Integrating Hepatitis C Treatment Into Routine Treatment of Substance Use Disorders

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Disclosure Information (Required)

- Presenter 1: Deanna Wilson, MD, MPH
  - No Disclosures
- Presenter 2: Divya Venkat, MD
  - No disclosures
- Presenter 3: Hannah Cawoski, PharmD
  - No disclosures
- Presenter 4: Stephanie Klipp, RN, CAAP, CARN
  - No disclosures

Learning Objectives

- Review the epidemiology and burden of hepatitis C in populations with substance use disorders.
- Identify the health-related consequences associated with hepatitis C infection.
- Explain the treatment options and review guidelines related to initiation of Hepatitis C pharmacotherapy and monitoring.
- Identify challenges, strategies, and best practices to engage specific sub-populations into Hepatitis C treatment as part of office-based substance use disorder treatment.

TC

- 29 yo woman presents to first clinic session at your office-based addiction treatment clinic
- She reports actively injecting IV heroin/fentanyl
  - Uses 15-20 bags per day
  - Started misusing opioids after MVA at age 15, transitioned to heroin at 17 and started injecting at 19
- Is interested in buprenorphine-naloxone maintenance
  - You give her instructions and prescription for home-based induction

Audience poll: Do you test her for hepatitis C?

- Yes, but should wait until she has at least 6 months abstinent from opioids so you can then offer treatment if positive
- Yes, and you should obtain bloodwork as soon as possible
- No, unlikely to be positive and she is too young for general screening guidelines
- No, because she denies any symptoms

Audience poll: Do you test her for hepatitis C?

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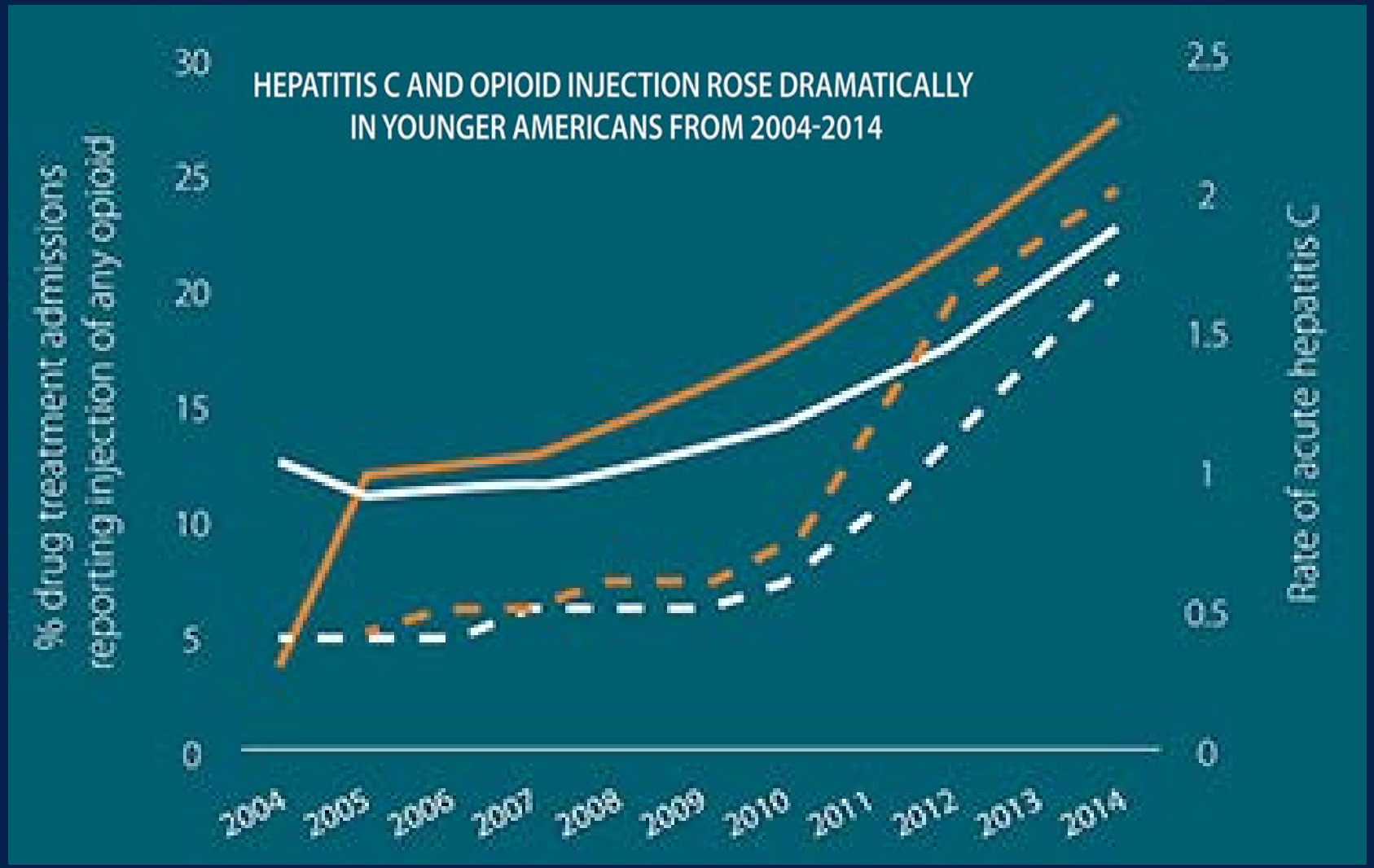
It is Best Practice to Test for HCV

- Most commonly reported bloodborne infection in US
  - 3.5 people in US with HCV
- IDU is primary risk factor for exposure
  - 39%- 77% prevalence depending on population with IDU
- Associated with significant morbidity and mortality
  - Leading cause for liver transplant and liver cancer in United States
  - Kills more people annually than HIV
- Now treatable with highly effective cure

Latimer, et al, 2009; NIDA, 2000; Trickey, et al, 2019; Ly, et al, 2016

Rising rates of HCV as surrogate for IDU



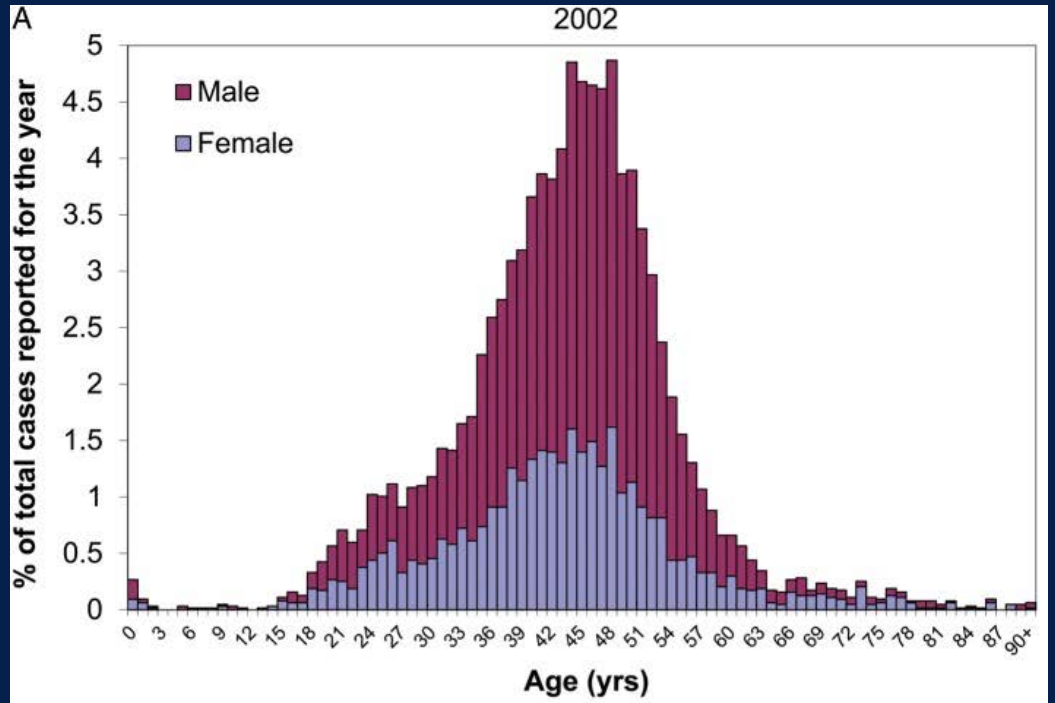
- Among people aged 18-29, HCV increased by 400% and admission for opioid injection by 622%

