

A Population-Based Intervention to Improve Care Cascades of Patients With Hepatitis C Virus Infection

John Scott,¹ Meaghan Fagalde,² Atar Baer,² Sara Glick,^{1,2} Elizabeth Barash,² Hilary Armstrong,² Kris V. Kowdley,³ Matthew R. Golden,^{1,2} Alexander J. Millman,⁴ Noele P. Nelson,⁴ Lauren Canary,⁴ Matthew Messerschmidt,⁵ Pallavi Patel,⁶ Michael Ninburg,⁷ and Jeff Duchin^{1,2}

Hepatitis C virus (HCV) infection is common in the United States and leads to significant morbidity, mortality, and economic costs. Simplified screening recommendations and highly effective direct-acting antivirals for HCV present an opportunity to eliminate HCV. The objective of this study was to increase testing, linkage to care, treatment, and cure of HCV. This was an observational, prospective, population-based intervention program carried out between September 2014 and September 2018 and performed in three community health centers, three large multiclinic health care systems, and an HCV patient education and advocacy group in King County, WA. There were 232,214 patients included based on criteria of documented HCV-related diagnosis code, positive HCV laboratory test or prescription of HCV medication, and seen at least once at a participating clinical site in the prior year. Electronic health record (EHR) prompts and reports were created. Case management linked patients to care. Primary care providers received training through classroom didactics, an online curriculum, specialty clinic shadowing, and a telemedicine program. The proportion of baby boomer patients with documentation of HCV testing increased from 18% to 54% during the project period. Of 77,577 baby boomer patients screened at 87 partner clinics, 2,401 (3%) were newly identified HCV antibody positive. The number of patients staged for treatment increased by 391%, and those treated increased by 1,263%. Among the 79% of patients tested after treatment, 95% achieved sustained virologic response. *Conclusion:* A combination of EHR-based health care system interventions, active linkage to care, and clinician training contributed to a tripling in the number of patients screened and a more than 10-fold increase of those treated. The interventions are scalable and foundational to the goal of HCV elimination. (*Hepatology Communications* 2021;5:387-399).

SEE EDITORIAL ON PAGE 355

An estimated 2.4 million Americans (1%) were chronically infected with hepatitis C virus (HCV) in 2013-2016,⁽¹⁾ and approximately

17,000-80,000 persons with hepatitis C die annually.⁽²⁻⁴⁾ New HCV infections increased nearly 3-fold from 2010 to 2015. During 2012-2013, the annual number of hepatitis C-related deaths exceeded the total number of deaths associated with the 60 other nationally notifiable infectious diseases combined, as reported

Abbreviations: CDC, Centers for Disease Control and Prevention; DAA, direct-acting antiviral; EHR, electronic health record; EMR, electronic medical record; HCV, hepatitis C virus; HCV-TAC, Hepatitis C Virus Test and Cure; HIV, human immunodeficiency virus; NASEM, National Academies of Science, Engineering, and Medicine; PCP, primary care provider; Public Health, Public Health of Seattle and King County; SVR, sustained virologic response.

Received June 17, 2020; accepted September 23, 2020.

Supported by the Centers for Disease Control and Prevention (6 NU 51PS004601 to J.S.).

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

© 2020 The Authors. *Hepatology Communications* published by Wiley Periodicals LLC on behalf of American Association for the Study of Liver Diseases. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

View this article online at wileyonlinelibrary.com.

DOI 10.1002/hep4.1627

Potential conflict of interest: Dr. Kowdley consults for and is on the speakers' bureau for AbbVie; he consults for, is on the speakers' bureau for, and received grants from Gilead. Dr. Ninburg received grants from AbbVie and Gilead. Dr. Scott advises Gilead. The other authors have nothing to report.

to the Centers for Disease Control and Prevention (CDC).⁽⁵⁾ The economic costs of chronic hepatitis C in the United States are in the billions of dollars each year.⁽⁶⁾ Despite this cost, there is a gap in the literature of reports of population-level interventions in the United States to identify and treat cases in order to achieve national targets for hepatitis C elimination.⁽⁷⁾

Data from the U.S. National Health and Nutrition Examination Survey found that among those born between 1945 and 1965 (“baby boomers”), 2.6% tested positive for the HCV antibody and 85% of those tested positive for HCV RNA,⁽⁸⁾ representing the majority of total infections. Although the prevalence of HCV infection is highest among baby boomers, there has been an increasing trend in new HCV infections among younger patients and in rural areas as a result of the opioid crisis and increased use of injection drugs.^(9,10) Indeed, the incidence of acute hepatitis C has increased dramatically in the past decade.^(11,12)

Highly effective direct-acting antiviral (DAA) therapy and simplified CDC and U.S. Preventive Services Taskforce hepatitis C screening guidelines recommending testing of all baby boomers provided new opportunities for persons with chronic HCV infection to be identified and treated.⁽¹³⁾ Sustained virologic response (SVR) for all genotypes using all-oral single-tablet DAA regimens to treat chronic HCV infections now exceed 95%, including populations once considered to be difficult to treat, such as patients who are human immunodeficiency virus (HIV)/HCV coinfecting, have cirrhosis, have severe renal impairment, or had failed therapy.⁽¹⁴⁻¹⁹⁾ Importantly, patients who achieve SVR have decreases in all-cause mortality and development of hepatocellular carcinoma.^(20,21) Because of the

availability of highly effective treatments for hepatitis C, expanded screening recommendations, and increased access to health care services, the National Academies of Science, Engineering, and Medicine (NASEM) and the U.S. Department of Health and Human Services National Viral Hepatitis Action Plan have called for the elimination of hepatitis C as a public health problem in the United States.^(7,22)

Despite these advances, significant challenges to hepatitis C elimination remain, including diagnosing at-risk vulnerable populations, linking diagnosed patients to care, and initiating curative antiviral treatment.⁽²²⁾ Collectively, these steps are referred to as the “care cascade.” This framework, which has been used extensively by public health agencies responding to the HIV epidemic,^(23,24) can be used to highlight gaps in care and prioritize intervention to improve clinical outcomes.⁽²⁵⁾ Numerous U.S. studies have examined the hepatitis C care cascade in the pre-DAA era.⁽²⁶⁾ A review by the CDC described these deficits at each step: as few as 50% of patients infected with HCV are aware of their diagnosis; once diagnosed, a minority of patients (32%-38%) are referred to care; 7%-11% of cases are treated; and 5%-6% are cured.⁽²⁷⁾

