Patrick M. Horne, MSN, APRN, FNP-BC, AF-AASLD
Assistant Director of Clinical Hepatology Research/Clinical Programs Coordinator
University of Florida
Division of Gastroenterology, Hepatology, and Nutrition
Section of Hepatobiliary Diseases

1

Disclosures

- Consulting: Abbvie and Gilead-HCV

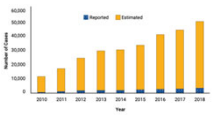
2

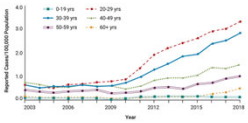
Hepatitis C Disease Burden in the U.S.

- Estimated 2.4 million infected
- Incidence increased 300% from 2009 to 2018
- 71% increase in rate of acute hepatitis C cases
  - Incidence highest in ages 20–39
- Bimodal distribution of newly reported cases in 2018
- Death rate in 2018 was 2.7 times higher for AI/AN and 1.9 times higher for blacks than whites
- U.S. has the third-highest number of HCV-related deaths after China and India

https://www.cdc.gov/hepatitis/policy/NationalProgressReport-HepC-ReduceInfections.htm.

3

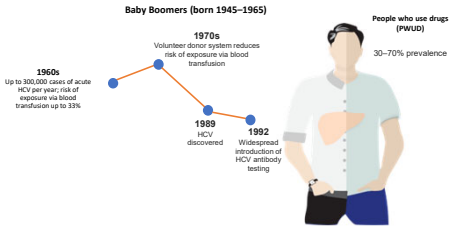




https://www.cdc.gov/hepatitis/policy/NationalProgressReport-HepC-ReduceInfections.htm.

4

Populations at Risk



Alter HJ. *Nat Med.* 2000;6:1082-1086.

5

Polling Question #1

- Which of the following is NOT a risk factor for contracting HCV:
  - A. Sharing needles
  - B. Receiving a blood transfusion in the 1980s
  - C. Drinking after someone infected with HCV
  - D. Homemade tattoos

6

Hepatitis C Risk Factors

Parenteral	Sexual	Perinatal
IVDU (most common risk factor for acute and chronic infection)	Multiple partners	High viral load
Intranasal cocaine	Traumatic sex	HIV +
Blood/blood product transfusions	HIV +	
Needle stick injury	Rectal intercourse	
Tattoos		
Body piercing		
Manicures		
Sharing household items		

7

Prevalence of HCV in HIV population

- Per the CDC, approximately 21% of adults with HIV who were tested for past or present hepatitis C virus (HCV) infection tested positive.
  - Although coinfection prevalence varies substantially according to risk group
  - As HCV is a bloodborne virus transmitted through direct contact with the blood of an infected person, coinfection with HIV and HCV is common (62%–80%) among injection-drug users who have HIV

https://www.cdc.gov/hepatitis/populations/hiv.htm

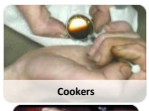
8

HCV Transmission and Recreational Drug Use

9

Transmission via Contact with Contaminated Blood: Preparation Equipment

Filters



Cookers

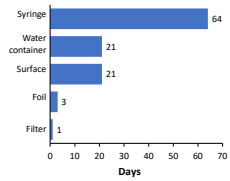
Water

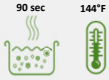
Surfaces

Zibbell J, CDC. Presented as part of Hepatitis C Prevention Opportunities Among PWID. April 28, 2015.

10

How Long Can HCV Survive on Inanimate Objects?





HCV-contaminated solution needs to be heated for almost 90 seconds and reach temperatures of 144°F for the virus to be at undetectable levels.

1. Paintsil et al. *J Infect Dis.* 2010; 2. Doerrbecker et al. *J Infect Dis.* 2011; 3. Thibault et al. *J Infect Dis.* 2011; 4. Doerrbecker et al. *J Infect Dis.* 2012; 5. Paintsil et al. *J Infect Dis.* 2014.

11

Hepatitis C and Other Drugs: More Than Just Injecting

- HCV can be spread through straws and pipes!
- HCV in nasal drug users ranges from 2.3% to 35.3%.
- HCV has been found on the stems of crack pipes.
- USPSTF and AASLD/IDSA guidance recommend screening for persons with history of intranasal drug use.
- Consider HCV in people who smoke crack or crystal meth, especially if linked to sex ("chem-sex").

