HCV in People who Inject Drugs (PWID)

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Disclosures

- **Speakers Bureau**: Clinical Care Options (HIV), Janssen Therapeutics (HIV), Viiv (HIV), Gilead Sciences (HIV, HCV), AbbVie (HCV), Bristol-Myers Squibb (HCV)

- **Scientific Advisor**: Gilead Sciences (HIV, HCV), Janssen Therapeutics (HCV), Bristol-Myers Squibb (HCV)

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- **Employer**: Family Health Centers of San Diego
Learning Objectives

At the end of this lecture, you will be able to:

• Describe the **epidemiology** of HCV in PWID
• Identify **unique challenges** in treating PWID
• Describe **clinical trials** including PWID
• Review **Guidance** on mgmt of HCV in PWID
What do we mean by PWID?

- Injected once?
- Injects regularly?
- Injects occasionally?
- Last injected 35 years ago?
- On stable OST and no longer injects?

• NSP: needle/syringe programme;
• OST: opioid substitution therapy;
• PWID: people who inject drugs
Epidemiology
Estimated HCV Prevalence: Global

- 3-4 million new infections/yr
- 150-180 million infections worldwide

Prevalence of infection:
- > 10%
- 2.5%-10%
- 1%-2.5%
- NA

Sources:
- Razavi et al AASLD 2013
Estimated HCV Prevalence in PWID Worldwide (millions)

Global estimate: ~10.0 million PWID (range 6.0–15.2)

Global prevalence: 67.0% of PWID
Estimated chronic HCV Prevalence: US

- NHANES¹: 2.7-3.2 million
- Adjusted for homeless, institutionalized, prisoners, military²: 5-7 million

Declining Prevalence of HCV Ab (1.3%) AND HCV RNA (1.0%)
Prevalence of HCV Antibody, by Year of Birth

Year of Birth


HCV Prevalence(%)

0 1.0 2.0 3.0 4.0 5.0 6.0 7.0

1945-1965

1988–1994

1999–2002
Hepatitis C Incidence in United States, 1982-2010

Estimated New Infections

Number of Cases

How is IDU contributing to HCV Epidemiology?

• Estimated 60% of prevalent HCV in US in current or former IDU’s¹, ²
• Estimated 29,718 new infections in 2013
  – 80% of incident HCV in PWID
• 3.8 Million have injected heroin at least once
  – 425,000 have injected in the last year
    • 289,000 actively injecting
• 64% of PWIDs are infected with HCV

Increasing Incidence of HCV in Young PWID
HCV testing at FHCSD – 12 month Results
Indiana HIV Outbreak - 2015

HIV Diagnoses by Week, Indiana HIV Outbreak (N=188)

- Detect and confirm
- Deploy emergency command, HIV testing, contact tracing, services
- Consolidate case management, HIV treatment, prevention services
- Retesting “blitz”

Adult prevalence as of February 1 2016

- Scott County (18,264*): 1.0 %
- Austin, if home for 80% of cases (3,143*): 4.6 %

Week Ending

Peters P et al., under review and Indiana State Department of Health

*estimated population age ≥18 years, U.S. Census
Management Challenges in PWID
Very few PWID treated in IFN era

<10% of PWID with HCV antibody positive were cured

PWID who receive HCV treatment

ETHOS: 5 OST clinics, 2 CHCs, 1 aboriginal center in New South Wales, Australia, 2009–2012

- Assessed by nurse: 387
- Referred to specialist: 236 (61%)
- Attended specialist appointment: 191 (49%)
- Started interferon-based treatment: 84 (22%)

Reasons for Non-Engagement

- Limited access to healthcare
- Poor quality of life
- Alcohol consumption
- Use of multiple substances
- Homeless or living in temporary accommodation (shelters, prison)
- Poorly educated (secondary education or less)

"I am treated as a criminal and this makes it hard to take care of my health"

"There are no friendly healthcare services near where I live"

"I would like to give up drugs, but I cannot get help"

"I cannot get opioid substitution therapy/syringes because it is illegal"

"Healthcare workers do not trust me, as if I just want drugs"

"Without clean needles and syringes, I have to share"
Pt-reported Barriers in OST & NSPs

Self-reported barriers to care among HCV-positive PWID (n=117)*
Reasons for non-referral/non-treatment in a testing/linkage program in Denver

- Mental illness
- Referral declined
- Lost to follow-up
- Medical disease
- Not documented
- Substance abuse

Number of HCV-infected individuals

- Mental illness: 11
- Referral declined: 14
- Lost to follow-up: 14
- Medical disease: 29
- Not documented: 46
- Substance abuse: 55

- Mental illness
- Substance abuse
- Medical disease
- Work on-going
- Lost to follow-up
- Not advanced liver disease

