Hepatitis C

Elimination Strategy

For AI/AN Communities

The objective of this document is to describe the rationale, program design and tool kit for implementing an HCV micro-elimination program in an AI/AN community.

This community could be a tribal or Indian Health Service (IHS) clinic, hospital or health system.

This document is designed to help tribal health advocates; decision-makers and medical providers address the HCV epidemic in their communities through programmatic and policy changes.

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SECTION I

Rationale for HCV micro-elimination program implementation in AI/AN communities:

THE PROBLEM

Hepatitis C virus (HCV) infection (HCV) is a public health threat in the United States and the leading cause of death among all reportable infectious diseases to the CDC[1]. In addition, HCV mortality is greater than 59 of the other reportable diseases combined. Approximately 80% of new HCV infections occur among people who inject drugs (PWID)[2]. The increases in acute HCV infections parallel increased treatment admissions for substance use disorders, mostly driven by the national opioid epidemic[3].

American Indians/Alaskan Natives are disproportionately affected by the HCV incidence, morbidity and mortality.

From 2015 to 2016 incidence rates of acute HCV among AI/ANs increased from 1.8 to 3.1 cases per 100,000[4]. In 2015, the incidence rate of HCV infections among AI/ANs was twice the rate of Whites. Prevalence is also higher in AI/AN, among veterans[5]; AI/ANs were tied with Hispanics for the second highest HCV infection prevalence at 6.4% - higher than the national average for veterans. The HCV-related mortality rate among AI/AN HCV is 10.8 per 100,000, compared to 4.5 per 100,000 nationally[6]. From 2011 to 2015, HCV mortality rates increased by 13% among AI/AN[7]. Rates of chronic liver disease and deaths due to cirrhosis are 2.3 times higher among AI/ANs compared to whites[8].

The drivers of this increase in HCV incidence are probably multifactorial and social determinants of health play an important role.

The correlation between the opioid epidemic and the HCV epidemic is striking.

From 2004 to 2014, HCV rates increased 400% and admission for opioid injection increased 622% among 18 to 29 year olds[3]. In 2016, AI/ANs had the second highest opioid overdose fatality rate at 13.9 deaths per 100,000[9]. Drug overdose deaths overall increased 519% among AI/ANs from 1999 to 2015[10].

To mitigate the impact of the HCV/Opioid syndemic it will be very important to address both epidemics simultaneously as well as the social determinants that are driving them. While use of syringe services and medication assisted treatments (MAT) for opioid use disorders are shown to reduce the risk of HCV infection[11], penetration of these programs in Indian Country is limited due to stigma, lack of funding and paraphernalia laws. In a study of American Indian men and women living on a Tribal reservation in Montana who inject drugs, 65% reported reusing syringes for injection, and 53% reported drawing from the same filter[12]. This is significant, as PWID are at greater risk of HCV infection if they reuse or share needles for injection[13].

THE PROBLEM

In July 2018, the CDC updated its map of jurisdictions determined to be experiencing or at-risk of viral hepatitis or HIV outbreaks as a result of the opioid crisis[14]. Currently, 226 jurisdictions across 26 states have been identified as vulnerable based on agency criteria. While the study brought greater urgency to the issue of HCV infections linked to the opioid crisis, it likely under-reports the vulnerability in jurisdictions with a high AI/AN population. This is because the indicators associated with acute HCV infections used in the study design did not include AI/ANs, despite the fact that AI/ANs have the second highest opioid overdose fatality rate nationwide.

Regional disparities in HCV infections among AI/ANs further demonstrate the disproportionate impact of the crisis on Tribal communities[15-19].

In Minnesota, the 2017 HCV prevalence rate for AI/ANs was 3,871 per 100,000, compared to 383 per 100,000 for Whites.

In Oregon from 2011-2015, acute HCV infections were twice as high among AI/ANs compared to other groups (0.92 per 100,000 compared to 0.45 per 100,000).

In Oklahoma, AI/ANs in 2017 had the second highest chronic HCV diagnosis rate at 9.1% , and the second highest acute HCV diagnosis rate at 13.6%.

In Arizona from 2011-2014, the age-adjusted average annual HCV mortality rate was at 8.6 per 100,000 among AI/ANs, compared to 5.9 per 100,000 among Whites.

THE SOLUTION

A multi-pronged approach will be needed to decrease the incidence, morbidity and mortality of HCV in AI/ANs communities, being the ultimate goal of HCV elimination.

There are several pillars that need to be in place to decrease transmission of HCV and improve the outcomes of those that are already infected. These are outlined on the next page:

THE SOLUTION

1. Political will and policy changes to eliminate HCV as a public health problem
2. Community education and activism
3. Expansion of the HCV screening programs
4. Development or expansion of the clinical infrastructure to link, evaluate and treat HCV (RNA +) individuals.
5. Implementation and or expansion of harm reduction programs such as Medication Assisted Treatment (MAT), Syringe Service Programs and Treatment as Prevention (TAP)
6. Development of a data collection and analysis system to evaluate the program's performance and guide the most effective interventions to achieve HCV elimination. Mathematical modeling could also be useful in predicting the elimination timeline based on progress achieved and guide future interventions.
7. Short and long term planning to address the social determinants in the community that are driving the epidemic.