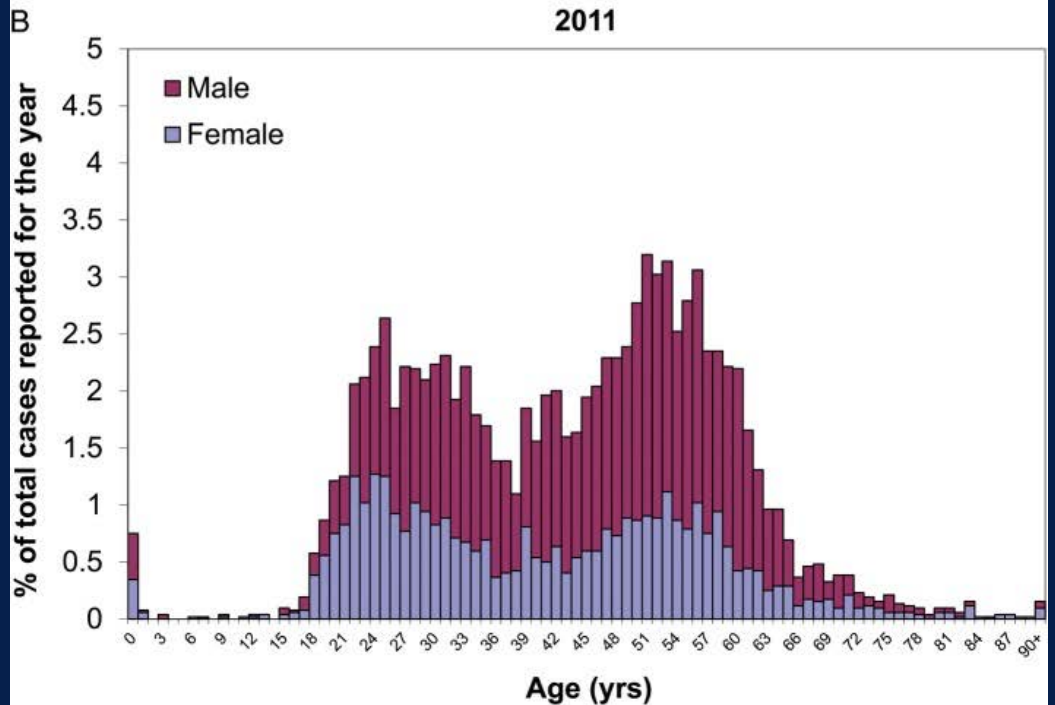
Any Opioid Injection (18-29)
Any Opioid Injection (30-39)
HCV Rate (18-29)
HCV Rate (30-39)

181,871 reported cases of chronic HCV and 33,900 estimated cases of acute HCV in 2015

https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html

HCV shifting to bimodal age distribution.





Kim AY, et al, 2013

Mechanisms of Infection

- Bloodborne infections transmitted through contaminated needles/syringes, cookers, tourniquets
- Accidental needle sticks from used syringes/needles
- Oral or skin bacteria introduced through unsterile practices of injection
  - Contaminated water to dissolve opioids
  - Dirty cookers or cotton used as filter
- Engaging in unprotected sexual contact
  - Higher risk of transmission for anal sex
- Increased engagement in transactional sex or sex work

Hepatitis C

- Single-strange, positive-sense RNA virus
  - At least seven genotypes; GT1 most common in US
- Most with acute HCV are asymptomatic or have mild clinical illness
  - Jaundice 20-30%
  - Avg time from exposure to symptoms is 2-12 weeks
- Antibodies positive within 4-10 weeks after infection
- HCV RNA indicates current infection—within 1-2 weeks after exposure

Schillie S, et al, 2020

Natural History of HCV

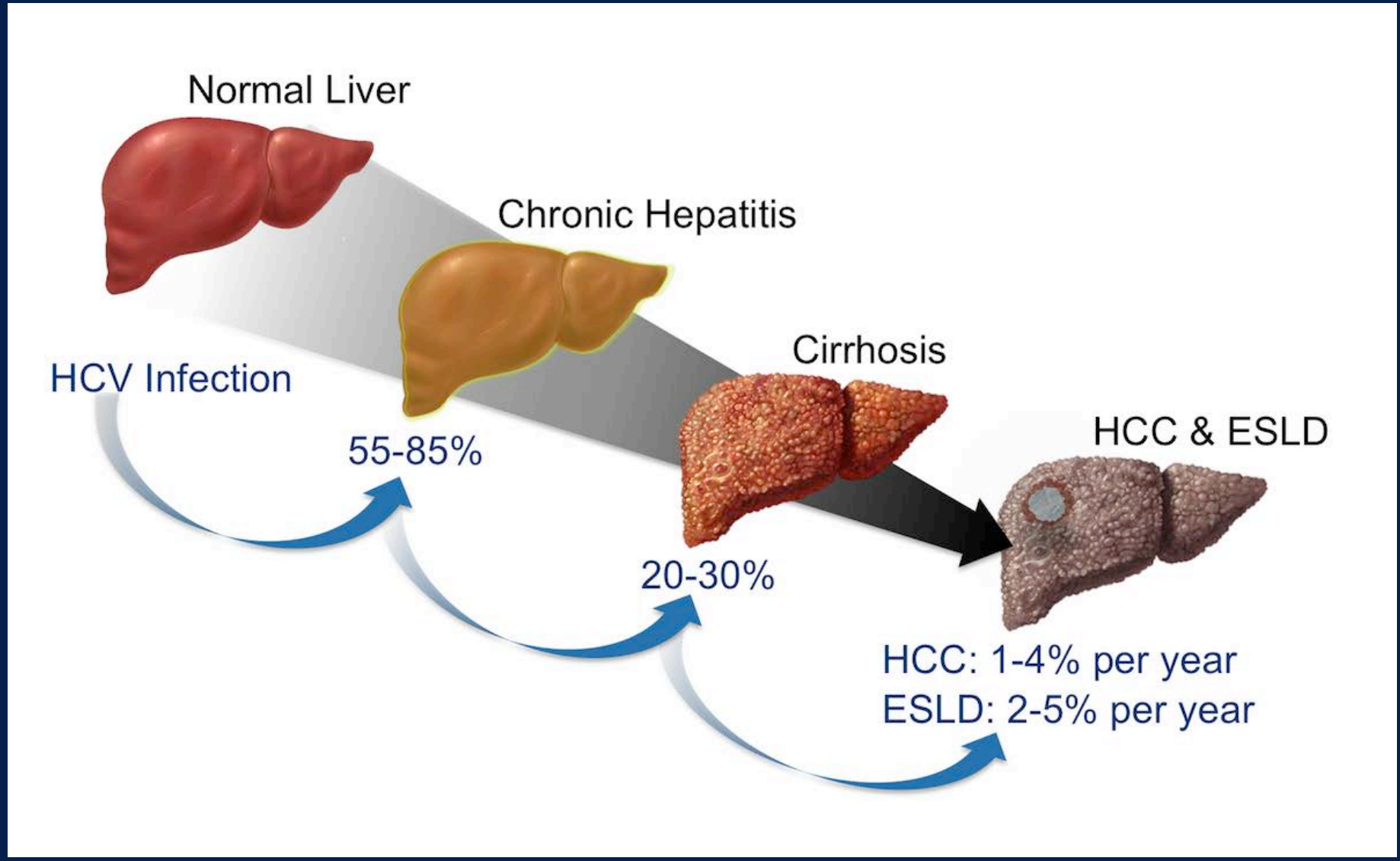
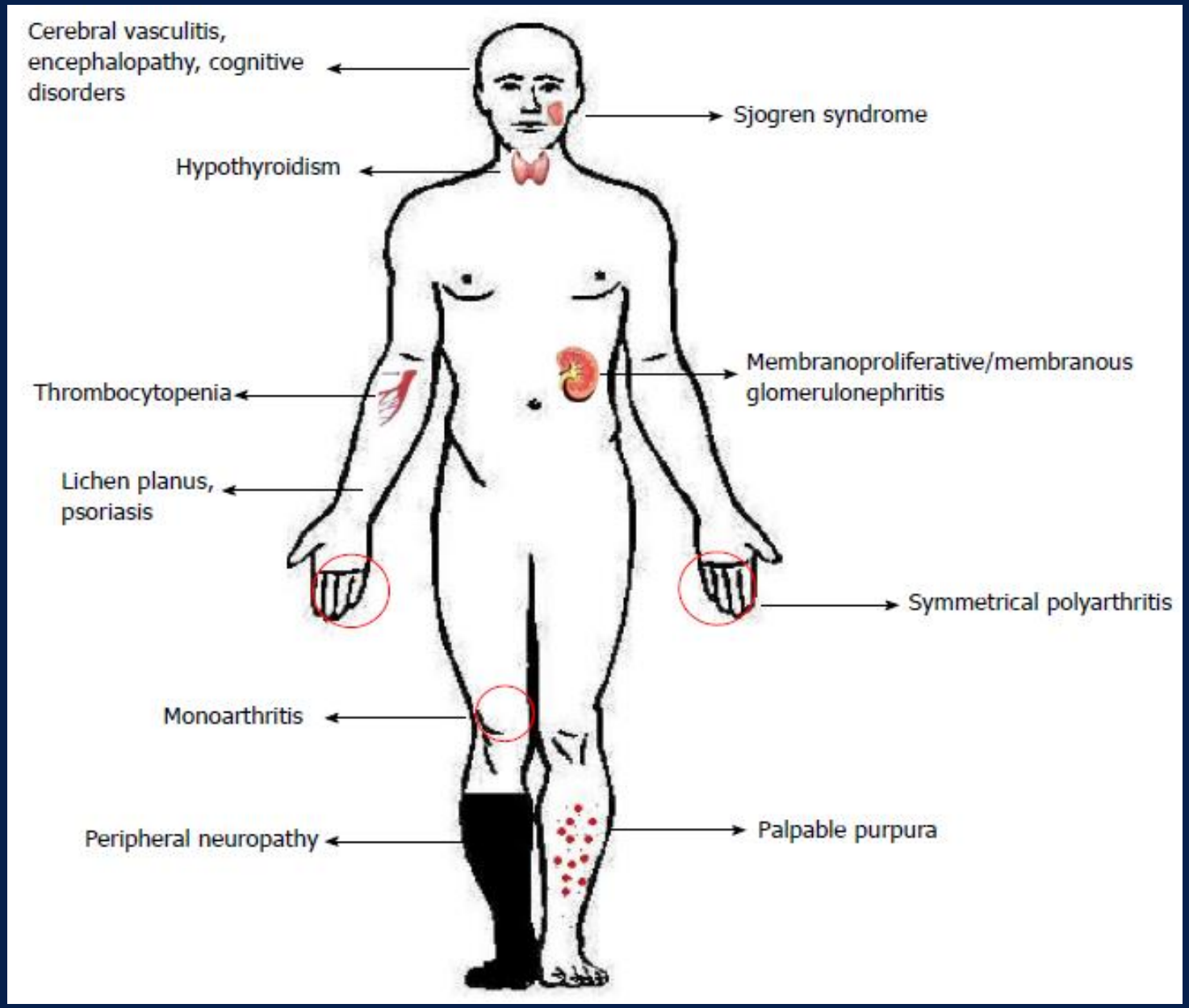


