How to Start an HCV Micro-elimination Program

Jorge Mera, MD, FACP

Disclosure

• The Cherokee Nation receives a grant from the Gilead Foundation for the HCV elimination program. Dr. Jorge Mera is the PI of the grant

• Dr. Jorge Mera has received speaker fees from Abbvie Pharmaceuticals
Outline

- HCV in Indian Country Basics
- HCV Elimination Basics
- Overview of HCV elimination
- Macro vs Micro elimination
- Overview of the Cherokee Nation Health Services (CNHS) and the HCV elimination program
- Conclusions
Change in HCV Incidence is Associated with Increases in Injection Drug Use

- ~31,000 new HCV infections in 2015
- 1:1 male:female ratio, predominantly white
- Highest incidence 20-29 years, non-urban areas

In the USA, 68% of Acute Cases of HCV Report IDU

Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)
Photograph courtesy of Jorge Mera, MD, permission to reproduce consented

IDU: Injection Drug Use
Indian Health Services: HCV Burden


Poverty
Domestic Violence
Mental Illness
Historical Trauma*
Cultural Disconnection
others

IDU
HCV
Prevention
Screening
Linkage to Care
Quality of Care

HCV

THE CHEROKEE TRAIL OF TEARS
The forced removal of more than 15,000 Cherokee from the eastern U.S. to Oklahoma resulted in the deaths of thousands. Fort Armistead, near Coker Creek in Monroe County, was used as a collection point along the historic Unicoi Turnpike.

Source: National Park Service

*Maria Yellow Horse Brave Heart, Journal of Psychoactive Drugs, Vol. 35, Iss. 1, 2003

45% Younger Than Baby Boomers
Feasibility Criteria for Elimination

<table>
<thead>
<tr>
<th>In General¹</th>
<th>Hepatitis C Virus</th>
<th>Check list</th>
</tr>
</thead>
<tbody>
<tr>
<td>No non-human reservoir and the organism can not multiply in the environment</td>
<td>No non human reservoir</td>
<td>✔</td>
</tr>
<tr>
<td>There are simple and accurate diagnostic tools</td>
<td>Serology widely available</td>
<td>✔</td>
</tr>
<tr>
<td>Practical interventions to interrupt transmission</td>
<td>Treatment as prevention, Needle and syringe programs, Medication assisted programs</td>
<td>✔</td>
</tr>
<tr>
<td>The infection can in most cases be cleared from the host</td>
<td>Treatment is 95% curative</td>
<td>✔</td>
</tr>
</tbody>
</table>

Adapted from Hopkins D. Disease Eradication. N Engl J Med 2013;368:54-63
HCV Elimination: Definitions and Goals

• **Definition:**
  – Elimination of hepatitis C as a *public health problem*

• **Goals:**
  – **National Viral Hepatitis Action Plan 2017-2020**¹
    • Decrease in new infections by 60% by the year 2020
    • Decrease in mortality by 25% by the year 2020
  
  – **National Academy of Sciences**²
    • Decrease the incidence of new infections by 90% by the year 2030
    • Decrease in mortality by 65% by the year 2030


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**WHO Impact Targets for Elimination of Hepatitis B and Hepatitis C as Public Health Threats**

<table>
<thead>
<tr>
<th>Target</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>90% reduction in new HBV and HCV infections</strong></td>
<td>6-10 million infections (in 2015) to 900,000 infections (by 2030)</td>
</tr>
<tr>
<td><strong>65% reduction in deaths from HBV and HCV</strong></td>
<td>1.4 million deaths (in 2015) to under 500,000 deaths (by 2030)</td>
</tr>
</tbody>
</table>
Key Concepts to Guide HCV Elimination

- Decrease the burden of HCV related liver diseases by treating the chronically infected population
  - Birth cohort (patients born between 1945-1965/1975*)
  - Anyone infected for 20+ years or with multiple liver comorbidities

- Decrease new infections by preventing transmission
  - Mainly target the younger population who are PWID
    - Treatment as prevention/MAT/Needle and syringe programs
  - Address unsafe medical practices
  - Address sexual transmission in MSM

