

# Treating Hepatitis C in the Indian Health Service

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# Disclosures

# Thanks

- Lisa Neel
- Brigg Reilley
- Amy Nguyen
- Karla Thornton
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- Jorge Mera
- Jessica Leston
- Matt Baker
- IHS Hepatitis C Providers

# Case Presentation

- A 52 year-old male American Indian store owner comes in to establish primary care with his new IHS physician. He does not drink alcohol but injected drugs once when he was in high school in 1978. He is found to have systolic hypertension, an LDL of 192 and an ALT of 48 after evaluation. Review of the EHR reminders shows that he is due for an influenza vaccine, and HIV serology and a Hepatitis C baby boomer screening test with reflex viral load. He is found to be HIV negative but HCV Antibody positive with a viral load of 150,000 iu/ml.

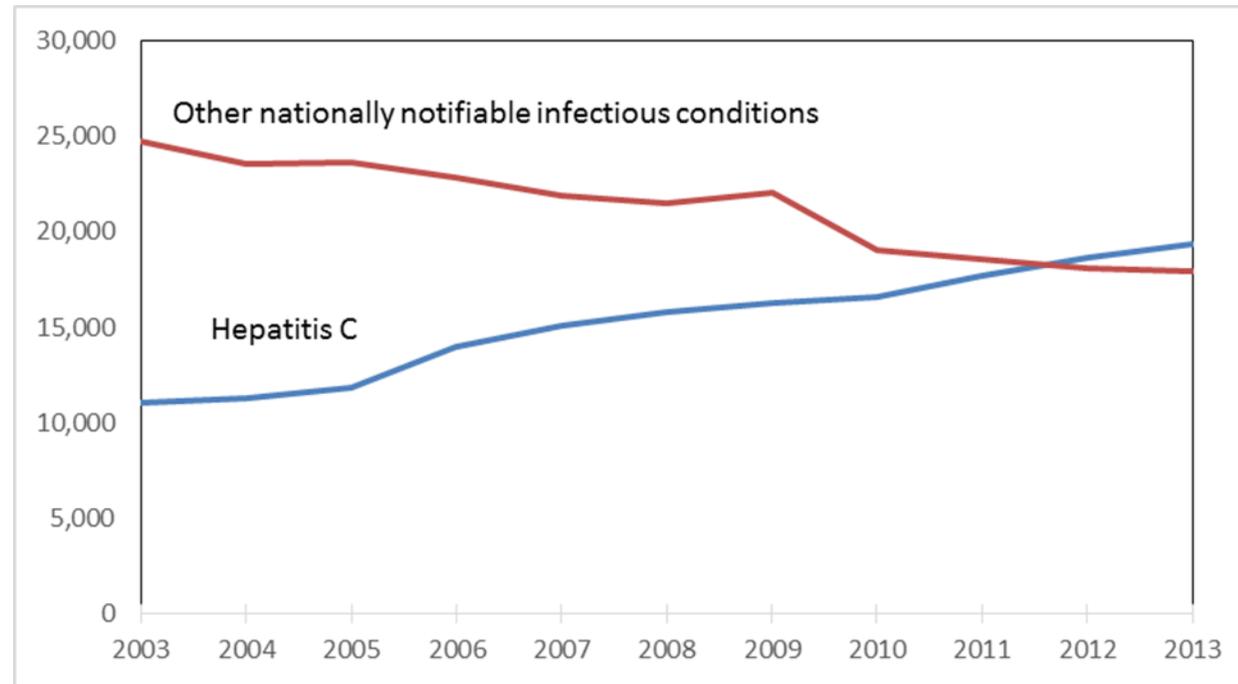
The Big Question...

**Why should we care?**

# The big unknown...

- 2.7-3.9 million Americans have HCV
- 45-85% don't know they have it
- Future cost to society is huge

