

## Cases: Issues in Hepatitis C in Active or Recently Active Substance Abuse and Renal Failure

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IAS-USA

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### Learning Objectives

After attending this presentation, learners will be able to:

- Describe special considerations for hepatitis C treatment for people with recent history of drug use
- Describe considerations for the treatment of hepatitis C for people with advanced chronic kidney disease

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### Off-Label Disclaimer

**I will discuss the following off-label use in this presentation:**

**Treatment of acute HCV infection**

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## Case

- 21 y/o woman with congenital ureteropelvic junction obstruction progresses to ESRD requiring dialysis by age 17. PMH also notable for ADHD, anemia, growth retardation. On waiting list for deceased donor renal transplant for 2 years. She presents with new HCV Ab seroconversion upon testing at dialysis center.
  - Negative testing 1 year earlier
  - Adherent to dialysis center visits
  - Use of intermittent substances, including snorted cocaine and heroin
  - Denies injection drugs, no new tattoos, no blood transfusions for over 10 years
  - Testing shows: ALT 274 U/L, HCV RNA 35,000 IU/mL, genotype 3a
  - HIV, syphilis negative, HBSAg negative, HBSAb negative

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## ARS Question 1

21 y/o woman with congenital UPJ obstruction progresses to ESRD requiring dialysis by age 17. PMH also notable for ADHD, anemia, growth retardation. On waiting list for deceased donor renal transplant for 2 years. She presents with new HCV Ab seroconversion upon testing at dialysis center. ALT 274 U/L, HCV RNA 35,000 IU/mL

What is the most likely scenario?

1. Chronic HCV (previous false negative antibody) with cocaine-related ischemic hepatitis
2. Chronic HCV (previous false negative antibody) with alcohol use
3. Acute HCV infection due to contaminated medical equipment
4. Acute HCV infection related to opioid drug use
5. Other

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### Recommendations for One-time HCV testing

One-time HCV testing is recommended for persons born between 1945 and 1965,\* without prior ascertainment of risk.

Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection.

#### Risk behaviors

- Injection-drug use (current or ever, including those who injected once)
- Intranasal illicit drug use

#### Risk exposures

- Long-term hemodialysis (ever)
- Getting a tattoo in an unregulated setting
- Healthcare, emergency medical, and public safety workers after needles, sharps, or mucosal exposures to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of transfusions or organ transplants, including persons who:
  - Were notified that they received blood from a donor who later tested positive for HCV infection
  - Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
  - Received clotting factor concentrates produced before 1987
  - Persons who were ever incarcerated

#### Other

- HIV infection
- Unexplained chronic liver disease and/or chronic hepatitis including elevated alanine aminotransferase levels
- Solid organ donors (deceased and living)

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Adapted from <http://www.aasld.org>

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**Recommendation for HCV Testing those with Ongoing Risk Factors**

Annual HCV testing is recommended for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV.

Slide 7 of 52 • Adapted from <http://hcv.aasld.org>

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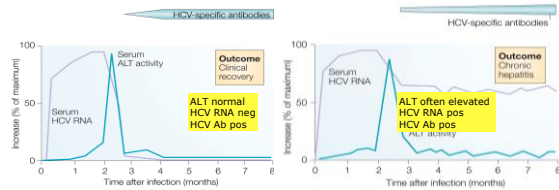
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**Outcomes of acute HCV**



Rehermann and Nascimbeni. Nat Rev Immunol 2005

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**Natural history of acute HCV**

Factors associated with viral clearance

- Female
- Young age
- Race (non-African-American)
- Immunocompetence
- Jaundice
- Cell-mediated immunity
- Genes related to the immune system
- Interleukin-28b (interferon-lambda)

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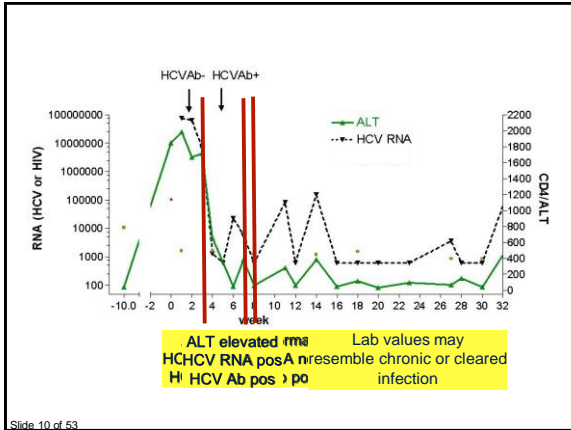
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### Diagnosing acute HCV

