How to Start an HCV Micro-elimination Program

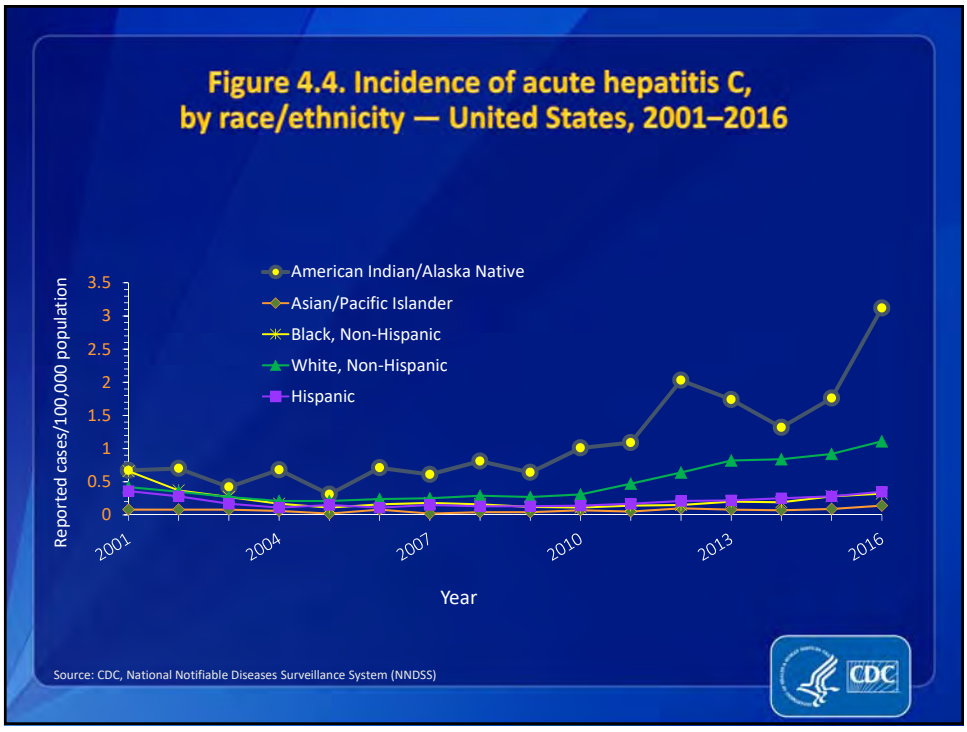
Jorge Mera, MD, FACP

Disclosure

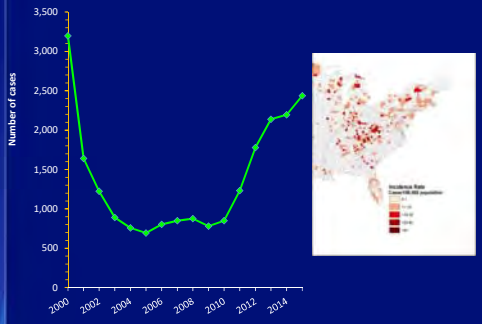
- The Cherokee Nation receives a grant from the Gilead Foundation for the HCV elimination program. Dr. Jorge Mera is the PI of the grant
- Dr. Jorge Mera has received speaker fees from Abbvie Pharmaceuticals

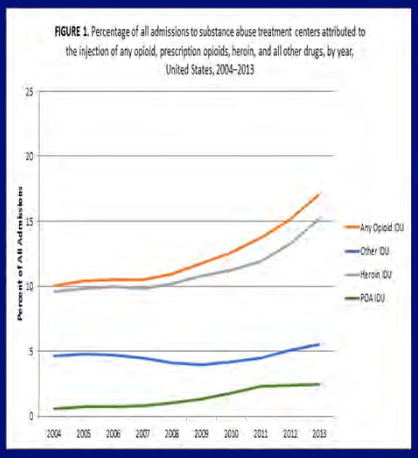
Outline

- 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

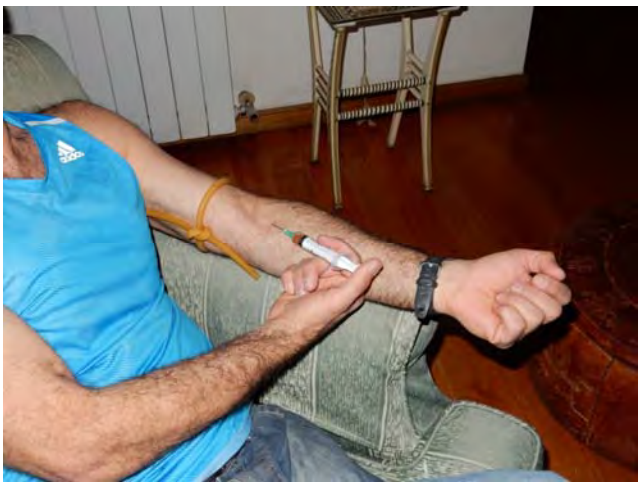




- ~31,000 new HCV infections in 2015
- 1:1 male: female ratio, predominantly white
- Highest incidence- 20-29 years, non-urban areas

Suryaprasad, CID 2014, Zibbell MMWR 2015, CDC unpublished data

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

Table 1 Number and rate of persons with an HCV diagnosis, 2005–2015, Indian Health Service