MICHAEL'S STORY

Michael Buckner (Cowlitz Tribe) contracted hepatitis C in 1982 while getting tattoos, but didn't learn he had the disease until 1996. He was suffering from a loss of energy, lack of motivation, and achy joints. Early treatments were long, difficult, and unsuccessful for Michael, causing him to get discouraged.

"The long-term effects of having Hep C all these years have cost me greatly," he said.

But recently, Michael was offered a new treatment–one that took just 12 weeks to cure him of Hep C.

"There were no side effects, and I'm happy to say I don't have hepatitis C anymore. I'm more active, have more energy, am less achy, and feel more positive." Michael urges others to get tested and treated, too.

"It's not going to go away unless you do something about it."

MICRO VS MACRO ELIMINATION

In 2018 a report[20] defined micro elimination as "pursuing elimination goals in discrete populations through multi-stakeholder initiatives that tailor interventions to the needs of these populations". In contrast, macro-elimination programs are usually done at a National or State level in which the major stakeholder is the government and it covers the whole HCV infected population. Interventions are designed by mathematical modeling using population-based information and resources needed for HCV screening, linkage to care, treatment and harm reduction are provided and readily available. In lieu of National or State macro-elimination programs, micro-elimination is a great opportunity to reduce the burden of HCV at a community or health system level.

These programs can build momentum, when combined with neighboring micro elimination-programs, that in turn may motivate and inspire macro elimination efforts.

Micro-elimination lacks the complexity and cost of macro-elimination programs but still have minimum requirements that include:

- Plan in place that describes how to tailor health resources and services to achieve high levels of HCV diagnosis and treatment in a defined population and period of time
- Achievable annual targets
- Multiple stakeholders involved in the planning, with key participants including government officials, health service providers and civil society representation
- Progress and outcomes monitored and publicly reported using indicators selected at the outset of the process.

COST EFFECTIVENESS OF SCREENING AND TREATMENT

Whereas current HCV screening strategies are focused on the baby boomer generation (those born from 1945 to 1965), they do not align with newer studies demonstrating the benefits of universal screening and expanded treatment access[21]. These studies have illustrated that screening all individuals over the age of 18 would lead to the identification of 256,000 additional HCV infections, result in 280,000 additional cures and 4,400 fewer cases of hepatocellular liver cancer at an incremental cost-effectiveness ratio of $28,000 per quality adjusted life year (QALY). The same study found that case detection and cure rates would increase 11% and 12% respectively, with a 21% reduction in liver-attributable mortality among the affected population. In a different study, HCV screening and treatment linkage for patients in methadone maintenance treatment programs were found to generate a net monetary benefit of $511,000 - $975,600. Using HCV medications at costs of $40,000 or less for a full regimen, 87% of analyses concluded treatment to be cost-effective, and nearly 8% concluded treatment to be cost-saving[22].

In recent years, HCV treatment costs have plummeted due to the availability of less expensive drug treatment regimen.

COST EFFECTIVENESS OF SCREENING AND TREATMENT

The retail cost of HCV treatment drugs has dropped from as high as $95,000 per patient in 2014 to $24,000 using new medications. However, the availability of cheaper medications has not translated into greater rates of treatment coverage for patients living with chronic HCV, mainly due to strict treatment eligibility requirements under Medicaid and by private insurers[22].

In 2018, a study on the benefits of screening and treating universal HCV screening in IHS beneficiaries[23]. Researchers compared the cost effectiveness of three different screening and treatment scenarios:

"Fast" scenario:
In which 100% of the eligible population are immediately screened and receive treatment.

"Medium" scenario:
In which 15% are screened per year and 50% of HCV-positive cases receive treatment.

"Slow" scenario:
In which only 8% are screened per year and 20% of positive cases receive treatment.

Assessing costs through 2030, researchers concluded total screening, treatment, and cirrhosis management costs at roughly $4.5 million for the "fast" scenario to be more cost-saving than the "slow" scenario with total costs at $11.5 million.

INNOVATIVE STRATEGIES: REIMBURSEMENT

Pharmacies in many I/T/U health programs are eligible for reimbursement by third-party payers for dispensing medications.

In the case of direct acting antivirals such as Harvoni and Mavyret, the reimbursement to the pharmacy program can be substantial, and help to support hepatitis c elimination efforts.