1. Scheinmann et al. *Drug Alcohol Depend.* 2007; 2. Hermanstyne et al. *J Public Health.* 2012.

12

Acute HCV in the U.S.

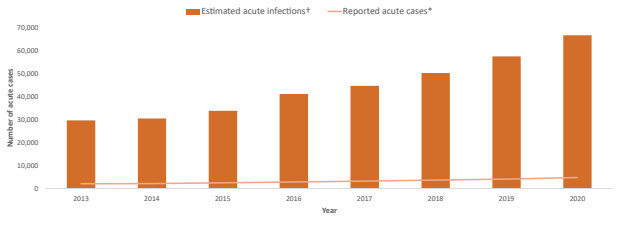
13

Polling Question #2

- The prevalence of acute hepatitis C is:
  A. Under reported
  B. Over reported
  C. Not reported

14

Figure 3.1 – Part 1 of 2
Number of reported cases* of acute hepatitis C virus infection and estimated infections† United States, 2013–2020



* Reported confirmed cases. For the case definition, see https://wwwn.cdc.gov/nndss/hepatitis-c-acute/

† The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases that met the classification criteria for a confirmed case by a factor that adjusted for underascertainment and underreporting. The 95% bootstrap confidence intervals for the estimated number of infections are displayed in the Appendix.

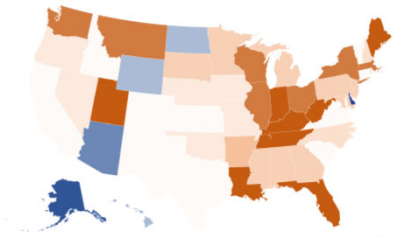
Reference: Kilmarx PH, Liu S, Roberts H, et al. Estimating acute viral hepatitis infections from nationally reported cases. Am J Public Health 2016; 106:682. PMC2951741.

Source: CDC, National Notifiable Diseases Surveillance System.

Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2020. https://www.cdc.gov/hepatitis/statistics/2020surveillance/index.htm. Published September 2022.

15

Figure 3.3
Rates* of reported cases† of acute hepatitis C virus infection, by state or jurisdiction
United States, 2020



Cases/100,000 Population

- 0.0–0.3
- 0.4–0.7
- 0.8–1.3
- 1.4–2.3
- 2.4–11.9
- No reported cases
- Data unavailable
- Not reportable

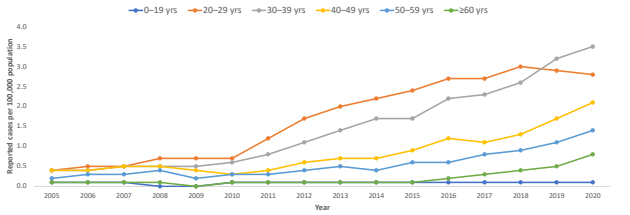
Color Key	Cases/100,000 Population	State or Jurisdiction
	0.0–0.3	NM, CA, ID, SC, TX, CO, VT, CT, KS, VA
	0.4–0.7	MO, NH, NV, IA, NE, OK, NC, OR
	0.8–1.3	MD, SD, AL, MN, PA, MI, GA, MS, NJ
	1.4–2.3	WA, IL, MT, OH, WI, NY, AR, MA
	2.4–11.9	TN, KY, UT, IN, DE, WV, LA, FL, ME
	No reported cases	HI, ND, WY
	Data unavailable	AZ, DC, RI
	Not reportable	AK

* Rates per 100,000 population.
† Reported cases that met the classification criteria for a confirmed case. For the case definition, see https://wwwn.cdc.gov/nndss/conditions/hepatitis-c-acute/

Source: CDC, National Notifiable Diseases Surveillance System.
Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2020. https://www.cdc.gov/hepatitis/statistics/2020surveillance/index.htm. Published September 2022.