Figure source: Lingala S, Ghany MG. Natural History of Hepatitis C. Gastroenterol Clin North Am. 2015;44:717-34.

Extrahepatic manifestations of HCV



Tampaki, Koskinas; 2014

Audience poll

- What characteristics associated with TC do NOT suggest a higher risk for spontaneous clearance (versus developing chronic hepatitis)?
  - White
  - Female
  - Age at infection
  - Infected via injection drug use
  - Reported symptomatic “hepatitis” (at age 20)

Audience poll

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  - White
  - Female
  - Age at infection
  - **Infected via injection drug use**
  - Reported symptomatic “hepatitis” (at age 20)

Ly, et al, 2016

Audience poll

- Who should be screened for Hepatitis C?
  - People born between 1945-1965
  - People born between 1945-1965 and people actively using intravenous drugs
  - Adults aged 18 to 79 years
  - People with a history of IV drug use and those actively using intravenous drugs

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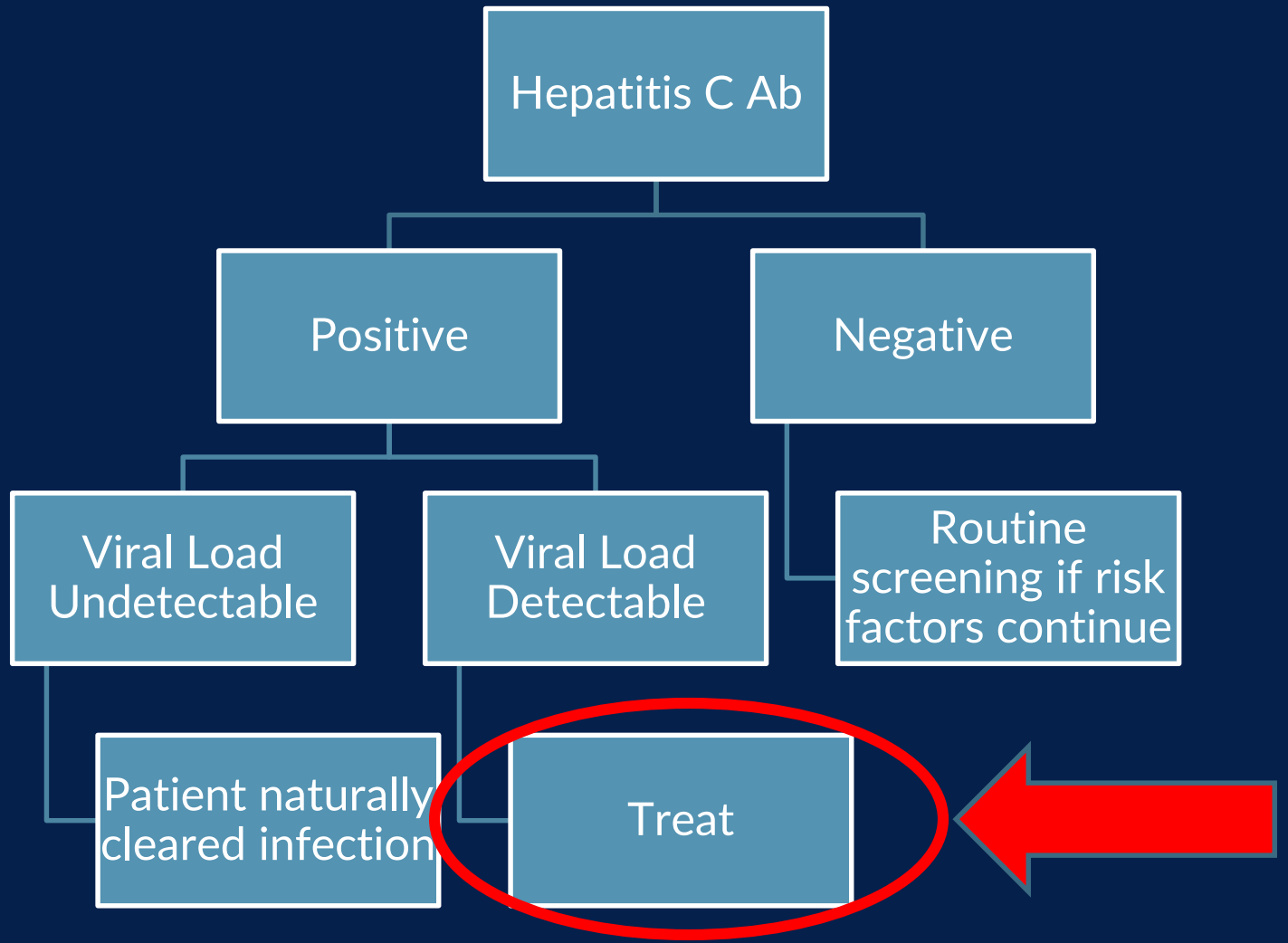
  - **Adults aged 18 to 79 years**
  - People with a history of IV drug use and those actively using intravenous drugs

Screening for Hepatitis C

Population	Recommendation	Grade
Adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B