HCV Macro-Elimination

- Launched at a National level
- Covers the whole HCV infected population
- Main Stakeholder is the government
- Resources available for widespread
  - Screening strategy
  - Engagement in Care
  - Treatment readily available and restrictions minimized
  - Harm Reduction
- Interventions designed by modeling and population based information
- Examples: Country of Georgia, Iceland, Australia etc.
Micro-Elimination

- **Concept**
  - Breaking down national elimination goals into smaller goals for individual population segments for which treatment and prevention interventions can be delivered more quickly and efficiently using targeted methods

- **Criteria**
  - Plan in place for how to tailor health resources and services to overcome known barriers and achieve high levels of HC diagnosis and treatment in one or more clearly definable populations of interest within a specified time frame
  - Achievable annual targets ideally based on mathematical modeling
  - Plan developed by multi-stakeholder process with essential participants including government officials, health services providers and civil society representation
  - Progress and outcomes are monitored and publicly reported using indicators selected at the outset of the process


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Micro-Elimination: Populations to be Targeted

- Aboriginal and Indigenous communities
- Birth cohorts with high HCV prevalence
- Children of HCV Infected mothers
- Hemodialysis recipients
- HIV/HCV Co-infected individuals
- Migrants from high-prevalence Countries
- People Who Inject Drugs
- People with hemophilia and other inherited blood disorders
- Prisoners

What do you need to know before you start a Micro-Elimination Program?

- What population are you going to target and why?
- What is the HCV prevalence of that population and what does your cascade of care look like?
- Who are your stakeholders going to be?
- What will be your goals?
- How are you going to measure them?
- What human resources will you have available?
- How are you going to get your DAAs for this population?
- What will be your harm reduction strategies?

### CNHS HCV Cascade of Care 2012

- **HCV RNA Estimate**: 1892 patients
- **HCV RNA Detected**: 263 patients (14%)
- **HCV Evaluation**: 179 patients (9%)
- **HCV Antiviral Treatment**: 1% (1 patient)

Estimated HCV Seroprevalence was 3.4%

*Cherokee Nation Health Services, 2018*
Impact of Electronic Health Record Reminder and Provider Education on HCV Screening in CNHS: 2012-2015

**Baby Boomers Screened**

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Clinic 1</td>
<td>11%</td>
<td>16%</td>
<td>11%</td>
</tr>
<tr>
<td>Clinic 2</td>
<td>11%</td>
<td>11%</td>
<td>12%</td>
</tr>
<tr>
<td>Clinic 3</td>
<td>12%</td>
<td>17%</td>
<td>9%</td>
</tr>
<tr>
<td>Clinic 4</td>
<td>22%</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Clinic 5</td>
<td>26%</td>
<td>8%</td>
<td>5%</td>
</tr>
<tr>
<td>Clinic 6</td>
<td>12%</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>Clinic 7</td>
<td>13%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Clinic 8</td>
<td>29%</td>
<td>63%</td>
<td>50%</td>
</tr>
<tr>
<td>Hospital</td>
<td>68%</td>
<td>64%</td>
<td>64%</td>
</tr>
</tbody>
</table>

GPRA Measures

**ECHO*: Moving Knowledge Instead of Patients

The *ECHO model improves CAPACITY and ACCESS simultaneously

*Extension for Community Health Outcomes
CNHS HCV Cascade of Care

Percentages for 715 hepatitis C virus (HCV) antibody-positive patients, showing cascade of care — Cherokee Nation Health Services, October 2012–July 2015

DOI: http://dx.doi.org/10.15585/mmwr.mm6518a2.

The Cherokee Nation HCV (Micro?)-Elimination Program
What do you need to know before you start a Micro-Elimination Program?

- What population are you going to target and why?
- What is the HCV prevalence of that population and what does your cascade of care look like?
- Who are your stakeholders going to be?
- What will be your goals?
- How are you going to measure them?
- What human resources will you have available?
- How are you going to get your DAAs for this population?
- What will be your harm reduction strategies?

