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Test Your Knowledge: An Interactive Session on Emerging Data and Expert Insights on Hepatitis B

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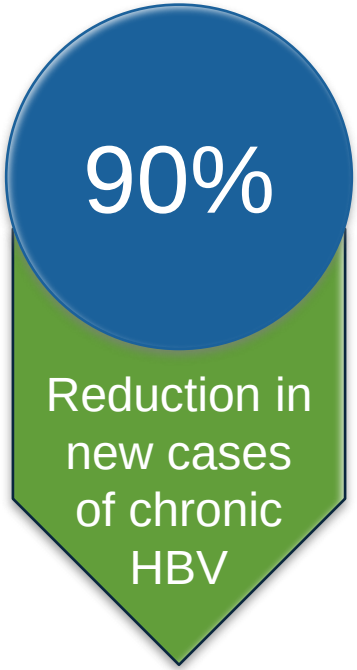
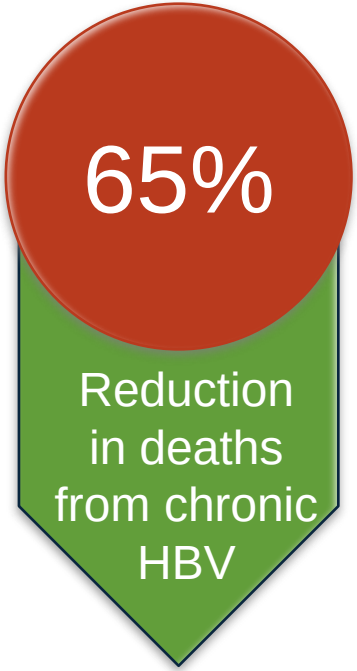
Learning Objective 1

Implement routine screening protocols for hepatitis B (HBV) in the primary care setting to derive guideline-directed care.

Global Viral Hepatitis Strategy Impact Targets for Elimination



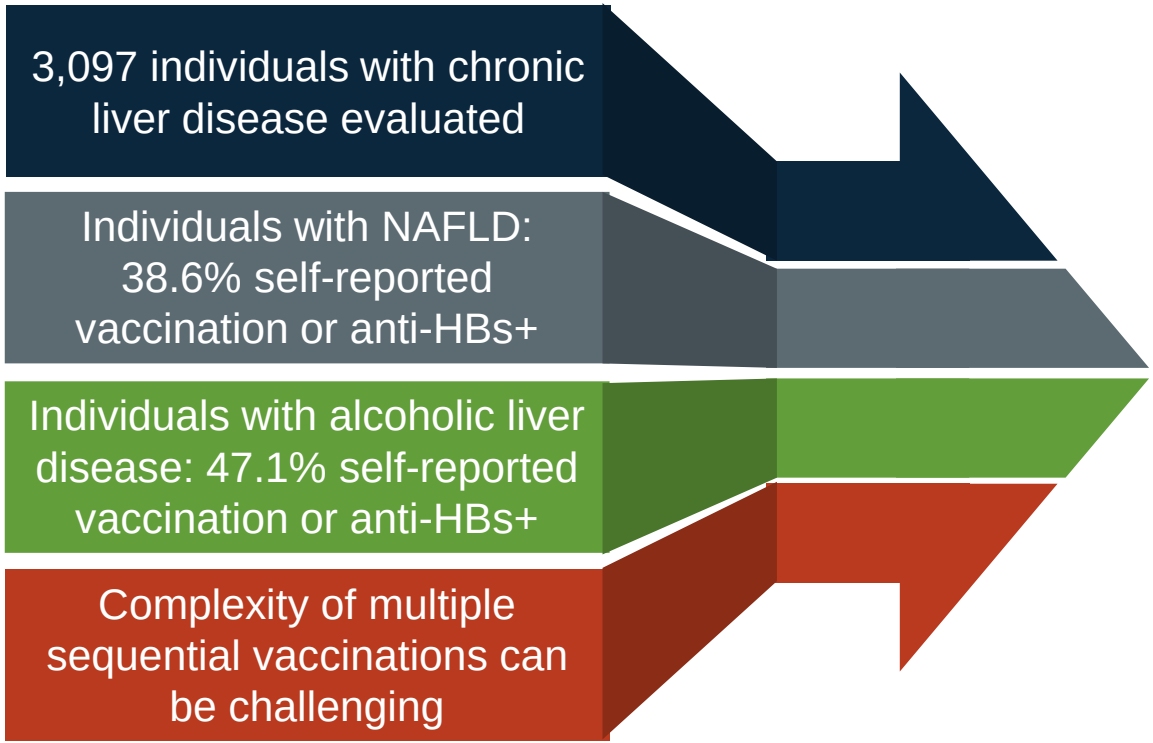
Reduce from 6-10M infections (2015) to 900,000 by 2030



Reduce from 1.4M deaths (2015) to under 500,000 by 2030

World Health Organization [WHO] Website. https://www.who.int/health-topics/hepatitis#tab=tab_1. Accessed March 29, 2021.

HBV Is a Vaccine Preventable Disease, but Vaccination Rates Are Alarmingly Low Among U.S. Adults with Chronic Liver Disease



NAFLD

Rates of vaccination and anti-HBs+ lowest among Hispanic (32.1%) and Non-Hispanic Whites (33.6%), highest among Asians (60.6%)

Alcoholic Liver Disease

Rates of vaccination and anti-HBs+ lowest among Hispanic (39.9%) and highest among Asians (74.6%)

Conclusions

Future efforts are needed to focus on targeted provider education or implementation of best practice alerts in electronic medical records to improve successful vaccination or documented immunity

