AETC AIDS Education & Training Center Program Northeast/Caribbean

ABCs of Viral Hepatitis

June 4, 2026

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MGH 1811

Disclosure Statement for Arthur Kim (updated May 15 26)

Grant/research support to institution, last 24 months: No industry support

Consultant/Scientific Advisory Board: Shionogi Inc. (DMC, SAB)

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

Use of antivirals for prophylaxis for HBV

Novel agents for HBV

Treatment for acute HCV

Funding: National Institutes of Health (NIAID)

Objectives

- Review the basics of who is at risk and the natural history of viral hepatitis
- Promote screening, testing, and prevention strategies for viral hepatitis
- Describe basic viral hepatitis evaluation and treatment

Case Question

- 34-year-old HIV+ man who has sex with men presents with fatigue, jaundice
  - on suppressive antiretroviral therapy, denies past or present use of injection drugs
  - Recent travel six weeks previously to Southern France and Italy
  - Ate seafood, some raw
  - Cocaine
  - Multiple sex partners (males)

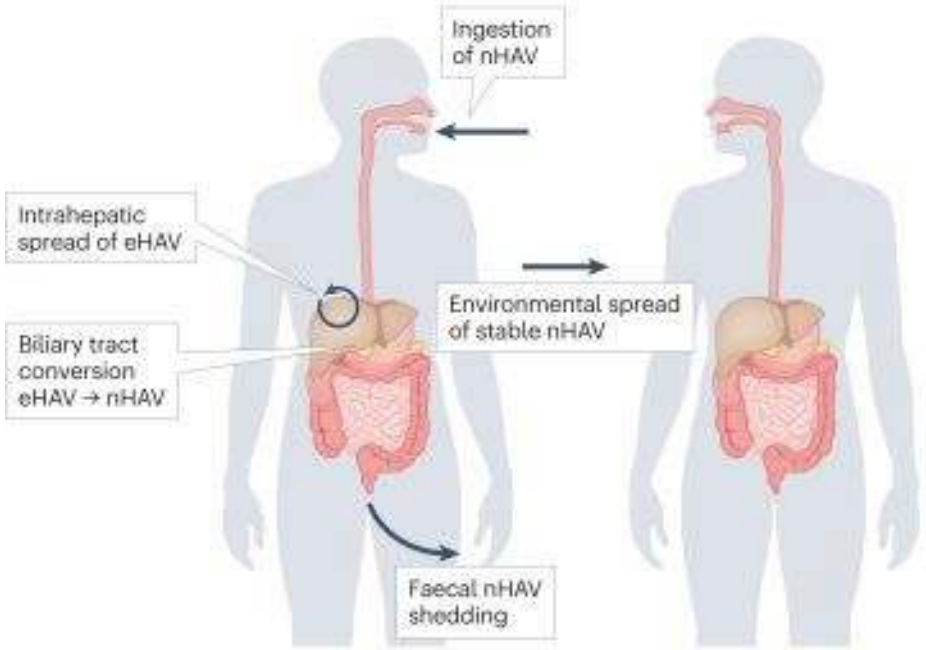
- ALT 2210 (U/L), Bilirubin 4.0

Which of the following diagnoses is most likely?

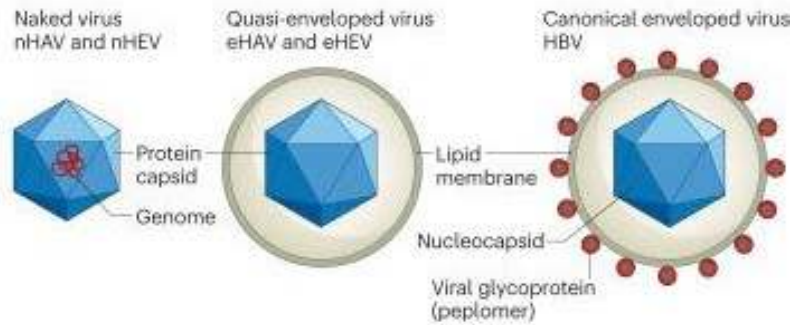
A. Acute hepatitis A
B. Acute hepatitis B
C. Acute hepatitis C
D. Cocaine use
E. Acute hepatitis E

Hepatitis A

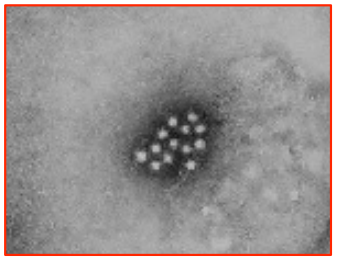
Fecal-oral spread



Quasi-enveloped, becomes naked in GI tract



Das et al. Nature Rev Microbiol 2023

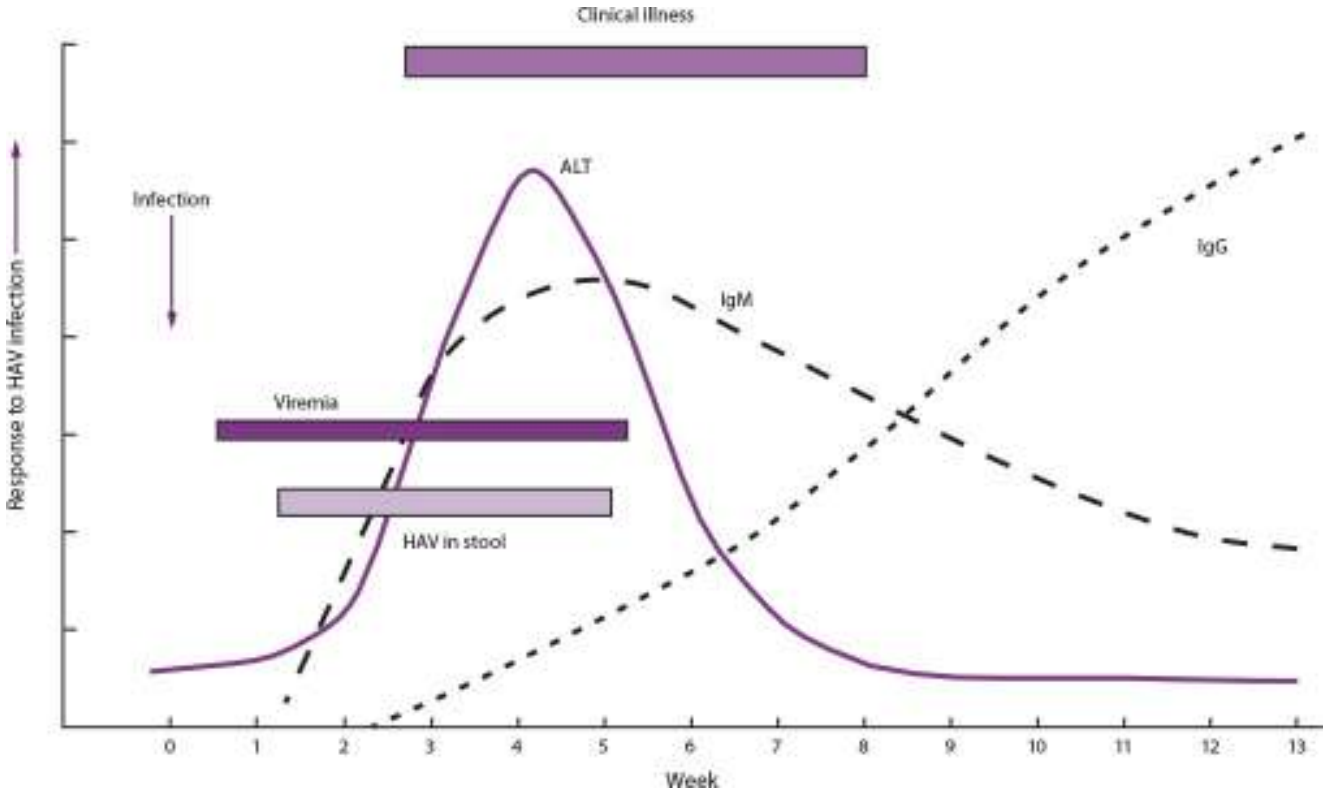


Hepatitis A

	Hepatitis A
Virology	Picornavirus no DNA intermediate 6 genotypes, serologic x-reactive Nonenveloped / Quasi-enveloped
Incubation period	Average 30 days Range 15-50 days
Rate of jaundice	<6 yrs <10% 6-14 yrs, 40-50% >14 years, 70-80%
Complications	Fulminant, cholestatic, relapsing (rare) Death higher if age > 50 and/or underlying liver dz
Chronic infection	None

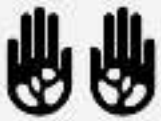
HAV: Virological, Immunological and Clinical Events

Longer incubation times than most viruses, infectivity precedes symptoms



Nelson et al. MMWR 2020

Hepatitis A transmission | Who are at-risk groups?



Not washing hands

Using drugs

Eating or drinking food with hepatitis A in it

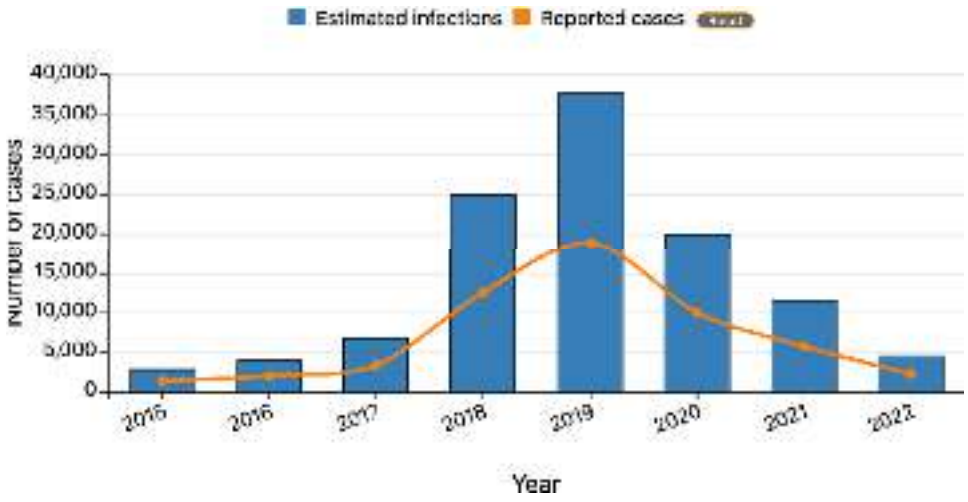
Having sex with someone who has hepatitis A

- People who use drugs
- People who are homeless
- Men who have sex with men
- People who have contact with someone who has hepatitis A
- Travelers to places where hepatitis A is common or where outbreaks are happening

Hepatitis A outbreaks in the United States centered around homeless/PWID

- Peaked in 2019

- Declined since 2020



Wikipedia re: 2019 hepatitis A outbreak; CDC surveillance data

Management of Hepatitis A outbreaks in the United States

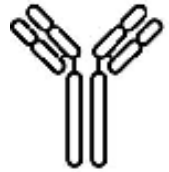
Hygiene

Clean water

Address overcrowding, homelessness

Hepatitis A vaccination for those nonimmune or unknown status

- Generally vaccinate, rather than rely on pre-vaccination testing



Gammaglobulin generally reserved for immunocompromised

- For post-exposure prophylaxis, hepatitis A vaccine found to be noninferior to gamma globulin, vaccine alone recommended in healthy persons age 1-40 years
- Guidelines have increased dose due to declines titers of neutralizing antibodies in the general US population

Victor et al. NEJM 2007; Updated Dosing for Immune Globulin MMWR 2017; ACIP Update MMWR 2020

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Hepatitis B

Virology	hepadnavirus DNA intermediate
Incubation period	Average 2-3 months Range 1-6 months
Rate of symptoms by age	Rare in infants, increases by age
Complications during acute infection	Rare in children Higher mortality in older individuals
Extrahepatic manifestation	Polyarteritis nodosa
Chronic infection	Some clear the virus “functionally” but not fully Others maintain chronic infection

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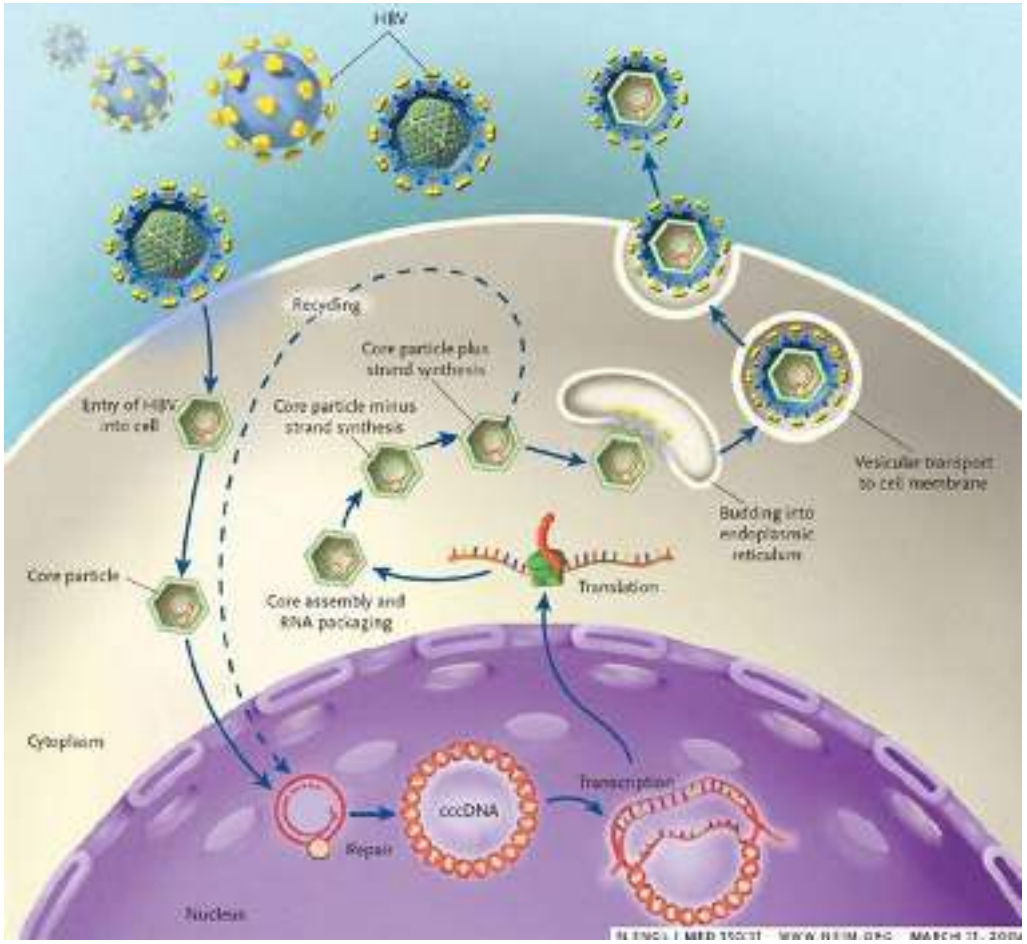
Hepatitis B life cycle



Reverse transcription of the DNA genome

covalently closed circular DNA (cccDNA) and integrated DNA (iDNA):

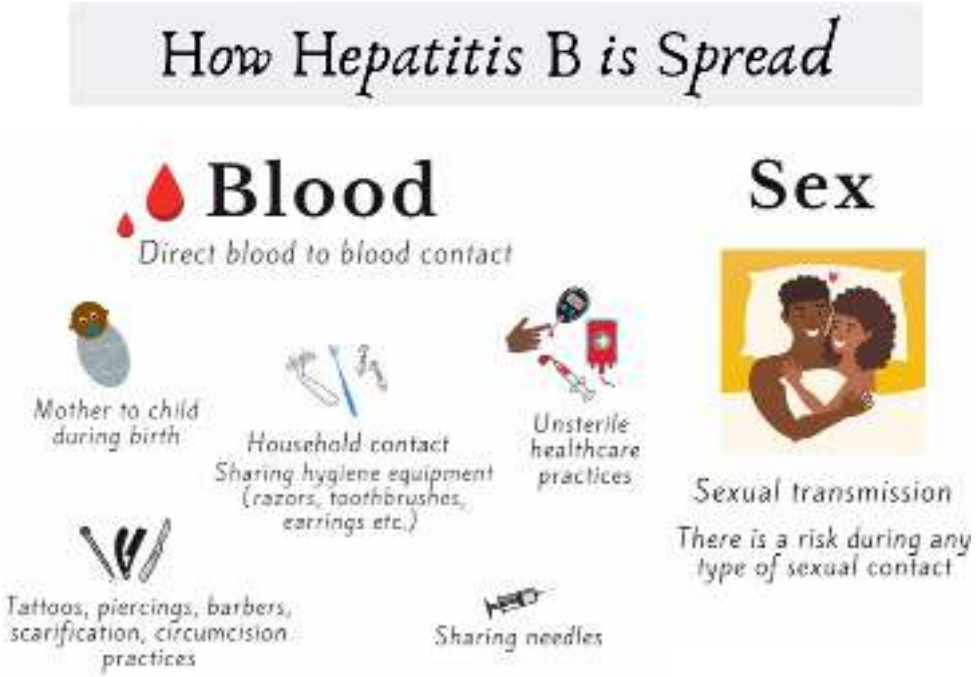
- Not easily cleared/cured
- Immune control
- Activation when immuno-suppressed

Not directly cytotoxic virus - immune response plays role in pathogenesis

Carcinogenic - leading cause of hepatocellular carcinoma worldwide

Ganem and Prince NEJM 2004; 350:1118-1129

Vertical transmission: Neonatal HBV vaccination and HBIg effective, suggesting transmission is predominantly at time of birth



Sexual transmission - higher prevalence in MSM, multiple sex partners, contact with sex workers