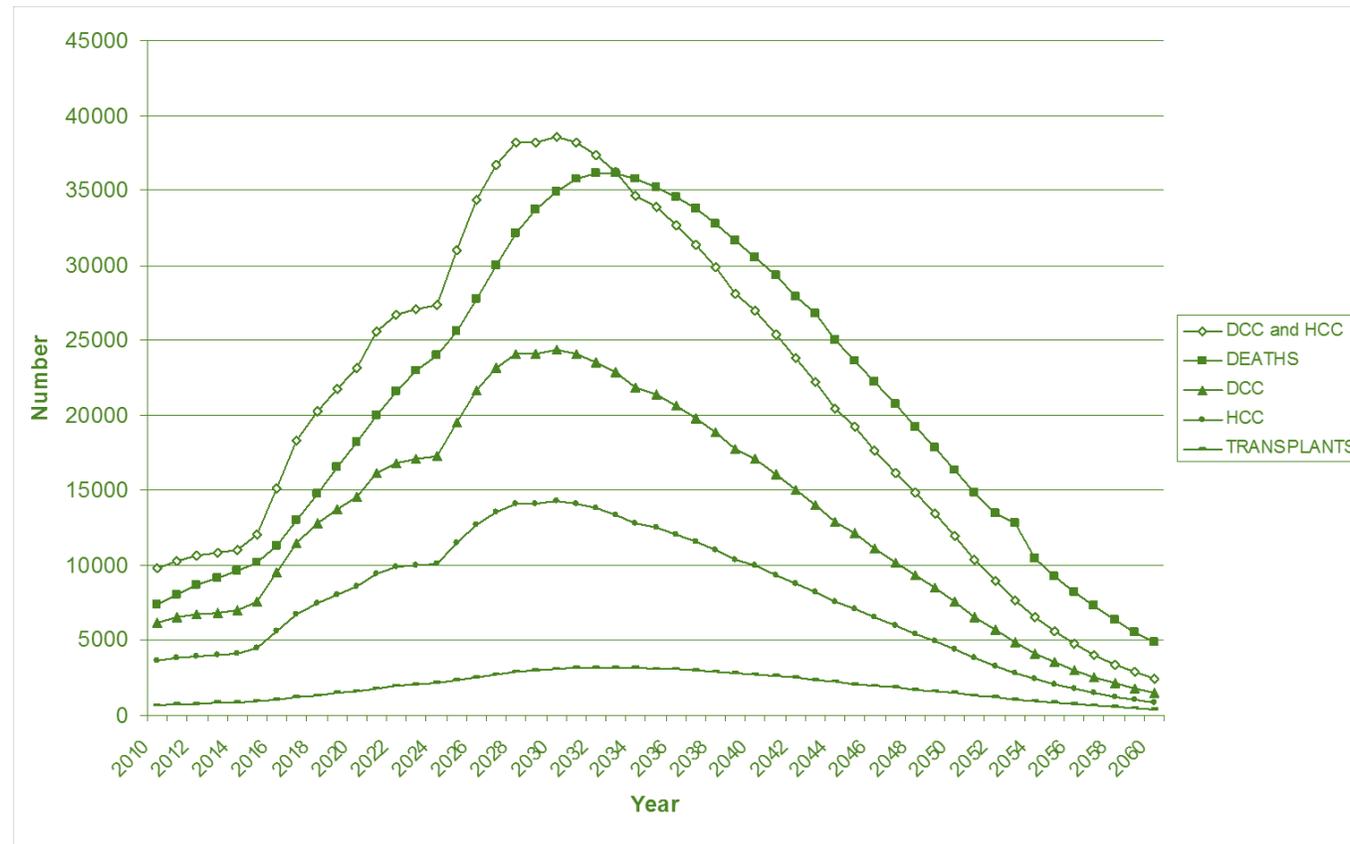
# HCV Deaths and Deaths from Other Nationally Notifiable Infectious Diseases,\* 2003- 2013



\* TB, HIV, Hepatitis B and 57 other infectious conditions reported to CDC

Holmberg S, et al. "Continued Rising Mortality from Hepatitis C Virus in the United States, 2003-2013"  
Presented at ID Week 2015, October 10, 2015, San Diego, CA

# Forecasted Annual Incident Cases of Decompensated Cirrhosis (DCC), Hepatocellular Carcinoma (HCC), Liver Transplants, and Deaths Associated with Persons with Chronic Hepatitis C Infection and No Liver Cirrhosis in the United States in 2005



Rein, DB, Wittenborn, JS, Weinbaum, CM Sabin, M, Smith, BD, Lesesne, SB. Forecasting the Mortality and Morbidity Associated with Prevalent Cases of Pre-Cirrhotic Chronic Hepatitis C Infections in the United States. *Journal of Digestive Liver Diseases* 2010.