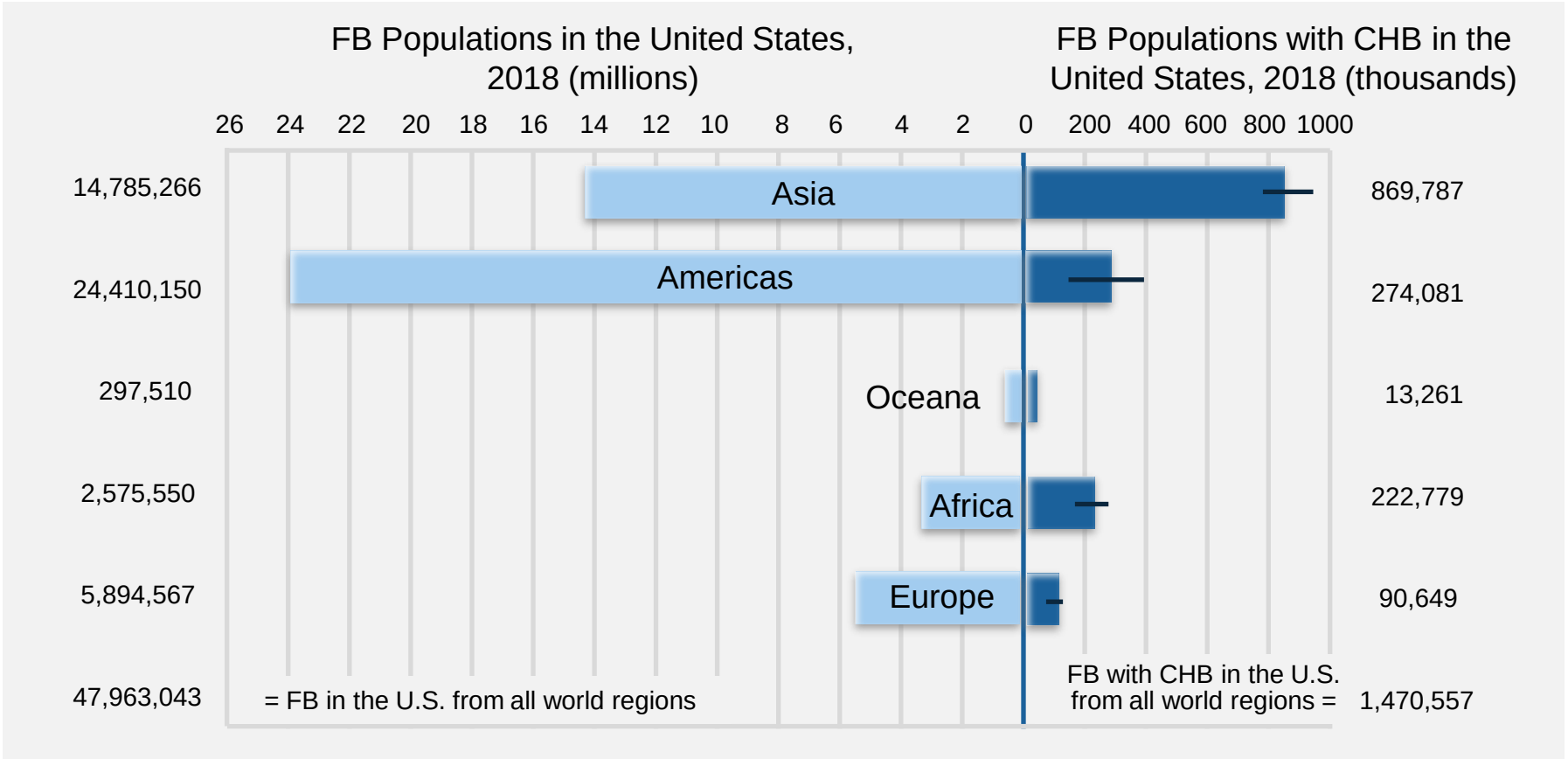
Wong RJ, et al. *Am J Med*. 2021 March 26. [Epub ahead of print]. PMID:33775642.

Who Should Be Vaccinated? Adults Who Are Recommended to Receive the Hepatitis B Vaccine

• At risk through sexual exposure	Sex partners of HBsAg+ persons
	Sexually active persons not in long-term, mutually monogamous relationship
	Persons seeking evaluation or treatment for sexually transmitted infection
	Men who have sex with men
• History of current or recent injection drug use	
• At risk for infection by percutaneous or mucosal exposure to blood	Household contacts
	Residents and staff of facilities for developmentally disabled persons
	Health care public safety personnel at risk for exposure to blood or blood contaminated body fluids
	Hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
	Person with diabetes mellitus who are age < 60 and ≥ 60 at the discretion of the treating clinician
• International traveler to countries with high or intermediate levels of endemic HBV	
• Persons with hepatitis C infection, chronic liver disease (including, but not limited to cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, ALT or AST level greater than 2x upper limit of normal	
• Persons with human immunodeficiency virus (HIV)	
• Incarcerated persons	
• Other persons seeing protection from HBV infection (even without acknowledgement of a specific risk)	

Schillie S, et al. *MMWR Morb Mortal Wkly Rep*. 2018;455-458.

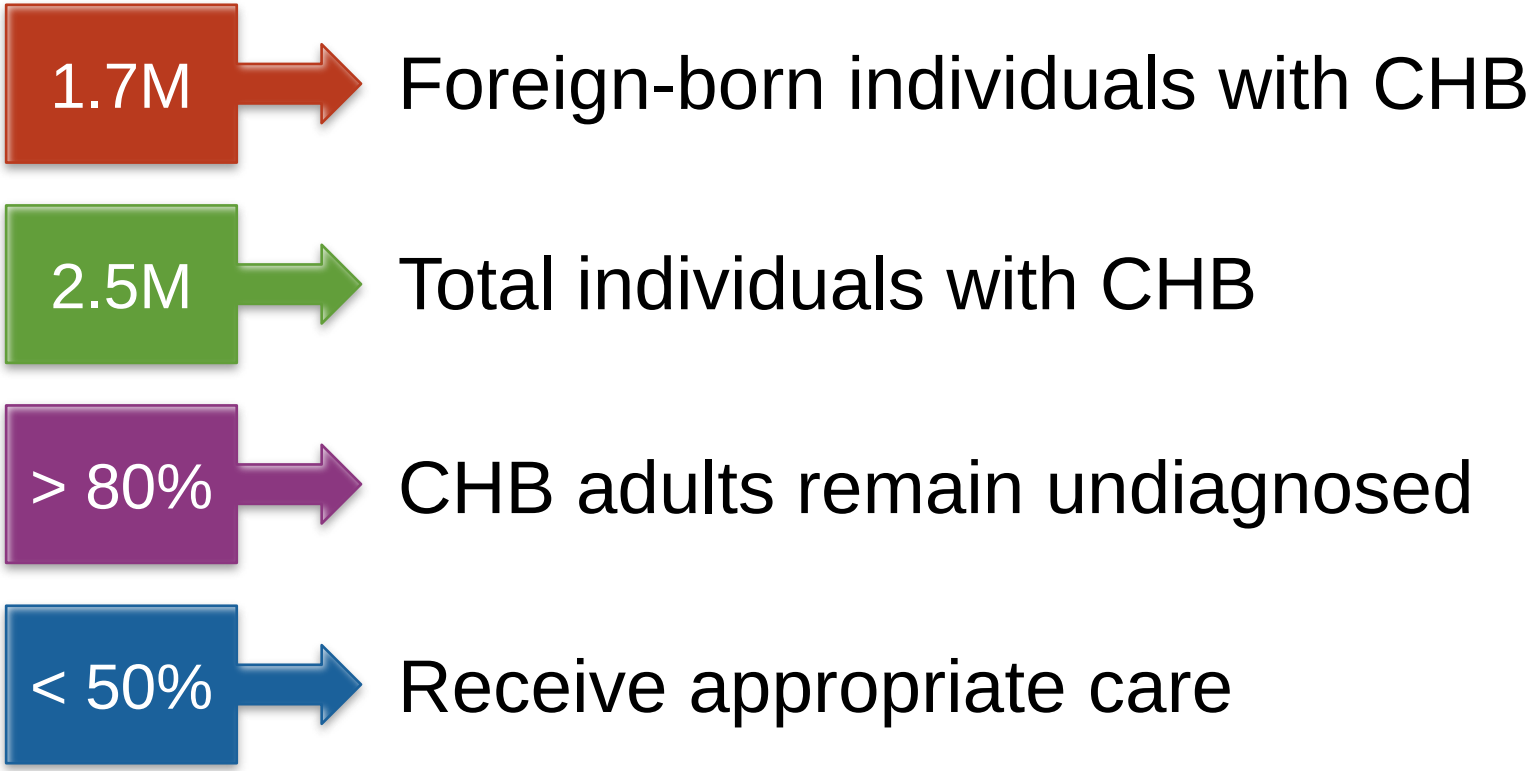
Prevalence of Chronic HBV Infection Among Foreign-Born Populations in the United States



CHB = chronic hepatitis B; FB = foreign-born

Wong RJ, Brosgart CL, Welch S, Block T, Chen M, Cohen C, Kim WR, Kowdley KV, et al. *Hepatology.* 2021 Mar 3. [Epub ahead of print]. PMID: 33655536.