16

Figure 3.4 – Part 1 of 2
Rates* of reported cases† of acute hepatitis C virus infection, by age group
United States, 2005–2020



* Rates per 100,000 population.
† Reported confirmed cases. For the case definition, see https://wwwn.cdc.gov/nndss/conditions/hepatitis-c-acute/

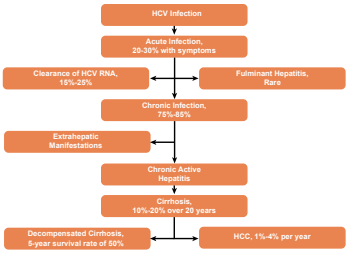
Source: CDC, National Notifiable Diseases Surveillance System.
Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2020. https://www.cdc.gov/hepatitis/statistics/2020surveillance/index.htm. Published September 2022.

17

Natural History

18

Natural History of HCV



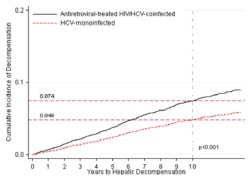
Chen & Morgan. 2006.

19

HCV-HIV coinfected patients do worse!

Worse outcomes historically

HIV infection remains independently associated with advanced liver fibrosis and cirrhosis in patients with HIV/HCV coinfection



Lo Re et al Ann Intern Med, 2014, Volume 160, Issue 6, p.369-379

Fierer et al Infect Dis, 2013, Volume 56, Issue 7, p.1038-1043

20

Screening for Hepatitis C

21

HCV Screening Recommendations

- One-time, routine HCV testing for all individuals aged 18 yeas or older
- One-time HCV testing in all persons less than 18 years old with activities, exposures, or conditions associated with an increased risk of HCV infection
- Prenatal screening in each pregnancy
- Periodic repeat HCV testing in all persons with activities, exposures, or conditions associated with an increased risk of HCV infection
- Recommended annual HCV testing for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP)

https://www.hcvguidelines.org/evaluate/testing-and-linkage.

22

People with HIV/AIDS should be vaccinated against hepatitis A and B and tested for hepatitis B and hepatitis C.

Beginning in 2020, CDC and the Advisory Committee on Immunization Practices (ACIP) began recommending that all people with HIV who are ≥1 year of age be vaccinated against hepatitis A and receive postvaccination serologic testing ≥1 month after completing the hepatitis A vaccine series.

Further, CDC and ACIP recommend that unvaccinated people with HIV receive hepatitis B vaccination. Vaccination should be followed by serologic testing to confirm adequate immune response. CDC recommends that people with HIV be tested for hepatitis B.

CDC now also recommends one-time hepatitis C testing of all adults (18 years and older), including those with HIV. CDC continues to recommend people with risk factors, like people who inject drugs, be tested regularly.

https://www.cdc.gov/hepatitis/populations/hiv.htm

23

Treatment of Hepatitis C

24

The AASLD/IDSA Recommendation for Linkage to Care

All persons with current active HCV infection should be linked to a practitioner who is prepared to provide comprehensive management.

Available at: www.hcvguidelines.org. Accessed October 11, 2022.

25

Polling Question #3

- Interferon is needed to get the highest HCV cure rates.
  A. True
  B. False

26

Principles of All Oral Regimens for HCV

- Combine drugs from different classes
  - Target multiple targets to increase efficacy
  - Decrease risk of viral resistance
- Near universal efficacy
- All oral, virtually no side effects, no interferon
  - Adverse events have minimal impact on patient's quality of life
- Methadone/buprenorphine/naloxone safe to use during therapy

27

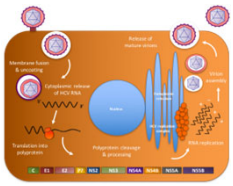
Direct-Acting Antiviral HCV Regimens

- Choice of regimen, treatment duration, and use of ribavirin depends on several factors
  - Presence/absence of compensated/decompensated cirrhosis
  - Prior treatment experience (IFN-containing vs. specific DAA classes)
  - Genotype (1–6) and subtype
  - Presence/absence of advanced kidney disease
  - Potential drug–drug interactions
- All oral, virtually no side effects, no interferon, nearly all ribavirin free
- Methadone/buprenorphine/naloxone safe to use during therapy
- Duration of HCV treatment: 8–16 weeks

28

Direct-Acting Antivirals (DAAs)