Parenteral transmission- Injection drug use (increasing), needlestick

- Unsafe injections (common worldwide, especially before universal precautions)
- Other nosocomial transmission, dialysis, transplant recipients (eg HBcAb positive liver recipient)

Iqbal K. et al. Clin Infect Dis 2015
https://www.cdc.gov/hepatitis/statistics/2021surveillance/hepatitis-b/table-2.3.htm
Figure from Hepatitis B Foundation

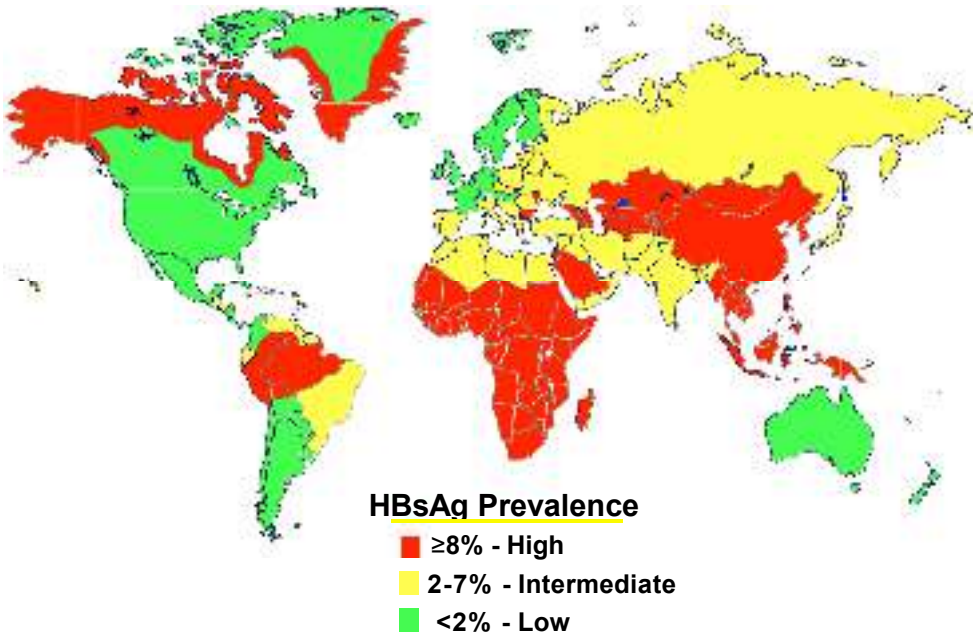
Perinatal Transmission of HBV

- As eAg seroconversion takes decades, many HBV-infected mothers have high HBV DNA
- As high as 90% to eAg mothers

- Neonatal HBV vaccination and HBIg effective, suggesting transmission is predominantly at time of birth
  - Even with these interventions, 9% transmission rate from eAg mothers
- 3rd trimester antiviral therapy, usually TDF, offered for HBV DNA > 200,000 IU/mL
- Breastfeeding - no association with transmission

AASLD 2018 Guidance for HBV; figure credit

Geographic Distribution of HBV



2 billion exposed to hepatitis B virus

296 million persons sAg positive (2019 WHO estimate)

Only 10.5% aware

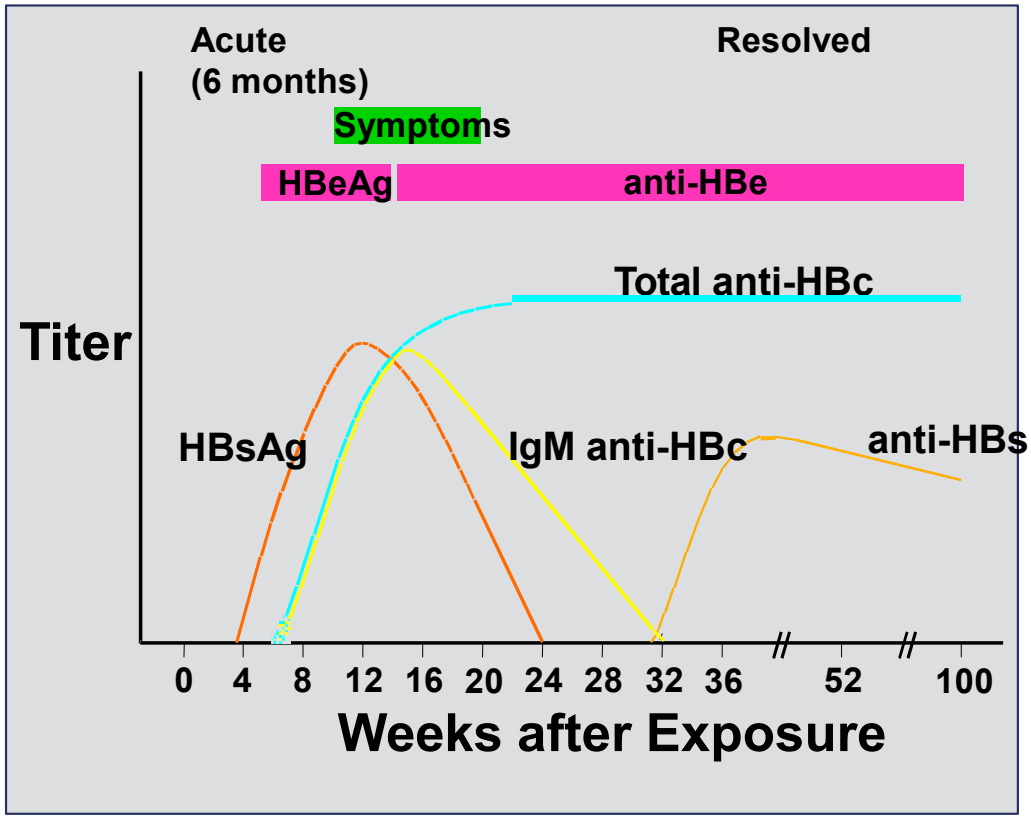
~1% coinfected with HIV/HBV

Deaths worldwide: est. 820,000 /year

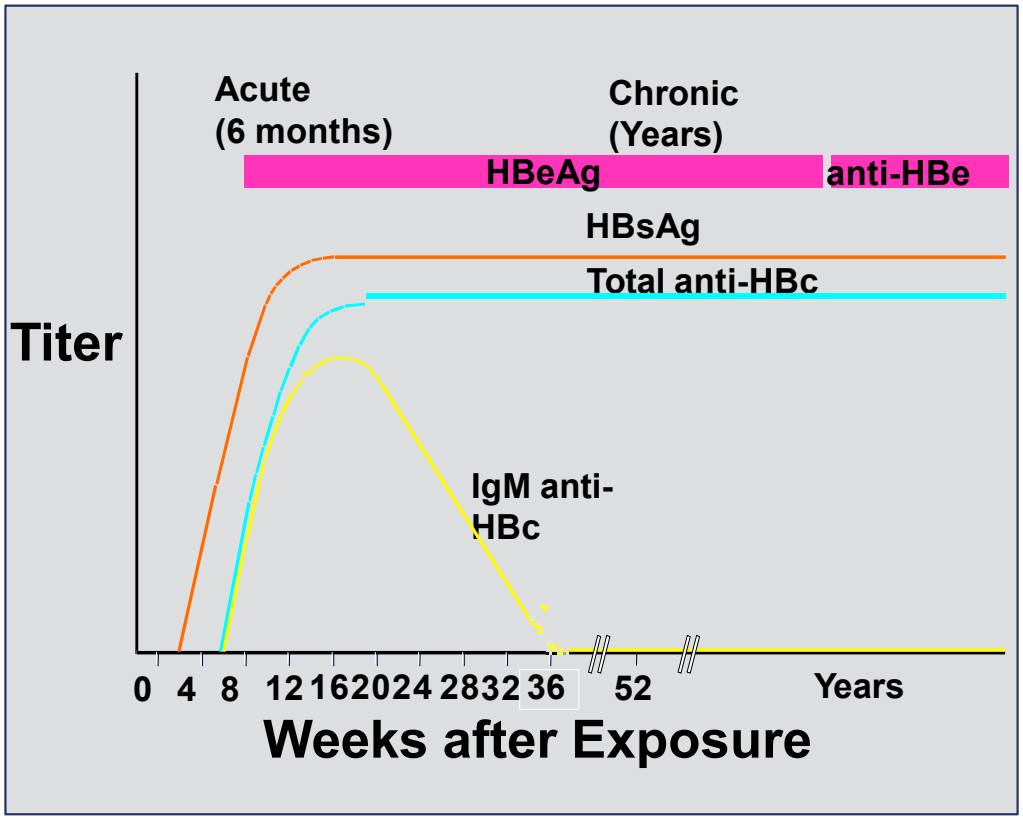
CDC Website; WHO Factsheet

Typical Serologic Courses of HBV

Recovery/resolved

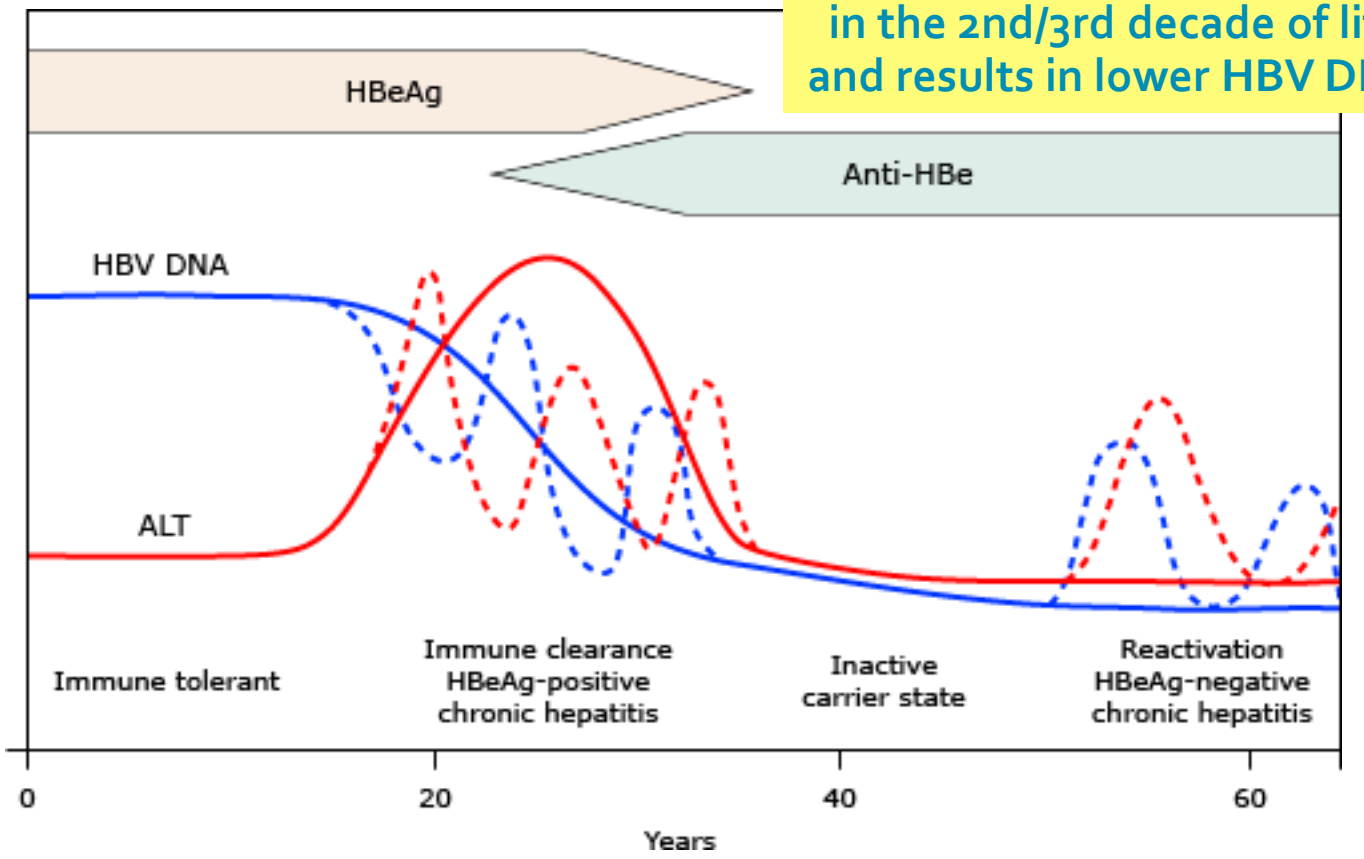


Progression to chronic



Prolonged course after infection early in life

eAg conversion occurs usually in the 2nd/3rd decade of life and results in lower HBV DNA



Reactivation may occur later in life, especially with immunosuppression

Yim HJ, Lok AS. Hepatology 2006; 43:S173

Classification / terminology for chronic HBV infection

	ALT normal	ALT abnormal
HBeAg positive (higher HBV DNA)	Immune tolerant	Chronic HBeAg positive hepatitis
HBeAg negative (lower HBV DNA)	Inactive carrier	Chronic HBeAg negative hepatitis

Interpretation of HBV diagnostic testing

Test	Acute Hepatitis B	Past Exposures (Immunity)	Previous Immunization	Chronic* Hepatitis B (replicative)	Chronic* Precore (replicative)	Inactive Carrier
HBsAg	+	-	-	+	+	+
Anti-HBs	-	+	+	-	-	-
HBeAg	+	-	-	+	-	-
anti-HBe	-	+/-	-	-	+	+
anti-HBc	+	+	-	+	+	+
IgM anti-HBc	+	-	-	-	-	-
HBV DNA (PCR)	+	-	-	>100,000 c/mL	>10,000 c/mL	- or low +

Use of "triple screen" accomplishes 3 goals

Goal	Test	Action Step
Identify chronic HBV	HBSAg	Refer for monitoring and treatment
Identify susceptible	anti-HBs	If negative, vaccinate
Identify risk of reactivation	anti-HBc	If immunosuppressed, monitor or prophylax

Whom to screen for HBsAg?
Older guidelines hard to remember
As of 2023: universal adult screening

Old recommendations (2005)

- ~~Persons born in prevalence regions >8%~~
- Tissue/blood/semen donors
- Hemodialysis patients
- Pregnant women
- Infants born to HBsAg positive women
- Household, needle-sharing, sex contacts of persons known to have HBsAg
- Sources of needlestick or other exposures to HCWs
- HIV positive persons

Groups added in update (2008)

- Persons born in prevalence regions >2%
- U.S. born persons not vaccinated as infants whose parents were born in regions >8%
- Injection drug users
- MSM
- Persons requiring immunosuppressive therapies
- Persons requiring cancer therapies (2020 ASCO)
- Elevated ALT/AST of unknown etiology

at least once during a lifetime for adults aged ≥18 years.

Why?

- Long latency before symptoms
- Risk for transmitting to others
- Risk for reactivation if immunosuppressed
- Testing is relatively inexpensive
- Safe and effective therapeutic options