USPSTF, 2020

Initial Screening



Initial Labs

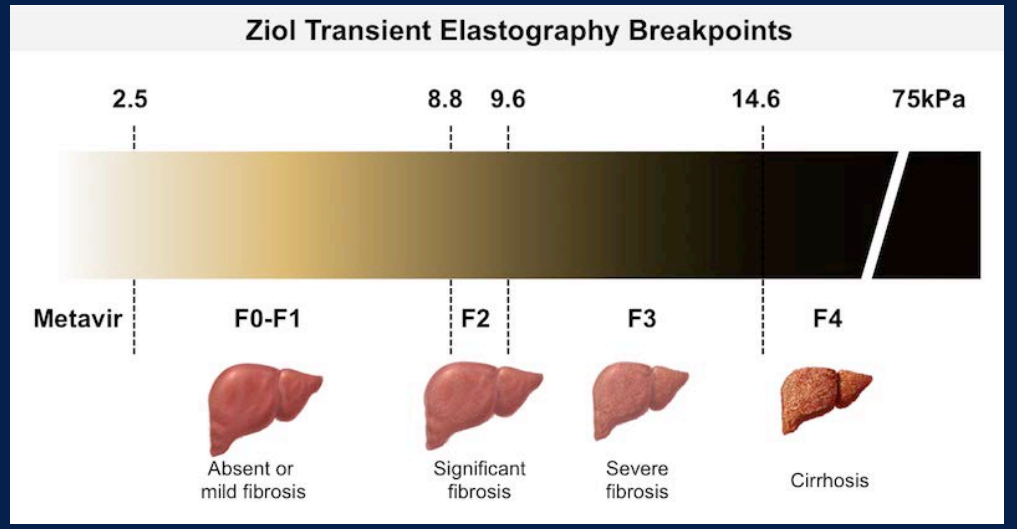
- Hepatitis C Genotype
- Fibrosure/Fibroscan
- HIV p24 antigen/antibody
- CBC with differential
- CMP
- PT/INR
- Pregnancy test if applicable
- Hepatitis A antibody
- Hepatitis B surface antigen, surface antibody, core antibody

Hepatitis vaccinations

- If Hepatitis A antibody negative, vaccinate prior to treatment initiation
- If Hepatitis B core antibody, surface antibody, and surface antigen are negative, vaccinate prior to treatment initiation

Review of Fibrosure and Fibroscan

- Fibrosure:
  - Blood test and quantitative marker for fibrosis
- Fibroscan:
  - Transient elastography using ultrasound
- Scored from F0 to F4
- F4 indicated cirrhosis



Cox-North, 2018

Checklist

Labs and Image Check List:

	Hepatitis C Genotype Results:
	HCV PCR
	Fibrosure/Fibroscan Results: If cirrhosis presented, compensated? Yes/no
	HIV P24 Antigen/antibody Results:
	CBC with Diff
	CMP
	PT/INR
	Pregnancy test Results:
	Hep A ab total Need Vaccine? Yes/no
	HBsAg, HBsAb, HBcAb Need Vaccine? Yes/No

Counseling

- Access to medications
- Social Determinants of Health screening
- Substance use history

ARTICLES | VOLUME 3, ISSUE 3, P153-161, MARCH 01, 2018

Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial

Jason Grebely, PhD • Prof Olav Dalgard, MD • Brian Conway, MD • Evan B Cunningham, PhD • Philip Bruggmann, MD • Behzad Hajarizadeh, PhD • et al. Show all authors

Grebely, 2018

Pharmacology

FDA Approved Medications

Hepatitis C Medication for Treatment-Naïve, Noncirrhotic Patients			
Genotype	Medication Combination	Duration of Treatment	Compensated Liver Cirrhosis (Child-Pugh A)
Genotype 1, 4, 5, 6	Sofosbuvir/Ledipasvir with or without Ribavirin	8 to 12 weeks	✓
All Genotypes	Sofosbuvir/Velpatasvir	12 weeks	✓
All Genotypes	Glecaprevir/Pibrentasvir	8 to 12 weeks	✓

Mavyret. Package Insert. AbbVie Inc; 2017.
Harvoni. Package Insert. Gilead Sciences, Inc; 2019.
Epclusa. Package Insert. Gilead Sciences, Inc; 2016

Pharmacology Simplified

Adult Patients with Chronic Hepatitis C (NO Cirrhosis and Treatment Naïve)		
All Genotypes	Glecaprevir (300 mg) / pibrentasvir (120 mg)	• 8 weeks of treatment • Take daily with food
All Genotypes	Sofosbuvir (400 mg) / velpatasvir (100 mg)	• 12 weeks of treatment • Take with or without food

AASLD and IDSA, 2020.

Pharmacology Simplified

Adult Patients with Chronic Hepatitis C (Compensated Cirrhosis (Child-Pugh A) and Treatment Naïve)		
Genotypes 1, 2, 3, 4, 5, 6	Glecaprevir (300 mg) / pibrentasvir (120 mg)	• 8 weeks of treatment • Take daily with food
Genotypes* 1, 2, 4, 5, 6	Sofosbuvir (400 mg) / velpatasvir (100 mg)	• 12 weeks of treatment • Take with or without food

*Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir.

AASLD and IDSA, 2020.

Drug-Drug Interactions (glecaprevir and pibrentasvir)

Drug Class	Effect of interaction
Antiarrhythmics: • Digoxin	↑ digoxin
Anticoagulants: • Dabigatran etexilate	↑ dabigatran
Anticonvulsants: • Carbamazepine	↓ glecaprevir ↓ pibrentasvir
Antimycobacterials: • Rifampin	↓ glecaprevir ↓ pibrentasvir
Ethinyl Estradiol-Containing Products: • Ethinyl estradiol containing medications such as combined oral contraceptives	↔ glecaprevir ↔ pibrentasvir

Mavyret. Package Insert. AbbVie Inc; 2017.

Drug-Drug Interactions (glecaprevir and pibrentasvir)

Drug Class	Effect of interaction
Herbal Products: • St. John's wort (hypericum perforatum)	 ↓ glecaprevir ↓ pibrentasvir
HIV-Antiviral Agents: • Atazanavir • Darunavir • Lopinavir • Ritonavir • Efavirenz	 ↑ glecaprevir ↑ pibrentasvir ↑ glecaprevir ↑ pibrentasvir ↑ glecaprevir ↑ pibrentasvir ↑ glecaprevir ↑ pibrentasvir ↓ glecaprevir ↓ pibrentasvir

Mavyret. Package Insert. AbbVie Inc; 2017.

Drug-Drug Interactions (glecaprevir and pibrentasvir)

Drug Class	Effect of interaction
HMG-CoA Reductase Inhibitors: • Atorvastatin • Lovastatin • Simvastatin • Pravastatin • Rosuvastatin • Fluvastatin • Pitavastatin	 ↑ atorvastatin ↑ lovastatin ↑ simvastatin ↑ pravastatin ↑ rosuvastatin ↑ fluvastatin ↑ pitavastatin
Immunosuppressants: • Cyclosporine	 ↑ glecaprevir ↑ pibrentasvir

Mavyret. Package Insert. AbbVie Inc; 2017.

Drug-Drug Interactions (sofosbuvir and velpatasvir)

Drug Class	Effect of interaction
Acid Reducing Agents: • Antacids • H2-receptor antagonists • Proton-Pump Inhibitors	↓ velpatasvir
Antiarrhythmics: • Amiodarone • Digoxin	Effect on amiodarone, sofosbuvir, and velpatasvir concentrations unknown ↑ digoxin
Anticancers: • Topotecan	↑ topotecan
Anticonvulsants: • Carbamazepine • Phenytoin • Phenobarbital • Oxcarbazepine	↓ sofosbuvir ↓ velpatasvir

Epclusa. Package Insert. Gilead Sciences, Inc; 2016

Drug-Drug Interactions (sofosbuvir and velpatasvir)

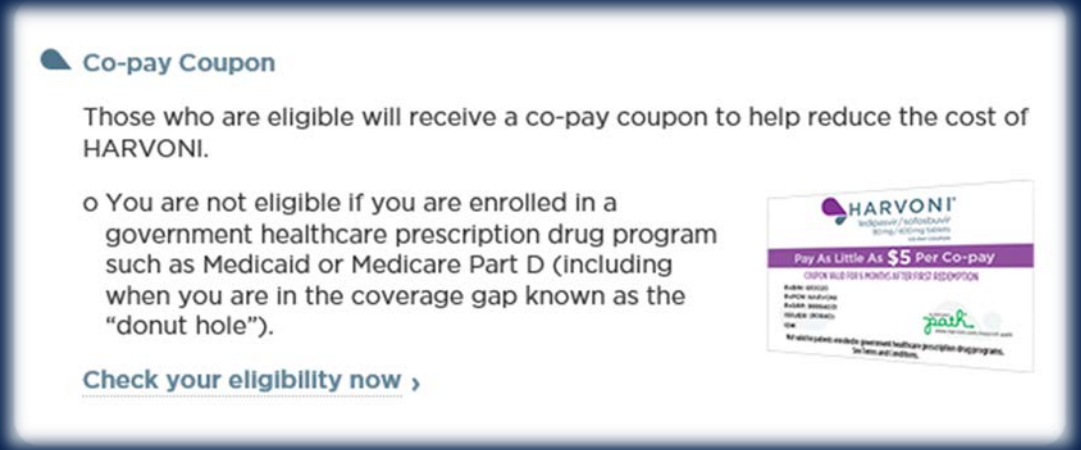
Drug Class	Effect of interaction
Antimycobacterials: • Rifabutin • Rifampin • Rifapentine	↓ sofosbuvir ↓ velpatasvir
HIV Antiretrovirals • Efavirenz • Regimens containing tenofovir DF • Tipranavir/ritonavir	 ↓ velpatasvir ↑ tenofovir ↓ sofosbuvir ↓ velpatasvir
Herbal Supplements: • St. John's wort (Hypericum perforatum)	↓ sofosbuvir ↓ velpatasvir
HMG-CoA Reductase Inhibitors: • Rosuvastatin • Atorvastatin	 ↑ rosuvastatin ↑ atorvastatin