As a step toward realizing the goal of elimination of hepatitis C as a public health problem, we developed a population-based public health and health care collaboration, the HCV Test and Cure (HCV-TAC) Coalition, with a focus on baby boomers. We report the results of the project, which employed enhancements to provider education, public health surveillance, health care system electronic medical records (EMRs) and data reporting capacity, and case management in order to increase the testing, linkage to care, treatment, and cure of persons with HCV

ARTICLE INFORMATION:

From the ¹Division of Allergy and Infectious Diseases, University of Washington, Seattle, WA, USA; ²Public Health – Seattle King County, Seattle, WA, USA; ³Liver Institute Northwest, Seattle, WA, USA; ⁴Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA; ⁵HealthPoint Community Health Center, Renton, WA, USA; ⁶Kaiser Permanente, Seattle, WA, USA; ⁷Hepatitis Education Project, Seattle, WA, USA.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO:

John Scott, M.D., M.Sc.
Division of Allergy and Infectious Diseases
University of Washington
325 Ninth Ave, Box 359938

Seattle, WA 98104, USA
E-mail: jdscott@uw.edu
Tel.: +1-206-744-3393

TABLE 1. STRATEGIES TO IMPROVE HCV CARE CASCADE ELEMENTS BY SITE, 2014-2018

Site	Case-Based Telemedicine	Online Tutorial	Didactics	Clinic Tutorials	Hybrid Tutorial & Teleconference Model	EMR Prompts	Clinic Education Materials
Large public hospital	X	X	X			X	X
Community clinic A	X	X					X
Community clinic B	X	X	X			X	X
Community clinic C	X	X	X			X	X
Private hospital			X				
Integrated health system		X	X	X	X		

infection in King County, the most populated county in Washington State.

Materials and Methods

From September 2014 to September 2018, Public Health of Seattle and King County (Public Health) developed the HCV-TAC Coalition, a collaboration with three community health centers, three large multiclinic health care systems (private, public, and capitated), and a hepatitis C patient education and advocacy group. Collectively, these health systems provide care for patients across a broad spectrum of racial and socioeconomic groups in King County. The three community health centers are federally qualified health centers and collectively served >100,000 patients in 2014. The public hospital, capitated, and private systems have 4, 20, and 30 primary care clinics, respectively; all participated in the HCV screening program. The HCV-TAC Coalition engaged partners on a quarterly basis, including experts in information technology, primary care clinicians, hepatology specialists, nurses, case managers, and project champions to review progress toward project milestones.

Our strategy included the following key components: identification and hepatitis C testing of eligible patients in accordance with CDC guidelines; developing a data system to integrate laboratory and clinical data into public health surveillance records; monitoring patients along the care cascade and providing case management to promote linkage to medical care and curative therapy when indicated; and enhancing hepatitis C treatment capacity among primary care providers (PCPs).

HCV-TAC partners used several interventions to increase hepatitis C screening in the outpatient primary care setting. Several sites modified their electronic health records (EHRs) to flag patients needing hepatitis C testing under health maintenance activities. Other sites put up CDC-produced posters in clinic waiting rooms to inform patients about hepatitis C screening for baby boomers, mailed screening reminders to baby boomer patients, and had reception staff give reminder cards at clinic check-in for baby boomers to ask their provider about hepatitis C testing.

To train PCPs to evaluate and care for patients with chronic hepatitis C, the HCV-TAC program

employed five different strategies: case-based telemedicine, an online tutorial, didactics, clinic tutorials, and a hybrid tutorial/teleconference model. A summary of educational and screening interventions are summarized in Table 1. The Extension for Community Health Outcomes project (Project ECHO) was developed at the University of New Mexico to safely and effectively treat common, complex, chronic diseases and monitor outcomes in rural and underserved areas.^(28,29) First used for the treatment of hepatitis C in New Mexico, Project ECHO was adopted by the University of Washington for regularly scheduled telehealth clinics that function as “knowledge networks,” bringing together interdisciplinary specialists from academic medical centers and community-based PCPs.

An online tutorial, HCV Online (www.hepatitisc.uw.edu), was adapted during the project period for use in King County. The publicly available website consists of an interactive online course covering 26 core competencies with learning objectives and practice goals. A 40-question multiple choice “boards style” examination is required for those seeking continuing medical education credits, and a certificate of completion is issued if 80% of the answers are correct. A progress tracker allows a supervisor to see multiple clinicians in a group and areas of knowledge deficits.

Hepatology and infectious disease specialists gave presentations to PCPs on hepatitis C evaluation and treatment and offered PCPs opportunities to shadow specialists seeing patients with HCV infection. One health care system pioneered a clinic tutorial/teleconference model in which PCPs were trained on hepatitis C evaluation and treatment and presented their cases to hepatitis C specialists in a regular teleconference and through an internal “eReferral” system. During the project, there were 252 PCPs working at six clinics who were trained on hepatitis C evaluation and treatment.

Public Health and a patient advocacy organization, the Hepatitis Education Project, worked with clinicians to provide case management designed to ensure patient linkage to care and progress through the HCV care cascade and to provide point of care testing, information, and medical and financial navigation services.

Public Health promoted public awareness of HCV infection and the importance of screening through

a dedicated web page, a blog, media releases, and in-depth stories in the local press and radio. Targeted outreach included communities of color and the Seattle syringe exchange. Educational information distributed to the public included materials from CDC’s Know More Hepatitis campaign.

In order to improve the quality of public health hepatitis C monitoring, we developed a hepatitis C data system that integrated clinical data from EHRs, laboratory reports, and case investigations into a unified data management system that facilitated public health investigations and monitoring of patients through the hepatitis C care cascade.⁽²⁹⁾

The State of Washington Human Research Review Section determined that the program did not require review by the Washington State Institutional Review Board.

ANALYTIC METHODS

Data were available for a baseline period (September 30, 2013, to September 29, 2014), and the project period, beginning with year 1 (September 30, 2014, to September 29, 2015) through the end of year 4 (September 30, 2017, to September 29, 2018). To be included in the study analysis, patients had to reside in King County and have at least one visit to a participating primary care or liver specialty clinic during the project period.

