Hepatitis C
Exploring the Link with Injection Drug Use

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Today’s Meeting Goals

- **WHO Envisions Viral Hepatitis elimination by 2030**
- **DISCOVER** How PWID Contribute to the Increasing Burden of Hepatitis C
- **UNDERSTAND** Why PWID Should Be Treated
- **REMEMBER** That Hepatitis C Is a Curable Disease
- **CONSIDER** Your Role in Screening, Diagnosing, and Referring PWID

PWID people who inject drugs; WHO, World Health Organization.
WHO Envisions Viral Hepatitis Elimination by 2030

Globally, more than 90% of the burden of hepatitis-associated mortality is due to sequelae of HBV and HCV infections

WHO prevention and treatment service coverage targets to eliminate HBV and HCV

1. HBV vaccinations for infants
2. Prevention of mother-to-child transmission of HBV
3. Blood and injection safety
4. Harm reduction*
5. Treatment
   • Diagnosis
   • Highly effective medicines

Impact of Service Coverage Targets Leading to Elimination of HBV and HCV by 2030

In the absence of additional prevention efforts, 19 million hepatitis-related deaths are anticipated from 2015 to 2030.

*Sterile syringe/needle set distributed per person per year for PWIDs.
HCV Treatment Can Prevent Onward Transmission

- Observed and modeled HCV chronic prevalence among PWID in Melbourne, Australia

![Graph showing HCV chronic prevalence among PWID in Melbourne, Australia, with data points and modeled scenarios.](clinicaloptions.com)
How Do PWID Contribute to the Increasing Burden of Hepatitis C?

PWID or PWIDs? People Who Inject Drugs
What Does the Term “PWID” Mean?

- “PWID” is a subjective term referring to any people who have ever injected drugs:
  - Once
  - Regularly
  - Occasionally
  - No longer (ie, on stable OST)
  - Previously (eg, ever in the past)

- PWID populations:
  - “Active” or “recent” PWID – injected drugs within 1 month to 1 year and are at risk for transmitting/acquiring HCV infection
  - “Former” PWID – ceased injecting drugs but may have existing HCV infection
  - People move between groups


Past or current injection drug use is the most important risk factor for HCV infection. – US Preventive Services Task Force
Injection Drug Use (IDU) Is the Primary Risk Factor for New HCV Infections in the United States

~3.5 million people living with chronic HCV in the United States

~60% are current or former PWID

With an estimated 34,000 new HCV infections in the United States in 2015, new infections have nearly tripled in the past 5 years, reaching a 15-year high.2,4,*

The greatest increases in new HCV infections, and the highest overall number of cases, were among young people aged 20-29 years, with injection drug use as the primary route of transmission.4

Changing Epidemiology of HCV in the US

- Screening → linkage to HCV care → DAA treatment cascade must be operative in all those at risk
- Treatment of PWIDs plus harm reduction efforts essential part of elimination efforts

HCV Outbreaks Associated With IDU Are Occurring Throughout the United States

CDC, Centers for Disease Control and Prevention.
Injection Networks Are Driving Hepatitis C Outbreaks

- Higher incidence of HCV infection (especially among younger PWID) in 2012 than in 2006 in at least 30 states, with the largest increases occurring in nonurban counties east of the Mississippi River*

Why Should PWID Be Screened and Treated for HCV Infection?
PWID Are Often Co-infected With HCV and HIV

Among the HIV-positive population in North America

12% of non-PWID have HCV co-infection

83% of PWID have HCV co-infection

~153,000 PWID in North America are co-infected with HIV/HCV

High Rates of HCV Infection Among PWID

- HCV transmission is highly efficient among PWID
  - Young injectors frequently acquire HCV soon after transitioning to injection.¹,*

**Host Factors**
- Young/new PWID tend to share drug preparation equipment (eg, drug cookers, filtration cotton, rinse water)¹
- Injectors† may increase other high risk behaviors (eg, MSM and multiple sex partners)²,³

**Viral Factors**
- HCV can survive on inanimate surfaces like cookers, and filters for days, and even longer in the barrel of a syringe¹
- In controlled healthcare environments, HCV is transmitted at up to a 10-fold rate relative to HIV following needlesticks⁴

