*Hepatitis Awareness*

# Evaluating Vaccination and Treatment of Hepatitis B for People Who Use Drugs

Monday, July 27, 2020 at 12:00 pm ET

PHILADELPHIA FIGHT

NATIONAL NURSE-LED CARE CONSORTIUM
a PHMC affiliate

Delaware Valley Community Health, Inc.

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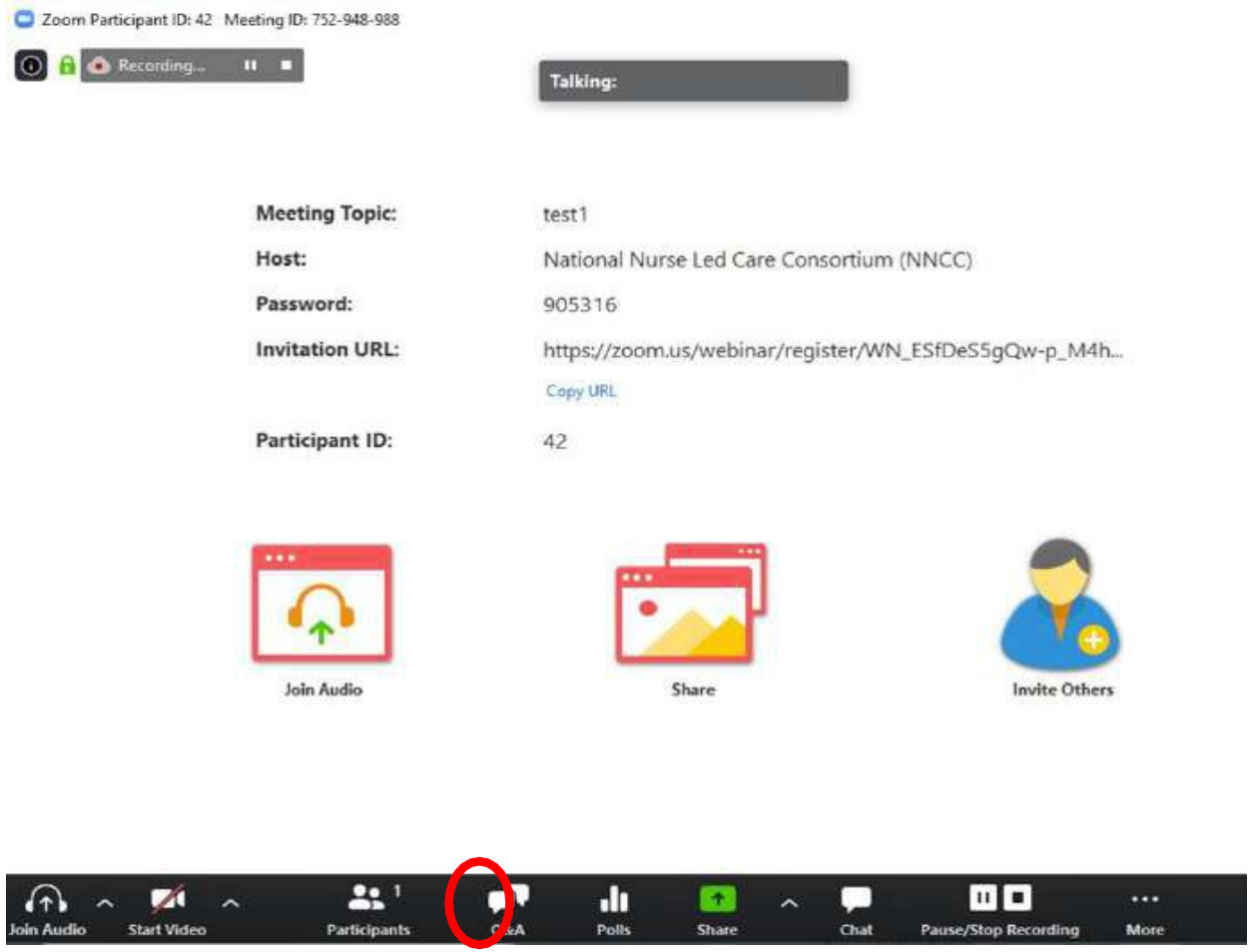

# Hepatitis B Epidemiology and Treatment

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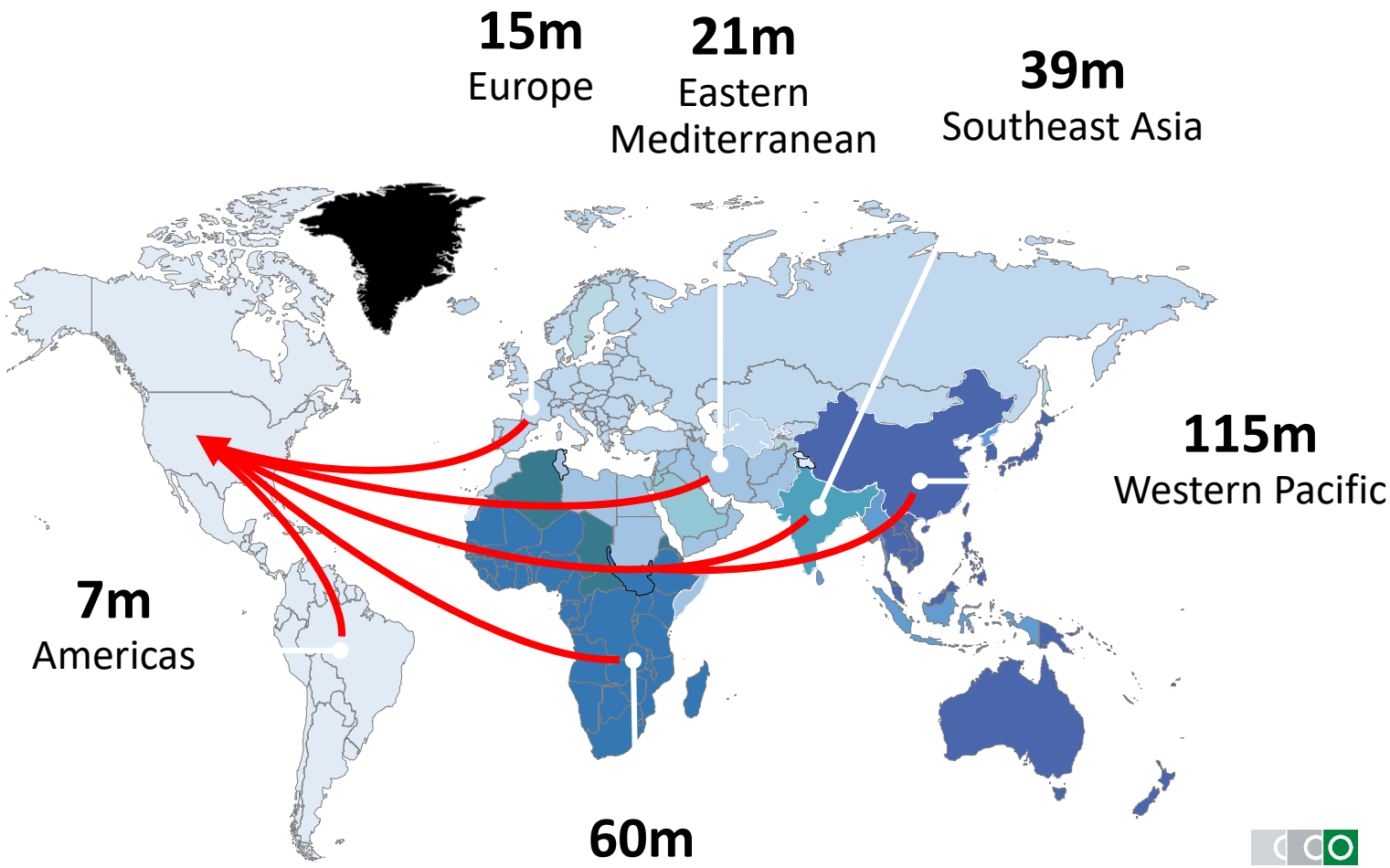
# Estimated Prevalence of CHB

## US Prevalence of CHB in Foreign-Born Persons in 2009[1]

| Birth Country | Total (M) | Midrange CHB Prevalence (%) |
|---|---|---|
| **All regions** | **38.4** | **3.5** |
| Asia | 10.6 | 7.3 |
| Central America | 14.4 | < 1.0 |
| Caribbean | 3.4 | 4.5 |
| South America | 2.6 | 1.3 |
| North America | 0.8 | < 1.0 |
| Oceania | 0.19 | 4.8 |
| Africa | 1.5 | 10.3 |
| Europe | 4.9 | 2.0 |

## Global Prevalence of CHB in 2015: 257 Million[2]




1. Kowdley. Hepatology. 2012;56:422. 2. WHO. Global hepatitis report, 2017.

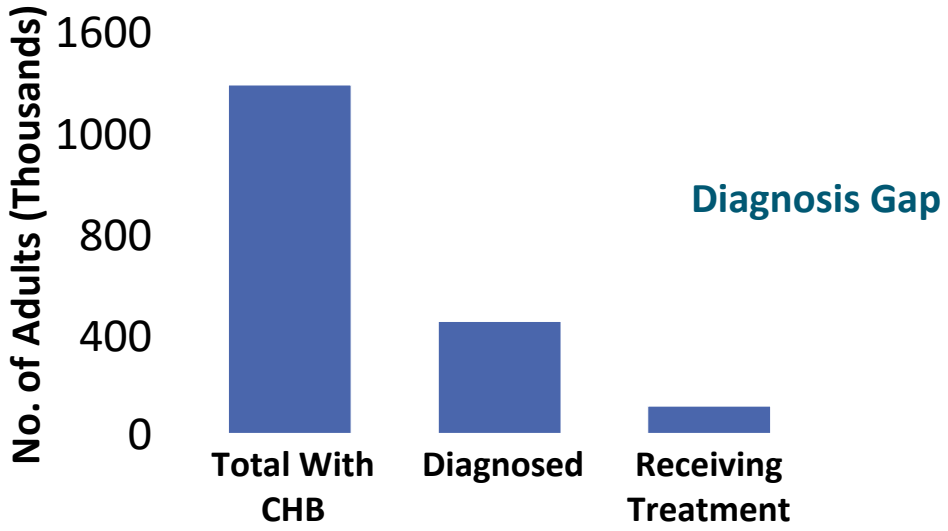
Slide credit: clinicaloptions.com

# Prevalence of CHB in the United States

- Including foreign-born persons, **850,000 to 2.2 million people in the US** are living with CHB,[1] including **400,000 to 800,000 Asians**[1,2]