Number of reasons:

- Substance abuse: 23
- Medical disease: 28

- Most common reasons: substance abuse and co-morbid medical disease.
Clinical Trials of HCV treatment in PWID
Retrospective analysis: ION-1, -2, -3: patients on stable OST

- No differences between OST and non-OST participants:
  - Overall SVR12 (94% vs. 97%, p=0.29)
  - Adherence to LDV/SOF ≥80% (94% vs. 96%, p=0.33)
  - Proportion with AEs (89% vs. 80%, p=0.07)

- No cases of HCV reinfection were observed up to SVR24

IFN: interferon; LDV: ledipasvir; OST: opioid substitution therapy; SOF: sofosbuvir; RBV: ribavirin; PWID: people who inject drugs
High SVR12 for pts on OST with OMV/PTV/RTV + DSV + RBV

Phase 2, open-label, single arm study of OMV/PTV/RTV + DSV for 12 weeks in GT 1 adult patients on stable OST with methadone or buprenorphine (N=38)

Virological response (%)

- EOT: 37/38
- SVR4: 37/38
- SVR12: 37/38

Grazoprevir/Elbasvir x 12 weeks in pts on OST (C-EDGE CO-STAR)

Phase 3, randomised, double-blind study in PWID on OST with GT 1, 4 or 6 (n=201)

- 17 patients did not achieve an SVR
  - 7 cases of relapse
  - 5 cases of re-infections
  - 5 patients were lost to follow-up or discontinued due to events unrelated to treatment failure

<table>
<thead>
<tr>
<th>GT</th>
<th>SVR 12 (%)</th>
<th>SVR 12 (n)</th>
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<tbody>
<tr>
<td>All GT</td>
<td>92</td>
<td>184/201</td>
</tr>
<tr>
<td>GT 1a</td>
<td>94</td>
<td>144/154</td>
</tr>
<tr>
<td>GT 1b</td>
<td>93</td>
<td>28/30</td>
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<tr>
<td>GT 4</td>
<td>92</td>
<td>11/12</td>
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<tr>
<td>GT 6</td>
<td>20</td>
<td>1/5</td>
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</table>
ELB/GRZ x 12 weeks in pts on OST – C-EDGE CO-STAR: Adherence

Phase 3, randomised, double-blind study in PWID on OST with GT 1, 4 or 6

Adherence

- 99% (199/201) patients completed 12 weeks of treatment with grazoprevir/elbasvir
- Majority of patients (97%) missed 3 doses or fewer
- Around 60% patients tested positive for illicit drug use during the study

Missed doses

<table>
<thead>
<tr>
<th>Number of missed doses</th>
<th>Number (%) patients</th>
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<tbody>
<tr>
<td>0</td>
<td>153 (76.9)</td>
</tr>
<tr>
<td>1</td>
<td>23 (11.6)</td>
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<tr>
<td>2</td>
<td>8 (4.0)</td>
</tr>
<tr>
<td>3</td>
<td>8 (4.0)</td>
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<tr>
<td>4</td>
<td>1 (0.5)</td>
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<tr>
<td>≥5</td>
<td>6 (3.0)</td>
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High SVR₁₂ for PWID in Community setting

121 consecutive patients from urban FQHC in the Bronx

- HCV Care Coordinator responsible for scheduling, reminder calls, prior authorizations
- Outcomes compared between People who use drugs (Opiate substitution therapy or positive Urine tox screens)
HCV Re-infection rates in PWID
Reinfection Rates Are Low Among PWID (‘ever’ injectors)

Pooled estimate of HCV reinfection risk for PWIDs¹:
2.4 (95% CI 0.9–6.1) per 100 person-years

- Reinfection rates among PWIDs may be higher:
  - In communities with high HCV prevalence²
  - For young PWIDs³–⁵
  - For active injection drug users³–⁵

Reinfection Rates Among Persons Who Ever Injected Drugs Per 100 Person-Years²

<table>
<thead>
<tr>
<th>Country</th>
<th>Rate</th>
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<tbody>
<tr>
<td>Canada</td>
<td>3.20</td>
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<tr>
<td>Netherlands</td>
<td>0.76</td>
</tr>
<tr>
<td>Norway</td>
<td>0.80</td>
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<tr>
<td>Germany</td>
<td>3.94</td>
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<tr>
<td>USA</td>
<td>2.63</td>
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<tr>
<td>Australia</td>
<td>4.70</td>
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Risk of HCV re-infection in low and high risk groups and HIV/HCV co-infection

