



Published in final edited form as:

Clin Infect Dis. 2020 April 15; 70(9): 2005–2007. doi:10.1093/cid/ciz832.

Cascade of Care for Alaska Native People With Chronic Hepatitis C Virus Infection: Statewide Program With High Linkage to Care

Brian J. McMahon^{1,2}, Lisa Townshend-Bulson¹, Chriss Homan¹, Prabhu Gounder², Youssef Barbour¹, Annette Hewitt¹, Dana Bruden², Hannah Espera¹, Julia Plotnik¹, James Gove¹, Timothy J. Stevenson¹, Sarah V. Luna^{1,†}, Brenna C. Simons^{1,2}

¹Liver Disease and Hepatitis Program, Alaska Native Tribal Health Consortium, Anchorage, Alaska;

²Arctic Investigations Program, Division of Preparedness and Emerging Infections, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Anchorage, Alaska

Abstract

Most persons with chronic hepatitis C virus (HCV) infection in the United States are undiagnosed or linked to care. We describe a program for the management of Alaska Native patients infection utilizing a computerized registry and statewide liver clinics resulting in higher linkage to care (86%) than national estimates (~25%).

Keywords

hepatitis C virus; Alaska Natives; linkage to care and treatment

Chronic hepatitis C virus (HCV) infection is a significant worldwide etiology of cirrhosis, liver failure, and hepatocellular carcinoma (HCC). In the United States, an estimated 3.5 million persons have HCV infection. Viral hepatitis is now responsible for more deaths in the United States than human immunodeficiency virus [1]. A recent meta-analysis estimated

Correspondence: B. J. McMahon, Liver Disease and Hepatitis Program, Alaska Tribal Health Consortium and Centers for Disease Control and Prevention, 4315 Diplomacy Drive, Anchorage, AK 99508 (bdm9@cdc.gov).

[†]Deceased.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Publisher's Disclaimer: *Disclaimer.* The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Potential conflicts of interest. B. J. M. is the Director of the Liver Disease and Hepatitis Program, which has received 2 grants from Gilead Sciences, but none of these grants supports any of his salary. These 2 grants have not been used to support the work done in this manuscript. L. T-B. is a co-investigator in one of the grants from Gilead Sciences, but this grant does not support her salary nor the work done for this manuscript. Y. B. is the Principal Investigator of one of the grants from Gilead Sciences, but this grant does not support his salary nor the work done for this manuscript. C. H., A. H., H. E., J. P., and J. G. are the authors who have a conflict have received support from a research grant from Gilead Sciences and a portion of these grants do support their salaries but this grant does not support their salary nor the work done for this manuscript. T. J. S. receives salary support from a Gilead Sciences investigator-sponsored research award. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

that only 50% of persons with HCV infection were aware of their diagnosis; of those, 43% had access to care and only 25% were tested for HCV RNA, the confirmatory test for HCV infection [2]. Despite the development of highly effective HCV direct antiviral agents (DAAs) resulting in greater than 90% sustained viral response (SVR), the majority of persons infected with HCV are not diagnosed or linked to care.

The Alaska Native Tribal Health Consortium (ANTHC) Liver Disease and Hepatitis Program (LDHP) has been involved in the care of Alaska Native/American Indian (AN/AI) persons with HCV infection since 1994. The LDHP focuses HCV infection screening on high-risk individuals and has a program for screening Baby Boomers (born 1945–1965). All persons positive for HCV serology are entered into a statewide HCV registry used for patient tracking and management. This paper examines the cascade of care—defined as the continuum from screening, diagnosis, linkage to care, evaluation for therapy, and treatment of HCV infection—for AN/AI persons with chronic HCV infection from January 2014 through December 2017.

METHODS

The ANTHC coordinates healthcare within the Alaska Tribal Health System (ATHS) for an estimated 160 000 AN/AI people throughout the state of Alaska, with more than 50% living in rural communities [3]. Primary care is provided in remote communities by community health aide practitioners [4]. In larger communities, both primary and secondary care is available at regional hospitals and clinics staffed by physicians and midlevel providers. In Anchorage, the Southcentral Foundation and the Alaska Native Medical Center (ANMC) provide primary and tertiary care, respectively. Further details of the population and healthcare delivery system have previously been described [3]. Electronic health records are used throughout ATHS facilities.