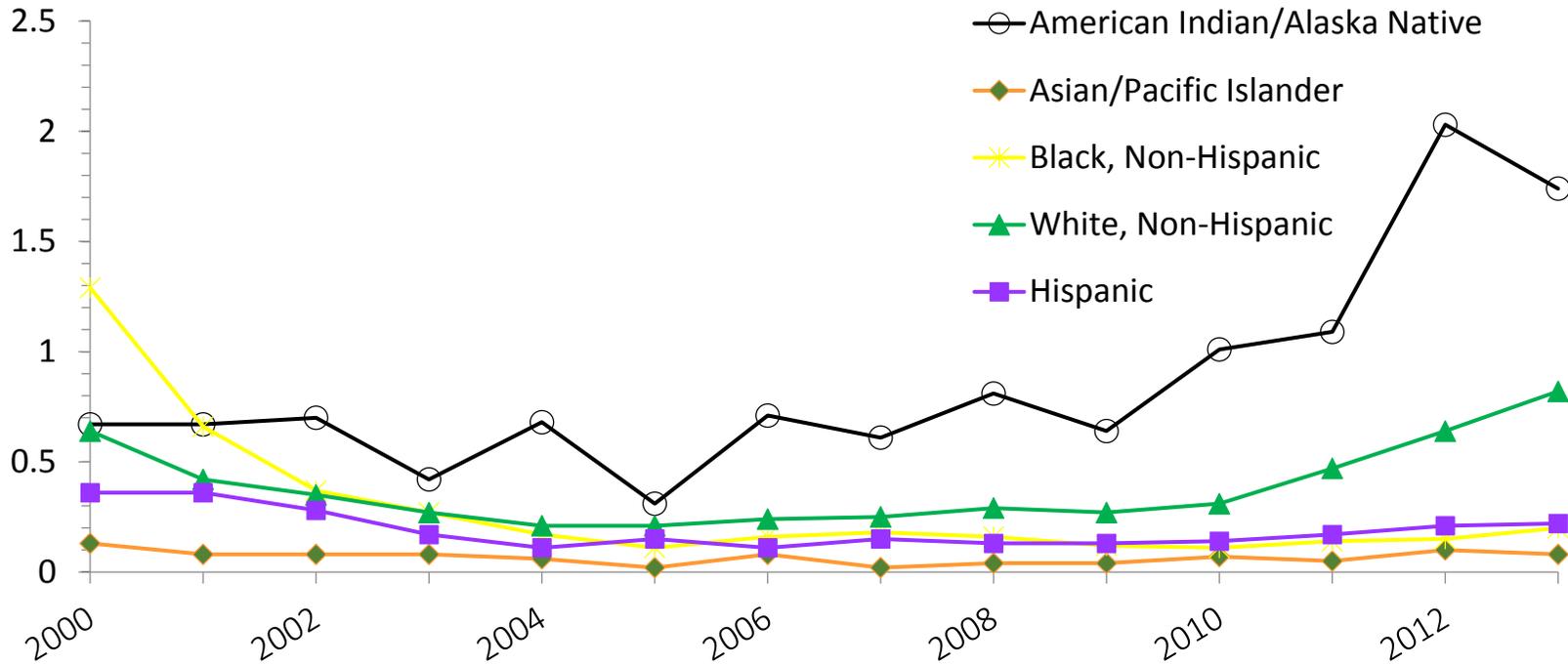
# Diabetes and Hepatitis C

- Risk increased by 70% compared to non-infected controls (OR 1.7)
- Successful HCV treatment associated with decrease in insulin resistance and reduction in incidence of diabetes mellitus

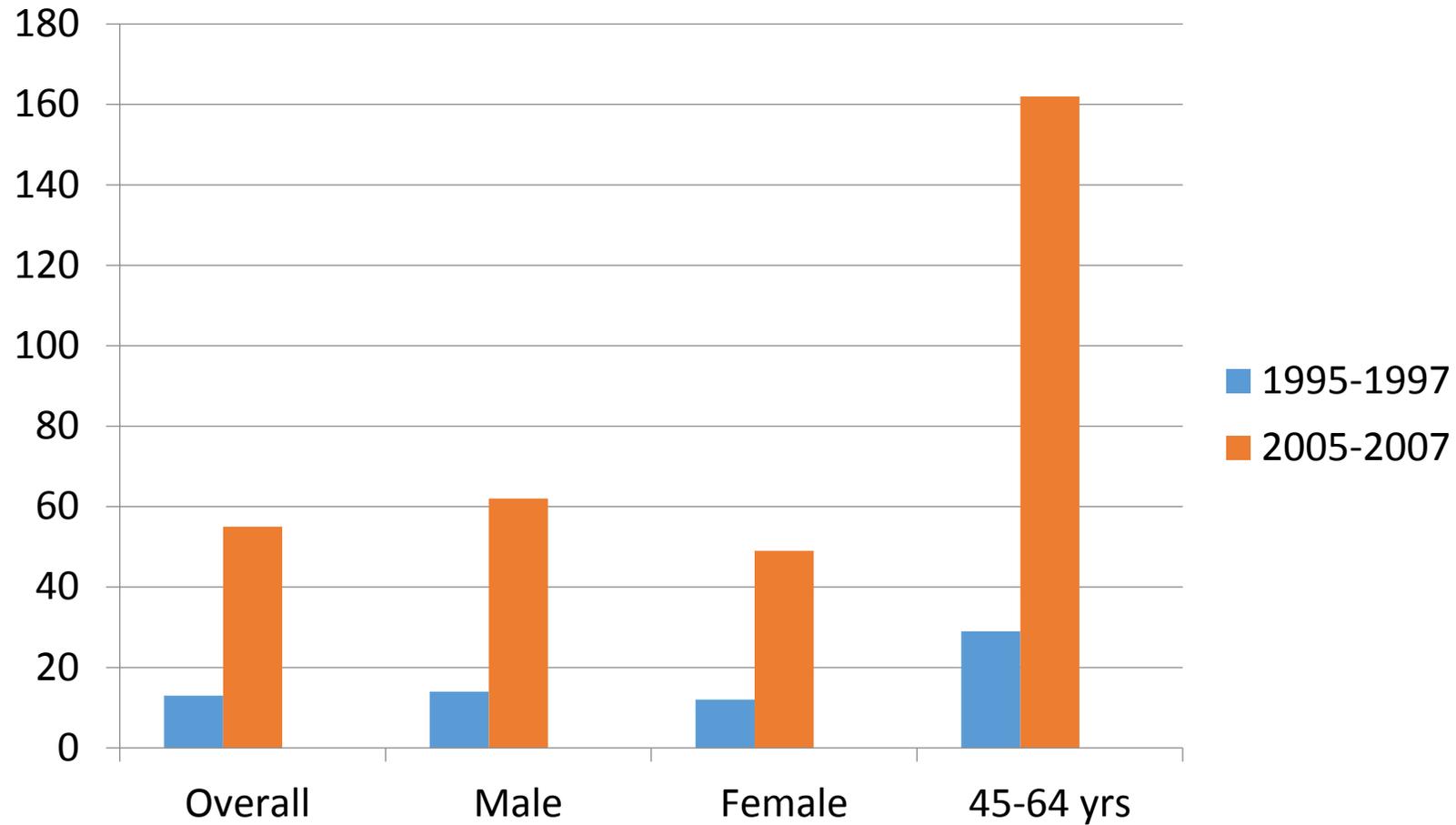
White DL, et al. Hepatitis C infection and risk of diabetes: a systematic review and meta-analysis. *Hepatology*. 2008;49(5):831.

How about the Indian Health Service?

