Viral Disease in Addiction Medicine

A Review of HIV and HCV Best Practices

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Disclosures

I have no conflicts of interest to declare.
I will discuss (and identify) off-label use of medication.
Brand names are used for drug recognition and do not imply endorsement.

Objectives

One

After participating in this session, attendees should be able to apply current screening recommendations for viral disease in patients living with addiction.

Two

After participating in this session, attendees should be able to prescribe HIV prophylaxis for patients with increased risk of sexual or injection-related transmission

Three

After participating in this session, attendees should be able to evaluate patients for HCV infection and consider starting treatment in appropriate patients.

I:

Epidemiology and screening

Epidemiology

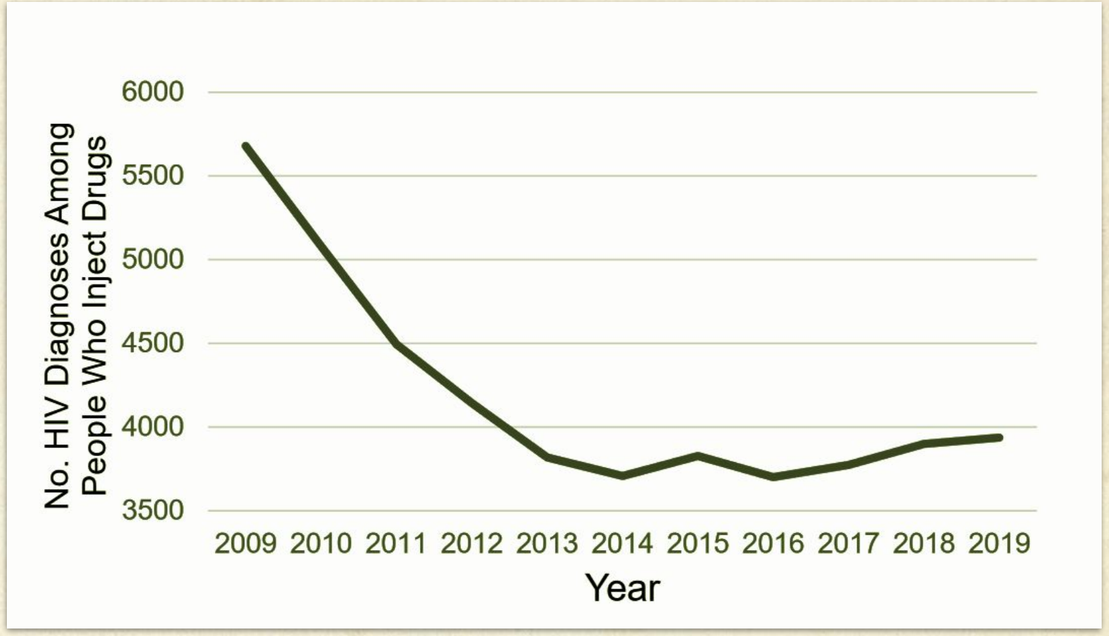
- Substance use is viewed as a significant risk factor for the development of both HIV and HCV
- While we often associate the transmission of viral disease with injection drug use, studies have shown elevated risk for HIV and HCV in patients who use non-injection drugs.
- The presence of Alcohol Use Disorder has been shown to be a risk for HCV positive patients to not receive treatment compared to peers
- Nationally, the trend has shifted overwhelmingly toward sexual transmission of HIV (89% of new cases in 2021) compared to injection drug use.
- In contrast, national data for HCV shows injection drug use to be the most common risk factor (57% of new cases in 2021) identified in cases where risk data was reported.
- In 2022, Minnesota reported 262 new cases of HIV and an estimated 32,543 patients with chronic HCV

Understanding “syndemics”

- Clustering of diseases (eg. substance use disorder and HIV) can be viewed through the framework of a *syndemic*, or a synergistic interaction between multiple epidemics which have shared determinants
- Beyond simple clustering and epidemiology, the syndemic framework tries to unite the health consequences of disease (eg. HIV/AIDS) with the social, economic, and environmental factors which drive those diseases (eg. poverty, low access to education)
- The association between substance use and HIV has been long known, prompting study of the “SAVA” syndemic beginning in the 1990s (Substance Abuse, Violence, and AIDS/HIV)
- While we often view viral disease as a consequence of specific behaviors (such as sharing injection supplies or poor clinical follow-up), these diseases share determinants beyond behavior such as access to housing, racial injustice, connection to the criminal justice system, and corporate profit motive.

