INFECTIONS ASSOCIATED WITH SUBSTANCE USE DISORDERS AND RELATED BEHAVIORS

- Diagnosis and Management

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DISCLOSURES

- over the last 5 years:
  - One-time advisory boards for AbbVie, Melinta and Shionogi
  - Research support from AbbVie
  - IDWeek 2022: one-time educational event sponsorship from Melinta

AGENDA

- Types of risk (harm) with SUD
- Overview of infections connected with SUD and related behaviors
- Prevention, diagnosis and management of SUD-associated infections in various settings

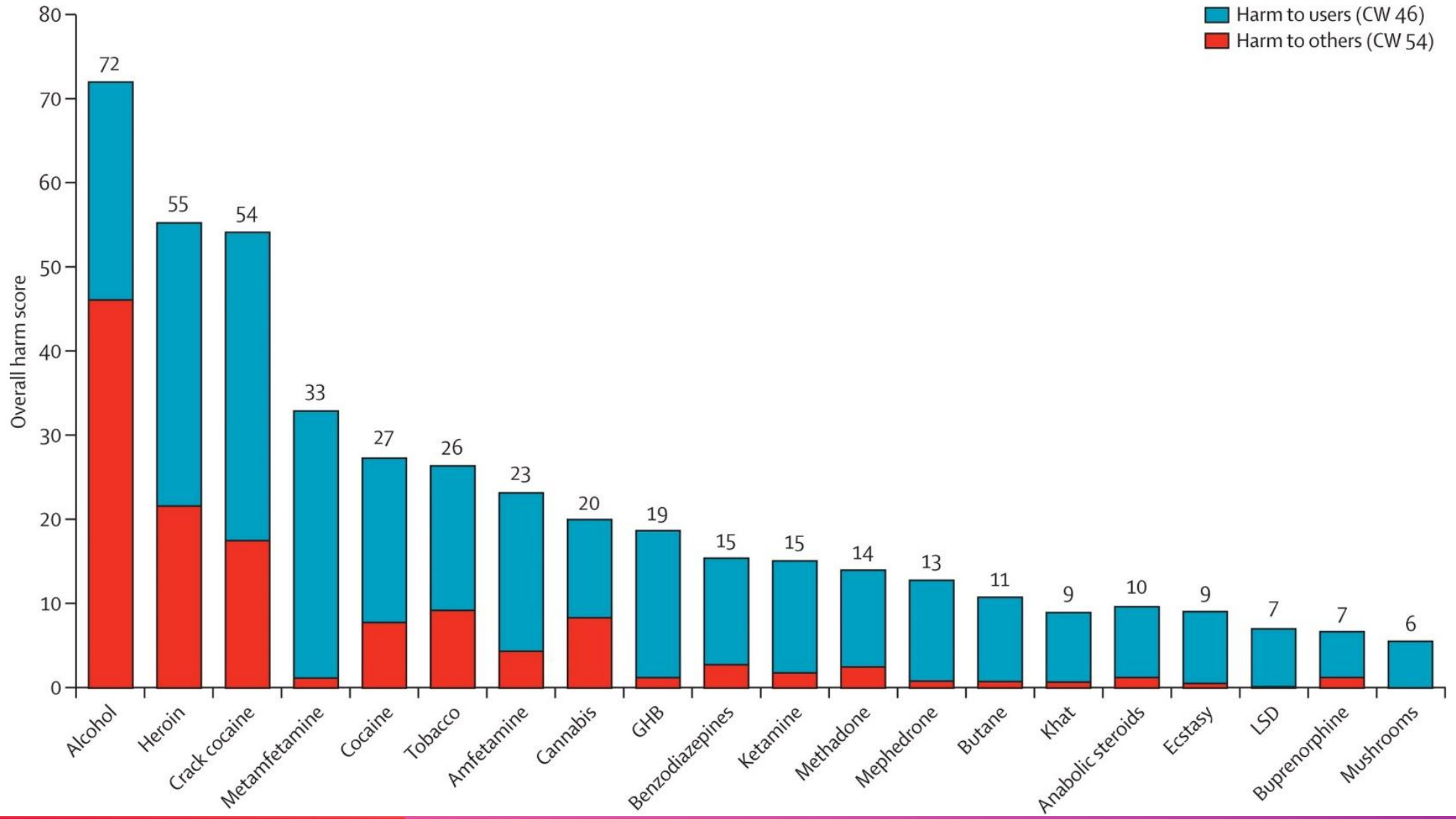
TYPES OF RISK (HARM) WITH SUD

Overdose; Abuse vs Addiction/Dependence

Socio-economic; Violence; Non-violent crime

Infections; Injury; Other Physical and Mental Health Problems

DRUG HARMS (IN THE UK)



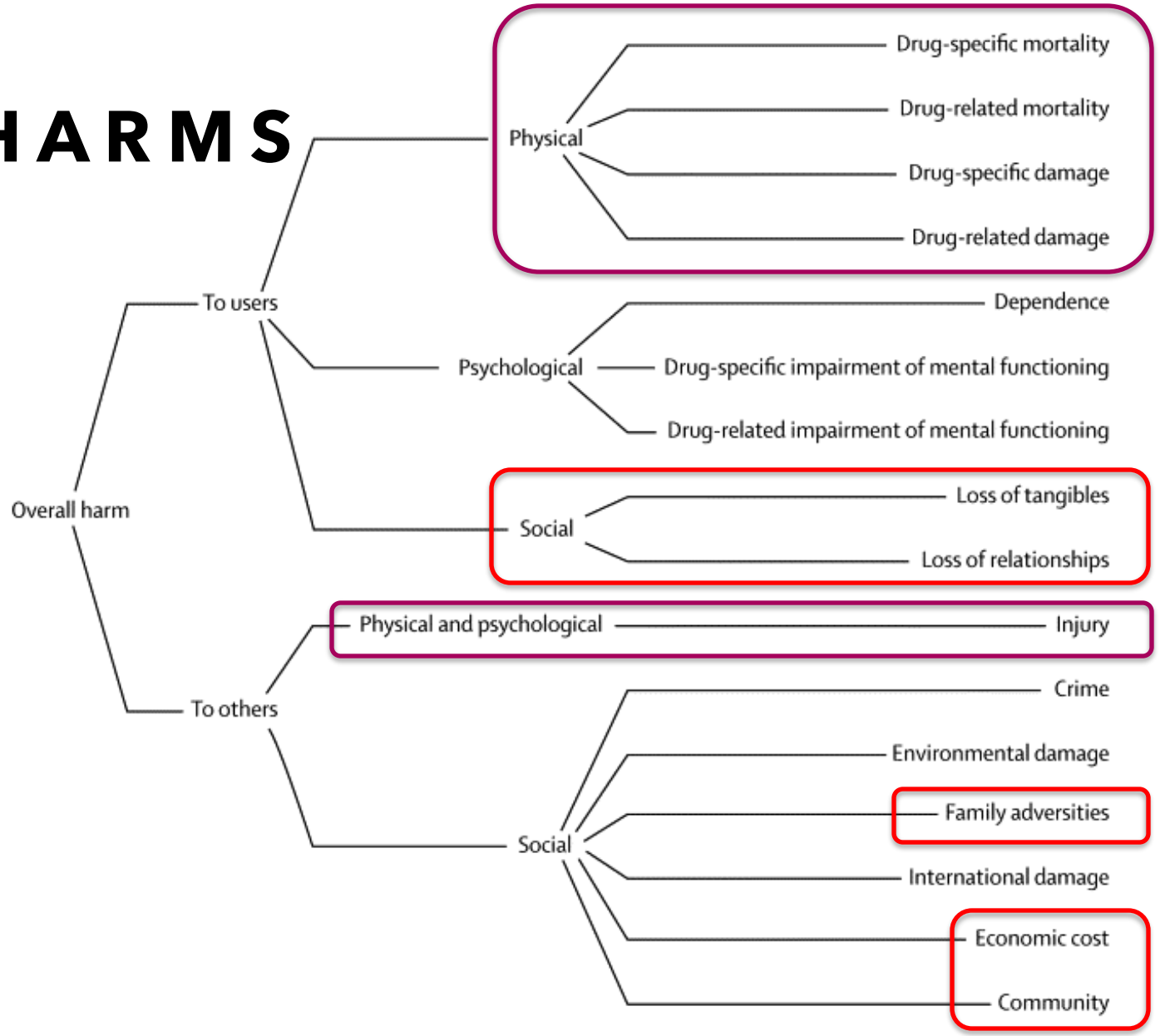
Nutt DJ. Lancet. 2010.

TYPES OF DRUG HARMS

Infection

&

consequences



Nutt DJ. Lancet. 2010.

NSDUH ANNUAL NATIONAL REPORTS: SAMHSA

WHO IS AT RISK?

PAST YEAR SUD AND MENTAL ILLNESS (AGE 18+):