NS3/4a protease:
simeprevir
paritaprevir
grazoprevir
voxilaprevir
glecaprevir



NS5B polymerase:
sofosbuvir
dasabuvir
elbasvir
pibrentasvir

NS5A replication complex:
ledipasvir, ombitasvir, daclatasvir, velpatasvir

29

Main HCV Players Today

- Protease based regimen:
  - glecaprevir/pibrentasvir (Mavyret)
    - FDA approved for genotypes 1-6, non and well compensated cirrhosis
- Sofosbuvir based regimens:
  - sofosbuvir-ledipasvir (Harvoni)
    - FDA approved for genotypes 1, 4, 5, and 6 with or without cirrhosis as well as compensated and decompensated
  - sofosbuvir-velpatasvir (Epclusa)
    - FDA approved for genotypes 1-6 with or without cirrhosis as well as compensated and decompensated c
- A little of both
  - Sofosbuvir-velpatasvir-voxilaprevir (Vosevi)
    - FDA approved as a salvage regimen

30

Important Information Needed at Diagnosis: Consultation with a Liver Specialist

- Make sure the patient is not cirrhotic; accurate staging of liver disease is important
  - History, physical exam
  - Laboratory data:
    - Focus on platelets
    - Subtle clues: decreased albumin
  - Hepatic imaging may be suggestive of cirrhosis
    - PV diameter > 12 mm; spleen > 12 cm, liver contour, large left lobe or caudate lobe
  - Non-invasive testing:
    - FIB4 or APRI
    - Fibrosure or equivalent serum tests
    - Elastography
- Use clinical judgment to reconcile conflicting results

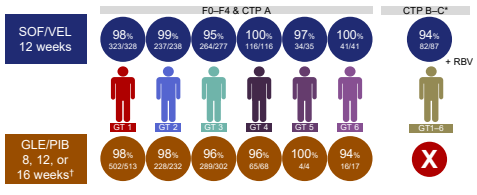
31

Hepatitis C Treatment Outcomes: Sustained Viral Response Rates

Genotype 1–6 F0-4 CTP A	Genotype 1–6 CTP B and C	Salvage Therapy
94–100%	94%	> 95%

32

High SVR Rates Achieved across Patient Types



*Safety and efficacy of SOF/VEL has not been assessed in patients with CTP class C cirrhosis; †As approved in the Canadian Product Monograph. These are not head-to-head studies, and direct comparisons cannot be made.
CTP: Child–Turcotte–Pugh; GLE/PIB: glecaprevir/pibrentasvir; GT: genotype; RBV: ribavirin; SOF/VEL: sofosbuvir/velpatasvir.
Agarwal K et al. ILC 2016 Poster #SAT-195; Gane E et al. AASLD 2017; Oral #74; Puoti M, et al. ILC 2017 Poster #SAT-233;
AbbVie Corporation. MAVIRET (glecaprevir/pibrentasvir) Product Monograph, August 2017; Gilead Sciences Canada Inc. EPCLUSA (sofosbuvir/velpatasvir) Product Monograph, April 2018.

33

Polling Question #4

- HCV-HIV co-infected patients respond differently to HCV treatment
  A. True
  B. False

34

Do HCV-HIV co-infected patient respond differently to treatment than HCV mono-infected patients?

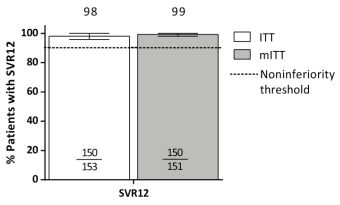
NO!!!!

35

Expedition 2 Study

Phase 3, multicenter, open-label study evaluating glecaprevir/pibrentasvir (300 mg/120 mg) in HCV genotype 1-6/HIV-1-coinfected adults without and with compensated cirrhosis for 8 and 12 weeks.

Patients were either HCV treatment-naive or experienced with sofosbuvir, ribavirin, or interferon, and antiretroviral therapy (ART) naive or on a stable ART regimen.



Breakthrough	1	1
Relapse	0	0
Missing data	1	–
Discontinued	1	–

Rockstroh et al. Clin Infect Dis. 2018 Sep 14;67(7):1010-1017.

36

ION-4 Study

A multicenter, single-group, open-label study involving patients coinfected with HIV-1 and genotype 1 or 4 HCV receiving an antiretroviral regimen of tenofovir and emtricitabine with efavirenz, rilpivirine, or raltegravir.

