

The Opioid Crisis

Peter G. Gulick, DO, FACP, FACOI, FIDSA
Professor
College of Osteopathic Medicine
Michigan State University

General Information

1. 1999-2014 Prescription of opioid drugs increased four fold
2. Narcotics account for 23% of prescriptions
 - 650,000 opioid prescriptions per day
 - Levels of pain remained constant
3. 1996 Oxycontin released
 - Contained large amount of oxycodone easily dissolved
 - Responsible for over 25% of prescribed narcotic drugs
 - US consumes over 80% of world's oxycodone supply

General Information

4. Over 2.4 million Americans meet definition of Severe Opioid Use Disorder (OUD)
5. In 2016, 9/10 people needing treatment for substance abuse disorder were not getting it
6. CDC put restrictions on prescription opioids
7. Shift toward IV heroin, fentanyl, and other synthetic opioids
 - Opioid death rate up
 - Increasing rate of HCV, HIV, HBV

Response to the Problem

1. Reduce over prescribing of opioid drugs

- In 2016 CDC released guidelines on opioid prescribing for chronic pain
- Every state has adopted prescription drug monitoring program (PDMP)
- States have offered CME Medical Education on best prescribing practices
- Training program on opioids for healthcare providers

Response to the Problem

2. Increased access to treatment
3. Need Medication Assisted Treatment (MAT) program
 - Have been shown to reduce risk of overdose deaths by 50%
 - Health costs decreased 50% with those on MAT
 - Only 10% of 27 million Americans addicted received treatment
 - 61% of counties in the US have no program
 - Insurances do not cover them
 - Physicians reluctant to get educated and prescribe the drugs

Response to the Problem

4. Medication Assisted Treatment (MAT)

➤ Medication approved

➤ Methadone

- Agonist (fully activates opioid receptors)
- High-strength and efficacy to reduce euphoria

➤ Buprenorphine (Suboxone)

- Partial agonist (partial agonist and activates opioid receptors to relieve cravings)
- Eligible to be prescribed by certified healthcare providers

➤ Naltrexone (Vivitrol)

- Antagonist (blocks opioid receptors)

Response to the Problem

Recommendations

1. Increase funding for addiction treatment programs
 - Grants from government, states
2. Maintain insurance coverage for people with drug use disorders
 - Medicaid to maintain full health coverage , inpatient, hospitalization, out patient detoxification program
 - Ensure insurance to enforce mental health parity in ACA
3. Increase access to buprenorphine treatment
 - Increase all healthcare provider access (NP, PA, MD, DO)
 - Have FQHC centers receive waivers to prescribe
4. Reduce administrative barriers to treatment
5. Support research for new treatment options

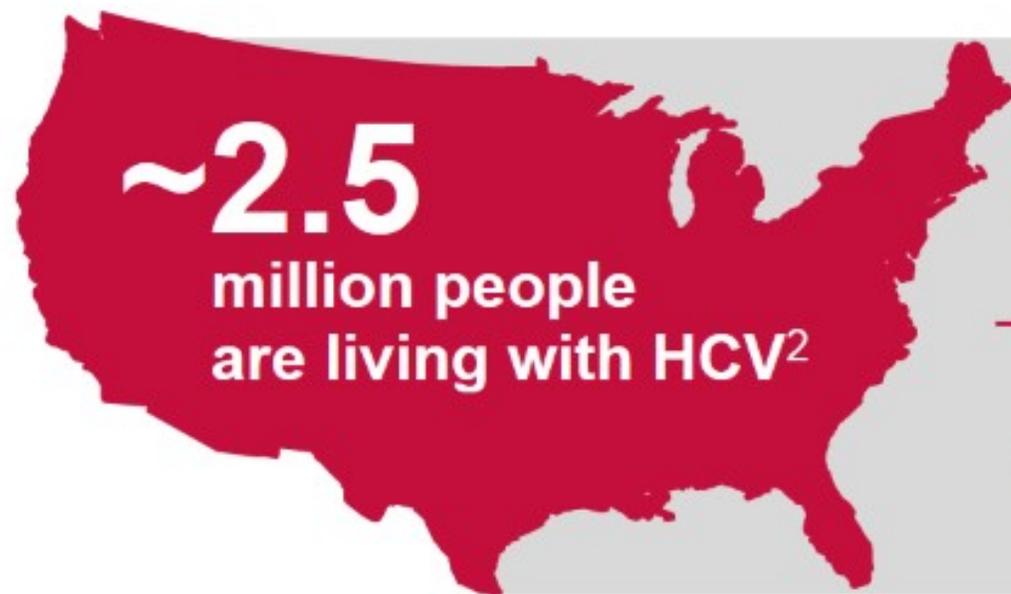
Current Epidemiological Trends in HIV and HCV Among PWID in the US