Data collection methods have been described.⁽²⁹⁾ Briefly, HCV-TAC partners extracted laboratory and clinical data from EHRs by identifying three subsets of patients who (A) had a hepatitis C-related diagnosis code, positive hepatitis C laboratory test, or prescription of hepatitis C medication; (B) were born between 1945 and 1965 and tested negative for HCV antibody; and (C) were born between 1945 and 1965 (baby boomer cohort) and had no record of hepatitis C testing.

Epidemiologists assessed baby boomer screening rates by project year for each partner site by identifying unique baby boomer patients with at least one visit to a partner clinic during that project year and calculating the percentage of those patients who had been screened for HCV antibodies before or during the year. If HCV antibody test results were available, test dates were used to determine when the screening occurred; if no laboratory data were available, the subset assigned by partners was used to determine

screening status (i.e., HCV positive, HCV negative, never screened). Among baby boomer patients who tested HCV antibody positive during the project period, we assessed the percentage of patients who (1) were not tested for HCV RNA; (2) had the same specimen immediately tested for HCV RNA (reflex RNA testing); and (3) were tested for HCV RNA at a later date.

To be included in the analysis of the hepatitis C care cascade, patients were required to have a positive HCV RNA test. A patient who was HCV positive was considered staged for treatment if either (1) they had laboratory test results allowing computation of an aspartate aminotransferase-to-platelet ratio index and HCV genotype testing or (2) had a liver fibrosis staging test (e.g., FibroSure, liver biopsy, FibroScan). Patients with a prescription for hepatitis C DAA medication but no information on staging were considered to have missing staging data. Patients with a prescription for hepatitis C DAA medication in the EHR were considered prescribed treatment. Treatment start and end dates were obtained from prescription information from EHRs. All patients with hepatitis C prescriptions had at least one treatment date, and treatment completion was calculated for those without a treatment end date using a 12-week treatment duration. Patients more than 12 weeks posttreatment completion were eligible for SVR testing to determine cure. Patients with detectable HCV RNA at SVR testing were considered treatment failures, and those with undetectable HCV RNA at SVR testing were considered cured. Progress over the project period in screening, uptake of reflex HCV RNA testing, and milestones on the care cascade were analyzed by comparing baseline to year 4 data using chi-square tests and *P* values with $\alpha = 0.05$ as significant. Data management activities and analyses were performed using SAS 9.4.

Results

HCV-TAC partners identified 232,214 patients residing in King County with at least one visit to a partner primary care or liver specialty clinic during the baseline or project period. Because the focus of the study was on baby boomers, nearly all the patients included in the analysis were born between 1945

and 1965 ($n = 225,363$). A diagram of patients and their testing outcomes is shown in Fig. 1, and patient demographics are described in Table 2.

HCV antibody test results were available for 80,204 baby boomer patients, including 2,627 patients screened before the project period. Of the 77,577 baby boomers screened for HCV antibody during the project period, 2,401 were antibody positive (3%). The proportion testing positive declined from 8% at baseline to 2.5% by year 4. After accounting for patients who were seen at multiple partner sites, there were 2,250 unique baby boomer patients who screened as HCV antibody positive during the project period. Some baby boomers who were HCV antibody positive were screened more than once during the project period, resulting in 2,613 positive antibody tests eligible for reflex RNA testing.

Of the 2,250 unique baby boomer patients who tested HCV antibody positive during the project period, 73% ($n = 1,635$) were HCV RNA positive and were included in the care cascade analysis, 561 patients were HCV RNA negative, and 54 had not received HCV RNA testing.

Among the 2,627 baby boomer patients screened before the project period, 211 (8%) were antibody positive; after accounting for patients who were seen at multiple partner sites, there were 192 unique persons who were HCV antibody positive. Of these 192 baby boomer patients, 156 (81%) were HCV RNA positive and were included in the care cascade analysis, 26 tested HCV RNA negative, and 10 had not received confirmatory HCV RNA testing.

There were 6,418 baby boomer patients identified as having HCV by medical history but had no available HCV antibody test results. After accounting for patients who were seen at multiple partner sites, there were 5,540 unique persons identified in this group, including 3,887 who were HCV RNA positive and were included in the care cascade analysis, 503 who tested HCV RNA negative, and 1,150 patients with no laboratory record of any positive HCV antibody or RNA test.

Partners also identified 6,851 persons diagnosed with hepatitis C who were not baby boomers. After accounting for patients seen at multiple partner sites, there were 6,038 unique persons identified; 2,592 were found to be HCV RNA positive and were included in the care cascade analysis, 650 tested RNA negative, and 2,796 had no laboratory record of positive HCV antibody or RNA testing.

Hepatitis C screening of baby boomer patients increased significantly from 18% of baby boomer patients to 54% of baby boomer patients from baseline to year 4 (Fig. 2). The increase was consistent across partner sites (Fig. 3) and most closely related temporally to the institution of EMR-based prompts, although relaxation of Medicaid restrictions also occurred halfway through the project, and this effect likely also factored. Interestingly, the large public hospital had the highest

screening at baseline but also the smallest change across the study period. The percentage of antibody positive tests reflexed for HCV RNA increased significantly during the project period from 46% (212 of 462) at baseline to 81% (427 of 529) in year 4 ($P < 0.0001$).

In total, 8,270 patients infected with HCV with a detectable HCV RNA test who resided in King County were included in the hepatitis C care cascade analysis (Table 3). The majority were non-Hispanic white (59%,