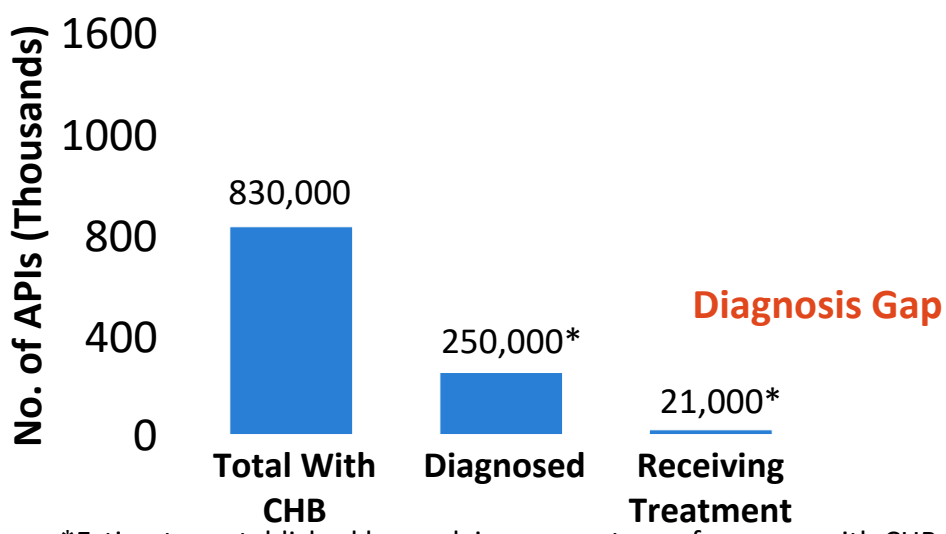
- 2013-2016 estimated CHB prevalence in **US** was 0.7%[3]

**Diagnosis and Treatment Gaps in US Population[3]**




- 2007 CHB prevalence among foreign-born **APIs in US** was 8.9%[4]

**Diagnosis and Treatment Gaps in US API Population[4,5]**




*Estimates established by applying percentage of persons with CHB diagnosed and treated in total population to number of APIs with CHB.

1. Harris. MMWR. 2018;67:541. 2. Kowdley. Hepatology. 2012;56:422. 3. Zhou. Clin Gastroenterol Hepatol. 2019. Epub.
4. Cohen. J Viral Hepat. 2008;15:12. 5. Cohen. J Viral Hepat. 2011;18:377.

Slide credit: clinicaloptions.com

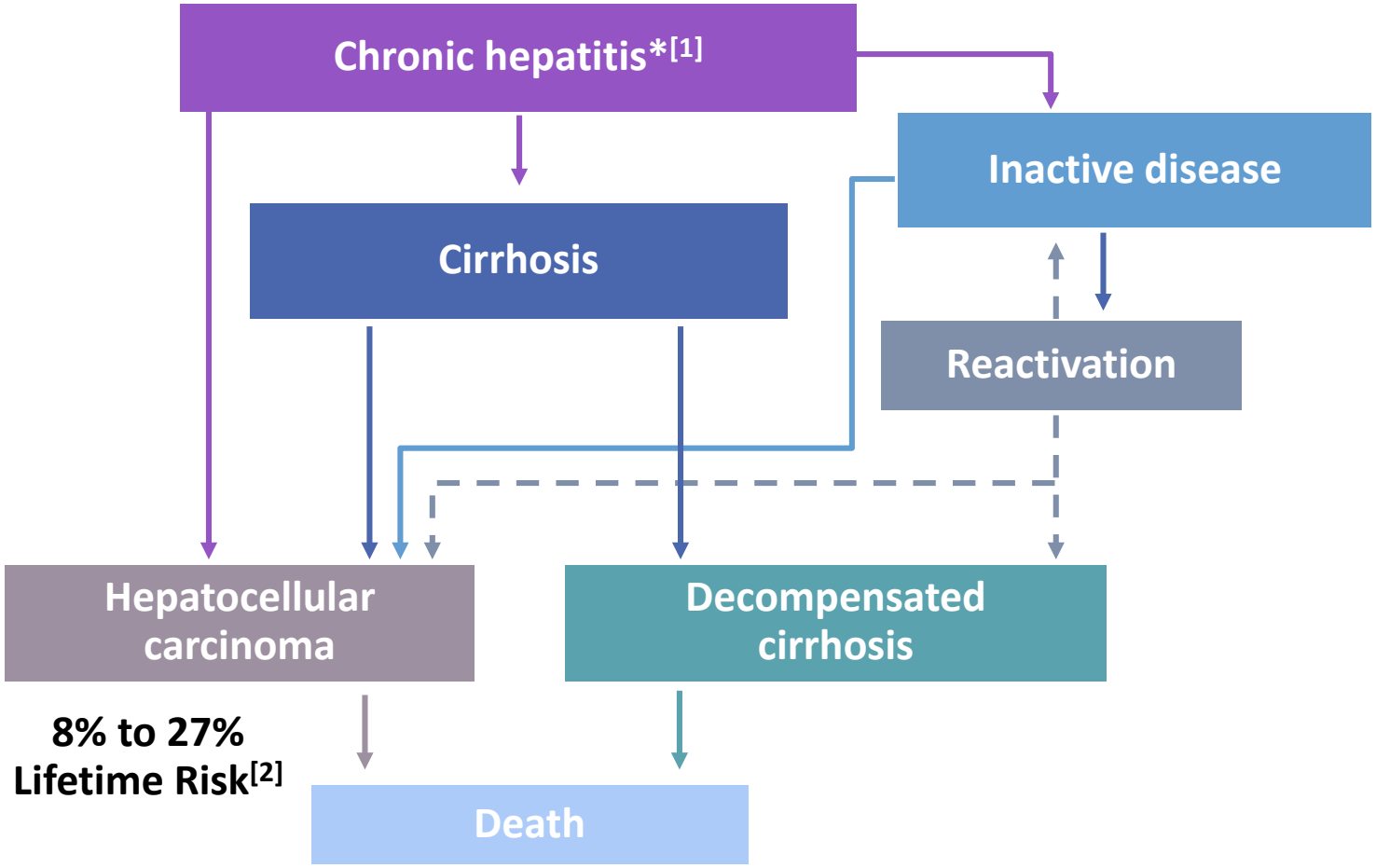
# Hepatitis B Epidemiology

- The incubation period from the time of exposure to onset of symptoms is 6 weeks to 6 months.
- HBV is found in highest concentrations in blood and in lower concentrations in other body fluids (e.g., semen, vaginal secretions, and wound exudates).
- HBV infection can be self-limited or chronic.

# Hepatitis B Clinical Features

- Incubation period 45-160 days (average 120 days)
- Nonspecific prodrome of malaise, fever, headache, myalgia
- Illness not specific for hepatitis B
- At least 50% of infections asymptomatic

# Hepatitis B Disease Progression and Impact




- Up to 40% of persons with CHB develop significant clinical consequences, including cirrhosis, liver failure, and HCC[3]
- 25% of persons with CHB will die prematurely from complications[4]

*Failure to clear HBsAg 6 mos after acute infection.

1. The elimination of hepatitis B. In: Buckley. Eliminating the public health problem of hepatitis B and C in the United States: Phase One Report. 2016. 2. Huang. JCO. 2011;29:3643. 3. Lok. NEJM. 2002;346:1682. 4. Harris. MMWR. 2018;67:541.

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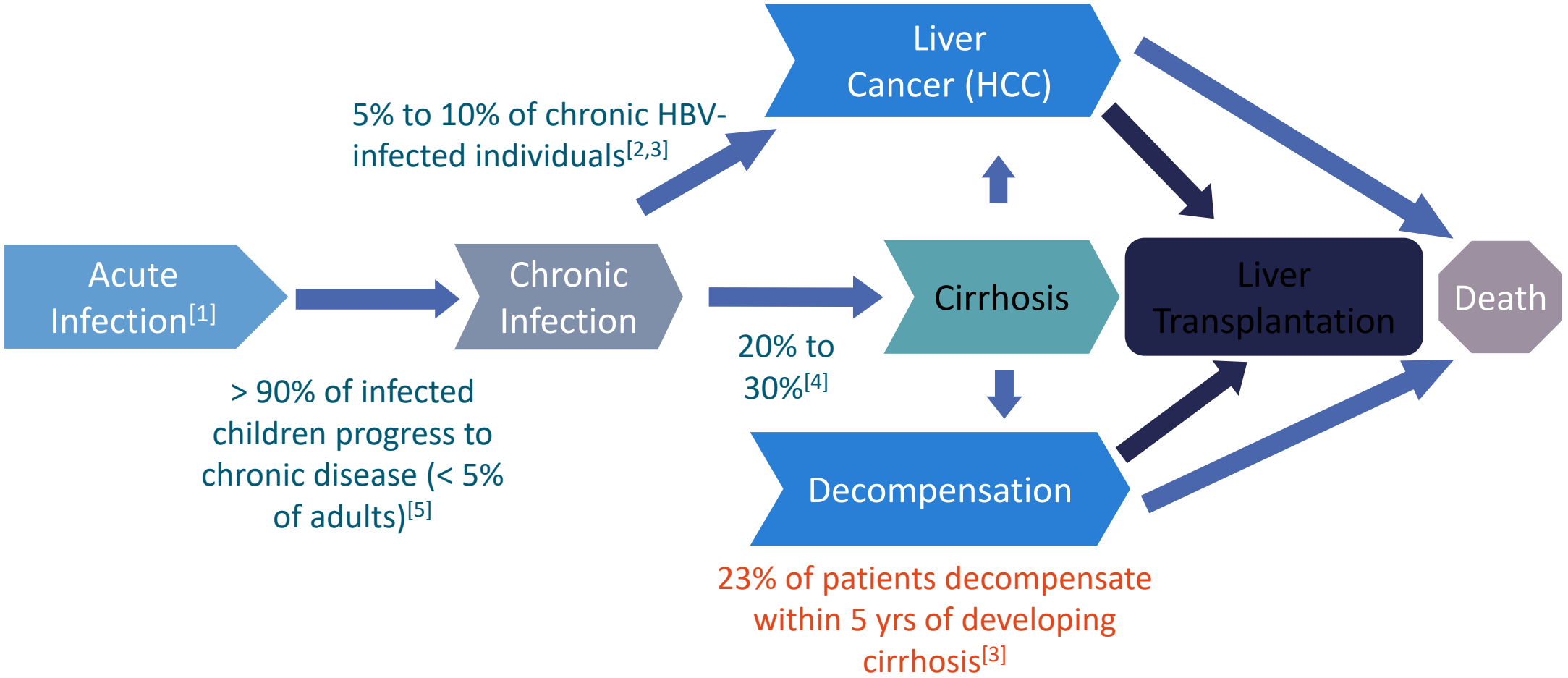
# Hepatitis B Disease Progression




1. The elimination of hepatitis B. In: Buckley. Eliminating the public health problem of hepatitis B and C in the United States: Phase One Report. 2016. 2. Iloeje. Liver Int. 2012;32:1333. 3. Fattovich. Hepatology. 1995;21:77. 4. Niederau. World J Gastroenterol. 2014;20:11595. 5. Weinbaum. MMWR Recomm Rep. 2008;57:1.