All patients received ledipasvir, an NS5A inhibitor, and sofosbuvir, a nucleotide polymerase inhibitor, as a single fixed-dose combination for 12 weeks. The primary end point was a sustained virologic response at 12 weeks after the end of therapy.

Response	Ledipasvir–Sofosbuvir for 12 Wk (N = 335)
	no. (%)
HCV RNA <LLOQ	
During therapy period	
At wk 2	272 (81)
At wk 4	331 (99)
After end of therapy	
At wk 4	324 (97)
At wk 12†	322 (96)
Virologic breakthrough during treatment	2 (1)
Relapse in patients with HCV RNA <LLOQ at end of therapy	10 (3)
Death	1 (<1)

Naggie et al. N Engl J Med. 2015 Aug 20;373(8):705-13.

37

ASTRAL-5 Study

A phase 3, open-label, single-arm study at 17 sites in the United States enrolled patients with HCV of any genotype and HIV-1 coinfection, including those with compensated cirrhosis.

All patients received sofosbuvir-velpatasvir once daily for 12 weeks. The primary endpoint was sustained virologic response 12 weeks after treatment (SVR12). Efficacy and safety were assessed in all patients receiving at least 1 dose of treatment.

Efficacy Analysis

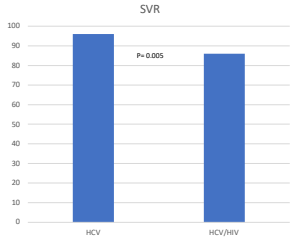
Characteristic	SOF - VEL for 12 wk (n = 106)
HCV RNA below the LLOQ during treatment, no./No. (%)	
Week 2	70/103 (68)
Week 4	95/103 (92)
Week 6	102/103 (99)
HCV RNA below the LLOQ after treatment, No. (%)	
Week 4	101 (95)
Week 12	
Overall, No. (%, 95% CI)	101 (95, 89–99)
By genotype, no./No. (%, 95% CI)	
Genotype 1a	63/66 (95, 87–99)
Genotype 1b	11/12 (92, 62–100)
Genotype 2	11/11 (100, 72–100)
Genotype 3	11/12 (92, 62–100)
Genotype 4	5/5 (100, 48–100)

Wyles, et al. Clin Infect Dis. 2017 Jul 1; 65(1): 6–12.

38

HCV/HIV Treatment Real World Outcomes

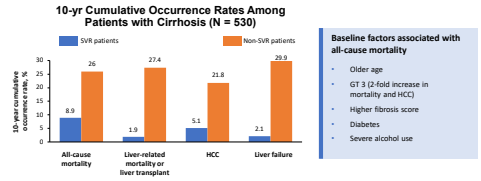
- HCV Treatment in NYC
- N= 350
  - 327 with complete datasets
  - HCV monoinfection= 253
  - HCV/HIV= 74
- Multiple DAA regimens used
- Duration- 12-24 weeks
- FACTORS ASSOCIATED WITH FAILURE in Univariate
  - Detectable HIV VL
  - Higher HCV VL
  - Lower CD4



Gayam V et al, GUT Liver, 2018

39

Impact of Antiviral Therapy



Baseline factors associated with all-cause mortality

- Older age
- GT 3 (2-fold increase in mortality and HCC)
- Higher fibrosis score
- Diabetes
- Severe alcohol use

*Median follow-up: 8.4 years.
Van der Meer A et al. *JAMA*. 2012;308:2584–2593.

40

Treatment: Safety

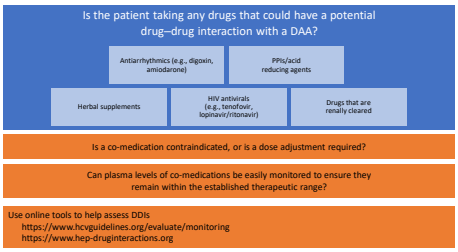
41

DAAs Can Be Safely Prescribed

- All DAAs are well-tolerated
- Minimal side effects as a class
  - Fatigue, headache, nausea (overall less than 10%)
- Avoid protease inhibitors in decompensated cirrhosis
- Be aware of potential drug–drug interactions

42

Reviewing Potential Drug–Drug Interactions Is Important



PPI = proton pump inhibitor.