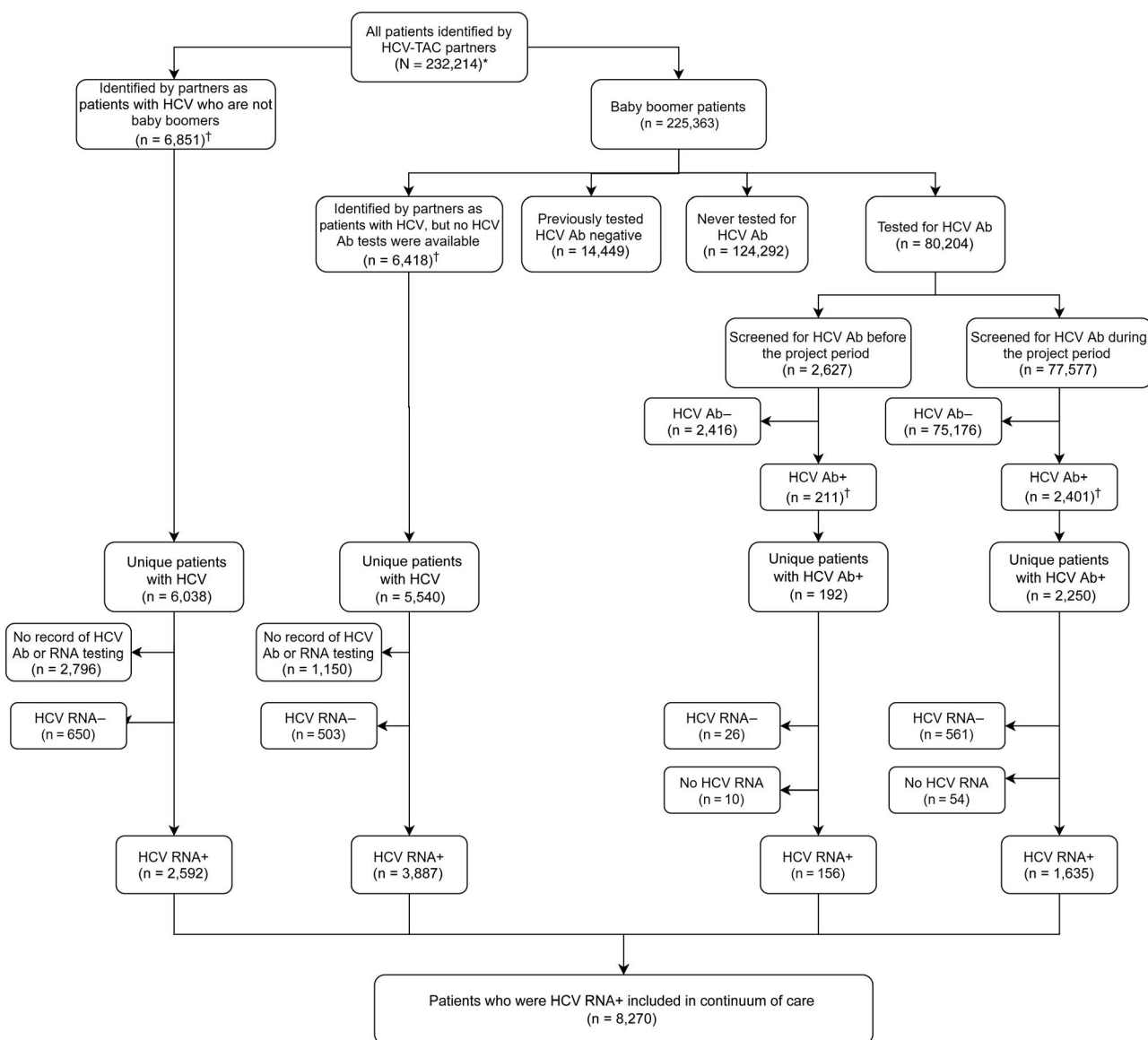


FIG. 1. Flow and classification of patients residing in King County identified by HCV-TAC partner organizations from September 30, 2013, to September 29, 2018. *Includes all patients identified by each HCV-TAC partner organization; individuals seen at more than one health care system are counted more than once in the total number. Records for patients with hepatitis C were deduplicated in the public health surveillance database. †Numbers may not match the next step because of lack of public health information, deduplication, and exclusion of persons not residing in King County. Abbreviation: Ab, antibody.

TABLE 2. CHARACTERISTICS OF ALL HCV-TAC PARTNER PATIENTS RESIDING IN KING COUNTY AND SEEN AT PARTNER CLINICS FROM SEPTEMBER 30, 2013, TO SEPTEMBER 29, 2018

Characteristic	Total (N = 232,214)		Baby Boomers (Born From 1945-1965) (n = 225,363)		Nonbaby Boomers (Not Born From 1945-1965) (n= 6,851)	
	Number	Percent (%)	Number	Percent (%)	Number	Percent (%)
Sex						
Female	122,791	52.9	119,816	53.2	2,975	43.4
Male	109,368	47.1	105,496	46.8	3,872	56.5
Unknown	55	0.02	51	0.02	4	0.06
Race/ethnicity						
Non-Hispanic white	140,915	60.7	137,493	61.0	3,422	50.0
Non-Hispanic black	26,058	11.2	24,878	11.0	1,180	17.2
Non-Hispanic Asian	31,458	13.6	30,530	13.6	928	13.6
Non-Hispanic AIAN	2,464	1.1	2,309	1.0	155	2.3
Non-Hispanic other or multiracial	4,326	1.9	4,124	1.8	202	3.0
Hispanic	15,449	6.7	14,714	6.5	735	10.7
Unknown	11,544	5.0	11,315	5.0	229	3.3
Uninsured at any time	37,238	16.0	35,075	15.6	2,163	31.6

Abbreviation: AIAN, American Indian Alaska Native.

n = 4,854), men (66%, n = 5,421), insured by Medicaid at some time (53%, n = 4,387), and seen at only one partner site (67%, n = 5,539). Thirteen percent of patients (n = 1,082) had advanced fibrosis (stage F3 or F4); 7% of patients were HIV positive (n = 607); and 29% were diagnosed with opioid use disorder (n = 2,403). Seventy-nine percent (n = 6,531) of patients infected with HCV were staged for treatment, and 53% (n = 4,347) were prescribed hepatitis C treatment. Among these patients, 79% (n = 3,413) received RNA testing 12 weeks after treatment end to determine SVR. Of those tested for SVR, 95% (n = 3,243) achieved SVR while 5% (n = 170) had detectable HCV RNA (Fig. 4).

The percentage of patients who were diagnosed with HCV infection and were staged ($P < 0.0001$), treated ($P < 0.0001$), and cured ($P < 0.0001$) increased significantly from the baseline period to year 4 (Fig. 5). The number of patients diagnosed increased by 76%, those staged for treatment (either by genotype or a fibrosis test) increased 3.9-fold, those treated increased 12.6-fold, and those achieving SVR increased 14.4-fold.