Slide credit: clinicaloptions.com

# Hepatitis B

## Typical interpretation of serologic test results for hepatitis B virus infection

| Serologic Marker | | | | Interpretation |
|---|---|---|---|---|
| HBsAg[1] | Total anti-HBc[2] | IgM[3] anti-HBc | Anti-Hbs[4] | |
| –[5] | – | – | – | Never infected |
| +[6,7] | – | – | – | Early acute infection; transient (up to 18 days) after vaccination |
| + | + | + | – | Acute infection |
| – | + | + | + or – | Acute resolving infection |
| – | + | – | + | Recovered from past infection and immune |
| + | + | – | – | Chronic infection |
| – | + | – | – | False-positive (i.e., susceptible); past infection; "low-level" chronic infection;[8] or passive transfer of anti-HBc to infant born to HBsAg-positive mother |
| – | – | – | + | Immune if concentration is ≥10 mIU/mL after vaccine series completion;[9] passive transfer after hepatitis B immune globulin administration |

Source: MMWR Recomm Rep. 2006; 55(RR-16):1–25.

# Natural History of HBV and Treatment Indications

| Parameter | HBeAg Positive | | HBeAg Negative | | Resolved HBV infection |
|---|---|---|---|---|---|
| | Chronic *Infection* | Chronic *Hepatitis* | Chronic *Infection* | Chronic *Hepatitis* | |
| Old terminology | Immune tolerant | Immune reactive HBeAg positive | Inactive carrier | HBeAg negative chronic hepatitis | HBsAg negative, anti-HBc positive |
| HBsAg | High | High/intermediate | Low | Intermediate | Negative |
| HBeAg | Positive | Positive | Negative | Negative | Negative |
| HBV DNA | > $10^7$ IU/mL | $10^4$ to $10^7$ IU/mL | < 2000 IU/mL* | > 2000 IU/mL | Undetectable |
| ALT | Normal | Elevated | Normal | Elevated† | Normal |
| Liver disease | None/minimal | Moderate/severe | None | Moderate/severe | None |
| Disease progression | Low | **Moderate to high** | Low | **Moderate to high** | None (HCC) |
| Treatment | Not indicated‡ | **Indicated** | Not indicated | **Indicated** | Not indicated§ |

*HBV DNA levels up to 20,000 IU/mL can occur without signs of chronic hepatitis. †Persistently or intermittently. ‡Treatment is indicated in some patients. § Prophylaxis for select cases.

EASL. J Hepatol. 2017;67:370.

Slide credit: clinicaloptions.com

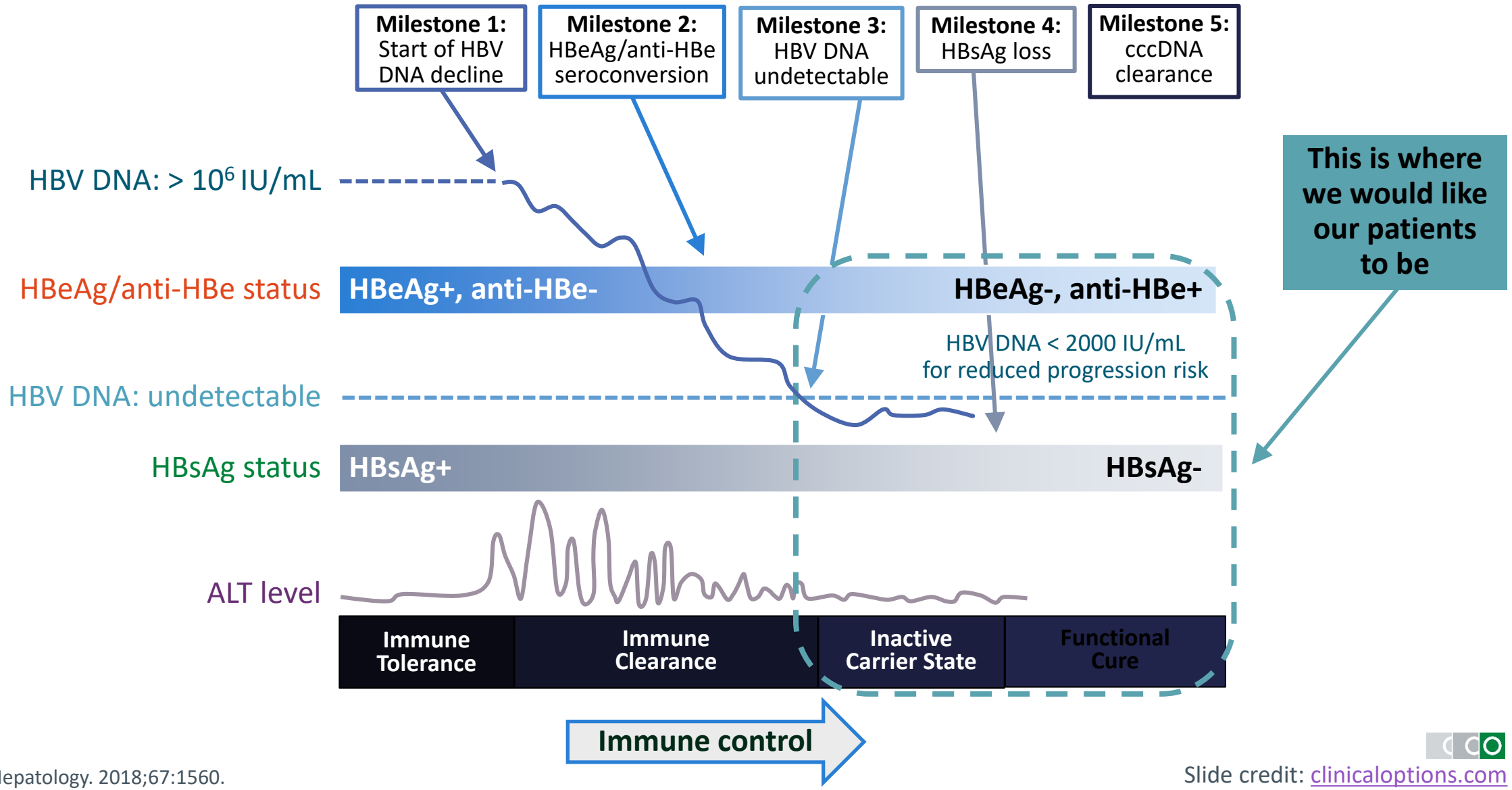
# 2018 AASLD Guidance: Defining Immune-Active vs Immune-Tolerant CHB

| Phase | Diagnostic Criteria |
|---|---|
| Immune-active CHB | ▪ HBsAg present for ≥ 6 mos<br>▪ Serum HBV DNA > 20,000 IU/mL in HBeAg+ CHB and > 2000 IU/mL in HBeAg- CHB<br>▪ Intermittently or persistently elevated ALT and/or AST levels<br>▪ Liver biopsy or noninvasive tests results show chronic hepatitis with moderate or severe necroinflammation ± fibrosis |
| Immune-tolerant CHB | ▪ HBsAg present for ≥ 6 mos<br>▪ HBeAg positive<br>▪ Very high HBV DNA levels (typically > 1 million IU/mL)<br>▪ Normal or minimally elevated ALT and/or AST<br>▪ Liver biopsy or noninvasive test results show no fibrosis and minimal inflammation |

Terrault. Hepatology. 2018;67:1560. www.aasld.org.

Slide credit: clinicaloptions.com

# Aiming for True Inactive Carrier Status




Terrault. Hepatology. 2018;67:1560.

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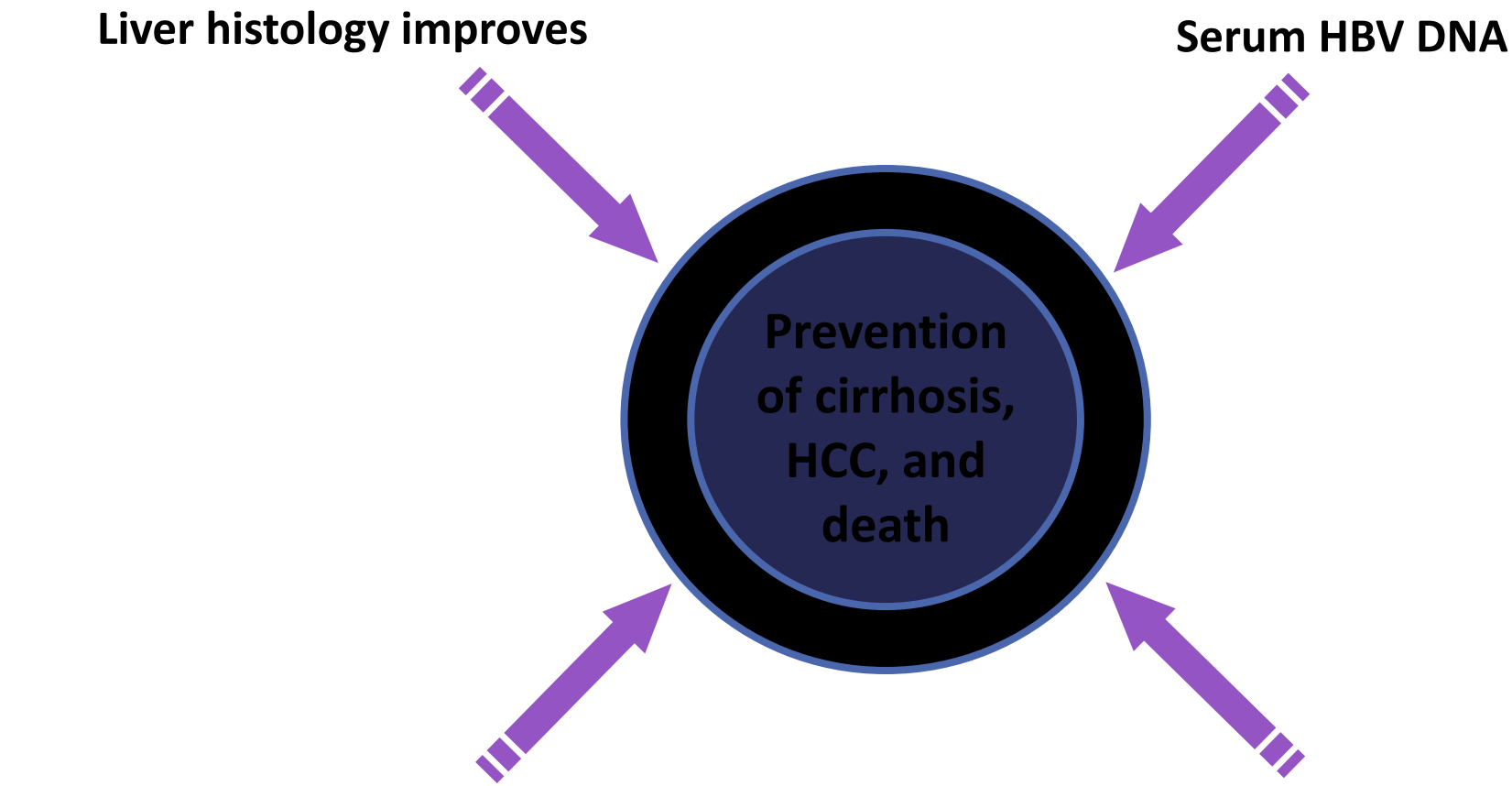
# Goals of Therapy for HBV




EASL. J Hepatol. 2017;67:370.