The Case for Universal HBV Screening to Close Gaps in Diagnosis and Early Linkage to Care



Wong RJ, Brosgart CL, Welch S, Block T, Chen M, Cohen C, Kim WR, Kowdley KV, et al. *Hepatology.* 2021 Mar 3. [Epub ahead of print]. PMID: 33655536.
Kim HS, et al. *J Viral Hepat.* 2017;24:1052-1066. Ogawa E, et al. *JAMA Netw Open*. 2020;3(4):e201844.

HBV Prevalence in High-Risk Groups

High-Risk Group	HBV Prevalence Estimate*
Veterans	0.3%-0.84%
Health care professionals	0.1%-8.1%
Men who have sex with men	Not available
Prisoners	0.9%-11.4%
Homeless individuals	0.4%-1.17%
People who inject drugs	11.8%
Patients with HCV coinfection	3.0%-8.4%
Patients with HIV coinfection	3.0%-8.4%

Other special populations

- Pregnant women
- Patients with diabetes or other metabolic disorders
- Newborns

*Prevalence data derived from hepatitis B surface antigen (HBsAg) positivity
HCV = hepatitis C virus
Lim JK, et al. *Am J Gastroenterol*. 2020;115:1429-1438.

HBV and Injection Drug Use

- Like HCV and HIV, injection drug use contributes significantly to acute HBV infection
- Areas of high prevalence of HBV in the United States align closely to those of the opioid epidemic

- Harm reduction, screening, and linkage to care are important for the care of the individual and spread of HBV to others

Centers for Disease Control and Prevention [CDC] Website. Last reviewed 2020. https://www.cdc.gov/hepatitis/hbv/index.htm. Accessed March 17, 2021.

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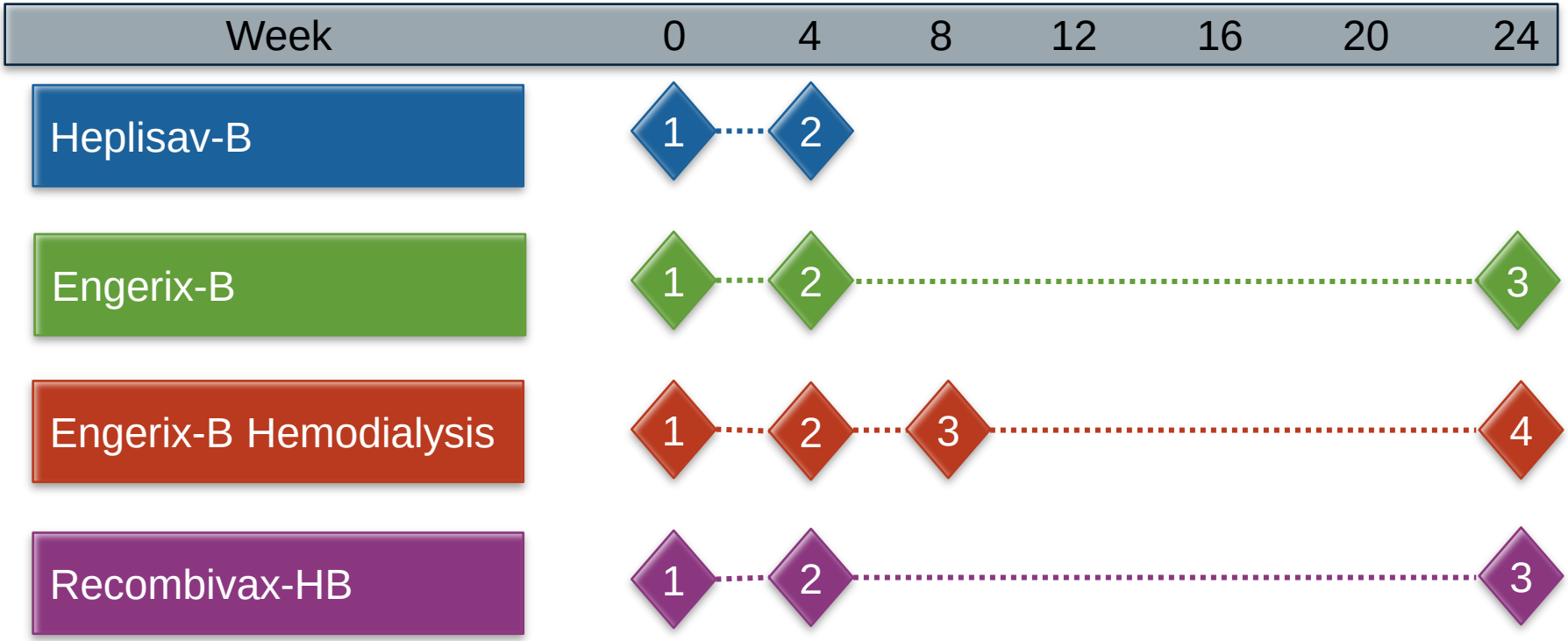
Faculty Discussion

Audience Questions Received
April 7, 2021

Recommended Hepatitis B Vaccines and Schedule in Adults



*Before a potential exposure such as international travel, Twinrix can be administered as an accelerated series at day 1, 7, 21-30 followed by 4th dose at 12 months

Tang AS, et al. Hepatitis B Online Website. 2020. https://www.hepatitisb.uw.edu/go/prevention-hbv/hbv-immunizations/core-concept/all#hbv-vaccines-schedules. Accessed April 17, 2021.

Five Steps to Stop HBV Stigma

- **KNOW THE FACTS**
  - Seek accurate information about how HBV is transmitted, who is at risk, and how to improve care and support for people affected by HBV
- **BE MINDFUL OF YOUR ATTITUDE AND BEHAVIOR**
  - Prejudices and judgmental thinking are learned and often commonplace
  - We can change our thinking and recognize people not as labels but as unique individuals
- **CHOOSE YOUR WORDS WISELY**
  - Use accurate and sensitive words when talking about people at risk for HBV
- **EDUCATE OTHERS**
  - Take opportunities to share facts and positive attitudes about people affected by HBV
  - If people present information that is not true, let them know that their negative words and misinformation affect people at risk for or living with HBV
- **TAKE ACTION**
  - Increase awareness about HBV-related stigma
  - If you witness a person with HBV experiencing discrimination, speak up!

Association of Asian Pacific Community Health Organizations [AAPCHO] Website. 2017. https://aapcho.org/wp/wp-content/uploads/2017/07/AAPCHO-HBV-Stigma-Toolkit-Sneak-Peek.pdf. Accessed March 29, 2021.