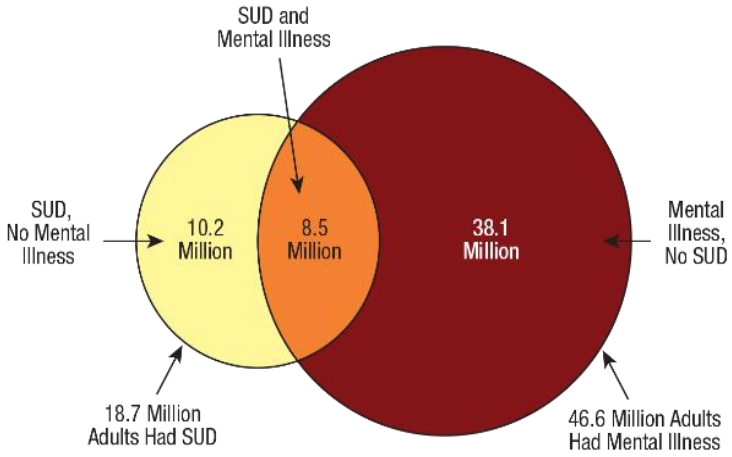
2017VS2019

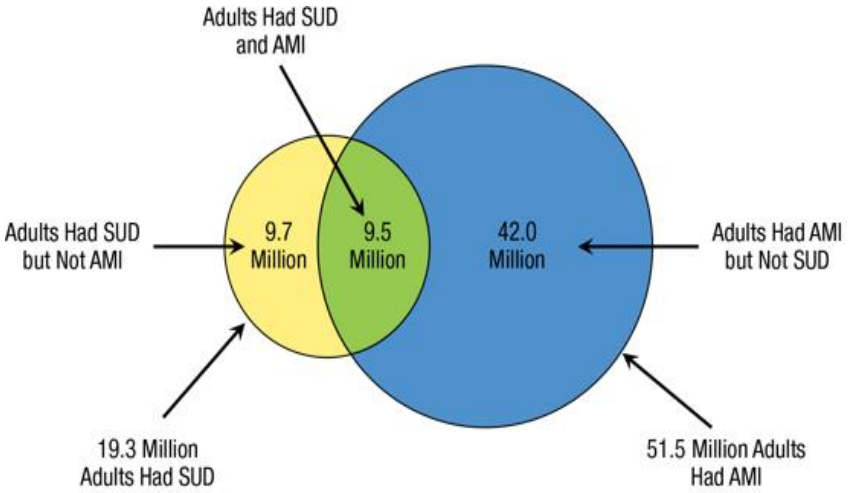
VS

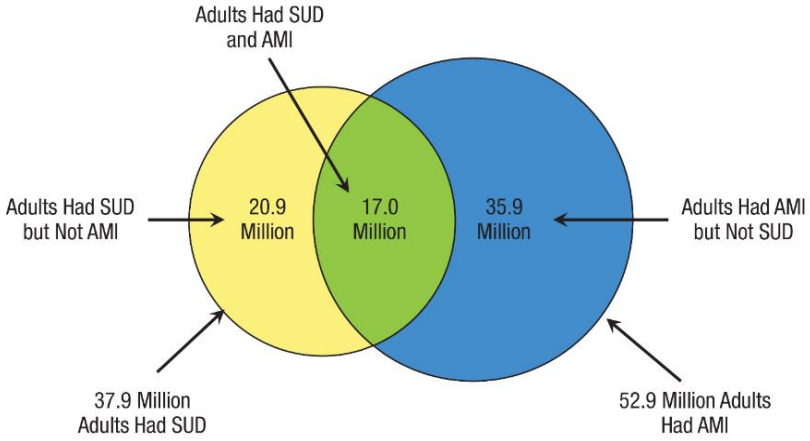
2020

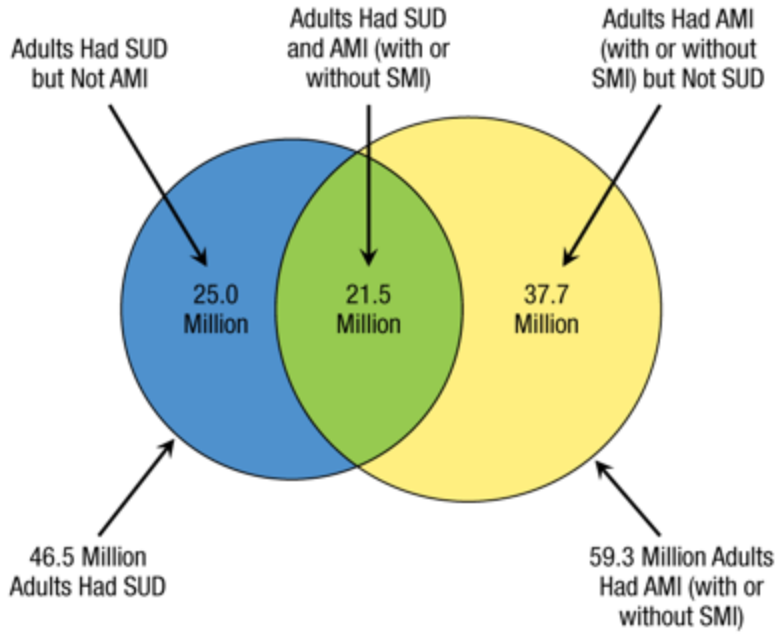
VS

2022







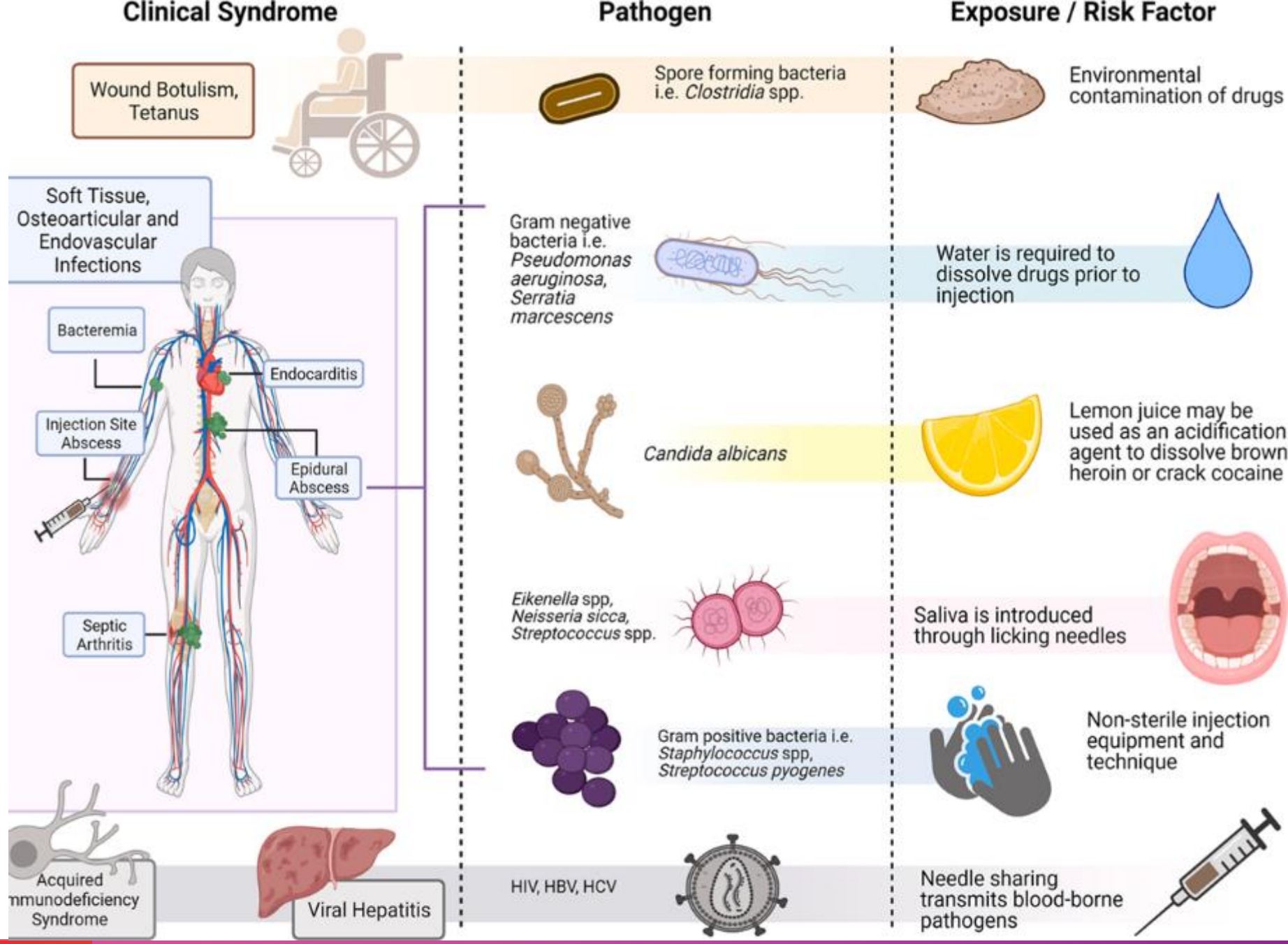


84.2 Million Adults Had Either SUD or AMI (with or without SMI)

OVERVIEW OF INFECTIONS CONNECTED WITH SUD AND ASSOCIATED BEHAVIORS

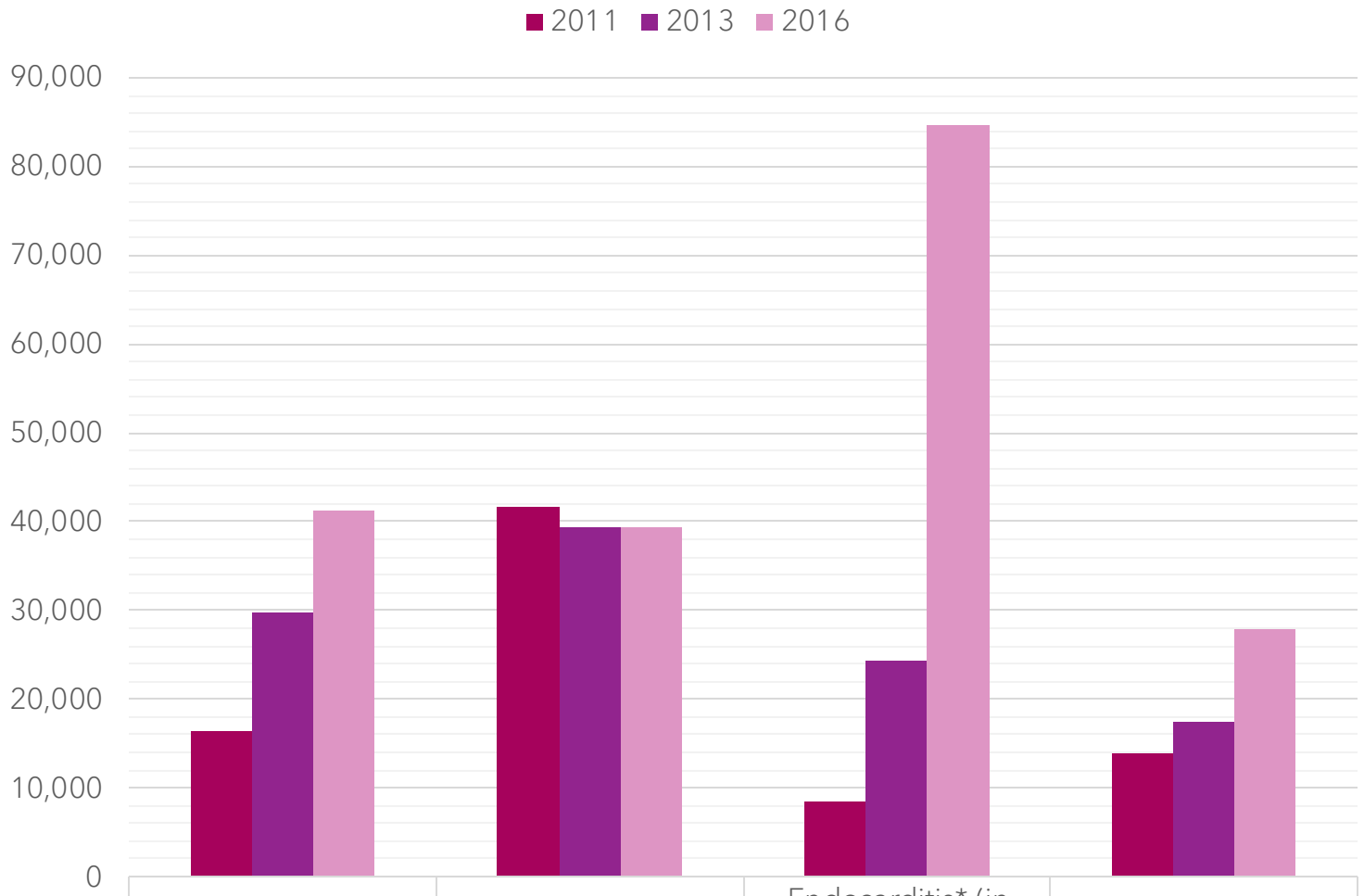
- Blood stream infections, Infective Endocarditis, Osteomyelitis, Deep Abscesses
- HIV
- Viral Hepatitis
- STIs
- MTB (mostly if hx/o homelessness or incarceration, HIV or epidemiologically relevant travel/country of origin)

CDC.gov: https://www.cdc.gov/pwid/index.html



Marks LR et al . Med Clin North Am. 2022.

INCIDENCE OF INFECTIONS



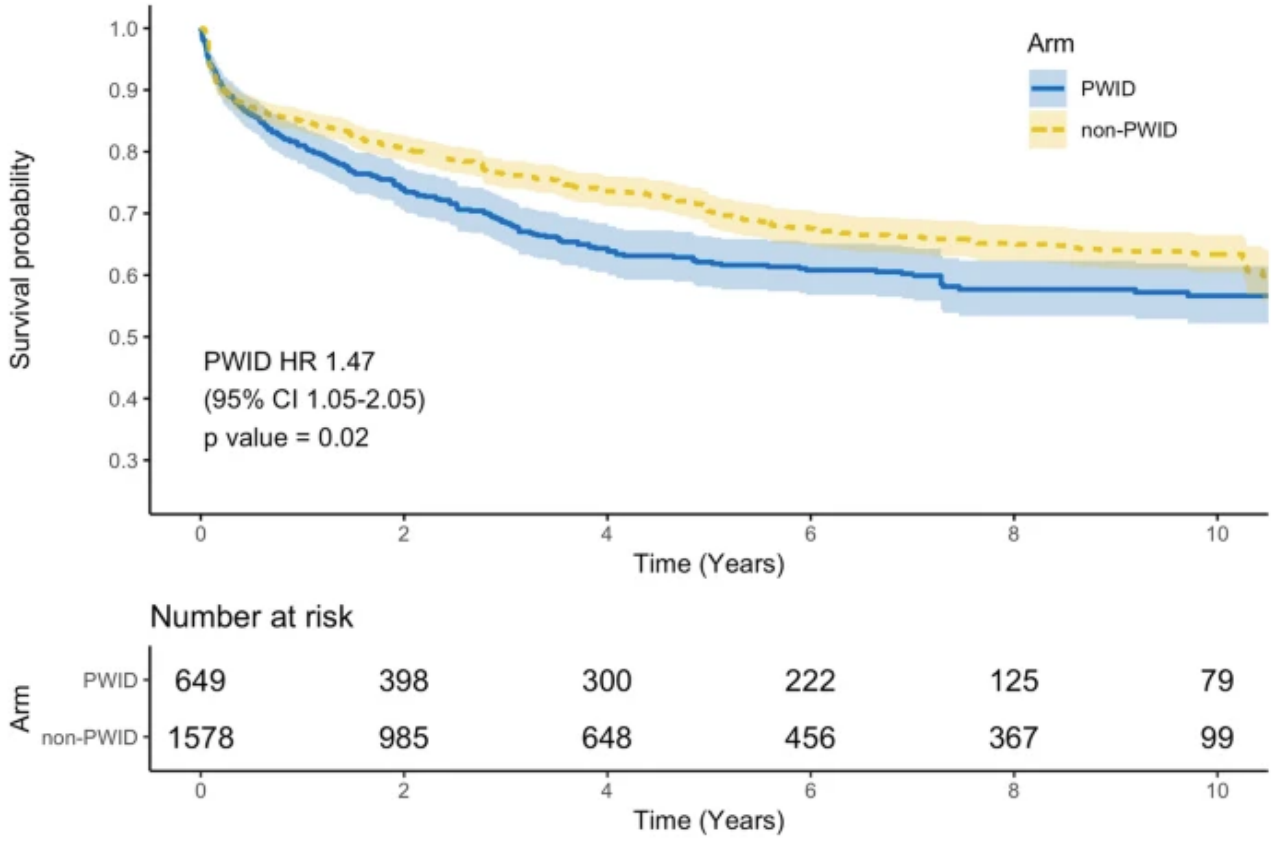
	HCV	HIV (~9% infected by IDU)	Endocarditis* (in North Carolina, x 100)	Syphilis
2011	16,500	41,623	8,505	13,970
2013	29,700	39,355	24,357	17,375
2016	41,200	39,459	84,671	27,814

- - *Schranz AJ, *Ann Intern Med*, 2019
- - CDC.gov: https://gis.cdc.gov/grasp/nchhstpatlas/charts.html

Blood stream infections, Infective Endocarditis, Osteomyelitis, Deep Abscesses

- PWID have increased incidence of bacterial and fungal infections due to using and sharing contaminated injection drug equipment and unsanitary injecting conditions
- Rates of invasive MRSA associated with IDU more than doubled from 2010–2018
- Hospitalization due IDU-related bacterial and fungal infections — cost over $700 million in 2012 alone
- Outcomes, particularly long-term, are worse in PWID

Fig. 2



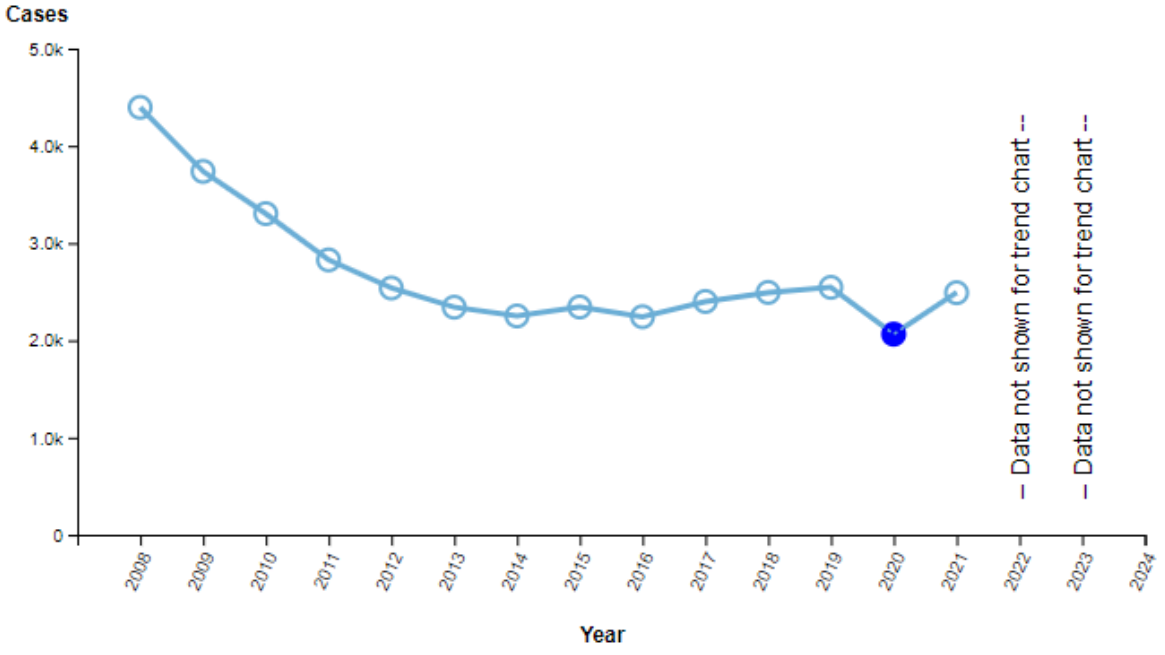
Survival of PWID and non-PWID after cardiac surgery for infective endocarditis. Abbreviations: non-PWID, people who do not inject drugs; PWID, people who inject drugs

CDC.gov: https://www.cdc.gov/pwid/index.html; https://www.cdc.gov/pwid/vulnerable.html;

Goodman-Meza D, *BMC Infect Dis* **19**, 918 (2019)

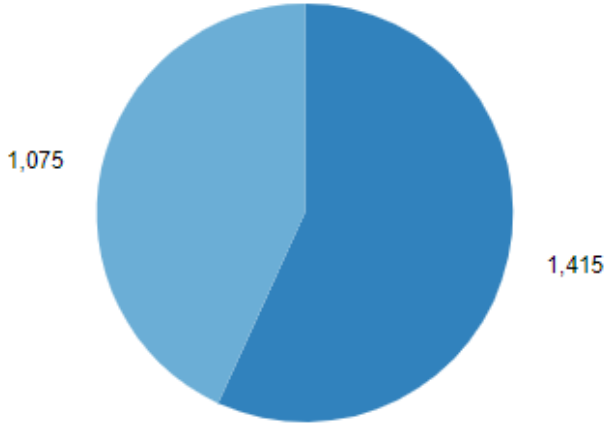
HIV Diagnoses

HIV diagnoses | 2021 | Ages 13 years and older | All races/ethnicities | Both sexes | Injection drug use | United States

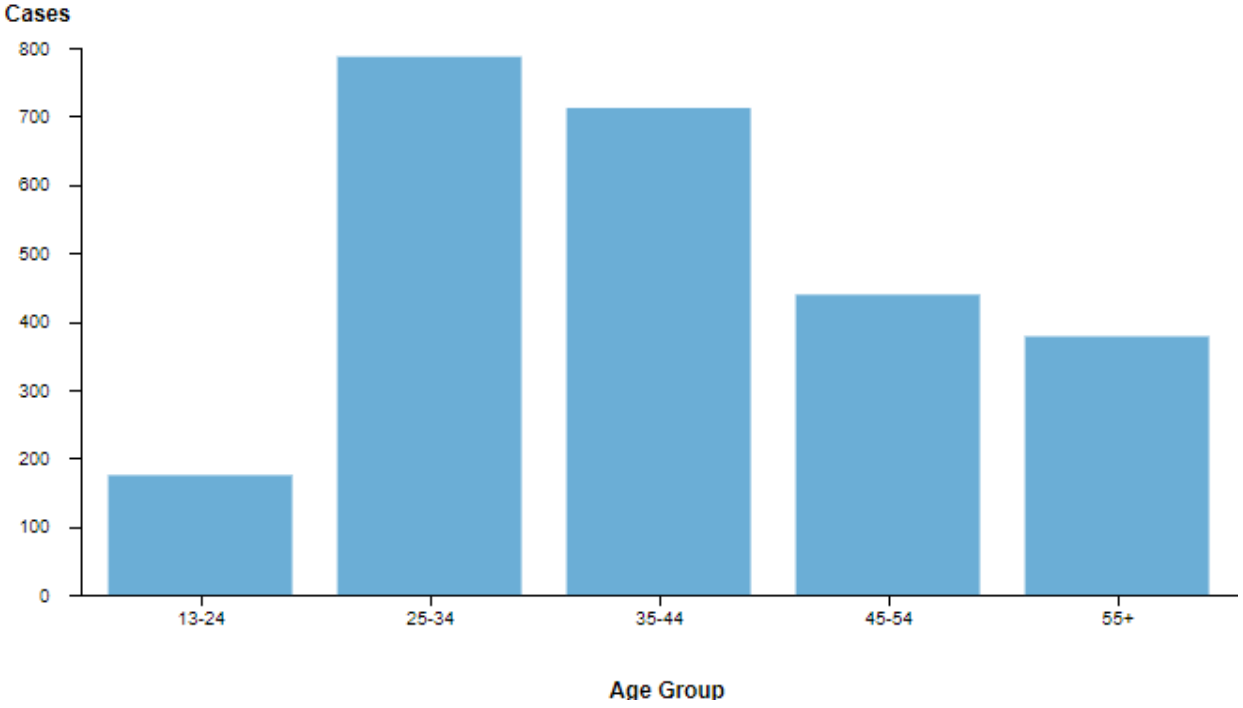


- 11% of all people with an HIV diagnosis in 2018 reported injection drug use
- average lifetime HIV-related medical cost for one person with HIV is $510,000

CDC.gov: https://gis.cdc.gov/grasp/nchhstpatlas/charts.html; https://www.cdc.gov/pwid/vulnerable.html



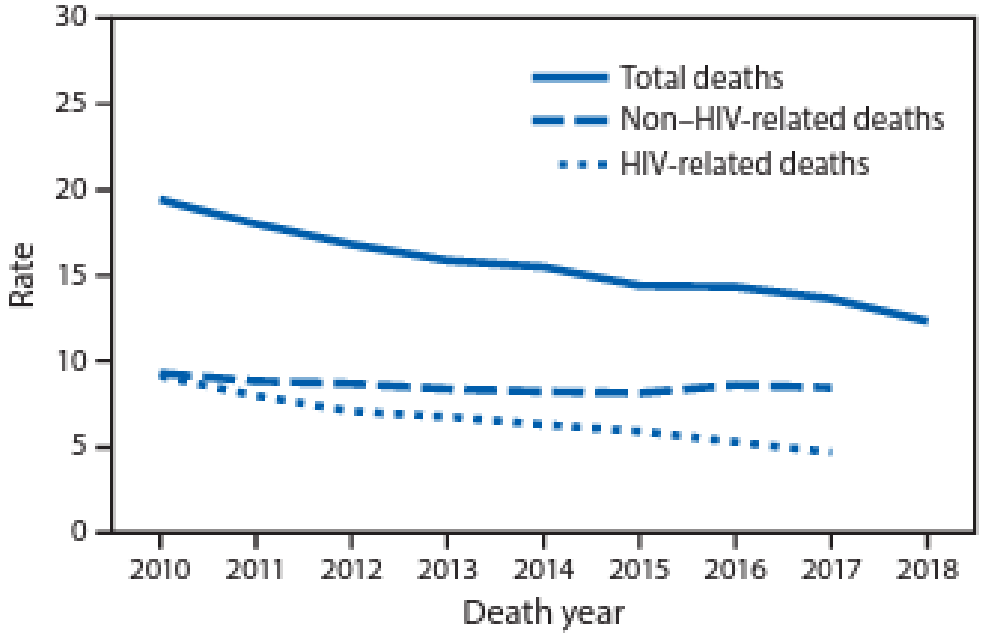
HIV diagnoses | 2021 | Ages 13 years and older | All races/ethnicities | Both sexes | Injection drug use | United States