Specific risks for HIV

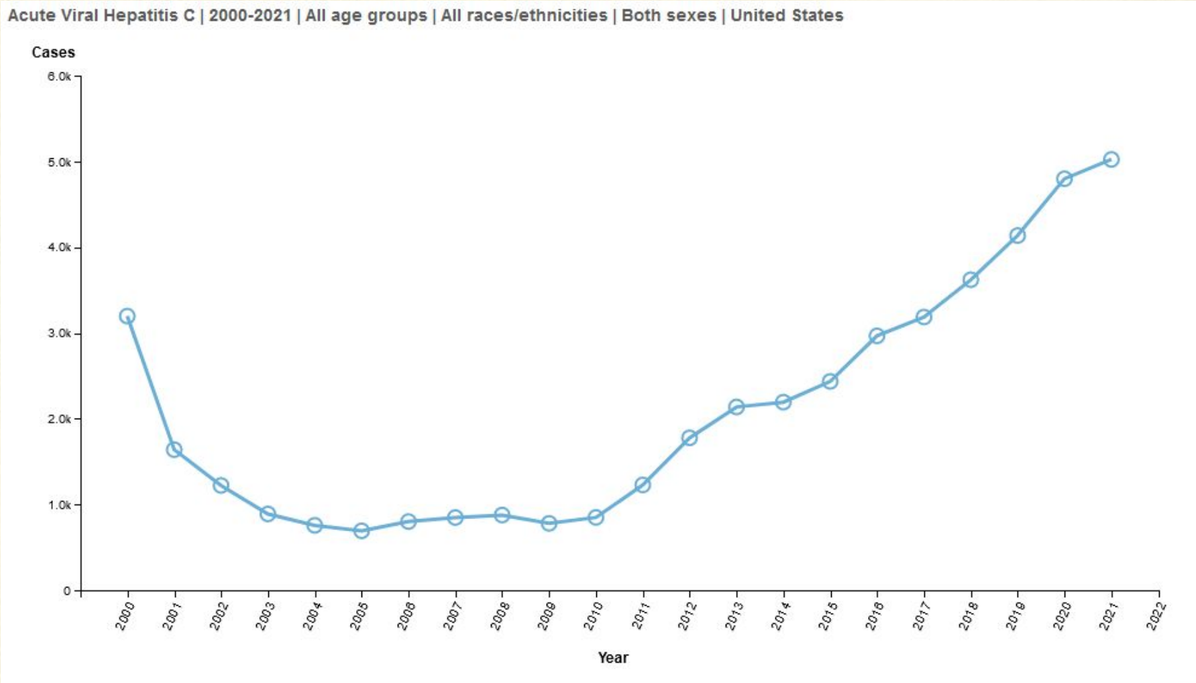
- Through extensive public health measures and access to safer injection supplies, HIV transmission among people who use drugs decreased 31% from 2009 to 2019
- Despite this, there has been minimal overall reduction in US HIV diagnoses year over year



https://www.cdc.gov/hiv/pdf/clinicians/materials/CDCHIVSlides2022EndingtheHIVEpidemic508.pdf

Specific risks for HCV

- Acute hepatitis C cases have been rising year over year, particularly among people who use drugs
- It is likely that increased awareness and access to testing play a role, though do not fully explain rise in cases
- Other risks include unlicensed tattooing, incarceration, health care exposures, transfusion, organ transplant, and sexual exposure