- A. In 2008-2014 HIV diagnosis in the US among PWID fell 48%
 - 50% decline in urban Black, Hispanic injections
 - HIV screening among PWID remains infrequent overall especially in rural areas
- B. Syringe needle exchange remains high in White PWID but declining in Black and Hispanic
 - PWID also remain sexually active with high-risk sexual practices
- C. Awareness of serostatus among PWID networks remains poor
 - 45% unaware of last injecting partners' serostatus especially in rural areas

Current Epidemiological Trends in HIV and HCV Among PWID in the US

- D. HCV incidence has increased with a threefold increase in acute HCV (2010-2015) especially in rural areas
 - Appalachian states highest rates
- E. Young white active injection users are the new risk for acute HCV
- F. HCV transmitted in blood easier than HIV (3-9% vs. 0.3%)
- G. HCV survives on an inanimate surface over 6 weeks versus HIV from 6 days to 4 weeks
 - High dead-space syringes harbor higher risk

Current and former PWID comprise more than half of the chronic HCV population in the United States¹



~40%

of PWID with recent injection drug use have HCV³

~80%

of new HCV infections in 2014 occurred among PWID⁴



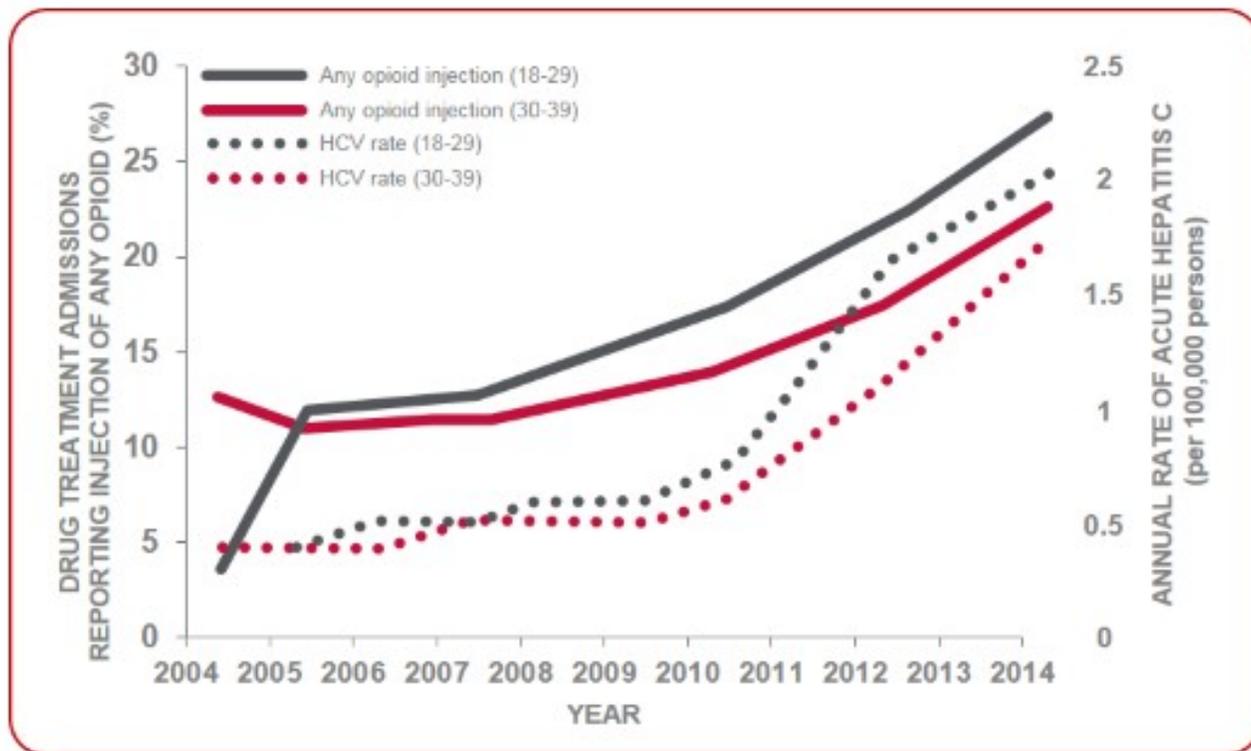
The United States has the second largest population of people with recent injection drug use who have HCV in the world: 895,000.^{3,a}

^a95% CI: 353,000-1,601,500.