	No. (rate/100,000)	Rate ratio (95% CI)[a]	P-value
Sex			
Male	15,362 (193)	Reference	Reference
Female	14,441 (166)	0.86 (0.84–0.88)	< .0001
Age (years)			
< 15	150 (3.3)	0.01 (0.01–0.01)	< .0001
15–24	2085 (67)	0.13 (0.13–0.14)	< .0001
25–39	8302 (235)	0.47 (0.46–0.49)	< .0001
40–54	14,234 (496)	Reference	Reference
55+	5032 (199)	0.40 (0.39–0.41)	< .0001
Birth cohort			
Born before 1945	1118 (101)	0.21 (0.20–0.22)	< .0001
Born 1945–1965 (baby boomers)	15,900 (478)	Reference	Reference
Born after 1965	12,785 (105)	0.22 (0.21–0.22)	< .0001
Region[b]			
Alaska	2743 (179)	0.81 (0.77–0.84)	< .0001
East	1051 (197)	0.89 (0.84–0.95)	.0005
Northern Plains East	1875 (166)	0.75 (0.71–0.79)	< .0001
Northern Plains West	4801 (224)	1.01 (0.98–1.05)	.4462
Southern Plains	7986 (221)	Reference	Reference
Southwest	5538 (98)	0.44 (0.43–0.46)	< .0001
West	5809 (286)	1.29 (1.25–1.34)	< .0001
Total	29,803 (179)		

Numbers include only the first HCV visit for a person in fiscal years 2005–2015. Rates are defined as the number of persons with an HCV ICD-9-CM diagnosis per 100,000 person years

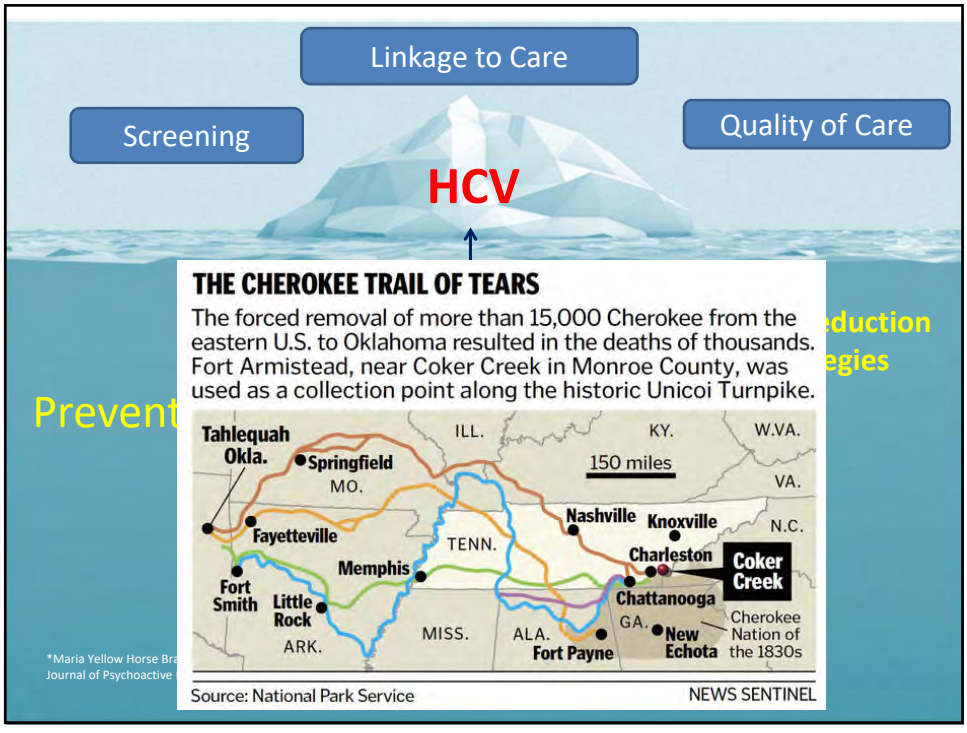
[a]CI Confidence Interval

[b]Regions comprised of multiple states include East (NC, MS, ME, CT, NY, LA, TX, RI, AL, MA, MD, IL, FL), Northern Plains East (MI, WI, MN) Northern Plains West (MT, WY, ND, SD, IA, NE), Southern Plains (KS, OK) Southwest (NM, AZ, CO, UT, NV), and West (CA, OR, ID, WA)