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⁴Examples of other modes of HCV transmission include transfusion, needlestick, sex, mother-to-child.
†Prescription opioids such as oxycodone have been associated with heightened risk of initiating injecting.
HCV Is Underdiagnosed and Undertreated, Even More for PWID

Cascade of Care*

HCV disproportionately impacts PWID, but treatment rates are lower relative to the overall HCV population

<table>
<thead>
<tr>
<th>Chronic HCV infection</th>
<th>Diagnosed and aware</th>
<th>Treated</th>
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</thead>
<tbody>
<tr>
<td>~3.5 Million&lt;sup&gt;1,†&lt;/sup&gt;</td>
<td>~2.1 Million&lt;sup&gt;2,‡&lt;/sup&gt;</td>
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<tr>
<td>~1.75 Million&lt;sup&gt;1,†&lt;/sup&gt;</td>
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<td>49%</td>
<td>~560,000&lt;sup&gt;1,†&lt;/sup&gt;</td>
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<td>≤~189,000&lt;sup&gt;3,§&lt;/sup&gt;</td>
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</tbody>
</table>

*All numbers are approximate. <sup>1</sup>2003-2013; <sup>2</sup>Estimated, 2005; <sup>3</sup>Estimated, 2014.
Perceived Barriers to HCV Care in the PWID Population

- In a single-center study in Denver, Colorado, individuals (born 1945-1965) with substance abuse were less likely to be referred compared with those without substance abuse, but if referred were equally likely to attend an HCV specialty visit (n=250)\textsuperscript{4,*}

\textsuperscript{*}Individuals born between 1945-1965 were screened for HCV through a testing and linkage-to-care program in 2 community clinics in Denver, Colorado. HCV evaluation and treatment courses were followed prospectively from January 2013–March 2015.
Major Global Organizations Recommend HCV Treatment for PWID$^{1-4}$

Chronic HCV Infection Can Result in Cirrhosis and Can Increase the Risk for Hepatocellular Carcinoma (HCC)* if Not Treated

*All percentages are approximate.
†20%-30% of individuals are symptomatic.


**Acute infection†**

**Chronic infection** 75%-85%

**Cirrhosis** (within the first 20 years) 10%-20%

**Clearance of HCV RNA** 15%-25%

**Potential extrahepatic manifestations**

**Decompensated cirrhosis** Up to 30% at 10 years

**HCC per year** 1%-4%
Individuals With HIV/HCV Co-infection Have Higher Mortality Rates Compared With Those Without HCV

- Overall, individuals with HIV/HCV co-infection have \(~2.5\text{x greater mortality rates and higher rates of liver mortality}\) (adjusted HR=14.0), compared with those without HCV \(*\)

\(*\)Data collected from the Antiretroviral Therapy Cohort Collaboration study involving ~32,000 HIV-infected persons (who initiated ART between 2002-2009) with known HCV status and IDU history. HCV+ was defined as positive antibody test or plasma HCV RNA.


Survival probability by HCV Status in PWID and HIV Populations
(ART Cohort Collaboration study; 2000-2009)

Effects of both HCV and IDU on mortality risk were greater in patients aged 30-49 years.
Unlike Some Chronic Conditions, HCV Can Be Cured

- The possibility of eliminating the virus and achieving a cure may be due to the manner in which the virus infects the host cells\(^1\)
  - HCV does not integrate into the nuclei of infected cells, whereas HBV and HIV DNA are incorporated into the nucleus of the cell\(^1\)

**Diagram:**

- HCV\(^1\)
  - viral RNA
- HBV\(^1\)
  - cccDNA\(^*\)
- HIV\(^1\)
  - proviral DNA\(^†\)

**Legend:**

- Nucleus
- Host Cell
- Host DNA

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\(^*\)HBV cccDNA: accumulates in hepatocyte nuclei, acting as a template for viral messenger RNA transcription.

\(^†\)HIV proviral DNA: integrates into the chromatin of infected cells, acting as the template for the transcription of viral genes.

\(^‡\)Including diabetes, hypertension, and hyperlipidemia.


Most chronic conditions\(^‡\) require lifelong management, but HCV is curable, with a treatment duration of 8-12 weeks with highly effective all-oral treatments.\(^1-4\)
In some instances, HCV treatment does not result in cure, or SVR, because the virus does not reach undetectable levels or because it does not stay undetectable after therapy completion.