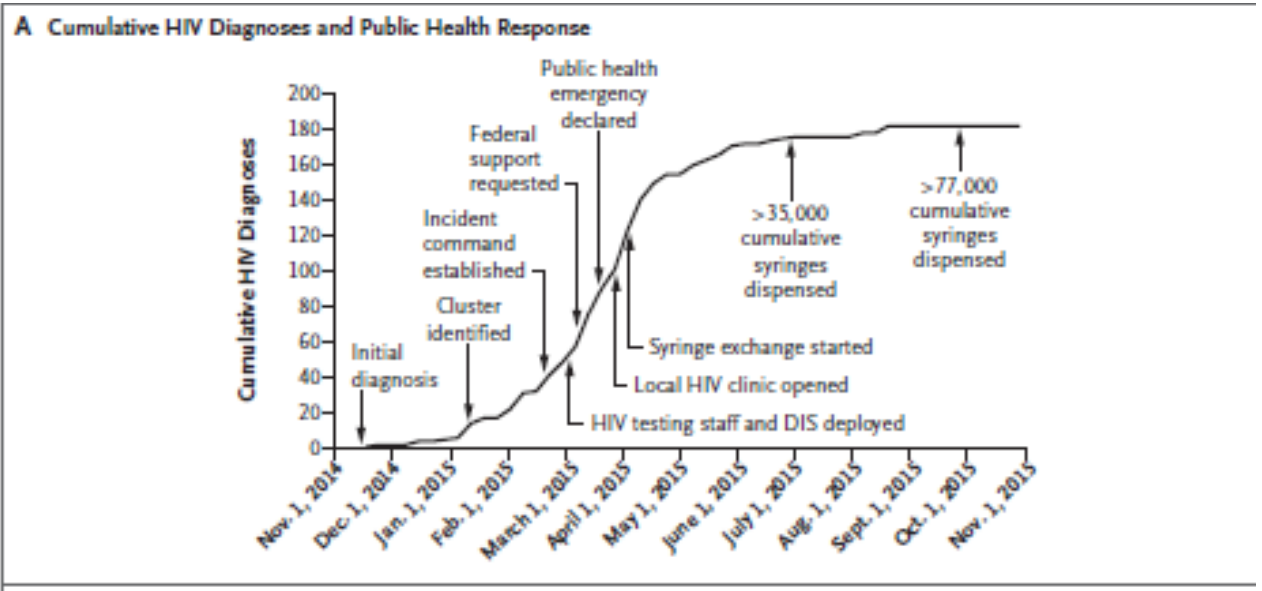
HIV Mortality

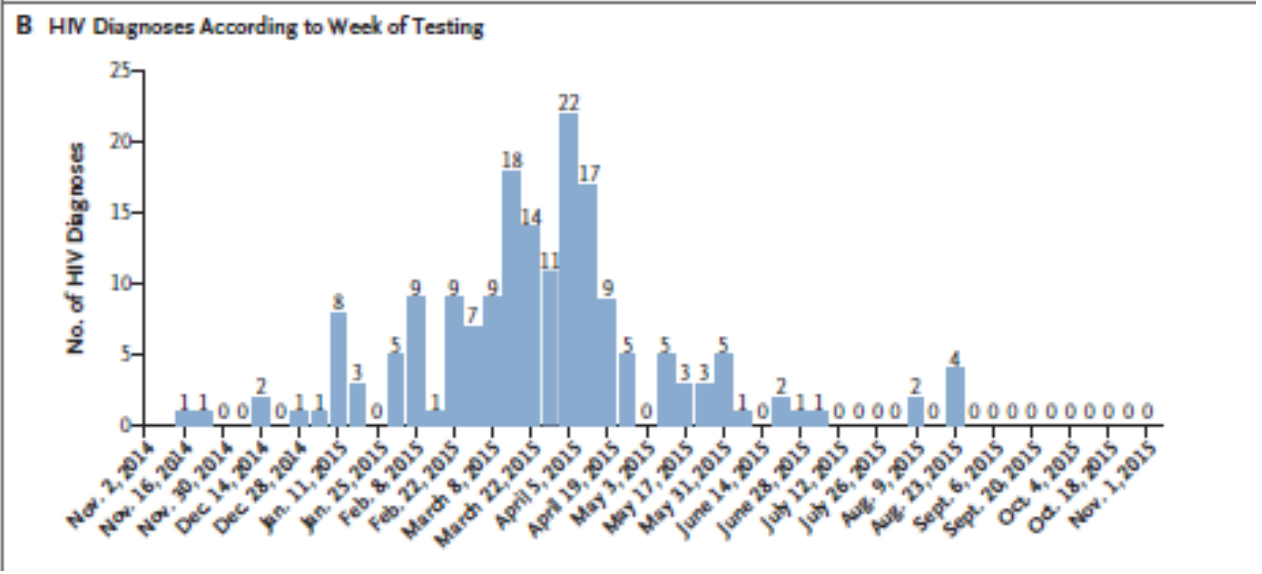
- Bosh KA, et al. MMWR Morb Mortal Wkly Rep 2020;69:1717–1724

FIGURE 1. Age-adjusted rates* of total deaths,† human immunodeficiency virus (HIV)–related deaths,§ and non–HIV-related deaths among persons aged ≥13 years with diagnosed HIV infection — United States, 2010–2018¶



* Rates per 1,000 persons with diagnosed HIV infection. Rates age-adjusted using the U.S. 2000 standard population.
† Deaths among persons with diagnosed HIV infection regardless of cause of death (n = 16,742 in 2010; n = 15,483 in 2018).
§ HIV-related deaths include deaths with an underlying cause with an *International Classification of Diseases, Tenth Revision*, code of B20-B24, O98.7, or R75. Non–HIV-related deaths include all other deaths with a known underlying cause.
¶ Deaths by cause available through 2017 because of reporting delays.

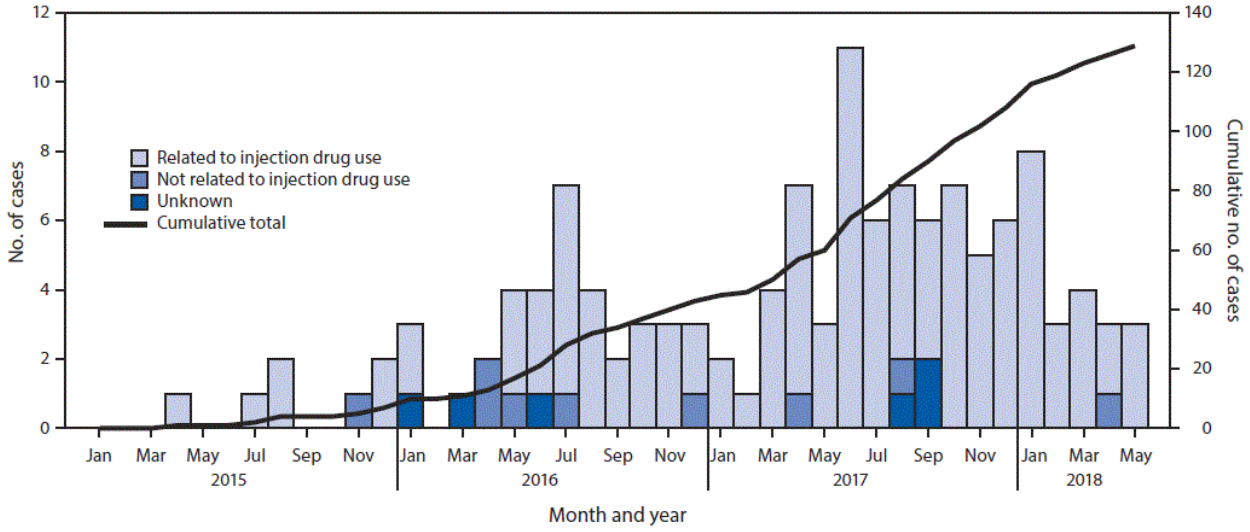




HIV OUTBREAK IN PWID - INDIANA

- HIV diagnoses in Scott County, Indiana, November 2016–August 2015
- 180 cases via IDU - oxymorphone

Peters PJ, NEJM, 2016



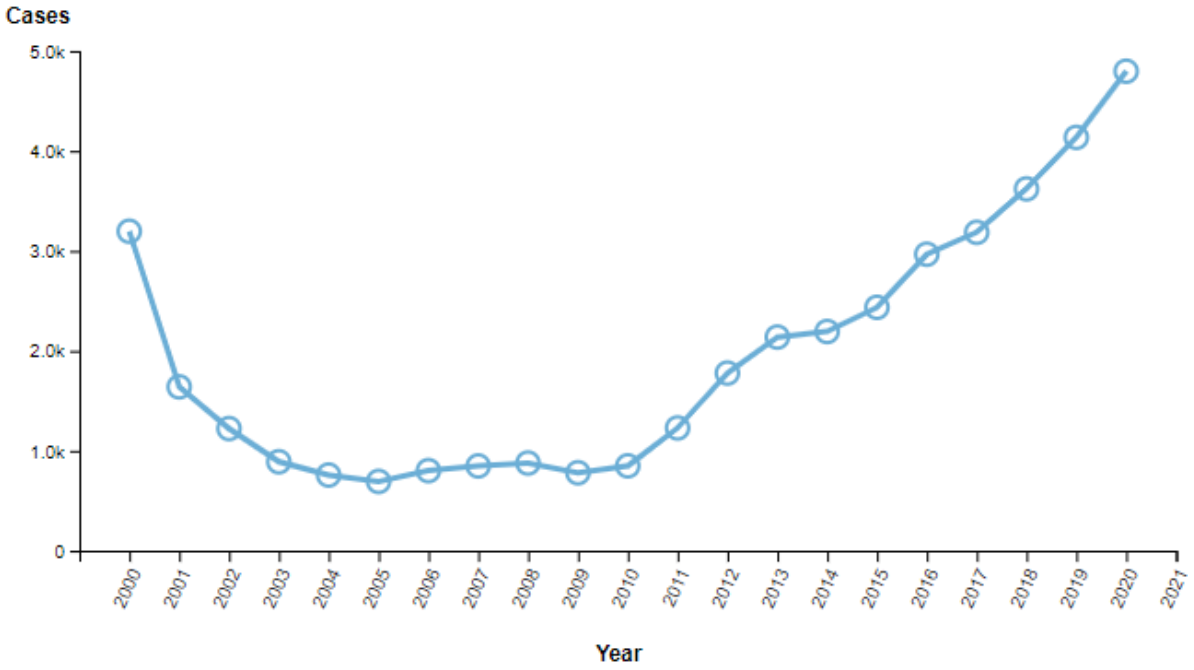
HIV OUTBREAK IN PWID – MASSACHUSETTS

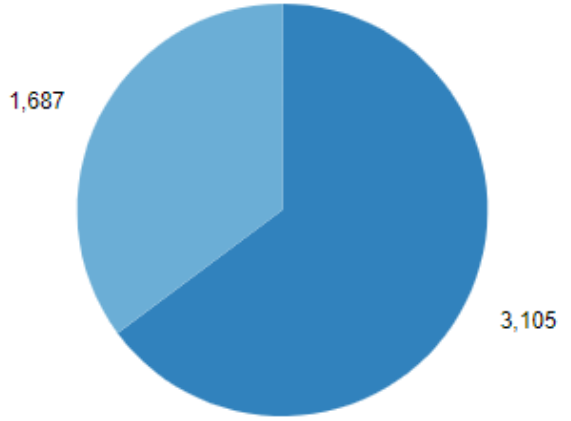
- HIV diagnoses in Lawrence and Lowell, Massachusetts, January 2015–May 2018
- 114 (88%) history of IDU, only 3% also reported male-to-male sexual contact
- 116 (90%) had laboratory evidence of past or current hepatitis C virus infection

Cranston K, MMWR Morb Mortal Wkly Rep 2019

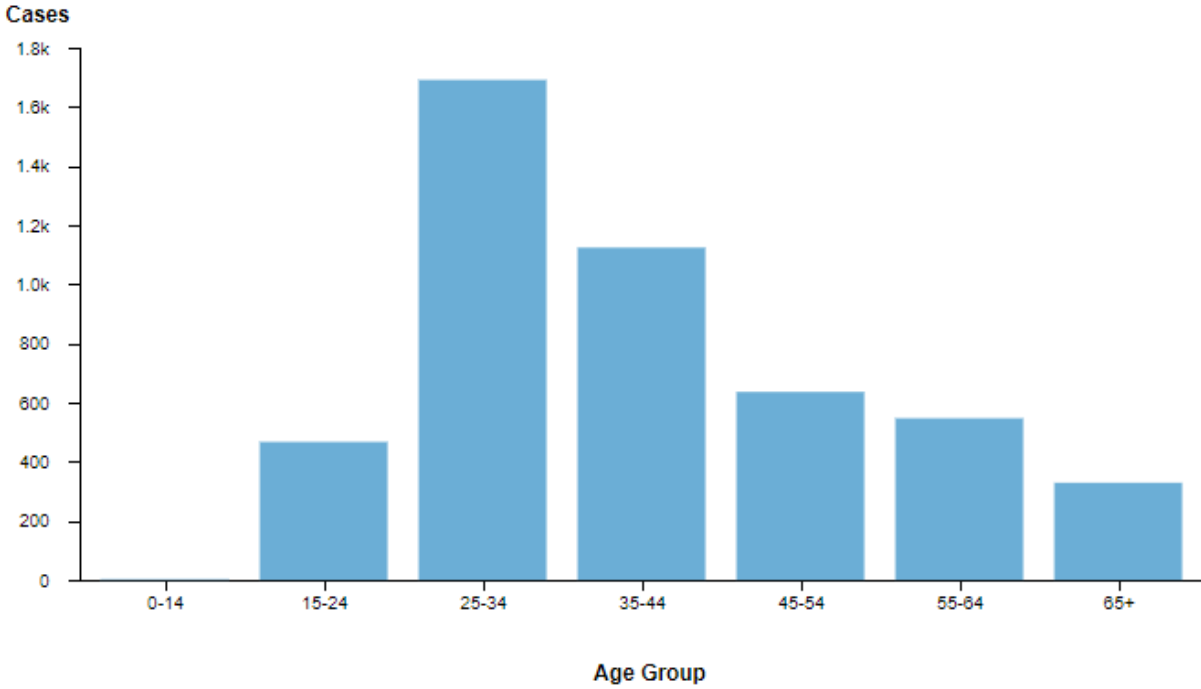
Viral Hepatitis - HCV

Acute Viral Hepatitis C | 2020 (COVID-19 Pandemic) | All age groups | All races/ethnicities | Both sexes | United States



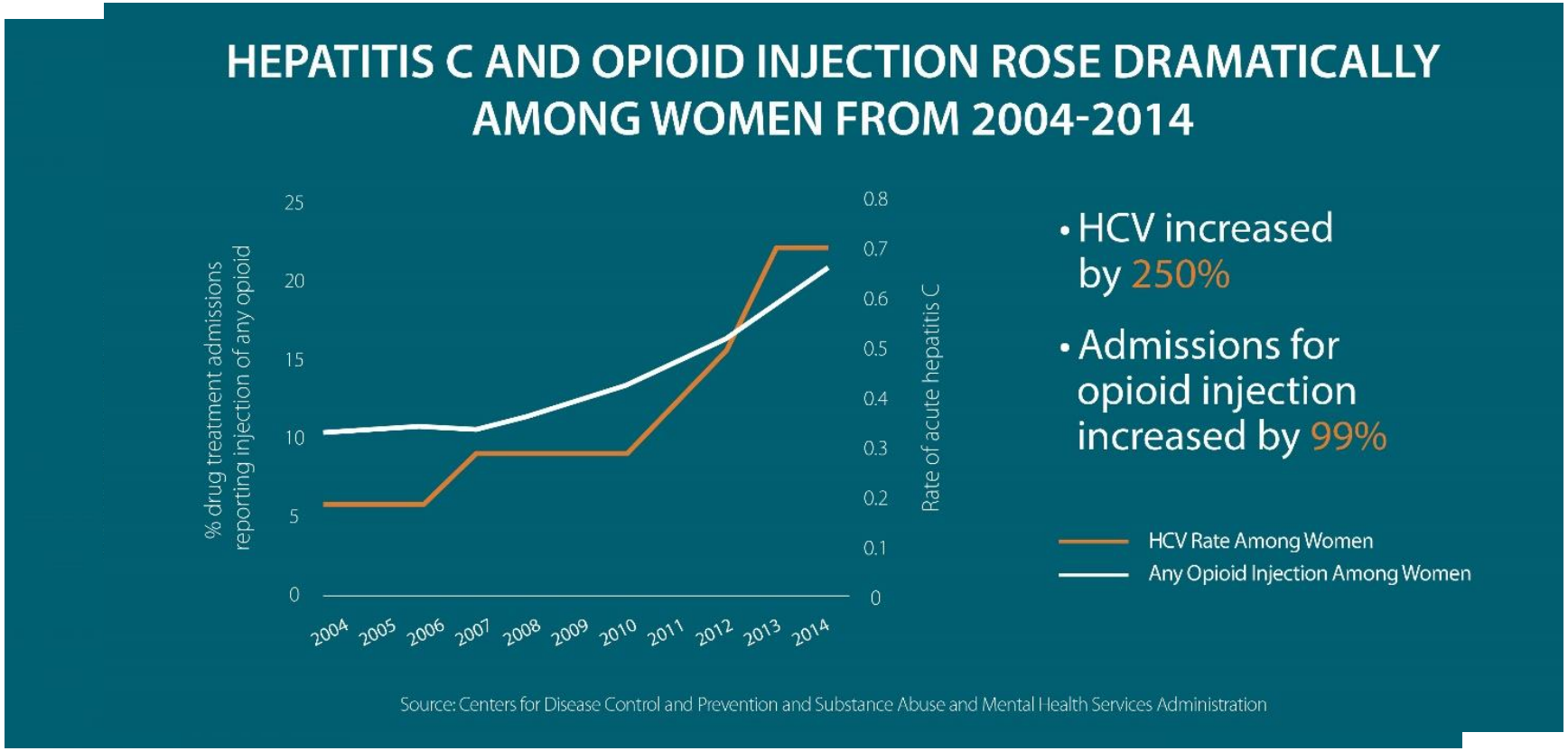


Acute Viral Hepatitis C | 2020 (COVID-19 Pandemic) | All age groups | All races/ethnicities | Both sexes | United States