Discussion

Over a period of 4 years, hepatitis C testing, linkage to care, treatment, and cure increased significantly for patients monitored by the HCV-TAC

program. The proportion of baby boomers who were screened increased from 18% at baseline to 54% at the end of the project period. This rate is higher than recent reports documenting an increased testing rate of baby boomers from 12.3% to 17.3% nationally.⁽³⁰⁾ The percentage of baby boomers who received reflex HCV RNA testing after screening antibody positive increased from 46% at baseline to 81% in year 4, ensuring timely diagnosis. There was a 3.9-fold increase in the number of patients staged for treatment and a 12.6-fold increase in the number of patients who started antiviral therapy, relative to the baseline period. Treatment failure among those assessed for SVR was low (5%), although a significant proportion of patients who completed treatment did not receive SVR assessment (21%).

The conclusions of our study confirm the findings of others. Turner and colleagues⁽³¹⁾ used the Screen, Treat, Or Prevent Hepatocellular Carcinoma (STOP-HCC) model to increase screening, linkage to care, and treatment in a primarily Hispanic safety net population. Of note, the researchers intended to use an EMR-based best practice alert to identify nonscreened baby boomer patients and then append an order for clinician approval. However, cost restrictions required a pivot to a more manual process of clinic staff review and order entry. They screened nearly half of their eligible baby boomer population,

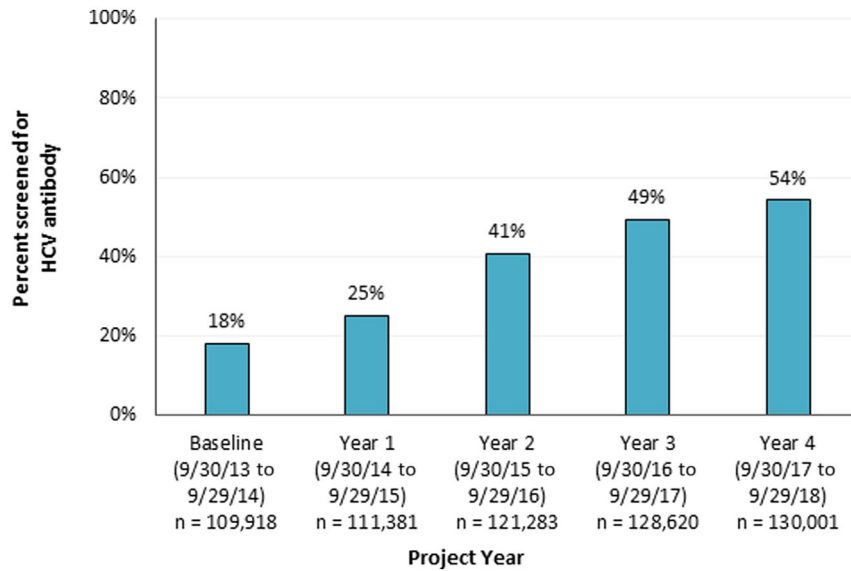


FIG. 2. Percentage of baby boomer patients residing in King County with visits to HCV-TAC partner clinics who have been screened for HCV antibody, by project year (September 30, 2013, to September 29, 2018).

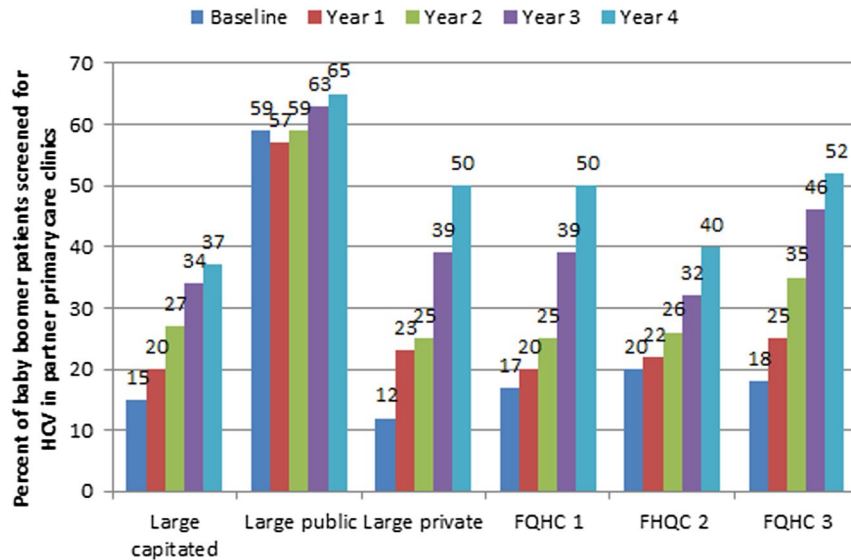


FIG. 3. Percentage of baby boomer patients screened for HCV in partner primary care clinics. Abbreviation: FQHC, federally qualified health center.

finding 520 confirmed patients who were viremic and ultimately treated 82, with 70 achieving a cure. A review of intervention strategies to increase HCV screening highlights the value of EMR-based interventions, with several studies showing double-digit percentage increases after using a best practice alert,

as well as emergency room screening and screening at the time of colonoscopy.⁽³²⁾ We were able to implement an EMR-based screening process at multiple settings and using different EMRs for a relatively modest amount of time and money; this intervention appeared to have the greatest effect on

TABLE 3. CHARACTERISTICS OF PATIENTS WITH DETECTABLE HCV RNA RESULTS RESIDING IN KING COUNTY AND SEEN AT PARTNER CLINICS FROM SEPTEMBER 30, 2013, TO SEPTEMBER 29, 2018, WHO WERE INCLUDED IN THE HCV CARE CASCADE ANALYSIS

Characteristic	Number	Percent (%)
Total patients HCV RNA positive	8,270	100
Born from 1945 to 1965	5,678	68.7
Sex		
Female	2,849	34.5
Male	5,421	65.6
Race/ethnicity		
Non-Hispanic white	4,854	58.7
Non-Hispanic black	1,894	22.9
Non-Hispanic Asian	508	6.1
Non-Hispanic AIAN	191	2.3
Non-Hispanic other or multiracial	177	2.1
Hispanic	521	6.3
Unknown	125	1.5
Homeless at any time	1,162	14.1
Insurance status		
Medicaid	3,829	46.3
Private insurance	2,202	26.6
Medicare	2,084	25.2
Self-pay or other insurance	136,140	1.7
Unknown	15	0.2
Uninsured at any time	1,472	17.8
On Medicaid at any time	4,387	53.1
HIV positive	607	7.3
Cirrhosis	2,396	29.0
Liver transplant	68	0.8
Chronic kidney disease	629	7.6
Diabetes	1,706	20.6
Opioid use disorder	2,403	29.1
HBV coinfection	665	8.0
History of injection drug use	1,886	22.9
History of alcohol use disorder	624	7.6
Genotype		
GT 1	4,208	50.9
GT 2	642	7.8
GT 3	729	8.8
GT 4	86	1.0
GT 5	6	0.1
GT 6	117	1.4
No record of genotype test	2,482	30.0
Tested for APRI at any time	8,120	98.2
Most recent fibrosis stage		
F0	820	9.9
F1	472	5.7
F2	938	11.3
F3	483	5.8