- Finding acute HCV requires a high clinical suspicion
- Consider in any new diagnosis with risk factors or newly elevated transaminases
- Many underreport or may not be aware of risk
- History
  - Ask about **past testing** of HCV,
  - Specifics of injection drug use (or sexual risks for HIV+MSM)
    - » Duration of behaviors, paraphernalia
  - Systematic screening results in increased identification
- Laboratory testing
  - HCV RNA even if HCV Ab negative
  - Repeat evaluations, seroconversions, viral fluctuations

Slide 11 of 53 Kim et al. Hepatology 2013

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### ARS Question 2

21 y/o woman with new diagnosis of acute HCV

Should we treat her HCV now?

1. Yes
2. No, wait for spontaneous clearance
3. No, recent drug use means she will reinfect herself after treatment

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**Recommendations for Testing, Managing, and Treating Hepatitis C**


*Recommendation Regarding HCV Treatment and Pregnancy (Whom to Treat)*

For women of reproductive age with known HCV infection, antiviral therapy is recommended before considering pregnancy, whenever practical and feasible, to reduce the risk of HCV transmission to future offspring.

**Rating:** Class I, Level B

- Women of reproductive age with HCV should be counseled about the benefit of antiviral treatment prior to pregnancy to improve the health of the mother and eliminate the low risk of mother-to-child transmission (MTCT).

Slide 13 of 52 Adapted from <http://hcvguidelines.org>

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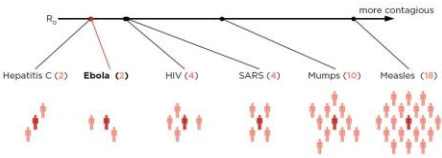
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### R<sub>0</sub> (basic reproductive number)

The number of people that one sick person will infect (on average) is called R<sub>0</sub>. Here are the maximum R<sub>0</sub> values for a few viruses.



**R<sub>0</sub> = C \* P \* D**

- **C** = # of contacts per unit of time
- **P** = probability of transmission per contact with infectious person
- **D** = duration that patient is infectious to others

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### R<sub>0</sub> (basic reproductive number)

**R<sub>0</sub> = C \* P \* D**

- **C** = # of contacts per unit of time
  - Smaller or limited networks may decrease C
- **P** = probability of transmission per contact with infectious person
  - Clean injection equipment may decrease P
- **D** = duration that patient is infectious to others
  - Behaviors that affect C and/or P amongst PWID cycle over time / locale.
  - Knowledge of infectious status may affect behaviors.
  - **Ultimately, duration of infectiousness is a major barrier as most infected persons remain infectious without treatment.**

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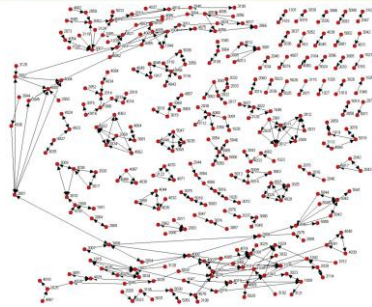
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**Treat social networks  
"Bring your friends"**



Hellard et al Hepatology 2014;  
Hellard et al JECH 2016

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**What were the effects of de-restricting access to DAAs in the Netherlands?**

**2014**

A-HCV n = 93  
Genotype 1= 75 (81%)  
Genotype 4= 18 (19%)

PYFU n = 8290

11.2/1000 PYFU  
(95% CI 9-14)

1.1% per year



**2016**

A-HCV n = 49  
Genotype 1= 34 (69%)  
Genotype 4= 15 (31%)

PYFU n = 8961

5.5/1000 PYFU  
(95% CI 4-7)

0.55% per year

- Late 2015: unrestricted access with very rapid uptake in Dutch HIV/HCV coinfection - ~70% treated
- No associated decrease in syphilis or LGV so behavior unlikely explanation
- Indirect evidence of "cure as prevention" for HCV

Rijnders et al. CROI Abstract 137LB

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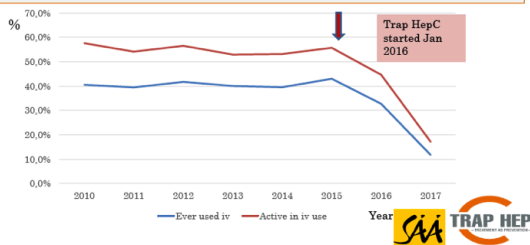
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**What were the effects of de-restricting access to DAAs in Iceland?**