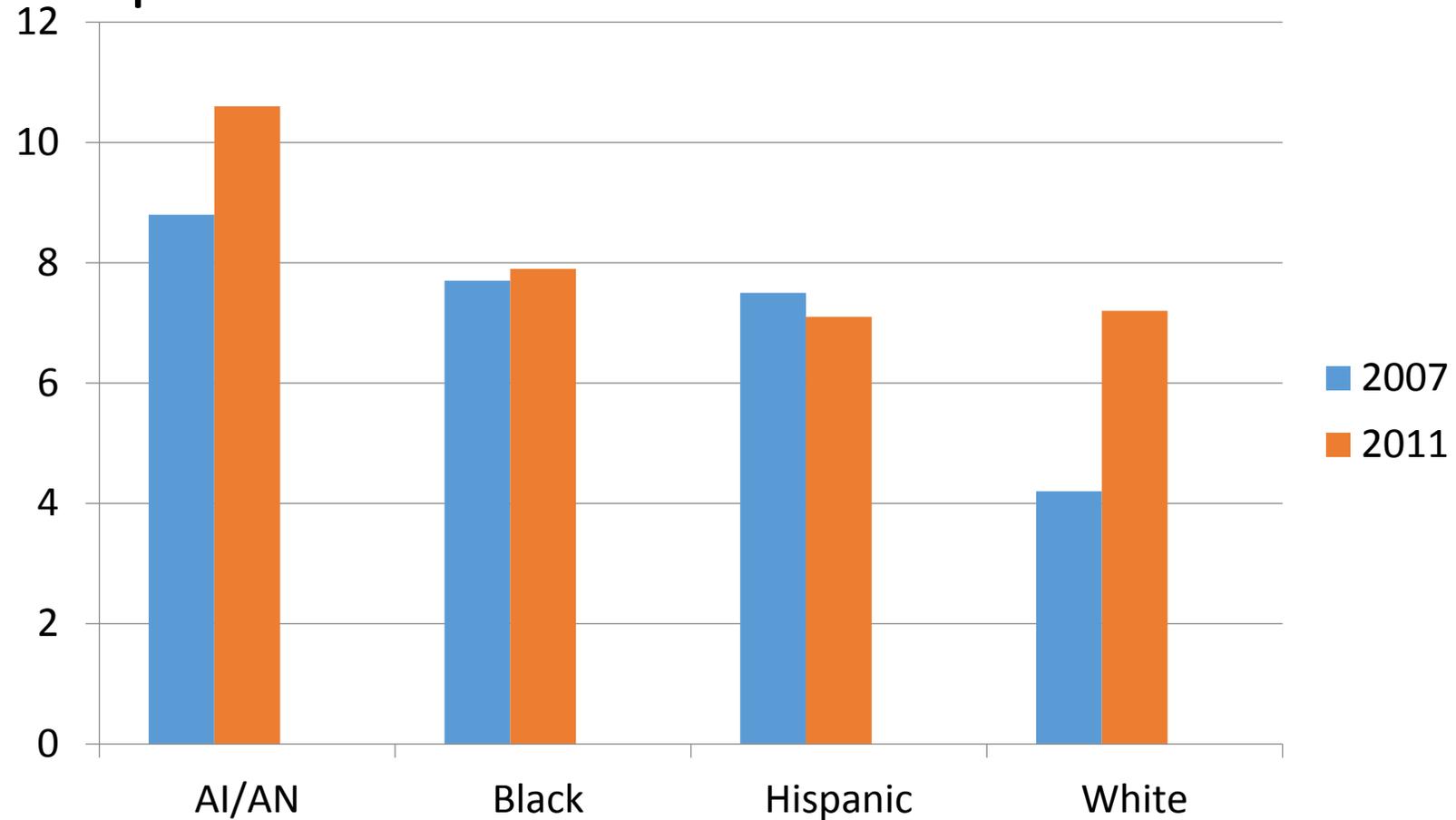
# Incidence of Acute Hepatitis C, by Race/Ethnicity — United States, 2000–2013



## A 300% Increase in Hepatitis C –related Hospitalization for AI/AN – 1995-2007



## HCV –Related Mortality by Race/Ethnicity- 2007 compared to 2011



# HCV in IHS

- “Barbell” shaped epidemiology curve
- 1945-1965 Birth Cohort patients, from exposure >20 years ago
- Younger patients, often from exposure to injecting drug use
- Initial data shows an estimated 50%-50% split of HCV burden in these two groups

# HCV Screening 1945-1965 birth cohort (federal SUs)

- 42% screened as of December 2015 (45,486/108,453)
- Wide variability in individual facilities (range 2%-82%)
- Tracked as Developmental GPRA measure
- EHR reminder available

# HCV estimates for IHS

- Among 1945-1965 birth cohort, HCV Ab+ seroprevalence range of 2%-12% depending on region
- Of birth cohort, most are historical infections and about 25% have advanced liver disease due to HCV and need priority treatment
- Estimate about 7000 chronic HCV+ IHS patients nationwide have stage 3 or 4
- Treatment estimates currently <250 patients/year

At this rate it will take 28 years to catch up!