TABLE 3. Continued

Characteristic	Number	Percent (%)
F4	599	7.2
No record of fibrosis staging	4,958	60.0
Number of partner sites patient was seen at		
1	5,539	67.0
2	2,315	28.0
3	387	4.7
4	29	0.4

Abbreviations: AIAN, American Indian Alaska Native; APRI, aspartate aminotransferase-to-platelet ratio index; GT, genotype; HBV, hepatitis B virus.

screening. We encourage EMR vendors to make this a standard feature in order to defray costs. Turner and colleagues⁽³¹⁾ faced the challenge of lack of reflex RNA testing for patients testing positive for HCV antibodies. We worked with local and national laboratories to implement reflex testing, thus eliminating a step in the care cascade. We recommend that all laboratories execute this strategy as well. Finally, the current study is unique in that it built partnerships between the local public health department and health systems, thus improving data and coordination of outreach activities.

The current study focused on baby boomers, but the majority of new infections occur in young people who inject drugs (PWID), who may be less likely to engage in primary care and more likely to be seen in mental health and/or substance abuse programs. Thus, programs which offer “wrap-around” services including DAA therapy may be successful.

Several factors contributed to the success of the HCV-TAC program. First, there was a strong collaboration between health care systems, patient advocacy organizations, and the public health department; this allowed for a coordinated and integrated approach to expanding screening of at-risk patients, sharing of clinical best practices, and promotion of health care system improvements, such as EHR modifications and reflex HCV RNA testing. Second, enhancements to clinical EHR and associated data systems increased the availability and utility of clinical data for public health population-level surveillance and program evaluation. A key element of our project was monitoring hepatitis C testing and treatment using a care

cascade framework analogous to that used successfully by public health systems to monitor HIV control. Third, we provided clinicians with high-quality hepatitis C training, including a wide variety of educational opportunities that provided the skills and resources for them to successfully treat hepatitis C. Finally, an important extrinsic factor influencing our success was the lifting of Washington State Medicaid restrictions for hepatitis C treatment based on fibrosis level after legal challenges in 2016. This watershed court ruling brought Washington State's Medicaid policy in line with American Association for the Study of Liver Diseases/Infectious Diseases Society of America HCV guidelines⁽³³⁾ and opened up treatment options for an estimated >50% of early stage patients known to be infected with hepatitis C who were previously ineligible for treatment.⁽³⁴⁾

Successful collaboration and data sharing between the health department and coalition partners led to significant improvements in hepatitis C surveillance. To assess baby boomer screening and uptake of reflex HCV RNA testing, we used a combination of laboratory test results and partner-identified classification of patient HCV infection status (never screened,

HCV negative, and HCV positive). This methodology allowed us to determine the hepatitis C screening status for all baby boomer patients at each clinic visit. Accordingly, we were able to track and report individual- and clinic-level progress toward screening goals over the course of the project period.

Deduplication and merging clinic EHR data with the public health surveillance database provided access to historical data for each patient diagnosed with hepatitis C, regardless of clinical provider, and tracked patients diagnosed with hepatitis C across health care systems. We found that a third of patients ($n = 2,731$) included in the hepatitis C care cascade were seen at more than one partner site during the baseline and project periods.

Of the nonbaby boomer patients identified as having HCV infection, a significant proportion did not have HCV laboratory results available for analysis (46%, $n = 2,796$ of 6,038 nonbaby boomer patients). EHRs identified these patients as having hepatitis C based on documentation of a hepatitis C diagnosis or DAA treatment, but without laboratory testing information it is not possible to verify HCV infection status. The high proportion of nonbaby boomer patients

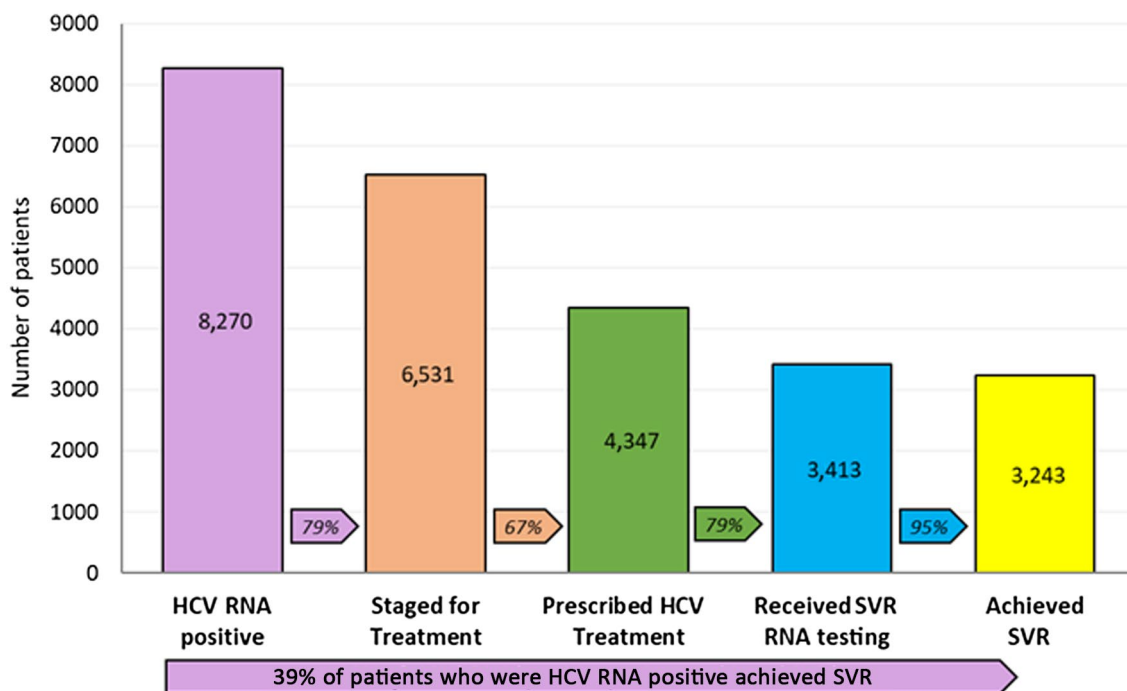


FIG. 4. Hepatitis C care cascade for patients with HCV RNA-positive results residing in King County and seen at partner clinics during the project period September 30, 2013, to September 29, 2018 ($n = 8,270$).