**Prevalence of HCV viremia among PWID at Vogur Addiction Hospital 2010-2017 – recent iv use**



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### Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)

| RECOMMENDED  | RATING |
|--|--------|
| Annual HCV testing is recommended for PWID with no prior testing, or past negative testing and subsequent injection drug use. Depending on the level of risk, more frequent testing may be indicated.                                      | Ia, C  |
| Substance use disorder treatment programs and needle/syringe exchange programs should offer routine, opt-out HCV-antibody testing with reflexive or immediate confirmatory HCV-RNA testing and linkage to care for those who are infected. | Ia, C  |
| PWID should be counseled about measures to reduce the risk of HCV transmission to others.  | I, C   |
| PWID should be offered linkage to harm reduction services when available, including needle/syringe service programs and substance use disorder treatment programs.   | I, B   |
| Active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment.   | Ia, B  |

### Recommendation for Testing for Reinfection in People Who Inject Drugs (PWID)

| RECOMMENDED   | RATING |
|---|--------|
| At least annual HCV-RNA testing is recommended for PWID with recent injection drug use after they have spontaneously cleared HCV infection or have been successfully treated. | Ia, C  |



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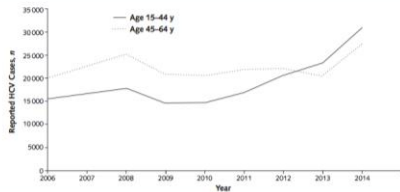
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### HCV is rising among reproductive-aged women and children in the U.S. 2006-2014

Figure. Number of reported cases of HCV infection among women aged 15-44 years and 45-64 years in the United States, 2006-2014.



Data source: Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System. HCV = hepatitis C virus.

Ly et al. Ann Intern Medicine 2017

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### ARS Question 3

Patient is ready to treat, genotype 3a  
 Fibrosure is confounded, Fibroscan shows 4 kPa  
 What would be your choice of antiviral regimen?

1. Ledipasvir/sofosbuvir x 6 weeks
2. Ledipasvir/sofosbuvir x 12 weeks
3. Elbasvir/grazoprevir x 12 weeks
4. Glecaprevir / pibrentasvir x 8 weeks
5. Glecaprevir / pibrentasvir x 12 weeks
6. Sofosbuvir / velpatasvir x 12 weeks
7. Something else

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## Treatment of HCV



"It's the only treatment option he has under his current health plan."

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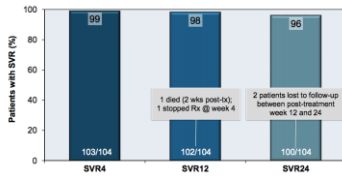
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## Glecaprevir and pibrentasvir (G/P): Renal impairment

- GT 1-6 for 12 weeks
- Stage 4 or 5 CKD
- GFR < 30 including HD
- 82% on HD
- TN or TE (42%) with IFN, P/R or SOF+P/R
- Including compensated cirrhosis (19%)
- GT1a 22%, GT1b 28%, GT2 16%, GT3 11%, GT4 19%, GT5 1, GT6 1



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Gane et al. NEJM 2017

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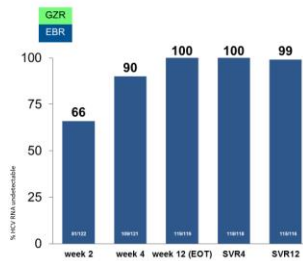
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## EBR/GZR - C-SURFER established safety and efficacy in patients with chronic kidney disease (CKD) stage 4/5



Treatment naive and experienced  
Mean age 56  
~6% cirrhosis

Hypertension or diabetes were primary etiologies  
Prior renal transplant n=17

SAE 14.4% in treatment  
SAE 16.8% in deferred



Roth et al. Lancet 2015

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Recommended regimens listed by evidence level and alphabetically for:

### Patients With CKD Stage<sup>a</sup> 4 or 5 (eGFR <30 mL/min or End-Stage Renal Disease)

| RECOMMENDED   | GENOTYPE         | DURATION                   | RATING            |
|---|------------------|----------------------------|-------------------|
| Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)                   | 1a, 1b, 4        | 12 weeks                   | I, B              |
| Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) <sup>b</sup> | 1, 2, 3, 4, 5, 6 | 8 to 16 weeks <sup>c</sup> | I, B <sup>c</sup> |

<sup>a</sup> Chronic kidney disease (CKD) stages: 1 = normal (eGFR ≥60 mL/min); 2 = mild CKD (eGFR 60-89 mL/min); 3 = moderate CKD (eGFR 30-59 mL/min); 4 = severe CKD (eGFR 15-29 mL/min); 5 = end-stage CKD (eGFR <15 mL/min).  
<sup>b</sup> This is a 3-tablet combination. Please refer to the prescribing information.  
<sup>c</sup> Patients in this group should be treated as would patients without CKD. Duration of glecaprevir/pibrentasvir should be based on presence of cirrhosis and prior treatment experience (please refer to appropriate section). As such, strength of rating may be lower for certain subgroups.