Natural History of Chronic HBV Infection

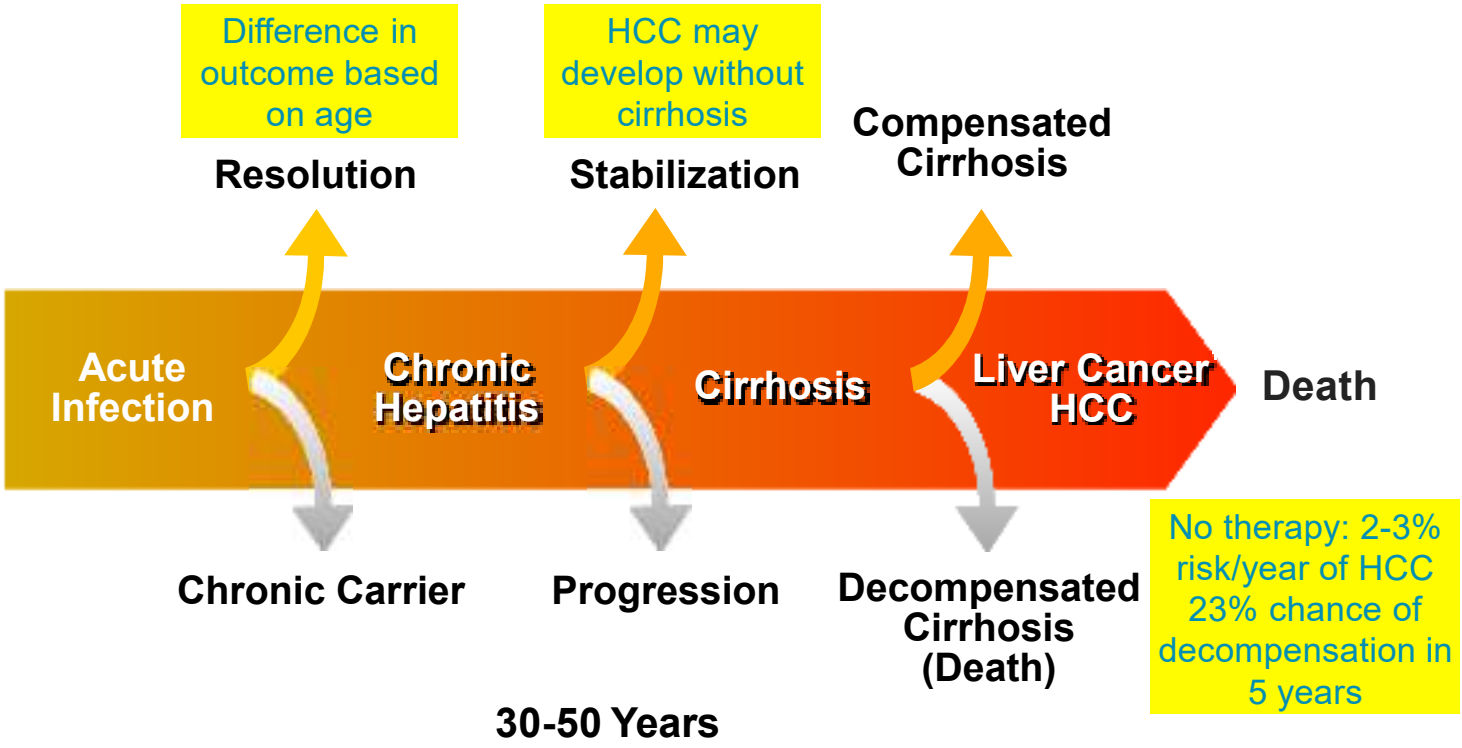


Figure Adapted from Feitelson, Lab Invest, 1994

Fattovich et al. Hepatology 1995

Recommended groups for HCC screening

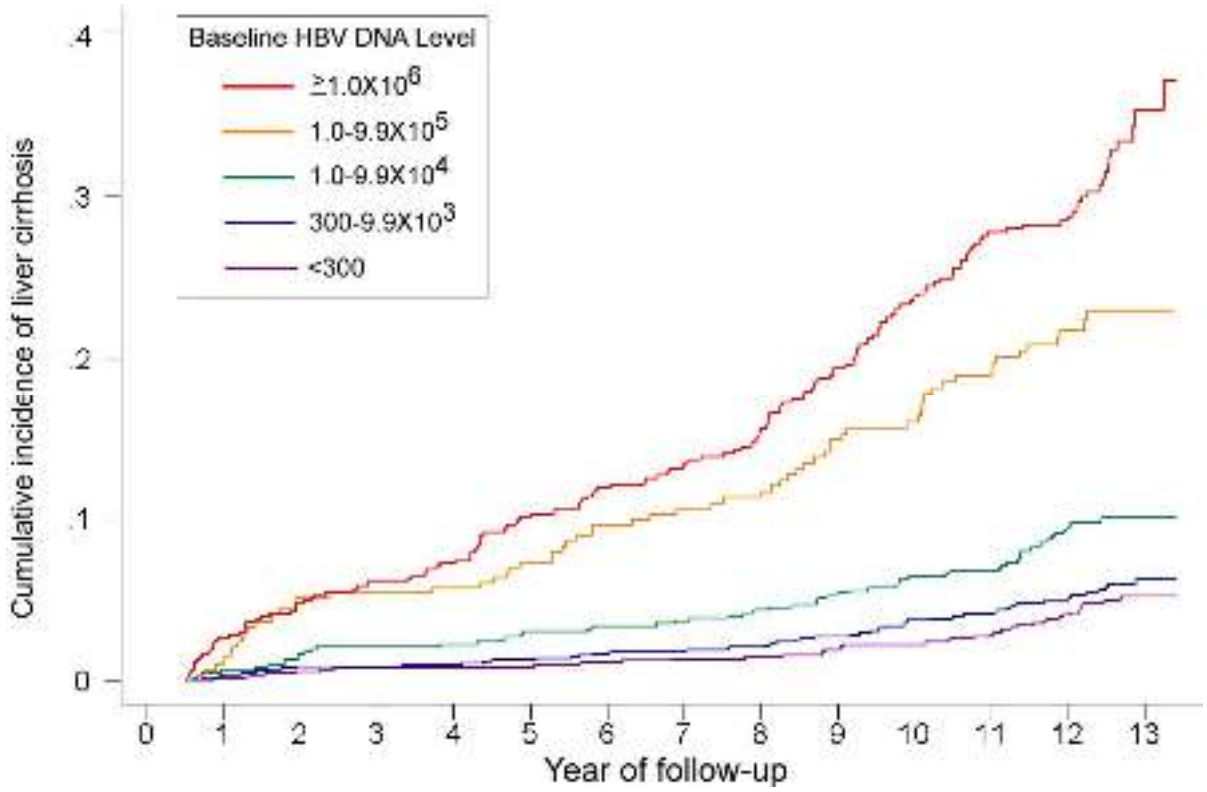
US +/- alfa-fetoprotein every 6 months if HBsAg and any of the following:

- Cirrhosis*
- first-degree relative with HCC*
- HDV co-infection
- Subsaharan African origin ≥ 20 years of age
- men > 40 years of age or women > 50 years of age from endemic countries
- HIV: men ≥ 18 years of age, women ≥ 40 years of age
- PAGE-B score > 10

*Continue screening after functional cure of HBV if cirrhosis, 1st degree relative with HCC, and/or functional cure occurs after age 40 for men or 50 for women

Marrero Hepatology 2018; 2023 AASLD HCC Practice Guidance; 2026 AASLD/IDSA Guidelines

The magnitude of HBV DNA predicts clinical outcomes (incidence of liver cirrhosis)



Iloeje U, Gastroenterology 2006;130:678-86

Whom to Treat - Chronic HBV

AASLD guidelines updated in 2018; all cirrhotics should be treated

	ALT normal	ALT abnormal*
HBeAg positive	Follow if no fibrosis, Treat if significant histology†	>20,000 IU/mL
HBeAg negative	Follow if no fibrosis, Treat if significant histology or fibrosis	>2,000 IU/mL

* ALT > 2x ULN (30 U/L men, 19 U/L women); †fibrosis ≥ 2/4 and necroinflammation ≥ 2/4
- Follow = HBV DNA, ALT q3-6 months

- Consider treatment below HBV DNA cut offs if significant fibrosis

Terrault NA, et al. Hepatology. 2018;67:1560.

Armamentarium of HBV drugs
Interferons and polymerase inhibitors

FDA approved

IFN-α−2b

Pegylated IFN-α-2a

Lamivudine (not used alone due to resistance)

Tenofovir (TDF or TAF)

Entecavir*

Adefovir

~~Telbivudine**~~

Not FDA approved

Emtricitabine

Pegylated IFN-α-2b

* Will select M184V in HIV positive individuals - test for HIV at baseline
** Discontinued October 2016

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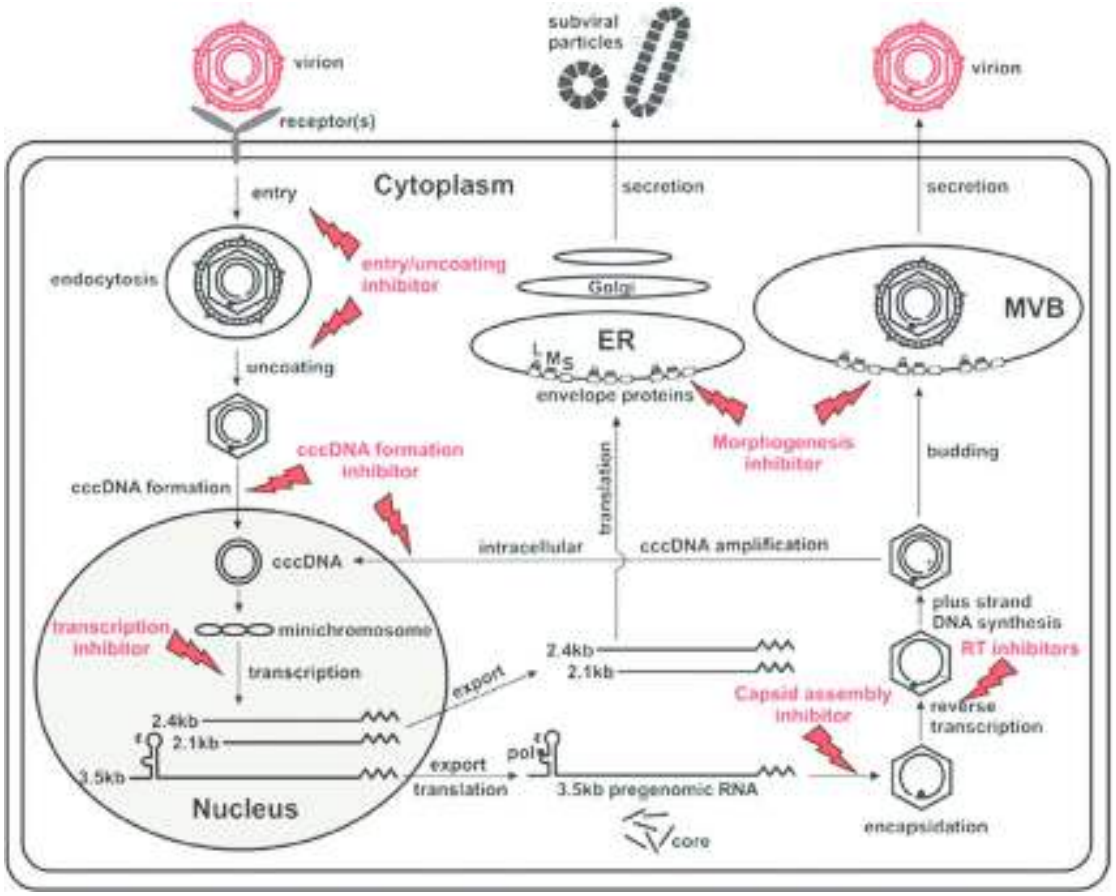
Why does HBSAg persist despite lack of HBV DNA?



Reverse transcription of the DNA genome occurs after encapsidation

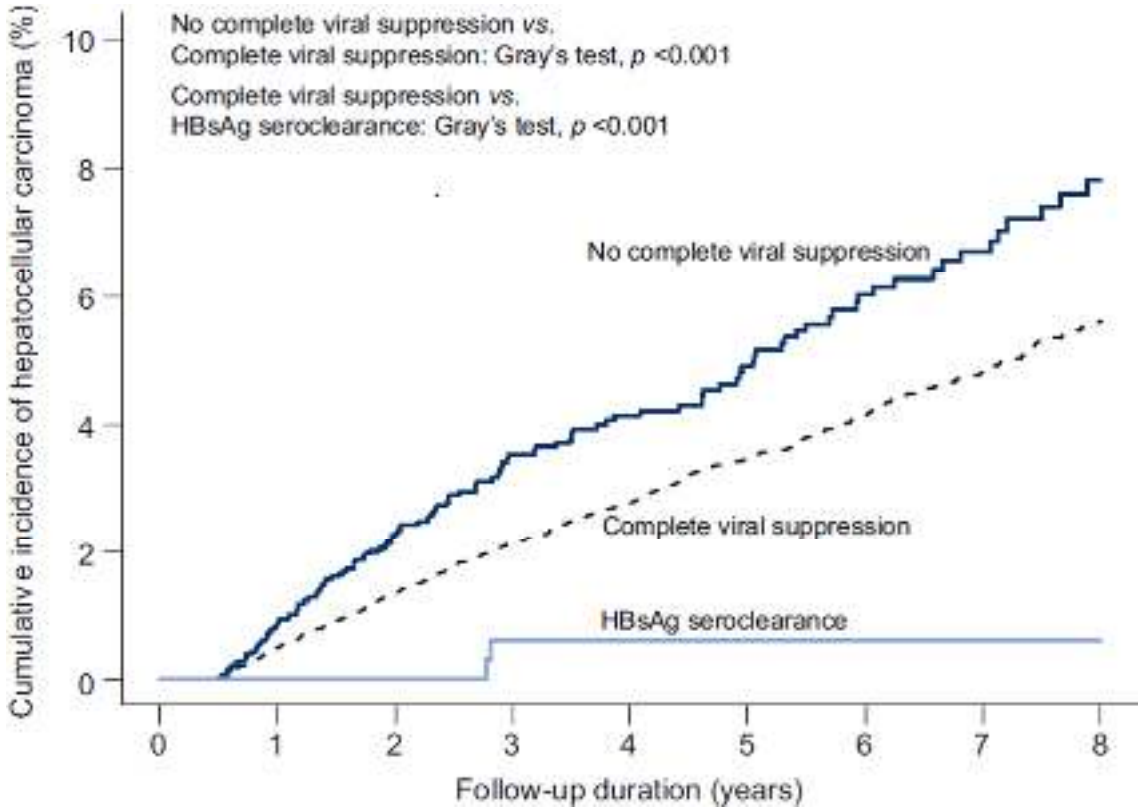
NRTIs suppress DNA but do not inhibit cccDNA, minimal effect on HBsAg

Subviral particles with envelope but not capsid nor DNA may be translated / secreted without DNA

Thus, patients may be **surface antigen positive** but without infectious particles containing DNA, and likely responsible for ongoing T-cell exhaustion

Rajbhandari and Chung Clin Trans Gastroenterol 2016

Impact of antiviral therapy on HBV-related HCC (Hong Kong, n=20,263 on TDF or ETV)



Functional cure possible but relatively rare on long term treatment (~1% year)

Yip et al. J Hepatol 2019

Functional cure of HBV: HBsAg loss, with or without HBsAb

HBsAg loss (HBV functional cure) is associated with:

- Decreased incidence of liver decompensation and HCC
- Increased survival overall
- Decreased levels of cccDNA (reservoir of HBV infection)

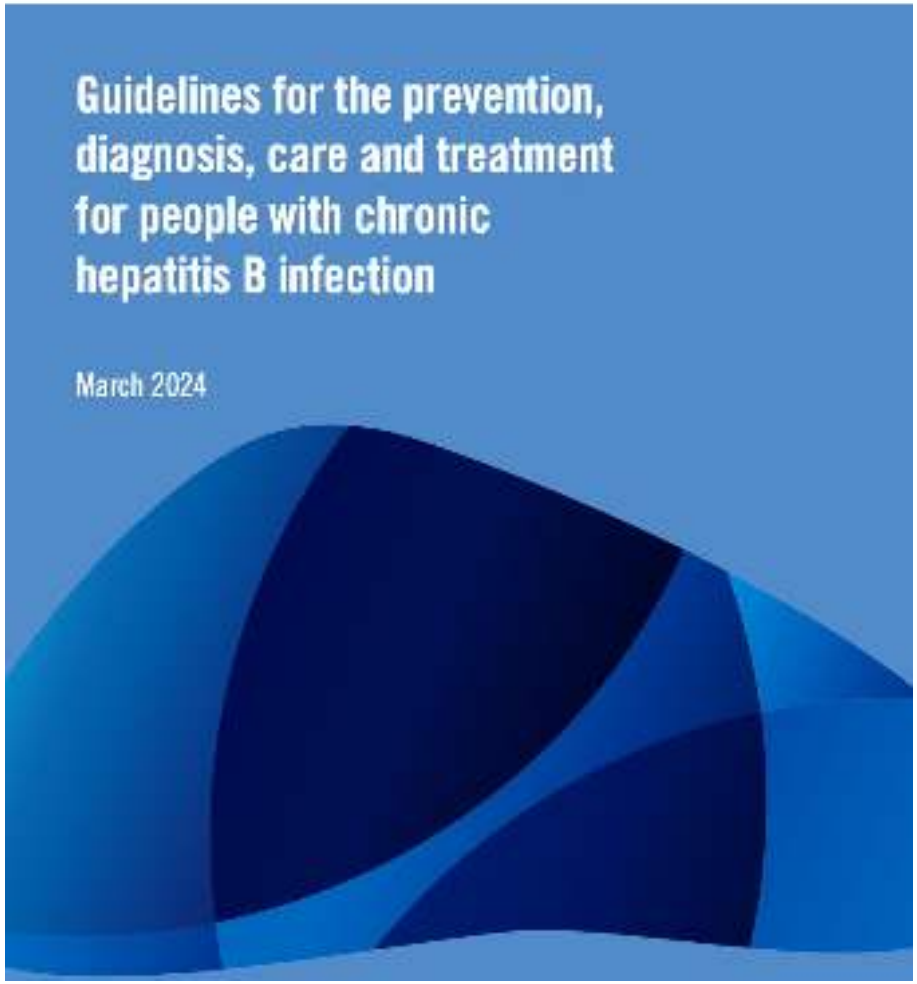
When does functional cure occur?

- Some achieve functional cure as natural history of disease
- Low rates of HBsAg loss (~1%/year) with current therapies
- Higher rates if HIV/HBV co-infected
- Higher rates with treatment interruption; but risks liver damage

Adapted from Debika Bhattacharya (UCLA)

World Health Organization

Released 29 March



2024 WHO Guidelines Highlights

Expanded Treatment Eligibility: Broadened criteria, allowing treatment accessto a larger population, including adolescents and when HBV DNA results are not available.

Alternative Antiviral Therapy Regimens: TAF, dual regimens (when more accessible than monoinfection)

Expanded Access to Antiviral Prophylaxis for Pregnant Women: Provisional option to use antiviral prophylaxis for all HBsAg-positive mothers

Enhanced HBV Diagnostics: Promoted alternative approaches using point-of-care (POC) DNA assays and reflex HBV DNA testing.

Testing for Hepatitis Delta Coinfection: Whom to test and how to test for chronic hepatitis D virus, including universal testing of HBsAg where feasible and reflex testing.

Key Approaches for Delivering High-Quality HBV Care: Eight key approaches including strategies to promote testing uptake, linkage to care/treatment or prevention, adherence, retention in care.

https://www.who.int/publications/i/item/9789240090903

HBV reactivation

What is HBV reactivation?

- HBV flares (abrupt increase in ALT)
  - preceded by HBV DNA increase
  - institution or withdrawal of immunosuppression
  - HBV core IgM may be positive

Who is at risk?