Slide credit: clinicaloptions.com

# Candidates for CHB Treatment in Patients Without Cirrhosis

| Treatment Threshold | APASL[1] (2015) | EASL[2] (2017) | US Algorithm[3] (2015) | AASLD[4] (2018) |
|---|---|---|---|---|
| HBV DNA, IU/mL | | | | |
| ▪ HBeAg positive | > 20,000 | > 2000* | ≥ 2000 | > 20,000 |
| ▪ HBeAg negative | > 2000 | > 2000* | ≥ 2000 | > 2000 |
| ALT | > 2 x ULN | > ULN* | > ULN | ≥ 2 x ULN |
| ▪ ULN for men | 40 IU/mL | 40 IU/L | 30 IU/L | 35 U/L |
| ▪ ULN for women | 40 IU/mL | 40 IU/L | 19 IU/L | 25 U/L |
| Key factors | HBV DNA, ALT | HBV DNA, ALT, age | HBV DNA, ALT | HBV DNA, ALT |
| Biopsy | Consider in certain groups | | | |

*If at least moderate necroinflammation and/or fibrosis.

1. Sarin. Hepatol Int. 2016;10:1. 2. EASL. J Hepatol. 2017;67:370. 3. Martin. Clin Gastroenterol Hepatol. 2015;13:2071. 4. Terrault. Hepatology. 2018;67:1560.

# Candidates for CHB Treatment: Where All Guidelines Agree

| Patient Characteristic | APASL[1] (2015) | EASL[2] (2017) | US Algorithm[3] (2015) | AASLD[4] (2018) |
|---|---|---|---|---|
| HBV DNA, IU/mL | | | | |
| ▪ HBeAg positive | 20,000 | 20,000 | 20,000 | 20,000 |
| ▪ HBeAg negative | > 2000 | > 2000* | ≥ 2000 | > 2000 |
| ALT | > 80 IU/mL | > 80 IU/mL | 80 IU/mL | 80 IU/mL |

*If at least moderate necroinflammation and/or fibrosis.

1. Sarin. Hepatol Int. 2016;10:1. 2. EASL. J Hepatol. 2017;67:370. 3. Martin. Clin Gastroenterol Hepatol. 2015;13:2071. 4. Terrault. Hepatology. 2018;67:1560.

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# AASLD Guidance Update: What's New

- The decision to treat persons with **ALT > ULN but < 2 x ULN** requires consideration of liver disease severity by biopsy or noninvasive testing
  - Other factors to consider: age, family history of HCC or cirrhosis, previous treatment history, extrahepatic manifestations
- Patients with low-level viremia (HBV DNA < 2000 IU/mL) and **compensated cirrhosis** should be treated, regardless of ALT
- All patients with **decompensated cirrhosis** who are HBsAg positive should be treated, regardless of HBV DNA, HBeAg status, or ALT
- **Adults older than 40 yrs of age who are otherwise immune tolerant** (ie, normal ALT and HBV DNA > 1 million IU/mL) with liver biopsy showing significant necroinflammation or fibrosis should be treated

Terrault. Hepatology. 2018;67:1560.

Slide credit: clinicaloptions.com

# First-line Treatment Options for CHB

| Status | Treatment | Notes |
|---|---|---|
| Preferred | ETV, TAF*, or TDF† | ▪ High potency, high genetic barrier to resistance |
| | PegIFN | ▪ Less safe with cirrhosis (reserve for mild CHB), contraindicated with decompensated cirrhosis |
| Not preferred | LAM, ADV, or TBV | ▪ Low genetic barrier to resistance |

*Efficacy and safety of TAF have not been established for CHB in patients with decompensated cirrhosis, pregnant women, or children; recommendations for these populations are subsequently limited. †If TDF is chosen, monitor renal function and BMD in at-risk patients.

ETV, TAF, and TDF have very favorable safety and resistance profiles

Terrault. Hepatology. 2018;67:1560. EASL. J Hepatol. 2017;67:370.

# Dosing of Preferred NA Therapies

| Agent | Approval Yr | | QD Dose | Lowest CrCl Without Dose Adjustment | Dose Reductions by CrCl, mL/min |
|---|---|---|---|---|---|
| | HIV | CHB | | | |
| ETV*[1] | -- | 2005 | 0.5 mg | 50 mL/min | ▪ 30-49: 0.25 mg QD *or* 0.5 mg Q48H<br>▪ 10-29: 0.15 mg QD *or* 0.5 mg Q72H<br>▪ < 10 (HD/CAPD): 0.05 mg QD *or* 0.5 mg QW |
| TDF[2] | 2001 | 2008 | 300 mg | 50 mL/min | ▪ 30-49: 300 mg Q48H<br>▪ 10-29: 300 mg Q72-96H<br>▪ < 10 (HD): 300 mg QW or after ~ 12 hrs HD‡ |
| TAF[3] | 2015† | 2016 | 25 mg | 15 mL/min | ▪ < 15: not recommended if no concurrent HD |

*Oral solution recommended for doses < 0.5 mg. †In fixed-dose combinations with other ARVs. ‡No data to make recommendation when eGFR < 10 mL/min if patient not receiving HD.

1. ETV PI. 2. TDF PI. 3. TAF PI.

Slide credit: clinicaloptions.com

# 2018 AASLD Guidance: Criteria for Selecting ETV vs TAF vs TDF

| Comparative Measure | ETV | TAF | TDF |
|---|---|---|---|
| Dose | 0.5 mg/day | 25 mg/day | 300 mg/day |
| Presence of LAM resistance | Increase dose | Active | Active |
| Anticipated pregnancy | Pregnancy Category C | No human data in pregnancy | Pregnancy Category B |
| Renal disease | Decrease dose if CrCl < 50 mL/min | Do not use if CrCl < 15 mL/min or if on dialysis* | Decrease dose if CrCl < 50 mL/min |
| Bone disease | Recommended | Recommended | Recommended |
| HIV coinfection | Only recommended in addition to complete ART regimen | Coformulated ART regimen | Coformulated ART regimen |
| Cost considerations | Generic available | No generic | Generic available |

*By contrast, EASL guidelines recommend either ETV or TAF in patients receiving hemodialysis. Since February 2019, TAF prescribing information notes that no dose adjustment is necessary in individuals with CrCl > 15 mL/min or in individuals with CrCl < 15 mL/min who are receiving hemodialysis.

Terrault. Hepatology. 2018;67:1560. www.aasld.org.

Slide credit: clinicaloptions.com

# 2018 AASLD Guidance: Nucleos(t)ide Analogues

- **ETV 0.5 mg/day, TAF 25 mg/day, or TDF 300 mg/day**
- Potent, high genetic barrier to resistance
- Drug-related monitoring
  - All: HIV at BL, lactic acid during therapy if clinical concern
  - TAF: serum creatinine and phosphorus; urine glucose and protein
  - TDF: BL CrCl, renal monitoring if renal risk, BL bone density

Terrault. Hepatology. 2018;67:1560. www.aasld.org.

Slide credit: clinicaloptions.com

# 2018 AASLD Guidance: Therapy Duration on NAs

- **For most, NA treatment duration is indefinite**
  - HBeAg-positive adults without cirrhosis who seroconvert to anti-HBe on therapy: **discontinue therapy** after a period of treatment consolidation *if this endpoint is met*
  - HBeAg-positive adults with cirrhosis who seroconvert to anti-HBe on NA therapy: **indefinite therapy***, unless there is a strong competing rationale for treatment discontinuation*
  - HBeAg-negative adults with immune-active CHB: **indefinite therapy**

Terrault. Hepatology. 2018;67:1560. www.aasld.org.

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# EASL Guidance: How to Monitor Patients Receiving HBV Therapy

- Liver tests every 3-4 mos in first yr, then every 6 mos thereafter
- Serum HBV DNA every 3-4 mos in first yr, then every 6-12 mos thereafter
- HBeAg/anti-HBe in HBeAg-positive patients
- HBsAg every 12 mos in patients with persistently undetectable HBV DNA
  - Those clearing HBsAg should be tested for anti-HBs
- Periodic renal monitoring in those treated with TDF and those at risk of renal disease treated with any NA
  - Serum creatinine and serum phosphate levels every 3 mos in first yr, then every 6 mos thereafter

EASL. J Hepatol. 2017;67:370.

Slide credit: clinicaloptions.com

# Long-Term Efficacy of HBV Therapies

- **5-Yr efficacy of ETV in HBeAg-positive patients in observed analysis[1]**
  - 94% with HBV DNA < 300 copies/mL
  - 80% with ALT normalization
- **8-Yr efficacy of TDF in ITT analysis[2]**
  - 74% with HBV DNA < 29 IU/mL (HBeAg-negative patients)
  - 58% with HBV DNA < 29 IU/mL (HBeAg-positive patients)
- **144-Wk efficacy of TAF in ITT analysis[3]**
  - 81% with HBV DNA < 69 IU/mL*

*Including 180 of 1046 pts who switched from TDF to TAF at wk 96

1. Chang. Hepatology. 2010;51:422. 2. Marcellin. AASLD 2014. Abstr 299. 3. Chan. AASLD 208. Abstr 235.

# 2018 AASLD Guidance: Efficacy of First-line Antiviral Therapies in Treatment-Naive Adults With CHB

| Outcomes From Separate Studies (Not Head to Head) | PegIFN* | ETV† | TAF‡ | TDF† |
|---|---|---|---|---|
| **HBeAg positive** | | | | |
| ▪ HBV DNA suppression,§ % (IU/mL) | 30-42 (< 2000-40,000) | 61 (< 50-60 IU/mL) | 73 (< 29) | 76 (< 60) |
| ▪ HBeAg loss, % | 32-36 | 22-25 | 22 | -- |
| ▪ HBeAg seroconversion, % | 29-36 | 21-22 | 18 | 21 |
| ▪ Normalization ALT, % | 34-52 | 68-81 | -- | 68 |
| ▪ HBsAg loss, % | 2-7 | 4-5 | 1 | 8 |
| **HBeAg negative** | | | | |
| ▪ HBV DNA suppression,¶ % (IU/mL) | 43 (< 4000) | 90-91 (< 50-60) | 90 (< 29) | 93 (< 60) |
| ▪ Normalization ALT, % | 59 | 78-88 | 81 | 76 |
| ▪ HBsAg loss,% | 4 | 0-1 | < 1 | 0 |

*Assessed 6 mos after completion of 12 mos of therapy. †Assessed after 3 yrs of continuous therapy. ‡Assessed after 2 yrs of continuous therapy. § HBV DNA < 2000-40,000 IU/mL for pegIFN; < 60 IU/mL for ETV and TDF; < 29 IU/mL for TAF. ¶HBV DNA < 20,000 IU/mL for pegIFN; < 60 IU/mL for ETV and TDF; < 29 IU/mL for TAF. ‖ALT normalization defined by laboratory normal rather than < 35 U/L for men and 25 U/L for women.