1. Grebely J, et al. *Clin Infect Dis*. 2013;57(7):1014-1420. 2. Chhatwal J, et al. Presented at: AASLD 2018, The Liver Meeting®, November 9-13, 2018; San Francisco, CA.
3. Grebely J, et al. *Addiction*. 2019;114(1):150-166. 4. Zibbell JE, et al. *Am J Public Health*. 2018;108(2):175-181.

AASLD=American Association for the Study of Liver Diseases;
CI=confidence interval.

From 2004-2014, HCV and opioid injection drug use increased significantly among people aged 18-39 years^{1,2}



Among people aged 18-29 years¹:



Rate of acute HCV



Admission for
opioid injection

Among people aged 30-39 years¹:



Rate of acute HCV



Admission for
opioid injection

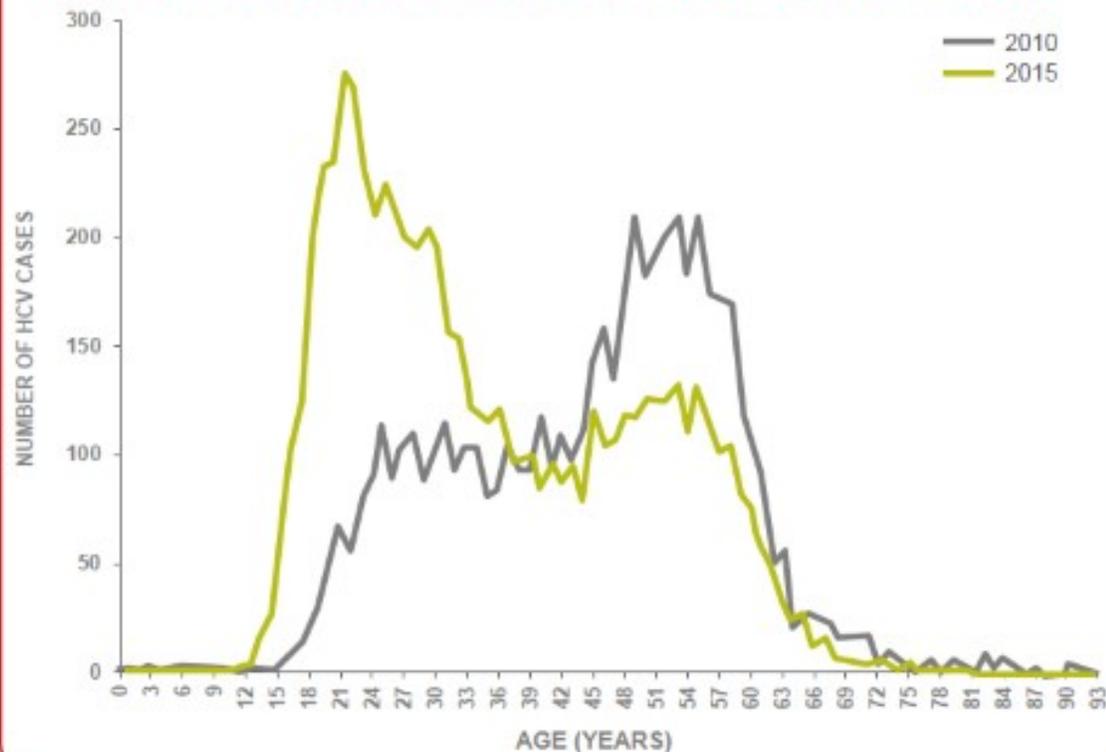
The national increase in acute HCV infection is associated with the nation's opioid epidemic.¹

1. Zibbell JE, et al. *Am J Public Health*. 2018;108(2):175-181. 2. CDC. <https://www.cdc.gov/nchstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html>. December 21, 2017. Accessed October 23, 2018.