Cherokee Nation

- Sovereign Nation within a Nation
- One of the 566 Federally recognized tribes and 2nd largest Indian Nation (~350,000 citizens)
- Tripartite government
- 14 county area (over 9,200 sq mi.)
- Capitol located in Tahlequah, Oklahoma
- Largest Tribal Health System in the USA

- One central hospital and 8 outlying clinics
- Medically serves 130,000 AI/AN
- Unified electronic health record.
- 80,928 unique patients ages 20-69 visit the health system in a 3 year period

AI/AN: American Indian/Alaskan Native  Source: Cherokee Nation Health Services, 2018
What do you need to know before you start a Micro-Elimination Program?

- What population are you going to target and why?
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CNHS HCV Cascade of Care 2015

What do you need to know before you start a Micro-Elimination Program?

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• What human resources will you have available?
• How are you going to get your DAAs for this population?
• What will be your harm reduction strategies?

CNHS HCV Elimination Program Goals
7/2015

- Secure political commitment
  - Tribal leadership support
  - Partnered with CDC
  - Partnered with Oklahoma State Health Department
  - ProjectECHO UNM
  - Partnered with Oklahoma University
- Expand the screening program
- Expand clinical capacity
- Decrease new infections
What do you need to know before you start a Micro-Elimination Program?

- What population are you going to target and why?
- What is the HCV prevalence of that population and what does your cascade of care look like?
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Goal #1: Secure Political Commitment

HCV Awareness Day
October 31, 2015

HCV Elimination Awareness Day
October 31, 2017

“As Native people and as Cherokee Nation citizens, we must keep striving to eliminate hepatitis C from our population.”
Chief Bill John Baker
Goal #2: HCV Screening Expansion

Screen 85% of Target Population (80,928 AI/AN)

**Universal Screening**
- Ages 20-69

**Non-Traditional Screening Sites**
- Emergency Department
- Urgent Care
- Dental Clinics
- OB/GYN

**Screening Modalities**
- EHR Reminders
- Point of care antibody test
- Lab Triggered screening

Why Universal HCV Screening?

- 80,928 AI/AN Ages 20-69 that access CNHS
- HCV (+) PWID Transmitting the Infection

Medication Assisted Treatment
Prison
Needle and Syringe Programs
Services Not Available at CNHS

Cherokee Nation Health Services, 2018

PWID: People Who Inject Drugs
AI/AN: American Indian/Alaskan Native
• “In addition to risk-based testing, one time HCV testing of persons 18 and older appears to be cost-effective, leads to improved clinical outcomes and identifies more persons with HCV than the current birth cohort recommendations. These findings could be considered for future recommendation revisions”.

Patient Location During Lab Triggered Screening: 12/2015 - 2/2017

97 patients with new positive HCV antibody screen at WW Hastings Hospital

97 patients with new positive HCV antibody screen at WW Hastings Hospital

67% of patients were detected in the Urgent Care/Emergency Department

Cherokee Nation Health Services, 2018

Goal #2: HCV Screening Expansion
Interventions and Outcomes

<table>
<thead>
<tr>
<th>Period</th>
<th>Interventions</th>
<th>Number of Unique Patients Screened (% seropositive)</th>
<th>Number of Patients Screened per month</th>
<th>% HCV Seropositive Patients Born after 1965</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2006 - 9/2012</td>
<td>High Risk Patients, Patients with cirrhosis, Patients with elevated LFT's</td>
<td>5,425 (10.8%)</td>
<td>57</td>
<td>?</td>
</tr>
</tbody>
</table>

Cherokee Nation Health Services, 2018
Goal #3: Link to Care, Treat, and Cure

Before HCV Evaluation
- Patient Navigator
- Medication Procurement Specialist
- Public Health Nurse
  - Link the patient to the clinic for appointment with HCV Provider
  - Initial point of contact between the clinic and the patient