Resources to Assist Patients Who Face HBV Stigma and Discrimination

- Hepatitis B Foundation
  - https://www.hepb.org/resources-and-support/know-your-rights/
- Association of Asian Pacific Community Health Organizations (AAPCHO)
  - https://aapcho.org/resources/
- American Liver Foundation
  - https://liverfoundation.org/
- CME Outfitters HBV Patient Education Hub
  - https://www.cmeoutfitters.com/hbv-patient-education-hub/

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USPSTF Recommendations for HBV Screening in Adolescents and Adults

- USPSTF recommends screening for HBV infection in adolescents and adults at increased risk of infection
  - Persons born in countries/regions with high prevalence of infection (≥ 2%), such as Asia, Africa, Pacific Islands, and parts of South America
  - U.S.-born persons not vaccinated as infants, whose parents were born in regions with very high prevalence (≥ 8%)
  - HIV-positive persons
  - Persons who inject drugs
  - Men who have sex with men
  - Household contacts or sexual partners of persons with HBV infection

U.S. Preventive Services Task Force [USPSTF] Website. 2020. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-b-virus-infection-screening. Accessed March 29, 2021.

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Hepatitis B Screening Recommendations

Risk Group	CDC	AASLD	USPSTF	ACP
Persons born in countries with ≥ 2% HBV prevalence	HBsAg*	HBsAg anti-HBs	HBsAg anti-HBs anti-HBc	HBsAg anti-HBs anti-HBc
Persons born in United States not vaccinated as an infant and whose parents were born in regions with high HBV endemicity (HBsAg prevalence ≥ 8%)	HBsAg*	HBsAg anti-HBs	HBsAg anti-HBs anti-HBc	No organizational recommendation
Men who have sex with men	HBsAg anti-HBs OR anti-HBc	HBsAg anti-HBs	HBsAg anti-HBs anti-HBc	HBsAg anti-HBs anti-HBc
Persons who inject drugs	HBsAg anti-HBs OR anti-HBc	HBsAg anti-HBs	HBsAg anti-HBs anti-HBc	HBsAg anti-HBs anti-HBc
Persons with HIV infection	HBsAg anti-HBs OR anti-HBc	HBsAg anti-HBs anti-HBc	HBsAg anti-HBs anti-HBc	HBsAg anti-HBs anti-HBc
Household, needle-sharing, or sexual contact with persons with HBV infection	HBsAg anti-HBs OR anti-HBc	HBsAg anti-HBs	HBsAg anti-HBs anti-HBc	HBsAg anti-HBs anti-HBc

*Consider anti-HBc or anti-HBs in persons with ongoing risk

AASLD = American Association for the Study of Liver Diseases; ACP = American College of Physicians; HBc = hepatitis B core antigen

Abara WE, et al. *Ann Intern Med*. 2017;167:794-804. Schillie S, et al. *MMWR Recomm Rep.* 2018;67:1-31. Terrault NA, et al. *Hepatology.* 2018;67:1560-1599. Weinbaum CM, et al. *MMWR Recomm Rep.* 2018;57:1-20.

Interpretation of HBV Serologic Test Results

Serologic Test Result	HBsAg	Total Anti-HBc	IgM Anti-HBc	Anti-HBs
Detected following vaccination or for 3-6 months following receipt of HBIG	−	−	−	+
• False positive (susceptible) • Past infection (resolved) • "Low level" chronic infection (unlikely to be infectious)	−	+	−	−
Chronic infection	+	+	−	−
Past infection, with recovery, immunity to new infection	−	+	−	+
Acute infection	−	+	+	−
Early acute infection or receipt of the vaccine within several weeks	+	−	−	−
Never infected, susceptible	−	−	−	−

- **Hepatitis B surface antigen (HBsAg):** Detected in high levels in serum during acute or chronic HBV infection. Its presence indicates the person is infectious.
- **Total hepatitis B core antibody (anti-HBc):** Appears at the onset of symptoms in acute HBV and persists for life. Indicates previous or ongoing infection.
- **IgM antibody to hepatitis B core antigen (IgM anti-HBc):** Positivity indicates recent infection with HBV (≤ 6 months). Its presence indicates acute infection.
- **Hepatitis B surface antibody (anti-HBs):** The presence of anti-HBs is generally interpreted as indicating recovery or immunity from HBV infection. Also present in a person who has been vaccinated.

HBIG = hepatitis B immune globulin

Centers for Disease Control and Prevention [CDC] Website. Last reviewed 2015. https://www.cdc.gov/hepatitis/resources/professionals/training/serology/training.htm. Accessed March 29, 2021.

Evaluation of HBsAg+ Patients

History/Examination

- ☐ Symptoms/signs of cirrhosis
- ☐ Alcohol and metabolic risk factors
- ☐ Family history of HBV or hepatocellular carcinoma (HCC)
- ☐ Hepatitis A vaccination status

Routine Laboratory Tests

- ☐ CBC comprehensive
- ☐ Comprehensive metabolic panel including:
  - AST/ALT
  - Total bilirubin
  - Alkaline phosphatase
  - Albumin
  - Creatinine
- ☐ INR

Serology/Virology

- ☐ HBeAg/anti-HBe
- ☐ HBV DNA
- ☐ Anti-HAV (total or IgG to determine need for vaccination if none documented
- ☐ Anti-HCV
- ☐ Anti-HDV
- ☐ Anti-HIV

Imaging/Staging Studies

- ☐ Abdominal ultrasound
- ☐ Elastography (e.g., FibroScan)
- ☐ Serum fibrosis assessment* (e.g., APRI, FibroSure, FIB-4)

*AST-to-platelet ratio index (APRI) and fibrosis-4 index (FIB-4) scores can be calculated using platelet count and AST and ALT from routine labs. Calculators with score interpretation are available. See *Hepatitis B Online* APRI calculator and FIB-4 calculator. FibroSure and FibroTest are commercially available blood tests that can be ordered as well

ALT = alanine transaminase; AST = aspartate transaminase; CBC = complete blood count; HAV = hepatitis A virus; HDV = hepatitis D virus; IgG = immunoglobulin G; INR = international normalized ratio

Tang AS, et al. Hepatitis B Online Website. 2020. https://www.hepatitisB.uw.edu/hbv-pcw/guidance. Accessed March 29, 2021.

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Fibrosis Staging: Early and Accurate Diagnosis of Hepatic Fibrosis and Cirrhosis

Augmented Reality Segment

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Visit the

Liver Disease Hub

After the live webcast, this activity will be available on the Liver Disease Hub where you'll find free resources and education for health care providers on hepatitis B

https://www.cmeoutfitters.com/liver-hub/

Fibrosis Staging: Early and Accurate Diagnosis of Hepatic Fibrosis and Cirrhosis

Noninvasive Methods for Assessing Cirrhosis and Fibrosis

Elastography

- Transient elastography (TE)
- Magnetic resonance elastography (MRE)
- 2D shear wave elastography (SD-SWE)

Serum Biomarkers

- FIB-4
- FibroTest
- FibroSure
- Aspartate aminotransferase-platelet ratio index (APRI)

- Liver biopsy remains the gold standard, but poor patient acceptance, variability, and complications limit wide application

European Association for Study of Liver [EASL], Asociacion Latinoamericana para el Estudio del Higado [ALEH]. *J Hepatol*. 2015;63(1):237-264.