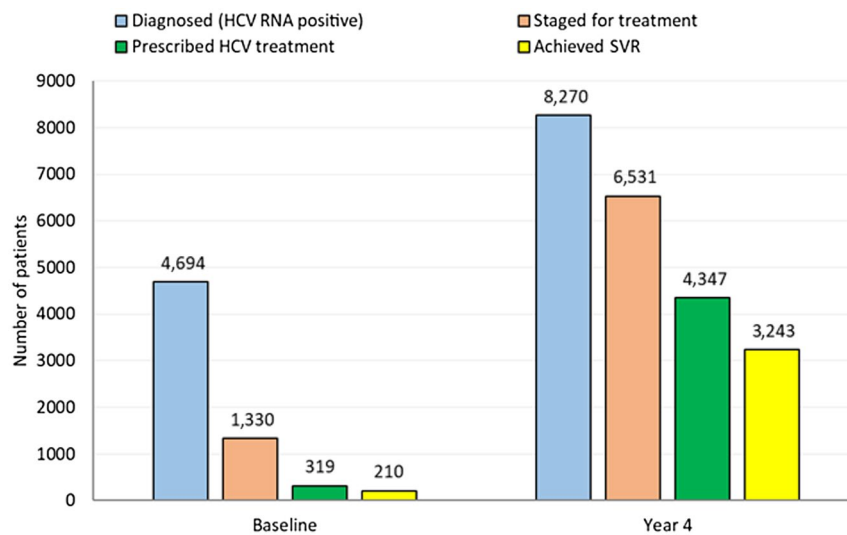


FIG. 5. Comparison of hepatitis C care cascade at end of baseline year (September 30, 2013, to September 29, 2014) and end of year 4 (September 30, 2017, to September 29, 2018).

without hepatitis C laboratory testing could reflect a history of past hepatitis C testing elsewhere and not reflected in the EHR or that partners were not properly extracting all available hepatitis C laboratory data from their EHR systems. In addition, a significant number of baby boomer patients did not get HCV testing. Because records were de-identified, the ability to study predictors of screening was limited.

Our findings have several important limitations. First, due to the movement of patients across health care systems, it is possible that partner EHRs could not identify all patients screened for hepatitis C in another health care system. Second, as described,⁽²⁹⁾ inaccurate calculations of treatment start and end dates based on prescription order dates in the EHR may have resulted in some patients being incorrectly categorized as never tested for SVR or failing treatment. We found 21% of patients who completed treatment did not have HCV RNA testing at least 12 weeks after stopping therapy. However, based on other studies from the Veterans Affairs and at specialty clinics outside of the registration clinical trials, it is likely that >90%-95% of those treated achieved cure.^(35,36) Third, cooperative agreement funding provided resources for database development, EHR enhancements, and clinician training, which may not be easily replicated in other settings without comparable investments. There were 4.5 full-time equivalent positions assisting in

this work, including dedicated epidemiologists, a public health nurse, a disease investigation specialist, program managers, and administrative support. Fourth, our study population may not be generalizable to other communities. For example, other parts of the United States have a greater proportion of African American and Latino patients. We attempted to address this limitation by recruiting health systems across demographic and socioeconomic strata. Additionally, there may be fewer PWID compared with the total population of persons infected with HCV because the focus of this study was the baby boomer cohort. Therefore, these results may not be generalizable to populations with different demographic characteristics or risk behaviors. Although a significant proportion of baby boomers were screened, approximately half were not, and reasons for not screening were not ascertained. Finally, the specific partners and interventions necessary to optimize population-level identification and treatment of persons with chronic HCV infection will reflect the local environment with respect to the epidemiology of chronic HCV infection, health care delivery, and public health systems.

NASEM has concluded that the elimination of HCV transmission and chronic infection as a public health problem is feasible in the United States.⁽²²⁾ Among the barriers to achieving elimination identified by NASEM are inadequate surveillance systems,

failure to identify infected persons, limited access to treatment medications due to high cost, and difficulty retaining high-risk persons in care. Our study has shown that with appropriate resources and a multifaceted strategy, major improvements in addressing barriers to hepatitis C elimination are possible.

Acknowledgment: We thank Dr. David Spach for his pioneering work on HCV Online and Ade Osinubi, M.S., and Aaron Harris, M.D., M.P.H., for their contributions.