During Evaluation
- Licensed Drug and Alcohol Counselor
  - If substance use disorder is present, appropriate referrals are made (MAT, Counseling, Psychiatry, etc.)
- Utilize ECHO for Primary Care providers

After Treatment Initiation
- Clinical Case Manager
- Pharmacist
- Community Health Worker
  - Follow the patient during treatment to help ensure adherence and follow up to SVR
  - Sometimes will include direct observed therapy (DOT)

Goals
- Link to care 85%
- Treat 85%
- Cure 85%

Cherokee Nation Health Services, 2018

CNHS HCV Clinical Capacity Expansion
1/2014 – 6/2018

- HCV Project ECHO Introduced
- HCV Elimination
- 24 Providers*
- Presence of Cirrhosis at Treatment Initiation
  - Overall 23.8%
  - Born 1945-1965 33%
  - Born after 1965 13%

*Providers included 1 Specialist, 8 Physicians, 8 Pharmacists and 7 Nurse Practitioners
Cure rates did not differ by provider type

Cherokee Nation Health Services, 2018
### HCV Treatment Outcomes of Pharmacist Managed Patients (5/2015-1/2017)

![Pie chart and bar graph showing treatment outcomes for pharmacist-managed vs. non-pharmacist-managed patients.]

<table>
<thead>
<tr>
<th></th>
<th>Pharmacist-Managed</th>
<th>Non Pharmacist-Managed</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention to Treat</td>
<td>83.6%</td>
<td>73.1%</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>(including patients lost to follow up)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pew Protocol</td>
<td>91.6%</td>
<td>93.2%</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>(Excluding patients lost to follow up)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Goal #4: Reduce the incidence of new HCV infections

**Public and Provider Awareness**
- Public Campaign
- Provider Training

**Contact Tracing**
- Acute HCV
- PWID

**Harm Reduction**
- Treatment as Prevention
- MAT
- NSP (NOT Available in Oklahoma)

MAT: Medication assisted treatment
NSP: Needle and syringe program

Cherokee Nation Health Services, 2018
CNHS: Chronology of MAT Escalation

<table>
<thead>
<tr>
<th>Date</th>
<th>MAT Waived Providers</th>
<th>Capacity to Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006 -2016</td>
<td>None</td>
<td>0 patients</td>
</tr>
<tr>
<td>2017</td>
<td>2 clinicians</td>
<td>60 patients</td>
</tr>
<tr>
<td>6/2018</td>
<td>1 Infectious Disease Nurse Practitioner and 1 Specialist</td>
<td>60 patients</td>
</tr>
<tr>
<td>12/2018</td>
<td>2 Emergency Physicians, 2 Hospitalists, 6 Primary care physicians, 1 CMO</td>
<td>330 patients</td>
</tr>
<tr>
<td>4/2019</td>
<td>4 Behavioral Health Nurse Practitioners</td>
<td>120 patients</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>570 patients</td>
</tr>
</tbody>
</table>

Medication Assisted Treatment with Buprenorphine/Naloxone
C. No person shall deliver, sell, possess or manufacture drug paraphernalia knowing, or under circumstances where one reasonably should know, that it will be used to plant, propagate, cultivate, grow, harvest, manufacture, compound, convert, produce, process, prepare, test, analyze, pack, repack, store, contain, conceal, inject, ingest, inhale or otherwise introduce into the human body a controlled dangerous substance in violation of the Uniform Controlled Dangerous Substances Act.