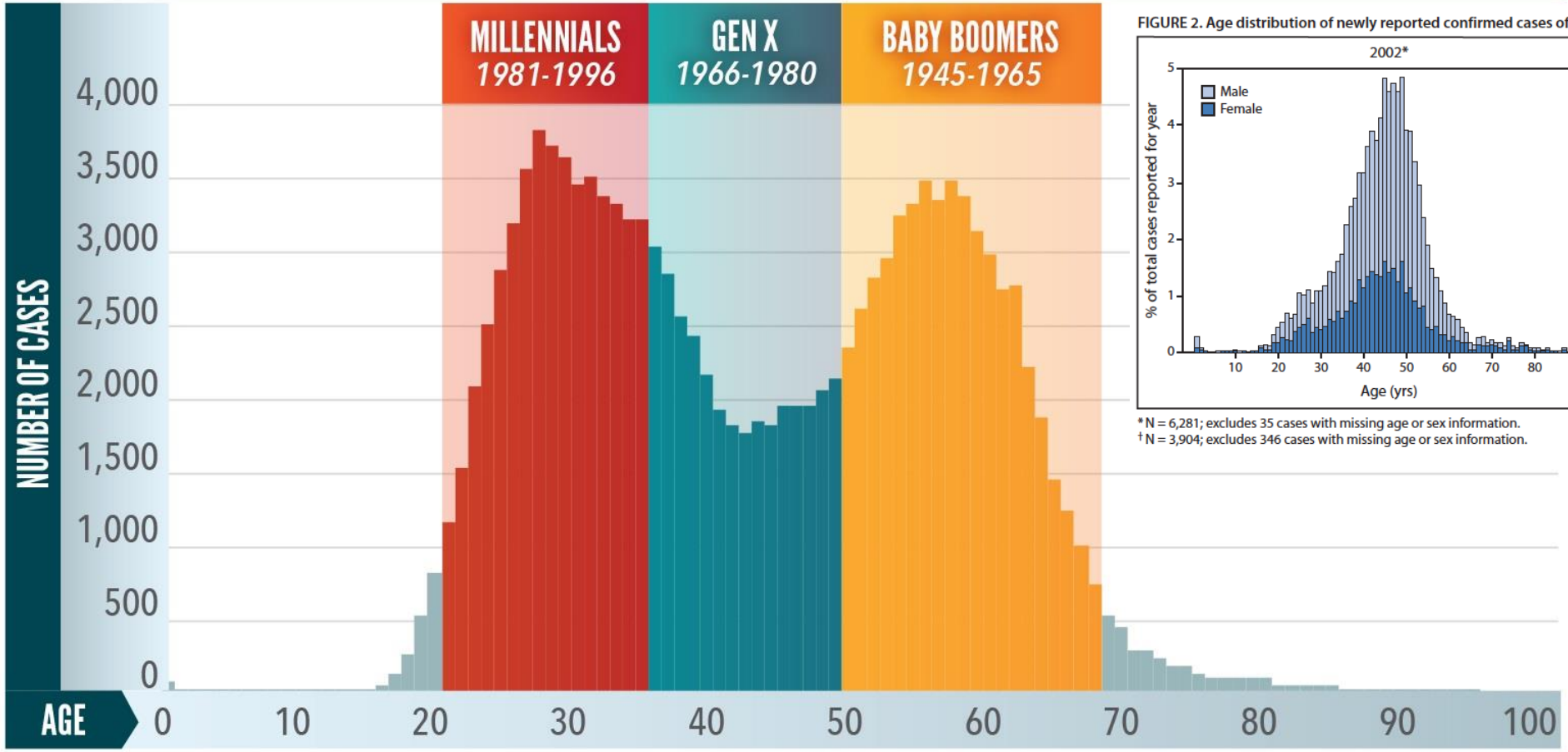
CDC.gov: https://gis.cdc.gov/grasp/nchhstpatlas/charts.html

Viral Hepatitis - HCV



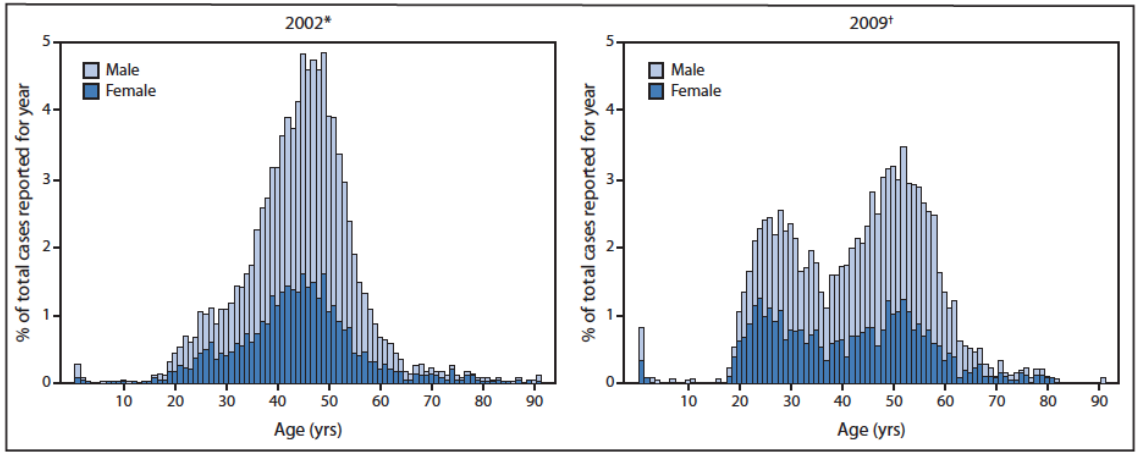
Zibbell JE, *American Journal of Public Health*, 2018
CDC.Gov: https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection.html

New Reports of Chronic Hepatitis C High in Multiple Generations



SOURCE: National Notifiable Diseases Surveillance System, 2018

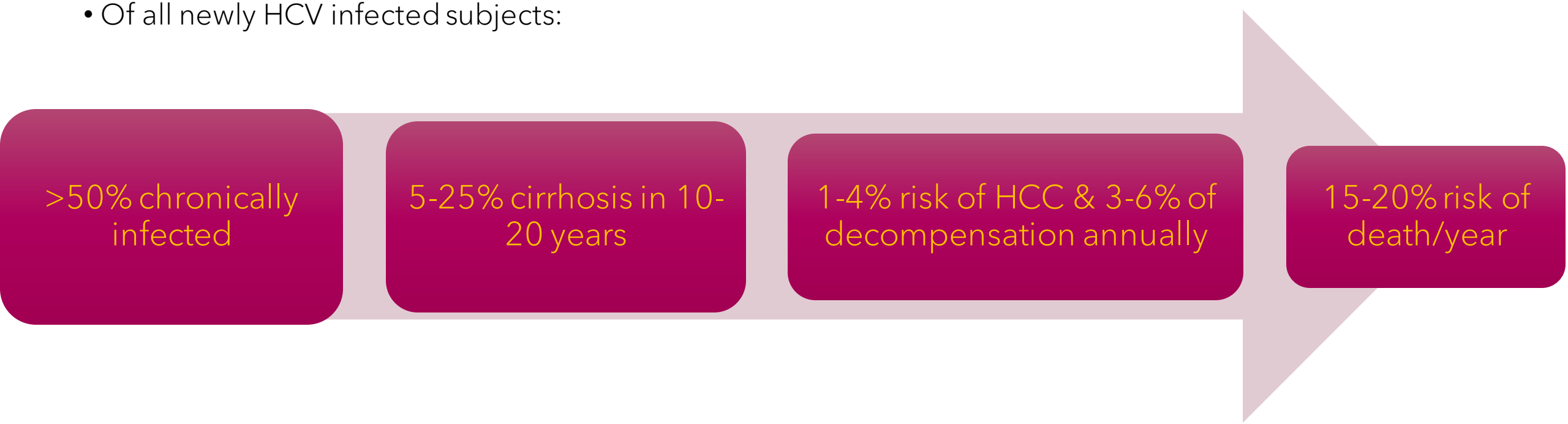
FIGURE 2. Age distribution of newly reported confirmed cases of hepatitis C virus infection — Massachusetts, 2002 and 2009



*N = 6,281; excludes 35 cases with missing age or sex information.
†N = 3,904; excludes 346 cases with missing age or sex information.

CDC.gov: https://www.cdc.gov/nchhstp/newsroom/2020/hepatitis-c-impacting-multiple-generations.html; https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6017a2.htm

- ~2.4 million people live with chronic HCV (1% of the population – 2013-2016 estimate)
- ~40% unaware of their infection
- Of all newly HCV infected subjects:



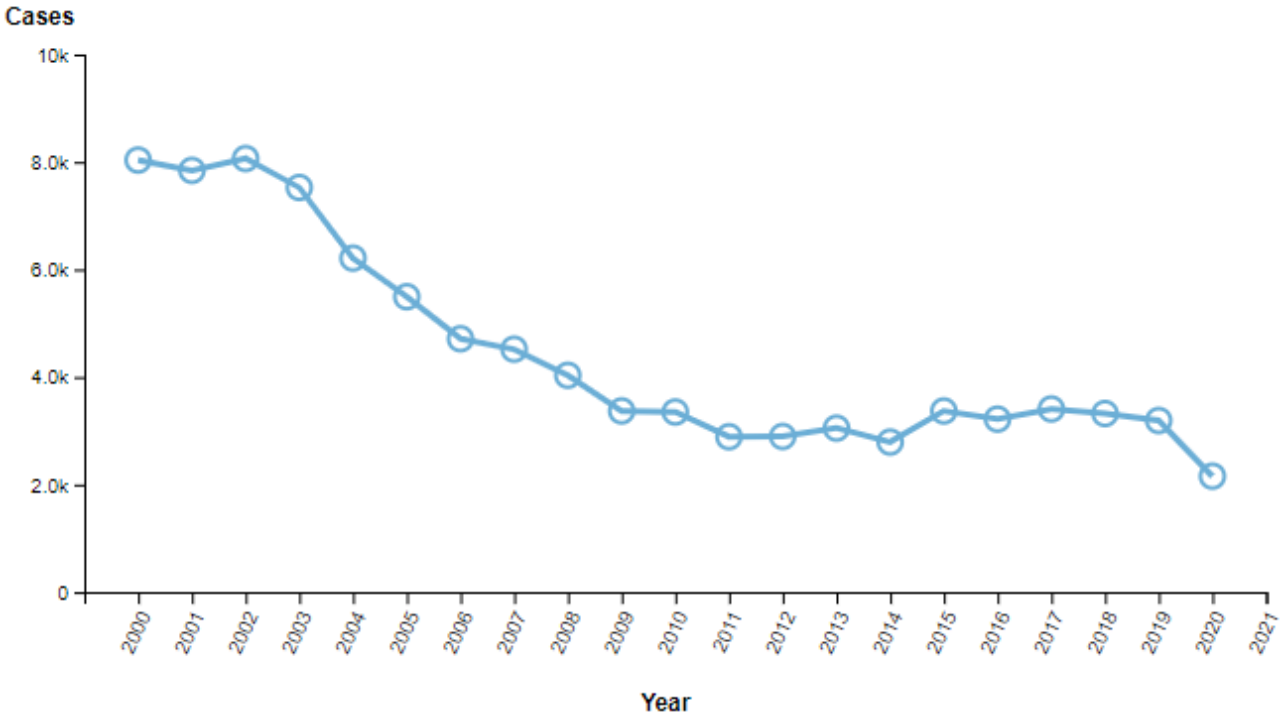
VIRAL HEPATITIS - HCV

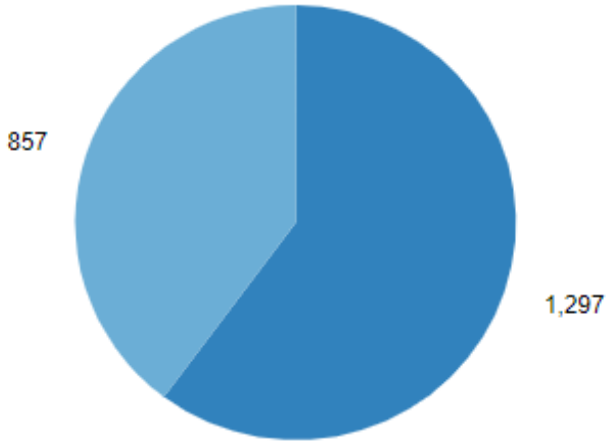
https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/hepatitis-c-basics/index.html;

https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm

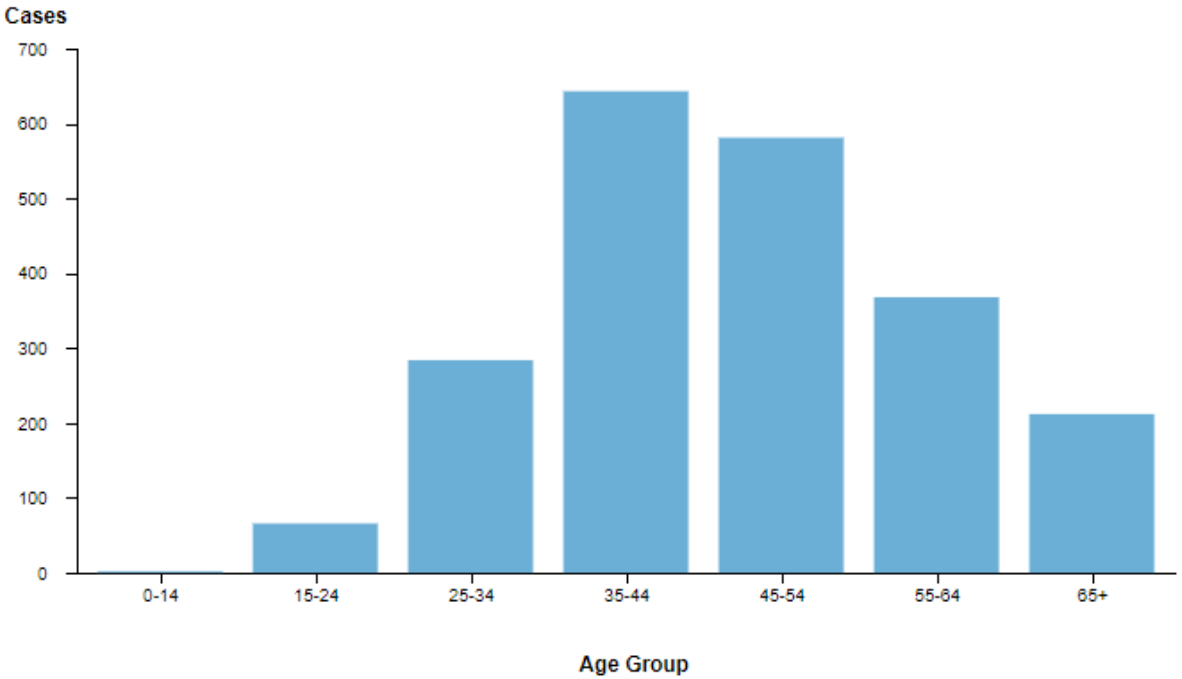
Viral Hepatitis - HBV

Acute Viral Hepatitis B | 2000-2020 (COVID-19 Pandemic) | All age groups | All races/ethnicities | Both sexes | United States





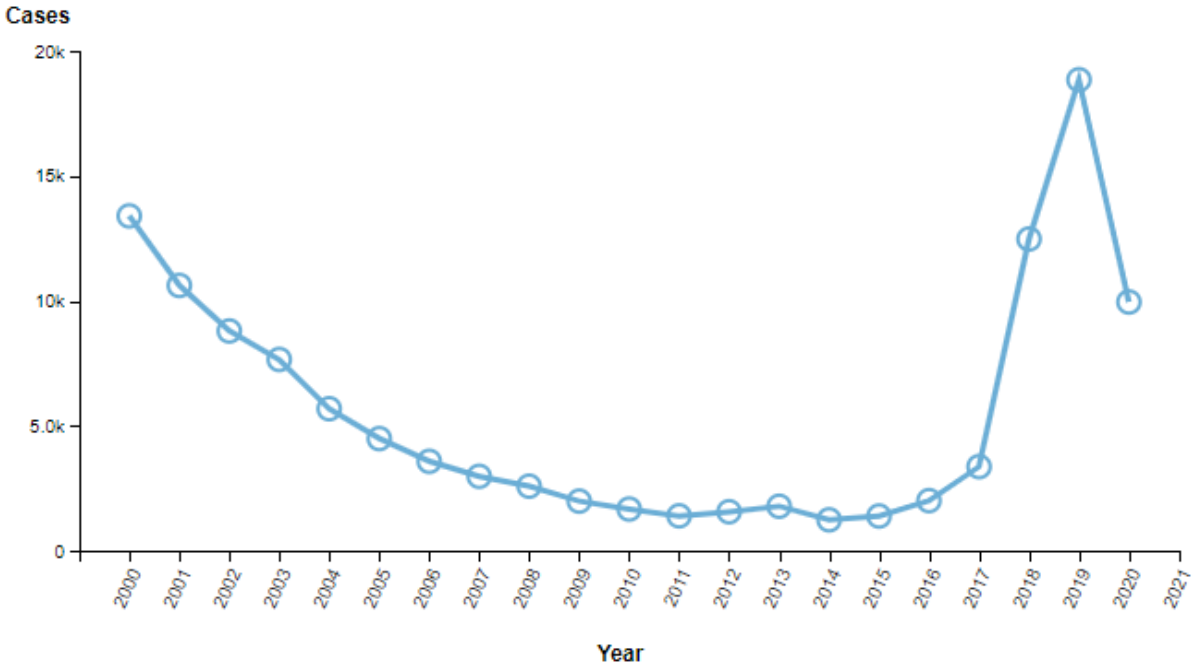
Acute Viral Hepatitis B | 2020 (COVID-19 Pandemic) | All age groups | All races/ethnicities | Both sexes | United States