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Annals of Internal Medicine

ORIGINAL RESEARCH

### Direct-Acting Antiviral Prophylaxis in Kidney Transplantation From Hepatitis C Virus–Infected Donors to Noninfected Recipients An Open-Label Nonrandomized Trial

Christine M. Durand, MD; Mary G. Bowring, MPH; Diane M. Brown, MSN; Michael A. Chattergoon, MD, PhD; Guido Masaccesi, BS; Nichole Bair, BSN; Russell Wesson, MChB; Ashraf Reyd, MBBSCh; Fizza F. Naqvi, MD; Dario Ostrowski, PhD; Jeremy Supraman, MD; Dorry L. Segur, MD, PhD; Mark Sulikowski, MD; and Nijal M. Desai, MD

**Background:** Given the high mortality rate for patients with end-stage kidney disease receiving dialysis and the efficacy and safety of hepatitis C virus (HCV) treatments, discarded kidneys from HCV-infected donors may be a neglected public health resource.

**Objective:** To determine the tolerability and feasibility of using direct-acting antivirals (DAAs) as prophylaxis before and after kidney transplantation from HCV-infected donors to non-HCV-infected recipients (that is, HCV D/R transplantation).

**Design:** Open-label nonrandomized trial. (ClinicalTrials.gov: NCT02781649)

**Setting:** Single center.

**Participants:** 10 HCV D/R kidney transplant candidates older than 50 years with no available living donors.

**Interventions:** Transplantation of kidneys from deceased donors aged 13 to 50 years with positive HCV RNA and HCV antibody test results. All recipients received a dose of grazoprevir (GZR), 100 mg, and elbasvir (EBR), 50 mg, immediately before trans-

plantation or 3 infection had sofosbuvir, 400 mg, added to GZR-EBR for 12 weeks of triple therapy.

**Measurements:** The primary safety outcome was the incidence of adverse events related to GZR-EBR treatment. The primary efficacy outcome was the proportion of recipients with an HCV RNA level below the lower limit of quantification 12 weeks after prophylaxis.

**Results:** Among 10 HCV D/R transplant recipients, no treatment-related adverse events occurred, and HCV RNA was not detected in any recipient 12 weeks after treatment.

**Limitation:** Nonrandomized study design and a small number of patients.

**Conclusions:** Pre- and posttransplantation HCV treatment was safe and prevented chronic HCV infection in HCV D/R kidney transplant recipients. If confirmed in larger studies, this strategy should markedly expand organ options and reduce mortality for kidney transplant candidates without HCV infection.

**Primary Funding Source:** Merck Sharp & Dohme Corp.

### Recommended Treatment for Patients With Acute HCV Infection

| RECOMMENDED   | RATING |
|---|--------|
| If the clinician and patient decide that a delay in treatment initiation is acceptable, monitoring for spontaneous clearance is recommended for a minimum of 6 months. When the decision is made to initiate treatment after 6 months, treating as described for chronic hepatitis C is recommended (see <i>Initial Treatment of HCV Infection</i> ). | Ila, C |
| If a decision is made to initiate treatment during the acute infection period, monitoring HCV RNA for at least 12 to 16 weeks before starting treatment is recommended to allow time for possible spontaneous clearance.  | Ila, C |

### Recommended Regimens for Patients With Acute HCV Infection

| RECOMMENDED  | RATING |
|--|--------|
| Owing to high efficacy and safety, the same regimens that are recommended for chronic HCV infection are recommended for acute infection. | Ila, C |

### When Antiviral Therapy Is Not Recommended



| NOT RECOMMENDED  | RATING |
|--|--------|
| For patients in whom HCV infection spontaneously clears, antiviral treatment is not recommended. | III, B |



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**Recommendations for Testing, Managing, and Treating Hepatitis C**

**What are exceptions to the waiting period for acute HCV?**

- HCV transmission prevention
  - a surgeon
  - a person with ongoing intravenous drug use
  - an HIV-positive man who engages in sex with other men
- Mitigation of clinical consequences
  - a patient with cirrhosis who is acutely superinfected with HCV)
- Reduction in the likelihood of loss to follow-up
  - a patient who may not be engaged in care in 3 to 6 months)