**Syringe Service Programs (SSP) and Medication Assisted Treatment (MAT) Prevent HCV Transmission**

SSP and MAT effective in reducing self-reported injecting risk behaviour

- Limited evidence for effect on HCV transmission

**New Cochrane systematic review**

- MAT alone decreases risk by 50%
- SSP alone decreases risk by 56% (in Europe)
- MAT + SSP jointly decreases risk by 71%

The CNHS Comprehensive HCV Care Model

Universal Screening ➔ Patient Navigator ➔ HCV Evaluation ➔ Treatment

Non-Adherence Risk Assessment
- Nurse
- BH Counselor
- HCV Provider (Start MAT if needed)
- Case Manager (DAA Procurement)
- Pharmacist
- Community Health Worker

DAA: Direct Acting Antiviral, MAT: Medication Assisted Therapy

CNHS HCV Cascade of Care
11/2012 - 12/2018

2012-2015 2015-2018 (Elimination Period)

Number of Patients

<table>
<thead>
<tr>
<th>Stage</th>
<th>2012-2015</th>
<th>2015-2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated HCV RNA Detected</td>
<td>2100</td>
<td>961</td>
</tr>
<tr>
<td>HCV RNA Detected</td>
<td>1327</td>
<td>566</td>
</tr>
<tr>
<td>Evaluated</td>
<td>1121</td>
<td>353</td>
</tr>
<tr>
<td>DAA Treatment</td>
<td>889</td>
<td>588</td>
</tr>
<tr>
<td>Cured</td>
<td>684</td>
<td>430</td>
</tr>
</tbody>
</table>

* Estimated HCV RNA calculated based on 3.46% Seroprevalence of the 47,919 patients screened from 2015-2018. Adjusting for 75% RNA positive rates on HCV Antibody positive patients

* This % only reflects those patients who have completed treatment and have SVR12 cure data available. Intention to treat cure rates are 85 % and treatment per protocol cure rates are 95 %.
**CNHS: Three Year HCV Elimination Goals Results (11/2015-12/2018)**

<table>
<thead>
<tr>
<th>Category</th>
<th>ITT</th>
<th>SVR12/treatment initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened/accessing care at CNHS</td>
<td>47,919/80,928</td>
<td>59.2%</td>
</tr>
<tr>
<td>Linked to care/current HCV</td>
<td>768/1174</td>
<td>65.4%</td>
</tr>
<tr>
<td>Treatment Initiated/link to care</td>
<td>588/820</td>
<td>71.7%</td>
</tr>
<tr>
<td>ITT SVR12 /treatment initiated</td>
<td>430/488</td>
<td>88.1%</td>
</tr>
</tbody>
</table>

ITT: Intention to Treat, SVR12: Sustained Virologic Response at 12 Weeks

**Phylogenetic analysis of the CN HCV HVR1 sequences**

(HVR1 NGS-Major, 264 bp in length)

HCV genotype distribution
Among CN cases (n=162)

- Genotype 1a: 60.5%
- Genotype 3a: 18.5%
- Genotype 1b: 5%
- Genotype 2a: 17.3%
- Genotype 2b: 9%
- Genotype 3b: 2%
- Other: 1%
Each node is a case.
Nodes are linked if cases share HCV strain (linkage by transmission).

7 transmission clusters, n=14

Unlinked cases, n=148

Transmission Network among CN Cases (n=162) Identified using Global Hepatitis Outbreak and Surveillance Technology (GHOST)

Conclusions

- Elimination of HCV is possible by the year 2030
- Effective interventions are available
- Priority issues must be addressed to meet elimination goals
- Micro-Elimination programs are feasible and needed in the absence of National Macro-Elimination programs
  - Planning and commitment can accelerate the process
- The CNHS HCV Micro-elimination program is based on
  - Presence of multiple Stakeholders
  - Universal Screening
  - Robust primary care work force (projectECHO)
  - Harm reduction interventions
    - Treatment as prevention/Medication assisted therapy
Reflection

“Eradication and elimination are laudable goals, they are the ultimate goals of public health. These goals carry great responsibility and there is no room for failure. The question is whether these goals are to be achieved in the present or some future generation”

Walter R. Dowdle “The Principles of disease Elimination and Eradication”
MMWR December 31, 1999/48(SU01);23-7

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Deirdre McAuley
Lisa Ortiz
Jeffrey Gastorf
Melissa Gastorf
Adam Sprankell
Jonathan White
Destini Goins
Robin Stand
Hannah Hill
Katherine Bazin
Shane Dominick
Sharon Smallwood
Brooke Dill

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