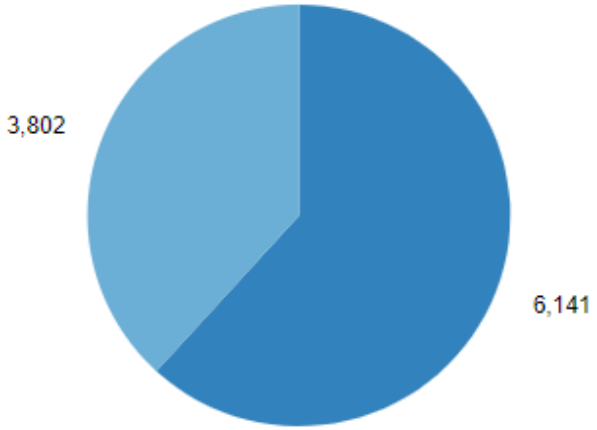


CDC.gov: https://gis.cdc.gov/grasp/nchhstpatlas/charts.html

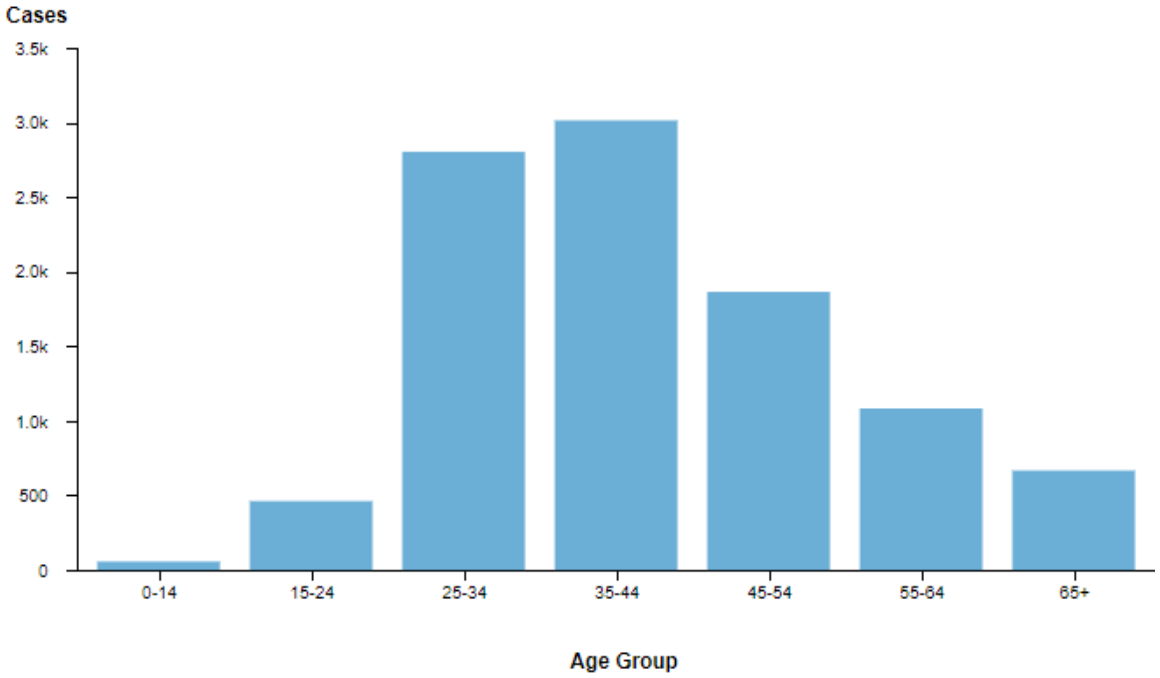
Viral Hepatitis - HAV

Hepatitis A | 2000-2020 (COVID-19 Pandemic) | All age groups | All races/ethnicities | Both sexes | United States





Hepatitis A | 2020 (COVID-19 Pandemic) | All age groups | All races/ethnicities | Both sexes | United States



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

HBV and HAV vaccination uptake

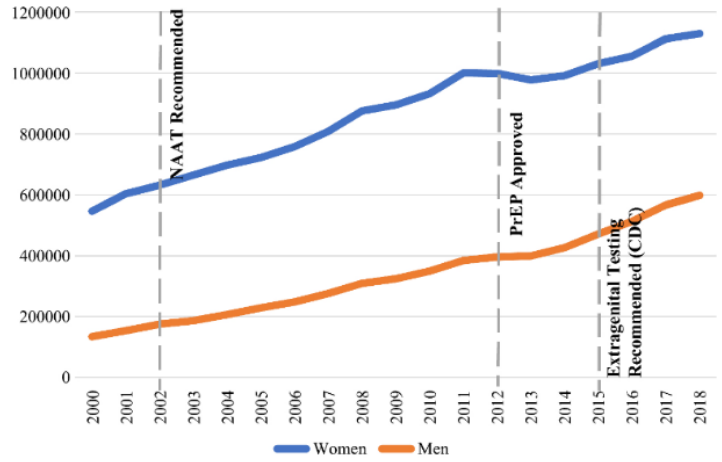
Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos
Hepatitis B (HepB)	1st dose	←2nd dose→			←3rd dose→			
Hepatitis A (HepA)					See notes		←2-dose series, See notes→	

- coverage for HBV in children increased from 63% to 86% between 1999-2016, though immunity waned as years progressed
- coverage for HAV has been lower: ~70% for both doses in 2017
- **substantial increases in incidence of HAV occurred since late 2016 due to ongoing outbreaks among people who use drugs and people experiencing homelessness as well as outbreaks among men who have sex with men => consider testing & vaccinating these populations early**

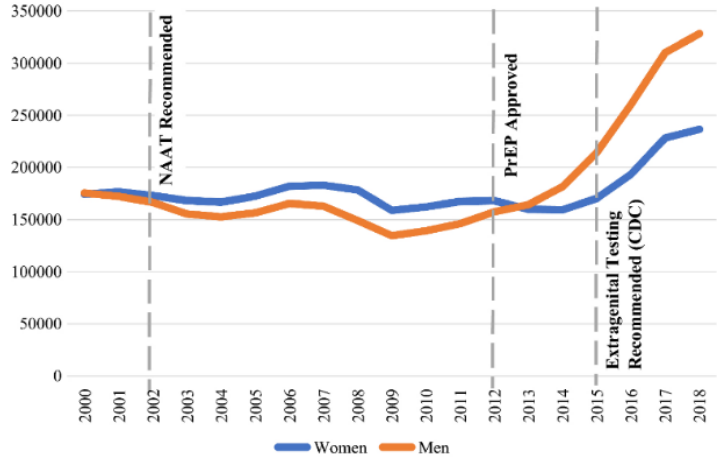
CDC.gov: https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html; https://www.cdc.gov/vaccines/acip/recs/grade/hep-a-catchup-etr.html; https://www.cdc.gov/hepatitis/outbreaks/hepatitisaoutbreaks.htm;
Le MH, *JAMA Netw Open.* 2020;3(11):e2022388

Sexually Transmitted Infections - STIs

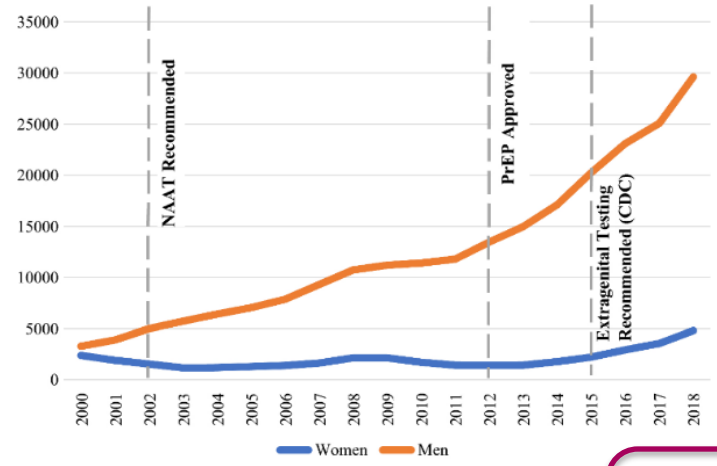
Chlamydia

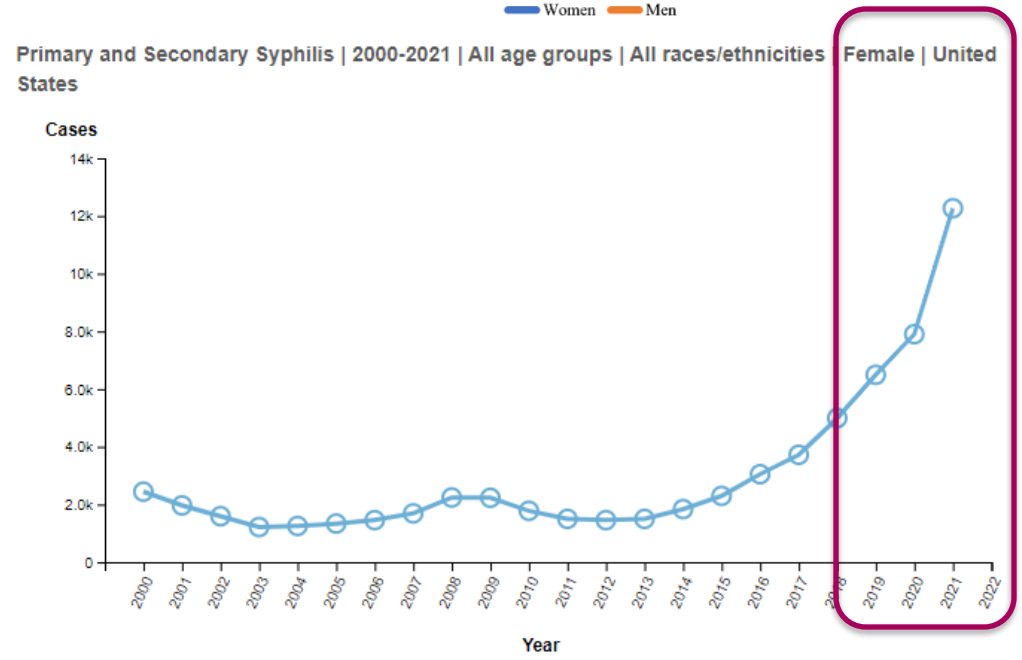


Gonorrhea



Primary/Secondary Syphilis (ref 1)





CDC.gov: https://gis.cdc.gov/grasp/nchhstpatlas/charts.html;
Scott-Sheldon LAJ, *Arch Sex Behav* 2020

STIs – contributing factors

- more vulnerable during altered state of consciousness and cooccurring mental health disorders
- higher propensity toward risk taking
- sex in exchange for drugs and/or money, particularly when contributing socio-economic factors are present

contrast, users of illicit drugs had a significantly higher level of unprotected sex at last intercourse over the 15-year period than those who had never used illicit drugs. Previous studies have shown an association between drug use and nonuse of condoms.[9,19]

Figure 1. **Percentage of High School Students Sexually Active in Past 3 Months by Past-Month Alcohol Use 1991-2005 YRBS (Vertical Bars Indicate 95% CIs)**

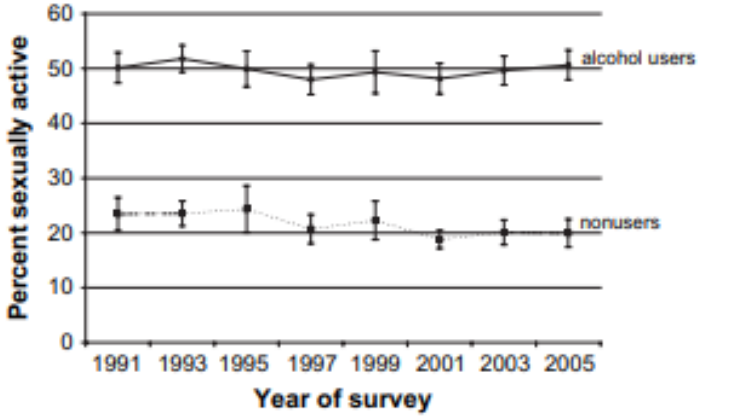
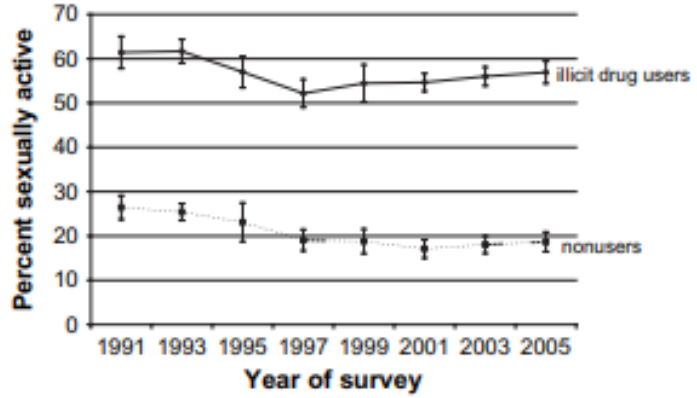


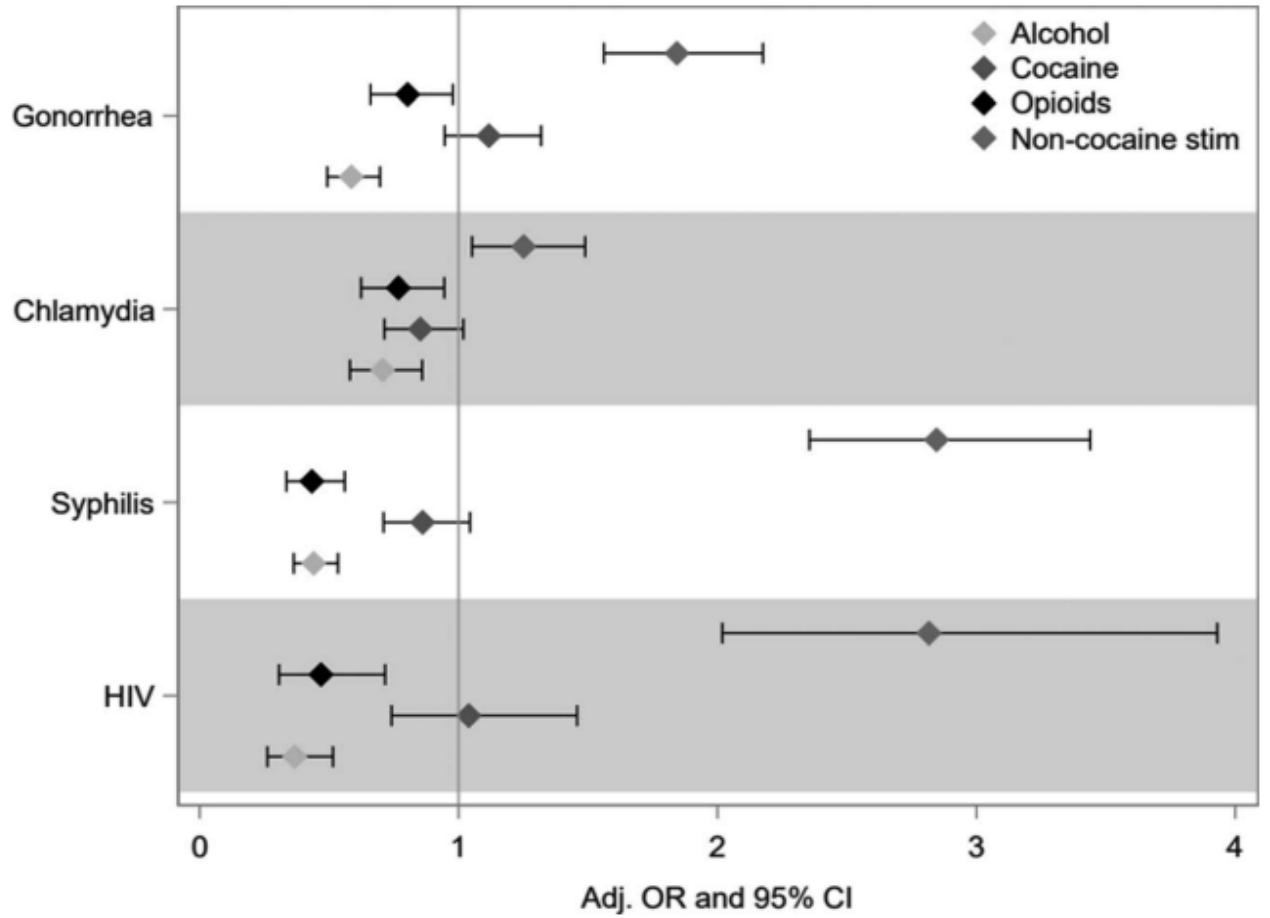
Figure 2. **Percentage of High School Students Sexually Active in Past 3 Months by Lifetime Illicit Drug Use 1991-2005 YRBS**



Anderson JE, Mueller TE. J Sch Health 2008

STIs – contributing factors

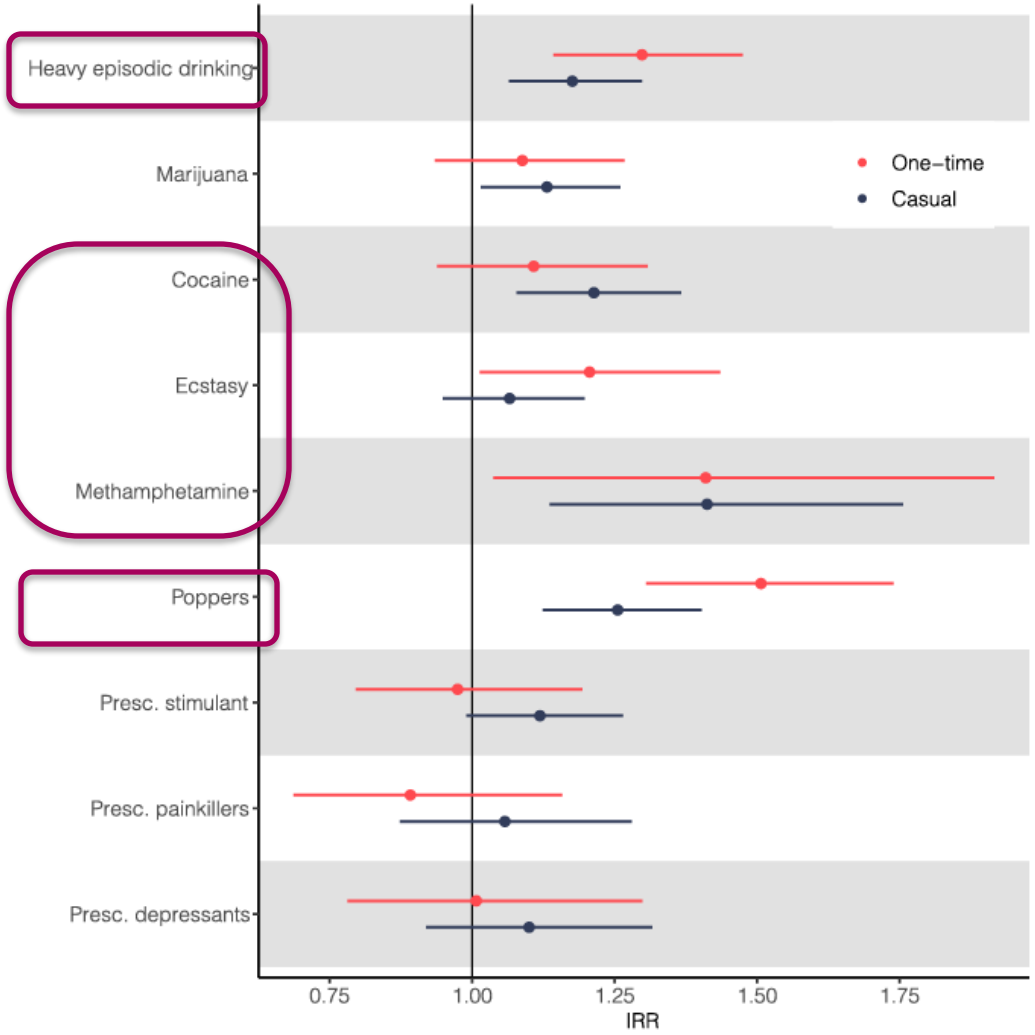
- no comparisons of STI rates in people w/o SUD vs with SUD were performed in this study



STIs – contributing factors

KEY POINTS

- There has been no significant improvement in the global rates of STIs over the past 20 years and dramatic increases over the past decade in rates of STIs in men who have sex with men in high-income settings
- Antimicrobial resistance in important STI pathogens, such as *Neisseria gonorrhoeae*, is an urgent global public health threat.
- Here, we will review recent findings regarding the efficacy of novel antimicrobial treatment strategies for key sexually acquired pathogens and discuss emerging biomedical prevention strategies for bacterial STIs.