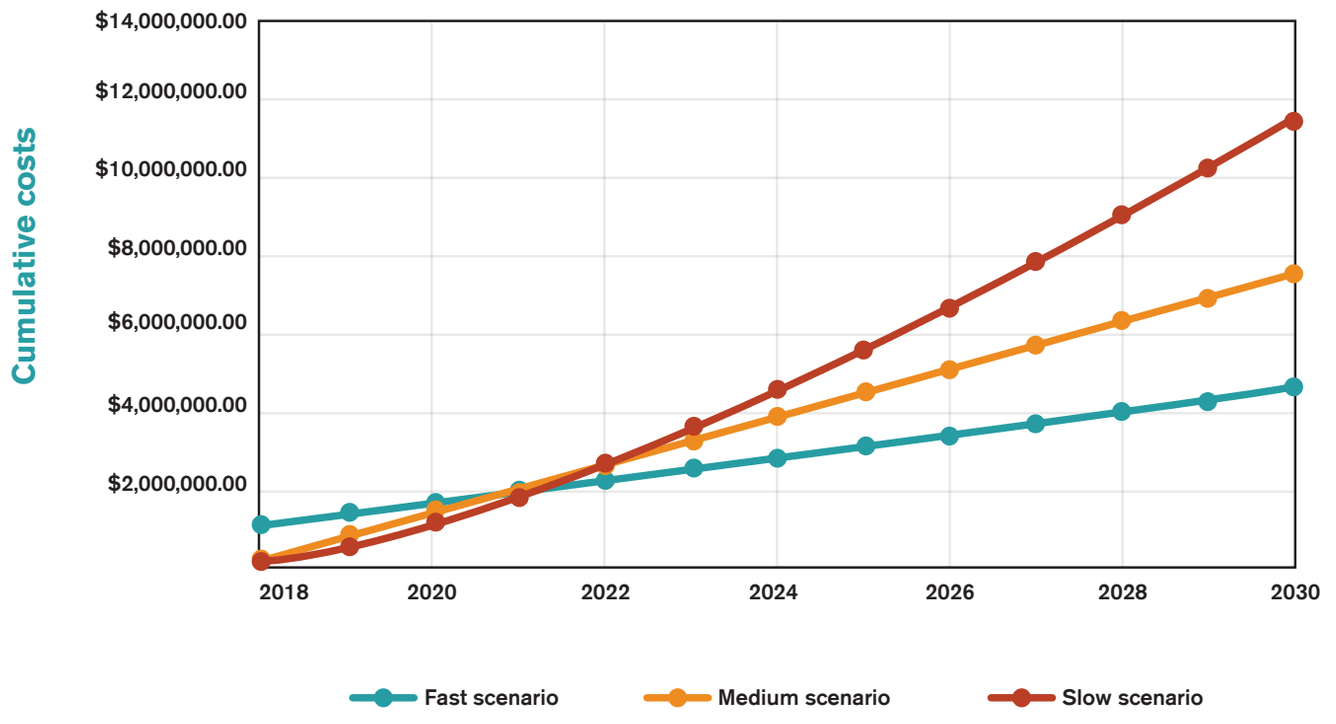
In Washington State, a tribal pharmacy program was able to increase pharmacy revenue by over 300% in one year by offering direct acting antivirals. This created the opportunity for the health program to hire a tribal member full-time to do outreach and harm reduction programming to support HCV elimination.

As the tribal member increased outreach activities more patients were tested and ultimately treated for chronic HCV, supporting both community health and the pharmacy bottom line.

COST EFFECTIVENESS OF SCREENING AND TREATMENT

Table 3: Costs accrued over time under different screening and treatment scenarios			
Scenario	**Year in which screening of full population**	**Number of cases that develop (2018-2030)**	**Total cost of screening, treatment, and management (2018-2030)**
Fast	2018	59	$4,543,430
Medium	2024	126	$7,058,654
Slow	2030	244	$11,487,583

Figure 5: **Cumulative costs over time under different screening and treatment scenarios**



These results led the IHS in 2019 to recommend screening for HCV all individuals 18 years or older and to incorporate three direct antiviral agents (DAAs) into its formulary, Sofosbuvir/Ledipasvir (Harvoni), Sofosbuvir/Velpatasvir (Epclusa) and Glecapravir/Pibrentasvir (Mavyret)

INNOVATIVE STRATEGIES: EXAMPLES OF IMPLEMENTATION

Several Tribes have developed innovative programs to improve HCV screening, testing, and access to treatment among their citizens. These initiatives show promise for future investments to ensure that all Tribes and AI/ANs are able to eliminate HCV in their communities.

- Launched in November of 2015, the Cherokee Nation HCV Elimination Project is a first-of-its-kind initiative. As of June 2019, the program has successfully screened 50,246 individual AI/AN for HCV between the ages of 20 to 69. Of those screened, the Tribe identified 1211 individuals with a current HCV infection, of which 78% have initiated antiviral treatment and 96% of those who have completed treatment and have sustained virological response data available have been cured[24]. The Cherokee Nation project has received national recognition for its innovative and highly successful approach towards HCV elimination.
- In response to rates of new HCV infections estimated to be 40 times higher than the neighboring non-Native community, the Lummi Tribal Health Center (LTHC) in Washington State began screening and treating Tribal citizens for HCV in 2017. LTHC sent providers to either the University of New Mexico Project ECHO HCV training, or the online HCV course from the University of Washington in order to build internal capacity for HCV treatment. the Tribe is currently on track to initiate treatment for 5 patients per month and eliminate HCV by 2021[22].

HCV is a curable disease. However, significant barriers to treatment access remain, particularly for IHS, Tribal, and urban Indian health systems.

HCV screening and treatment are shown to be highly cost-effective and can improve quality of life. Multiple sites in IHS and tribal health systems are initiating or expanding their HCV and some are initiating elimination programs. The science is here as well as the political commitment and awareness; this is the time for action and start the process of HCV elimination in AI/AN communities.