In 1 study, of those patients who reached SVR, 99% had undetectable levels of HCV RNA up to 4 years after cessation of treatment. These patients do not experience viral recurrence and may be considered to be cured.3

*Cure, also known as SVR, is defined as no detectable HCV in the blood at least 12 weeks after completion of therapy.1,2

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Treatment for HCV Has Evolved

- Before 2011 (interferon era)
  - HCV treatment had serious side effects
  - Could last up to a year
  - Cure rates* (SVR) were 40%-50% for the most common genotype¹

- Now (interferon-free)
  - Few side effects
  - All genotypes
  - Cure rates about 95%²,³,*

* Cure, also known as SVR, is defined as no detectable HCV in the blood at least 12 weeks after completion of therapy.

HCV-TARGET: Real-World Efficacy and Safety of SOF/VEL for GT1-6 HCV

- Pts treated per local standard of care at academic (n = 45) and community medical centers (n = 19) in North America (n = 60) and Europe (n = 4)
  - N = 451 for SOF/VEL; N = 119 for SOF/VEL + RBV
99% SVR12 rate with 8-wk regimen in DAA-naive pts with GT2 HCV—noninferior to 95% historical control (SOF + RBV for 12 wks)

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</table>

*Slide credit: clinicaloptions.com*
PWID Across the Spectrum Can Be Treated for HCV

**Active Injectors**
- Among active injectors, frequent drug use (daily/every other day) has an impact on adherence, treatment completion, or treatment efficacy; occasional drug use does not\(^1,*\)

**Opioid Agonist Therapy**
- Among patients on opioid agonist therapy, HCV treatment outcomes improved among those treated for opioid addiction compared with nonaddiction-treated drug users\(^2,*\)

**Former Injectors**
- Among former injectors, successful HCV outcomes are more likely to be achieved if PWID are stabilized for addiction and then undergo HCV therapy\(^3,*\)

*Studies utilized IFN/RBV as the treatment arm.

*IFN, interferon.*
IFN Era: Adherence Among PWID is Comparable to the Overall HCV Population (2001-2007)¹

Non-PWID who initiated treatment (N=655)
79% completed treatment

PWID who initiated treatment (N=844)
71% completed treatment

Adherence in PWID is similar using newer IFN-free regimens.²

Reinfection Is Rare, Even Among High-Risk Groups

- A global meta-analysis of 14 articles that assessed HCV recurrence in high-risk patients; 12 evaluated the risk in PWID*

Reinfection rate among high-risk populations (PWID and Prisons)
19.06/1000 PYFU†

North American and European Reinfection Rates for PWID

<table>
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<tr>
<th>Location</th>
<th>North American Studies</th>
<th>European Studies</th>
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<td>0</td>
<td>1</td>
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</tr>
<tr>
<td>United States</td>
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<td>1</td>
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</tr>
<tr>
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<td>24</td>
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<tr>
<td>Re-infections</td>
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<td>2</td>
<td>3</td>
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</table>

PYFU, person-years of follow-up.

*Studies included adults (aged ≥18 years) who achieved SVR12 or SVR24 post-treatment with IFN-based therapies.
†Includes 2 studies conducted in prisons and was not specific to PWID.
Harm Reduction Facilities Can Increase Adoption of Lower-risk Alternative Injection Practices

Comprehensiveness of State Laws Pertinent to Prevention of HCV Infection Among PWID*

- Assessment of whether a state had established
  - Authorization of syringe exchange statewide or in selected jurisdictions
  - Exemption of needles or syringes from the definition of drug paraphernalia
  - Decriminalization of possession and distribution of syringes or needles for participants of a legally authorized syringe service program
  - Avoidance of criminal prosecution for possession of drug paraphernalia by disclosing possession of a needle or sharp object to an arresting officer
  - Allowance for the retail sale of syringes without a prescription to PWID

*United States, 2016.
What Role Can You Play in the Treatment and Management of PWIDs?
You Are the First Line of Communication for Patients With Addiction

*Screening for HCV antibodies does not have to be with a blood test. It can be via oral swab, or an even simpler approach, asking the patient questions about injecting drugs even once then proceed to the blood test for HCV RNA.*