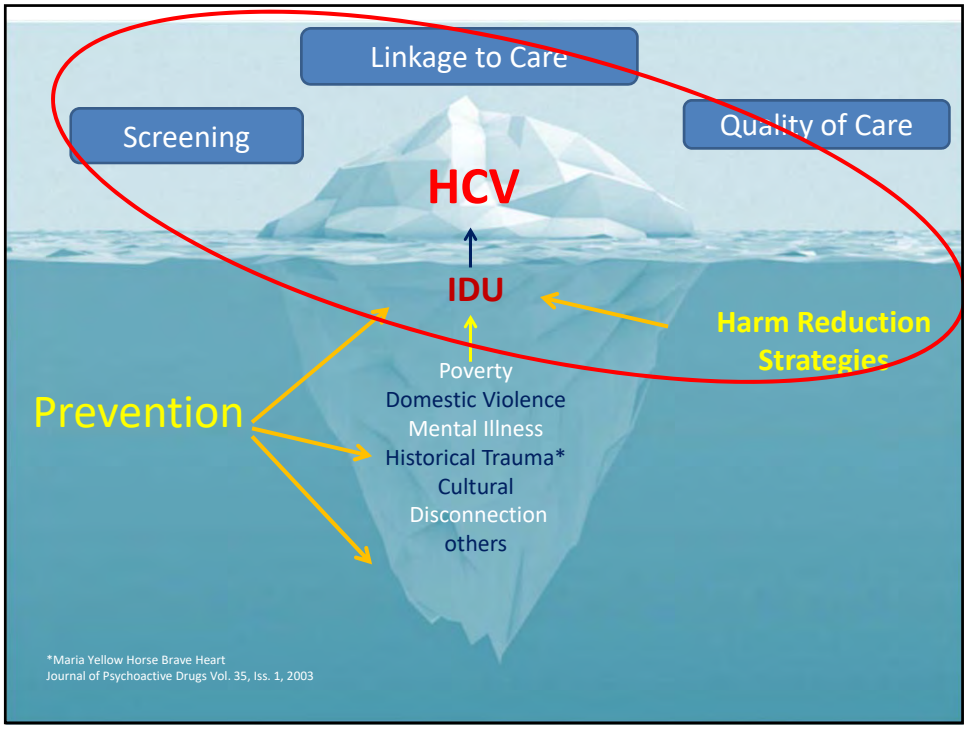
45% Younger Than Baby Boomers

Radley A et al. Assessing Disparities in the rates of HCV Diagnoses Within American Indian or Alaska Native Populations Served by the U.S. Indian Health Service, 2005-2015. 2018 Journal of Community Health. https://doi.org/10.1007/s10900-018-0528-7

www.hcvguidelines.org | Last Updated: May 24, 2018



*Maria Yellow Horse Bra
Journal of Psychoactive



Feasibility Criteria for Elimination

In General[1]	Hepatitis C Virus	Check list
No non- human reservoir and the organism can not multiply in the environment	**No non human reservoir**	✓
There are simple and accurate diagnostic tools	**Serology widely available**	✓
Practical interventions to interrupt transmission	**Treatment as prevention** **Needle and syringe programs** **Medication assisted programs**	✓
The infection can in most cases be cleared from the host	**Treatment is 95% curative**	✓

Adapted from Hopkins D. **Disease Eradication.** N Engl J Med 2013;368:54-63

HCV Elimination: Definitions and Goals

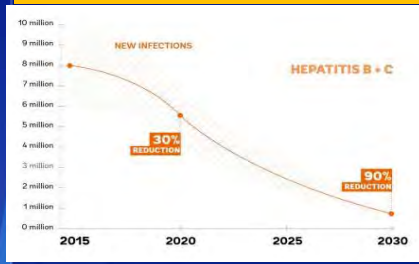
- **Definition**:
  - Elimination of hepatitis C as a ***public health problem***

- ***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

1. https://www.cdc.gov/hepatitis/hhs-actionplan.htm 2. National Academies of Sciences, Engineering, and Medicine. 2017. ***A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report.*** Washington, DC: The National Academies Press

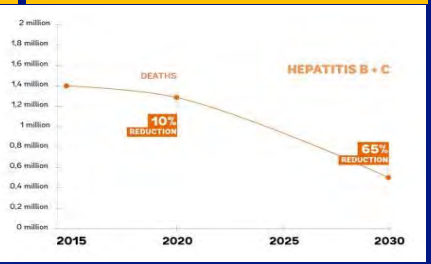
WHO Impact Targets for Elimination of Hepatitis B and Hepatitis C as Public Health Threats

90% reduction in new HBV and HCV infections



6-10 million infections (in 2015) to 900,000 infections (by 2030)

65% reduction in deaths from HBV and HCV



1.4 million deaths (in 2015) to under 500,000 deaths (by 2030)

Division of Viral Hepatitis

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

Edlin BR, Winkelstein ER. 2014. Antiviral Research. 110:79-93
Grebely J, Dore GJ. 2014. Antiviral Research. 104:62-72
*Shah H, Bilodeau M, et al. CMAJ June 04, 2018 190 (22) E677-E687

PWID: People Who Inject Drugs
MAT: Medication Assisted Treatment
MSM: Men who have Sex with Men

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

Lazarus JV, Safreed-Harmon K, Thursz MR et al. The Micro-Elimination Approach to Eliminating Hepatitis C: Strategic and Operational Considerations. Seminars in Liver Disease, 2018,38 (3);181-192.