https://gis.cdc.gov/grasp/nchhstpatlas/charts.html

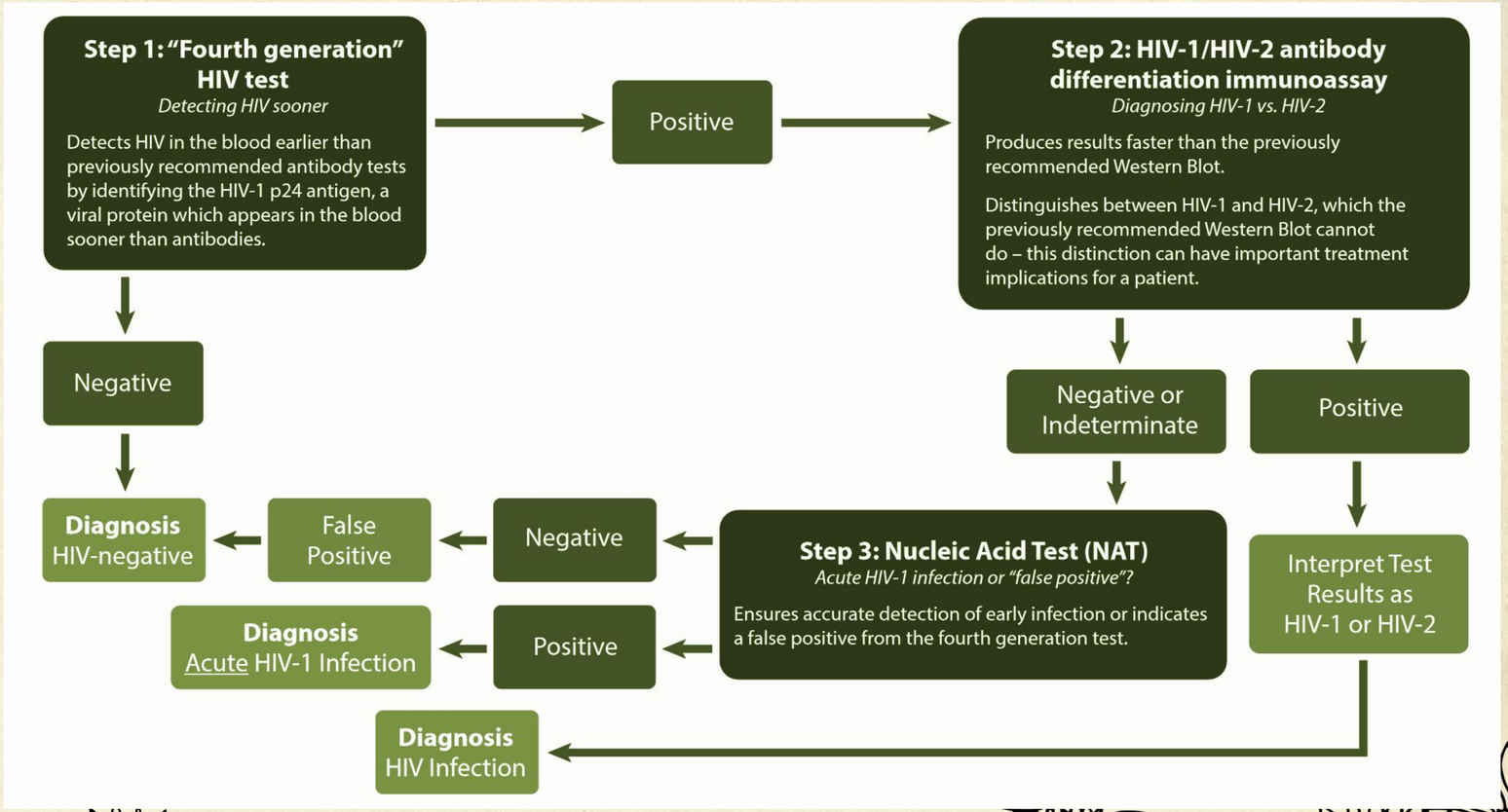
Screening

- Who should be screened?
  - HIV: CDC 2017 recommends screening for all people ages 13-64 and all pregnant people at least once, USPSTF 2019 recommends screening ages 15-65 once.
  - HIV: CDC recommends screening at least annually for people with increased risk (injection drug use, sexual risk factors)
  - HCV: CDC 2020 recommends screening every person over age 18 at least once, and “routine periodic” screening for people with increased risk. USPSTF 2020 recommends screening all people ages 18-79 once. Screen all pregnant people.
  - All patients who seek bacterial STI testing should be offered HIV/HCV testing, and all patients requesting viral testing (with or without obvious risk factors) should be offered testing.

Screening

Image Source: Centers for Disease Control, New CDC Recommendations for HIV Testing in Laboratories, 2014
https://www.cdc.gov/nchhstp/newsroom/docs/2014/hiv-testing-labs-flowchart.pdf

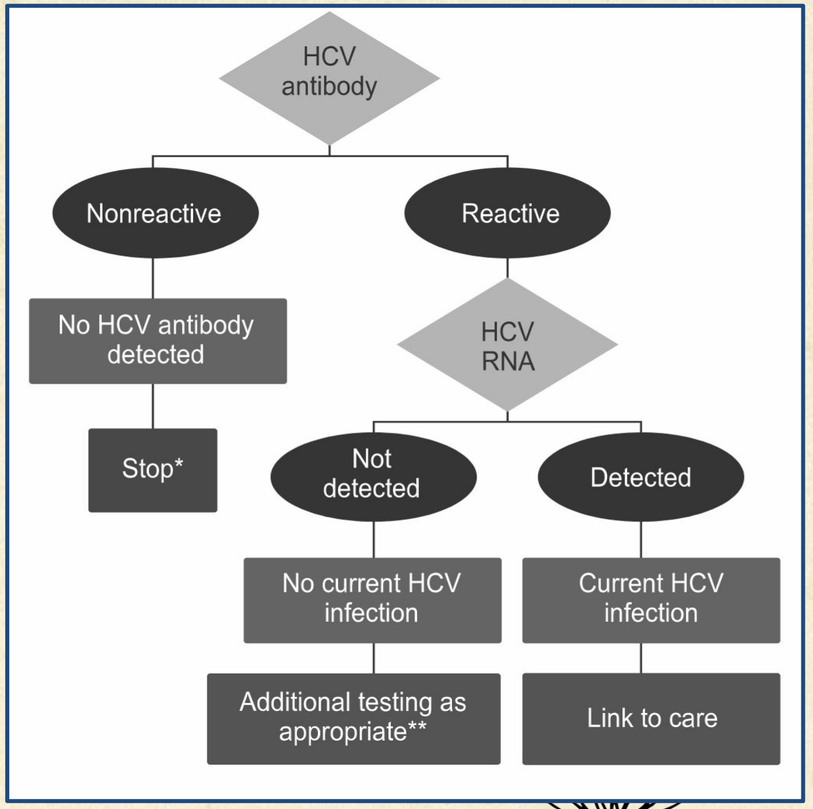
- How should I screen for HIV?
  - Step 1: HIV 1/2 Antigen/Antibody Immunoassay (4th generation)
  - Step 2: HIV 1/2 Antibody Differentiation Assay
  - If concerned for acute infection, start with HIV-1 NAT
  - Western Blot no longer recommended