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**Clinical trials of acute HCV with DAAs, interferon-sparing**

| Study               | Location / n                      | HIV  | GT  | Design / Regimen          | Status                 | SVR          |
|---------------------|-----------------------------------|------|-----|---------------------------|------------------------|--------------|
| DARE-C II           | Australia n=19                    | Both | All | SOF/RBV x 6 weeks         | Completed              | 32% (6/19)   |
| NYAHCNS             | NYC n=12                          | All  | 1   | SOF/RBV x 12 weeks        | Completed              | 92% (11/12)  |
| SWIFT-C Group 1     | US, multiple (ACTG) n=17          | All  | All | SOF/RBV x 12 weeks        | Completed              | 59% (10/17)  |
| SWIFT-C Group 2     | US, multiple (ACTG) n=27          | All  | 1,4 | LDV/SOF x 8 weeks         | Completed              | 100% (27/27) |
| SOL                 | Europe, multiple n=26             | All  | 1,4 | LDV/SOF x 6 weeks         | Completed              | 85% (22/26)  |
| HepNet Acute HCV IV | Europe, multiple n=20             | No   | 1   | LDV/SOF x 6 weeks         | Completed              | 100% (20/20) |
| DAHHS-2             | Netherlands/Belgium n=60          | All  | 1,4 | EBR/GZR x 8 wks           | Active, not recruiting | 98%* (62/63) |
| SAHIV               | France n=50                       | All  | 1,4 | EBR/GZR x 8 wks           | Recruiting             |              |
| REACT               | Europe/Australia/Canada/USA n=250 | Both | All | RCT SOF/VEL 6 vs 12 weeks | Recruiting             |              |
| TARGET3D            | UK, Australia, NZ / n=90          | Both | All | G/P 5 weeks then 4 weeks  | Recruiting             |              |

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Martiniello et al. Hepatology 2016; El Saeed et al. HIV Clin Trials; Nagge et al. CID 2017; Rockstroh et al. Lancet Infect Dis 2017; Detering et al. Lancet Infect Dis 2017; clinicaltrials.gov search 9/15/2018. DAHHS-2 counted reinfection as successful SVR

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**Can PWID be cured with novel HCV regimens?**

Annals of Internal Medicine ORIGINAL RESEARCH

**Elbasvir-Grazoprevir to Treat Hepatitis C Virus Infection in Persons Receiving Opioid Agonist Therapy**

**A Randomized Trial**

Gregory J. Dore, MD; Frederick Altice, MD; Alain H. Litwin, MD; Olav Dalgaard, MD; Edward J. Gane, MD; Oren Shibolet, MD; Anna Luettikemeyer, MD; Ronald Nahass, MD; Cheng-Yuan Peng, MD; Brian Conway, MD; Jason Greasley, PhD; Anita Y.M. Howe, PhD; Isaias N. Gendrano, MPH; Erluo Chen, MPH; Hsueh-Cheng Huang, PhD; Frank J. Doolko, PhD; David C. Nisckle, PhD; Bach-Yen Nguyen, MD; Janice Wahl, MD; Elvav Barr, MD; Michael N. Robertson, MD; and Heather L. Platt, MD; on behalf of the C-EDGE CO-STAR Study Group\*

Dore et al. Ann Intern Med 2016

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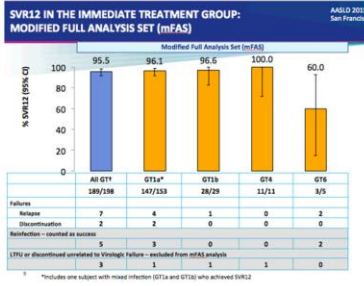
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## C-EDGE COSTAR

Treatment naive PWID on opiate agonist therapy for 3 months, keeping 80% of appointments

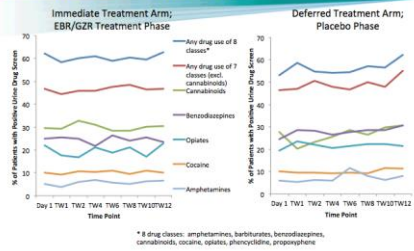


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Dore et al. Ann Intern Med 2016