# What can be done in the IHS?

- Enhance Screening
- Enrolling positive patients in care
- Treating all patients with Hepatitis C at every IHS Area

# IHS Screening Rates

**TABLE 2. Hepatitis C virus antibody testing (cumulative) among persons born during 1945–1965, by Indian Health Service federally operated facilities and region,\* 2015**

<b>Region</b>	<b>No. of facilities</b>	<b>Total eligible population</b>	<b>No. tested (% coverage)</b>	<b>Coverage range among facilities</b>
Northern plains	21	31,206	9,927 (31.8)	18.4%–66.6%
Southern plains	12	9,579	3,009 (31.4)	6.5%–70.5%
Southwest	21	64,120	26,424 (41.2)	1.9%–69.4%
East	3	602	188 (31.2)	15.6%–44.7%
Pacific coast	6	6,812	2,444 (35.9)	21.3%–75.1%
<b>Total</b>	<b>62</b>	<b>112,319</b>	<b>41,992 (37.4)</b>	<b>1.9%–75.1%</b>

\* *Northern plains*: Iowa, Minnesota, Montana, Nebraska, South Dakota; *Southern plains*: Oklahoma, Texas; *Southwest*: Arizona, Colorado, New Mexico, Nevada, Utah; *East*: Maine, Massachusetts, North Carolina; *Pacific coast*: Idaho, Oregon, Washington.

# Hepatitis C testing

- Test of Choice in 2016:
  - Screening EIA with reflex Reverse Transcriptase PCR
    - Qualitative PCR- yes no answer
    - Quantitative PCR- how much virus is present preferred

# Hepatitis C screening recommendations

- Continue **Risk based** screening
  - h/o Injection and Inhaled Drug Use
  - HIV infected
  - Alcoholics
  - Unexplained hepatitis
- CDC recommendations: **Screen all Baby Boomers** born between 1945 and 1965 (inclusive)
  - Utilize EHR Reminders as a proven practice to enhance screening

# Hepatitis C Evaluation

- Obtain the following
  - Hepatitis C viral load
  - Hepatitis C genotype
  - HIV serology
  - Hepatitis B, Hepatitis A antibodies
- Vaccinate for Hep A and Hep B if not immune

# Cirrhosis assessment

- Blood Tests

- Commercial assays (Fibrosure) → expensive

- Liver biopsy → Risky, invasive, expensive

- **APRI score:**  $\text{AST/ULN AST/Platelet count} \times 100$

- $>0.7$  → Hepatic fibrosis (Sens 77%, Spec 72%)

- $> 1.0$  → Cirrhosis (Sens 76%, Spec 72%)

# Cirrhosis surveillance

- Upper endoscopy to evaluate for varices
- Ultrasound and Alpha Fetoprotein every 6-12 months

# Who to treat

Ultimate goal:

Treat every patient infected with HCV

# Who to treat

- Factors to consider when deciding about therapy:
  - **Advanced Fibrosis** (Metavir 3 score on biopsy or commercial assayt)
  - Compensated **Cirrhosis** (Metavir 4)
  - **Liver Transplant** patient with HCV
  - Coinfection with HIV or HBV
  - **Extrahepatic Disease**
    - Cryoglobulinemia with vasculitis
    - Proteinuria,Nephrotic Syndrome, MPGN

# Who to treat

- High risk to transmit HCV
  - HIV positive Men who have Sex with Men
  - Injection drug users
  - Incarcerated
  - Dialysis

# Who not to treat

- People with short life expectancy (<12 months) that cannot be remediated by treating HCV or doing a liver transplant

# Hepatitis C Evaluation

- Mental Health Evaluation
- Treat substance abuse (prefer sobriety **BUT NOT MANDATORY**)
- Ensure Birth control
- Screen for TB and Diabetes
- Assess income and insurance status
  - Drug assistance programs
  - Health Insurance

# HCV Direct Acting Agents

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- NS3-4A **P**rotease inhibitors “**previr**”
  - Simeprevir, Paritaprevir, Grasoprevir
- NS5**B** Polymerase inhibitor “**buvir**”
  - Nucleoside – Sofosbuvir
  - Non-nucleoside – Dasabuvir
- NS5**A** replication complex inhibitor “**asvir**”
  - Ledipasvir, Ombitasvir, Daclatasvir, Elbasvir



# Hepatitis C Treatment

- Genotype 1a:

- Elbasvir/grazoprevir 1 po daily (Zepatier<sub>TM</sub>)
- Ledipasvir /Sofosvubir 1 po daily (Harvoni<sub>TM</sub>)
- Paritaprevir /Ritonavir /Ombitasvir/ Dasabuvir Ribavirin (Viekira Pak<sub>TM</sub>)
- Sofosbuvir/Simepravir +/- Ribavirin daily

- Duration

- Usually 12 weeks
- See guidelines for patients with cirrhosis or baseline drug resistance

# Hepatitis C Treatment

- Genotype 1b:
  - Elbasvir/grazoprevir 1 po daily for 12 weeks
  - Ledipasvir/Sofosbuvir 1 po daily (Harvoni<sub>TM</sub>) for 12 weeks
  - Paritaprevir /Ritonavir /Ombitasvir/ Dasabuvir (Viekira Pak<sub>TM</sub>) for 12 weeks (add ribavirin if cirrhotic)
  - Sofosbuvir 400 mg plus Simepravir 150 mg for 12 weeks (treat 24 weeks if cirrhotic)

# Hepatitis C Treatment

- Genotype 2
  - Daclatasvir/Sofosbuvir daily for 12 weeks if not cirrhotic
  - Ribavirin daily plus Sofosbuvir daily
  - Duration
    - for 12 weeks if not cirrhotic, 16-24 weeks if cirrhotic