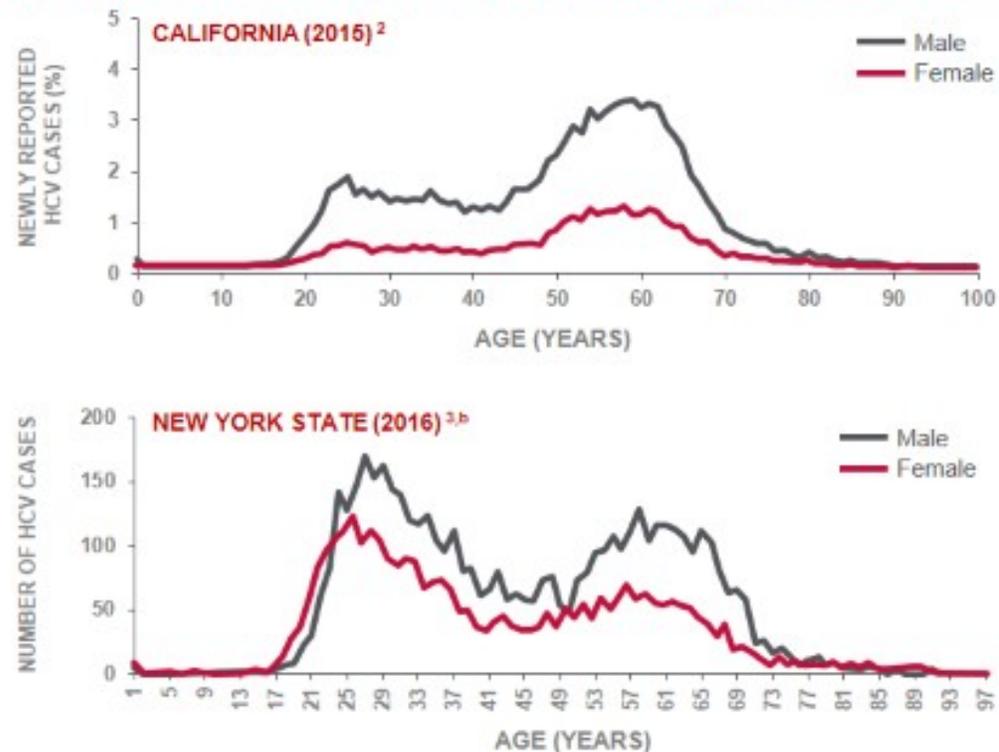
CDC=Centers for Disease Control and Prevention.

Increased injection drug use in adolescents and young adults is shifting the demographics of HCV infection in the United States¹⁻³

BETWEEN 2010 AND 2015, THERE WAS A SHIFT IN HCV INFECTIONS FROM AN OLDER TO A YOUNGER POPULATION (INDIANA DATA)^{1,a}



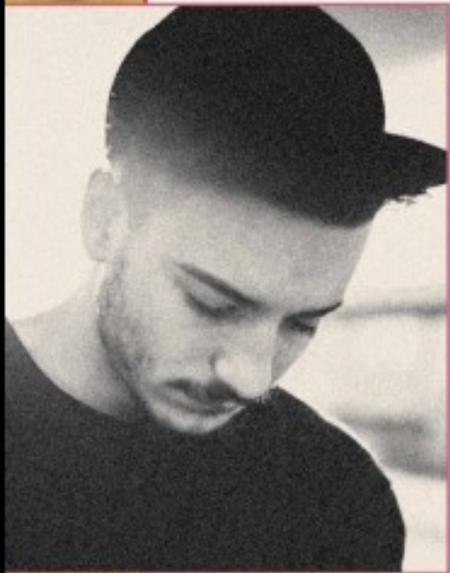
RECENT HCV INCIDENCE DATA DEMONSTRATE A COMPARABLE BIMODAL AGE DISTRIBUTION AMONG NEW HCV INFECTIONS IN MEN AND WOMEN



^aAdapted from the Indiana State Department of Health's Hepatitis C Epidemiological Report 2015. ^bExcludes cases from New York City.

CDC=Centers for Disease Control and Prevention.

1. Indiana State Department of Health. <https://www.in.gov/isdh/files/2015%20Hepatitis%20Epidemiologic%20Profile%20FINAL.pdf>. Accessed October 19, 2018. 2. California Department of Public Health, STD Control Branch. https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Converted_ChronicHCV_SurvRpt_Graphs.pdf. June 2017. Accessed October 19, 2018. 3. New York State Department of Health. https://www.health.ny.gov/community/youth/development/docs/nys_youth_sexual_health_plan.pdf. Updated 2018. Accessed October 19, 2018.