## What is the rate of positive toxicology screens?

### URINE DRUG SCREEN RESULTS: DAY 1 TO TREATMENT WEEK 12

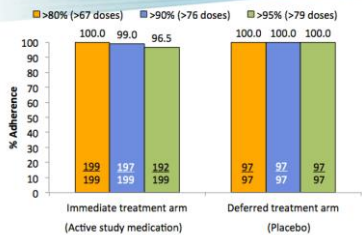


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Dore et al. Ann Intern Med 2016

## What was adherence in PWID?

### ADHERENCE



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Dore et al. Ann Intern Med 2016

## SIMPLIFY - successful treatment, 74% active injectors

- Open label, SOF/VEL x 12 weeks for chronic HCV and recent IDU
- Australia, NZ, NA, Europe

Table 1: Baseline characteristics (n=103)

|   | SOF/VEL (12 weeks)<br>n=103, n (%) |
|---|------------------------------------|
| Age <60 years                                   | 25 (24)                            |
| Female sex                                      | 29 (28)                            |
| OAT and injecting drug use (in the last month)* |                                    |
| No OAT, no injecting                            | 12 (12)                            |
| No OAT, injecting                               | 33 (32)                            |
| OAT, no injecting                               | 35 (34)                            |
| OAT, injecting                                  | 43 (42)                            |
| HCV genotype                                    |                                    |
| 1   | 36 (35)                            |
| 2   | 5 (5)                              |
| 3   | 60 (58)                            |
| 4   | 2 (2)                              |
| Fibrosis stage (METAVIR)**                      |                                    |
| F0-F1   | 59 (57)                            |
| F2-F3   | 27 (26)                            |
| F4  | 9 (9)                              |



Figure 2: Proportion of the study population who achieved ETR and SVR12. ITT analysis includes all patients who should have reached the SVR12 time point by data extraction.

Grebely et al. *Lancet Gastroenterol Hepatol* 2018

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## HCV and medication-assisted therapies

- Numerous studies show compatibility of HCV medications with methadone and buprenorphine
- Integrated analysis across phase III ION studies (ledipasvir/sofosbuvir) showed no decrement in SVR
- Naltrexone
  - No changes in dosing for mild-to-moderate hepatic impairment
  - Early studies associated naltrexone use with hepatotoxicity; however, many patients had other reasons for transaminase elevations, such as HCV
  - Later studies have suggested safety; warnings about hepatotoxicity were removed from label
- Generally, advise choosing MAT independent of HCV and liver status (except decompensated cirrhosis)

Grebely et al. *CID* 2016; <http://pcssmat.org/wp-content/uploads/2014/10/PCSS-MAT-NTX-Liver-Safety-GuideLine1.pdf>

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## Case

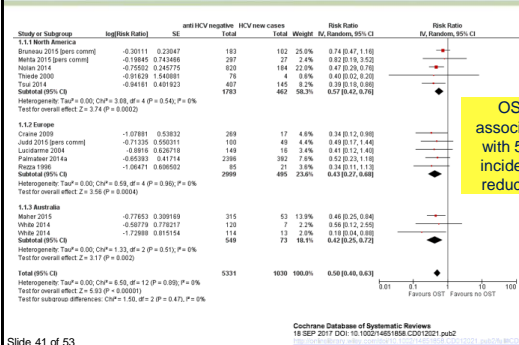
- 23 y/o woman with acute HCV infection
- Genotype 3 infection, HCV RNA doesn't clear
- She initiates therapy with G/P

What other counseling measures are important?

Liver health  
Reinfection  
Other associated risks

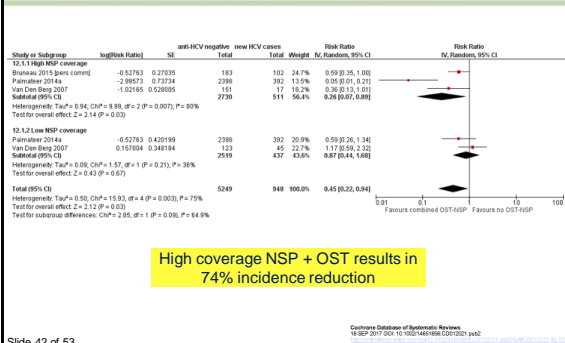
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## Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs



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## Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs



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## Contrasts in opioid abuse services

Netherlands  
pop 16.8 million



Amsterdam:  
Universal access  
to methadone & NEP

Massachusetts  
pop 6.75 million



39 methadone programs  
opioid overdose  
2x national average

Indiana  
pop 6.6 million



13 methadone programs  
# clients rose from 3,646 in 1996  
to 14,269 in 2011 to 15,500 in 2014  
58% were between 18 and 34 years old,  
44% women compared to  
just 20% women a decade ago.