# Hepatitis C Treatment

- Genotype 3
  - Daclatasvir/Sofosbuvir daily for 12 weeks if not cirrhotic (24 if cirrhotic)
  - Ribavirin daily plus Sofosbuvir plus PEG-Interferon daily for 12 weeks

# Monitoring Therapy

- Monitor CMP, CBC after 1 month of therapy
- Monitor HCV viral load
  - 4 weeks after starting therapy
  - At the end of therapy
  - 12 weeks after completing therapy (SVR)

# Cure Rates (Sustained Virologic Response)

- Genotype 1
  - Harvoni<sub>TM</sub> 97-99%
  - Viekira Pak<sub>TM</sub> 95.3%
- Genotype 2 94%
- Genotype 3 84%

# How do we afford treatment for our patients?

- HCV disproportionately affects AI/AN
- Early treatment is proven to reduce long-term morbidity and mortality.
- New treatments involving once-daily therapy for 12 weeks are better tolerated and have improved adherence.
- Drug costs remain a major barrier to patient access to treatment.

Opinion

## VIEWPOINT

### The Need to Expand Access to Hepatitis C Virus Drugs in the Indian Health Service

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The American Indian/Native Alaska population is disproportionately affected by hepatitis C virus (HCV). The most recent national data show American Indian/Alaska Native people with both the highest rate of acute HCV infection and the highest HCV-related mortality rate of any US racial/ethnic group.<sup>1</sup> In 2013, the latest national data available, rates of acute HCV infection were 1.7 per 100 000 American Indian/Alaska Native persons.<sup>1</sup> From 2009 through 2013, their HCV-related mortality rate increased by 23.2%, accounting for 324 deaths in 2013.<sup>1</sup> The American Indian/Alaska Native mortality rate of 12.2 deaths per 100 000 population is more than double the national rate of 5.0 per 100 000.<sup>1</sup> Although prevalence data are limited, one national study estimates 120 000 persons living on Indian reservations are positive for the HCV antibody.<sup>2</sup> Another study has shown American Indian/Alaska Native veterans born from 1945 to 1965 have an antibody-positive seroprevalence of 10%.<sup>3</sup>

The Indian Health Service (IHS) is a government agency entrusted to be the primary source for the provision of health care for the American Indian/Alaska Native population. The provision of health services to

Indians/Alaska Natives. Direct-acting antiviral regimens have high rates of achieving sustained virologic response with few contraindications or adverse effects. These advances represent a major shift in treatment options for HCV and may likely reduce HCV-related deaths. Among persons with compensated HCV-related cirrhosis, measured by sustained virologic response, successful treatment can lead to a survival curve similar to that of the general population.<sup>5</sup>

Yet these new HCV drug therapies must be accessible to have meaningful health benefits for patients. Many state Medicaid programs and insurance companies have imposed restrictions to contain costs. Some of these policies mandate significant liver damage as a requirement for eligibility, such as having stage 3 (precirrhosis) or stage 4 (cirrhosis) of the liver on the METAVIR scoring system. These criteria present a quandary: earlier treatment can prevent advanced liver disease, but late-stage liver disease is needed to qualify for treatment. For a clinician, explaining this circular logic to a patient can be frustrating for both parties.

Although direct-acting antiviral drugs have been cited as being cost-effective, cost-effectiveness does not necessarily mean affordable. The public sector in general and IHS specifically have budget constraints that shape treatment decisions; per capita user health expenditures range from \$3099 per year in the IHS compared with \$8097 per year for the US general population.<sup>4</sup> Only a limited number of American Indian/Alaska

#### Access to treatment for IHS patients should be a federal priority to fulfill its obligations to tribal nations and American Indian/Alaska Native people.

members of federally recognized tribes developed from government-to-government relationships between the federal government and Indian tribes. This relationship, established in 1787, is based on Article I, Section 8, of the Constitution and has been given form and substance by numerous treaties, laws, Supreme Court decisions, and executive orders. The IHS is under the US Department of Health and Human Services and comprises a network of health care facilities that collectively serves nearly 2.2 million people

Native patients belong to tribes that have notable incomes stemming from natural resource or gaming royalties. With 1 in 4 American Indian/Alaska Native people living below the poverty line and with an average household income of just higher than \$30 000, paying even a small proportion of the out-of-pocket cost for this potentially life-saving medical treatment is not an option for most patients.

Another federal agency that provides direct patient care, the Department of Veterans Affairs (VA), has added HCV drugs to its formulary and created