43

DDIs with Sofosbuvir Based Regimens and ART

Potential Interaction
Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP)
Sofosbuvir/Velpatasvir

Quality of Evidence: Moderate

Summary:

Coadministration of emtricitabine/tenofovir-DF with sofosbuvir/velpatasvir has been shown to increase tenofovir concentrations by ~40-55% when used with an HIV regimen containing a pharmacokinetic enhancer (ritonavir or cobicistat), and also with regimens containing raltegravir, efavirenz or rilpivirine. The safety of increased tenofovir concentrations in these settings has not been established. The potential risks and benefits associated with coadministration should be considered, particularly in patients at increased risk of renal dysfunction. If other alternatives are not available, patients receiving sofosbuvir/velpatasvir concomitantly with tenofovir-DF and a boosted HIV protease inhibitor should be monitored for adverse reactions related to tenofovir-DF. No dose adjustment is recommended for patients receiving sofosbuvir/velpatasvir concomitantly with tenofovir-DF and raltegravir or rilpivirine. The increased exposure of tenofovir could potentiate adverse reactions associated with tenofovir disoproxil fumarate, including renal disorders and renal function should be closely monitored. Coadministration of sofosbuvir/velpatasvir and efavirenz containing regimens is not recommended as it is expected to decrease plasma concentrations of velpatasvir.

https://www.hiv-druginteractions.org/interactions/96963 Accessed October 11, 2022

44

DDIs with Glecaprevir/Pibrentasvir and ART

HIV-Antiviral Agents:		
Atazanavir	↑ glecaprevir ↑ pibrentasvir	Coadministration is contraindicated due to increased risk of ALT elevations *[see Contraindications (4)]*.
Darunavir Lopinavir Ritonavir	↑ glecaprevir ↑ pibrentasvir	Coadministration is not recommended.
Efavirenz	↓ glecaprevir ↓ pibrentasvir	Coadministration may lead to reduced therapeutic effect of MAVYRET and is not recommended.

Mavyret PI https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209394s000lbl.pdf. Accessed October 11, 2022

45

Use of Addiction Medications with DAA Therapy

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/ Velpatasvir/ Voxilaprevir
Buprenorphine	x	x	x	x	x
Methadone	x	x	x	x	x
Naloxone	x	x	x	x	x
Naltrexone	x	x	x	x	x

ALL ARE COMPATIBLE.

46

HBV Testing before DAA Therapy for Chronic Hepatitis C

EASL

Patients commencing DAA-based treatment for hepatitis C should be tested for HBs antigen, anti-HBc antibodies, and anti-HBs antibodies (B1).

AASLD

All patients initiating HCV DAA therapy should be assessed for HBV coinfection with HBsAg, anti-HBs, and anti-HBc (B1).

Options	Risk
HBsAg –ve/anti-HBc -ve	No risk
HBsAg –ve/anti-HBc +ve	Very low risk
HBsAg +ve/anti-HBc +ve	Moderate risk (depending on HBV DNA)

47

Important DAA Safety Information: FDA Box Warning for All DAAs

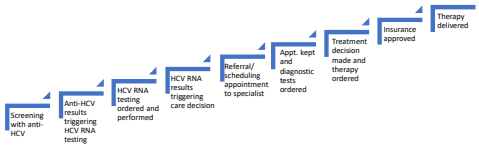
- Test all patients for evidence of current or prior hepatitis B virus (HBV) infection before initiating treatment with any DAA.
- HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV DAAs and were not receiving HBV antiviral therapy.
- Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Cases have been reported in patients who are HBsAg positive, in patients with serologic evidence of resolved HBV, and in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV DAAs may be increased in patients taking these other agents. Monitor HCV/HBV coinfected patients for hepatitis flare up or HBV reactivation during HCV treatment and post-treatment follow-up.
- Initiate appropriate patient management for HBV infection as clinically indicated.