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**Screen for HCV antibodies**

Test at-risk patients with a blood test to detect the presence of HCV antibodies*

**Diagnose with an HCV RNA test**

A blood test for the presence of HCV RNA will confirm an HCV diagnosis in patients who test positive for HCV antibodies

**Refer to an experienced HCV clinician**

Refer your patients with HCV to an experienced HCV clinician for treatment evaluation, regardless of symptoms

*Screening for HCV antibodies does not have to be with a blood test. It can be via oral swab, or an even simpler approach, asking the patient questions about injecting drugs even once then proceed to the blood test for HCV RNA.*
The First Step Is to Diagnose HCV: HCV Antibody Test

If the Result Is Negative

• It is highly unlikely that your patient has been exposed to HCV\textsuperscript{1}
• However, if exposure is suspected in the past 6 months, consider re-testing for HCV antibodies or ordering an HCV RNA test\textsuperscript{3}

If the Result Is Positive

• Your patient has been exposed to HCV\textsuperscript{1}
• You will need to confirm a chronic HCV diagnosis with an HCV RNA test\textsuperscript{3}

The Second Step Is to Confirm HCV Diagnosis: HCV RNA Test

To confirm the diagnosis, a blood test for the presence of HCV RNA is necessary.

**TEST FOR HCV RNA**

- **HCV RNA Not Detected**
  - The patient has been exposed to HCV but is not chronically infected.
  - Approximately 20%-50% of patients clear HCV spontaneously.
  - Such patients do not need further medical evaluation for HCV infection.

- **HCV RNA Detected**
  - The patient should be referred to an HCV specialist for additional tests and treatment evaluation.
  - Further testing includes a genotype test and may include a liver biopsy and/or liver ultrasound to determine disease progression.

An HCV Ab reflex to the HCV RNA confirmation test automatically confirms Ab-positive samples with an HCV RNA test.


What to Do if HCV RNA Is Not Detected

The patient is not chronically infected with HCV
No further medical evaluation for HCV infection is required

Discuss the results with your patient:
  - Tell the patient that he or she is not chronically infected, and that no further testing or treatment is needed
  - Confirm that he or she understands how the virus is spread and the situations in which he or she could be exposed
  - Explain that he or she will always test positive for HCV antibodies
  - Explain that he or she is not immune, and can be infected with repeat exposure

What to Do if HCV RNA Is Detected

- The patient is infected with HCV
- Consider ordering an HCV genotype test (optional)
- Refer the patient to an HCV specialist for additional tests and treatment evaluation
- **Discuss** the diagnosis with your patient:
  - **Tell** your patient that he or she is infected with HCV and will be referred to a specialist for more tests and possible treatment
  - **Explain** that HCV is a progressive disease that can lead to serious liver-related complications
  - **Emphasize** that HCV can be curable and that treatment options are available
Refer HCV-Positive Patients to HCV Specialists

Refer Promptly

- After their diagnosis is confirmed with an HCV RNA test, your patients with chronic HCV should be promptly referred to an HCV specialist, regardless of viral load or liver enzyme levels
  - Viral load or liver function tests may not be reliable indicators of liver damage
  - Most patients with chronic HCV are asymptomatic until serious liver complications arise

Quality Referral

- Confirm diagnosis with an HCV RNA test
- Refer to a specialist who has experience with treating HCV

Discuss Referral With Your Patient

- 24%-57% of patients with HCV miss their first appointments with a specialist
- There are several common reasons for patient nonadherence:
  - Patients may not recognize the urgency of treating a disease with few symptoms
  - Lack of insurance coverage
  - Fear of social rejection and stigmatization
- Explain why referral is necessary
- Describe the liver complications that can arise from delaying treatment
- Make it clear that therapy can lead to cure
- Assure your patient that you will stay in contact

Hepatitis C: Barriers to Treatment

- Unidentified patients
- Too few treating providers
- Patients frequently fail to see an “expert”
- Local care is better?
  - Patient is on site
  - Relationship with local provider
  - Project ECHO® teaches skills in a case-based format
Project ECHO®

- Extension for Community Health Outcomes
- Getting care to people instead of getting people to care
- Deliver knowledge
  - Right place
  - Right time
Learning to Drive