Epclusa. Package Insert. Gilead Sciences, Inc; 2016

Assistance Programs

- Utilize patient support phone numbers or websites
- Prior Authorizations to help patients get medications approved through insurance
- Assistance for uninsured patients
- Utilize specialty pharmacies who assist with the prior authorization process, shipping of the medication, and patient phone call follow-ups

Assistance Programs



HEPCONNECT

- Primary focus:
  - Expand screening and linkage to care
  - Support harm reduction and community education
  - Activate healthcare infrastructure

- Indiana, North Carolina, Tennessee, West Virginia

FOCUS (Frontline of Communities in the U.S.)

- A public health initiative that aims to
  - Decrease the stigma underlying viral testing and diagnosis
  - Bring HCV screening and linkage to care into alignment with the Centers for Disease Control (CDC), the U.S. Preventative Services Task Force (USPSTF), and state and local health department guidelines

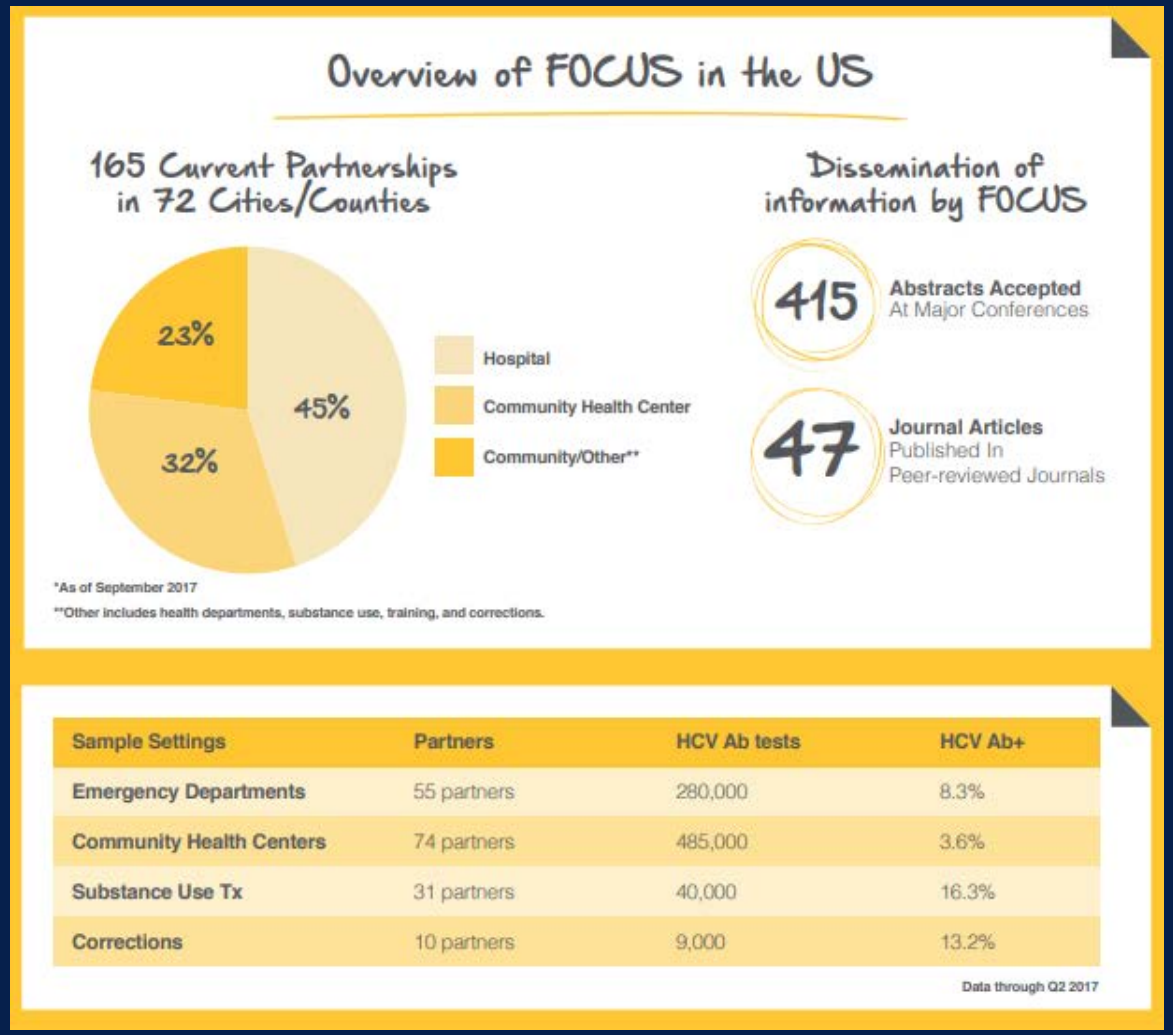
Gilead, 2020

FOCUS (Frontline of Communities in the U.S.)

- 2010: initiation of screening and linking to care for HIV
- 2014: HCV testing added to program
- 2016: 300,000 HCV tests were completed in 21 counties
- 2017: 1,000,000 HCV tests were completed in 45 counties

Ozaeta, 2017
Sajed, et al, 2017.

FOCUS (Frontline of Communities in the U.S.)