48

Linkage to Care

49

Challenges in Screening –
Linkage to Care – Access to Treatment



50

Barriers to Care

51

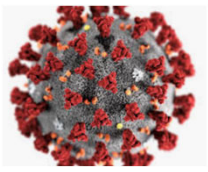
- Lack of political will and no champion
- Social stigma toward affected populations
- Lack of disease education amongst population, providers, policymakers
- Increase in acute cases
  - Opioid epidemic
  - Perinatal
- Two-step testing needed for diagnosis
  - Lack of widespread use of point-of-care testing
- Screening guidelines not universally followed

52

- Cost of testing and treatment
- No national treatment policy
  - **Restrictive state DAA policies for affected populations**
- Inadequate linkage to care and lack of treaters
- Lack of vaccine
- COVID effects

53

- Decreased screening due to lack of visits
- HCV treatment put on "back burner"
- Increased opioid and alcohol use lead to more acute cases
- Decreased state revenues to fund public health projects



54

Treatment of PWUD

55

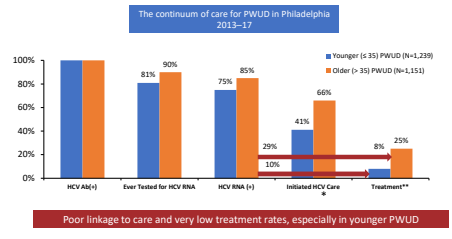
Specific Challenges Faced by PWUDs

- Stigmatization regarding diagnosis of HCV
- Poor knowledge and inaccurate perceptions about HCV infection, its long-term consequences, and associated treatment
- Perceived low need for treatment
  - Absence of noticeable symptoms
  - Belief that HCV is a "benign disease"
- In many states, restrictions on HCV medication provisions still exist
- Variations in reimbursement for HCV therapy create challenges in expanding pool of treating providers

1. Barua S, et al. *Ann Intern Med.* 2015; 163(3): 215-223. doi:10.7326/M15-0406;
2. Canary LA, et al. *Ann Intern Med.* 2015; 163(3): 226-228. doi:10.7326/M15-0320; 3. Grebely J, et al. *Nat Rev Gastro Hep.* 2017;14:641-651.

56

Continuum of Care in PWUD



*In HCV Care = seeing a specialist or having another RNA > 180 days from 1st RNA result.
**Treatment = report that treatment initiated or the infection resolved.
Addish E et al. AASLD. 2018. Abstract 1632.

57

HCV Treatment in PWUD Is a Priority

- A study determined the optimal HCV treatment prioritization strategy for IFN-free DAA regimens by disease stage and risk status incorporating treatment of PWUD.
- A dynamic HCV transmission and progression model compared the cost-effectiveness of treating patients early vs. delaying until cirrhosis for patients with mild or moderate fibrosis, where chronic HCV prevalence was 20%, 40%, or 60% in PWUD.
- Study found that **treatment of mild-to-moderate HCV in PWUD is more cost-effective than delaying treatment until cirrhosis develops.**

Martin NK et al. *J. Hepatol.* 2016;65:17–25.

58

HCV Treatment in PWUD

- Treatment has no impact on ORT or increased drug use.
- Drug use within 6 months of HCV therapy does not affect response.
- *However*, more frequent drug use decreases HCV treatment efficacy.

Social functioning and attendance are better indicators of treatment outcome, as they are independently associated with SVR after adjusting for drug use.

SLIDE PER Grebely, J.
1. Van Thiel. *AJG.* 2003; Mauss. *Hepatology.* 2004; 2. Grebely. 2nd ISHCSU, Belgium 2011; 3. Sylvestre. *JSAT.* 2005; 4. Grebely. *J Gastro Hepatol.* 2007; 5. Dore G, et al. *Gastroenterology.* 2010; 6. Matthews. *CID.* 2005.

59

HCV Elimination in Active PWUD

- Adult, active PWUD treated
- 25 cohorts, 6 countries
  - Decomp F4 and prior NS5a exposure excluded
- 340 patients, 15% F4, 73% diagnosed with a mental disorder, 27% homeless, 21% incarcerated
- Treatment adherence < 90% observed in 24 patients (8%)
- 86 patients either lost to follow-up (79%) or had non-virologic failure
- SVR-12 was 98% in the remaining 254 patients

Teti E et al. AASLD 2020. #915.