Screening

Image Source: https://www.hepatitis.va.gov/hcv/screening-diagnosis/screening-algorithm.asp

- How should I screen for HCV?
  - Step 1: HCV Antibody screen, **this can be positive in initial/acute infection or cleared prior infection**
  - Step 2: HCV RNA, if viral load is present this is consistent with active infection. Does not necessarily differentiate acute vs chronic infection.



II:

HIV Prevention

HIV Prevention

- HIV should be viewed as a preventable disease where all physicians can have an impact
- HHS established the “Ending the HIV Epidemic” initiative in 2019 with a goal of ending the HIV epidemic by 2030
  - First goal: 75% reduction in new cases by 2025 (looking unlikely…)
  - Second goal: 90% reduction in new cases by 2030
- While not curable, HIV is a treatable infection and patients on antiretroviral medication can live long and healthy lives without transmitting virus to others (Undetectable = Untransmittable)
- Patients seeking HIV prevention resources often face stigma and difficulty with access
  - Syringe Service Programs - illegal in some states, limited/no access in rural areas
  - PrEP - not provided in all clinics (do you know your closest PrEP clinic?)
  - PEP - not prescribed routinely, many patients unaware of this option

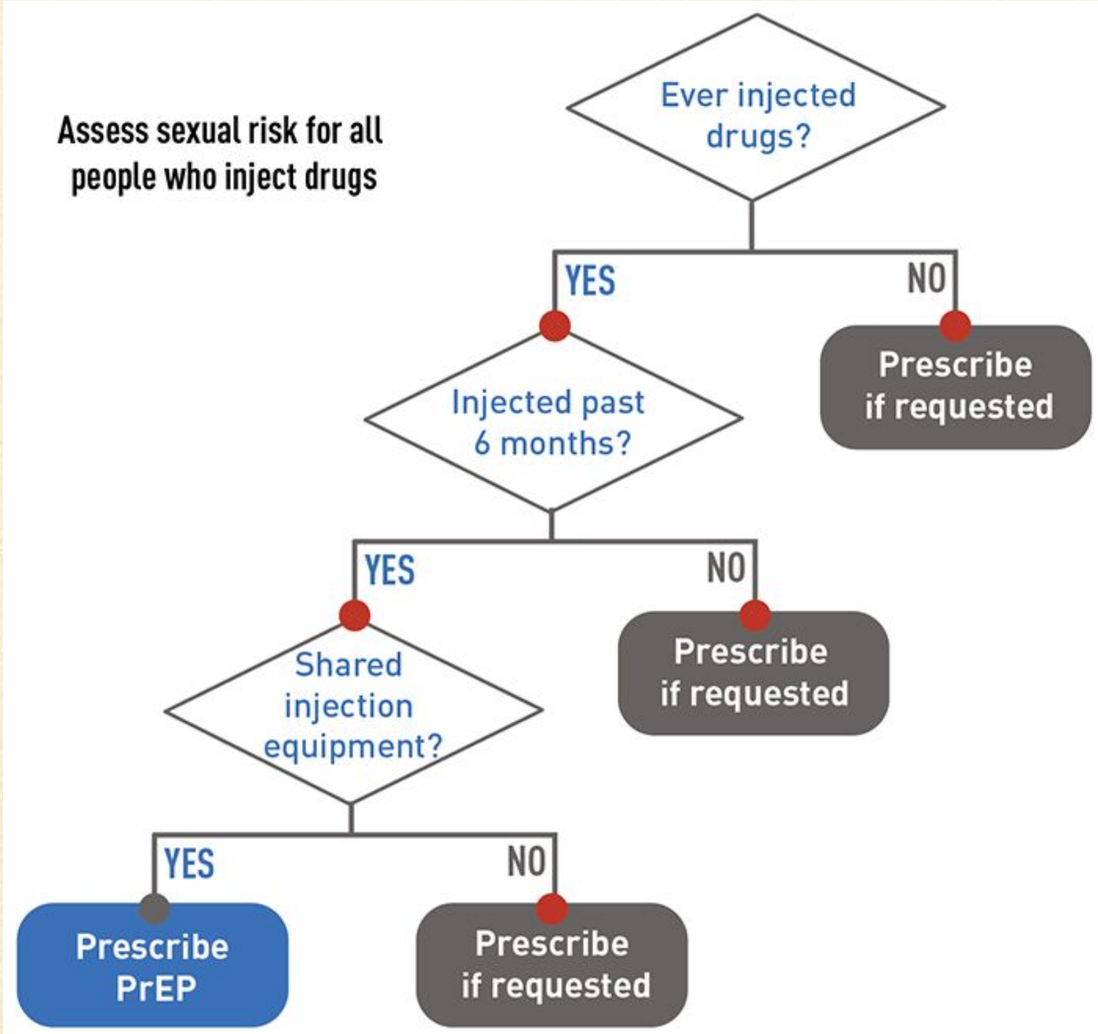
Primary Prevention

- We can encourage patients to reduce their risk of HIV exposure from injection…
  - Always use clean injection supplies and never share supplies (includes preparation supplies)
  - Dispose of injection supplies safely
  - If sterile injection supplies are not available, can bleach-sterilize supplies
  - Take advantage of syringe service programs
- …as well as their risk from sexual activity
  - Encourage universal condom use and make condoms easily available in clinical settings
  - Use water-based/silicone-based sexual lubricants to protect condoms from breaking or slipping
  - Any sexual activity that involves contact with bodily fluids can carry HIV risk
  - Get tested frequently if you have increased risk, and encourage partners to test