- Steroids, transplant, chemotherapy / biologics
  - (esp. anti-CD20 Ab)
- Rare cases with HCV antiviral therapy in HBsAg / HCV coinfection (8-12 weeks into treatment)
- Risk lower if HBV DNA neg and/or SAb pos

How to manage? Monitoring (low risk) versus prophylaxis (high-risk)

- Monitoring HBV DNA, which rises before LFTs
- Entecavir/tenofovir generally used due to higher threshold for resistance than lamivudine

Lok et al AASLD Guidelines 2009; Hammond et al. Biol Blood Marrow Transplant 2009; Wright et al. Am J Transplant 2014

Although rare, HBV flares can be clinically severe and deadly

CORRESPONDENCE

Hepatitis B reactivation after tenofovir withdrawal in an HIV-infected patient with history of cured hepatitis B virus infection and poor immunological status

Mican, Rafael; Busca Arenzana, Carmen; Vasquez, Julia; Daroca, German; Perez-Valero, Ignacio; Martin-Carbonero, Luz

Hepatitis B Infection or Reactivation After Switch to 2-Drug Antiretroviral Therapy: A Case Series, Literature Review, and Management Discussion

Shilpa Vasishta, MD,[a] Douglas Dieterich, MD,[b] Michael Mullen, MD,[a] and Judith Aberg, MD[a]

Liver enzyme elevation after lamivudine withdrawal in HIV–hepatitis B virus co-infected patients: the Swiss HIV Cohort Study

C Bellini, O Keiser, J-P Chave, JM Evison, J Fehr, L Kaiser, R Weber, P Vernazza, E Bernasconi, A Telenti, M Cavassini, the Swiss HIV Cohort Study

A Fatal Outcome after Cessation of Nucleotide Analogue Therapy in a Patient with Chronic Hepatitis B: A Case Report

Sylvia M. Brakenhoff[a] Heng Chi[a] Pieter Friederich[b] Michail Doukas[c] Caroline den Hoed[c,d] Hajo J. Flink[b] Robert J. de Knegt[c] Robert A. de Man[a]

Methods

- **OPERA cohort:** Electronic health records from >14K people with HIV in the US (96 clinics, 22 states, 1 US territory)
- **Study inclusion:**
  - HIV/HBV co-infection (HBsAg+ and/or HBcAb+)
  - Interruption: stopped TDF or TAF for ≥45 days (16APR2001 - 10MAY2023)
  - ≥1 ALT, HBsAg or HBV DNA during the interruption

Table 1. HBV reactivation risk based on HBV serology

	HBsAg	HBcAb	HBsAb
High	+	+/−/?	+/−/?
Moderate	−/?	+	−/?
Low	−/?	+	+

Figure 2. Incidence of HBV reactivation

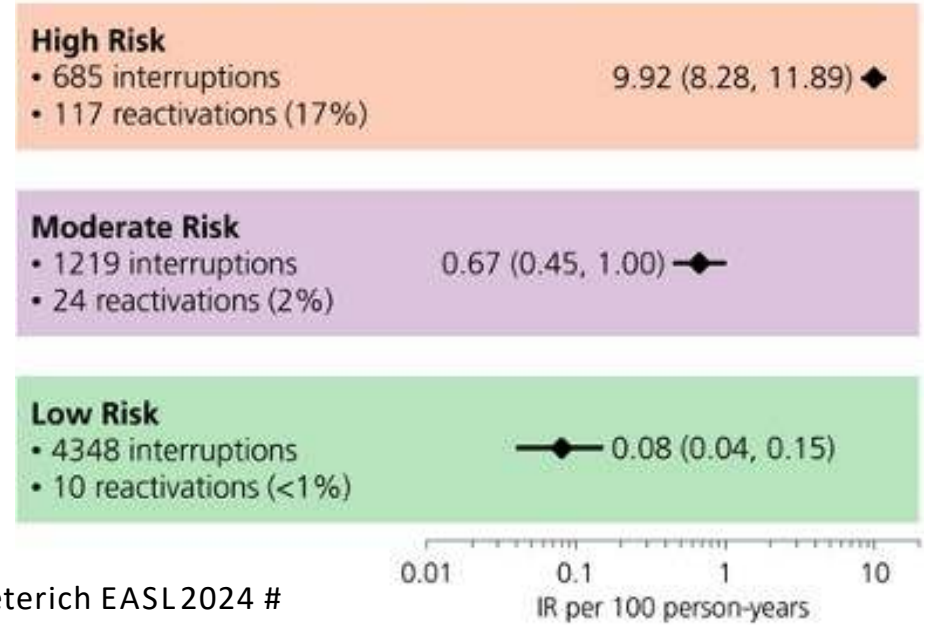
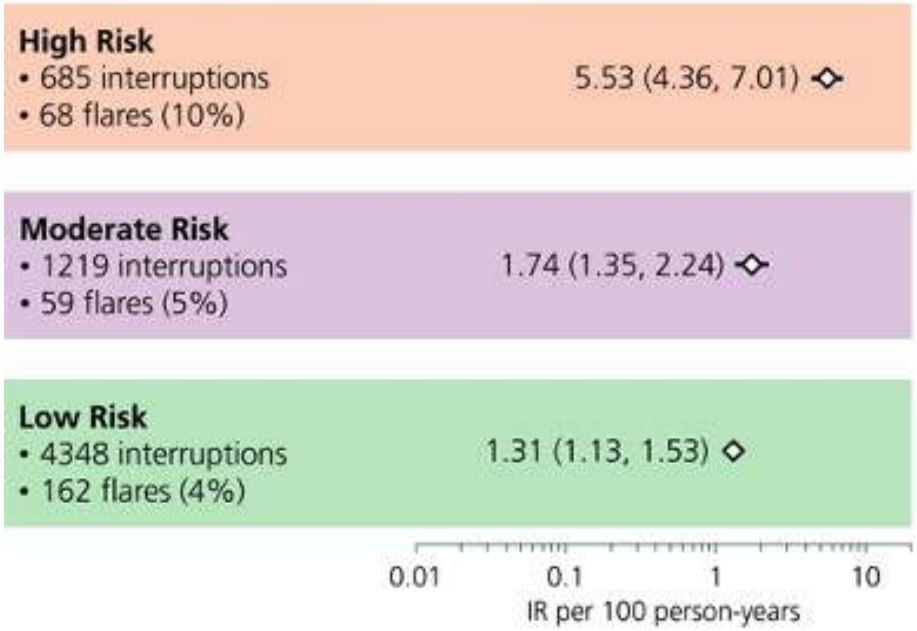
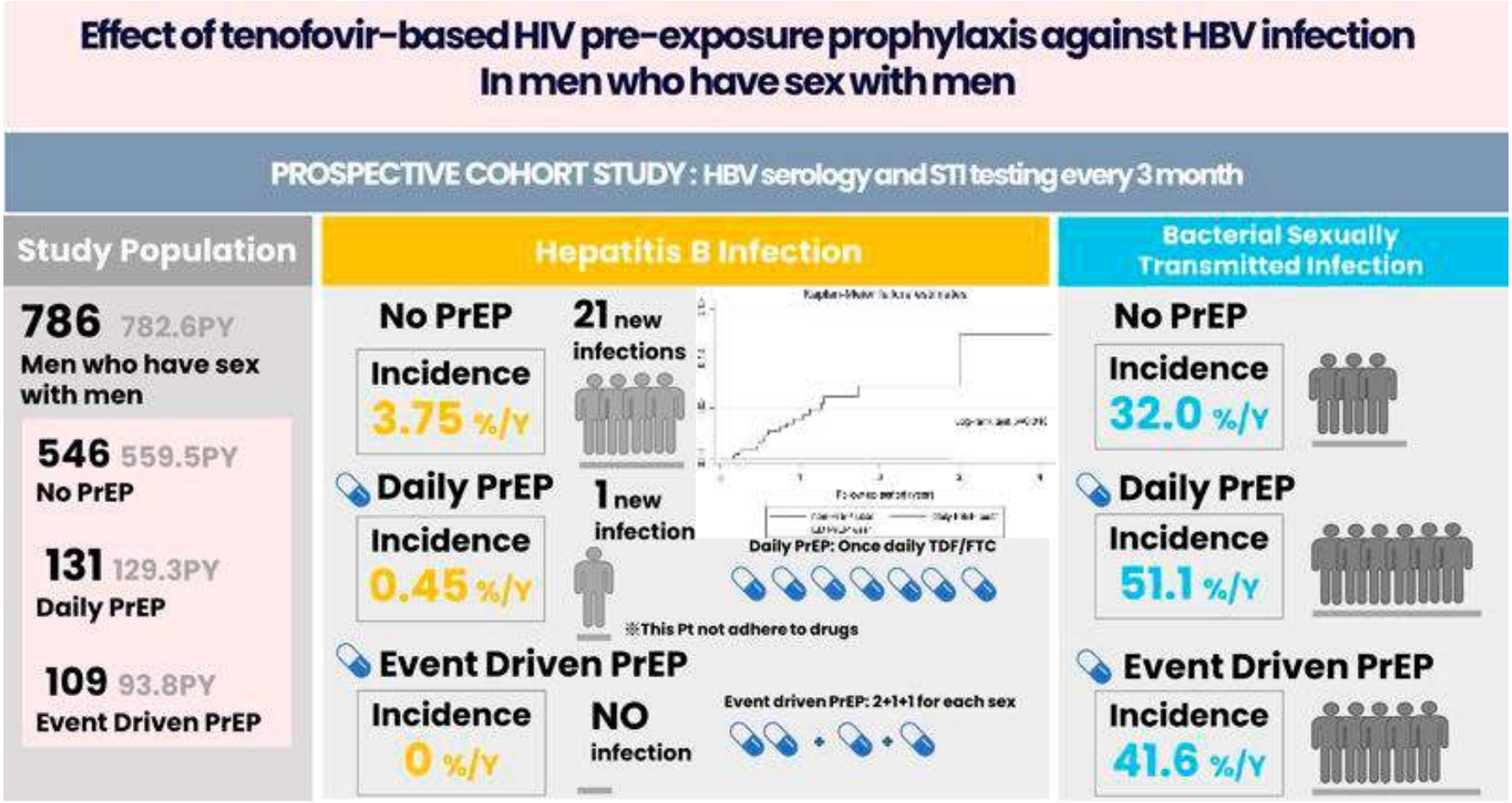


Figure 3. Incidence of hepatitis flare



Dieterich EASL 2024 #

Effect of tenofovir-based HIV pre-exposure prophylaxis against HBV infection In men who have sex with men



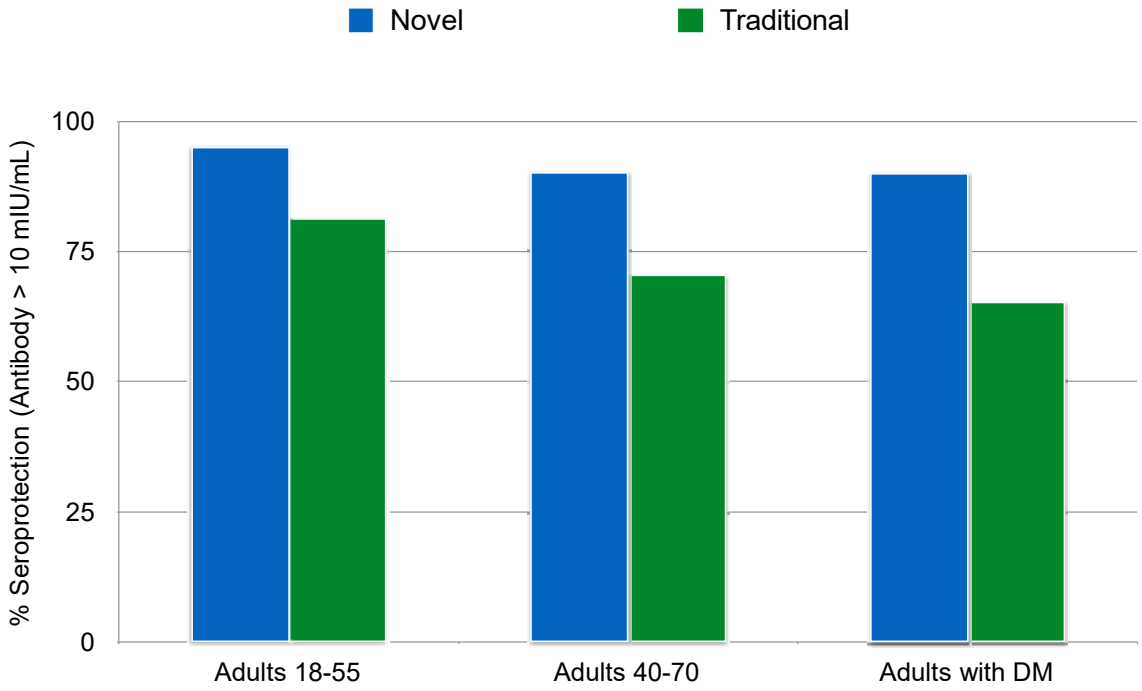
PrEP: Taking TDF/FTC for preventing HIV, Daily PrEP: Participants take drugs everyday, Event Driven PrEP: Participants take drugs on demand. ex) 2-1-1.

Mizushima et al. Hepatology 2023

HEPATOLOGY

TLR-adjuvanted vaccine FDA-approved in 2018

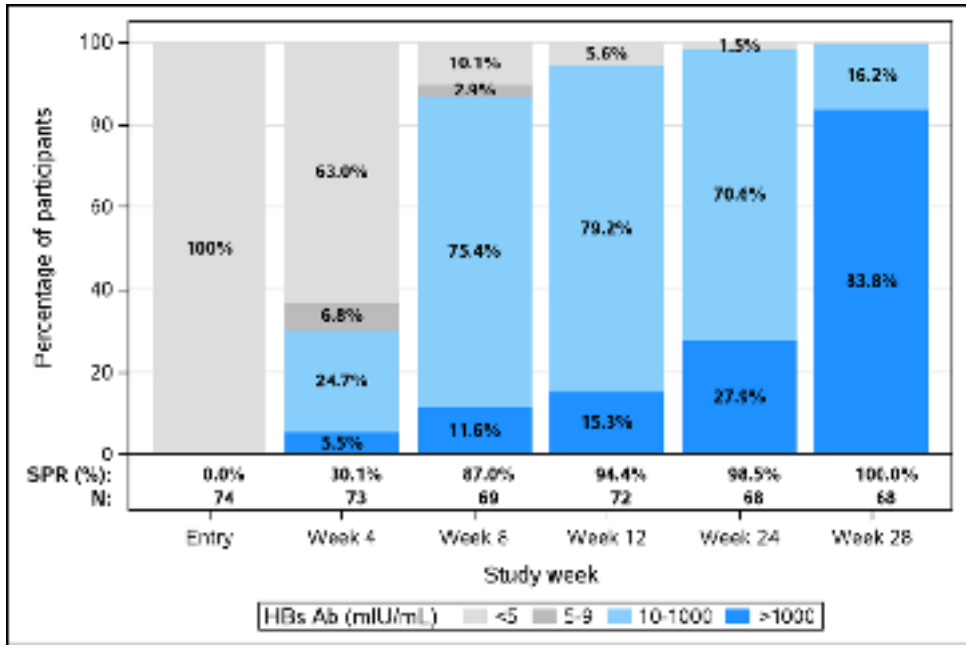
- Novel adjuvant, cytosine phosphoguanine (CPG) oligodeoxynucleotide stimulates TLR9
- Approved for adults, 2 shot series, 4 weeks apart
- Enhanced immunogenicity compared to traditional vaccine
- Higher rates of local reactions (redness/swelling)



Campbell Methods Mol Bio 2017; HEPLISLAV-B package insert

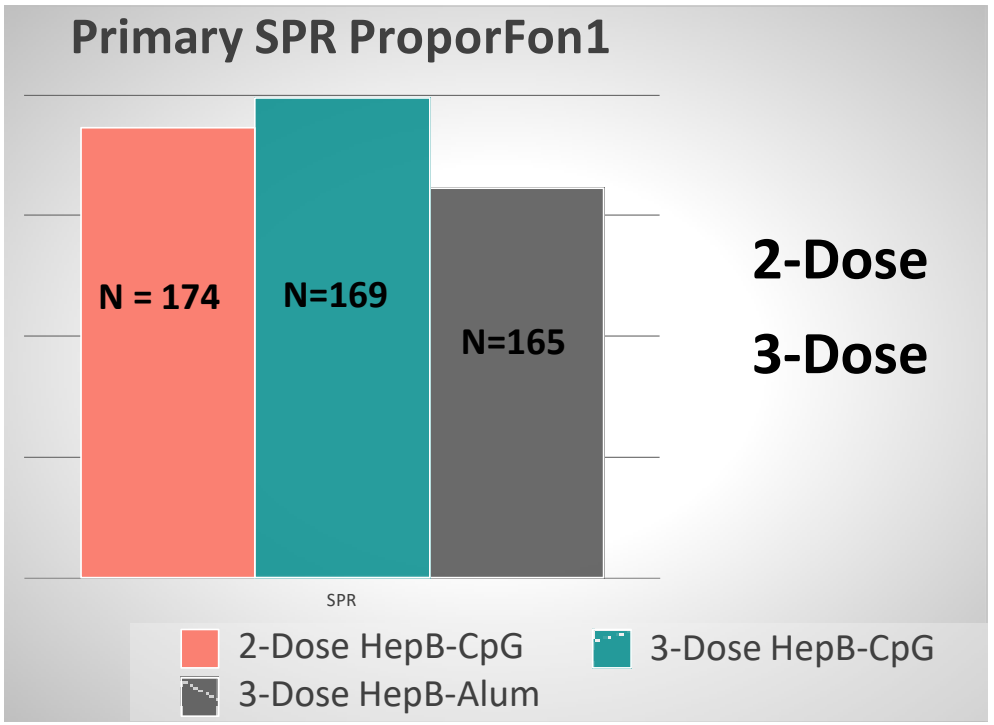
A5379 BEe-HIVe Study: CpG vaccine for People with HIV

A5379 People with HIV, HBV **vaccine naive**
100% seroprotection rate (SPR) after 3 doses



Marks et al. CID 2023
Marks et al. JAMA 2025

A5379 People with HIV, HBV **vaccine nonresponders**
2-dose and 3-dose arms superior to 3-dose alum



CDC recommends HBV vaccination to prevent sexual transmission

Sexual Transmission and Viral Hepatitis

Certain adults who are sexually active should be vaccinated against hepatitis B.