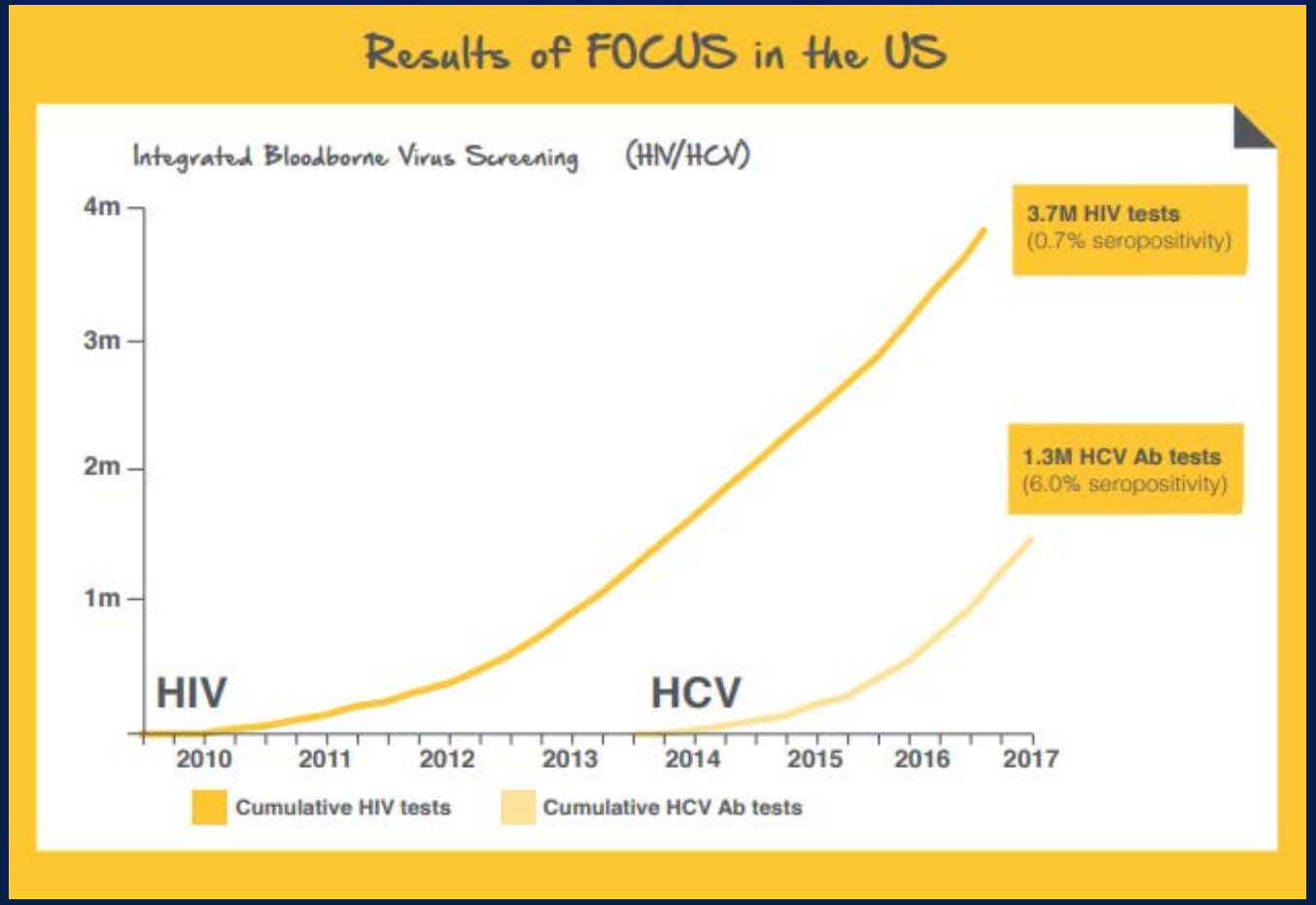


Sample Settings	Partners	HCV Ab tests	HCV Ab+
Emergency Departments	55 partners	280,000	8.3%
Community Health Centers	74 partners	485,000	3.6%
Substance Use Tx	31 partners	40,000	16.3%
Corrections	10 partners	9,000	13.2%

Data through Q2 2017

Sajed, et al, 2017.

FOCUS (Frontline of Communities in the U.S.)



Sajed, et al, 2017.

Hepatitis C Project ECHO

- Virtual session for primary care providers to increase the treatment of HCV in the under-served population
- *Community HCV teleECHO meets every Wednesday 3-5 pm MST*
- Submit blinded patient cases for review by experts

Hepatitis C Project ECHO

Project ECHO® (Extension for Community Healthcare Outcomes)

HCV Community Initial Case Presentation Form

Presentation Date:_____ Site:_____ Clinician:_____

General Information/Demographics

Patient ECHO ID:	**Age:**	**Sex at Birth:** ☐Male ☐Female	**Gender Identity:**
Race: ☐ American Indian or Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian / Other Pacific Islander ☐ White			**Ethnicity:** ☐ Hispanic or Latino ☐ Not Hispanic or Latino
Insurance: ☐ None ☐ Medicare ☐ Medicaid, MCO (if in NM, please specify: ☐ Presbyterian ☐ BCBS ☐ Western Sky ☐ Unknown) ☐ Commercial Health Insurance ☐ Other:_____			

Liver Related History	☐ Cirrhosis	Any evidence of clinical decompensation? ☐ Ascites ☐ Hepatic Encephalopathy ☐Variceal Bleed
	☐ Previous HCV Treatment	Year: Drug Regimen: Duration of Treatment:
	☐ Hepatocellular Carcinoma	Year of Diagnosis:

Medical Diagnoses	☐ Diabetes Mellitus ☐ Hepatitis B, Chronic ☐ HIV ☐ Other Relevant Diagnoses:	☐ Seizure Disorder ☐ Solid Organ Transplant --- Year: Organ: ☐ Rheumatoid Arthritis

Psychiatric Diagnoses	☐ Depression ☐ Anxiety ☐ Other:

UNM and Project ECHO, 2019

Special Cases

Returning to use

- 28 year-old man with history of severe opioid use disorder and was on bup-nx 16 mg daily treated in combined primary care and OBOT program
- Shortly after connecting to your clinic, he was treated for HCV with SVR.
- Had been in sustained remission for the past two years, but had recent return to use in setting of increased stressors and worsening MH 2/2 COVID. Missed his last two appointments for MOUD.
- Patient presented to clinic today to receive treatment for an abscess in hand. Reports that he has returned to regular IDU. Does not want to stop right now nor does he want to start MOUD again. Reports actively injecting daily, and sharing needles.

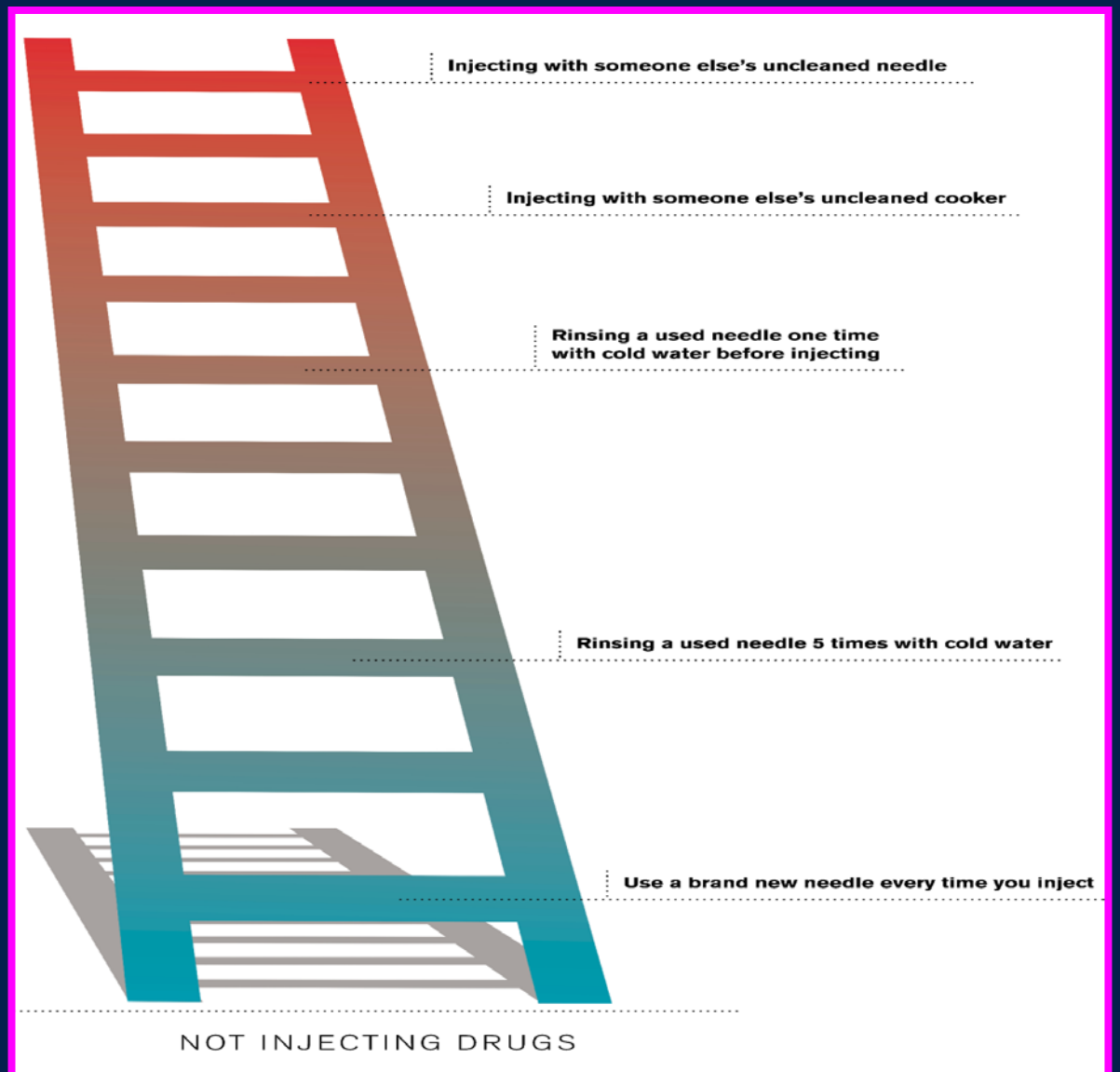
Returning to use

- What do you do for this patient?

- Narcan and overdose prevention education
- Referral to needle and syringe exchange
- Safe injection practices

So what do you say?