Williams E, et al., Curr Opin Infect Dis 2021; substance use and casual sex in MSM => Janulis P, et al., Drug Alcohol Depend. 2023

PREVENTION, DIAGNOSIS AND MANAGEMENT OF SUD-ASSOCIATED INFECTIONS IN VARIOUS SETTINGS

- HIV
- Viral Hepatitis
- STIs

HIV, VIRAL HEPATITIS & STI

- Regular screening of asymptomatic PWUD as well as PWUD with fever, jaundice, malaise/fatigue/body-aches, skin rash/lesions, genital lesions/discharge, etc.
- Targeted blood work (HIV/viral hepatitis serology and/or PCR; TPA +/- RPR), CSF VDRL and cell counts/chemistries (if neurosyphilis suspected, including intra-ocular), GC/Chlamydia/Trich NAAT from genital swabs/urine, throat and or rectum (based on exposure history), HSV serology and/or PCR from lesions, etc. (i.e. skin/hair parasites, Mycoplasma genitalium, Chancroid, Granuloma inguinale (Donovanosis), HPV-associated cancers, MPox)
- Counselling on prevention AND harm reduction techniques

HIV, VIRAL HEPATITIS & STI

BOX 1. The Five P's approach for health care providers obtaining sexual histories: partners, practices, protection from sexually transmitted infections, past history of sexually transmitted infections, and pregnancy intention

1. Partners
- "Are you currently having sex of any kind?"
- "What is the gender(s) of your partner(s)?"

2. Practices
- "To understand any risks for sexually transmitted infections (STIs), I need to ask more specific questions about the kind of sex you have had recently."
- "What kind of sexual contact do you have or have you had?"
  - "Do you have vaginal sex, meaning 'penis in vagina' sex?"
  - "Do you have anal sex, meaning 'penis in rectum/anus' sex?"
  - "Do you have oral sex, meaning 'mouth on penis/vagina'?"

3. Protection from STIs
- "Do you and your partner(s) discuss prevention of STIs and human immunodeficiency virus (HIV)?"
- "Do you and your partner(s) discuss getting tested?"
- For condoms:
  - "What protection methods do you use? In what situations do you use condoms?"

4. Past history of STIs
- "Have you ever been tested for STIs and HIV?"
- "Have you ever been diagnosed with an STI in the past?"
- "Have any of your partners had an STI?"

Additional questions for identifying HIV and viral hepatitis risk:
- "Have you or any of your partner(s) ever injected drugs?"
- "Is there anything about your sexual health that you have questions about?"

5. Pregnancy intention
- "Do you think you would like to have (more) children in the future?"
- "How important is it to you to prevent pregnancy (until then)?"
- "Are you or your partner using contraception or practicing any form of birth control?"
- "Would you like to talk about ways to prevent pregnancy?"

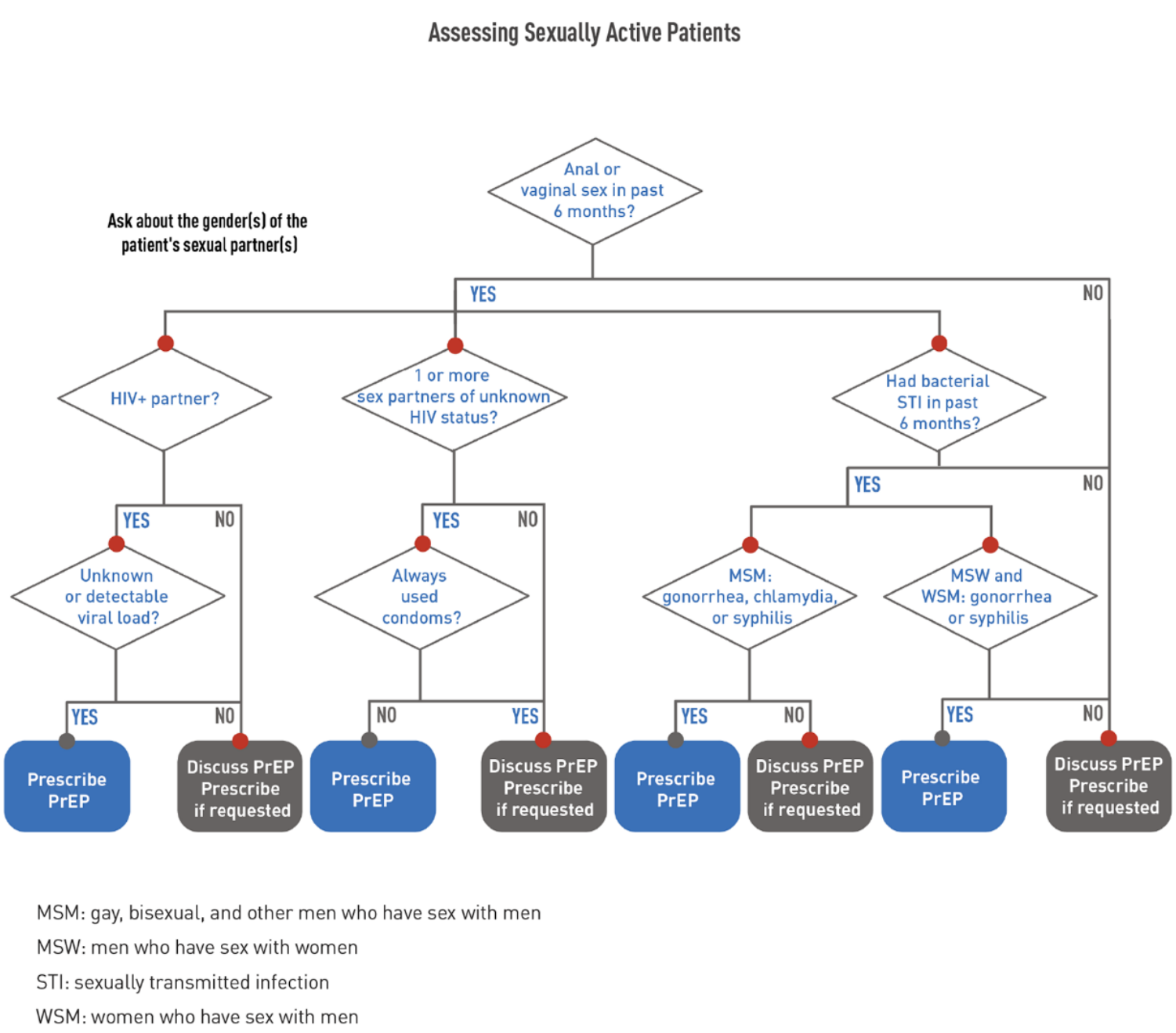
https://www.cdc.gov/std/treatment-guidelines/default.htm

HIV PrEP

Oral sex

- carries little to no risk for transmission of HIV
- transmission of HIV is possible if an HIV-positive man ejaculates in his partner's mouth during oral sex
- risk of transmitting HIV through oral sex increases if: oral ulcers, bleeding gums, genital sores, and the presence of other sexually transmitted diseases (STDs), which may or may not be visible

https://www.hiv.gov/hiv-basics/hiv-prevention/reducing-sexual-risk/preventing-sexual-transmission-of-hiv/



https://www.cdc.gov/hiv/clinicians/prevention/prescribe-prep.html

HIV PrEP

Transmission Route	Type of PrEP	Effectiveness Estimate	Interpretation
Sexual	Oral PrEP[1-3]	~99%	Consistently using PrEP as prescribed ensures maximum effectiveness.
	Injectable PrEP[4,5]	≥99%	Injectable PrEP with CAB may be even more effective than daily oral F/TDF at reducing the risk of getting HIV from sex.
Injection Drug Use	Oral PrEP[6,7]	≥74%	This estimate is based on tenofovir alone and not necessarily when taken daily. Two-drug oral therapies and taking oral PrEP medication daily may increase its effectiveness.
	Injectable PrEP	Unknown	The effectiveness of injectable PrEP with CAB at reducing the risk of getting HIV from injection drug use has not yet been studied.

https://www.cdc.gov/hiv/clinicians/prevention/prescribe-prep.html

HIV PrEP

- injectable cabotegravir associated with decreased risk of HIV infection vs oral TDF/FTC (RR=0.33 [95% CI, 0.18-0.62] in MSM and transgender women [n = 4490] and RR=0.11 [95% CI, 0.04-0.31] in cisgender women [n = 3178]).

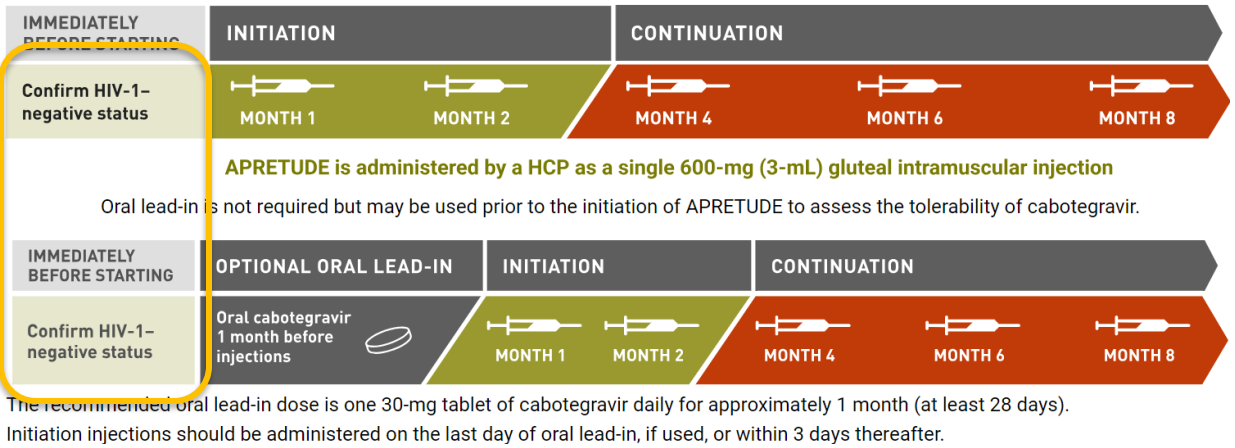
Long-acting injectable cabotegravir vs daily oral TDF/FTC				
HPTN 083 Landovitz et al,[6] 2021 International Median, 1.4 y Good	A: Cabotegravir long-acting injectable (600 mg at wk 5, 9, 17, and every 8 wk afterward) and oral placebo (n = 2282) B: Oral TDF/FTC (300 mg/200 mg once daily) and injectable placebo (n = 2284)	Cisgender men who have sex with men and transgender women who have sex with men	Age (median): 26 vs 26 y Men who have sex with men: 88% vs 87% Transgender women who have sex with men: 12% vs 13%	Received injection with no delay ≥2 wk: 91.5% vs 74% (plasma, tenofovir level >40 ng/mL [consistent with ≥4 doses/wk])
HPTN 084 Delany-Moretwle et al,[7] 2022 Sub-Saharan Africa Median, 1.24 y Good	A: Cabotegravir (600 mg in a 3-mL intramuscular injectable every 8 wk) (n = 1592) B: Daily TDF/FTC (300 mg/200 mg) (n = 1586)	High-risk women Reported at least 2 episodes of vaginal intercourse in the previous 30 d at risk of HIV infection based on an HIV risk score	Age (median): 25 vs 25 y Black race: 97.2% vs 96.5% Gender identity: 99.9% vs 99.8% female, 0% vs 0.2% male, and 0.1% vs 0% transgender male	Received injection with no delay ≥2 wk: 93% vs 42% (plasma, tenofovir level ≥40 ng/mL)

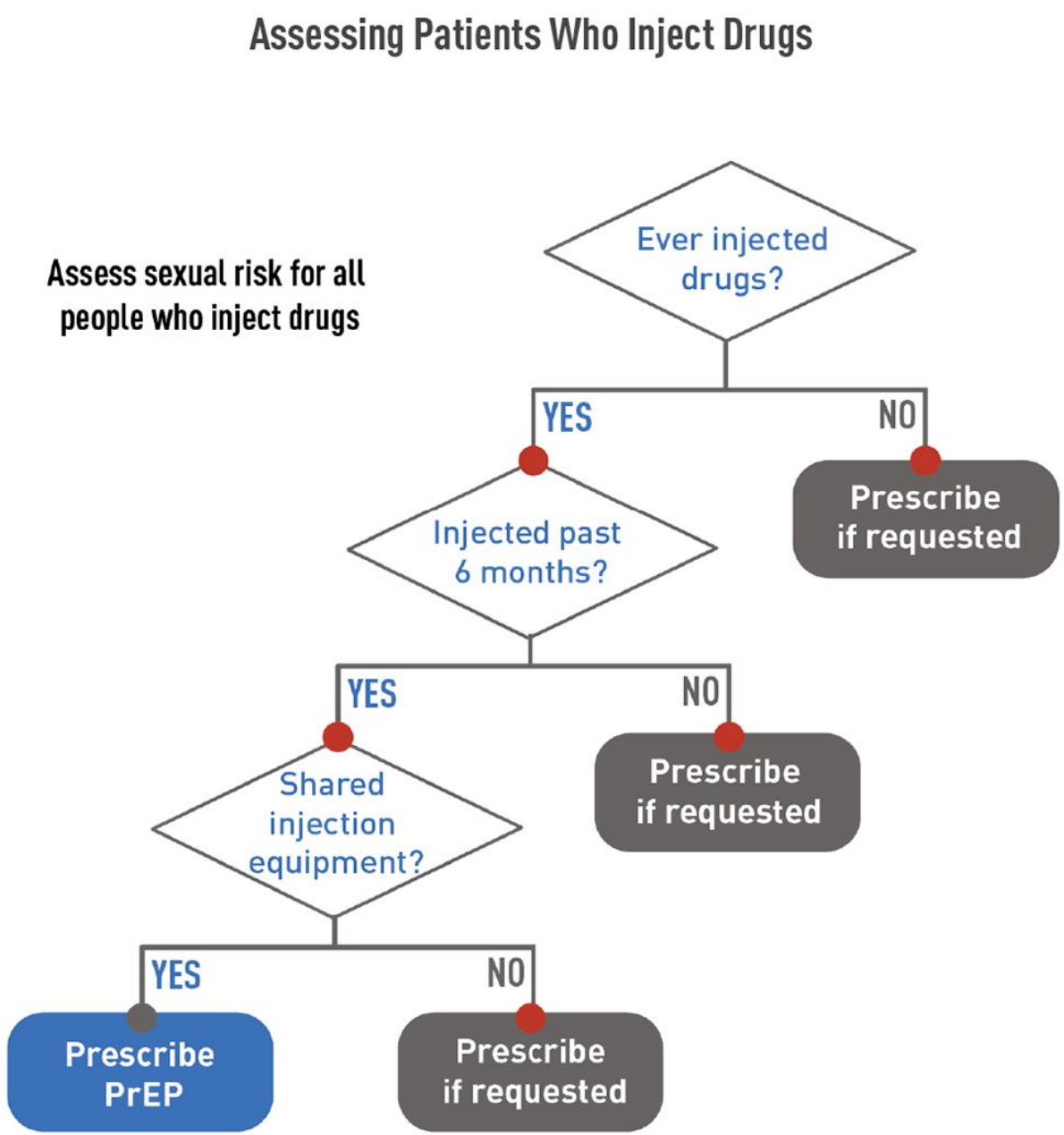
HIV PrEP

Types

- Oral PrEP: emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) or emtricitabine/tenofovir alafenamide (FTC/TAF)

- Injectable: cabotegravir IM (Apretude) => do not use Apretude in HBV+ patients (Oral PrEP acts as treatment of HBV at the same time)