The Liver Disease and Hepatitis Program Hepatitis C Virus Registry

The LDHP maintains a computerized registry of all patients who tested positive for HCV antibody (anti-HCV), which includes extensive laboratory, clinical, and demographic data used primarily for management of AN/AI persons with chronic HCV infection. All patients in the HCV registry receive a letter every 6 months asking them to attend their local clinic for liver function tests. Those patients with evidence of cirrhosis receive a second letter, at 6-month intervals, recommending a liver ultrasound for HCC surveillance. Each clinic, provider, and regional facility receive a list of patients to be tested in their respective areas. Testing for anti-HCV is performed at the ANMC, and positive serum samples are reflex tested for HCV RNA. Pertinent laboratory tests, including liver function tests and complete blood count, are uploaded biweekly into the Alaska Native Hepatitis C (AK-HepC) Registry database. The LDHP also conducts regularly scheduled hepatology field clinics at 10 ATHS hospitals throughout Alaska.

From the mid-1990s, all eligible patients have been offered Food and Drug Administration (FDA)–approved drugs for HCV infection treatment based on guidelines from the American Association for the Study of Liver Diseases/Infectious Diseases Society of America [5]. Direct antiviral agent treatment is provided regardless of liver fibrosis stage or medical

coverage. All currently licensed DAA medications are made available as soon as they are FDA approved. For rural communities, LDHP uses telephone consults, telemedicine, virtual (Vidyo®) clinics, tele-radiography, and other means to support local providers in caring for patients with HCV infection.

In addition, a nurse/patient navigator aids compliance by determining patient eligibility, providing patient education regarding HCV infection and treatment, and aiding any medical coverage needs. The patient navigator tracks patient progress during treatment and reminds patients of appointments with frequent phone calls and text messages. Since 1995, the LDHP has reported the clinical outcomes of chronic HCV infection [4, 6, 7].

Cascade of Care

The cascade of care takes a population perspective of illness by following the patient pathway through screening, diagnosis, testing, linkage to care, and treatment. We tracked the following numbers: (1) persons tested for HCV infection, (2) persons with a positive anti-HCV test, (3) persons with chronic HCV infection as determined by the presence of HCV RNA, (4) persons linked to a knowledgeable provider, (5) persons who meet eligibility for treatment, and (6) persons who have received antiviral therapy (Figure 1).

We characterized linkage to care as the proportion of persons who visited with a primary care provider or liver specialist for HCV laboratory and treatment evaluation or received a letter reminding them to make an appointment to see a provider for HCV infection. Treatment eligibility is determined by whether patients keep at least 2 consecutive clinic appointments: the first to explain the treatment regimen and draw serum samples for testing; the second to review laboratory results and start DAA treatment. The Alaska Area and Centers for Disease Control and Prevention Institutional Review Boards as well as the regional Tribal health organizational review boards in Alaska all approved the study. This manuscript has been reviewed by the Alaska Native Tribal Health Consortium and Southcentral Foundation tribal review boards.

RESULTS

We analyzed persons who visited the LHDP liver clinic for an appointment or blood draw between 1 January 2014 and March 2017. We identified 3443 persons with an anti-HCV positive test in our database; 97% had HCV RNA testing performed (Figure 1). As of 31 December 2017, 660 persons had died, 1058 (38%) were HCV RNA negative or had resolved their HCV infection within 1 year, 46 had no confirmation test performed, and 98 had been cured with interferon-based therapy. This left 1581 persons remaining who were HCV RNA positive for 12 months or longer. Of the 1581 persons identified with chronic HCV infection, 125 (8%) were lost to follow-up. Of the remaining 1358 persons linked to care, 999 (74%) had been evaluated for DAA antiviral therapy, and the 359 patients who had not been evaluated had been sent repeated letters requesting that they make an appointment for treatment. Of the 999 evaluated for treatment, 872 (87%) persons were deemed eligible for treatment and 127 (13%) were not. As of 31 December 2017, of the 872 persons deemed treatment ready, 669 (77%) have started therapy, leaving 203 (25%) who were awaiting treatment. Sustained viral response was achieved in 96% of those who completed therapy.