Brian

22-year-old male, recent injection drug use with an opioid use disorder

PATIENT PROFILE

- Caucasian
- Dropped out of college and is unemployed
- Covered by parents' commercial insurance

MEDICAL HISTORY

- **Comorbidity:** Depression

TREATMENT CONSIDERATIONS

- Recently entered 7-day treatment facility
- Receiving buprenorphine

How does the disease burden of HCV in PWID impact your decision to screen a patient like Brian for HCV infection?

Barriers to HCV care in PWID

Provider-level Barriers

- Perception that patients who inject drugs are poor candidates for treatment¹
- Concerns regarding patient adherence^{1,2}
- Perception that substance use may affect treatment outcomes²
- Concerns about the risk of HCV reinfection^{1,2}

System-level Barriers

- Complexity of referrals¹
- Limited infrastructure for HCV assessment and treatment in primary care and substance use treatment facilities that treat marginalized populations²
- Treatment access restrictions³
- Treatment cost^{1,2}

Patient-level Barriers

- Low perceived need for treatment²
- Lack of knowledge of HCV serostatus¹
- Fear of side effects¹
- Lack of insurance¹
- Low socioeconomic status¹
- Stigma from HCPs and system²
- Distrust of healthcare system¹



Education and training should address misconceptions and stigmatization of PWID with evidence-based guidelines.^{4,5}

1. Zeremski M, et al. *World J Gastroenterol*. 2013;19(44):7846-7851. 2. Grebely J, et al. *J Infect Dis*. 2013;209(Suppl 1):S19-S25. 3. Center for Health Law and Policy Innovation at Harvard Law School. https://www.chlpi.org/wp-content/uploads/2013/12/State-of-HepC_2017_FINAL.pdf. October 23, 2017. Accessed October 21, 2018. 4. Aspinall EJ, et al. *Clin Infect Dis*. 2013;57(Suppl 2):S80-S89. 5. Muething L, et al. IDSA/AIDS Week 2015. Poster 1029.

Barriers to Prevent Rural PWID from Accessing HIV/HCV Testing and Treatment

A. Lack of Specialty Health Care

- PCP with no experience with HIV/HCV care
- PCP with no experience with care of PWID with MAT methods

B. Cost, Insurance, and Rationing of Care

- HIV care
 - Ryan White helps bridge those without insurance
- HCV care
 - No program for underinsured
 - In rural areas only 32% are insured
 - Use of DAA in substance abuse remains controversial with concerns of nonadherence and reinfection

What is the Efficacy of HIV/HCV Treatment Among PWID

- A. PWID have historically been less likely to persist in HIV care, receive ART, and achieve viral suppression
 - More urban areas with MAT programs are achieving success as non-users
 - Rural areas have less care and PLWH enter care more advanced with higher mortality
- B. PWID with HCV show high cure rates with DAA of 96-97% if on Medication Assisted Therapy (MAT)
 - Rural areas don't have established MAT programs

Long Road from Screening to Cure

Linkage to Outpatient Care

- Current sites
 - Infectious Disease, GI, Hepatology
- Future sites
 - Integrated sites
 - Primary Care, substance abuse, mental health, opioid (MAT) sites all linked
 - Education opportunities
 - To get certified to treat HCV and approved by insurances and states
 - More health care providers involved (MD, DO, PA, NP, Pharmacists)

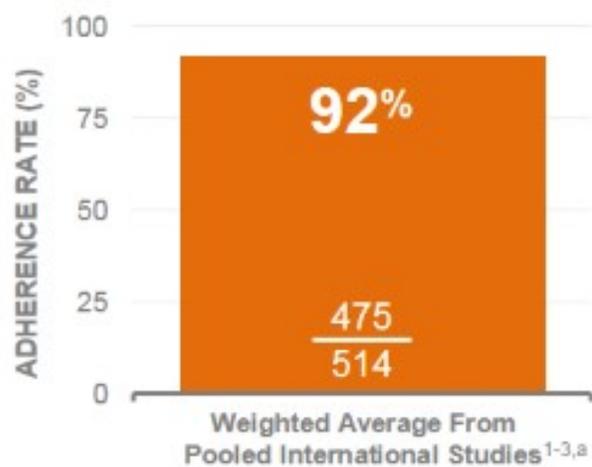
How to Optimize HIV/HCV Treatment Outcomes Among PWID