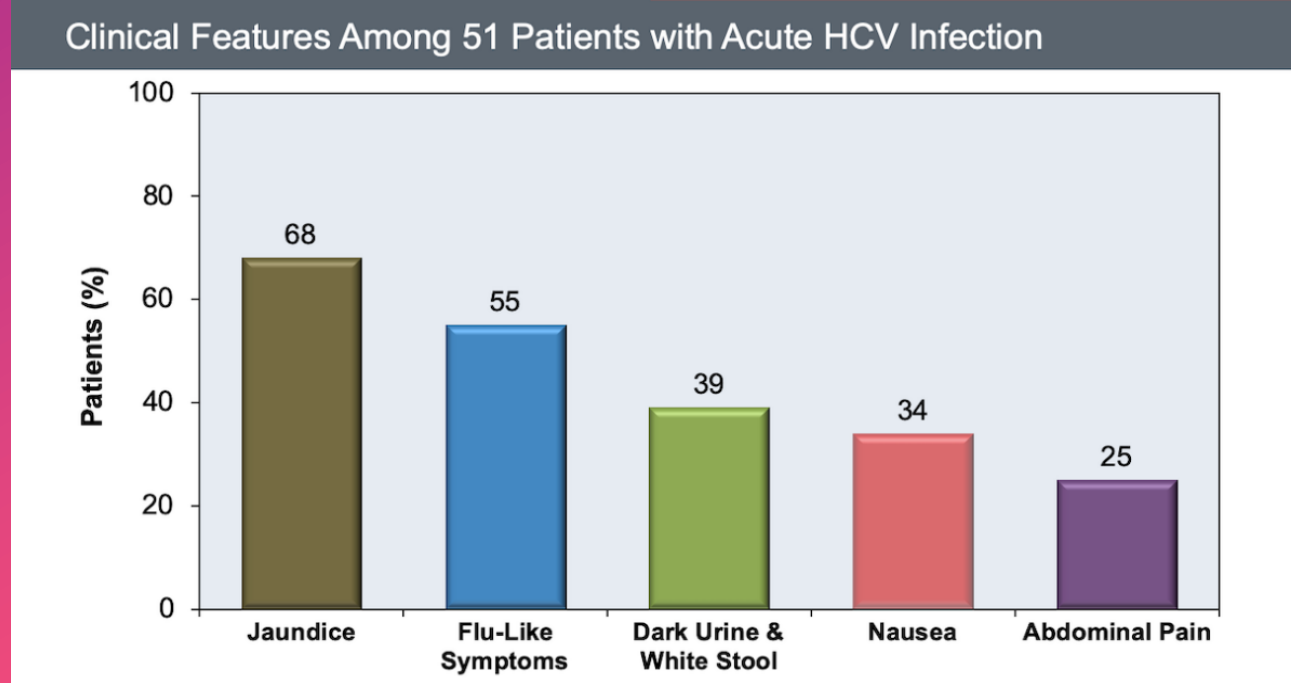
https://www.cdc.gov/hiv/clinicians/prevention/prescribe-prep.html; https://apretudehcp.com/dosing/

Viral Hepatitis: A,B,C,D,E

- A,E => fecal-oral transmission; A not chronic (E can be chronic in immunocompromised => ribavirin); HAV IgM; HEV IgM (HEV RNA PCR exists)
- B,C,D => blood-borne; D only together with B; often chronic (C > B; D infrequent)
- A, B vaccine preventable (C,D,E not)

https://www.niddk.nih.gov/health-information/liver-disease/viral-hepatitis/what-is-viral-hepatitis; https://www.cdc.gov/hepatitis/abc/index.htm

HCV OVERVIEW



Gerlach JT, et al. Gastroenterology. 2003;125:80-8

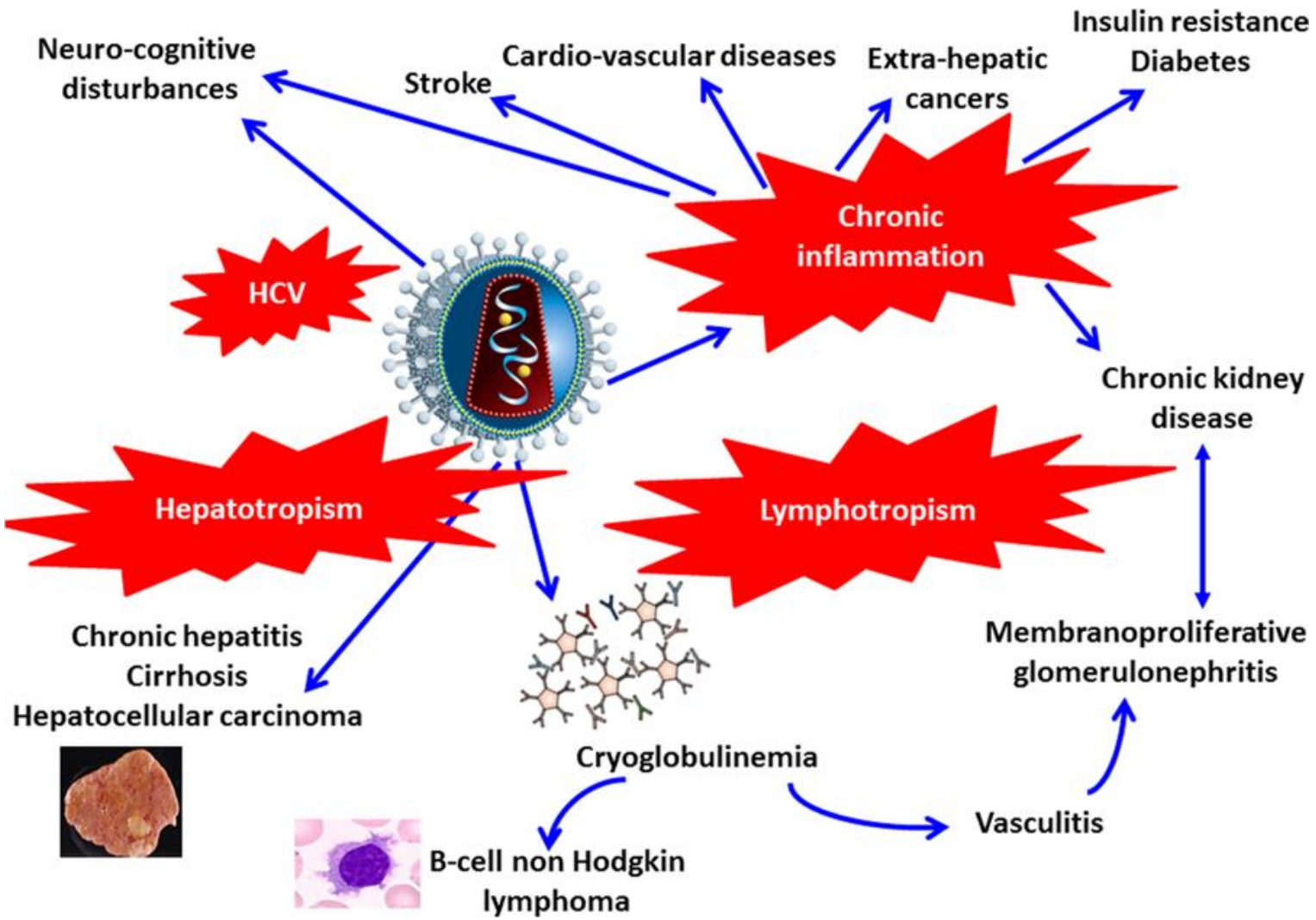
Chronic HCV symptoms:

- **Most commonly asymptomatic!**
- Fatigue
- Depression
- Joint pain and/or muscle pain
- Symptoms consistent with advanced chronic liver disease

CDC FAQ: HCV for Healthcare Professionals

HCV OVERVIEW

POL S, GENES AND IMMUNITY, 2019



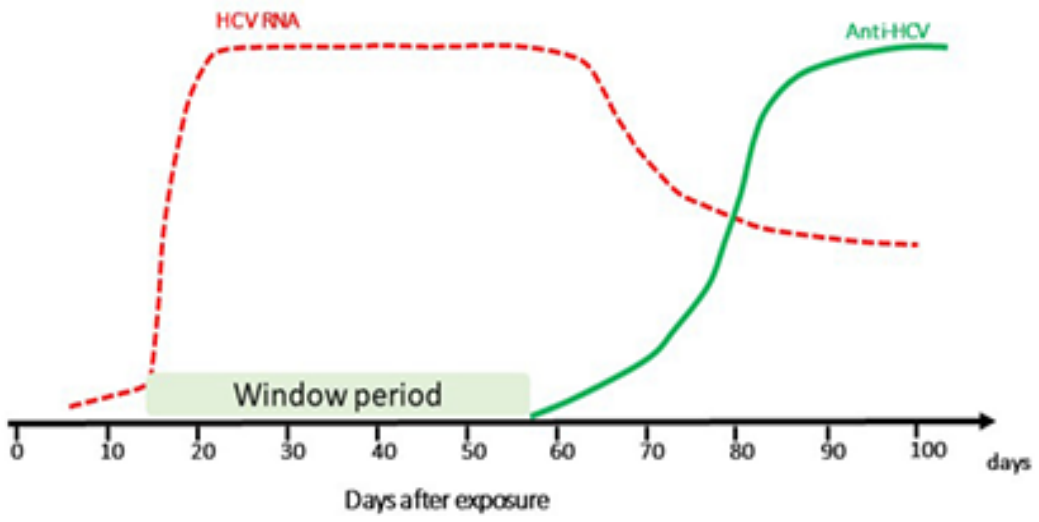
HCV OVERVIEW

Interpretation of Hepatitis C Virus Test Results: Guidance for Laboratories

LABORATORY MARKERS OF HCV INFECTION

Currently available Hepatitis C Virus (HCV) antibody tests have a window period from exposure to HCV to detection of antibody of approximately 8-11 weeks. Nucleic acid amplification tests (NAT) can detect HCV RNA approximately 1-2 weeks after exposure. This means that for the first eight weeks following exposure to HCV antibody tests may not be able to detect HCV antibodies, and for the first 1-2 weeks following HCV exposure NATs may not be able to detect HCV RNA.

Figure 1: Laboratory Markers of HCV Infection (provided by S. Kamili, DVH, CDC)



HCV Linkage to Care

WHO?

ID (non-cirrhotic or compensated cirrhosis, co-infections: HIV, frequent IDU-related SSTIs, hx/o IE, STIs or pos PPD)

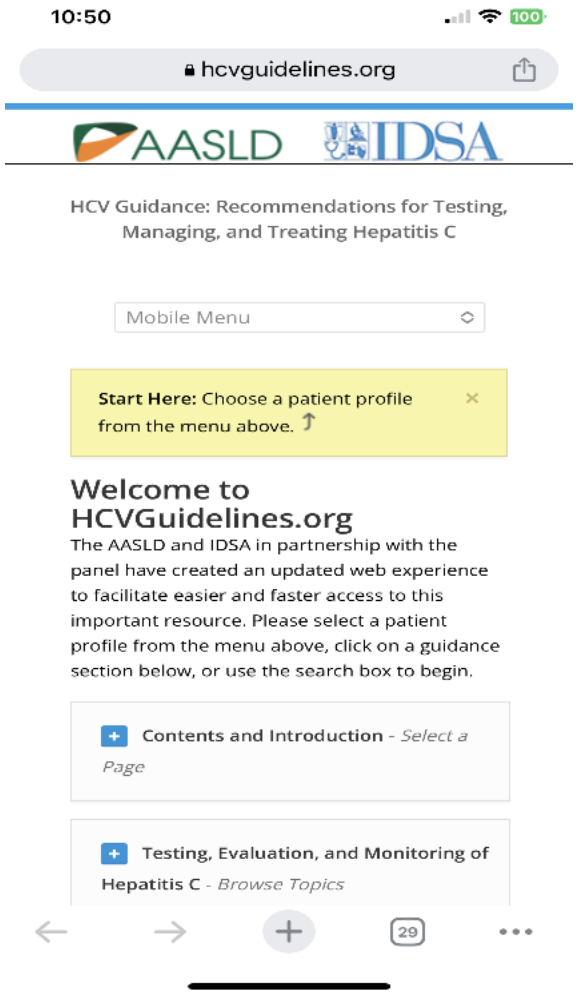
GI (advanced liver diseases, HCC, need for liver transplantation, concurrent chronic pancreatitis with insufficiency, other/unrelated GI co-morbidities)

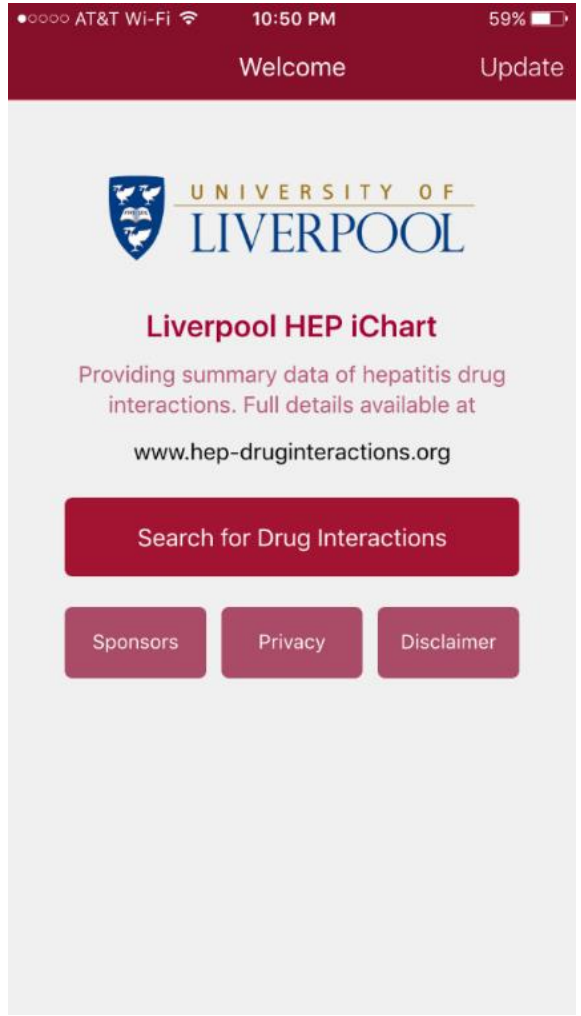
No matter who helps, if **HCV is a result of IDU** – patient still needs mostly you, an addiction specialist! For substance abuse management, psychopharmacology and psychotherapy.

HCV Treatment

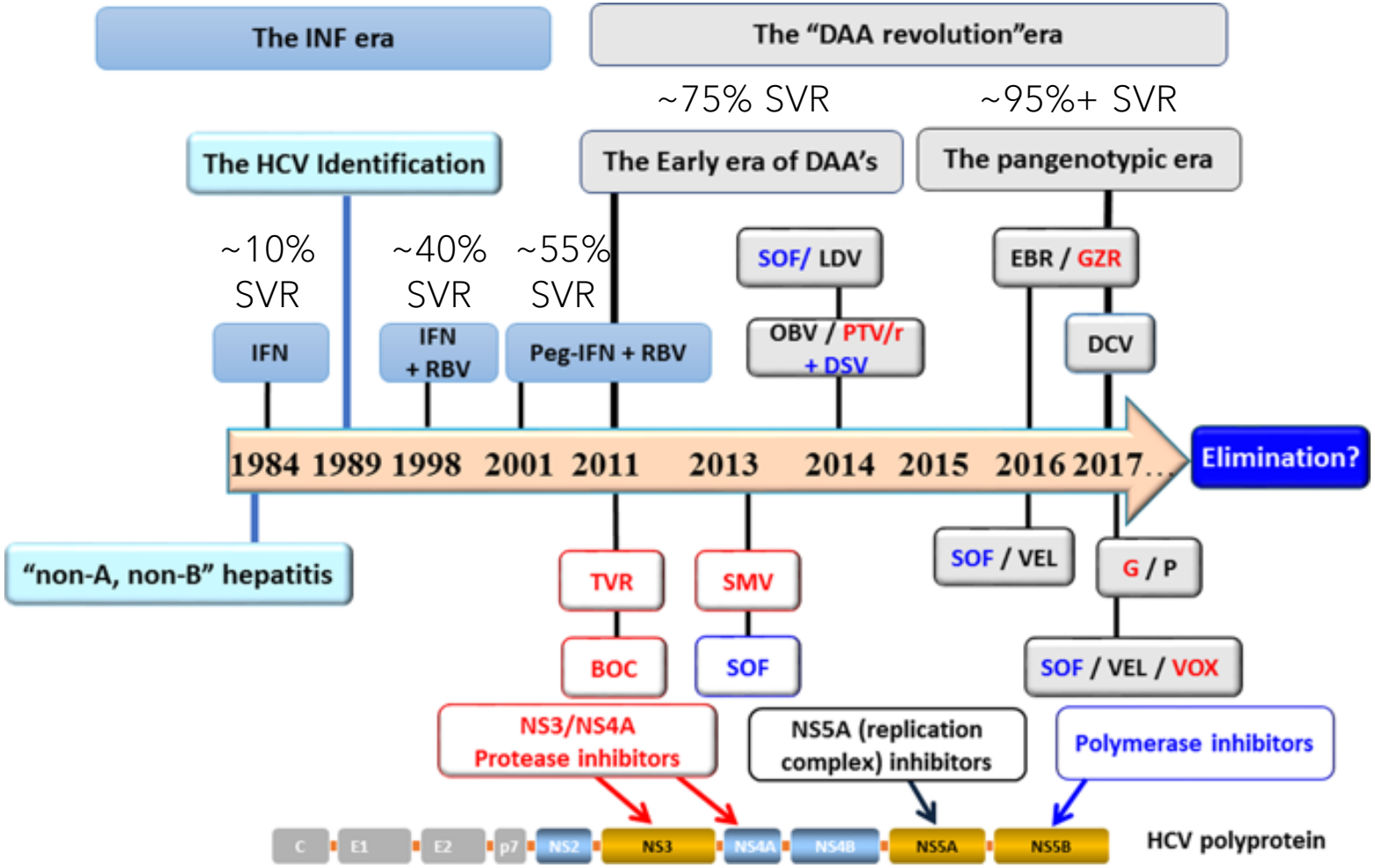
For any patient with HCV – please check hcvguidelines.org
Step by step guidance on full A-to-Z evaluation and important considerations

For patients starting or already on HCV treatment – please check hep-druginteractions.org
Patients should consult you prior to starting new medications or supplements





HCV Treatment



Pol S, *Genes and Immunity,* 2019

RECOMMENDED REGIMENS*	
Glecaprevir (300 mg) / pibrentasvir (120 mg) taken with food for a duration of 8 weeks	**Sofosbuvir (400 mg) / velpatasvir (100 mg)** for a duration of 12 weeks

HCV Treatment for Patients w/o Cirrhosis or with Compensated Cirrhosis

Need to know prior to treatment: stage of liver disease (including ?HCC), comorbidities

Patients should consult you prior to starting new medications or supplements – for current DDI, please check hep-druginteractions.org