Micro-Elimination: Populations to be Targeted

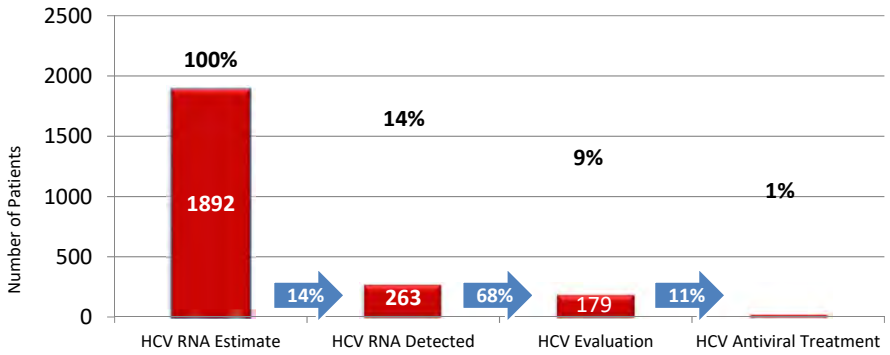
- Aboriginal and Indigenous communities
- Birth cohorts with high HCV prevalence
- Children of HCV Infected mothers
- Hemodialysis recipients
- HIV/HCV Co-infected individuals
- Migrants from high-prevalence Countries
- People Who Inject Drugs
- People with hemophilia and other inherited blood disorders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

Lazarus JV, Safreed-Harmon K, Thursz MR et al. The Micro-Elimination Approach to Eliminating Hepatitis C: Strategic and Operational Considerations. Seminars in Liver Disease, 2018,38 (3);181-192.

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?

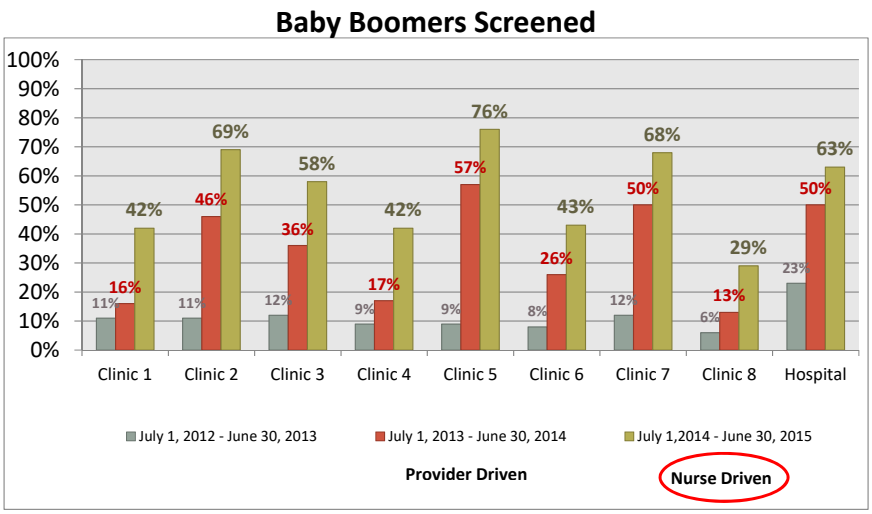
CNHS HCV Cascade of Care 2012



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



GPRA Measures

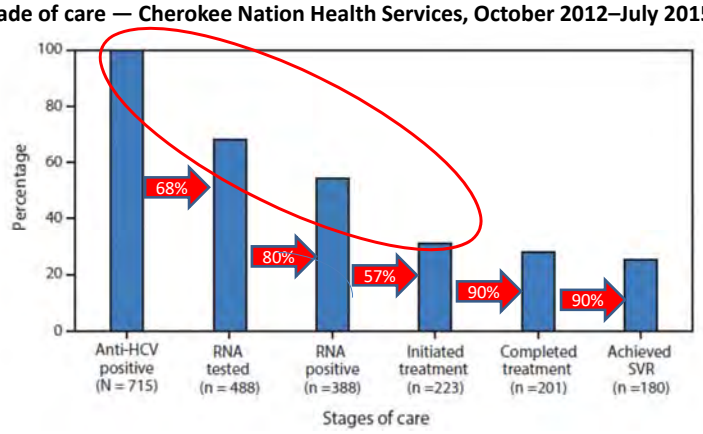
ECHO*: Moving Knowledge Instead of Patients

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



Mera J, Vellozzi C, Hariri S, et al. Identification and Clinical Management of Persons with Chronic Hepatitis C Virus Infection — Cherokee Nation, 2012–2015. MMWR Morb Mortal Wkly Rep 2016;65:461–466.
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**

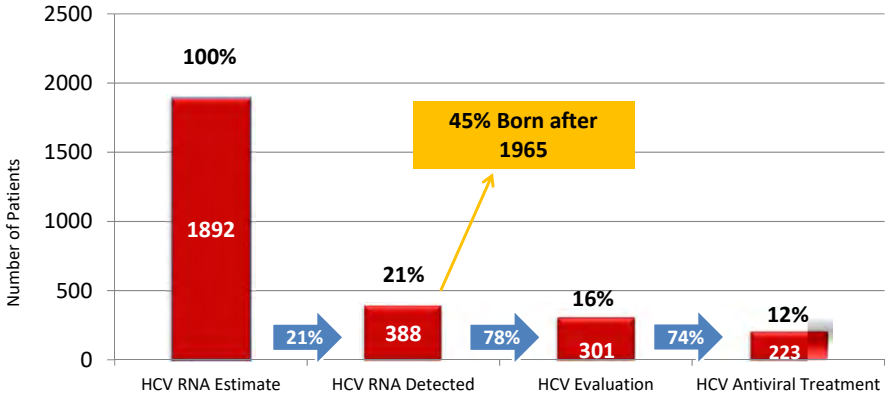
AI/AN: American Indian/Alaskan Native

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?
- 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 2015



Adapted from: Mera J, Vellozzi C, Hariri S, et al. Identification and Clinical Management of Persons with Chronic Hepatitis C Virus Infection — Cherokee Nation, 2012–2015. MMWR Morb Mortal Wkly Rep 2016;65:461–466.