SECTION II

Building an HCV Elimination Program

PLANNING

1. Building partnerships with the institutions that are willing and capable of collaborating with the elimination program and determining who are the stakeholders of the program are the first major steps.

   Ideally the stakeholders should include a **representative from the community**, **funding agency** (if applicable), **local health department**, **university** (if applicable), **leadership** (tribal and administrative), **medical providers** and **harm reduction agencies** (if available in the area). Once this is established, tasks and responsibilities for each stakeholder should be determined as well as a clear agenda with a timeline.

2. **Measuring the baseline burden of HCV in the micro-elimination target population.** Proportions of positive HCV antibody and detectable HCV RNA should be determined to have an estimate of the seroprevalence and the prevalence of current HCV infection respectively. Other baseline measurements that may be useful in monitoring progress are the incidence of liver cancer and the prevalence of HCV related liver cirrhosis. If an epidemiologist is available, this task should be assigned to them. If not, ways of obtaining a baseline measurement of the HCV burden in the community where the HCV micro-elimination program will be implemented can be done by:

   a. Contacting the local health department/State Health Department. They may have incidence and prevalence data available for your target population.

   b. Retrospectively analyzing the prevalence of HCV antibodies in the individuals representing the target population who have been screened in a defined period of time. This data can usually be obtained from your reference laboratory. This measurement can be refined with time as more screening data is available but could be an important baseline measurement. Stratifying the results by age or birth cohort and gender is recommended.

   c. Prospectively screen the first consecutive 200-400 individuals ages 18 or older that are representative of your target population.

   These measurements should be calculated at least on a yearly basis to monitor the success of the program.

TARGET POPULATION DEFINITION

Each facility should decide what will be their target population to implement the HCV micro-elimination program; this can be based on geography, AI/AN access to the health system, infrastructure, availability of MAT programs, and availability of Syringe Service Programs etc. A combination of target populations can be included. The most important factor in choosing the target population is actually being able to access them. It is also very important to choose a target population in which you have a high likelihood in finding the at risk population that are transmitting the infection (example: PWID) and / or have a high morbidity due to HCV (baby boomers).

Examples:

- Individuals who inject drugs
- Individuals who are incarcerated
- Individuals who are homeless
- Individuals registered in the health system
- Individuals who access the health system
- Geographic boundaries of the reservation
- Specific services within the health system
- Syringe Services Programs
- Medication-Assisted Treatment (MAT) programs
- Specific departments:
    - Emergency/UC departments
    - Behavioral health
    - Hemodialysis units
    - OBGYN
    - Med-Surg
    - Other

INNOVATIVE STRATEGIES: CORRECTIONAL FACILIITES

It is estimated that 12-35% of inmates in jails and prisons have an HCV infection[26]. Jails and prisons, including tribal facilities, thus offer a unique opportunity for HCV elimination.

Treating HCV in correctional facilities is cost effective and by reducing the pool of individuals with current HCV infection released to the community it may also have a favorable impact in reducing HCV transmission in the community[27].

The National Academies of Sciences, Engineering and Medicine report on Hepatitis B and C Elimination recommended that correctional settings should be a focus of HCV screening and treatment efforts[28]. Unfortunately very few correctional facilities have a formal HCV program. However, there are examples of local I/T/U facilities collaborating with corrections to coordinate the screening, treatment, and follow-up of patients with HCV. These partnerships are instrumental to access this underserved population.

DEFINITION OF HCV MICRO-ELIMINATION GOALS IN **COMMUNITIES**:

The goal of HCV elimination is to reduce the burden of the disease to a level that it is not a public health problem. That requires reduction in mortality as well as transmission of the infection. The goal of any micro elimination program should be in alignment with the National goals, which are:

> 90% reduction in incidence by 2030
>
> 65% reduction in mortality by 2030

In 2017 the CDC released a report that recommended obtaining the HCV incidence and mortality measurements for the year 2014 to use as the baseline for comparison with future measurements[29]. At the micro-elimination level this could be difficult and in some cases misleading. Difficult because mortality data may not be accurate for AI/AN due to ethnic misclassification, or the diagnosis of HCV may have not been included in the death certificate, thus underreporting the impact of HCV mortality in AI/AN. Misleading because when HCV screening is expanded, there may be an apparent increase in the new cases of HCV diagnosed because more patients are being tested. In addition, in geographic regions with a low population density the HCV mortality rate may be difficult to interpret. Therefore, it may be more precise to use as baseline the incidence and mortality data obtained during the first year of the micro-elimination program and not what occurred in 2014.

Despite these issues, we still recommend trying to pursue these measurements to improve the capacity to obtain them as part of the process.

DEFINITION OF HCV MICRO-ELIMINATION GOALS FOR **INDIVIDUAL PROGRAMS**:

Programs with small populations may have a very difficult time calculating HCV incidence, and programs that target populations that are immersed in non-native populations may have problems measuring mortality. Therefore, the standard definition of elimination may not be appropriate for measuring the micro-elimination programs success. For individual programs reporting metrics that measure system level performance would be more appropriate.

For example: The number of patients engaged in treatment as a fraction of patients with a positive HCV RNA.