Terrault. Hepatology. 2018;67:1560.

Slide credit: clinicaloptions.com

# Efficacy and Limitations of Currently Available HBV Therapies

## Efficacy

- Result in potent viral suppression
- Reverse hepatic fibrosis/cirrhosis
- Prevent progression to liver failure

## Limitations

- Result in low rate of HBsAg loss
- Decrease but do not eliminate risk of HCC
- Require long duration (lifelong in some patients) to maintain benefit, resulting in high costs, potential drug resistance, and prolonged adverse events

EASL. J Hepatol. 2017;67:370.

Slide credit: clinicaloptions.com

# 2018 AASLD Guidance: Monitoring of CHB Patients Not on Antiviral Therapy

| | Immune-Tolerant CHB | Inactive CHB | Resolved CHB |
|---|---|---|---|
| **Definition of Population** | HBeAg positive, high HBV DNA | HBeAg negative, normal ALT, low HBV DNA | HBsAg loss |
| **Recommended Monitoring for Population** | **ALT: every 3-6 mos**<br>▪ If ALT level rises to > ULN, evaluate ALT and HBV DNA more frequently<br><br>**HBeAg status: every 6-12 mos**<br>▪ Treat if HBeAg+ with HBV DNA > 20,000 IU/mL for 3-6 mos and ALT > 2 x ULN<br><br>**Liver biopsy or noninvasive assessment of fibrosis**<br>▪ Consider with slight, persistent ALT elevation, particularly if > 40 yrs of age and infected for long duration | **ALT and HBV DNA: every 3 mos for first yr, then every 6-12 mos**<br>▪ If ALT level rises to > ULN, evaluate ALT and HBV DNA more frequently<br><br>**HBsAg: annually** | **ALT and HBV DNA monitoring no longer required**<br><br>**HCC surveillance**<br>▪ Continue if individual has cirrhosis, a first-degree family member with HCC, or a long duration of infection |

**If treatment is not indicated, actively monitor as candidacy may change with disease progression**

Terrault. Hepatology. 2018;67:1560. www.aasld.org.

Slide credit: clinicaloptions.com

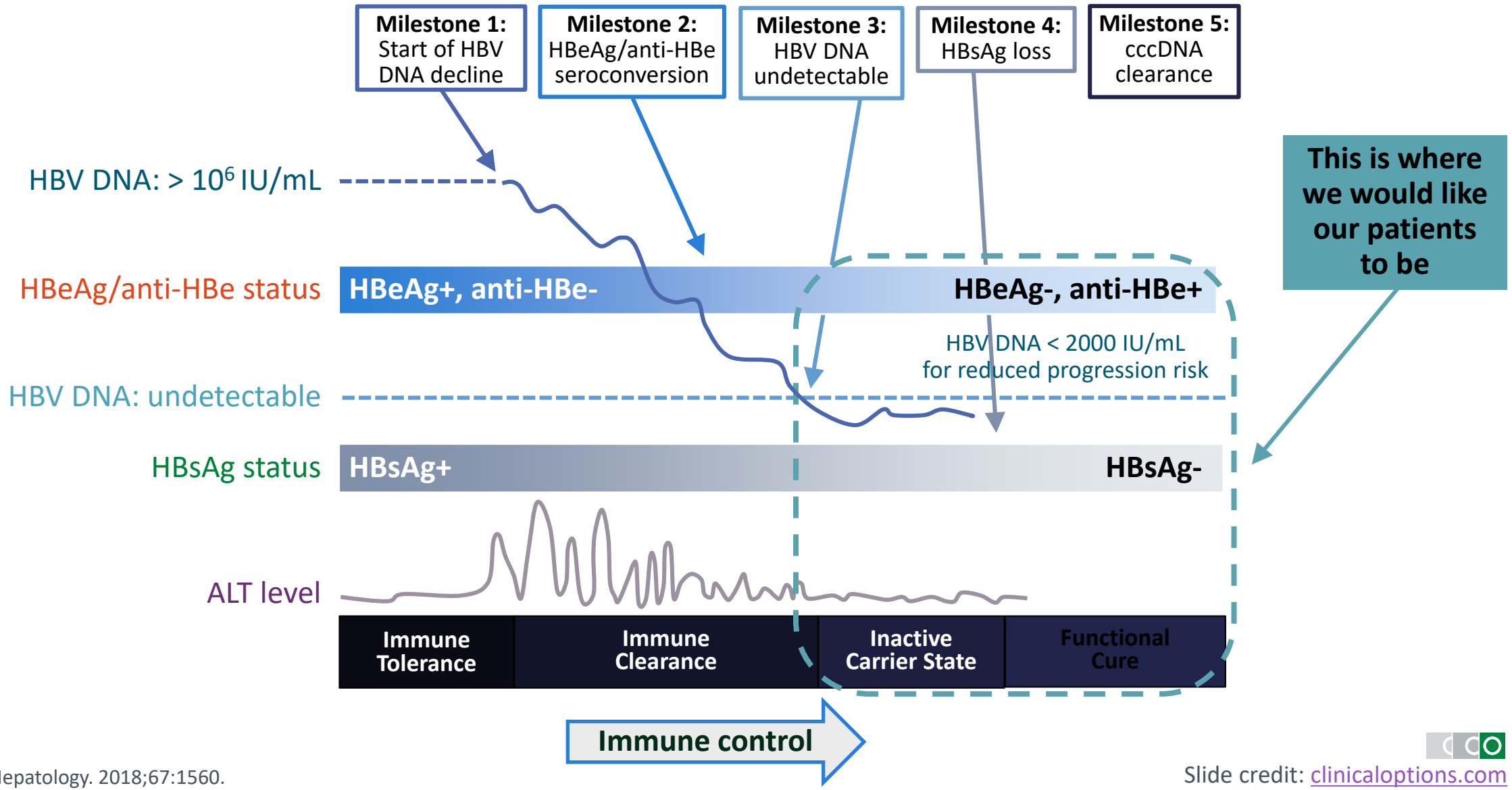
# AASLD Guidelines: Recommendations for HCC Screening

- Hepatitis B carriers at high risk[1]
  - All patients with cirrhosis
  - Patients with first-degree family member with history of HCC
  - Asian or black men older than 40 yrs of age
  - Asian women older than 50 yrs of age
  - Coinfected with HDV
- Liver ultrasound with or without AFP in high risk patients every 6 mos[1,2]

1. Terrault. Hepatology. 2018;67:1560. 2. Heimbach. Hepatology. 2018;67:358.

Slide credit: clinicaloptions.com

# Aiming for True Inactive Carrier Status




Terrault. Hepatology. 2018;67:1560.

Slide credit: clinicaloptions.com

# HBV in PWID: Serologic Markers and Vaccination

KATIE HUYNH MS,PA-C, AAHIVM-S

# Screening for HBV

# WHO SHOULD BE SCREENED?

- **Persons born in high and intermediate endemic areas (≥2% prevalence)**
- **US-born children of immigrants from high endemic areas (≥8%; only if not vaccinated as infants in the US)**
- **Household and sexual contacts of HBV carriers**
- **Persons who have injected drugs**
- **Persons with multiple sexual partners or history of STIs**
- **Men who have sex with men**
- **Inmates of correctional facilities**
- **Pts with chronically elevated ALT/AST**
- **Individuals infected with HIV or HCV**
- **Patients undergoing dialysis**
- **PrEP and PEP pts**
- **All pregnant women**
- **Infants born to HBV carrier mothers**



CDC recommendations for HBV screening. doi:10.1371/journal.pone.0092266.g002

# HBV is a silent killer

- Chronic HBV infection usually asymptomatic, even with liver cancer and well-compensated cirrhosis
- Liver panel may be normal
- As many as 2 out of 3 chronically infected persons are unaware of HBV infection
- Those born after 1992, not vaccinated as infants
- *With increase of injection drug use, rise in not only HCV but HBV as well*

# PATIENT BARRIERS TO SCREENING

- Lack of understanding (screening, mother to child transmission)
- *Lack of venous access*
- Cultural beliefs/shame
- Privacy
- Value of testing/treatment
- Asymptomatic
- Financial
- Language

# PATIENT EDUCATION/ENGAGEMENT

- Highlight ways in which HBV infection is transmitted and can be prevented
- Emphasize that HBV can be prevented through a highly effective vaccine
- Highlight that there are highly effective HBV treatments to prevent bad long-term outcomes

# CLINICIAN BARRIERS

- Too many things to keep track of and accomplish in too short a time at primary care visit
- HBV serological results are confusing
- No venous access in PWID
- Unclear/undocumented vaccination history
- HBV guidelines are conflicting and/or confusing
- No reminders built into clinic system (electronic health records, etc.)

# SOLUTIONS FOR CLINICIAN BARRIERS

- Make HBV risk assessment and appropriate screening routine parts of care
  - EHR prompts, add risk assessment to standard intake forms, use flow chart
- Understand HBV screening guidelines to identify at-risk persons
- Identify effective ways to engage patients in HBV screening
- Learn how to effectively screen for HBV and interpret serologies
- Identify opportunities for prevention through HBV vaccination
- Understand when/how to refer patients to specialists for HBV care
- Identify social service resources for patients (insurance, immigration, care access) and refer when appropriate

# HBV Serologic Markers

# HEPATITIS B SEROLOGY - STEP ONE

- **HBsAg: Hepatitis B surface antigen**
  - Marker of active infection
  - Chronic HBV: HBsAg positive for at least 6 months
- **Anti-HBs (or HBsAb): Antibody to HBsAg**
  - Marker of immunity to hepatitis B
- **Anti-HBc: Total hepatitis core antibody (IgG)**
  - Previous exposure or false positive
- ***If acute HBV is suspected: IgM Anti-HBc**



Source: Adapted from McMahon, BJ, Peters, M. http://www.aasld.org/education/Pages/HBVSlides.aspx. Accessed March 12, 2010.