Clinical Calculators

APRI Calculator[1]

$$\text{ARPI} = \frac{\dfrac{\text{AST Level (u/L)}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet count } (10^6/\text{L})} \times 100 =$$

- Score > 1.0 had predictive value of 72% for cirrhosis
- Score > .7 had predictive value of 72% for significant fibrosis
- APRI alone is likely not sufficiently sensitive to rule out significant disease

Fibrosis-4 (FIB-4) Calculator[2]

$$\text{FIB-4} = \frac{\text{Age (yrs)} \times \text{AST Level (u/L)}}{\text{Platelet count } (10^6/\text{L}) \times \sqrt{\text{ALT (U/L)}}} =$$

- FIB-4 score < 1.45 had negative predictive value of 90% for advanced fibrosis
- FIB-4 score > 3.25 had positive predictive value of 65% for advanced fibrosis
- Those with FIB-4 score > 1.45 often go on to liver elastography[3]

Online calculators available on the Hepatitis C Online Website at https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4 and https://www.hepatitisc.uw.edu/page/clinical-calculators/apri

1. Lin, et al. *Hepatology*. 2011;53:726-736. 2. Sterling RK, et al. *Hepatology.* 2006;43:1317-1325. 3. Sterling R. MDCalc Website. https://www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis. Accessed March 29, 2021.

Which Noninvasive Method to Choose?

Test	Advantages	Disadvantages
TE (Fibroscan)	• Most widely used, validated technique • User friendly • Quality criteria well-defined • High performance for cirrhosis • Prognostic value in cirrhosis	• Unable to discriminate between intermediate stages of fibrosis • Applicability (80%) lower than serum biomarker • False positive in acute hepatitis
2D SWE	• Can be implemented on regular US machine • Measure of liver stiffness in real time • High performance for cirrhosis	• Unable to discriminate between intermediate stages of fibrosis • Quality criteria not well-defined
MRE	• Can be implemented on a regular MRI machine • Examination of whole liver • High performance for cirrhosis	• Further validation warranted especially vs. TE • Requires an MRI facility • Time-consuming/costly
Serum biomarkers	• Well validated in patients with chronic hepatitis • FIB-4 and APRI are most widely used and validated tests	• More evidence in hepatitis C than in HBV • Performances are better for detecting cirrhosis than significant fibrosis

US = ultrasound

European Association for Study of Liver [EASL], Asociacion Latinoamericana para el Estudio del Higado [ALEH]. *J Hepatol*. 2015;63(1):237-264.

Patient Education and Counseling: Encouraging a Healthy Lifestyle

- Schedule regular visits with your liver specialist or health care provider
- Get the hepatitis A vaccine
- Avoid drinking alcohol and smoking
- Talk to your provider before starting any herbal remedies or vitamin supplements
- Check with your pharmacist about any over-the-counter drugs
- Avoid inhaling chemical fumes that could damage your liver
- Eat a healthy diet
- Avoid eating raw or undercooked shellfish
- Check for signs of mold on food
- Reduce your stress through healthy diet, rest, and exercise
- Everything you eat, drink, breathe, or absorb through the skin is eventually filtered by the liver!

PROTECT YOUR LIVER!

HEPATITIS B FOUNDATION

Hepatitis B Foundation Website. https://www.hepb.org/assets/Uploads/Living-with-Chronic-Hepatitis-B.pdf. Accessed March 29, 2021.

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Learning Objective 2

Optimize efficacy and safety profiles of current agents when initiating or switching treatment in patients with HBV.

Results from HBV screening are returned for your 46-year-old male patient:

HBsAg+

HBeAg-

ALT: 90 u/L

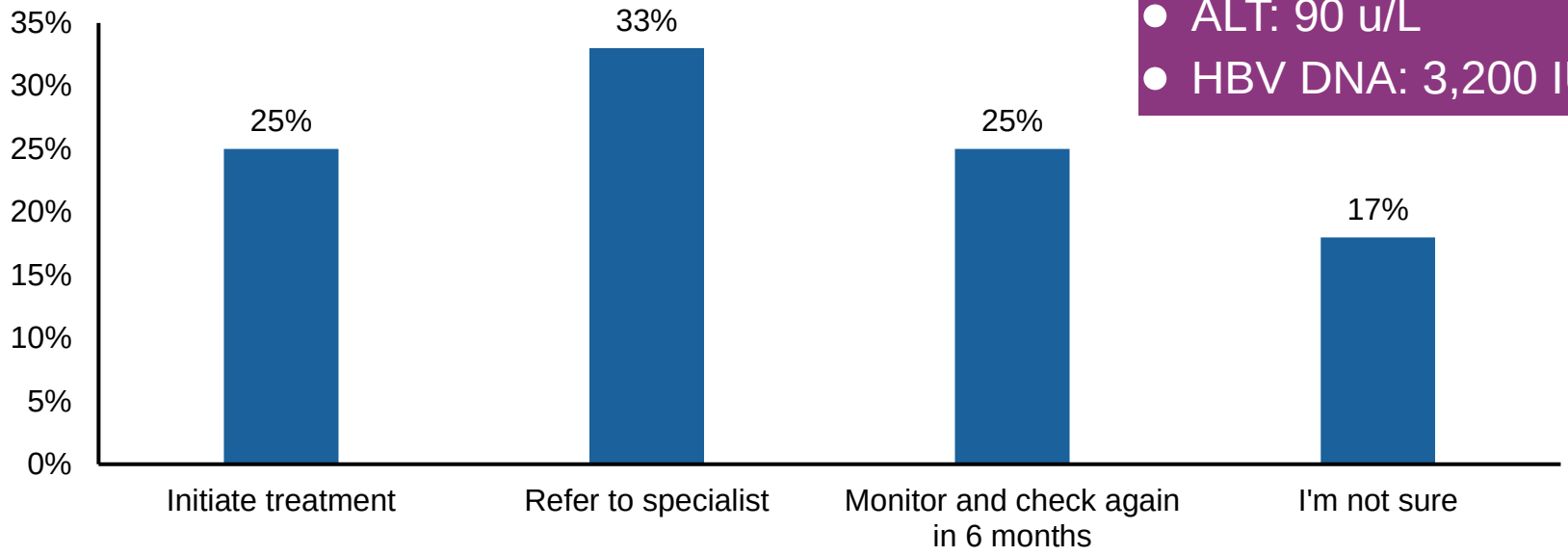
HBV DNA: 3,200 IU/mL

What is your next step?

A. Initiate treatment
B. Refer to specialist
C. Monitor and check again in 6 months
D. I’m not sure

Results from HBV screening are returned for your 46-year-old male patient: what is your next step?

- HBsAg+
- HBeAg-
- ALT: 90 u/L
- HBV DNA: 3,200 IU/mL



Results recorded on April 7, 2021

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A National Strategy for the Elimination of Hepatitis B and Hepatitis C

Recommendation 5-2

The American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) should partner with primary care providers (PCPs) and their professional organizations to build capacity to treatment of HBV and hepatitis C (HCV) in primary care. The program should set up referral systems for medically complex patients.