Center for Health Information and Access. Access to substance use disorder treatment in Massachusetts, April 2015, available at <http://www.chiamass.gov/assets/Uploads/SUD-REPORT.pdf>  
Center for Health Policy, IUPUI. Opioid Treatment Programs in Indiana – The Use of Medication in Addiction Treatment, January 2013.

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### Outbreaks of other viruses: HAV, HBV, HIV

**Hepatitis B cases in Maine**  
Hepatitis B is an infectious disease spread primarily by sharing hypodermic needles or through sexual contact.

| Year | Cases |
|------|-------|
| 2007 | 1     |
| 2008 | 1     |
| 2009 | 1     |
| 2010 | 1     |
| 2011 | 1     |
| 2012 | 1     |
| 2013 | 1     |
| 2014 | 1     |
| 2015 | 1     |
| 2016 | 1     |
| 2017 | 27    |

**HIV CASES ON THE RISE IN S. INDIANA**

WASHINGTON COUNTY, IN | JACKSON COUNTY, IN  
FERRY COUNTY, IN | SOFTY COUNTY, IN  
CLARK COUNTY, IN

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### PWID are at risk for re-infection for HCV and other infections

- Preventive measures:
  - Parenteral exposures
    - Clean needles, syringes, cookers, cottons, water
    - Opiate agonist therapy may be protective
  - Safe tattoos
  - Sexual transmission
  - HAV & HBV immunization
  - Prevention of skin, soft tissue infections, endocarditis
    - Especially young men, watch for use of anabolic steroids

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### Reinfection incidence in PWID following SVR

| Study               | Study Design         | Country                    | n   | # reinfection | Incidence reinfection |
|---------------------|----------------------|----------------------------|-----|---------------|-----------------------|
| Dore 2016           | OST (100%)           | International, multicentre | 301 | 6             | 4.6 (1.7, 10.0)       |
|                     | Recent PWUD (58%)    | Prospective                |     |               |                       |
| Midgard 2016        | Lifetime PWID (100%) | Norway                     | 94  | 12            | 2.0 (1.0, 3.5)        |
|                     | Recent PWID (39%)    | Prospective                |     |               |                       |
| Weir 2016           | Lifetime PWID (100%) | Scotland                   | 277 | 7             | 1.7 (0.7, 3.5)        |
|                     |                      | Retrospective              |     |               |                       |
| Pineda 2015         | HIV-positive (100%)  | Spain                      | 84  | 4             | 1.2 (0.3, 3.1)        |
|                     | Lifetime PWID (86%)  | Prospective                |     |               |                       |
| Conway 2013         | Recent PWID (100%)   | Canada                     | 70  | 4             | 2.9 (1.1, 7.2)        |
|                     |                      | Prospective                |     |               |                       |
| Deshai 2013         | Recent PWID (100%)   | Canada                     | 20  | 2             | 6.3 (1.7, 20.3)       |
|                     |                      | Prospective                |     |               |                       |
| Edlin 2013          | Recent PWID (100%)   | US                         | 15  | 1             | 2.2 (0.9, 11.5)       |
|                     |                      | Not reported               |     |               |                       |
| Hilsden 2013        | Recent PWID (100%)   | Canada                     | 23  | 1             | 2.8 (0.0, 14.5)       |
|                     |                      | Prospective                |     |               |                       |
| Marco 2013          | Incarcerated (100%)  | Spain                      | 119 | 9             | 5.3                   |
|                     | Recent PWID (86%)    | Retrospective              |     |               |                       |
| Ruzic 2013          | HIV-positive (15%)   | Serbia                     | 20  | 0             | 0 (0.0, 3.7)          |
|                     | Former PWID (100%)   | Retrospective-prospective  |     |               |                       |
| Grady 2012          | Recent PWUD (100%)   | The Netherlands            | 42  | 1             | 0.8 (0.0, 3.7)        |
|                     |                      | Prospective                |     |               |                       |
| Manolakopoulos 2012 | Lifetime PWID (100%) | Greece                     | 61  | 5             | 4.1 (1.8, 9.2)        |
|                     | Recent PWID (57%)    | Retrospective              |     |               |                       |

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Martinello et al, Curr HIV/AIDS Rep 2017

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**What were re-infection rates in CO-STAR?  
Overall 2.3 reinfections / 100 person-years**