CDC and the Advisory Committee on Immunization Practices (ACIP) recommend hepatitis B vaccination for

- sexually active people with more than one sex partner during the previous 6 months;
- people seeking evaluation or treatment for a sexually transmitted disease;
- sex partners of people with hepatitis B; and
- men who have sex with men (MSM).

CDC recommends one-time hepatitis C testing of all adults (18 years and older) and regular testing for people with risk factors.

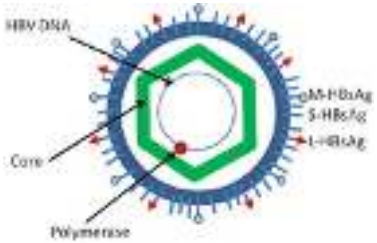
https://www.cdc.gov/hepatitis/populations/stds.htm

Vaccinate after testing!
HBV vaccine may result in false positive tests

After the collection of blood for serologic testing, persons who have not completed a vaccine series should be offered vaccination per ACIP recommendations at the same visit or at an associated provider visit. Blood collection before vaccination is recommended because transient HBsAg positivity has been reported for up to 18 days after vaccination.

https://www.cdc.gov/mmwr/volumes/72/rr/rr7201a1.htm?s_cid=rr7201a1_w

Hepatitis B Virus Take Home Points



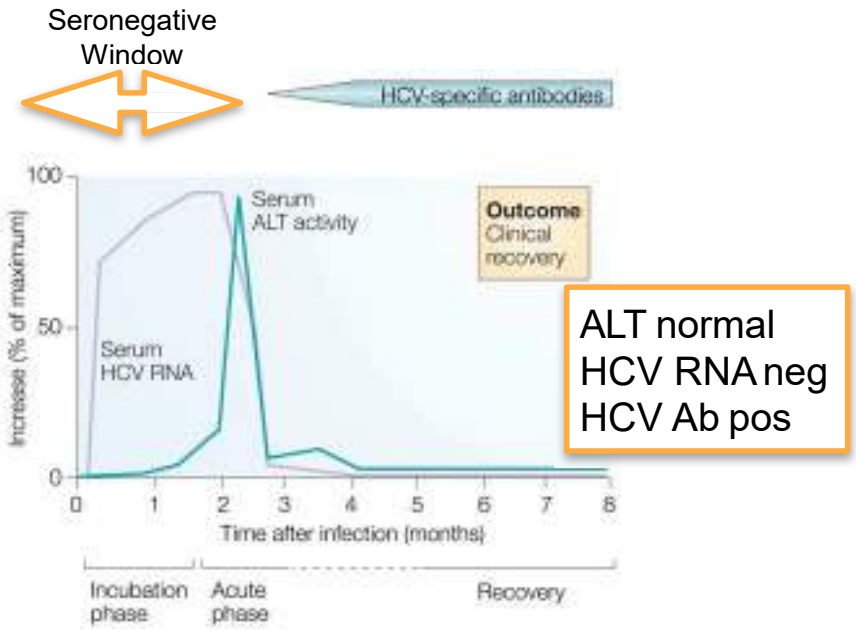
- ***HBV is a DNA virus with variable outcomes***
  - May convert from stable to dynamic stages
- ***HBV represents an enormous global burden of liver disease***
  - Assess ALT at least twice yearly
  - Assess fibrosis and screen for liver cancer
  - Screening all adults with “triple screen”- HBcAb, HBsAg, HBsAb
  - Prevention, especially vaccination (all adults up to age 60)
    - CpG vaccine superior immunologic response
- ***Antiviral (entecavir, TDF, TAF) treatments effective***
  - Expanding WHO treatment guidelines
  - Novel therapies will aim towards a functional cure

Hepatitis C: causative agent of non-A, non-B hepatitis discovered in 1989

Virology	Hepacivirus (RNA-dependent RNA polymerase - no DNA intermediate) Extremely variable virus
Incubation period	Average 2-3 months Range 0.5-6 months
Rate of symptoms during acute phase	Usually asymptomatic or minimally symptomatic
Complications	Renal disease, cryoglobulinemia After decades of chronic infection, cirrhosis
Chronic infection	Some clear the virus fully Others progress to chronic infection

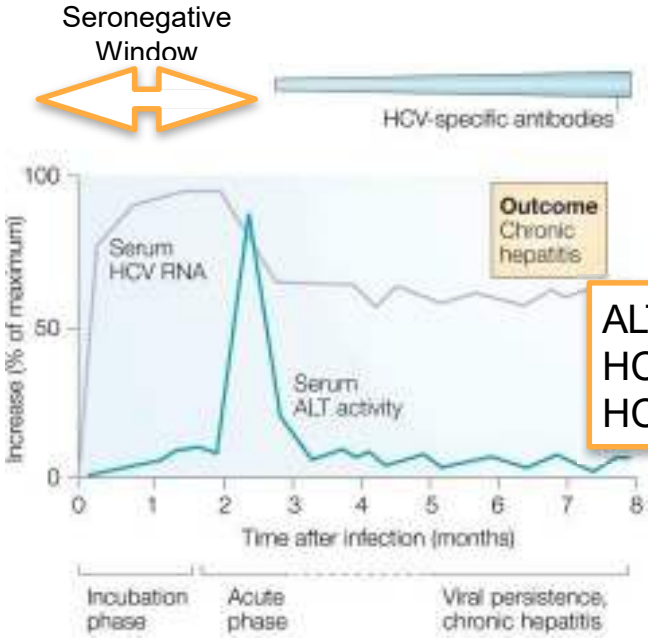
Binary outcomes of hepatitis C

Cleared infection



ALT normal
HCV RNA neg
HCV Ab pos

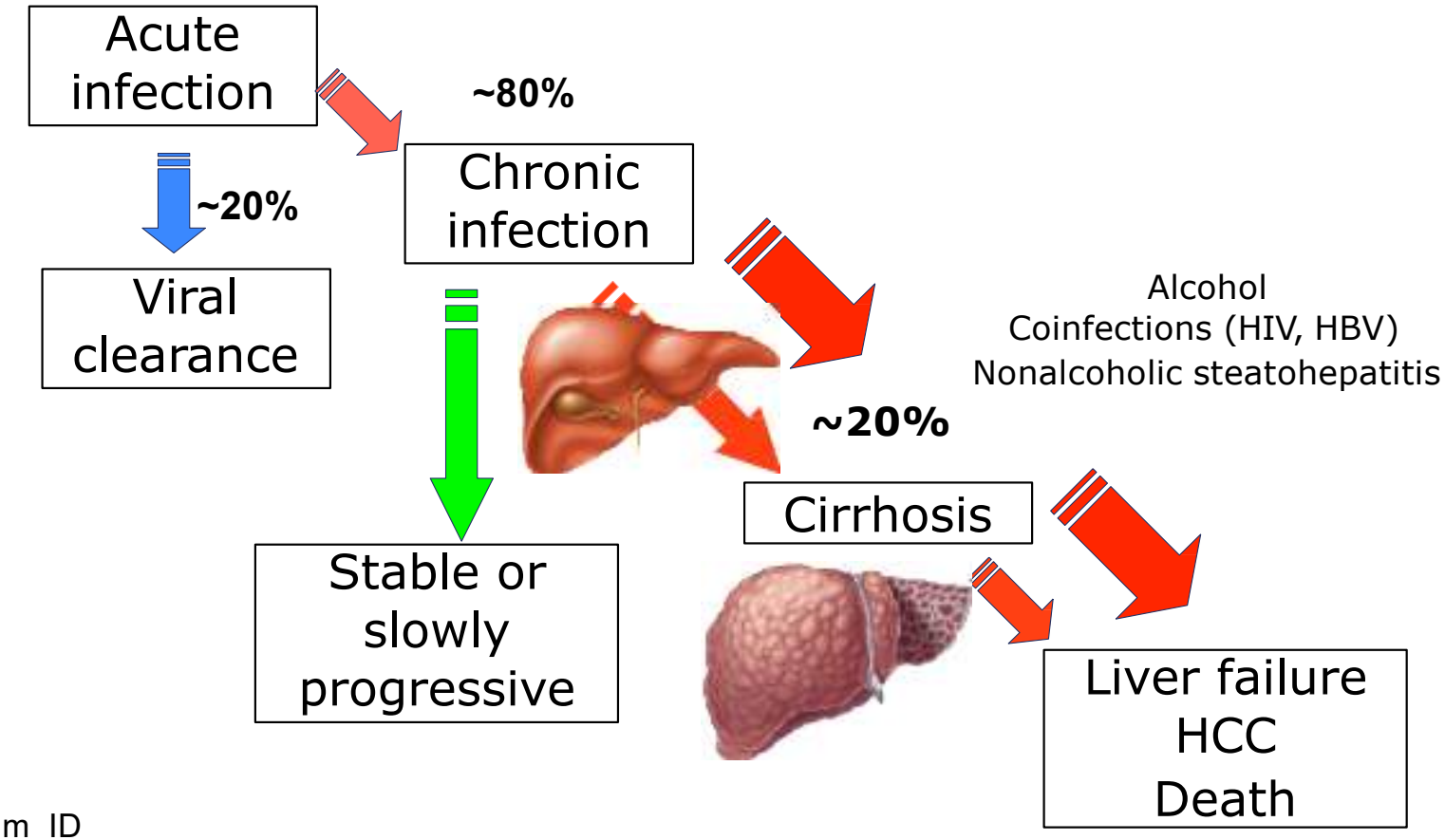
Chronic infection



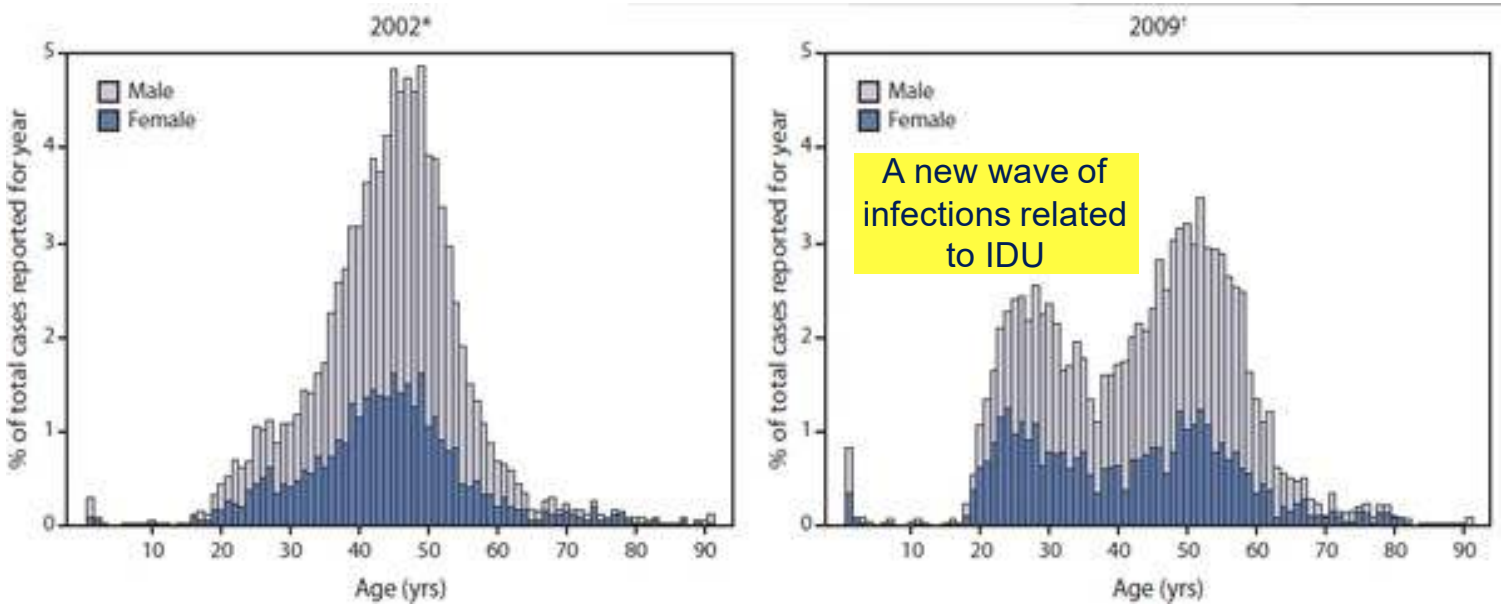
ALT often elevated
HCV RNA pos
HCV Ab pos

Rehermann and Nascimbeni Nat Rev Immunol 2005

Natural history of HCV



MMWR: Age distribution of newly reported confirmed cases of hepatitis C virus infection --- Massachusetts, 2002 and 2009



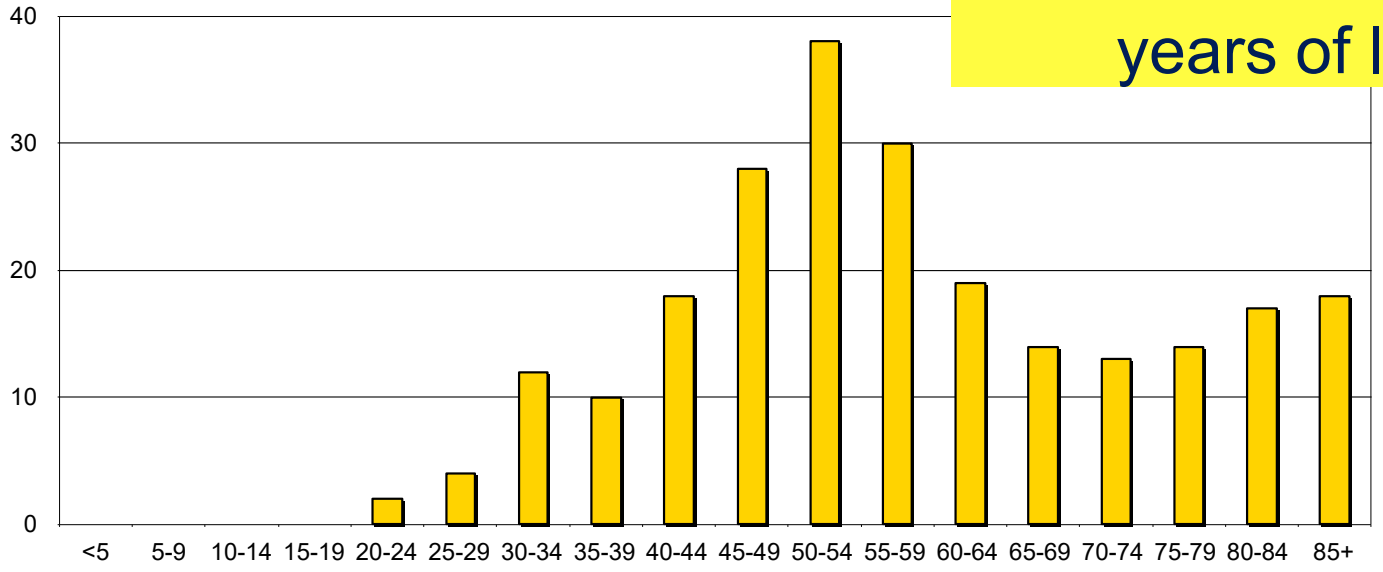
* N = 6,281; excludes 35 cases with missing age or sex information.
† N = 3,904; excludes 346 cases with missing age or sex information.