- Learning by watching

- Learning by doing
Force Multiplier in Medicine:

- Expand the pool of people who can deliver high quality expert care
- Demonopolize Knowledge
Project ECHO® ≠ Telemedicine
Models: Provider-to-patient vs Provider-to-Provider

Telemedicine
Provider-to-Patient
1-to-1

Telemedicine
Provider-to-Provider
1-to-1

Project ECHO®
Tele-mentoring
One-to-many
Case-based with CME
Force multiplier
Sanjeev Arora, MD
University of New Mexico

Project ECHO® Hubs, USA

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Making the Most of our Assets
Using Primary Care to Manage Complex Disease

- No difference between university and community care - different from all prior studies
- Sense of community among providers

ASCEND Study: HCV Treatment by Primary Care Providers (2016)

- Multicenter, open-label, phase 4 study (n=600 HCV patients)
  - 2 urban health centers, 16 providers
  - Ledipasvir/sofosbuvir
  - Similar patient types for all
    - Male (69%), black (96%), HIV-coinfected (23%), cirrhosis (20%)
  - HCV treatment experienced (18%)

<table>
<thead>
<tr>
<th><strong>HCV</strong></th>
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<tbody>
<tr>
<td><strong>Free screenings, public info of risk factors</strong></td>
<td>Perform HCV Antibody or Rapid HCV Antibody test</td>
</tr>
<tr>
<td><strong>Positive Patients Identified</strong></td>
<td>If anti-HCV positive, client offered HCV RNA with GT</td>
</tr>
<tr>
<td><strong>Resources Assessed</strong></td>
<td>If client is HCV (+), staff informs via ph or mail</td>
</tr>
<tr>
<td><strong>Appropriate Referral</strong></td>
<td>Resources: FQHC, County, Indigent Clinic</td>
</tr>
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Community health improves because of locally available care delivered by local providers with enhanced skills.

Appropriate cases may be referred to a medical center.
Over 700 cases presented

- Over 3,000 patients treated without assistance
- Over 345 providers in 6 states have been educated
  - Texas, Louisiana, South Carolina, Alabama, Florida and Tennessee
Community Providers

Community Provider Participation

- MD: 42%
- NP: 40%
- PA: 8%
- Other: 10%
- 40%
Referral Best Practices

✔ Explain what to expect when meeting with an HCV specialist

✔ Explain what an HCV diagnosis means, that HCV is curable, and that interferon-free (no injections) options exist that offer all-oral treatments

✔ Assist with scheduling the specialist appointment and emphasize the importance of keeping the appointment

✔ After the specialist appointment, stay in touch with your patient and the specialist
Various Clinical Models Have Demonstrated Improved Linkages to HCV Care

“Evaluation by a practitioner who is prepared to provide comprehensive management, including consideration of antiviral therapy, is recommended for all persons with current (active) HCV infection.”

— AASLD/IDSA Recommendations for Testing, Managing, and Treating Hepatitis C

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<tr>
<th>Co-located or Integrated Care</th>
<th>Telehealth</th>
<th>Referral</th>
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<tbody>
<tr>
<td>• Designed to impact loss to follow-up¹</td>
<td>• Delivers service to underserved populations²</td>
<td>• Referral for HCV infection to an experienced HCV clinician¹</td>
</tr>
<tr>
<td>• Potentially affects access to treatment¹</td>
<td>• Links specialists to communities²</td>
<td>• Multidisciplinary approach to treatment has the potential to mitigate barriers to HCV care¹</td>
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*HCV treatments were Peg-IFN+RBV-based therapies (pre-DAA). Treatment duration was 48 weeks for genotype 1 and genotype 4; 24 weeks for other genotypes. Studies utilized SVR24 as primary endpoint.

Treatment at Early-Stage Disease May Be Associated With Higher SVR Rates and Less Severe Complications

- **Treat Early**
  - Treatment is more effective at early-stage disease\(^1\);*
- **Treat in place**

“[Clinicians] should treat HCV-infected patients with antiviral therapy with the goal of achieving an SVR, preferably early in the course of their chronic HCV infection before the development of severe liver disease and other complications.”

– AASLD/IDSA HCV Guidance\(^2\)

*Studies utilized SVR24, the standard protocol before 2013 for measuring attainment of SVR.