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 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?
- 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?

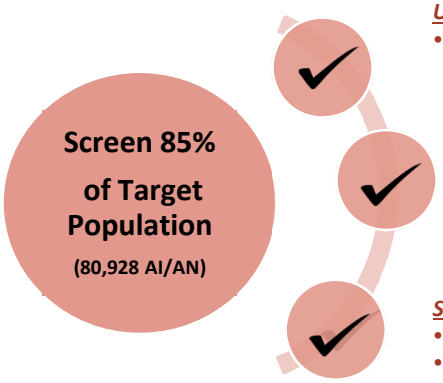
Goal #1: Secure Political Commitment

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



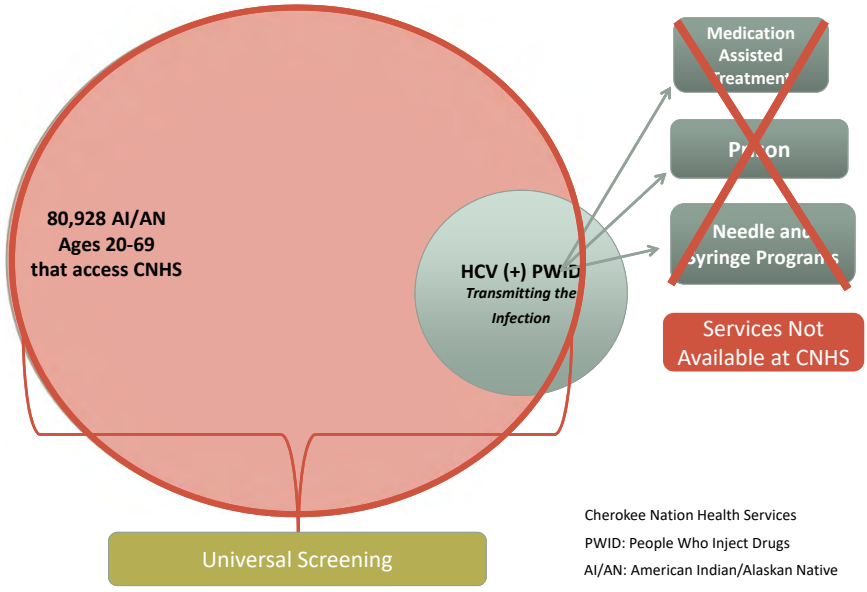
Universal Screening
- Ages 20-69

Non-Traditional Screening Sites
- Emergency Department
- Urgent Care
- Dental Clinics
- OBGYN

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

Cherokee Nation Health Services, 2018

Why Universal HCV Screening?

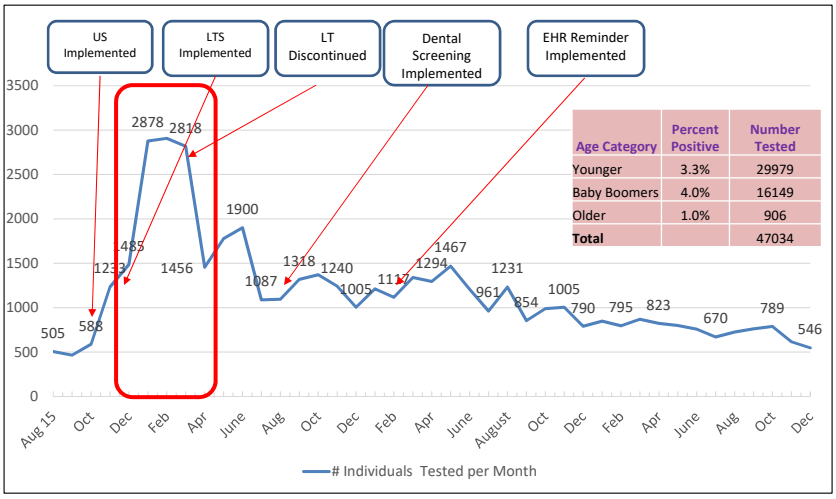


Cherokee Nation Health Services
PWID: People Who Inject Drugs
AI/AN: American Indian/Alaskan Native

Cost-effectiveness: HCV Testing Expansion

- *"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".*
  - Barocas JA et al. **Population-level Outcomes and Cost-Effectiveness of Expanding the Recommendation for Age-based Hepatitis C Testing in the United States** *Clinical Infectious Diseases*, Volume 67, Issue 4, 1 August 2018, Pages 549–556