Meta-analysis of 66 studies in 11,071 patients

Low risk
- 43 studies; N=9,419
- FU=4.1±2.1 years

High risk (PWID/prisoners)
- 16 studies; N=819
- FU=2.9±1.6 years

HIV/HCV co-infected
- 7 studies; N=833
- FU=3.1±1.2 years

Recurrence rate/100 patient years

- Low risk: 0.23 (95% CI 0.18–0.28)
- High risk: 2.80 (95% CI 2.06–3.71)
- HIV/HCV co-infected: 4.78 (95% CI 3.97–5.71)
HCV Can Be Managed in PWIDs Across the Spectrum

Active Injectors

- Occasional drug use does not impact adherence, treatment completion, or treatment efficacy\(^1\)
- Frequent drug use (daily/every other day) does\(^1\)

Opioid Agonist Therapy

HCV treatment outcomes improved among those treated for opioid addiction compared to untreated individuals\(^2\)

Former Injectors

Successful HCV outcomes are more likely to be achieved if PWIDs are stabilized for addiction and then undergo HCV therapy\(^3\)

Risk of HCV Transmission and Progression in PWIDs

Population Level
- Risk of HCV transmission

Individual Level
- Risk of liver-related morbidity and mortality

Highest prevalence of PWIDs

Years of age
- 15
- 25
- 35
- 45
- 55
- 65

• Lower risk of advanced liver disease
• Higher risk of HCV transmission due to the propensity of young/new PWIDs to share needles and syringes

• Moderate risk of advanced liver disease
• Moderate risk of HCV transmission

• Higher risk of advanced liver disease
• Lower risk of HCV transmission

ICPVH 2016
INTERNATIONAL CONFERENCE ON VIRAL HEPATITIS

FAMILY HEALTH CENTERS OF SAN DIEGO
Summary

• PWIDs are disproportionately affected by HCV
  – 60% of prevalent and 80% incident infections in US
• Ample evidence of increasing HCV incidence among young people using opiates
• Growing body of clinical trials and ‘real world’ studies showing comparable SVR rates
• Professional societies recommend comprehensive approach involving Opiate Substitution therapy, case management, HCV treatment
Questions?
Extra Slides: Drug-drug interactions
Potential for drug interactions between OST and DAAs

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<tr>
<th></th>
<th>DCV</th>
<th>LDV/SOF</th>
<th>OMV/PTV/RTV + DSV</th>
<th>SMV</th>
<th>SOF</th>
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<td>Buprenorphine</td>
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<td>Methadone</td>
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- ◯ No clinically significant interaction expected
- ■ Potential interaction – may require close monitoring, alteration of drug dosage or timing of administration
### Potential for drug interactions between antidepressants, antipsychotics and DAAs

Adapted from EASL. J Hepatol 2015;63:199–236.

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<td><strong>Antipsychotics</strong></td>
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Extra Slides:
Published Guidelines
### 2015 INHSU recommendations on management of HCV among PWID

**Prevention**
- Access to OST and sterile injecting equipment as part of widespread harm reduction programmes

**Screening**
- Annual screening via anti-HCV with RNA confirmation of positive tests
- Non-invasive liver fibrosis assessment should be offered to enhance screening

**Assessment**
- Pre-assessment should include HCV education and evaluation of social situation
- Models of integrated HCV care to increase linkage between addiction and HCV services to support successful pre-assessment

**Treatment**
- SOF, LDV/SOF, OMV/PTV/RTV + DSV ± RBV, DCV or SMV are suitable regimens depending on local availability and patients’ disease characteristics

**Management**
- Individualised and delivered in a multidisciplinary team
- Access to harm reduction programmes

**Prisoners**
- Screening and assessment should be offered
- Treatment is feasible and should be offered
• PWID should be routinely tested for HCV antibodies and, if negative, every 6–12 months (B1)
• Provided with clean drug injecting equipment and access to OST as part of widespread comprehensive harm reduction programmes, including in prisons (B1)
• Pre-therapeutic assessment should include evaluation of housing, education, cultural issues, social functioning and support, finances, nutrition, and drug and alcohol use. PWID should be linked into social support services and peer support if available (A1)
• A history of IDU and recent drug use at treatment initiation are not associated with reduced SVR and decisions to treat must be made on a case-by-case basis (B1)
• The anti-HCV regimens that can be used in PWID are the same as in non-PWID. No dose adjustment for methadone or buprenorphine is required but monitoring for opioid toxicity or withdrawal should be undertaken. More data are needed for daclatasvir (B1)
• PWID should receive treatment because of the elevated risk of HCV transmission (IIa, Level C)
• Annual HCV testing is recommended for PWID and for HIV seropositive MSM (Class IIA, Level C)
• Adherence and efficacy rates are comparable to those of patients who do not inject drugs
• The rate of reinfection in PWID who are treated is lower (2.4/100 py) than that of incident HCV in this population (6.1-27.2/100 py)