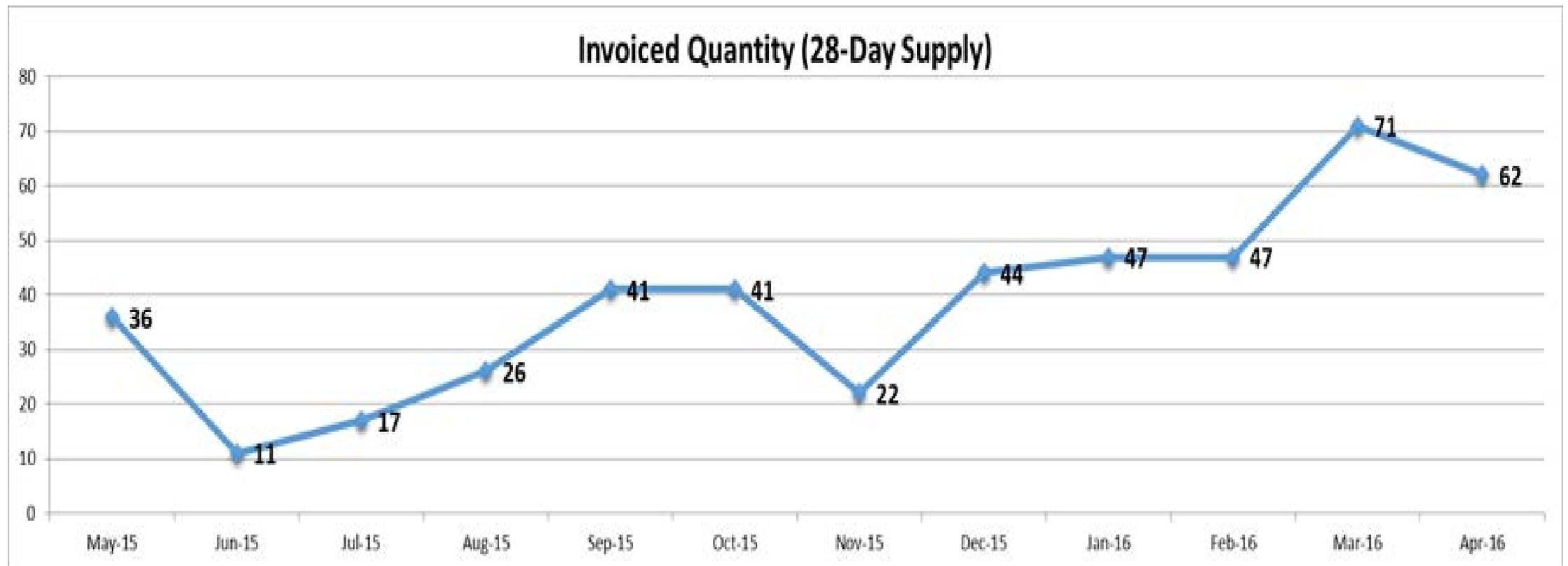
# Paying for Treatment

- Formulary or non-formulary approaches are utilized in some sectors of IHS.
- CMS and some third party insurers will pay for antiviral therapy for HCV infection.
  - Why?
    - Liver transplant cost ~\$300,000 + \$25,000/yr for antirejection drugs
    - Cirrhosis cost ~\$25,000 per admission
  - Various eligibility criteria can still limit access
- Patient Assistance Programs
  - Drug company sponsored programs that provide free medication
    - Most meet low-income eligibility
    - Non-formulary status has been critical

# IHS Treatment Costs

<b>Drug</b>	<b>IHS Price</b>	<b>VA (CMOP)*</b>
<b>Ledipasvir/sofosbuvir (Harvoni®)- 28 tablets</b>	\$12,604.16	\$5,267.00
<b>Ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak®)- 28 dose cards</b>	\$12,274.70	\$5,216.76
<b>Elbasvir/grazoprevir (Zepatier®)- 28 tablets</b>	\$12,214.55	\$5,216.76
<b>Ombitasvir/paritaprevir/ritonavir (Technivie®)- 28 Day Pack</b>	\$12,274.70	\$5,216.76
<b>Daclatasvir 30mg (Daklinza®)- 28 tablets</b>	\$14,144.82	\$12,372.91
<b>Daclatasvir 60mg (Daklinza®)- 28 tablets</b>	\$14,264.42	\$12,372.91
<b>Simeprevir (Olysio®)- 28 capsules</b>	\$14,714.26	\$14,714.26
<b>Sofosbuvir (Sovaldi®)- 28 tablets</b>	\$15,223.92	\$15,223.92

# IHS Anti-HCV Drug trends



# Paying for Treatment

- Klamath Tribal Health & Family Services
  - “We make it our goal to attempt to provide successful treatment to every patient who is in need. This is emphasized to our providers and to patients.”
    1. Appointment with PCP to evaluation/treatment.
    2. Maintain an HCV panel
    3. Refer “reasonable candidates” to local gastroenterology group
    4. If therapy recommended, provide support in obtaining medication
      - a. Oregon Health Plan (Medicaid) or Medicare
      - b. Private Insurance
      - c. Patient Assistance Programs
      - d. Local non-formulary process



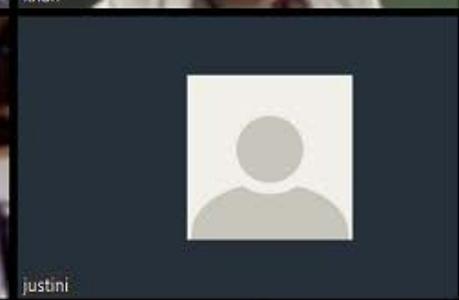
# Paying for Treatment

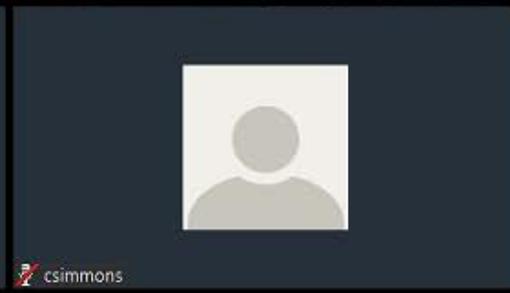
- Klamath Tribal Health & Family Services
  - Rationale for Treatment
    - HCV treatment is a one-time per patient expense (for most patients)
    - Proactively work to accommodate HCV treatment costs into pharmacy budget
      - Effectively bill insurance programs for drugs
      - Work to sign up all eligible patients for third-party resources (CMS, private insurance)
      - Manage the clinic formulary well (“Listen to the IHS NPTC. They seem to know what they are doing.”)
      - Utilize internal drug use policies to improve use and reduce costs.
      - Hire a pharmacy billing technician. Improved collections should more than pay for the position.
      - Utilize VA prime vendor, not HRSA 340b
    - Recognize that cumulative drug costs for other chronic diseases approach or exceed the costs for HCV treatment course (rheumatoid arthritis, diabetes, psychiatric conditions, etc.)
  - “Long story short, don’t nit pick any one drug cost. Effective overall pharmacy management can help to mitigate most unexpected one-time pharmacy costs.”