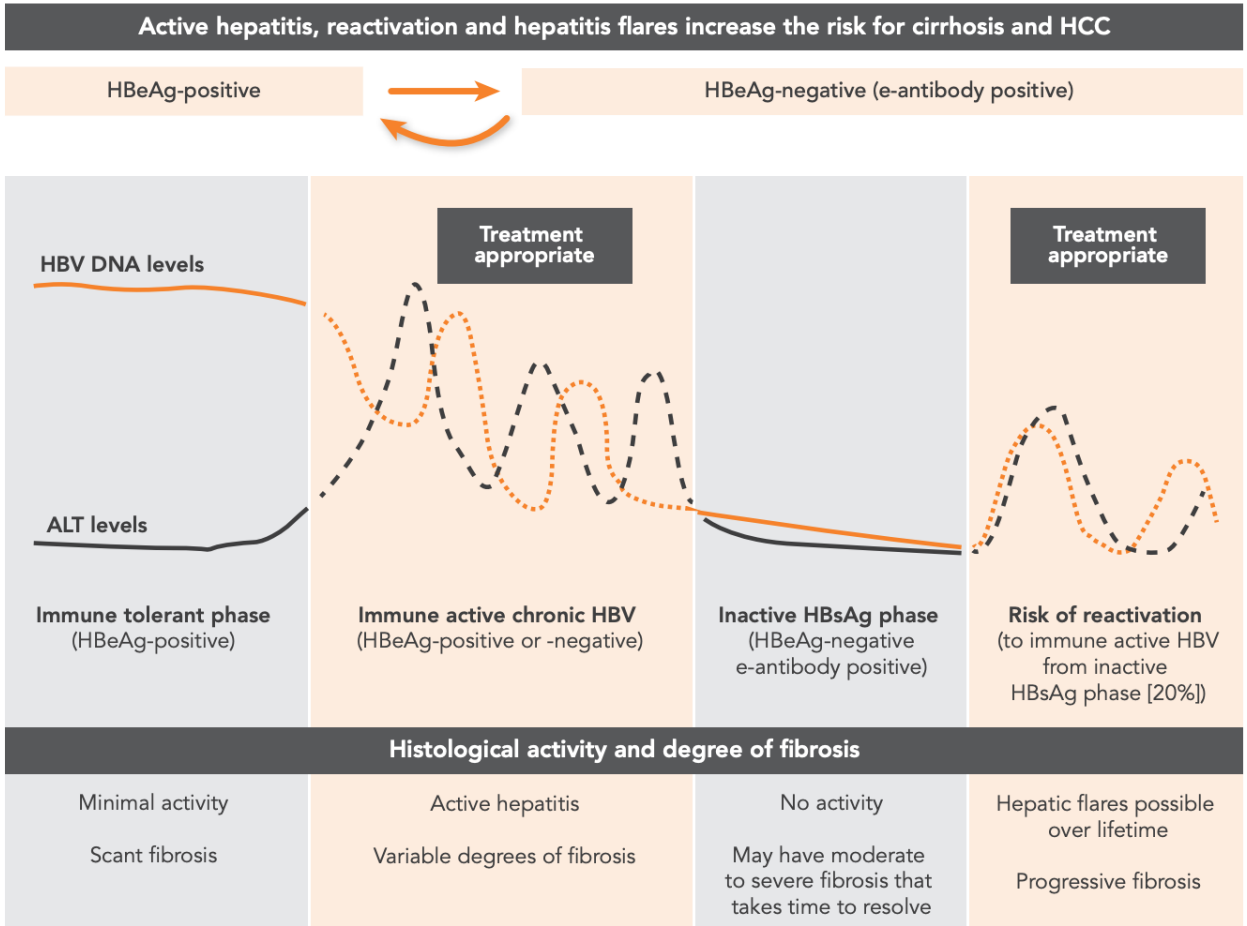
National Academies of Sciences, Engineering, and Medicine 2017. *A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report.* Washington, DC: The National Academies Press. https://doi.org/10.17226/24731. Accessed March 29, 2021.

Goals of HBV Treatment

- Achieve sustained suppression of HBV replication
  - Decrease the morbidity and mortality related to CHB
  - Reduce the risk of progression to cirrhosis- and liver-related complications, including HCC
  - Improve long-term survival

Terrault NA, et al. *Hepatology*. 2018;67(4):1560-1599.

Phases of Chronic HBV



Canadian Liver Foundation Website. 2013. https://www.liver.ca/wp-content/uploads/2017/09/HBV-QR-EN-_FINAL_Web.pdf. Accessed March 29, 2021.

Treatment and Management of Patients with HBV*

Cirrhosis	HBV DNA (IU/mL)	ALT (U/L)	Management
YES	Any	Any	• **TREAT** with antiviral medication • Monitor HBV DNA and ALT every 6 months • Refer to specialist for screening endoscopy and, if needed, for other cirrhosis-related complications • HCC surveillance, including in persons who become HBsAg- • All patients with decompensated cirrhosis† should be referred to a hepatologist
NO	> 2,000	Elevated‡	• **TREAT** with antiviral medication • Monitor HBV DNA and ALT every 6 months • Monitor HBeAg and anti-HBe every 6 months in patients who are HBeAg+ at the time of treatment initiation to evaluate for seroconversion from HBeAg+/anti-HBe- to HBeAg-/anti-Hbe+ • Check HBsAg annually if/when HBeAg-
		Normal	• **Monitor** HBV DNA and ALT every 6 months • Liver fibrosis assessment every 2-3 years
	≤ 2,000	Elevated‡	• **Evaluate** other etiologies for elevated ALT • Monitor HBV DNA and ALT every 6 months
		Normal	• **Monitor** HBV DNA and ALT every 6 months and HBsAg every year for seroclearance

*In contrast to other HBV guidelines that have incorporated HBeAg status into treatment initiation decisions for non-cirrhotic HBsAg+ patients, this guidance for PCPs uses only HBV DNA and ALT to determine initial treatment indication in non-cirrhotic HBsAg+ patients. †Patients should be considered to have decompensated cirrhosis and promptly referred to a hepatologist if any of the following are present: jaundice, ascites, variceal hemorrhage, hepatic encephalopathy, or a Child-Turcotte-Pugh (CTP) score ≥ 7 (see Hepatitis B Online CTP calculator). ‡Elevated ALT defined as > 25 U/L in females and > 35 U/L in males that is persistent for at least 3-6 months