60

Antiviral Therapy Guidelines in PWUD

AASLD/IDSA

Recent/active IDU should *not* be seen as contraindication to HCV therapy.[1]

EASL

Treatment should be prioritized in those at risk of transmitting HCV, *including* active PWUD, due to the high risk of transmission.[2]

1. www.hcvguidelines.org. 2. EASL. *J Hepatol.* 2018.

61

High Rates of HCV Reinfection and Retreatment in a Cohort of PWUD with HCV Cure: Two-Year Follow-Up Data (ANCHOR Study)

- ANCHOR is a prospective cohort study evaluating PWUD with chronic HCV, opioid use disorder, and ongoing injection drug use.
- Study set in a syringe service program in the DC area.
- 82 SVR patients were followed for a median of 96 weeks.
- Reinfection after SVR was defined as genotype switch or new detectable viral load after SVR.
- 9 patients (10.9%) were reinfected.
- Reinfection was not associated with reported opioid agonist therapy or drug use.

Kattakhuzy S et al. AASLD 2020. #968.

62

Reinfection

- 4114 HCV-infected patients treated with DAAs who achieved SVR and had ≥ 1 subsequent HCV RNA measurement were analyzed.
- 40 reinfections (defined as a positive RNA measurement after SVR) were identified.
- Reinfection rates were higher among recent and former PWUD vs. non-PWUD:
  - Recent PWUD (3.1/100 PYs; IRR 6.7; 95% CI 1.9–23.5)
  - Former PWUD (1.4/100 PYs; IRR 3.7; 95% CI 1.1–12.9)
  - Non-PWUD (0.3/100 PYs)

Rossi C et al. *J Hepatol.* 2018;69:1007-1014. doi: 10.1016/j.jhep.2018.07.025.

63

Overcoming Barriers to Care

64

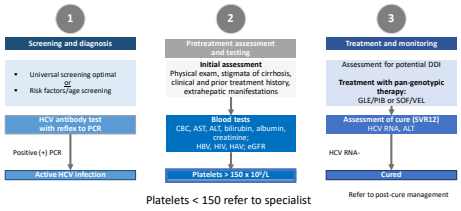
Barrier	Solution
Lack of political will and no champion	Remains to be seen
Social stigma toward affected populations	Educate public, but more difficult in today's political climate
Lack of disease education amongst population, providers, policymakers	Widespread education
Opioid epidemic	Harm reduction programs and rehab programs
Perinatal	Screen and treat during pregnancy
Two-step testing	Develop and implement POC testing
Screening guidelines not universally followed	Mandate?

65

Barrier	Solution
Cost of testing and treatment	Eliminate co-pays, provide gratis if not insured
No national treatment policy	Remove all state-imposed barriers and enact policy to treat everyone with HCV with DAAs
Linkage to care and lack of treaters	Expand to PCPs, NP/PA, pharmacists
Lack of vaccine	Research and development
COVID	Hopefully it will go away

66

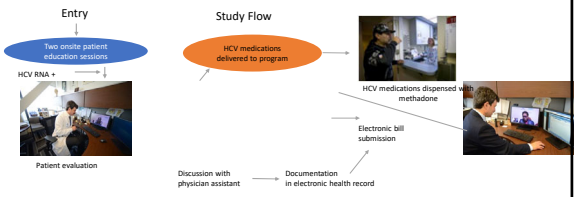
Simplified Algorithm for Management of Hepatitis C Infection



Dieterich et al. *Gastroenterology & Hepatology*. volume 15, issue 5, supplement 3, May 2019.

67

Overcoming Barriers: Telemedicine-Based HCV Evaluation



Talal AH et al. *Clin Infect Dis*. 2019;69:323-331. doi: 10.1093/cid/ciy899.

68

Conclusions

- Prevalence of chronic HCV remains steady.
- Incidence of acute HCV continues to increase.
- Harm reduction programs are needed to prevent acute HCV infections.
- DAA cure is achieved in > 95% of cases.
- For the first time, HIV co-infected patients have the same cure rates.
- DAA therapy is safe and well-tolerated.
- DAA therapy reduces mortality from liver and extra-hepatic causes.
- Barriers to HCV treatment remain in the U.S.
- Screening and linkage to care remain the bottleneck to HCV cure.
- Treatment of HCV-infected PWUD is recommended, is effective, and is an important step toward reduction of HCV infections and eventually eradication.

69

Thank you!

70