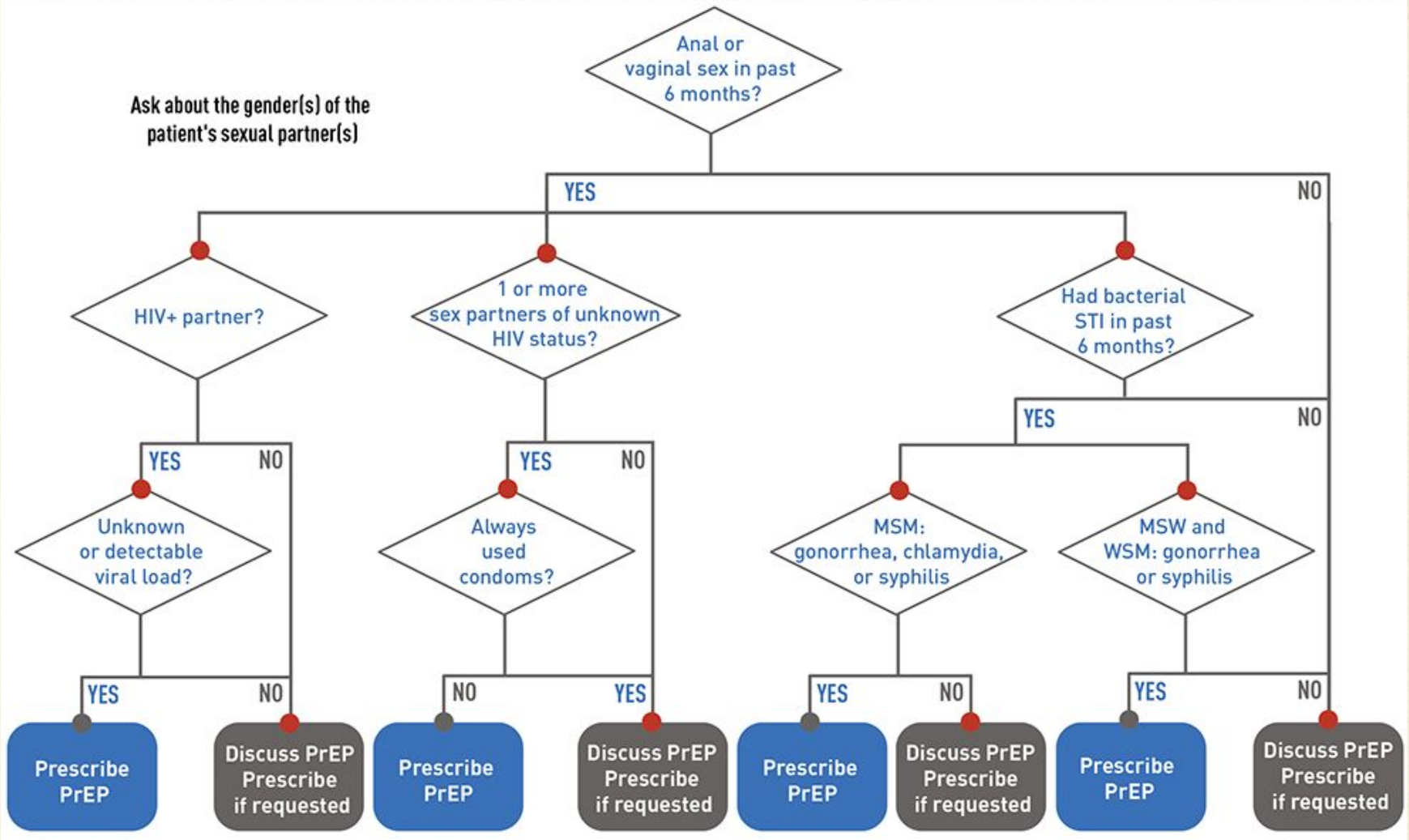
Pre-Exposure Prophylaxis

- Use of antiretroviral medications to reduce risk of initial HIV infection
- Has been shown in multiple studies to reduce risk by 99% or greater **when taken correctly**
- USPSTF recommends the prescription of PrEP for all people with increased risk of infection (Grade A)
- No significant interactions with common MOUD (buprenorphine, methadone)