Onofrey et al MMWR: May 6, 2011 / 60(17);537-541

Death Rates Among HCV Cases in Massachusetts, by age at death, 2000-2009

The highest average annual mortality rate for those with HCV was among the 50 to 54 year age group, with 38 deaths per 100,000

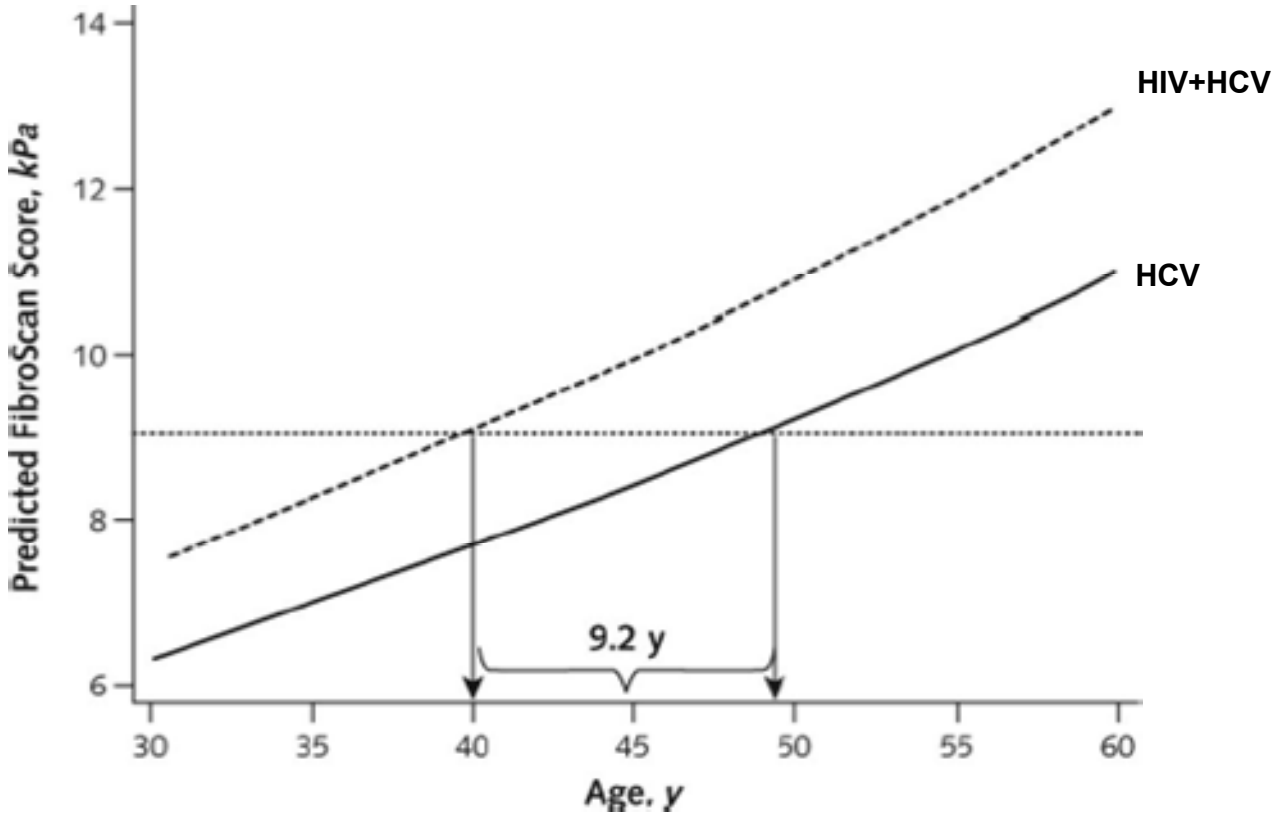
HCV associated with 20 years of lost life



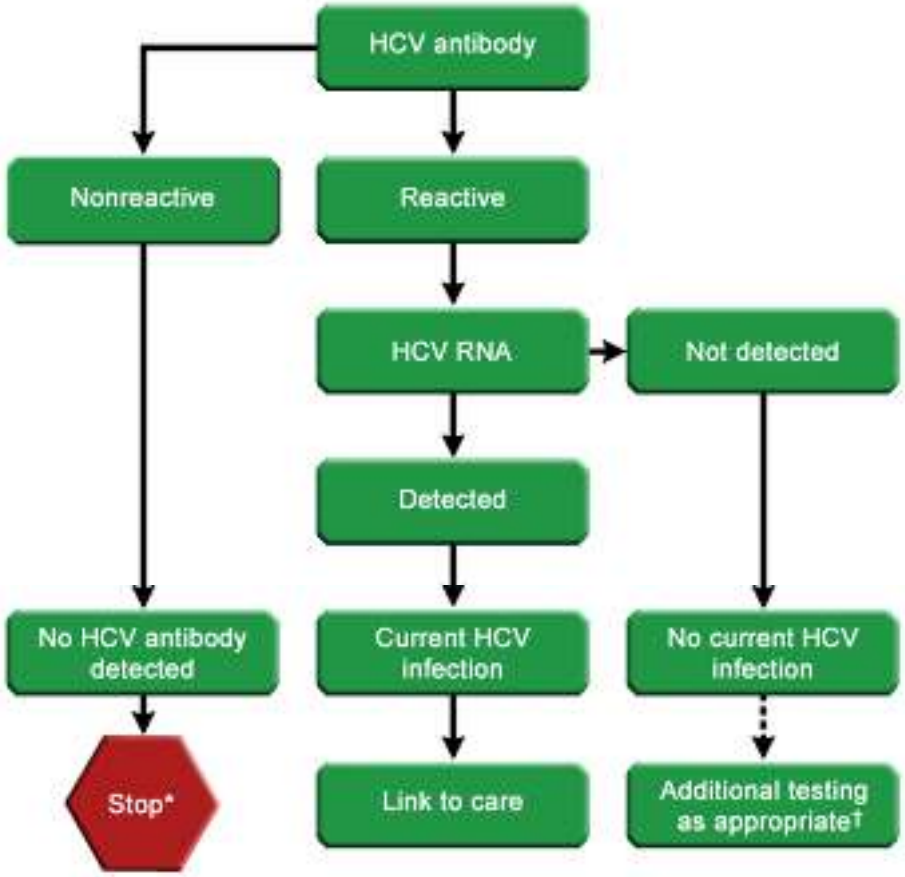
HCV data Source: MDPH Office of Integrated Surveillance and Informatics Services, data as of 2/10/12
HCV diagnosis date is the earliest known date of documented HCV infection

Slide courtesy: Dan Church, MA DPH

HIV associated with higher rates of HCV-related liver fibrosis - ~10 years of acceleratation compared to HCV monoinfection



Diagnosis of HCV



Multiple kits / tests available, FDA-approved

Antibody 98% specific
Plasma/sera

Rapid antibody testing available

Costs
~$15-25 antibody
~$63 HCV RNA

Reflex tests useful to reduce need to return for RNA testing

HCV antibody is your screening test
RNA confirms "current" or active infection

http://www.hcvguidelines.org

Screening of adults aged 18-79 in the U.S. recommended by the USPSTF as of March 2020

Recommendation Summary

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

- Aligns with previous recommendations by AASLD / IDSA and draft recommendations by CDC
- New infections are now largely driven by transmission via injection drug use and occur in younger adults outside the “baby boomers”
- Addresses a key gap and provides the first step towards identifying persons living with HCV, a necessary step for treatment

https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-c-screening
https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2021/05/routine-hepatitis-c-virus-screening-in-pregnant-individuals

Rules of 3: risk after needlestick

HBV	30%
HCV	3% (~1-2%)
HIV	0.3%

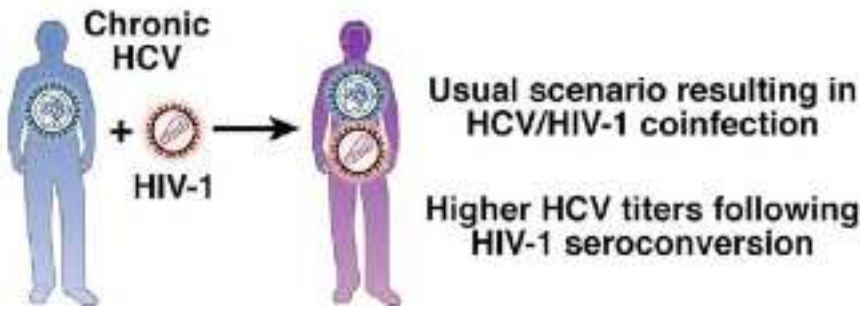
@Arthur_Kim_ID

Transmission of HCV

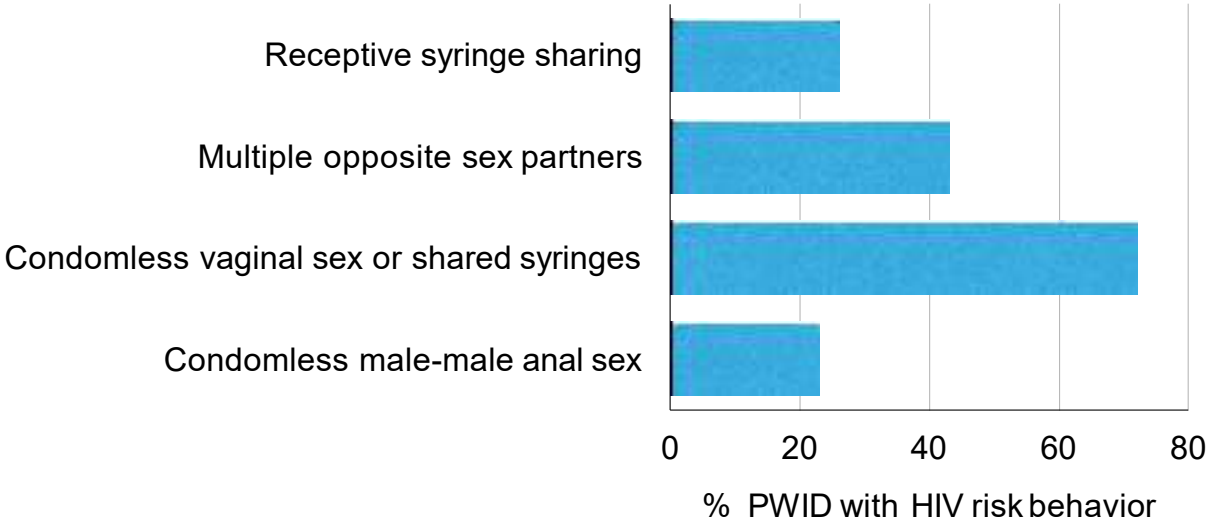
- Parenteral ~1% risk per exposure
- Perinatal ~ 6% from viremic mother to child
- Sexual: generally inefficient, except when HIV

Eyster et al. Ann Intern Med 1992, Terrault et al. Hepatology 2013, Benova et al. Clin Infect Dis 2014

Order of Co-infection: HCV Before HIV



- ~1 in 15 new U.S. HIV infections in 2020 occurred in PWID
- 6% of 11,348 PWID tested were positive for HIV (NHBS)
- Among PWID at risk for acquiring HIV
  - –57% reported having a recent HIV test
  - –46% self reported HCV infection



Co-infection Outbreak: Scott County, Indiana

- 135 cases as of report
- Investigation triggered by HIV surveillance
- Injection of oxymorphone
- Multigenerational use of injection drugs
- 84.4% (114/135) diagnosed with HCV infection

Morbidity and Mortality Weekly Report

Community Outbreak of HIV Infection Linked to Injection Drug Use of Oxymorphone — Indiana, 2015

Caitlin Conrad[1], Heather M. Bradley[2], Dita Broz[2], Swamy Buddha[1], Erika L. Chapman[1], Romeo R. Galang[2,3], Daniel Hillman[1], John Hon[1], Karen W. Hoover[2], Monita R. Patel[2,3], Andrea Perez[1], Philip J. Peters[2], Pam Pontones[1], Jeremy C. Roseberry[1], Michelle Sandoval[2,3], Jessica Shields[4], Jennifer Walthall[1], Dorothy Waterhouse[4], Paul J. Weidle[2], Hsiu Wu[2,3], Joan M. Duwve[1,5] (Author affiliations at end of text)

On April 24, 2015, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

On January 23, 2015, the Indiana State Department of Health (ISDH) began an ongoing investigation of an outbreak of human immunodeficiency virus (HIV) infection, after Indiana disease intervention specialists reported 11 confirmed HIV cases traced to a rural county in southeastern Indiana. Historically, fewer than five cases of HIV infection have been reported annually in this county. The majority of cases were in residents of the same community and were linked to syringe-sharing partners injecting the prescription opioid oxymorphone (a powerful oral semi-synthetic opioid analgesic). As of April 21, ISDH had diagnosed HIV infection in 135 persons (129 with confirmed HIV infection and six with preliminarily positive results from rapid HIV testing that were pending confirmatory testing) in a community of 4,200 persons (*1*).

The age range of the 135 patients is 18–57 years (mean = 35 years; median = 32 years); 74 (54.8%) are male. A small number of pregnant women were diagnosed with HIV infection and started on antiretroviral therapy during pregnancy. As of April 21, no infants had tested positive for HIV. Of the 135 persons with diagnosed HIV infection, 108 (80.0%) have reported injection drug use (IDU), four (3.0%) have reported no IDU, and 23 (17.0%) have not been interviewed to determine IDU status. Among the 108 who have reported IDU, all reported dissolving and injecting tablets of oxymorphone as their drug of choice. Some reported injecting other drugs, including methamphetamine and heroin. Ten (7.4%) female patients have been identified as commercial sex workers. Coinfection with hepatitis C virus has been diagnosed in 114 (84.4%) patients.

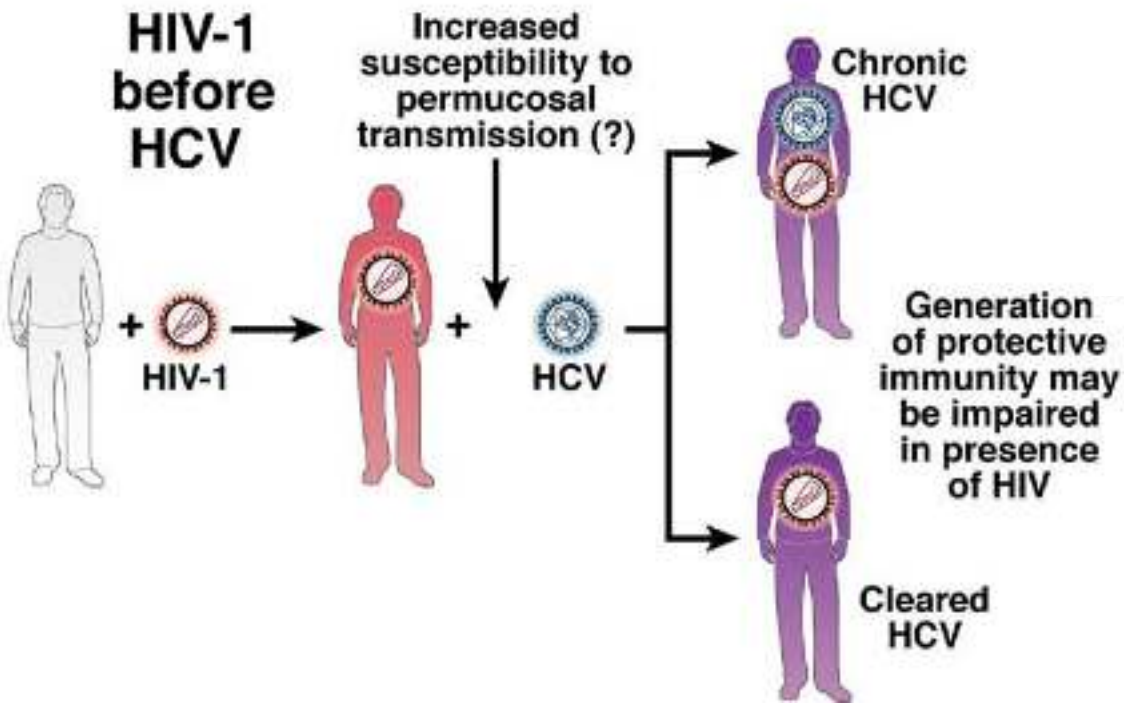
identified as syringe-sharing or sex partners, and 54 (42.2%) are social contacts regarded as at high risk for HIV infection.

Injection drug use in this community is a multi-generational activity, with as many as three generations of a family and multiple community members injecting together. IDU practices include crushing and cooking extended-release oxymorphone, most frequently 40 mg tablets not designed to resist crushing or dissolving. Syringes and drug preparation equipment are frequently shared (e.g., the drug is dissolved in nonsterile water and drawn up into an insulin syringe that is usually shared with others). The reported daily numbers of injections ranged from four to 15, with the reported number of injection partners ranging from one to six per injection event.

Like many other rural counties in the United States, the county has substantial unemployment (8.9%), a high proportion of adults who have not completed high school (21.3%), a substantial proportion of the population living in poverty (19%), and limited access to health care (*1*). This county consistently ranks among the lowest in the state for health indicators and life expectancy (*2*).

ISDH worked with the only health care provider in the immediate community, local health officials, law enforcement, community partners, regional health care providers and CDC to launch a comprehensive response to this outbreak. A public health emergency was declared on March 26 by executive order (*3*). The response has included a public education campaign, establishment of an incident command center and a community outreach center, short-term authorization of syringe exchange, and support for comprehensive medical care including HIV and hepatitis C virus care and treatment as well as substance abuse counseling and treatment. State and local health departments

Order of co-infection: HIV before HCV



A "Perfect Storm" for HCV transmission

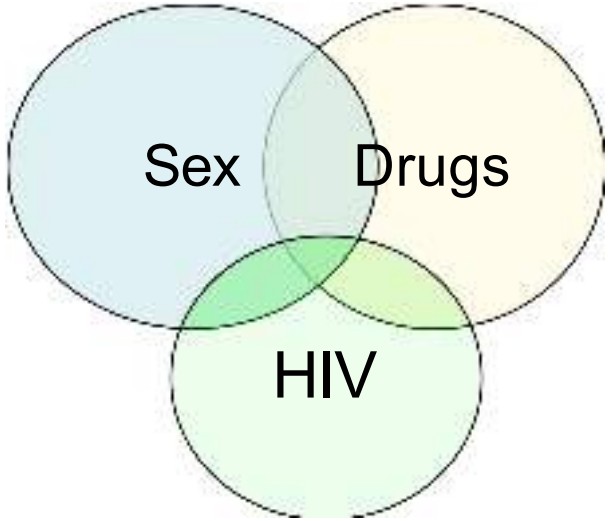
Bloody practices

Semen exposure

Ulcerative STDs

Sildenafil

Internet



"Chemsex"