DISCUSSION

Our program has achieved many successful elements in our ultimate goal for elimination of HCV for the AN/AI people. These elements include high percentages of persons with HCV RNA testing (97%), linkage to care (>80%), and DAA-based treatment eligibility determination (>85%).

Our program faces unique logistics in delivery of care, as many persons with HCV live in rural communities throughout Alaska, some without road access to medical facilities. Success requires a great deal of coordinated care with many providers, including community health aide practitioners. Our program can act as a model for regions of the world where many persons with chronic HCV infection live in both urban and remote communities. The epidemiology of HCV infection in the AI/AN population is similar to that of the US population, but AI/AN persons with chronic HCV infections have higher rates of liver failure, HCC, and liver-related death [3, 4]

With the advent of high efficacy and minimal side-effect DAA-based therapies for HCV infection, it is imperative to link untreated persons to care to prevent long-term liver disease complications. Direct antiviral agent drug costs are decreasing as a treatment barrier. As shown during interferon treatment regimens, curing HCV infection in persons with cirrhosis reduces the subsequent risk of developing HCC by 70% and of liver failure by 90% [8]. Half of our persons infected with HCV achieving an SVR have advanced liver fibrosis (Metavir F3 and F4). Curing persons with no or mild fibrosis protects from future risk of adverse outcomes. Economically, HCV treatment will prove worthwhile in reducing medical costs associated with adverse outcomes.

Several reports about the cascade of care in major health care organizations have been published. Two programs with considerable government funding, one in the US Veterans Affairs healthcare system and the other in Australia, are on the way to eliminating HCV in these populations [9, 10]. However, in other North American populations, there is a deficit in screening high-risk populations for HCV infection and subsequent drop off in the proportions of HCV-positive persons undergoing an HCV RNA test (60%–70%), those who are referred to knowledgeable providers (34%–76%), and those who are treated (12%–34%) [11, 12]. The drop-off rate from testing anti-HCV positive results for HCV RNA in our cohort was only 3%.

Our goal is to treat all persons with HCV infection. Establishing strong case-management tools such as computerized registries and reminder systems for patients with HCV infection could also link persons infected with HCV to care and treatment programs, including in communities with practitioners with limited formal training. Cascade of care programs are moving systems, and periodic evaluation of the components are of value to ensure ongoing success in the management and care for persons with chronic HCV infection.

Acknowledgments.

The authors dedicate this article to their colleague and beloved friend, Dr Sarah Luna, who was tragically killed at the age of 31 in a floatplane crash on route to participate in a remote community clinic.

Financial support. This work was supported by a grant from the Centers for Disease Control and Prevention (U01 PS001097) and the Alaska Native Tribal Health Consortium.

References

1. Mitchell AE, Colvin HM, Palmer Beasley R. Institute of Medicine recommendations for the prevention and control of hepatitis B and C. *Hepatology* 2010; 51:729–33. [PubMed: 20186842]
2. Edlin BR, Eckhardt BJ, Shu MA, Holmberg SD, Swan T. Toward a more accurate estimate of the prevalence of hepatitis C in the United States. *Hepatology* 2015; 62:1353–63. [PubMed: 26171595]
3. McMahon BJ, Hennessy TW, Christensen C, et al. Epidemiology and risk factors for hepatitis C in Alaska Natives. *Hepatology* 2004; 39:325–32. [PubMed: 14767985]
4. McMahon BJ, Bruden D, Bruce MG, et al. Adverse outcomes in Alaska natives who recovered from or have chronic hepatitis C infection. *Gastroenterology* 2010; 138:922–31.e1. [PubMed: 19909749]
5. AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. *Hepatology* 2015; 62:932–54. [PubMed: 26111063]
6. McMahon BJ, Bruden D, Townshend-Bulson L, et al. Infection with hepatitis C virus genotype 3 is an independent risk factor for end-stage liver disease, hepatocellular carcinoma, and liver-related death. *Clin Gastroenterol Hepatol* 2017; 15:431–437.e2. [PubMed: 27765729]
7. Bruden DJT, McMahon BJ, Townshend-Bulson L, et al. Risk of end-stage liver disease, hepatocellular carcinoma, and liver-related death by fibrosis stage in the hepatitis C Alaska Cohort. *Hepatology* 2017; 66:37–45. [PubMed: 28195349]
8. Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies. *Ann Intern Med* 2013; 158:329–37. [PubMed: 23460056]
9. Belperio PS, Chartier M, Ross DB, Alaigh P, Shulkin D. Curing hepatitis C virus infection: best practices from the U.S. Department of Veterans Affairs. *Ann Intern Med* 2017; 167:499–504. [PubMed: 28973196]
10. Wade AJ, Macdonald DM, Doyle JS, et al. The cascade of care for an Australian community-based hepatitis C treatment service. *PLoS One* 2015; 10:e0142770. [PubMed: 26562516]
11. Geboy AG, Nichols WL, Fernandez SJ, Desale S, Basch P, Fishbein DA. Leveraging the electronic health record to eliminate hepatitis C: Screening in a large integrated healthcare system. *PLoS One* 2019; 14:e0216459. [PubMed: 31120906]
12. O’Neil CR, Buss E, Plitt S, et al. Achievement of hepatitis C cascade of care milestones: a population-level analysis in Alberta, Canada. *Can J Public Health* 2019 doi:10.17269/s41997-019-00234-z. [Epub ahead of print]