REFERENCES

- 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.
- Ly KN, Xing J, Monina Klevens R, Jiles RB, Ward JW, Holmberg SD. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med* 2012;156:271-280. Erratum in: *Ann Intern Med* 2012;156:840.
- Mahajan R, Xing J, Liu SJ, Ly KN, Moorman AC, Rupp L, et al.; Chronic Hepatitis Cohort Study (CHeCS) Investigators. Mortality among persons in care with hepatitis C virus infection: the chronic hepatitis cohort study (CHeCS), 2006-2010. *Clin Infect Dis* 2014;58:1055-1061. Erratum in: *Clin Infect Dis* 2014;58:1792.
- Ly KN, Xing J, Klevens RM, Jiles RB, Holmberg SD. Causes of death and characteristics of decedents with viral hepatitis, United States, 2010. *Clin Infect Dis* 2014;58:40-49.
- Campbell CA, Canary L, Smith N, Teshale E, Ryerson B, Ward JW. State HCV incidence and policies related to HCV preventive and treatment services for persons who inject drugs—United States, 2015-2016. *MMWR Morb Mortal Wkly Rep* 2017;66:465-469.
- 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.
- National Academies of Sciences, Engineering, Medicine. A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report. Washington, DC: The National Academies Press; 2017.
- Denniston MM, Jiles RB, Drobeniuc J, Klevens RM, Ward JW, McQuillan GM, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. *Ann Intern Med* 2014;160:293-300.
- Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. *Clin Infect Dis* 2014;59:1411-1419.
- Zibbell JE, Iqbal K, Patel RC, Suryaprasad A, Sanders KJ, Moore-Moravian L, et al.; Centers for Disease Control and Prevention (CDC). Increases in hepatitis C virus infection related to injection drug use among persons aged ≤ 30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. *MMWR Morb Mortal Wkly Rep* 2015;64:453-458.
- Zibbell JE, Asher AK, Patel RC, Kupronis B, Iqbal K, Ward JW, et al. Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004 to 2014. *Am J Public Health* 2018;108:175-181.
- Centers for Disease Control and Prevention. Viral hepatitis: 2016 surveillance. <https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm>. Accessed February 2019.
- Smith BD, Morgan RL, Beckett GA, Falck-Yvetter Y, Holtzman D, Teo G-G, et al.; Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. *MMWR Recomm Rep* 2012;61:1-32. Erratum in: *MMWR Recomm Rep* 2012;61:886.
- Zeuzem S, Foster GR, Wang S, Asatryan A, Gane E, Feld JJ, et al. Glecaprevir-pibrentasvir for 8 or 12 weeks in HCV genotype 1 or 3 infection. *N Engl J Med* 2018;378:354-369.
- Gane EJ, Shiffman ML, Etzkorn K, Morelli G, Stedman CAM, Davis MN, et al.; GS-US-342-1553 Investigators. Sofosbuvir-velpatasvir with ribavirin for 24 weeks in hepatitis C virus patients previously treated with a direct-acting antiviral regimen. *Hepatology* 2017;66:1083-1089.
- Naggie S, Cooper C, Saag M, Workowski K, Ruane P, Towner WJ, et al.; ION-4 Investigators. Ledipasvir and sofosbuvir for HCV in patients coinfecting with HIV-1. *N Engl J Med* 2015;373:705-713.
- Bourlière M, Gordon SC, Flamm SL, Cooper CL, Ramji A, Tong M, et al.; POLARIS-1 and POLARIS-4 Investigators. Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection. *N Engl J Med* 2017;376:2134-2146.
- Kowdley KV, Gordon SC, Reddy KR, Rossaro L, Bernstein DE, Lawitz E, et al.; ION-3 Investigators. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. *N Engl J Med* 2014;370:1879-1888.
- Wyles D, Poordad F, Wang S, Alric L, Felizarta F, Kwo PY, et al. Glecaprevir/pibrentasvir for hepatitis C virus genotype 3 patients with cirrhosis and/or prior treatment experience: a partially randomized phase 3 clinical trial. *Hepatology* 2018;67:514-523.
- Veldt BJ, Heathcote EJ, Wedemeyer H, Reichen J, Hofmann WP, Zeuzem S, et al. Sustained virologic response and clinical outcomes in patients with chronic hepatitis C and advanced fibrosis. *Ann Intern Med* 2007;147:677-684.
- Butt AA, Wang X, Moore CG. Effect of hepatitis C virus and its treatment on survival. *Hepatology*. 2009;50:387-392.
- Office of Infectious Disease and HIV/AIDS Policy, U.S. Department of Health and Human Services. National Viral Hepatitis Action Plan, 2017-2020. <https://www.hhs.gov/hepatitis/viral-hepatitis-action-plan/index.html>. Published January 17, 2020. Accessed June 23, 2020.
- Mayer KH. Introduction: Linkage, engagement, and retention in HIV care: essential for optimal individual- and community-level outcomes in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2011;52(Suppl. 2):S205-S207.
- Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis* 2011;52:793-800.
- Linas BP, Barter DM, Leff JA, Assoumou SA, Salomon JA, Weinstein MC, et al. The hepatitis C cascade of care: identifying priorities to improve clinical outcomes. *PLoS One* 2014;9:e97317.
- Yehia BR, Schranz AJ, Umscheid CA, Lo Re V. The treatment cascade for chronic hepatitis C virus infection in the United States: a systematic review and meta-analysis. *PLoS One* 2014;9:e101554.
- Holmberg SD, Spradling PR, Moorman AC, Denniston MM. Hepatitis C in the United States. *N Engl J Med* 2013;368:1859-1861.
- Arora S, Geppert CMA, Kalishman S, Dion D, Pullara F, Bjeletich B, et al. Academic health center management of chronic diseases through knowledge networks: Project ECHO. *Acad Med* 2007;82:154-160.

- 29) Baer A, Munn M, Drake C, Sohlberg E, Barash E, Glick S, et al. Design of an enhanced public health surveillance system for hepatitis C elimination in King County, Washington. *Public Health Rep.* 2020;135:33-39.
- 30) Patel E, Mehta S, Boon D, Quinn T, Thomas D, Tobian A. Limited coverage of hepatitis C virus testing in the United States, 2013-2017. *Clin Infect Dis* 2019;68:1402-1405.
- 31) Turner BJ, Rochat A, Lill S, Bobadilla R, Hernandez L, Choi A, et al. Hepatitis C virus screening and care: complexity of implementation in primary care practices serving disadvantaged populations. *Ann Intern Med* 2019;171:865-874.
- 32) Tsay CJ, Lim JK. Assessing the effectiveness of strategies in US birth cohort screening for hepatitis C infection. *J Clin Transl Hepatol* 2020;8:25-41.
- 33) AASLD-IDSA HCV Guidance Panel. Hepatitis C guidance 2018 update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. *Clin Infect Dis* 2018;67:1477-1492.
- 34) Thein H-H, Yi Q, Dore GJ, Krahn M. Estimation of stage-specific fibrosis progression rates in chronic hepatitis C virus infection: a meta-analysis and meta-regression. *Hepatology* 2008;48:418-431.
- 35) Ioannou GN, Beste LA, Chang MF, Green PK, Lowy E, Tsui JI, et al. Effectiveness of sofosbuvir, ledipasvir/sofosbuvir, or paritaprevir/ritonavir/ombitasvir and dasabuvir regimens for treatment of patients with hepatitis C in the Veterans Affairs National Health Care System. *Gastroenterology* 2016;151:457-471.e5.
- 36) Terrault NA, Zeuzem S, Di Bisceglie AM, Lim JK, Pockros PJ, Frazier LM, et al.; HCV-TARGET Study Group. Effectiveness of ledipasvir-sofosbuvir combination in patients with hepatitis C virus infection and factors associated with sustained virologic response. *Gastroenterology* 2016;151:1131-1140.e5.