# HEPATITIS B SEROLOGY - STEP TWO
## IF HBsAg IS POSITIVE

- **HBeAg: hepatitis B “e” antigen**
  - Surrogate marker of high viral load
- **Anti-HBe (or HBeAb): antibody to HBeAg**
  - Precore or basal core promoter mutation: associated with lower viral load
- **HBV DNA Viral Load: active viral replication**

# INTERPRETATION OF HBV SEROLOGIES (SLIDE 1 OF 2)

| | | |
|---|---|---|
| • HBsAg<br>• Anti-HBc<br>• Anti-HBs | • negative<br>• negative<br>• negative | • Susceptible |
| • HBsAg<br>• Anti-HBc<br>• Anti-HBs | • negative<br>• positive<br>• positive | • Immune due to natural infection |
| • HBsAg<br>• Anti-HBc<br>• Anti-HBs | • negative<br>• negative<br>• positive | • Immune due to hepatitis B vaccination |

# INTERPRETATION OF HBV SEROLOGIES (SLIDE 2 OF 2)

| | | |
|---|---|---|
| • HBsAg<br>• Anti-HBc<br>• IgM anti-HBc<br>• Anti-HBs | • positive<br>• positive<br>• positive<br>• negative | • Acutely infected |
| • HBsAg<br>• Anti-HBc<br>• IgM anti-HBc<br>• Anti-HBs | • positive<br>• positive<br>• negative<br>• negative | • Chronically infected |
| • HBsAg<br>• Anti-HBc<br>• Anti-HBs | • negative<br>• positive<br>• negative | • Interpretation unclear; 4 possibilities:<br>• Resolved infection (most common)<br>• False-positive anti-HBc, thus susceptible<br>• “Low level” chronic infection<br>• Resolving acute infection |

# Isolated HBV Core Ab Positive

1) Remote **resolved HBV infection** with waning of anti-HB surface Ab to level <10 IU, can give one vaccinate and check (this would determine if resolved infection or false positive)or just complete entire series

2) **False positive** never actually never exposed to HBV, need full series of vaccination

3) Chronic infection, i.e. **occult HBV** with HB surface Ag that has escaped detection either due to low production or mutations in envelope protein;  advised to check DNA if negative, vaccinate, very common in HIV

4) "**Window phase**" of acute HBV infection between loss of HB surface antigen and emergence of anti-HB surface Ab; test for IgM Core Ab, check DNA or wait and screen for HBV surface Ab in a few mos

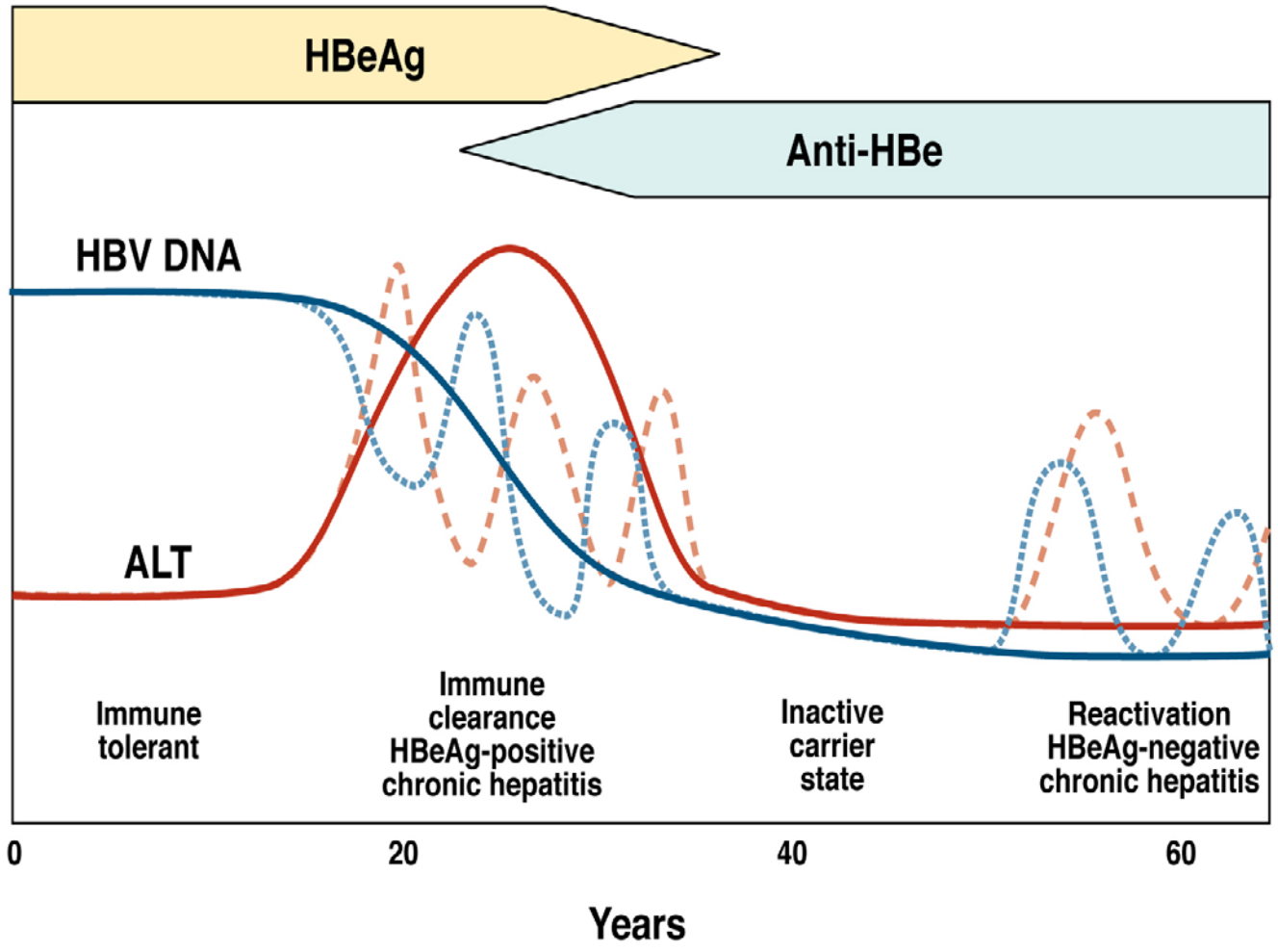
# Isolated HBV Core Ab Positive

**Isolated Core Ab** (most confusing results found in screening)

Factors associated with isolated core Ab:

- HIV infection (found in 20-45% in HIV-infected cases)
  - CD4 count <100 cells/mm3
- Chronic hepatitis C infection
- Older age

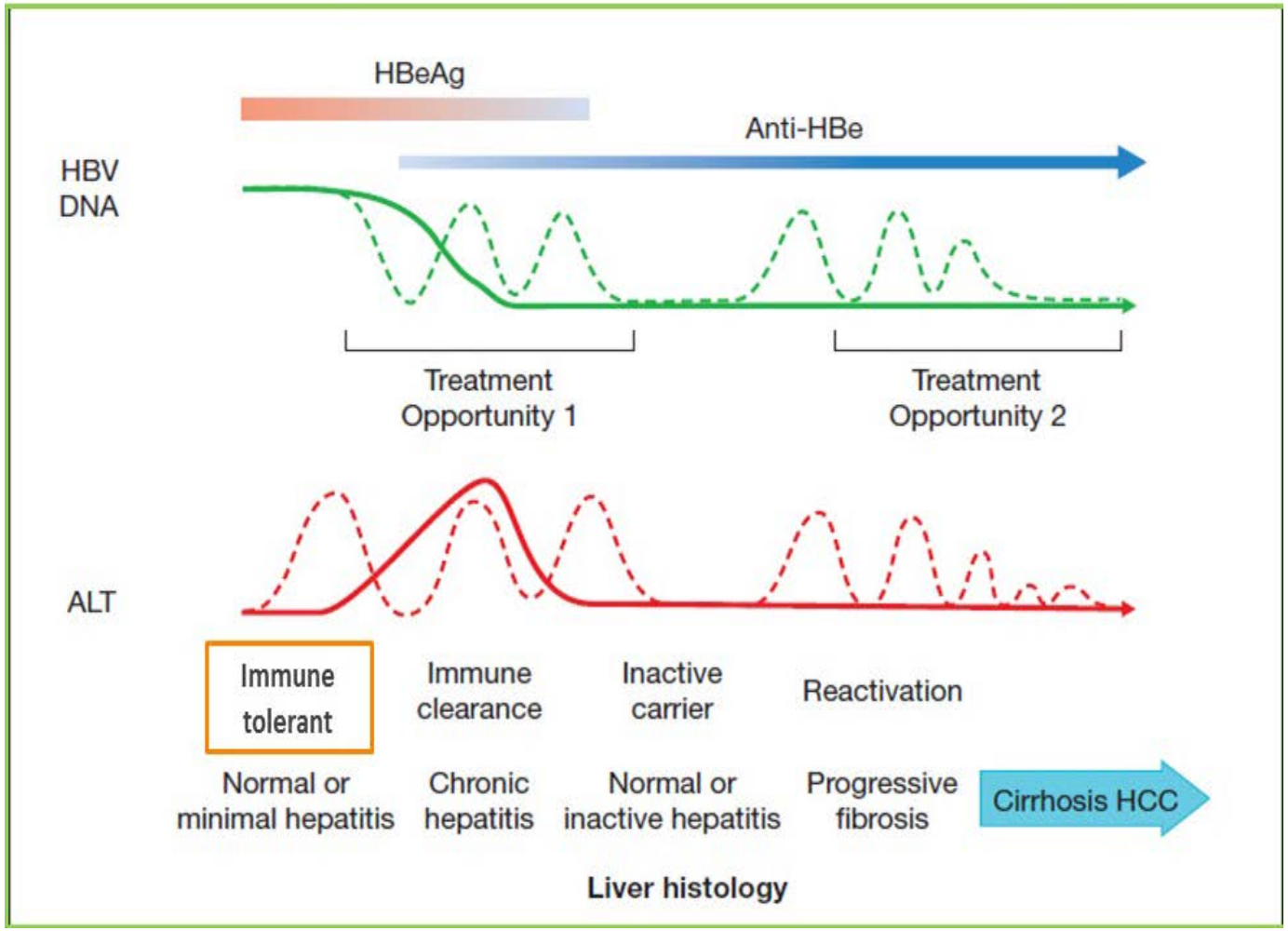
# CLINICAL PHASES OF HBV



# NOMENCLATURE UPDATE

Original terminology

Updated terminology






Source: Chan et al. Zakim & Boyer's Hepatology 2012.