- PrEP regimens are **deficient regimens**, meaning if a patient were to develop HIV (before or after starting PrEP) they would be at risk for developing drug resistance
- Given the increased risk seen in patients who use drugs (including non-injection drugs), **low-barrier access to PrEP can save them and their partners from a lifelong infection**

Who needs PrEP?



Who needs PrEP?



3 FDA Approved Options

TRUVADA (TDF-FTC)

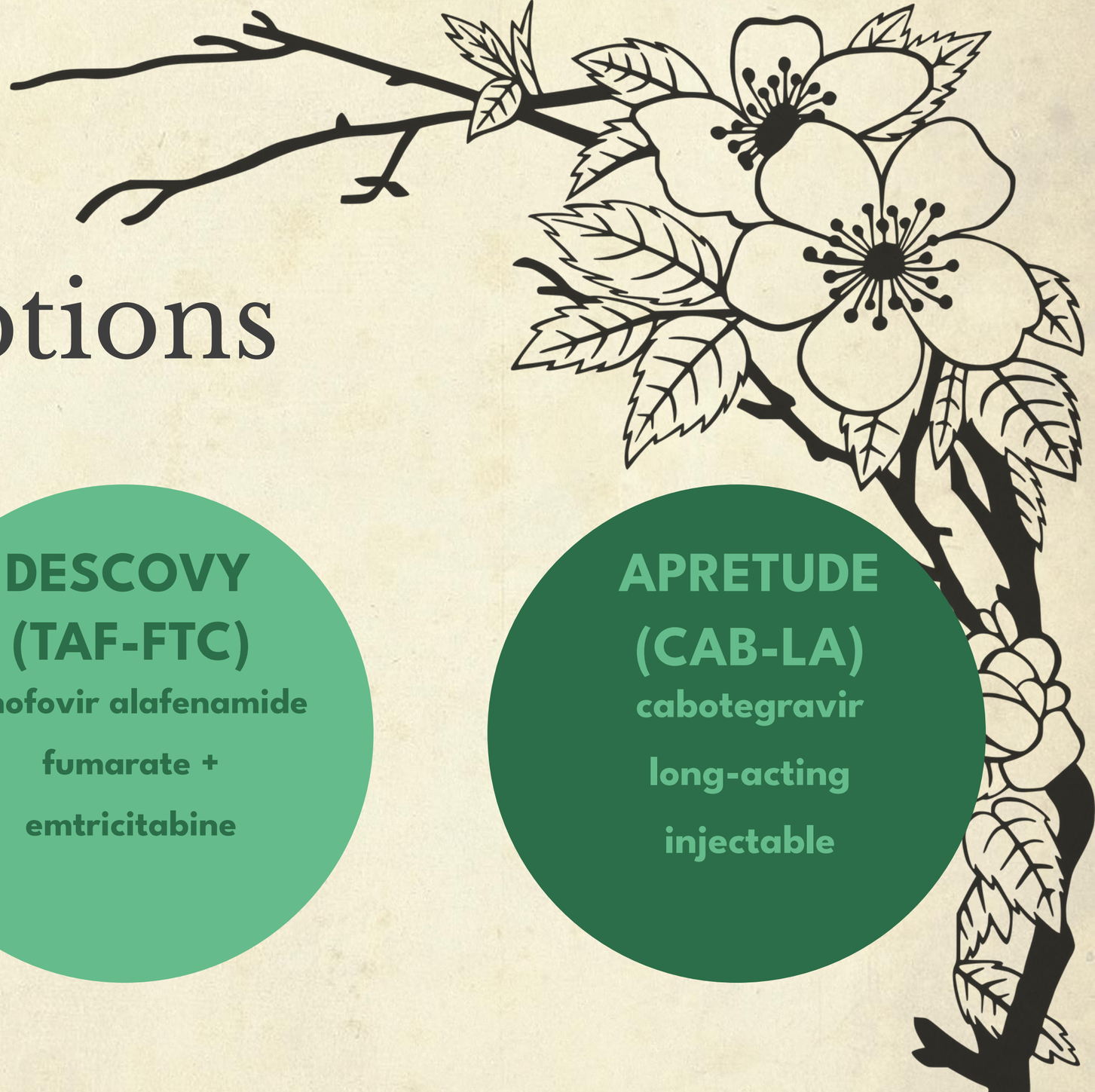
tenofovir disoproxil fumarate + emtricitabine