Higher levels of virus in plasma and semen

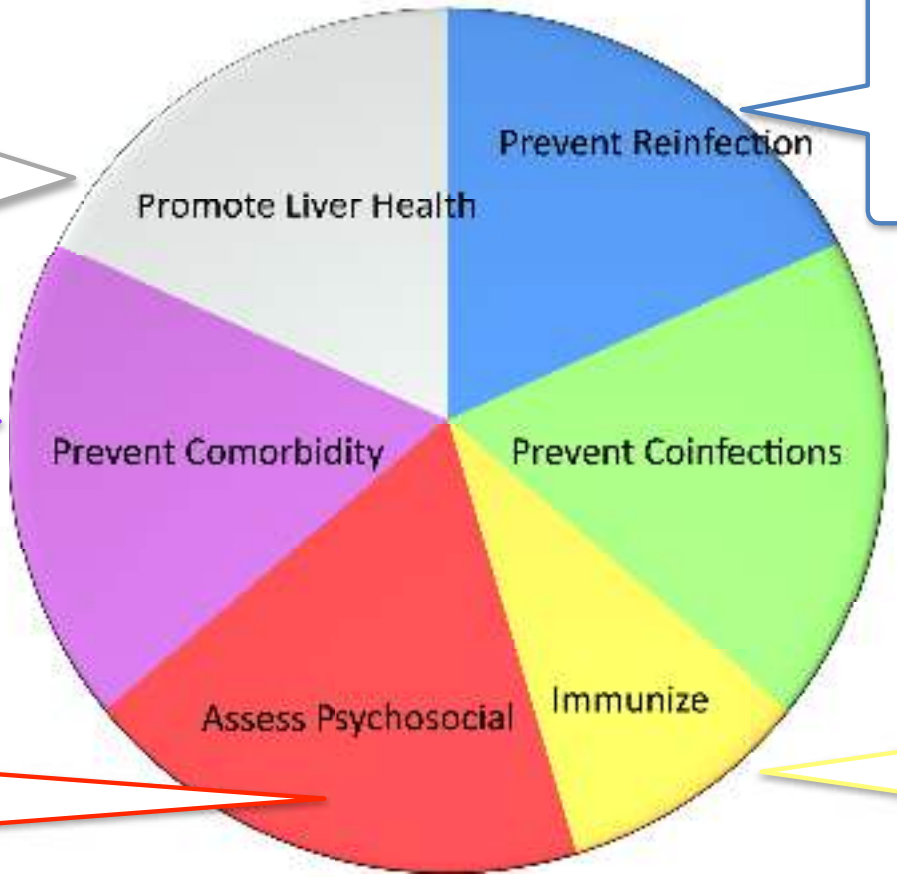
Immune deficiency, especially at GI mucosa

Diagnosing new HCV in HIV+ MSM

- Ask about high-risk behaviors (bloody practices, exposure to semen, chemsex), which may be under-reported, and screen for HCV
- Screen when presenting with STDs
- React to minor changes in ALT
- Minimally, **yearly antibodies recommended**, be aware of delayed seroconversion
- HCV RNA for seronegative window / re-infections; low / fluctuating levels suggestive
- q6m or q12m intervals results in delayed diagnosis in majority of cases
- Treat during acute phase to prevent onward transmission (treatment as prevention)

Sun et al. OFID 2023, Fierer CID 2024; Ingiliz HIV Med 2024

HCV care is not only about DAAs



Diagnose advanced fibrosis (exam, noninvasive means)
Diagnose HCC
Counsel alcohol reduction
Discuss herbals/hepatotoxicity

Parenteral (Harm Reduction)
Sexual (esp. if HIV+)
Household (Razors/Toothbrushes)

Obesity
Tobacco
Cardiovascular Prevention

HIV (PREP)
STDs (screening, counseling)
Bacterial infections

Substance use
Psychiatric disorders
Housing
Support system

Hepatitis A
Hepatitis B
Influenza
Pneumococcal
(F3+)

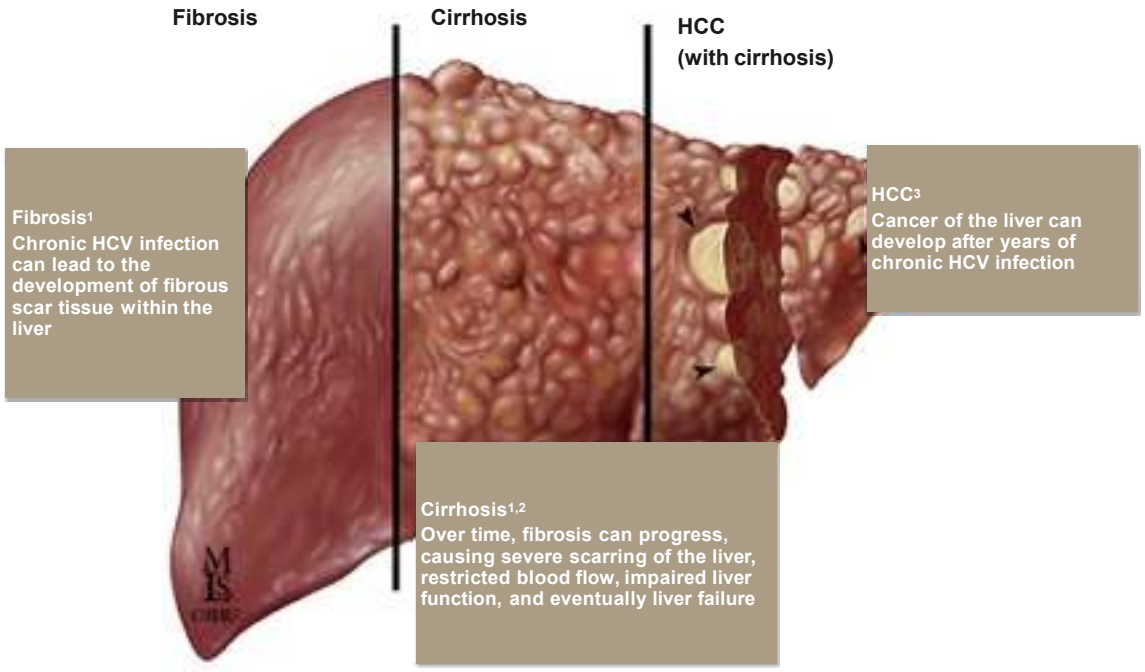
AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA
Infectious Diseases Society of America

Recommendations for Counseling those with Current (Active) HCV Infection and Pretreatment Assessment

Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening).



- Adapted from http://hcvguidelines.org

1. Highleyman L. Hepatitis C Support Project. http://www.hcvadvocate.org/hepatitis/factsheets_pdf/Fibrosis.pdf. Accessed August 18, 2011. 2. Bataller R, et al. *J Clin Invest.* 2005;115:209-18.
3. Medline Plus. http://www.nlm.nih.gov/medlineplus/enxy.article/000280.htm. Accessed August 28, 2012. 4. CDC. http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm. Accessed May 8, 2012.

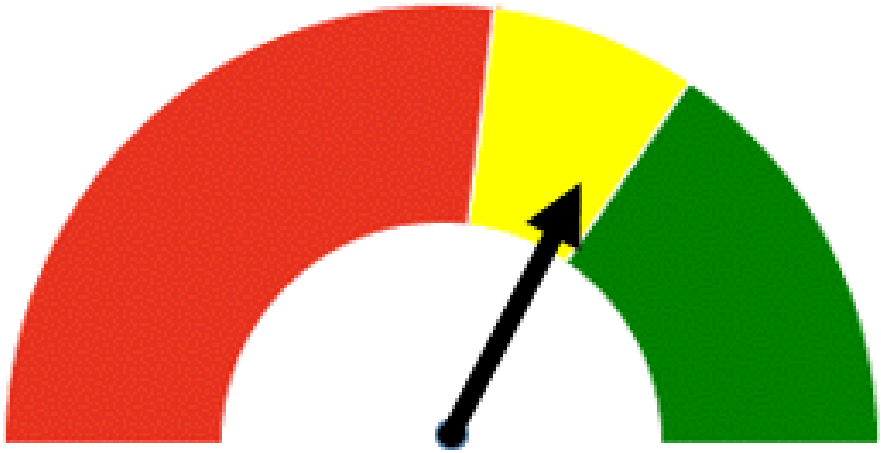
Liver Fibrosis "Harm Reduction"
What to avoid and what to promote

weight gain

marijuana

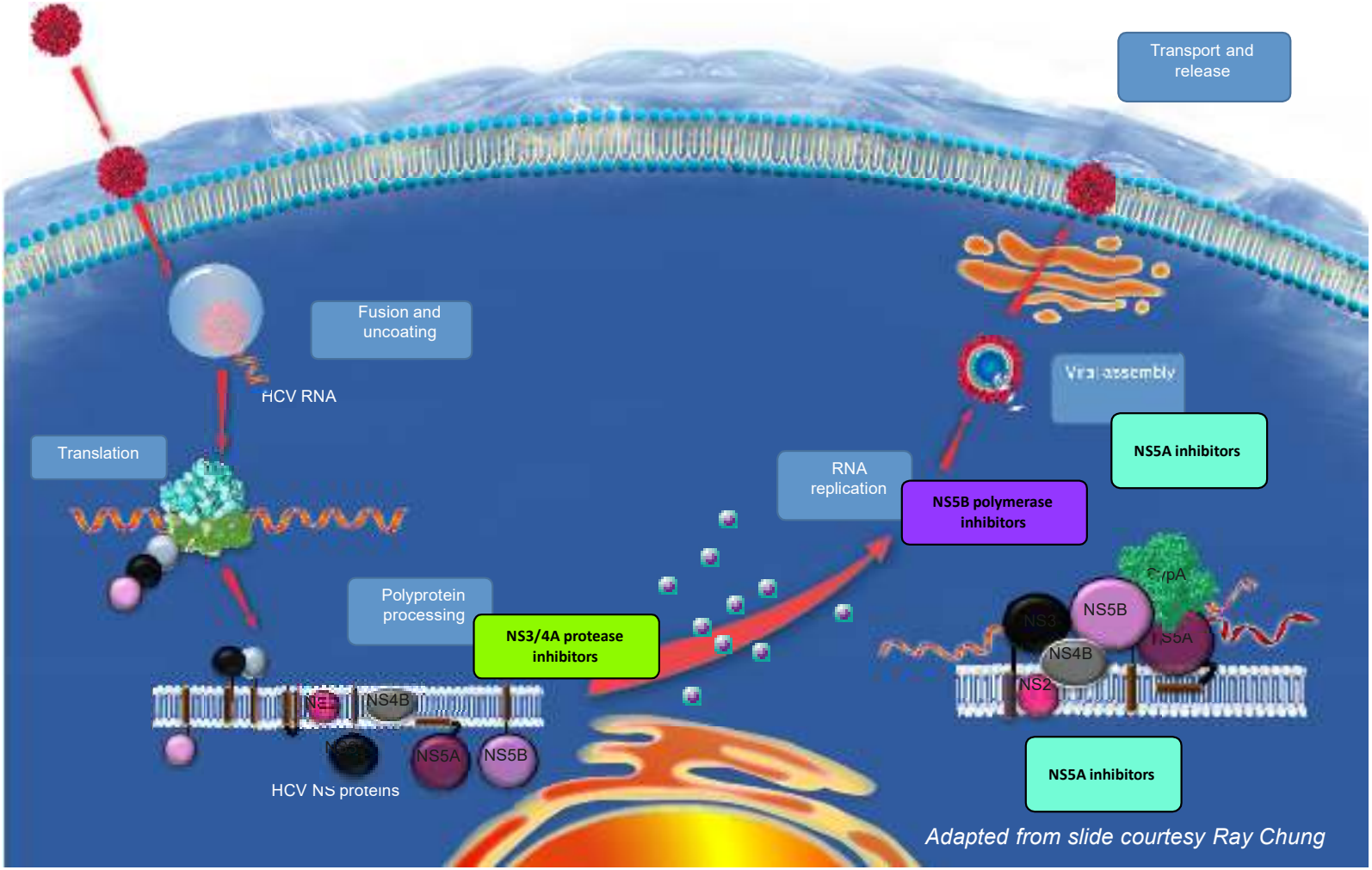
milk thistle

alcohol deleterious

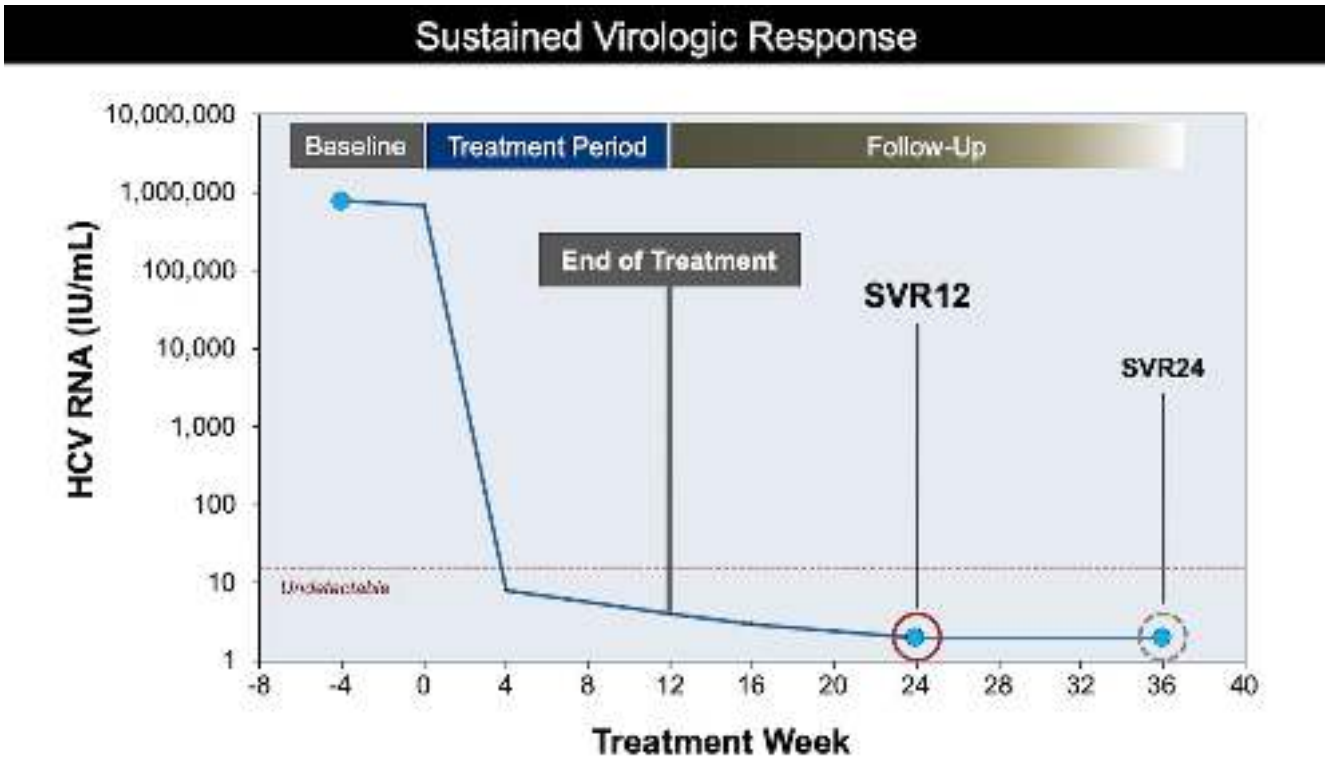


coffee beneficial

Therapeutic Targets in the HCV Replication Cycle

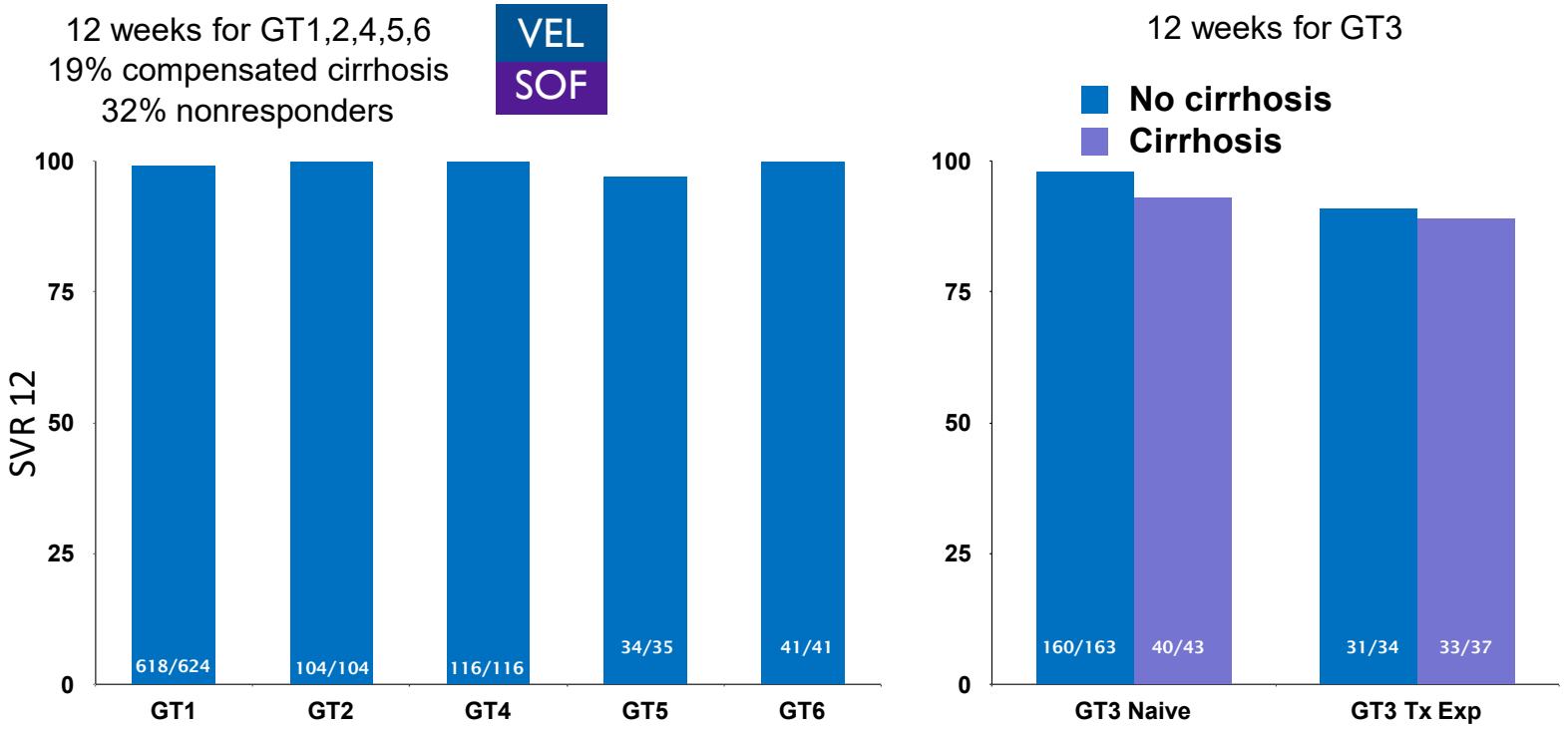


Cure = "Sustained virologic response" or negative HCV RNA **12** weeks after treatment end



https://www.hepatitisc.uw.edu/go/treatment-infection/monitoring/core-concept/all

Response rates for 12 weeks of pangenotypic regimen SOF/VEL for Genotypes 1-6

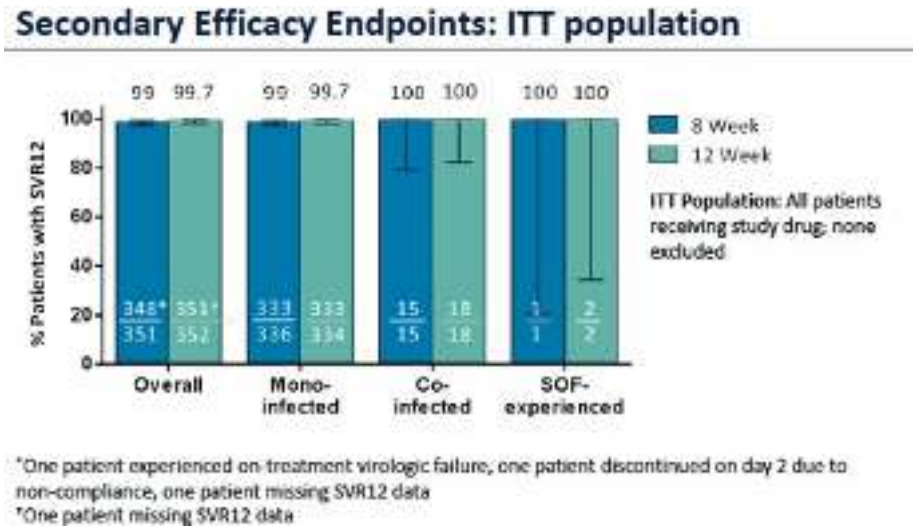


8 week arms of phase II trial: lower SVRs at 100 mg VEL dos (81-88%)