# HBV Vaccination

# HBV Vaccine Facts

- HBV can potentially be eradicated worldwide with vaccination
- Infant coverage has went from 3% in 1992 to 84% in 2016  worldwide
- Adults in US have approx 25% rate of completing three dose series
- Despite this HBV in US still decreased 90% from 1990 to 2015
- ***New HBV continue to be seen, especially in young PWID***
- *Non Responders: 5-10% of patients will not have immunity after completing series*



HTTPS://WWW.UPTODATE.COM/CONTENTS/HEPATITIS-B-VIRUS-IMMUNIZATION-IN-ADULTS?SEARCH=HEPATITIS%20B%20VACCINE&SOURCE=SEARCH_RESULT&SELECTEDTITLE=2~146&USAGE_TYPE=DEFAULT&DISPLAY_RANK=1

# Vaccine Options

Recombinant hepatitis B vaccines (conventional)

- Recombivax HB (10 mcg HBsAg/mL)
- Engerix-B (20 mcg HBsAg/mL)
- Twinrix (HAV and HBV)

All given 0,1,6 mos

Recombinant hepatitis B vaccine (CpG-adjuvanted)

- Heplisav-B (20 mcg HBsAg/0.5 mL)

Given 0,1 mos

- Shown to be more effective in those nonresponsive to conventional HBV vaccine. Consider in nonresponder and those with predicted less follow up. Less safety data. Not for use in pregnancy.

# HBV Schedule

Recommended doses of formulations of recombinant hepatitis B vaccines licensed in the United States for persons age 18 and older, by age group and vaccine type*

| | Age group and associated conditions | Volume (mL) | Dose HBsAg (mcg) | Recommended schedule¶ |
|---|---|---|---|---|
| Single-antigen vaccines | | | | |
| **Recombivax HB** | | | | |
| Pediatric/adolescent formulation | 18 through 19 years | 0.5 | 5 | 0, 1, and 6 months$^{\Delta}$ |
| Adult formulation | ≥20 years | 1 | 10 | |
| Dialysis formulation | ≥20 years and receiving dialysis$^{\Diamond}$ | 1 | 40 | 0, 1, and 6 months |
| **Engerix-B** | 18 through 19 years | 0.5 | 10 | 0, 1, and 6 months$^{\Delta}$ |
| | ≥20 years | 1 | 20 | |
| | ≥20 years and receiving hemodialysis$^{\Diamond}$ | 2$^{\S}$ | 40 | 0, 1, 2, and 6 months |
| **Heplisav-B**$^{¥}$ | ≥18 years | 0.5 | 20 | 0 and 1 months |
| Combination vaccine | | | | |
| **Twinrix** (combined HepB-HepA vaccine) | ≥18 years | 1 | 20 | Standard: 0, 1, and 6 months<br>Accelerated: 0, 7, and 21 to 30 days, and 12 months |

# Alternative Dosing

- An interruption in the vaccination schedule does not require restarting the entire series of vaccination or adding extra doses. If the vaccination series is interrupted after the first dose the second dose should be administered as soon as possible, the second and third doses should be separated by an interval of at least two months.
- An accelerated Twinrix dosing schedule (with doses given at 0, 7, and 21 to 30 days, and a booster at 12 months) is approved.
- An accelerated 0, 1, 2 and 12 mos is approved for Recombivax and Energix (used frequently in travelers)
- ***Accelerated doing schedules should be considered in PWID population***

# Response

- Longer than recommended intervals between doses do not reduce final antibody concentrations
- In some patients, protective hepatitis B surface antibody (anti-HBs) titers may be attained after only one or two doses of vaccine; however, completion of the full course (three doses) of vaccine is recommended to maximize the anti-HBs titer and the duration that anti-HBs can be detected.
- In general, the duration in which anti-HBs titer remains **above protective level >10 miu/mL** is proportional to the peak titer achieved after completion of vaccination.
- *5-10% of patients will not have immunity (>10miu/ml) after completing series*
- Consider revax series one more time with 40mcg dose
- The rate of protection decreases with increasing age from more than 90 percent in children and young adults, to 86 percent in the fourth decade, **and 47 percent in the sixth decade**

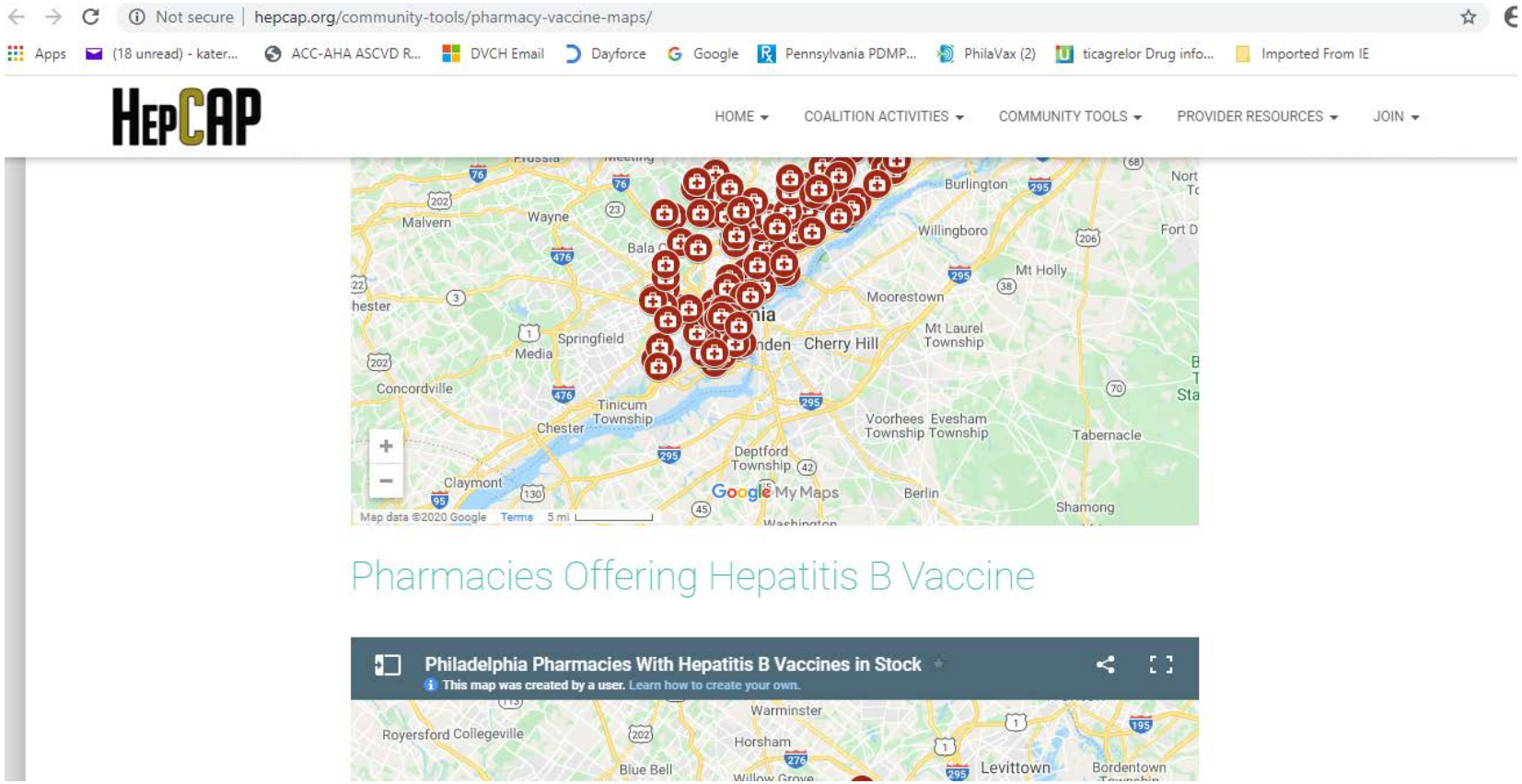
# Hepatitis B Vaccine in populations with low follow up rates

- HBV vaccine administered intramuscularly produces a protective antibody response in approximately 30%-55% of healthy adults aged <40 years after the first dose
- 75% after the second dose, and >90% after the third dose.
- Even if compliance with vaccination series not perfect, one dose better than none, 2 better than 1 ……
- Concerns about series completion is not a reason not to initiate first dose
- INITIATE VACCINE AT EARLIEST CONTACT

# Alternatives to in office Vaccination

- Pharmacies: http://www.hepcap.org/community-tools/pharmacy-vaccine-maps/
- Mobile or episodic healthcare services
- Link HBV vaccinations to community HIV and HCV testing
- Utilization of syringe service programs
- Financial incentives
- Improved communication among providers with pt held vaccine records and/or Philavax(central database)
- Other ideas?

# Philadelphia Pharmacy Map for HAV &HBV vaccines

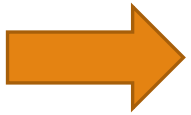


# Hepatitis B Immunization for isolated anti-HBc:

- Hepatitis B Immunization for isolated anti-HBc:
  - Can do either boost & check or complete series
  - Can consider anti-HBs assessment to differentiate boost/check or simply complete series
- Vaccinate early in HIV (before patient's CD4 gets <350)
- Always check anti-HBs 1-2 months after vaccination completed for HIV positive pts
- Keep in mind: Magnitude & duration of HBV vaccine response is often lower in HIV-infected patients due to a variety of factors (lowCD4, detectable HIV RNA, occult HBV, other health concerns)

# PrEP guidelines and HBV

# PrEP screener



| Who Should Consider HIV Pre-Exposure Prophylaxis (PrEP)? | |
|---|---|
| MSM | • Bacterial STI (syphilis, chlamydia, gonorrhea) in past 6 months<br>• HIV-positive sexual partner<br>• Condomless anal intercourse (receptive or insertive) in past 6 months with a partner of unknown HIV status<br>• Commercial Sex Work |
| Heterosexual Women and Men | • HIV-positive sexual partner<br>• Frequent condomless sexual intercourse with individuals at high risk of HIV infection (people who inject drugs, commercial sex workers, MSM or bisexual male partners)<br>• Commercial sex work |
| People who Inject Drugs | • HIV-positive injecting partner<br>• Sharing of injection equipment in the past 6 months |
| Persons using HIV PEP for Sexual exposures | |
| Persons of transgender experience or those with transgender partners with any of the above risk factors | |

# HBV in PrEP Guidelines

- Vaccination against HBV is recommended for all adolescents and adults at substantial risk for HIV infection, especially for MSM.
- Therefore, HBV infection status should be documented by screening serology before TDF/FTC is prescribed as PrEP
- Those patients determined to be susceptible to HBV infection should be vaccinated. Those patients found to be HBsAg positive should be evaluated for possible treatment either by the clinician providing PrEP care or by linkage to an experienced HBV care provider.
- PrEP should not be withheld if HBV screening unavailable
- 2:1:1 dosing or “Event Driven” PREP should NOT be considered in patients with chronic or suspected HBV



HTTPS://WWW.CDC.GOV/HIV/PDF/RISK/PREP/CDC-HIV-PREP-GUIDELINES-2017.PDF

# HBV screening in PrEP: reactivation risk

Emtricitabine and tenofovir (both TDF and TAF) can be used to treat HBV, and discontinuation of these medicines can cause rebound hepatitis. HBV infection is not a contraindication to PrEP, but all persons considered for PrEP with F/TDF or F/TAF must be screened for HBV; if they start PrEP, when they stop the medication their liver function can be closely monitored for reactivation of HBV replication that could result in hepatic damage.