DEFINITION OF HCV MICRO-ELIMINATION GOALS FOR INDIVIDUAL PROGRAMS:

Individual programs should set goals that are **realistic** according to the available resources but that will also **meet the patient demand** and **standard of care** by AASLD guidelines.

There are two options, which are not exclusive:

Option One:

If a backlog of diagnosed untreated HCV patients is present, goals should be set for a yearly percent reduction of the backlog. Based on real world data (VA health system, Cherokee Nation Health Services) 20-30 percent reduction per year can be achieved.

Option Two:

If a backlog is not present a percentage of each step of the cascade of HCV care should be set (see bullet # 5 below)

Other goals related to harm reduction should also be set, for example:

- MAT: % of individuals with an opioid use disorder on MAT
- Measurement of individuals with opioid use disorder should be developed and implemented.
- If SSP are available:
- Number of syringes dispensed per customer per month/year
- Treatment as prevention
- Number of HCV infected individuals that injected drugs within the past 6 months that have initiated DAA therapy

ELIMINATION TARGETS FOR IHS CLINICS, HOSPITALS, TRIBAL FACILITIES

a. Screen 90 % of the AI/AN target population 18 years and older at least once in a lifetime (additional testing based on risk factors)

b. Obtain an HCV RNA in 90 % of those who have tested positive for an antibody

c. Initiate treatment with DAA in 90 % of those who test positive for HCV RNA

d. Document treatment completion in 90 % of those who have initiated treatment

e. Document cure in 80 % of those who have completed treatment.

ELIMINATION TARGETS FOR IHS CLINICS, HOSPITALS, TRIBAL FACILITIES:

To avoid disparities, when using the above targets it is important that the percentage is not applied to the overall target population, but instead that **specific goals are reached within the subpopulations**.

For example, let us assume that a micro-elimination program whose target population are the individuals who access care in a specific Indian Health Clinic. Of these individuals 10% are PWID, and the HCV screening target of the program is to reach 90 % of the population overall. If the PWID populations are not defined and targeted independently the 10% of the individuals that may be missed can be 100% of the PWID population in this scenario. This would be a problem since the PWID subpopulation, should actually be a primary target for HCV elimination program to interrupt HCV transmission. Setting 90% screening goals for the population overall, with subpopulation targets can be useful. A way to prevent this problem would be as follows:

Example: The goal is not only to screen 90% of the total population who accesses the Indian Health Clinic, but also to screen 75% of those individuals who are PWID and access the clinic. For this, a screening tool to detect PWID who are part of your target population should be developed.

CASCADE OF CARE (COC)

The function of the CoC is to depict how many members of a population have progressed through each stage in a sequence of stages required for effective disease control, eg. HCV RNA positive, engaged in care, initiated treatment, etc[30]. This will help the individual program **prioritize interventions for improvement** at the different stages. With the objective of standardizing reports and interpretation of data a recent consensus has suggested focusing on 4 components of the cascade. This does not mean that an individual program can have more components, but for reporting purposes only 4 are required.

INFECTED
Estimated HCV RNA prevalence (RNA) during the time period of interest

TREATED
Started treatment in (year): Initiated treatment during the period of interest

DIAGNOSED
With chronic HCV (Detectable RNA) : Diagnosed during or before the period of interest, was alive at the end of the period of interest and not cured before the period of interest

CURED
Achieved SVR in (year): Cured at any time during the period of interest

As an example, if the period of the CoC under consideration were between January 1, 2017 and December 31, 2018 the individuals that would be considered eligible to be included in the cascade would be: Individuals 18 years of age or older who had a detectable RNA on any day between 1/1/2017-12/31/2018, were alive in 12/31/2018 and did not clear the infection by 12/31/2018

POLICY RECOMMENDATIONS NECESSARY TO ACHIEVE HCV ELIMINATION PROGRAM GOALS

1. Universal HCV screening
    a. 18 years of age and older
    b. Pregnant females
2. Definition of target population
3. Medication procurement strategy
    a. Patient Assistance Program
    b. Medicaid
    c. Medicare
    d. Private Insurance
    e. IHS
    f. Own formulary
    g. 340B
    h. VA pricing
4. HCV care team and workflow
    a. Patient navigator
    b. Clerk
    c. LPN
    d. RN (Case manager)
    e. Licensed alcohol and drug use counselor
    f. Pharmacist
    g. Clinician (Physician, APRN, PA)
    h. Community health worker
5. Measurements of outcome
    a. Cascade of Care
    b. HCV Related Mortality
    c. HCV Related Morbidity (Cirrhosis, HCC)
    d. HCV Incidence
    e. Other

SECTION III

HCV Micro-Elimination: A skills-based clinical toolkit

PRE-TREATMENT

- Screening
- Electronic Patient Management Tool
- Outreach and follow-up

DIAGNOSIS AND LIVER STAGING

- Lab Ordering and Reporting
- Outreach and follow-up

TREATMENT AND CURE

- Project ECHO
- Medication Acquisition
- Outreach and follow-up

NOTE: For additional guidance the AASLD and IDSA guidelines are located in appendix A

PREVENT NEW INFECTIONS AND REINFECTION

Access to safe injection supplies

Linkage to behavioral health and MAT

PRE-TREATMENT

Increase the number of patients in the community who know their HCV status

Screening

The Indian Health Service has recommended one-time HCV Ab screening for all patients over the age of 18 (Universal Screening). Screening using HCV Ab with a Reflex to RNA increases the number of patients who know their status and decreases time to treatment.