A. Substance Abuse Treatment

- Drug abuse support key to improving care for PLWH with addiction
 - Use of MAT program improves HIV outcomes
 - Make HIV providers aware of guidelines for HIV patients with chronic pain
- HCV patients in MAT programs do very well with DAA therapies and are more adherent and less likely to get reinfected

Adherence rates with DAA therapy among PWID/PWUD are high¹⁻³

ADHERENCE RATES WITH DAA THERAPY AMONG PWID/PWUD¹⁻³



The PWID/PWUD population included individuals who were actively using or injecting drugs, receiving MAT, HCV/HIV coinfecting, and/or housing unstable.¹⁻³

▶ **Regardless of active drug or injection drug use, studies have shown PWID/PWUD to be adherent to HCV therapy.¹⁻³**

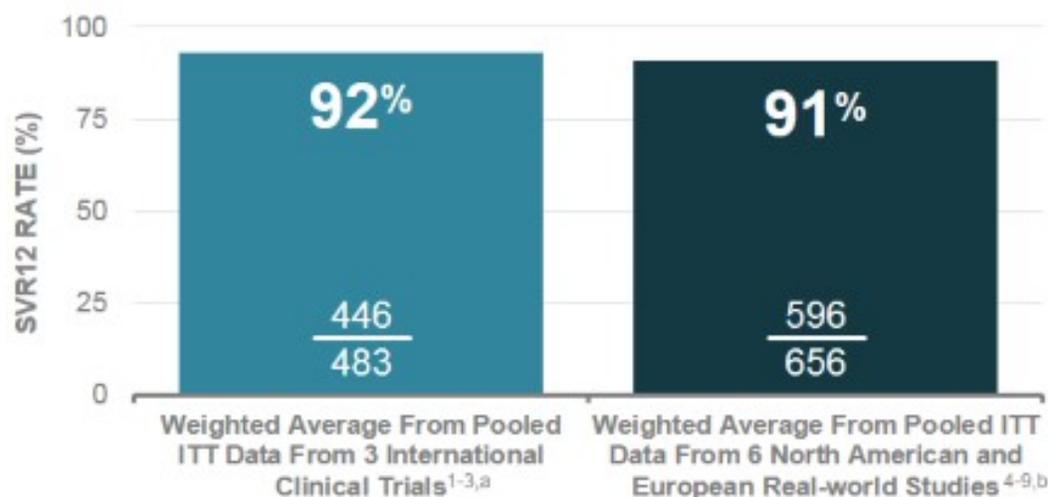
^aThree clinical trials or post-hoc analyses, including a study of 301 treatment-naïve subjects with HCV GT 1, GT 4, or GT 6, who were ≥80% adherent to opioid agonist therapy (C-EDGE CO-STAR); a study of 149 GT 1 subjects (58 with a history of injection drug use) receiving OST from a post-hoc analysis of 12 Phase 2 and 3 clinical trials of a DAA; and a study of 100 subjects with chronic HCV and recent opioid injection use (≤3 months) treated for 12 weeks with a DAA (ANCHOR). In the C-EDGE CO-STAR study, adherence was monitored by electronic diary. Subjects were considered adherent if they reported taking ≥95% of their pills. In the post-hoc analysis, adherence was calculated by dividing the number of total pills received by the total expected number of pills. Subjects were considered adherent if they had taken ≥90% of their expected pills. In the ANCHOR study, adherence was calculated based on the number of pill bottles used. Adherent subjects were those who completed 3 bottles.¹⁻³

1. Dore GJ, et al. *Ann Intern Med.* 2016;165(9):625-634. 2. Grebely J, et al. *Open Forum Infect Dis.* 2018;5(2):ofy001.
3. Rosenthal E, et al. Presented at: AASLD 2018, The Liver Meeting[®], November 9-13, 2018, San Francisco, CA.

DAA=direct-acting antiviral; GT=genotype;
MAT=medication-assisted therapy.