Feld et al. NEJM 2015; Foster et al. NEJM 2015; Everson et al. Ann Intern Med 2015

Glecaprevir and pibrentasvir (G/P): pangenotypic regimen

- ENDURANCE-1 examined 8 versus 12 weeks in GT1 non-cirrhotic patients with or without HIV



- 8 weeks G/P achieved 95% SVR in non cirrhotic genotype 3 patients in ENDURANCE-3

Zeuzem et al. NEJM 2018

Short course therapy with glecaprevir/pibrentasvir for early hepatitis C virus infection: PURGE-C

Kim et al., 2025 | *Clinical Infectious Diseases*

IDSA

BACKGROUND: What is the efficacy of short course therapy (4 weeks) of glecaprevir / pibrentasvir for early HCVinfection?

Single-arm open-label

Enrolled between November 2019 and January 2023
Recent HCV infection, including re-infections
All genotypes

Eleven sites within the United States and 1 site in Brazil from the Advancing Clinical Therapeutics Globally (ACTG) Network

- ✓ New elevation of ALT with HCV RNA or
- ✓ Positive HCV RNA with prior recent negative antibody or HCV RNA
- ✗ Cirrhosis
- ✗ Other causes of acute hepatitis (eg HAV or HBV)

Total participants n = 45

Included 23 (51%) persons with HIV

Recurrent viremia after Tx n = 6

Re-treatment for those with recurrent viremia

SVR 12 (HCV RNA < LLOQ 12 or more weeks after therapy cessation	84% (38 of 45)	100% (4 of 4)

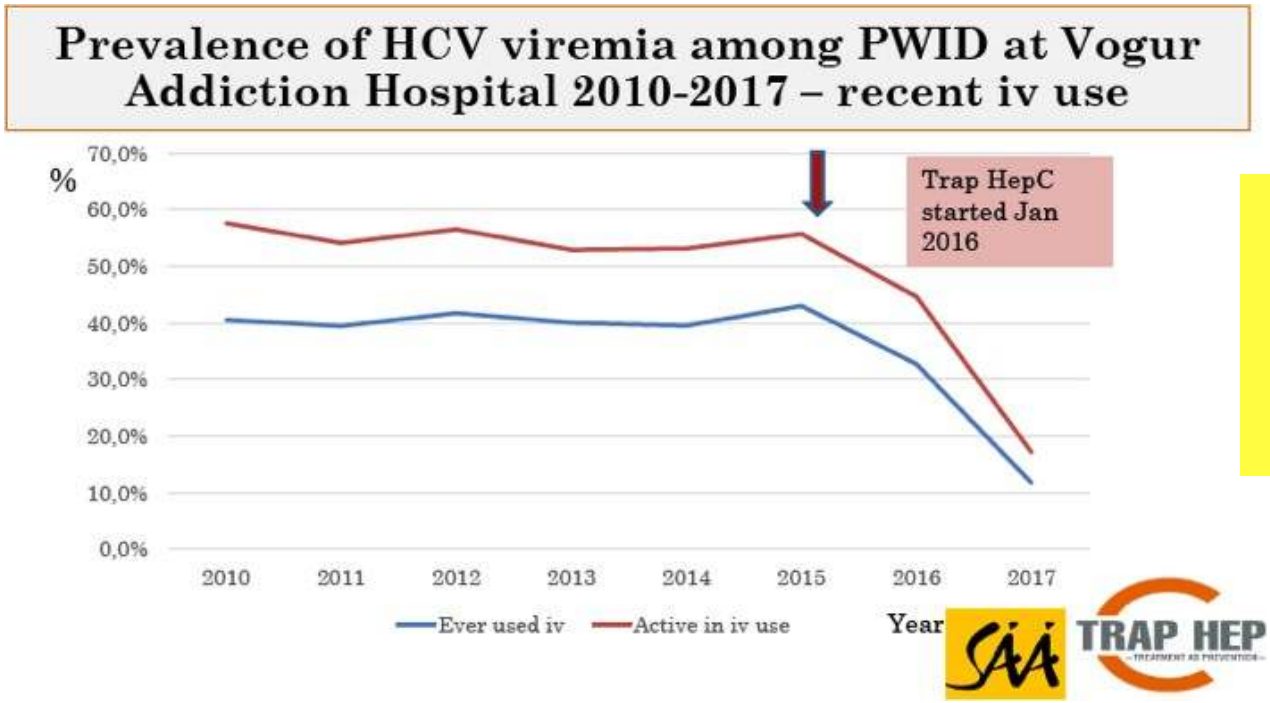
One participant achieved SVR4 but withdrew from the study due to incarceration. Of 6 participants with recurrent viremia, 5 exhibited high baseline HCV RNA, no resistance was detected and 4 achieved SVR12 with a salvage regimen.

About 84% of persons with early HCV who receive 4 weeks of G/P may be cured; those who relapse do not appear to exhibit resistance and can be successfully re-treated. Shorter courses may be pragmatic when a longer course is unlikely to be completed, especially in the context of treatment as prevention.

Clinical Infectious Diseases https://doi.org/10.1093/cid/ciaf305

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaf305/8215794

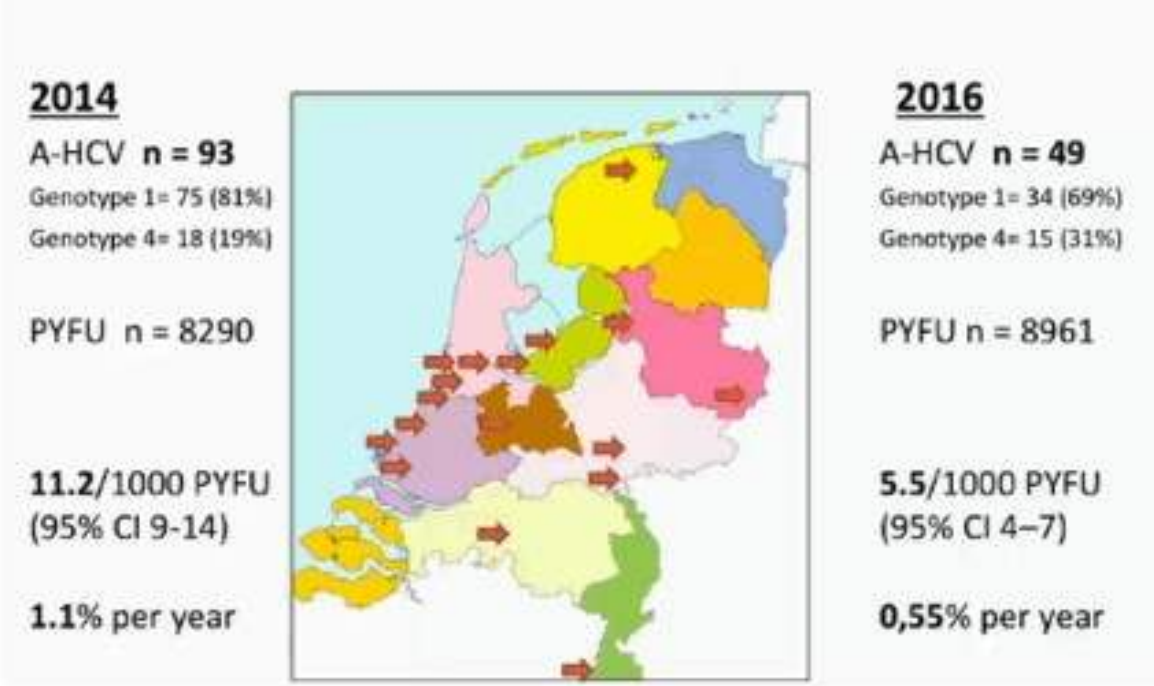
"Cure as Prevention" De-restricting Access to DAAs for PWID in Iceland Resulted in Lower Prevalence



Indirect evidence of treatment as prevention

Thorarinn Tyrfingsson et al. EASL 2018

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

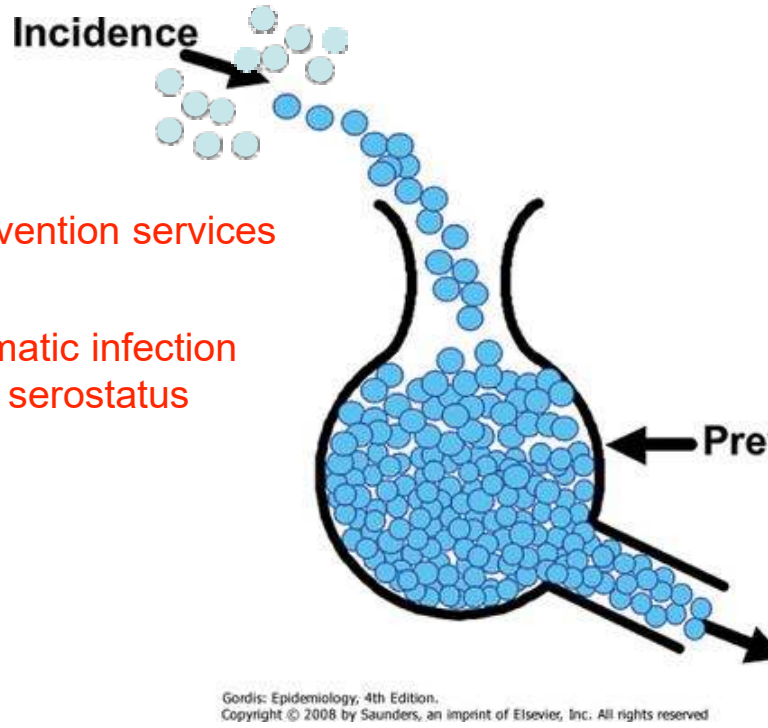


- Late 2015: unrestricted access with very rapid uptake in Dutch HIV/HCV coinfection - ~70% treated
- No associated decrease in syphilis or LGV so behavior unlikely explanation
- indirect evidence of “cure as prevention” for HCV

Rijnders et al. Clin Infect Dis 2017

Incidence, prevalence and sustaining an epidemic

Rising opiate use



Lack of prevention services

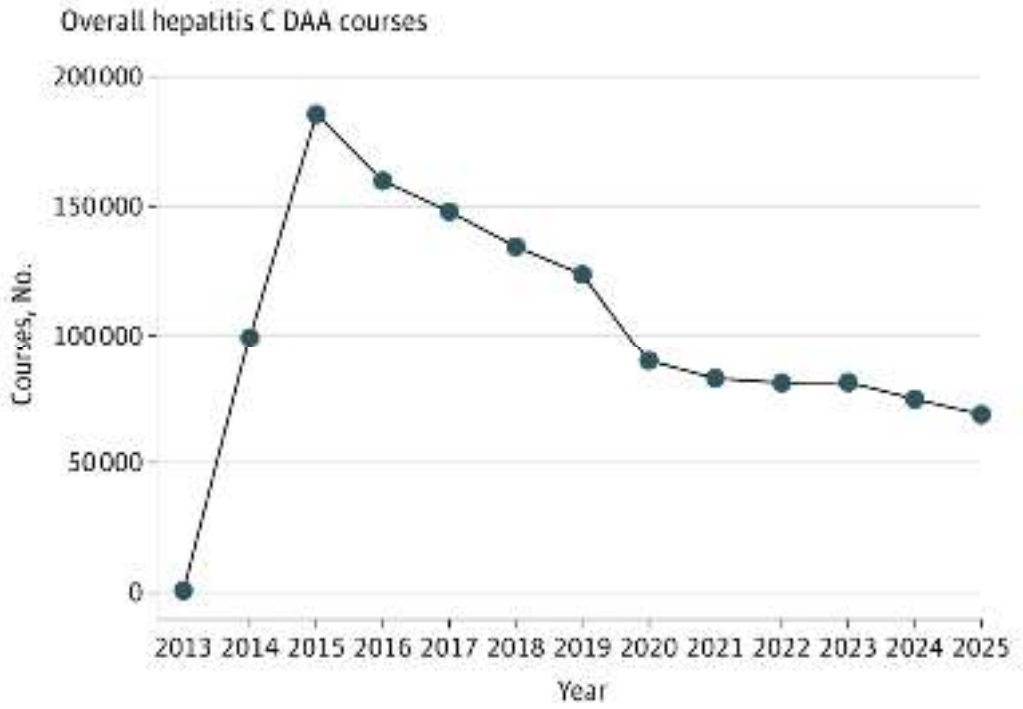
Asymptomatic infection
Unknown serostatus

Barriers to care,
access restrictions and
cost of treatment

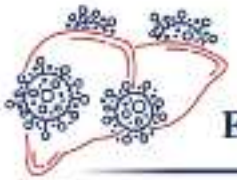
U.S. HCV treatment is behind elimination goals

Symphony Health Metys database, which estimates US prescription counts based on a large sample of retail, mail-order, and specialty pharmacy data

To meet elimination goals, needed >260,000 Tx/year



Kishore et al. JAMA 2026; NASEM 2017 Report



Launching a National Hepatitis C Elimination Program in the United States

On June 4, 2025, Senators Cassidy (R-LA) and Van Hollen (D-MD) introduced the bipartisan *Cure Hepatitis C Act*.

~$10B bill that would fund a national drug procurement program and provide funding for public health implementation.

The Congressional Budget Office estimated **the bill would save $6.6B** though reductions in HCV-related complications.

Slide Credit Carolyn Wester, CDC

119TH CONGRESS
1ST SESSION

S. _____

To require the Secretary of Health and Human Services to carry out activities to eliminate hepatitis C virus in the United States.

IN THE SENATE OF THE UNITED STATES

Mr. CASSIDY (for himself and Mr. VAN HOLLEN) introduced the following bill; which was read twice and referred to the Committee on

---

A BILL

To require the Secretary of Health and Human Services to carry out activities to eliminate hepatitis C virus in the United States.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Cure Hepatitis C Act of 2025".

HCV Summary

- Bloodborne infection, drug use epidemic has driven new cases
  - Epidemic overlaps with other viral infections (eg HAV/HBV/HIV)
- Leading cause of liver disease - **Silent** but deadly
  - Universal screening of adults recommended by AASLD/IDSA/ USPSTF
- Treatment of HCV is very effective
  - Viral cure (SVR12) is associated with reduction of liver-related complications and lack of onward transmission
- Prevention - No vaccine available, DAAs not used for PEP
  - **Harm reduction is effective!**
- While elimination is possible, multiple barriers remain

Selected References for Further Reading

- HAV
  - Desai and Kim. Management of hepatitis A in 2020-2021. JAMA2020;324(4);383-384
- HBV
  - AASLD HBV Guidelines: https://www.aasld.org/sites/default/files/HBVGuidance_Terrault_et_al-2018-Hepatology.pdf
  - ACIP: Adult vaccination recommendations update 2022 https://www.cdc.gov/mmwr/volumes/71/wr/mm7113a1.htm
  - CDC: Screening and Testing for Hepatitis B Infection 2023 https://www.cdc.gov/mmwr/volumes/72/rr/rr7201a1.htm
- HCV
  - Online Resource (funded by CDC, managed by University of Washington): https://www.hepatitisc.uw.edu/
  - Guidance from AASLD/IDSA: http://www.hcvguidelines.org
  - Kaplan DE. In the Clinic Hepatitis C Virus Ann Intern Med 2020.
  - CDC Recommendations for Hepatitis C Screening Among Adults 2020. https://www.cdc.gov/mmwr/volumes/69/rr/rr6902a1.htm

Thank you

- Arthur Y. Kim, MD
- @Arthur_Kim_ID on BlueSky