Identify, monitor, and link to treatment all patients in the community who need treatment for the Hepatitis C Virus (HCV). Expanded screening programs, electronic disease registries, and community outreach and follow-up with CHR or peers are needed in this phase of HCV elimination.

Lab Ordering and Reporting

An electronic system identifying all patients who have been screened, diagnosed, had liver staging, and are either in treatment or completed treatment, serves as the information hub to guide the elimination program.

PRE-TREATMENT: SCREENING

All patients over the age of 18 should be screened, at least once in their lifetime, for the Hepatitis C Virus (Universal Screening).

	Available Resources	Rationale
HCV screening should be made available outside of usual clinical visits (Eg Health Fairs, Emergency/Urgent Care Departments, Harm Reduction Programs, Jails, Opioid Treatment Programs, Dental Clinics).		Many high-risk patients do not regularly access primary care.
For persons who inject drugs, at least annual screening for HCV is recommended.	• AASLD/IDSA Recommendation for Screening HCV in Persons Who Inject Drugs	During the first few years of injection drug use the rate of HCV injection can exceed 40%.
Standing orders or standing protocols for HCV screening can streamline workflow and include non-providers in screening services.	• Example Standing Order (page 8)	Expand access to screening services in the absence of providers.
Point of Care Testing (Eg OraQuick®) can provide a rapid HCV screening result in 20 minutes with a finger stick blood test.	• OraQuick Product Information	Rapid tests can provide a test result for patients who are difficult to reach for follow-up and can be provided in community settings where a full blood draw is not possible.
Whenever blood draw is available (venipuncutre) to draw labs, providers should always order HCV Ab with a Reflex to RNA.	• LabCorp Info: HCV Ab with Reflex to RNA • Quest Lab Info: HCB Ab with Reflex to RNA	This strategy provides screening and diagnosis in one step, accelerating time to treatment.

PRE-TREATMENT: ELECTRONIC PATIENT MANAGEMENT TOOL

An electronic system identifying all patients who have been screened, diagnosed, had liver staging, and are either in treatment or completed treatment, serves as the information hub to guide the elimination program.

	Available Resources	Rationale
Many clinics use excel or access to create patient management tools. Most tools, unfortunately, require a dedicated team member to hand enter information from the Electronic Health Record into the database.	Examples of Patient Management Tools: • NPAIHB Links to Clinical Resources • Example Excel Management Tool • Example Access Database	The ability to quickly identify a patient at any point from HCV screening to treatment completion and cure is critical for understanding HCV elimination in your community.
Clinical Decision support tools in RPMS can assist in identifying and tracking patients who are in need of screening or additional follow up (ex: labs or liver staging) and to monitor treatment progress.	• HCV Screening Reminder Resources • iCare Resources	Use RPMS Reminders to identify and track patients through screening and treatment process to identify and close gaps in follow up
Programs that use RPMS/EHR can use iCARE to create the initial outline of a patient management tool.	• Video "How to use iCare for HCV Management"	Use iCare to manage patients leveraging the CMET (Care Management Event Tracking) functionality and/or the RPMS Reminders mentioned above. These tools can work hand in hand.

DIAGNOSIS AND LIVER STAGING

Increase the number of patients who start treatment for chronic HCV

Lab Ordering and Reporting

Many patients who need treatment for HCV are lost to follow-up from screening to the start of treatment. Developing standardized lab order sets and clinical workflow for screening and liver staging that minimize office visits and blood draws, will increase the number of patients who will start treatment.

DIAGNOSIS AND LIVER STAGING: LAB ORDERING AND REPORTING

Developing standardized lab order sets and clinical workflows that minimize the number of office visits or blood draws will increase the number of patients who start treatment for HCV.

	Available Resources	Rationale
Creating flexible and convenient clinical delivery processes that move patients from screening to HCV diagnosis in a single visit.	• Example Workflow/ Protocol	Creating clinical delivery models that meet the needs of this patient group is critical to eliminating HCV.
Providers should always order HCV Ab with a Reflex to RNA when ordering a blood draw for patients who have an unknown HCV Ab status.	• LabCorp Info: HCV Ab with Reflex to RNA • Quest Lab Info: HCB Ab with Reflex to RNA	This strategy provides screening and diagnosis in one step accelerating time to treatment.
Lab directors/managers/supervisors and EHR IT staff can play a critical role in accelerating the number of patients who are treated for HCV by creating standardized HCV screening and staging quick-order sets.	• Video "How to Create a Quick Order Set for HCV"	Creating standardized order sets can be a good training tool for providers who are new to treating HCV.
Calculating a patient's APRI or FIB-4 score is a validated non-invasive approach to determine the degree of fibrosis or cirrhosis for a patient.	• APRI Calculator • FIB-4 Calculator	Clinical calculators use AST, ALT and Platelet values which can be ordered in any lab. No imaging, special tests, or outside referrals are necessary.
Standardized HCV quick order sets along with standing orders or standing protocols can support nursing staff to provide high value outreach to complete HCV diagnosis and liver staging prior to treatment.	• Example HCV Case Management Protocol • Example Order Set	
Identifying a process for tracking lab results and entering them into the electronic patient management tool will ensure all patients who have chronic HCV are identified, and create an opportunity for recalling high risk patients who need periodic HCV RNA testing.		Additional eyes on the chart to track lab results can support the care for complex patients.