Studies have shown that PWID/PWUD achieve high SVR12 rates with DAA therapy¹⁻⁹

SVR12 RATES WITH DAA THERAPY AMONG PWID/PWUD¹⁻⁹



SVR12 rates for HCV DAA therapy were similar for pooled data from clinical trials and real-world studies.¹⁻⁹

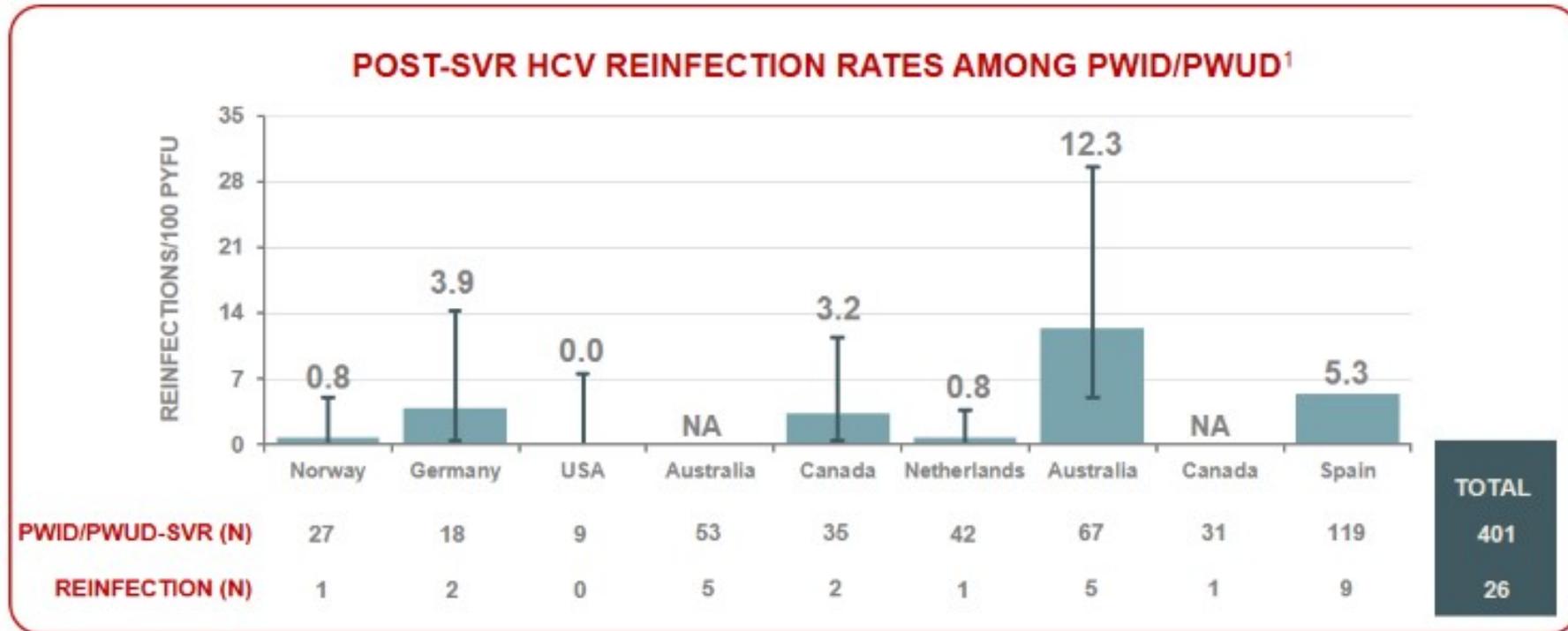
PWID/PWUD were cured regardless of active injection drug or MAT use.¹⁻⁹

*Three clinical trials or post-hoc analyses, including one of 301 subjects treated with 1 DAA regimen between September 2, 2014 and December 9, 2014 in 12 countries, Puerto Rico, and the United States; one of 149 subjects (58 with a history of injection drug use) treated with 1 of 2 DAA regimens between September 10, 2012 and April 28, 2016 at multiple international sites; and one of 38 subjects treated with 1 DAA regimen beginning in April 2013 at 8 sites in the United States.¹⁻³
^bSix real-world studies, including one of 291 patients (256 with a history of injection drug use, and 134 with drug use within ≤6 months of enrollment) treated with 1 of 5 DAA regimens between March 2014 and December 2017 at a Canadian clinic; one of 138 patients (103 with a history of injection drug use) treated with 1 of 5 DAA regimens between October 2015 and October 2017 at a Canadian clinic; one of 53 patients (45 with active injection drug use within ≤30 days) treated with 1 of 7 DAA regimens between June 2014 and December 2016 at a clinic in New York City; one of 50 Swiss patients (6 with illegal intravenous drug use) treated with DAAs between October 2014 and January 2017; one of 173 Scottish patients (129 with history of intravenous drug use) treated with 1 of 3 DAA regimens prior to September 30, 2016; and one of 50 French patients (6 with opioid injection use) treated with 1 of 5 DAA regimens from 2014 on.⁴⁻⁹