# Supports for Treatment

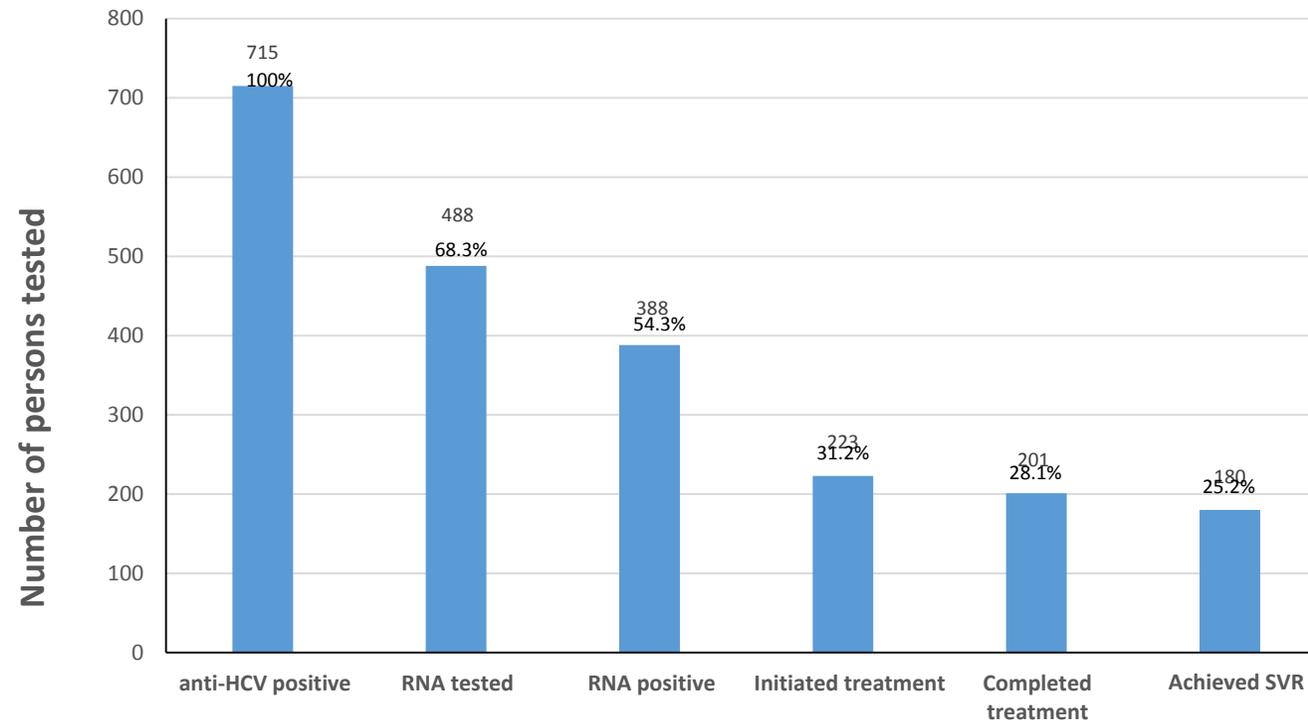
- Previously, many patients with HCV received treatment under the care of hepatologist or infectious disease specialist.
- The safety of newer treatments and the growing number of patients is shifting care more and more to primary care.
- Extension for Community Healthcare Outcomes (ECHO)
  - UNM developed model for teleconsultation
  - IHS- 1<sup>st</sup> & 3<sup>rd</sup> Wed., 12:00-1:00 pm MDT



 <p>Gail Daniels-McLaughlin IHS - Standing...</p>	 <p>Project ECHO IT Support</p>	 <p>Kellie Goudreau, MS, PAC &amp; Sarah Pa...</p>	 <p>rray</p>	 <p>jorge-mera</p>
 <p>paul.bloomquist</p>	 <p>ANGuyen2</p>	 <p>Standing Rock</p>	 <p>bmoran</p>	 <p>khan</p>
 <p>IHS HCV</p>	 <p>ademuth</p>	 <p>Brigg Reilley</p>	 <p>Jessica Leston</p>	 <p>justini</p>

 <p>Judy.Rose(White Earth)</p>	 <p>csimmons</p>	 <p>White Earth</p>	 <p>6059647724</p>
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# Cherokee Nation HCV Program Cascade of Care



# Recommendations

- Screen for Hepatitis C Infection (High-risk, Baby Boomers).
- Use a confirmatory test for all positives.
- Educate all HCV + patients on liver protection (alcohol/drugs), prevention of spread, and vaccinate against Hepatitis A & B.
- Create a HCV panel and risk-stratify patients.
- Use a multi-pronged approach to providing treatment (CMS, third-party, patient assistance programs, CMOP).
- Utilize ECHO supports.

Hepatitis C Rx:

**You can do this!!**

# Contact us

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