People on DM medications should be monitored for hypoglycemia

People on warfarin should be monitored for subtherapeutic INR

Otherwise no monitoring needed

https://www.hcvguidelines.org/

HCV FOLLOW UP AFTER TREATMENT

- SVR-12 testing (HCV RNA 12 or more weeks after treatment completion)

- If SVR achieved:
  - Non-cirrhotic patients do not need additional f/u
  - It is recommended that cirrhotic patients be screened every 6 months for HCC (US +/- AFP)

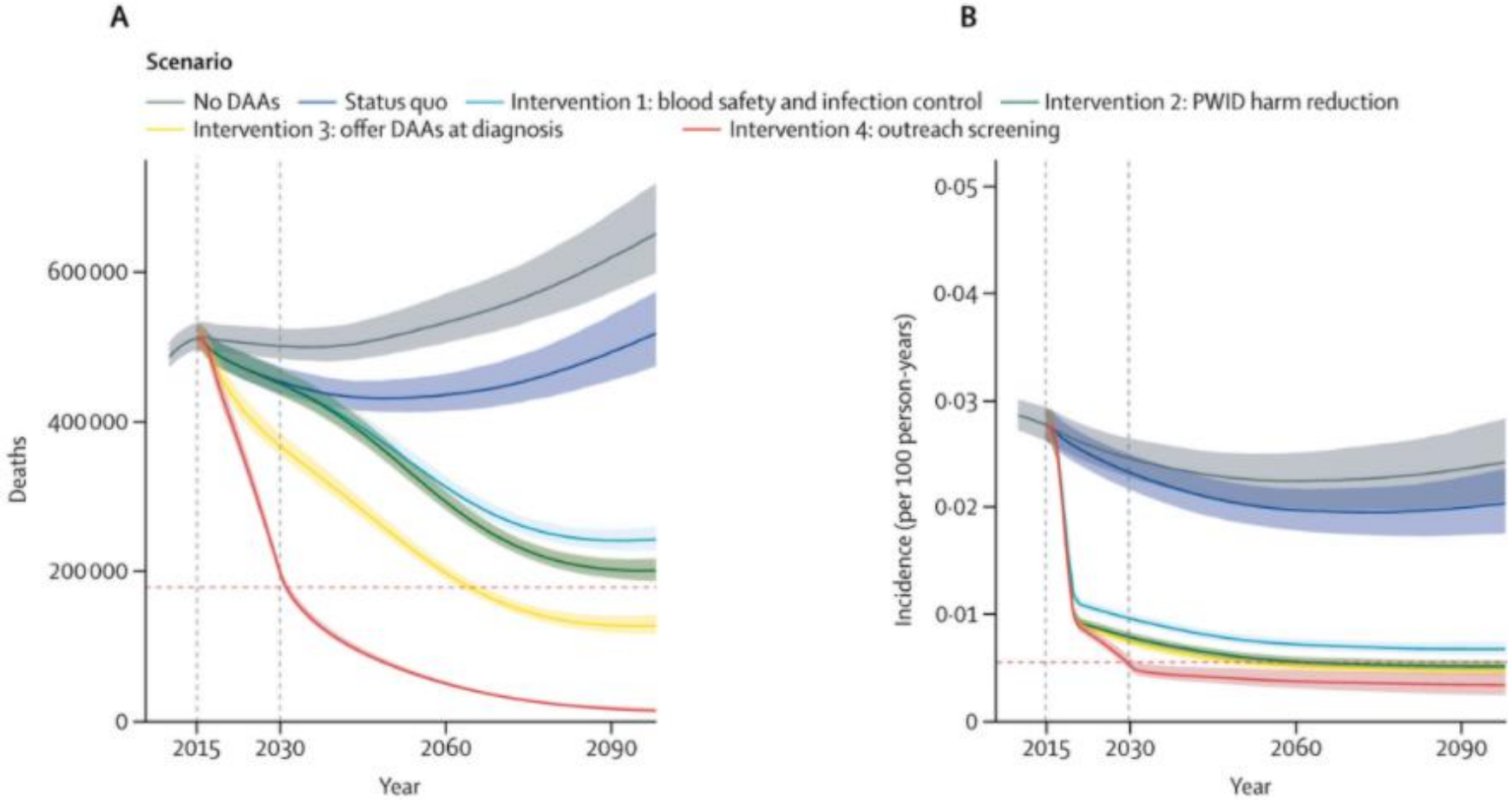
- If SVR not achieved:
  - Evaluate the reasons for failure and prepare for retreatment if appropriate
  - Monitor for progression of liver disease and development of other HCV complications

ACUTE HCV INFECTION

- No Pre- or Post-exposure prophylaxis is currently recommended after exposure

- Treatment is recommended w/o waiting for spontaneous resolution (currently the same regimens and duration as for chronic infection)

https://www.hcvguidelines.org/unique-populations/acute-infection



HCV ELIMINATION GOALS:
-80% INCIDENCE
&
-65% MORTALITY
BY 2030 (WHO)

HEFFFERNAN A, ET AL.. *LANCET* 2019

No further IDU	IDU: DID NOT share needles/syringes	IDU: DID share needles/syringes
1.5/100 person-years	2.4/100 person-years	17.9/100 person-years

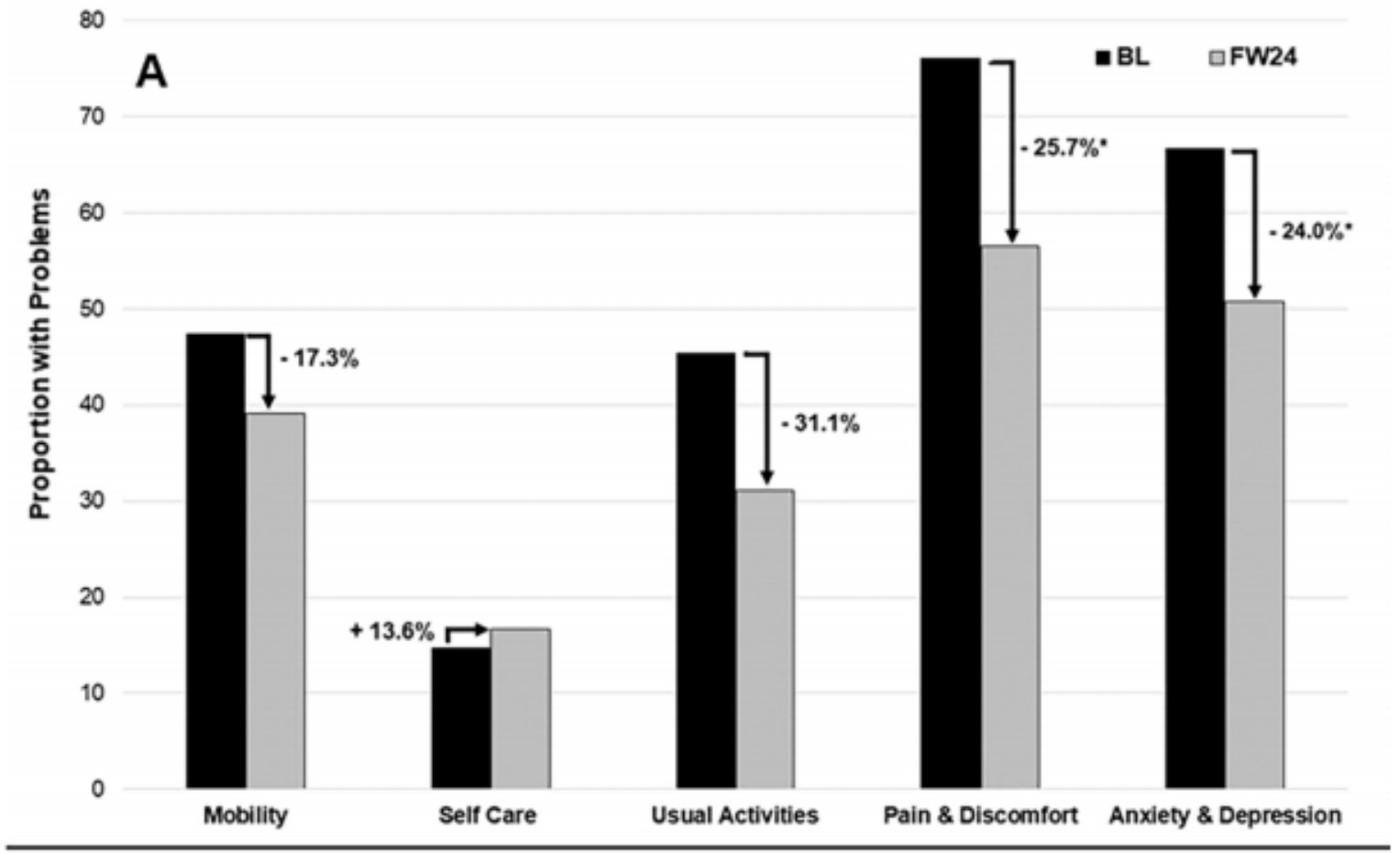
HCV ELIMINATION GOALS: POTENTIAL PROBLEMS WITH HCV REINFECTION AFTER TREATMENT

CUNNINGHAM EB, ET AL.. *CLIN INFECT DIS.* 2021

HCV ELIMINATION GOALS: HCV TREATMENT LED TO SUSTAINED IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE FOR PWID ON OAT WHO ACHIEVED SVR

GORMLEY MA, ET AL.. *CLIN INFECT DIS*. 2021

Figure 1



STIs Prevention - Vaccines

Available and recommended for:

- HAV (2 doses over 6 months)
- HBV (3 doses over 6 months; can be given together with HAV as Twinrix)

=> HAV & HBV are typically started in early childhood and onward

- HPV (2 doses up to age 15 min 5 months apart; 3 doses from 15-45 at 0,1,6-12 months)

=> can start at age 9 and can be considered until the age of 45

- Mpox for MSM and others at risk (SQ JYNNEOS x2 4-weeks apart)

Available but not yet recommended:

- Gonorrhea – Bexsero (MenB-4C vaccine) 2 doses 2 months apart were 40% effective and 1 dose 26% effective

Abara WE, et al.. *Lancet Infect Dis.* 2022

https://www.cdc.gov/std/treatment-guidelines/default.htm (accessed 7/29/23); https://www.cdc.gov/poxvirus/mpox/vaccines/index.html (accessed 7/29/23)

STIs Prevention - PEP

Available and variably recommended by authorities:

- Doxycycline 200 mg PO x1 24-72 hrs after unprotected sex (~80% reduction of Chlamydia and Syphilis, and ~50% reduction of Gonorrhea)

- CDC guideline proposal
  https://www.federalregister.gov/documents/2023/10/02/2023-21725/guidelines-for-the-use-of-doxycycline-post-exposure-prophylaxis-for-bacterial-sexually-transmitted

Lutkemeyer AF, et al.. *N Engl J Med.* 2023; Molina JM, et al.. Abstract #119, CROI 2023

A PrEP Cohort

Analyses	Doxycycline (no. of quarterly visits with event /total no. of visits (%))	Standard Care (no. of quarterly visits with event /total no. of visits (%))	Relative Risk (95% CI)	P Value
Primary analysis				<0.001
Any STI	61/570 (10.7)	82/257 (31.9)	0.34 (0.24–0.46)	
Secondary analysis				
Any gonorrhea	52/570 (9.1)	52/257 (20.2)	0.45 (0.32–0.65)	
Urethral	5/570 (0.9)	12/257 (4.7)	0.19 (0.06–0.55)	
Pharyngeal	38/570 (6.7)	34/257 (13.2)	0.50 (0.32–0.78)	
Rectal	25/570 (4.4)	29/257 (11.3)	0.40 (0.23–0.69)	
Any chlamydia	8/570 (1.4)	31/257 (12.1)	0.12 (0.05–0.25)	
Urethral	1/570 (0.2)	6/257 (2.3)	0.07 (0.01–0.59)	
Pharyngeal	2/570 (0.4)	4/257 (1.6)	0.22 (0.04–1.14)	
Rectal	7/570 (1.2)	23/257 (8.9)	0.14 (0.06–0.32)	
Any early syphilis	2/570 (0.4)	7/257 (2.7)	0.13 (0.03–0.59)	
Subgroup analysis: any STI				
Age				
≤30 yr	15/165 (9.1)	31/91 (34.1)	0.27 (0.15–0.47)	
>30 yr	46/405 (11.4)	51/166 (30.7)	0.37 (0.25–0.55)	
No. of STIs in previous 12 mo				
1	21/227 (9.3)	34/129 (26.4)	0.35 (0.20–0.60)	
>1	40/343 (11.7)	48/128 (37.5)	0.31 (0.21–0.46)	

0.01 0.1 0.5 1.0

Doxycycline Better Standard Care Better

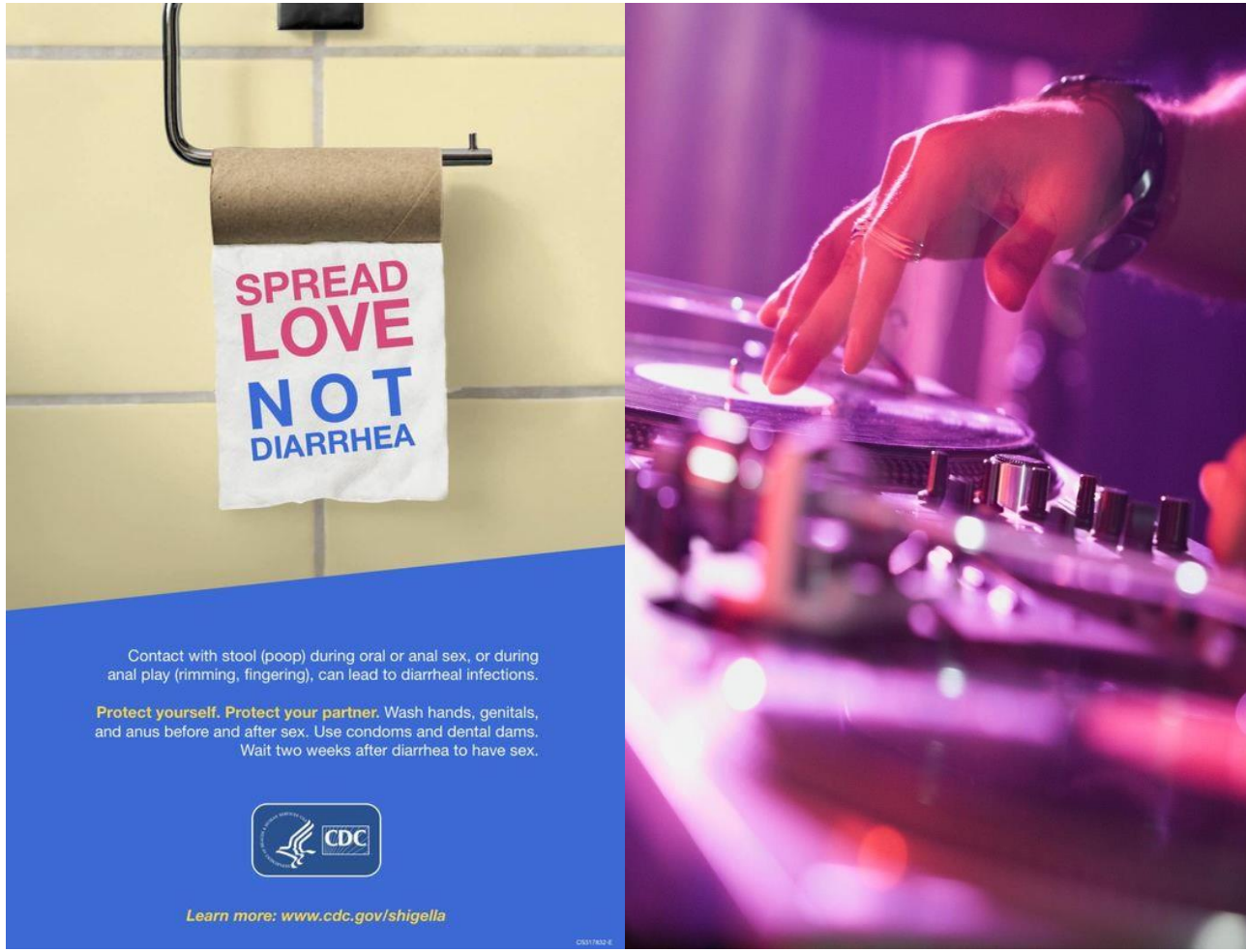
B PLWH Cohort

Analyses	Doxycycline (no. of quarterly visits with event /total no. of visits (%))	Standard Care (no. of quarterly visits with event /total no. of visits (%))	Relative Risk (95% CI)	P Value
Primary analysis				<0.001
Any STI	36/305 (11.8)	39/128 (30.5)	0.38 (0.24–0.60)	
Secondary analysis				
Any gonorrhea	27/305 (8.9)	26/128 (20.3)	0.43 (0.26–0.71)	
Urethral	3/305 (1.0)	5/128 (3.9)	0.23 (0.05–1.02)	
Pharyngeal	15/305 (4.9)	13/128 (10.2)	0.49 (0.23–1.03)	
Rectal	16/305 (5.2)	20/128 (15.6)	0.33 (0.17–0.63)	
Any chlamydia	12/305 (3.9)	19/128 (14.8)	0.26 (0.12–0.57)	
Urethral	2/305 (0.7)	2/128 (1.6)	0.36 (0.06–2.27)	
Pharyngeal	1/305 (0.3)	2/128 (1.6)	0.22 (0.03–1.86)	
Rectal	9/305 (3.0)	17/128 (13.3)	0.23 (0.10–0.54)	
Any early syphilis	2/305 (0.7)	3/128 (2.3)	0.23 (0.04–1.29)	
Subgroup analysis: any STI				
Age				
≤30 yr	9/30 (30.0)	6/19 (31.6)	0.95 (0.41–2.23)	
>30 yr	27/275 (9.8)	33/109 (30.3)	0.32 (0.19–0.54)	
No. of STIs in previous 12 mo				
1	23/196 (11.7)	8/55 (14.6)	0.78 (0.36–1.72)	
>1	13/109 (11.9)	31/73 (42.5)	0.28 (0.15–0.53)	

0.01 0.1 0.5 1.0

Doxycycline Better Standard Care Better

THANK YOU!



https://www.cdc.gov/shigella/posters.html