HCV Antibody Tests and Screening Interventions November 2015 – December 2018

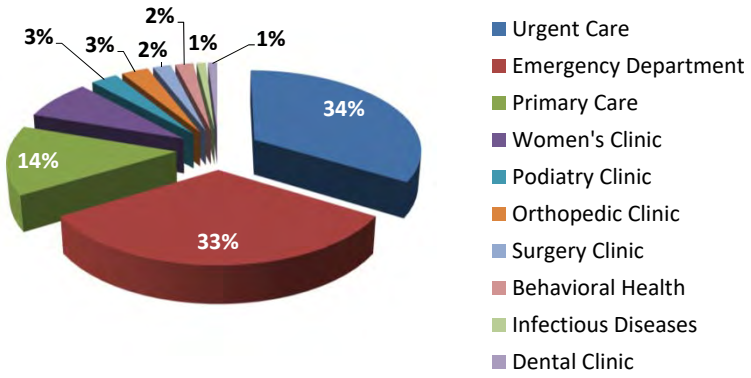


Age Category	Percent Positive	Number Tested
Younger	3.3%	29979
Baby Boomers	4.0%	16149
Older	1.0%	906
Total		47034

US: Universal Screening, LTS: Lab Triggered Screening, EHR: Electronic Health Record

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

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

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

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

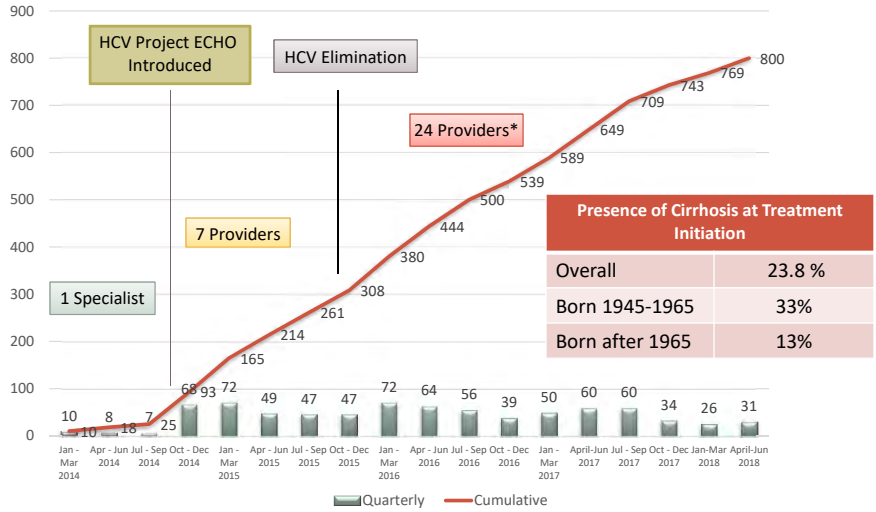
- Follow the patient during treatment to help ensure adherence and follow up to SVR
- Sometimes will include direct observed therapy (DOT)

Goals

Link to care 85% | Treat 85% | Cure 85%

Cherokee Nation Health Services, 2018

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



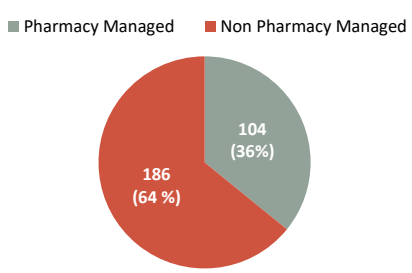
Presence of Cirrhosis at Treatment Initiation	
Overall	23.8 %
Born 1945-1965	33%
Born after 1965	13%

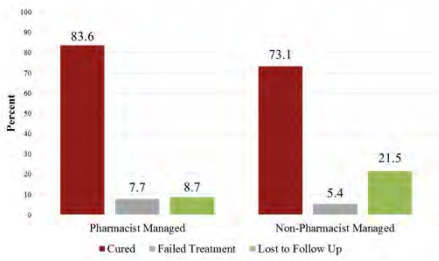
*Providers included 1 Specialist, 8 Physicians, 8 Pharmacists and 7 Nurse Practitioners

Cure rates did not differ by provider type

Cherokee Nation Health Services, 2018

HCV Treatment Outcomes of Pharmacist Managed Patients (5/2015-1/2017)





	Pharmacist-Managed	Non Pharmacist-Managed	p-value
Intention to Treat (Including patients lost to follow up)	83.6%	73.1%	p = 0.041
Per Protocol (Excluding patients lost to follow up)	91.6%	93.2%	p = 0.8

David C, David D, Essex W, Deming P , Qualls C, Mera J. Presented at AASLD, Washington DC, 2017

Goal #4: Reduce the incidence of new HCV infections

Public and Provider Awareness	Contact Tracing	Harm Reduction
• Public Campaign • Provider Training	• Acute HCV • PWID	• Treatment as Prevention • MAT • NSP (NOT Available in Oklahoma)

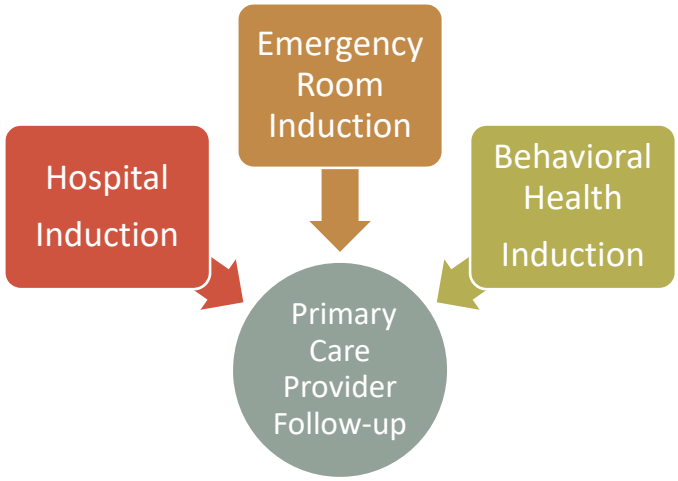
MAT: Medication assisted treatment
NSP: Needle and syringe program