- Be concrete
- Recognize the goal is to help move people from more to less harmful behaviors

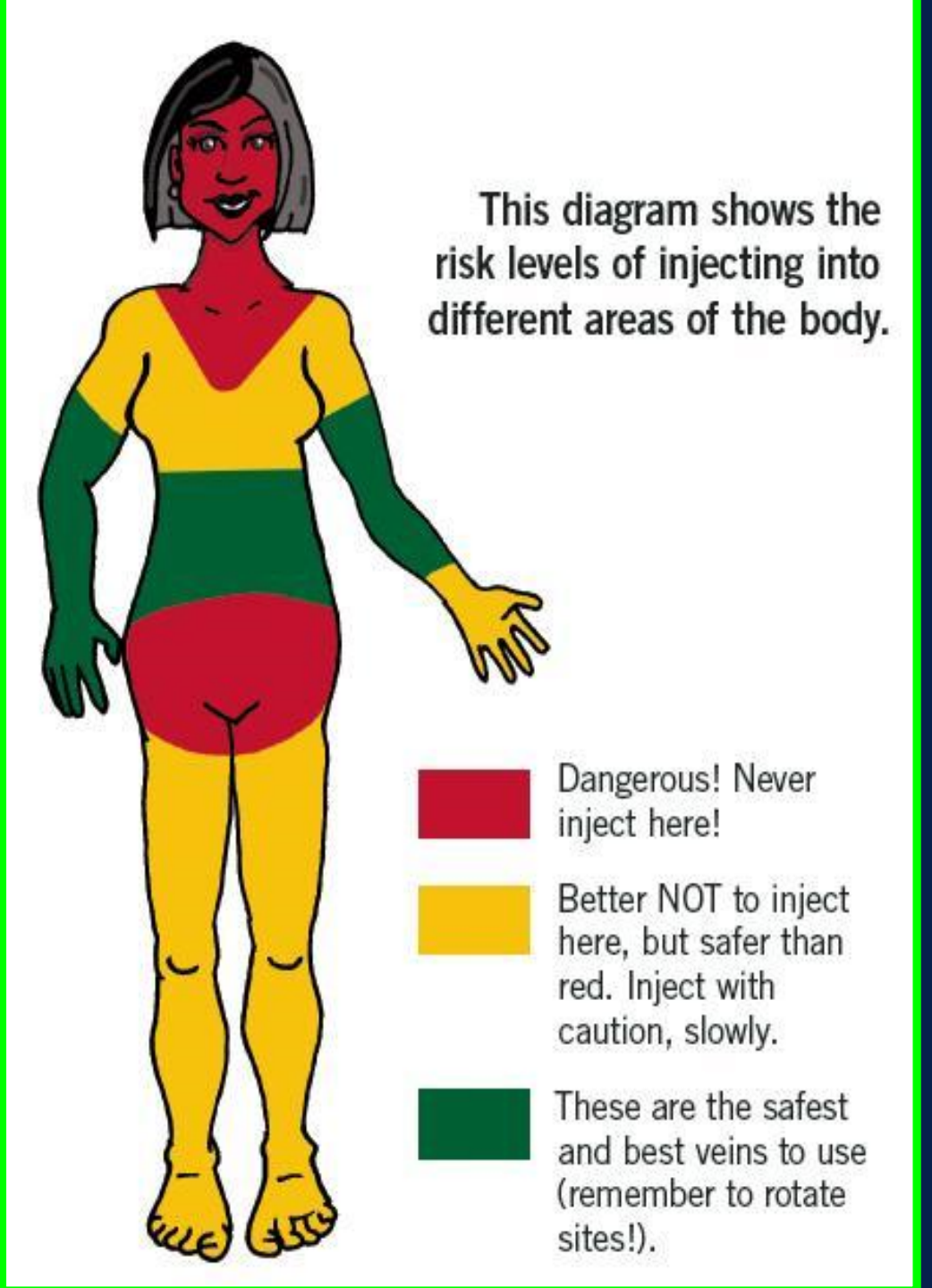


Safe injection education

- Choose safe place to inject
  - Access to clean water
  - Safe from crime/risk of arrest
- Have a partner and alternate use (in case of overdose)
  - Have naloxone available and someone sober to give it
- Carefully choose materials
  - Most use 25 to 28 G needles
    - Smaller the size puncture wound, less risk for infection
    - If many impurities (e.g. tar heroin), will need larger needle

"Getting off right." Harm Reduction Coalition, 2021.

Choose safer injecting sites



"Getting off right." Harm Reduction Coalition, 2021.

Safe injection education

- One shot= one new needle and syringe
  - If using needle again for even a few uses, it will become more dull
    - Results in larger puncture wound
    - Sharpening needle can lead to burr→ cause damage to veins or break off in vein
- No sharing needles, syringes, cookers, spoons, cottons
  - Even sharing non-needles can lead to HIV and HCV transmission

"Getting off right." Harm Reduction Coalition, 2021.

Safe injection education

- If you HAVE to reuse needle or syringe
  - Flush with cold water immediately after using
  - Then flush with undiluted bleach (2 min)
    - Necessary for 2 minutes to kill HBV (Unclear if kills HCV)
  - Rinse with cold water to remove bleach
- Cottons (filters)
  - 100% cotton from q-tip or cotton ball is cleanest
  - Rayon and synthetic fibers don't absorb as well
  - Cigarette filters not safe to use
  - Needs to be fresh every time you shoot up– "cotton fever"

"Getting off right." Harm Reduction Coalition, 2021.

Safe injection practices

- Use sterile water to dissolve drug
- If no sterile water, then can boil water for 10 minutes and seal in a jar
- If no boiled water, then fresh, cold tap water or bottled water
- If no sink, then water from toilet tank (NEVER BOWL)
- Wash hands prior to injecting with soap and water
- Clean skin prior to injecting with alcohol wipe

"Getting off right." Harm Reduction Coalition, 2021.

- 33 year old F with severe opioid use disorder, on buprenorphine maintenance
- She was diagnosed with HCV five years ago
- Recent recent screening confirmed positive for HCV, with a + viral load.
- Patient was interested in pursuing treatment for HCV due to inc in fatigue, but at her next visit her POC HCG is positive
- Patient reports that she as been trying to get pregnant, but is scared about passing HCV to her infant
- What do we do for this patient?

HCV On Pregnancy Outcomes

- Findings mixed—increased risk of adverse perinatal outcomes (eg, preterm delivery, LBW infants) with maternal HCV infection
  - BUT confounded by comorbid SUD
- Pregnant women with cirrhosis ARE at inc risk for poor maternal and neonatal outcomes
  - Should be referred to Maternal Fetal Medicine
- Maternal child transmission of HCV
  - 5% to 15%
    - 3% to 5% develop chronic HCV
  - Ok to breastfeed if no bleeding nipples/skin breaks
  - No specific risk factor predicts transmission and no specific intervention (eg, antiviral, mode of delivery, or others) has been demonstrated to reduce HCV transmission

Pulijic, 2016; Tan 2008; Jhaveri, 2015; Shebl, 2009; Mast, 2005; Ceci, 2001; AASLD-IDSA, 2021

Repeat HCV RNA after delivery

- Spontaneous clearance of HCV can occur in the postpartum period.
  - Up to 10% of postpartum women became HCV RNA undetectable
  - A 25% rate of spontaneous resolution that was strongly associated with the favorable IL28B allele
  - Re-test HCV RNA after delivery
- Refer for postpartum treatment

Honegger, 2013; Hatttori, 2003; Lin, 2000; Hashem 2017; AASLD-IDSA, 2021

- A 42 yo F with 22 years of IV opioid us
- She is newly engaged into treatment for OUD and just completed her fourth week of starting bup-nx maintenance
- She stopped injecting completely, hasn't used illicit opioids in two weeks, and is feeling better and is now interested in screening for her HCV
- Patient's antibody screening come back for HCV and HIV as positive, and the reflex with a + viral load of each.
- Patient is overwhelmed by the news of this co-infection, and is unsure about what do?
- **What do we do for this patient?**
- Refer to GI for Hepatology, patient's with co-infection may experience significant or rapid onset of liver damage, and new special considerations when deciding on treatment. Also refer for treatment of HIV (eligible for tx at time of diagnosis)

AASLD-IDSA, 2021

- 54 year old M who is homeless presents for initial visit for bup-nx induction
- Patient actively using IDU methamphetamines and heroin
- Interested in getting tested for bloodwork as recent outbreak of Hep A at his encampment

Laboratory findings

- HCV with a positive viral load
- Hep A + antibody positive
- Hep B surface antigen positive, HBV core antibody positive

Review of hepatitis B

Interpretation of Hepatitis B Serologic Test Results				
HBsAg	**Anti-HBc**	**IgM Anti-HBc**	**Anti-HBs**	**Interpretation**
–	–	–	–	Susceptible to HBV infection
–	+	–	+	Immune due to natural hepatitis B infection
–	–	–	+	Immune due to hepatitis B vaccination
+	+	+	–	Acute HBV
+	+	–	–	Chronic hepatitis B infection
–	+	–	–	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

Figure from: https://www.hiv.uw.edu/go/co-occurring-conditions/hepb-coinfection/core-concept/all

Audience poll: What do you offer patient?