HTTPS://WWW.CDC.GOV/HIV/PDF/RISK/PREP/CDC-HIV-PREP-GUIDELINES-2017.PDF

# HBV Reactivation

- All candidates for immunosuppressive, cytotoxic, or immunomodulatory, HCV therapy should be tested for HBsAg and anti-HBc testing before immunosuppression
- All HBsAg+, patients should initiate anti-HBV prophylaxis before immunosuppressive or cytotoxic therapy, Recommend prophylaxis with entecavir, TDF, or TAF
- HBsAg–, anti-HBc+ patients could be carefully monitored with ALT, HBV DNA, and HBsAg with the intent for on-demand therapy after having DNA screen

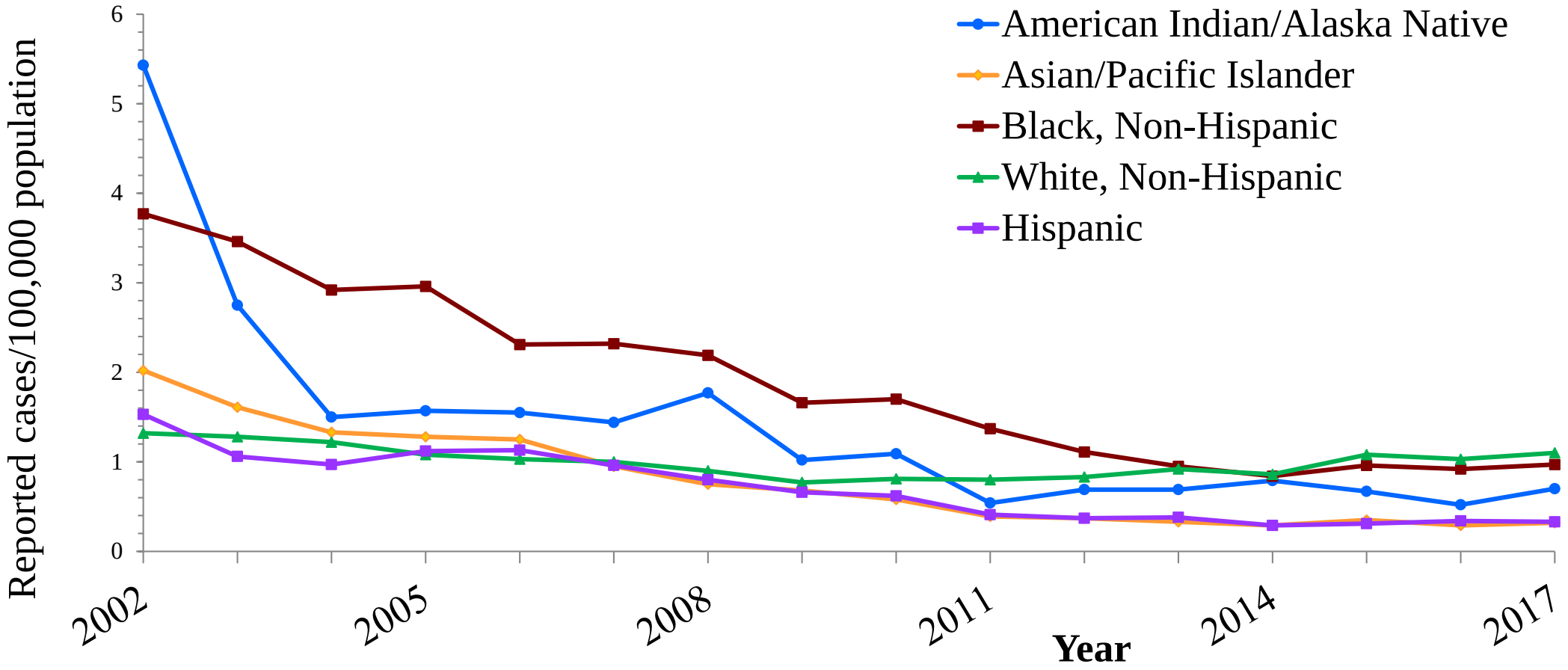
# HBV in PWID

- PWID are at high risk of transmission of blood borne viruses, including hepatitis B virus (HBV)
- The opioid epidemic and increasing rates of injection drug use are propelling infections in certain populations
- PWID are often ‘hard-to-reach’ and difficult to follow to series completion; novel methods to engage this population are critical to success
  - Vaccinating without checking titers
  - Accelerated vaccination schedules
  - Heplisav vaccination

# HCV vs HBV

- Screening more complicated
- HBV preventable with vaccination/HCV is not
- HCV curable, HBV not curable
- Finite treatment with HCV, indefinite with HBV
- Risk factors different, but do overlap
- HCC screening guidelines different

# Figure 3.5. Rates of reported acute hepatitis B, by race/ethnicity — United States, 2002–2017



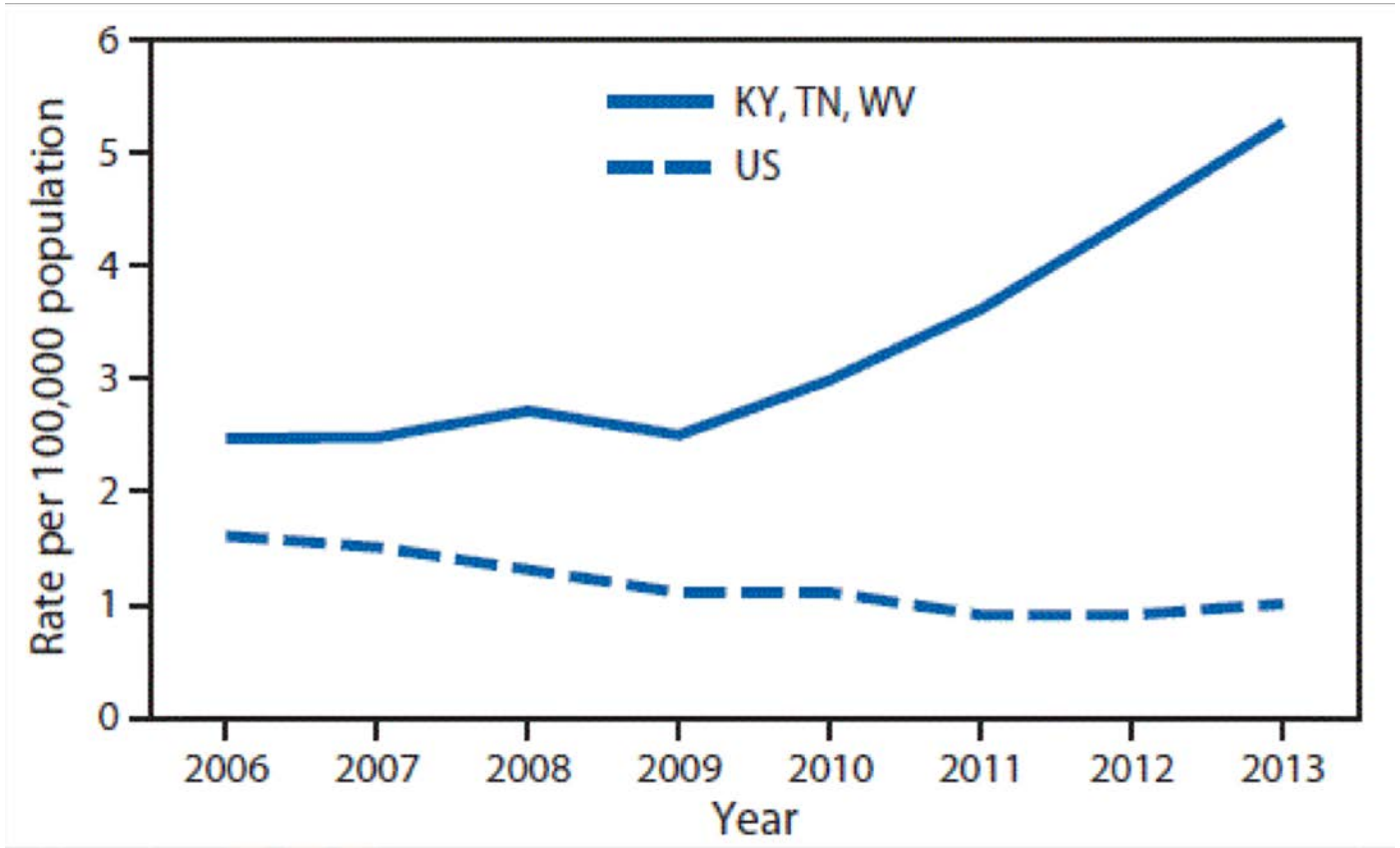

Source: CDC, National Notifiable Diseases Surveillance System.

# Injection drug use and acute HBV - 2016

- 48% of reported cases provide any risk data
- 22% with any information on risk have risk factors identified
- *Of those, 53% report a history of injection drug use*
- In 2015, 43% of identified risk factors were associated with injection drug use

Source: National Notifiable Diseases Surveillance System

# Increases in HBV infection among PWID: Kentucky, West Virginia, Tennessee




Harris, et al, *MMWR*, 2016

# Injection drug use and HBV

- Highly efficient. Can be spread through drug paraphernalia, not just needles and syringes
- Long survival period on inanimate objects
- One drop of blood with HBV, HCV and HIV
  - 30% chance of getting HBV
  - 1.8% chance of getting HCV
  - .03% chance of getting HIV

Hagan H, et al, 2010; CDC 2016

# Conclusions

- HBV related to IDU is increasing
- Despite being a highly mobile, hard-to-reach population that often is reluctant to access medical care, ***PWID can successfully complete a 3-dose series for HBV vaccination***
- Prioritizing screening and vaccination among PWID is essential in Philadelphia
- You are not in this alone, local health departments are prioritizing HBV among community-based organizations, work with other PWID focused groups.
- Establish linkage to care channels

# Questions?

Please type your questions into the Q&A box.

Christine Simon
csimon@phmc.org

World Health Organization

# WHO Commemoration of World Hepatitis Day 2020

## High-level Global Talk Show: Towards a “Hepatitis-free future”
## 28 July 2020 @ 7:00-9:15 pm EST

On July 28, WHO will celebrate World Hepatitis Day 2020 under the theme “Hepatitis-free future” and launch the new recommendations for the prevention of mother-to-child transmission of the hepatitis B virus (HBV).
Join high-level speakers and experts from WHO, member states, key partners and civil society to hear about the progress towards elimination of viral hepatitis as a public health threat.

**To join the webinar, please register in advance with the zoom platform here:**
**https://who.zoom.us/webinar/register/WN_7koOuWhQRXGFtqXZZZMUwA**

# NEW RESOURCE

## Hepatitis C Virus (HCV) Cost Calculator

Our HCV Cost Calculator uses a numerical value-based model of health center staff training, screening, and treatment regimen to estimate the cost-benefit comparison and return on investment (ROI) to the health center.

No cost to use on NURSELEDCARE.ORG

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