**INCREASED RISK OF REINFECTION BASED ON REPORTED INJECTION DRUG USE DURING FOLLOW-UP**

199 participants enrolled in Part B  
From the end of treatment through all available follow-up

|   |   |
|---|---|
| 74 participants (37%)<br>reported injection drug use                          | 125 participants (63%)<br>reported NO injection drug use                      |
| Rate of reinfection:<br>4.2 reinfections/100 person-years<br>95% CI: 1.5, 9.2 | Rate of reinfection:<br>0.4 reinfections/100 person-years<br>95% CI: 0.0, 2.3 |

3 of 10 re-infections cleared viremia spontaneously

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Dore et al. AASLD 2017

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**“Toolbox” for HCV prevention for PWID**

| Before exposure   | Point of transmission  | After exposure   |
|---|--|--|
| <ul style="list-style-type: none"> <li>HCV testing and counseling</li> <li>Drug treatment</li> <li>Reducing transmission from positive partners</li> <li>Vaccine</li> </ul> | <ul style="list-style-type: none"> <li>Change injecting behavior</li> <li>Clean injecting equipment</li> <li>Syringes/needles</li> <li>“extras”</li> <li>Safe injecting locations</li> </ul> | <ul style="list-style-type: none"> <li>Viral titer testing</li> <li>Antiviral treatment</li> </ul> |

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Adapted from Kim Page, UNM

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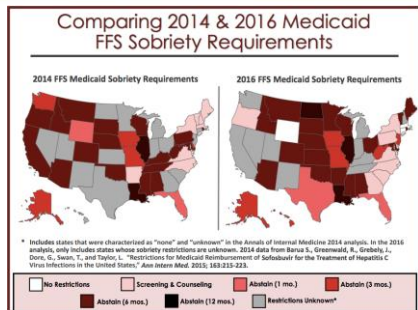
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**Restrictions often specifically exclude PWID**



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[https://www.chpi.org/wp-content/uploads/2013/12/HCV-Report-Card-National-Summary\\_FINAL.pdf](https://www.chpi.org/wp-content/uploads/2013/12/HCV-Report-Card-National-Summary_FINAL.pdf)

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## Co-localization of HCV care

- HIV/HCV co-infection clinics
- Integrated primary care/ SUD / HCV/HIV/STD care
- Training PCPs and SUD providers to treat HCV
- Training specialists that treat HCV regarding SUD
- ECHO models
- ? mobile clinics

**Perspective**  
AUGUST 24, 2017

**Stretching the Scope — Becoming Frontline Addiction-Medicine Providers**

Robert B. Rawson, M.D., and Christopher F. Rowley, M.D.

**O**n our infectious diseases (ID) consult service, we recently cared for Mr. C., a young man with *Staphylococcus aureus* (staph) culture, endocarditis, septic arthritis, and pneumonia that were consequences of his episode of acute ID. Several weeks later, he had started taking any number of pills, and eventually when the size of pills became prohibitive, had prepared an injecting heroin. His days were consumed by the struggle of the heroin he kept getting Mr. C. on the street. Despite his deep desire to stop using, he was initially an

Although Mr. C. had done well on buprenorphine in the past, accumulating several months of recovery, he first encountered the prospect of starting the process again in the days after his injecting heroin. His days were consumed by the struggle of the heroin he kept getting Mr. C. on the street. Despite his deep desire to stop using, he was initially an

As the opioid use and over-dose epidemic rages in United States, having witness to the physical and psychosocial consequences of addiction has become part of many physicians' daily work. Despite our position on the epidemic's front lines, the remarkable reality is that we remain often passively uninvolved and unchallenged in addressing our most difficult. Though we have

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Rappoport and Rowley, NEJM 2017

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## What physicians/providers can do

- Diagnosis and testing
- Screening for other infections
- Counseling about risk reduction, transmission
- Provide treatment
- Provide culturally competent care
- Don't let your clinic be the barrier!
- Build teams: enlist peers, other providers
- Advocate for harm reduction & derestricting access to DAAs



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## Conclusions and recommendations regarding HCV and PWID

- In 2018, HCV can be prevented, diagnosed, and cured for PWID
- To achieve elimination, we must:
  - Reduce silence by increasing testing and knowledge of HCV
  - Reduce stigma
  - Address substance use
  - Build structures that enhance access to comprehensive care
  - Prevent new cases, via harm reduction, medication assisted therapies, development of vaccine
  - Remove counterproductive restrictions to treatment based on lack of evidence, cost-containment, and discrimination
  - People: Enlist patients, peers, providers, policymakers

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## Question-and-Answer

Remember to raise your hand and wait until you have the microphone before you ask your question—we are recording!

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IAS-USA

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