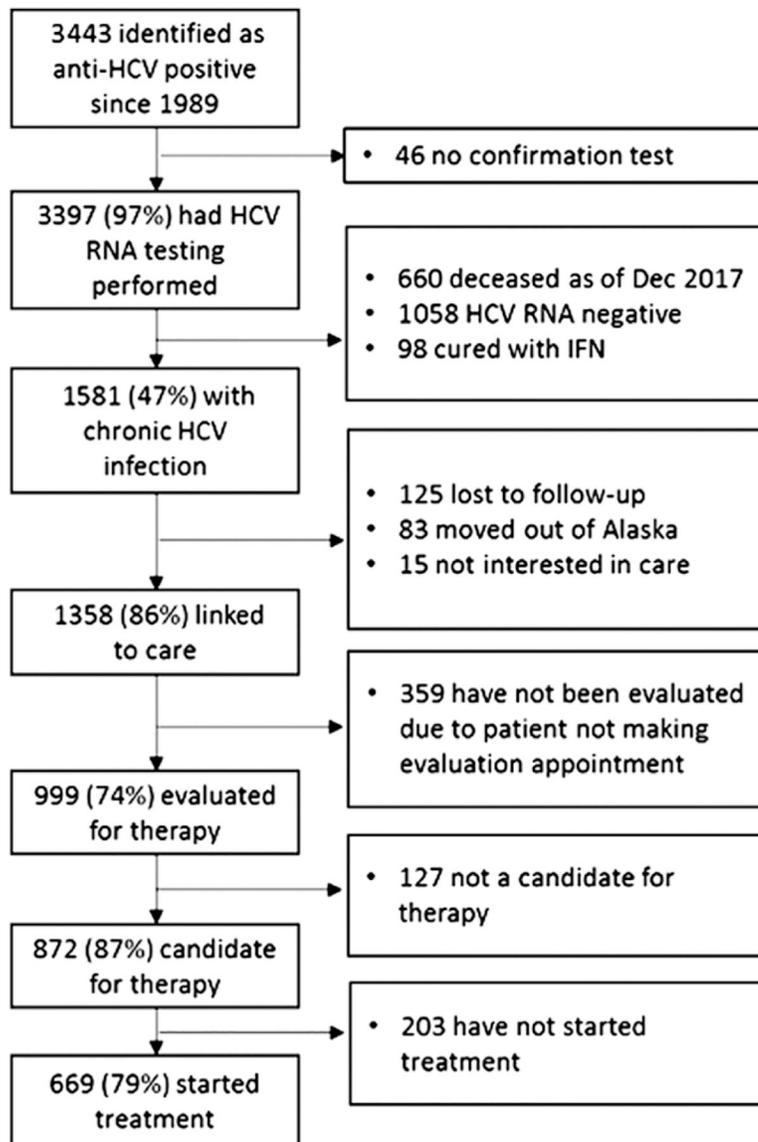


Figure 1. Hepatitis C virus cascade of care for Alaska Native persons living in Alaska, 2014–2017. Abbreviations: HCV, hepatitis C virus; IFN, interferon.