Cherokee Nation Health Services, 2018

CNHS: Chronology of MAT Escalation

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

Medication Assisted Treatment with Buprenorphine/Naloxone

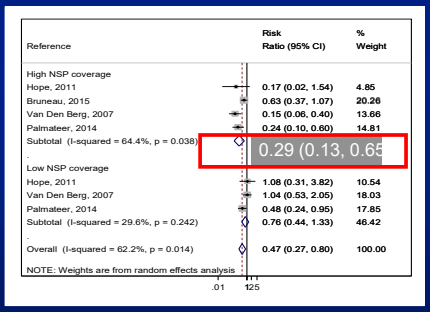


2014 Oklahoma Statutes
Title 63. Public Health and Safety

- 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.

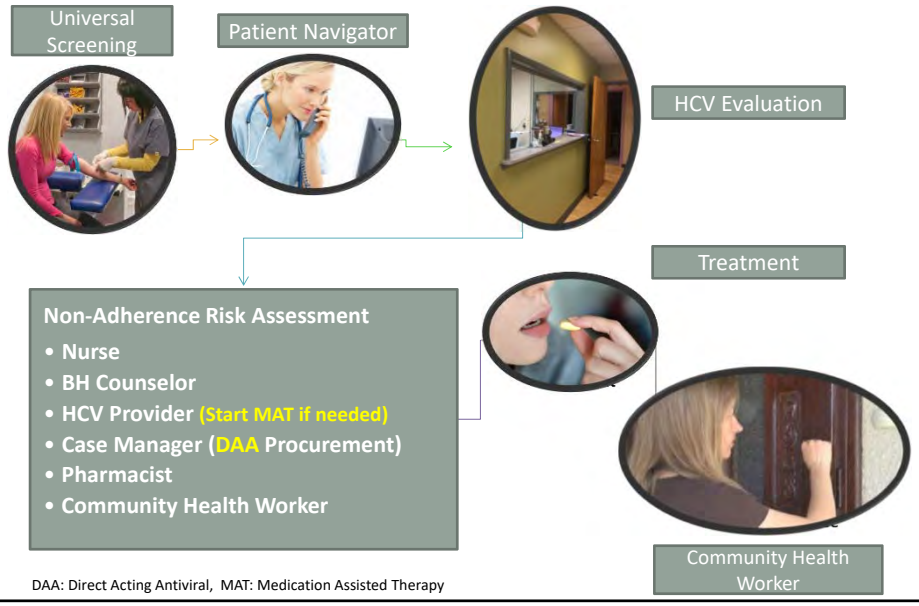
Syringe Service Programs (SSP) and Medication Assisted Treatment (MAT) Prevent HCV Transmission

- **SSP and MAT effective in reducing self-reported injecting risk behaviour**
  - Limited evidence for effect on HCV transmission[1,2]
- **New Cochrane systematic review[3]**
  - MAT alone decreases risk by 50%
  - SSP alone decreases risk by 56% (in Europe)
  - **MAT + SSP jointly decreases risk by 71%**



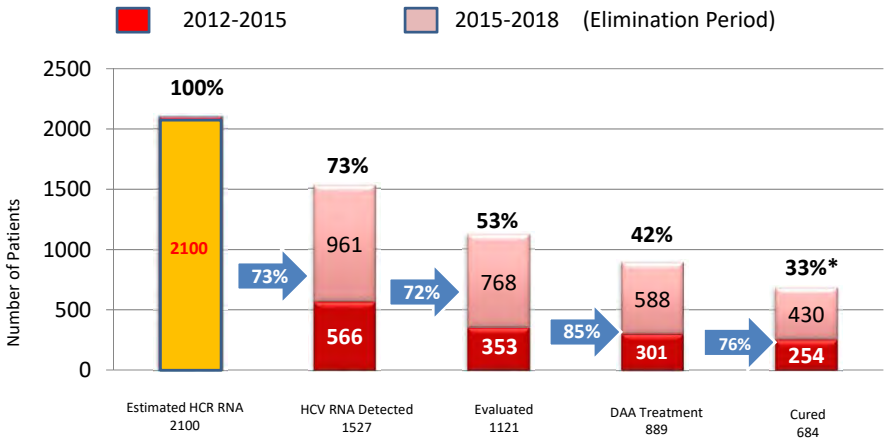
1 Palmateer , Addiction 2010, 2 Hagan, JID 2011, 3 Platt Cochrane Database Syst Rev. 2016;2016(1)