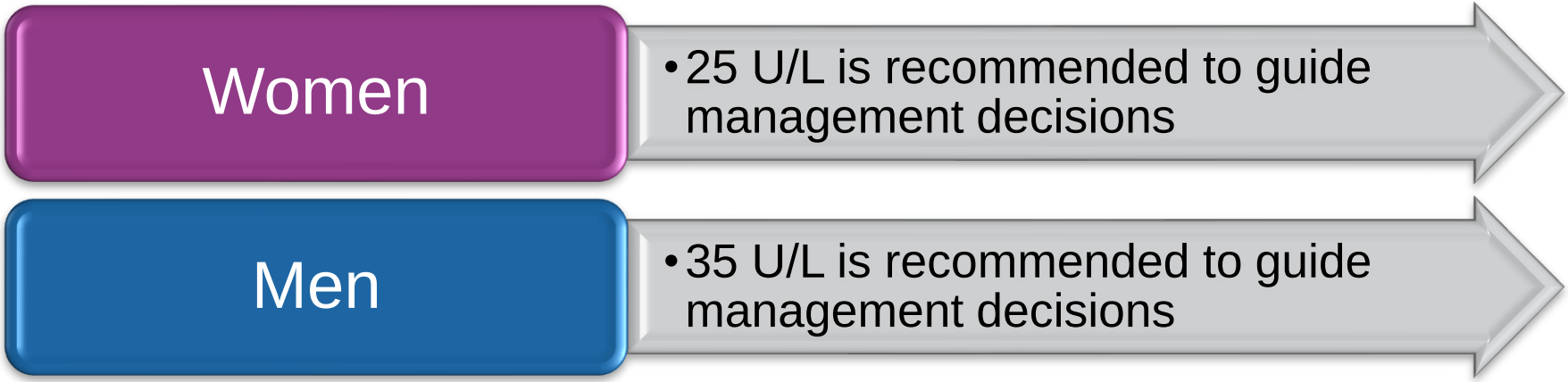
Tang AS, et al. Hepatitis B Online Website. 2020. https://www.hepatitisB.uw.edu/hbv-pcw/guidance. Accessed March 29, 2021.

Audience Response

What do the ACG guidelines define as the upper limit of normal ALT for women and men?

A. 40 U/L for women and 50 U/L for men
B. 25 U/L for women and 35 U/L for men
C. 30 U/L for women and 40 U/L for men
D. 40 U/L for women and 60 U/L for men
E. I'm not sure

What Are Normal ALT Values in Healthy Adults?



- Elevated ALT or AST above the upper limit of normal (ULN) in a population without identifiable risk factors is associated with increased liver-related mortality
- A normal ALT level may **not** exclude significant liver disease
- There is a linear relationship between ALT levels and body mass index (BMI) that should be assessed

Kwo PY, et al. *Am J Gastroenterol*. 2017:112(1):18-35.

Initiating Treatment for HBV: Key Options

Drug	Adult Dose	Pregnancy Category*	Side Effects	Monitoring on Treatment
Entecavir	Standard: 0.5 mg by mouth daily Decompensated liver disease: 1 mg by mouth daily Take 2 hours before or after food	Formerly FDA category C Limited pregnancy exposure, pregnancy exposure registry available Insufficient human data to assess risk of major birth defects No adverse effects observed in animal studies	Headache, fatigue, dizziness, nausea reported in ≥ 3% Post-marketing surveillance includes infrequent reports of: • Lactic acidosis • Severe hepatomegaly	Adjust dose with CrCl < 50 mL/min Avoid in pregnant patients Avoid in patients with prior exposure to lamivudine or known lamivudine resistance Lactic acid levels if clinical concern
Tenofovir disoproxil fumarate (TDF)	300 mg by mouth daily Take without regard to food	Formerly FDA category B Pregnancy exposure registry available Extensive data from pregnant women with HIV or HBV infections indicate no increase in pregnancy complications or major birth defects	Nausea (9%) Post-marketing surveillance includes infrequent reports of: • Nephropathy • Fanconi syndrome • Osteomalacia • Lactic acidosis	Adjust dose with CrCl < 50 mL/min Serum creatinine at baseline; if at risk for renal impairment, serum creatinine and phosphorus, and urine glucose and protein at least annually Consider bone density study at baseline and during treatment in persons with history of fracture or risks for osteopenia Lactic acid levels if clinical concern
Tenofovir alafenamide (TAF)	25 mg by mouth daily Take with food	Pregnancy exposure registry available No adverse effects observed in animal studies	Headache (12%) Lactic acidosis/severe hepatomegaly with steatosis is a warning for TAF due to rare reports with use of TDF	Avoid with CrCl < 15 mL/min if not receiving hemodialysis (HD) Dose after HD in those on HD If at risk for renal impairment, serum creatinine and phosphorus, and urine glucose and protein as clinically indicated Lactic acid levels if clinical concern

CrCl = creatinine clearance; FDA = U.S. Food and Drug Administration; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Tang AS, et al. Hepatitis B Online Website. 2020. https://www.hepatitisB.uw.edu/hbv-pcw/guidance. Accessed March 29, 2021.
Terrault NA, et al. *Hepatology*. 2018;67(4):1560-1599. Terrault NA, et al. *Hepatology*. 2016;63:261-283.

Treatment Recommendations for Patients Without and With Cirrhosis

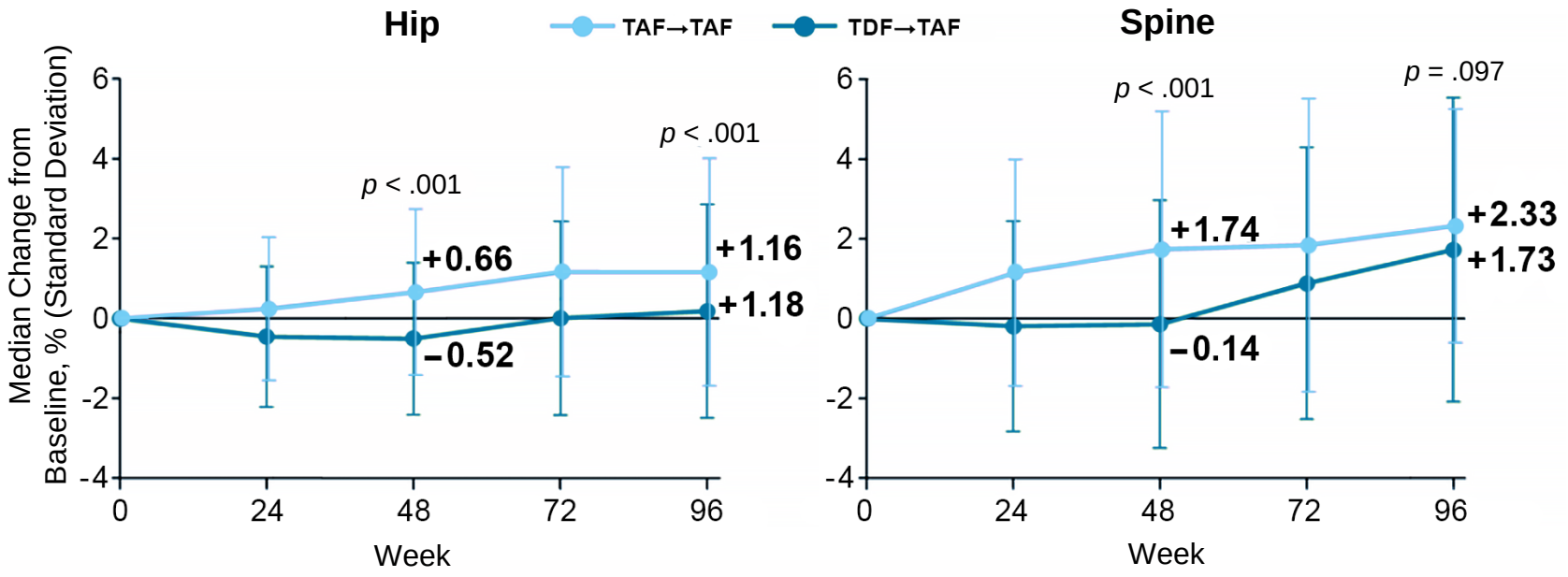
HBeAg-Positive or HBeAg-Negative CHB

Without Cirrhosis			Compensated Cirrhosis			Decompensated Cirrhosis‡‡	
Preferred	Alternative	Not Preferred	Preferred	Potential	Not Preferred	Preferred	Not Preferred
TDF TAF	Adefovir	Lamivudine	TDF TAF	Peg-IFN alfa-2a†	Lamivudine	TDF	
Entecavir	Telbivudine*		Entecavir		Telbivudine	Entecavir	
Peg-IFN alfa-2a							