TREATMENT AND CURE

Increase the number of patients who are cured of chronic HCV

Telehealth

Hepatitis C is being successfully treated and cured by primary care providers in I/T/U clinics across the country. As an example, Project ECHO (Extension for Community Healthcare Outcomes) provides regular access to Hepatologists and Infectious Disease Specialists via telemedicine to support HCV treatment by primary care physicians, mid-levels, and pharmacists. For more information please visit www.indiancountryecho.org.

Medication Acquisition

Direct Acting Antiviral medications that treat HCV are over 95% effective and have minimal side effects. However, their high cost has created some barriers to access. In most cases, patients can receive these medications through their State Medicaid Plans, Medicare, private insurance, IHS pharmacies or through Patient Assistance Programs operated by the pharmaceutical companies.

TREATMENT AND CURE: PROJECT ECHO

Hepatitis C is being successfully treated and cured by primary care providers in I//T/U clinics across the country with the support of Project ECHO.

	Available Resources	Rationale
The Northwest Portland Area Indian Health Board (NPAIHB) coordinates an HCV treatment ECHO clinic for I/T/U programs. Other HCV ECHO programs are available as well and run by academic medical centers such as the University of New Mexico and the University of Washington.	• ECHO Case Form • About Indian Country ECHO	Project ECHO improves providers knowledge and skill in treating HCV, and brings specialty care directly to I/T/U clinics.
Utilizing collaborative practice agreements, clinical pharmacists can play an important role in treating patients for HCV.	• Example Documents	A significant portion of HCV treatment is protocol driven (much like diabetes) and well suited for clinical pharmacists
Determining the appropriate direct acting antiviral medication for a patient is straightforward and guided by published algorithms.	• HCV Treatment Guidelines AASLD/IDSA • ECHO Treatment Decision Tree	Treatment decisions are highly protocol driven. Follow the decision trees.
There are many no cost trainings, both in person and on-line for providers to learn about diagnosing and treating chronic HCV.	• University of Washington HCV Online Training • Indian Country ECHO Trainings	
There are very few medication interaction/contraindications with the new direct acting antiviral medications. However, use the specialized drug interaction checker prior to ordering HCV treatment.	• HCV Drug-Drug Interaction Checker	Most HCV treatment regimens only last between 8-12 weeks. If a patient's chronic medication needs to be changed, it's usually only temporary.

TREATMENT AND CURE: MEDICATION AND ACQUISITION

The majority of patients with HCV will be able to receive Direct Acting Antiviral medications through either a State Medicaid Plan, Medicare, private insurance, IHS pharmacy or through Patient Assistance Programs (Charity Care) operated by the pharmaceutical companies.

	Available Resources	Rationale
Each State Medicaid Plan has different prior authorization requirements for acquiring DAAs. It's important to review these to make sure you have the right documentation to meet your State's Medicaid requirements.	• Hepatitis C: State of Medicaid Access	State Medicaid is a key third party payer
Almost all pharmaceutical companies who provide DAAs offer some form of Patient Assistance Program (charity care) for eligible patients, which can be accessed if a patient is uninsured or denied the medication by their primary insurance provider.	• Patient Assistance Program Guidelines • Income Documentation Guidelines • Sample Income Statements	Streamlining medication access can greatly reduce time-to-treatment and increase the number of patients who can be treated.
For programs that operate their own pharmacy, providing access to DAAs for patients whose pharmacy benefit covers the medication can significantly improve program budgets. Exploring options to opt-out of specialty pharmacy benefits from commercial payers can also be advantageous, especially for self-insured tribal employee health plans.		

FOLLOW UP AND OUTREACH

Decrease time to cure.

Follow-up and Outreach

Many patients who need treatment for HCV require additional support to make and keep appointments, may benefit from transportation and appreciate follow-up for missed appointments.

In most clinical settings, it can take up to a week from the time labs are ordered, sent out, and results returned. Creating a connection with patients and planning for outreach with phone calls, letters, home visits, and scheduling future appointments with transportation is often necessary to make sure patients who test positive for HCV get the treatment they need.

After patients start treatment, it's important to follow-up periodically to ensure there are no barriers to taking the medication. Some patients may become incarcerated, enter substance use disorder treatment, or lose housing while taking DAA's. Helping patients continue to receive their medications across care settings can be critical to help patients complete their HCV treatment.

FOLLOW-UP AND OUTREACH

Community health workers, peer workers, and other healthcare team members are critical to help patients navigate the stages of HCV treatment, and also to maintain close connections between visits for some patients.