The CNHS Comprehensive HCV Care Model



DAA: Direct Acting Antiviral, MAT: Medication Assisted Therapy

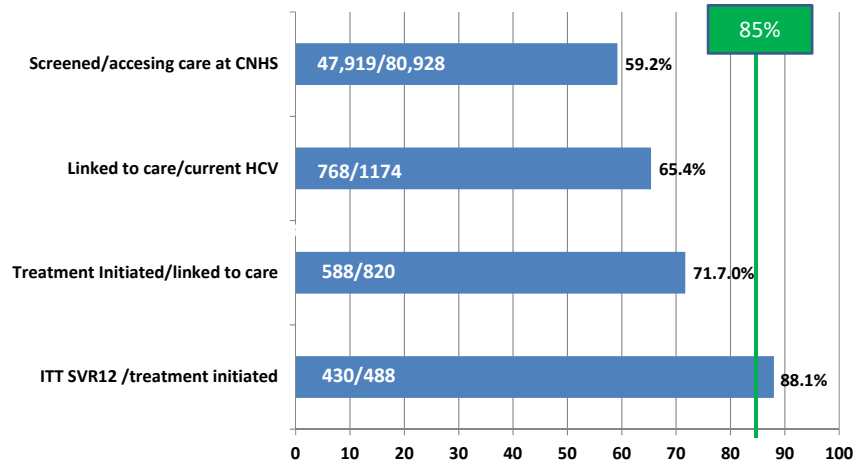
CNHS HCV Cascade of Care 11/2012 -12/2018



Estimated HCV RNA calculated based on 3.46% Seroprevalence of the 47,919 patients screened from 2015-2018. Adjstuing 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 %

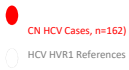
CNHS: Three Year HCV Elimination Goals Results (11/2015-12/2018)



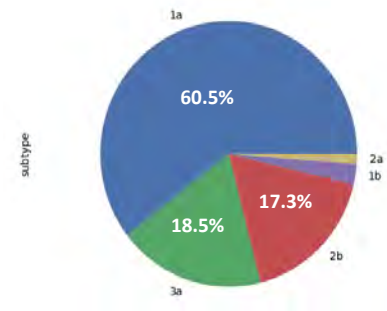
ITT: Intention to Treat, SVR12: Sustained Virologic Response at 12 Weeks

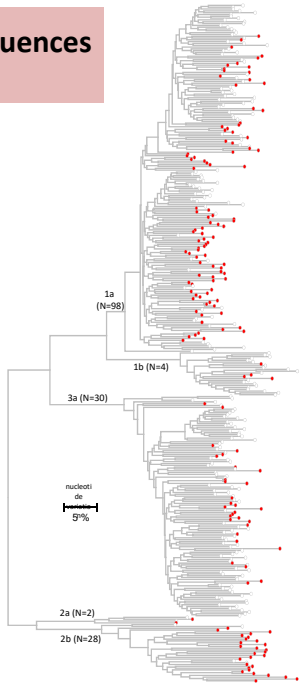
Phylogenetic analysis of the CN HCV HVR1 sequences

(HVR1 NGS-Major, 264 bp in length)

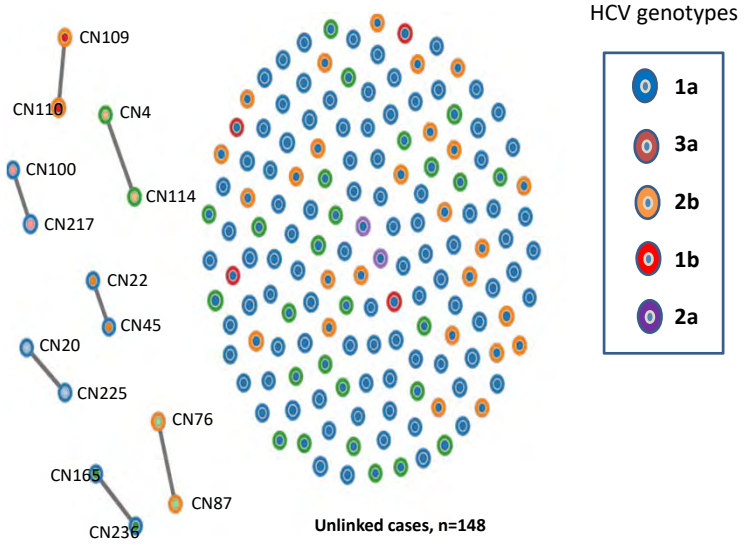


HCV genotype distribution Among CN cases (n=162)





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



7 transmission clusters, n=14

Each node is a case.
Nodes are linked if cases share HCV strain (linkage by transmission).

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

Acknowledgements

Stephanie Hammons
Charles Grim
Casi Jennings
Robin Fishinghawk
R. Stephen Jones
Tara Ritter
Doug Nolan
Carla Carter
Sharon Spinks
Tamme Garrison
Kendra Round
Amy Meigs
Jana Smith
James Baker
Dwayne David
Nicole Gibe
Kellye Parker
Kathryn Holloway
Barbara Beach
Brian Hail
Jennifer Tredway
Gaye Wheeler
Amy Cook
Kaleb Chamberlain
April Haddock
Latosha Zugelder
Brittany English
Shawn Sanders
Gina Luginbill
Michael Vowell
Travis Fleming
Tony Gustin
James Stallcup
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
Anna Miller
Sharon Smallwood
Natasha Barr
Kristen Walker
Kristen Adams
Jade Jordan
Centers for Disease Control and Prevention
Oklahoma State Department of Health
University of Oklahoma Health Sciences Center
Gilead Foundation