1. Dore GJ, et al. *Ann Intern Med*. 2016;165(9):625-634. 2. Grebely J, et al. *Lancet Gastroenterol Hepatol*. 2018;3(3):153-161. 3. Lalezari J, et al. *J Hepatol*. 2015;63(2):364-369. 4. Alimohammadi A, et al. *Open Forum Infect Dis*. 2018;5(6):ofy120. 5. Nouch S, et al. *Int J Drug Policy*. 2018;59:76-84. 6. Eckhardt BJ, et al. *Open Forum Infect Dis*. 2018;5(4):ofy048. 7. Scherz N, et al. Presented at: EASL, The International Liver Congress™ 2017, April 19-23, 2017; Amsterdam, The Netherlands. Poster SAT-245. 8. Boyle A, et al. Presented at: EASL, The International Liver Congress™ 2017, April 19-23, 2017; Amsterdam, The Netherlands. Poster THU-214. 9. Trabut JB, et al. *J Addict Med*. 2018;12(5):346-352.

ITT=intention-to-treat, SVR12=sustained virologic response at 12 weeks after the end of treatment.

Reinfection rates among PWID/PWUD are generally low



▶ The rate of reinfection in the PWID population (2.4/100 PY) is lower than the rate of incident HCV infection in the general population of PWID (6.1 to 27.2/100 PY).²

1. Cunningham EB, et al. *Nat Rev Gastroenterol Hepatol*. 2015;12(4):218-230. 2. AASLD/IDSA HCV Guidance. <http://www.hcvguidelines.org>. Updated May 24, 2018. Accessed August 24, 2018.

NA=not available; PYFU=person-years of follow-up.

HCV care continuum¹⁻³



A successful HCV care continuum for PWID requires strategies to improve HCV diagnosis, link infected persons with HCV care, increase treatment initiation, and increase viral cure.¹

1. Grebely J, et al. *Int J Drug Policy*. 2015;26(10):893-898. 2. Meyer JP, et al. *Int J Drug Policy*. 2015;26(10):922-935. 3. AASLD/IDSA HCV Guidance. <http://www.hcvguidelines.org>. Updated May 24, 2018. Accessed August 24, 2018.

Chronic HCV patients should be linked to care and treatment

LINKAGE TO CARE

“Ideally, treatment of HCV-infected PWID should be delivered in a multidisciplinary care setting with services to reduce reinfection risk and manage the common social and psychiatric comorbidities in this population.”
—AASLD/IDSA Recommendations for Testing, Managing, and Treating Hepatitis C¹

Current Care Pathway



Referral

- Referral to an experienced HCV clinician¹
- Multidisciplinary approach to treatment has the potential to mitigate barriers to HCV care¹

Alternative Care Pathways



ECHO/Telehealth

- Delivers service to underserved populations²
- Links specialists to communities, including rural populations²
- Similar safety and efficacy to non-telehealth settings for patients with HCV^{3,4,a}



Co-located or Integrated Care

- Reduce loss to follow-up¹
- Increase access to treatment¹

^aHCV treatments were Peg-IFN + RBV-based therapies (pre-DAA). Treatment duration was 48 weeks for GT 1 and GT 4; 24 weeks for other GTs. Studies used SVR24 as their primary endpoint.

1. AASLD/IDSA HCV Guidance. <http://www.hcvguidelines.org>. Updated May 24, 2018. Accessed August 24, 2018. 2. University of New Mexico. <http://echo.unm.edu/about-echo/model/>. Accessed April 23, 2017. 3. Arora S, et al. *N Engl J Med*. 2011;364(23):2199-2207. 4. Rossaro L, et al. *Dig Dis Sci*. 2013;58(12):3620-3625.

Peg-IFN=pegylated interferon alfa.

How to Optimize HIV/HCV Treatment Outcomes Among PWID

B. Co-Location of Services

- Co-location of mental health, substance use, social work, and pharmacy services in single venue
- HIV opioid users more likely to use buprenorphine if administered at parent HIV clinic
- HIV/HCV receiving psychiatric care at parent clinic makes adherence, compliance with visits and medication better
- Patient navigators help to guide patients with IDU, homelessness, alcohol use, mental health to better treatments with HIV/HCV