	Available Resources	Rationale
The most important function of an outreach worker is to create connection with the patient and let them know that healthcare programs want to help them treat HCV.	• Motivational Interviewing	Seventy percent of new cases of HCV occur in patients who are injecting drugs. Many patients have had negative experiences with the health care system.
Formalized processes to risk stratify patients can help guide outreach activities, but flexibility is a key to successful outreach.	• Risk Stratify Example	Not every patient who needs treatment for HCV will need outreach support. Identifying patients early in the process could help increase patient engagement.
Creating the opportunity for home lab draws (RN's or phlebotomists) can help patients who live long distances from the heath facility or have difficulty with transportation.		Bringing services to the patient is required for a successful outreach program.
Outreach workers are critical members of the care team and should have access to the electronic health record and other electronic patient management tools.		Outreach workers can be trained to flag charts, make notes about outreach, and fill in the gaps between office visits.

PREVENT NEW HCV INFECTIONS AND RE-INFECTION

Access to Safe Injection Supplies

Seventy percent of new HCV infections occur in persons who inject drugs with the majority of new cases impacting young people. Providing all patients access to safe injection supplies is an evidenced based public health approach to prevent both HCV and HIV infections.

Linkage to behavioral health and medications for opioid use disorder

Many patients who have HCV also have a mental health diagnosis such as depression, and/or substance use disorder. Starting treatment or maintaining sobriety prior to HCV treatment is not an evidenced based practice and should not be a prerequisite to treatment; however, helping patients access behavioral health services, alcohol use disorder treatment, and medications for opioid use disorder such as buprenorphine or methadone is important for overall patient health.

PREVENT NEW HCV INFECTIONS AND RE-INFECTION

Access to safe injection supplies such as syringes is an evidenced based public health approach to reduce HCV and HIV transmission.

	Available Resources	Rationale
Safe injection supplies should be made available to all patients who need them. Policies requiring patients to return a "dirty" needle in exchange for a "clean" needle is an outdated approach and will create unnecessary program barriers for patients.	• CDC Syringe Service Programs	Offering harm reduction programs will expand the patient population your health programs reach and identify patients at high risk for being infected or infecting others with HCV.
Many Tribes and the majority of States have passed laws making safe injection supplies legal to protect public health.	• Eastern Band of Cherokee • State Laws	
If possible, integrate safe injection supply distribution as a part of usual primary care services.		This approach can decrease stigma and improve patient comfort in accessing harm reduction services.

DIFFERENT HEALTHCARE TEAM MEMBERS CAN LEARN HCV ELIMINATION SKILLS

TREATMENT AND CURE

Physicians
Mid-levels
Pharmacists

SCREENING

Physicians
Mid-levels
Pharmacists
Nurses/PHN
CHR

LAB ORDERING AND REPORTING

Pharmacists
Nurses/PHN
CHR

MEDICATION ACQUISITION

Physicians
Mid-levels
Pharmacists
Nurses/PHN
CHR
Patient Navigator

ELECTRONIC PATIENT MANAGEMENT TOOL

Pharmacists
Nurses/PHN
CHR

LINKAGE TO BEHAVIORAL HEALTH AND MEDICATIONS FOR OPIOID USE DISORDER

Physicians
Mid-levels
Pharmacists
Nurses/PHN
CHR
Peers

FOLLOW UP AND OUTREACH

Pharmacists
Nurses/PHN
CHR
Patient Navigator

ACCESS TO SAFE INJECTION SUPPLIES

Physicians
Mid-levels
Pharmacists
Nurses/PHN
CHR
Peers

SECTION III

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SECTION IV

Appendix A

Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Adults with chronic hepatitis C (any genotype)
who do not have cirrhosis
and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Cirrhosis assessment**: Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis
- **Medication reconciliation:** Record current medications, including over-the-counter drugs, and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing**

  Within 6 months of initiating treatment:
  - Complete blood count (CBC)
  - Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
  - Calculated glomerular filtration rate (eGFR)

  Any time prior to starting antiviral therapy:
  - Quantitative HCV RNA (HCV viral load)
  - HIV antigen/antibody test
  - Hepatitis B surface antigen

  Before initiating antiviral therapy:
  - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Advise patients to avoid excess alcohol use.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Until retreatment occurs, assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Advise patients to avoid excess alcohol use.

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at www.hcvguidelines.org. Updated: August 27, 2020

Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- **Current or prior** episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m^2) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation**: Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing** (see next column)

Within 3 months of initiating treatment

- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Before initiating antiviral therapy

- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Genotype 1-6:

Glecaprevir (300 mg)/pibrentasvir (120 mg) taken with food for a duration of 8 weeks

Genotype 1, 2, 4, 5, or 6:

Sofosbuvir (400 mg)/velpatasvir (100 mg) for a duration of 12 weeks

NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.

ON-TREATMENT MONITORING

- Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.
- Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis
- Patients with ongoing risk for HCV infection (eg, IV drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Patients should abstain from alcohol to avoid progression of liver disease.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, creatinine, and INR is recommended.
- Patients should abstain from alcohol to avoid progression of liver disease.

AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment can be found at www.hcvguidelines.org.

IDSA Infectious Diseases Society of America

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For more information about in HCV in Indian Country, please visit http://www.npaihb.org/hcv/.

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