- Treat the hep B, then treat the hep C
- Refer out to hepatology
- Treat the hep C, then treat the hep B
- Do not treat HCV due to active use, refer to GI for Hep B treatment

Managing HBV and HCV Coinfection

- Worldwide prevalence of coinfection1–15%.
- Faster progression of disease
  - Faster to rate of cirrhosis
  - Higher rates of Hepatocellular carcinoma d
- HCV viral replication in coinfected cells is typically dominant over HBV replication
- **Treatment of HCV without suppression of HBV increases the risk for HBV reactivation**

Mavilia , Wu, 2018.

Managing HBV and HCV Coinfection

- Low or undetectable HBV DNA can receive prophylactic HBV tx for duration of treatment until SVR12
- OR
- Check q4weeks for HBV reactivation with HBV DNA testing
  - Start treatment if >10-fold or >1000 IU/mL
- Refer to GI/Hepatology/ID

Mavilia , Wu, 2018.

Who should we refer?

- Decompensated cirrhosis
- HIV or Hepatitis B co-infection
- Suspicion for hepatocellular carcinoma
- Concern for other liver diseases
- History of organ transplant

- Patient is 61 year-old male in treatment for about a year on 8 mg bup-NX BID
- Patient endorses he was interested in hep c screening, and provider ordered testing.
- Patient had positive ab and RNA and decided to start treatment.
- Patient started his oral regiment, and at his 4-week set of labs, patient's viral load was almost the same as beginning or treatment. At 8 weeks the patient's viral load had increased again, and at 12 weeks, the viral load had increased substantially.
- What do we do for this patient?

Unexpected responses to therapy

- Drug-drug interactions
- Adherence to medication
- Not taking as recommended
  - Are they taking with meal (required depending on drug)?
- Other possible liver pathologies
- Concerns for resistance
  - Would need referral to GI/Hepatology for resistance testing

Final Takeaways

- HCV is the most common bloodborne disease in the US
  - Higher prevalence among populations that use drugs
- New treatments are highly effective and straightforward for providers to integrate into routine office-based substance use disorder treatment
- Active drug use is NOT a contraindication to successful treatment
- Most populations can be treated safely in non-specialty settings, but consider referral for pregnant women, patients with comorbid HBV or HIV, or patients with an atypical response to treatment

References

1. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, 2021. https://www.hcvguidelines.org/sites/default/files/full-guidance-pdf/AASLD-IDSA_HCV-Guidance_TxN-Simplified-Tx-No-Cirr_e.pdf. Accessed March 2, 2021.
2. CDC. Hepatitis C and opioid injection, 2017. https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html. Accessed March 4.
3. Ceci O, Margiotta M, Marello F, et al. Vertical transmission of hepatitis C virus in a cohort of 2,447 HIV-seronegative pregnant women: a 24-month prospective study. *J Pediatr Gastroenterol Nutr*. 2001;33(5):570-575.
4. Cox-North P, Schuhart M. Evaluation and Staging of Liver Fibrosis. Hepatitis C Online, University of Washington 2018. https://www.hepatitisc.uw.edu/go/evaluation-staging-monitoring/evaluation-staging/core-concept/all. Accessed February 27, 2021.
5. Epclusa. Package Insert. Gilead Sciences, Inc; 2016
6. Gilead. HepConnect 2020. https://www.gilead.com/purpose/partnerships-and-community/hepconnect. Accessed March 2, 2021.
7. Gilead. HCV Elimination 2020. https://www.gilead.com/purpose/advancing-global-health/hcv-elimination#:~:text=The%20FOCUS%20Program%20is%20a,state%20and%20local%20health%20department. Accessed March 2, 2021.
8. Grebely J, Dalgard O, Conway B, et al. Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. *Lancet Gastroenterol Hepatol*. 2018;3(3):153-161. doi:10.1016/S2468-1253(17)30404-1
9. Harvoni. Package Insert. Gilead Sciences, Inc; 2019.

10. Hashem M, Jhaveri R, Saleh DA, et al. Spontaneous viral load decline and subsequent clearance of chronic HCV in postpartum women correlates with favorable IL28B allele. *Clin Infect Dis*. 2017;65(6):999-1005.
11. Hattori Y, Orito E, Ohno T, et al. Loss of hepatitis C virus RNA after parturition in female patients with chronic HCV infection. *J Med Virol*. 2003;71(2):205-211.
12. Honegger JR, Kim S, Price AA, et al. Loss of immune escape mutations during persistent HCV infection in pregnancy enhances replication of vertically transmitted viruses. *Nat Med*. 2013;19(11):1529-1533.Jhaveri, 2015;
13. Kim AY, Onofrey S, Church DR. An epidemiologic update on hepatitis C infection in persons living with or at risk of HIV infection. *J Infect Dis*. 2013;207 Suppl 1(Suppl 1):S1-S6. doi:10.1093/infdis/jis927 Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults — United States, 2020. MMWR Recomm Rep 2020;69(No. RR-2):1–17. DOI:
14. Latimer WW, Hedden SL, Floyd L, et al. Prevalence and correlates of Hepatitis C among injection drug users: The significance of duration of use, incarceration and race/ethnicity. *J Drug Issues*. 2009;39(4):893-904. doi:10.1177/002204260903900406Lin HH, Kao JH. Hepatitis C virus load during pregnancy and puerperium. *BJOG*. 2000;107(12):1503-1506.
15. Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising Mortality Associated With Hepatitis C Virus in the United States, 2003-2013. *Clin Infect Dis*. 2016;May 15;62(10):1287-1288. doi: 10.1093/cid/ciw111. Epub 2016 Mar 1. PMID: 26936668.
16. Mavilia MG, Wu GY. HBV-HCV Coinfection: Viral Interactions, Management, and Viral Reactivation. *J Clin Transl Hepatol*. 2018;6(3):296-305. doi:10.14218/JCTH.2018.00016
17. Mavyret. Package Insert. AbbVie Inc; 2017.
Mast EE, Hwang L-Y, Seto DSY, et al. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. *J Infect Dis*. 2005;192(11):1880-1889.
18. NIDA. (2000, March 1). Facts About Drug Abuse and Hepatitis C. Retrieved from https://archives.drugabuse.gov/news-events/nida-notes/2000/03/facts-about-drug-abuse-hepatitis-c on 2021, February 28

19. Ozaeta M. FOCUS: (On the) Frontline of Communities in the U.S. http://paetc.org/wp-content/uploads/2017/10/A.-Integrating-HEP-C-with-HIV-Care-Programs.pdf. Accessed March 2, 2021.
20. Sajed N, Hutchison K, Rossaro L, et al. Support of Global Ef
21. Puljic A, Salati J, Doss A, Caughey AB. **Outcomes of pregnancies complicated by liver cirrhosis, portal hypertension, or esophageal varices**. *J Matern Fetal Neonatal Med*. 2016;29(3):506-509.
22. forts Toward Elimination of Hepatitis C Virus. https://www.gilead.com/-/media/files/pdfs/other/hcv-infographic.pdf?la=en&hash=F1E4CE9BF88246ACFCDD319EC9B0F2D4. Accessed March 2, 2021.
23. Shebl FM, El-Kamary SS, Saleh D'aA, et al. **Prospective cohort study of mother-to-infant infection and clearance of hepatitis C in rural Egyptian villages**. Abdel-Hamid M, Mikhail N, Allam A, et al., eds. *J Med Virol*. 2009;81(6):1024-1031.
24. Tampaki M, Koskinas J. Extrahepatic immune related manifestations in chronic hepatitis C virus infection. *World J Gastroenterol* 2014; 20(35): 12372-12380
25. Tan J, Surti B, Saab S. **Pregnancy and cirrhosis**. *Liver Transpl*. 2008;14(8):1081-1091.
26. The University of New Mexico 2021. https://hsc.unm.edu/echo/institute-programs/hcv-community/. Accessed March 2, 2021.
27. The University of New Mexico and Project ECHO 2019. https://hsc.unm.edu/echo/_docs/program-docs/hcv_initial_form.pdf. Accessed March 2, 2021.
28. Trickey A, et al. The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. *The Lancet*. 2019; 4(6):P435-444.
29. US Preventive Services Task Force, Owens DK, Davidson KW, et al. Screening for Hepatitis C Virus Infection in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement [published online ahead of print, 2020 Mar 2]. *JAMA*. 2020;10.1001/jama.2020.1123. doi:10.1001/jama.2020.1123