DESCOVY (TAF-FTC)

tenofovir alafenamide fumarate + emtricitabine

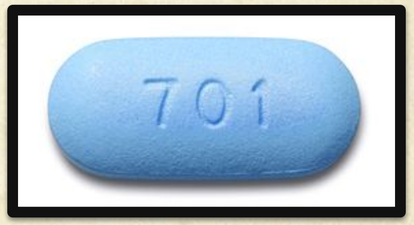
APRETUDE (CAB-LA)

cabotegravir long-acting injectable



Oral PrEP Options

- tenofovir disoproxil fumarate + emtricitabine (TRUVADA)
  - Indicated for those assigned male and female at birth
  - Approved for adults and adolescents weighing at least 35kg
  - Indicated for both sexual exposure risk and injection drug use
  - Now available as a generic! <$40/mo with coupons or mail order
  - Can be free with federal programs
- tenofovir alafenamide fumarate + emtricitabine (DESCOVY)
  - Indicated only for those assigned male at birth
  - Approved for adults and adolescents weighing at least 35kg
  - Not yet studied in people assigned female at birth or people who inject drugs
  - Lower incidence of renal and bone density complications



Injectable PrEP

- cabotegravir long-acting injectable (APRETUDE)
  - Indicated for those assigned male and female at birth
  - Approved for patients with sexual exposure risk
  - 2 monthly injections followed by injections every 2 months
  - Useful in patients with impaired renal function
  - Should be continued until risk has reduced, medication may remain in system

How to Prescribe Oral PrEP

- Before prescribing PrEP:
  - Test **renal function** (not needed for injectable PrEP) and **HIV status** with Ag/Ab test within 1 week before starting
  - Confirm no medication-medication interactions
- Prescribe **no more than a 90 day** supply of TAF/FTC or TDF/FTC
- Every 3 months: HIV testing for all, bacterial STI testing at all appropriate sites (genital, oral, rectal, blood) for MSM and trans women who have sex with men
- Every 6 months: Bacterial STI testing for all sexually active patients at all appropriate sites, renal function testing if age >=50 or starting CrCl <90 mL/min
- Every 12 months: Renal testing for all people on TAF/FTC or TDF/FTC, assess weight and lipids for people on TAF/FTC

How to Prescribe LAI PrEP

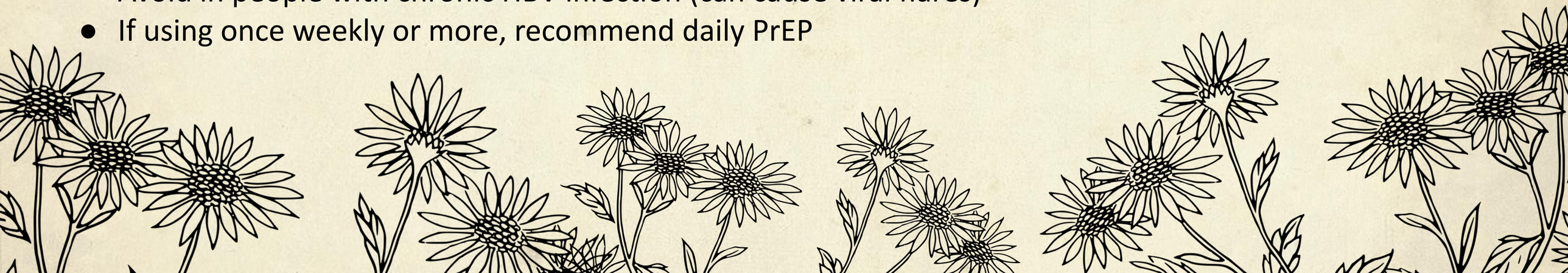
- For cabotegravir: **test HIV every visit** (2 months), bacterial STI testing every 4 months (MSM/TWSM), every 6 months for heterosexual patients. No need to monitor CrCl.
- For cabotegravir: counsel on increased risk of resistance if they discontinue cabotegravir and later contract HIV (possibly up to 3-4 years)
- Oral cabotegravir is available to test tolerance of medication before starting CAB-LA if desired
  - Not approved for use as PrEP

Possible future option: dapivirine vaginal ring

- Available in Europe, application to FDA withdrawn in 2021/2022

2-1-1 PrEP for MSM

- There are several studies (exclusively in men who have sex with men, MSM) indicating event-driven PrEP may be effective for prevention of HIV transmission
- This regimen is not currently approved by the FDA or endorsed by the CDC, but CDC now has prescribing guidelines for patients and physicians interested in using this method
- In 2-1-1 dosing, the patient takes TDF/FTC (Truvada) doses based on when they plan to have sex:
  - Two pills 2-24 hours before sex
  - One pill 24 hours after the first two-pill dose
  - One pill 48 hours after the first two-pill dose
- Should not be prescribed to people other than adult MSM
- Avoid in people with chronic HBV infection (can cause viral flares)
- If using once weekly or more, recommend daily PrEP



Post-Exposure Prophylaxis

- All persons with an exposure to HIV (sexual contact, injection drug use) should be offered PEP within 72 hours of exposure
  - Must involve an infectious body fluid (semen, blood, vaginal/rectal secretions, other fluid contaminated by blood)
  - Source must have a known or reasonable suspicion for HIV infection
  - The fluid must come in contact with a mucous membrane or bloodstream
- Immediately test for HIV (4th gen test), HBV/HCV, STIs (if applicable), pregnancy, and renal function (if using a tenofovir-containing regimen)
- See CDC 2016 PEP Guidelines for regimens and table of follow-up testing
- Continue PEP for 28 days regardless of severity of exposure
- Offer to presumptively treat for STIs if indicated

III:

HCV Diagnosis and Treatment

Hepatitis C Diagnosis

- Patients with positive antibody results should immediately have sample tested for HCV RNA
  - Often available as a reflex lab test
  - Consider testing RNA first in patients with known prior infection
- Presence of viral RNA consistent with active HCV infection, acute or chronic
- All patients with active (current) HCV infection should be connected with treatment
- Consider acute HCV (may be antibody negative but RNA positive) in patients with known discrete exposure, symptoms (eg. fever, jaundice), or abnormal LFTs
- AASLD currently recommends **against** waiting for possible spontaneous clearance before referral to treatment
- AASLD recommends referral to addiction medicine for patients with HCV and SUD

Pathways to HCV Treatment

- Many states no longer require specialist (eg. ID, hepatology) involvement for Medicaid coverage of treatment (including Minnesota), providers in other fields experienced in HCV treatment can initiate
- Pangenotypic regimens have simplified treatment in many cases (though insurance still often requests genotype testing)
- HCV treatment medication remains very expensive ($5,000 - $25,000 for full course)
- Some states still impose restrictions on patients living with addiction preventing them from accessing treatment (this does not include Minnesota)
- Patients with barriers to care may find specialist access difficult, may benefit from integrated HCV care

Pre-Treatment Evaluation

- Any time prior to treatment:
  - HCV Genotype (retest if concern for re-infection)
  - Hep A total ab
- Within 1 year of initiating treatment:
  - HCV viral load
  - HIV
  - Hepatitis B Testing (surface antigen, surface ab, core ab)
- Within 6 months of initiating treatment:
  - CBC, INR, Creatinine/eGFR
  - Liver Function panel
  - Assessment of liver fibrosis (biopsy not required, see next slide)

$$\text{FIB4 index} = \frac{(\text{age} \times \text{AST})}{\text{platelet count} \times \sqrt{\text{ALT}}}$$

FIB4 < 1.45 and normal platelets/albumin = unlikely fibrosis

FIB4 = 1.45-3.25 or abnormal platelets/albumin = further evaluation

FIB4 > 3.25 = likely cirrhosis

Evaluating for fibrosis:

- **Hepatic elastography** (eg FibroScan™)
- FibroSure or similar (blood test, variable data)
- Liver biopsy (invasive, painful)

Initiating Treatment

- Ensure no medication-medication interactions
  - Many interactions exist, including statins and PPIs
  - Consider collaboration with clinical pharmacist if available
- Generally insurance will dictate medication choice, ensure choice is appropriate for HCV genotype
- Most regimens are 8 or 12 week, specific to the medication
- Counsel on medication adherence and reducing risk of re-exposure
- No laboratory monitoring required on treatment for most patients
- Obtain HCV viral load and LFTs 12 weeks after completing treatment (SVR12)
- If concern for treatment failure, refer to specialist to consider re-treatment
- No follow-up testing required after SVR12 unless ongoing risk for exposure

Reasons to consider referral

- Prior Hepatitis C treatment
- End stage renal disease (eGFR < 30)
- HIV
- Hepatitis B surface antigen positive
- Currently pregnant
- Known or suspected hepatocellular carcinoma
- Prior liver transplant
- Cirrhosis

Resources

- Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2021 Update—A Clinical Practice Guideline (CDC)
- Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV (CDC)
- Clinician's Quick Guide: Oral HIV PrEP (CDC)
- UCSF 2-1-1 PrEP handout for MSM
- AASLD Simplified HCV Treatment Guidelines
- Liverpool HCV Drug Interaction Checker
- Liverpool HIV Drug Interaction Checker

Questions?

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