Note: therapies are approved for monotherapy only
*Per AASLD guidelines, lamivudine and telbivudine not preferred due to relatively high rate of resistance; adefovir not preferred due to weak antiviral activity and relatively high rate of resistance in HBeAg-negative studies; telbivudine is no longer available in the United States
†Early cirrhosis only
‡TAF or entecavir should be considered in patients with decompensated cirrhosis who have renal dysfunction and/or bone disease
Peg-IFN = pegylated interferon
Lok AS, et al. *Hepatology* 2016;63(1):284-306. Martin P, et al. *Clin Gastroenterol Hepatol*. 2015;13(12):2071-2087. EASL. *J Hepatol*. 2012;57:167-185. Liaw Y-F, et al. *Hepatol Int.* 2008;2:263-283. Terrault NA, et al. *Hepatology*. 2016;63(1):261-283. Terrault NA, et al. *Hepatology*. 2018;67(4):1560-1599.

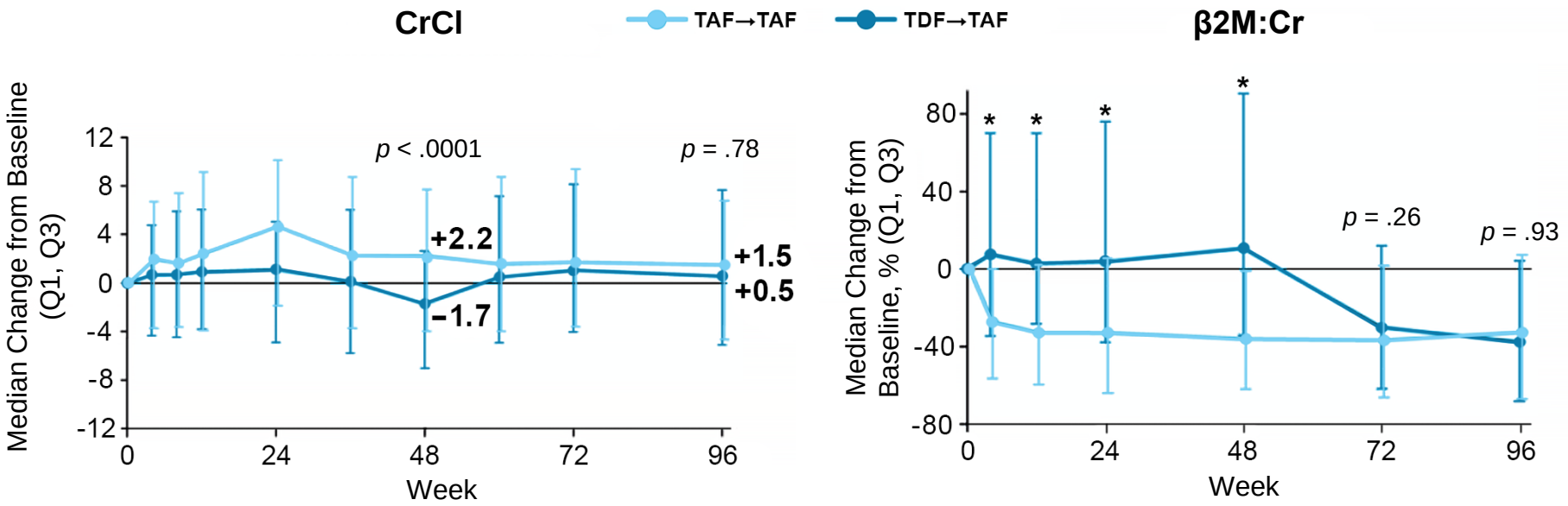
Bone Health: Impact of Switching from TDF to TAF at 96 Weeks

Hip and Spine Bone Mineral Density Through Week 96



Khalili M, et al. Presented at ACG 2020 Virtual Annual Scientific Meeting & Postgraduate Course. October 23-28, 2020.

Changes in Renal Parameters at 96 Weeks After Switching from TDF to TAF



β2M:Cr = β2-microglobulin creatinine

Khalili M, et al. Presented at ACG 2020 Virtual Annual Scientific Meeting & Postgraduate Course. October 23-28, 2020.

CME OUTFITTERS

Learning Objective 3

Routinely monitor patients with HBV every 6 months for disease progression, hepatocellular carcinoma (HCC), and HBV reactivation in patients who are immunosuppressed.

Risk Factors for HBV-Associated HCC

- Host factors
  - Family history
  - Older age
  - Male sex
  - Genetics/ethnicity
  - Diabetes/obesity
- Environmental factors
  - Smoking
  - Alcohol use
  - Aflatoxin exposure
- Viral factors
  - HBV integration site into host DNA
  - Virally translated proteins (HBsAg, HBx, HBeAg, HBcAg)
  - HBV Genotype C

Pandyarajan V, et al. *Int J Mol Sci.* 2021;22(2):479.

Indications for HCC Surveillance

- All persons with cirrhosis, including persons who become HBsAg-
- Populations even in the absence of cirrhosis
  - Asian or Black/African males older than age 40
  - Asian females older than age 50
  - Persons with a family history of HCC
  - Persons with hepatitis D virus coinfection
- Liver ultrasound with or without serum alpha-fetoprotein (AFP) every 6 months
  - More frequent monitoring or other imaging modalities such as CT or MRI with and without contrast may be indicated to evaluate new liver lesions

Tang AS, et al. Hepatitis B Management: Guidance for the Primary Care Provider. 2020. https://www.hepatitisB.uw.edu/hbv-pcw/guidance.

Case Study: Gerald

- 62-year-old man with history of metastatic angio-immunoblastic T cell lymphoma presented to the hospital for his 6th cycle of EPOCH chemotherapy and was found to have abnormal liver chemistries, prompting admission to the oncology ward
- No history of tobacco, alcohol, or recreational drugs
- No known history of liver disease
- At the time of initiation of chemotherapy:
  - HBsAg-
  - HBsAb-
  - Total anti-HBc+
  - IgM anti-HBc-
- Liver chemistries typically remained within normal limits, although there were elevations to less than 2x the ULN noted prior to cycle 5 with subsequent normalization after completion of the cycle

EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin

Saffo S, Lim JK. *Clin Liver Dis (Hoboken).* 2020;16(5):198-203.

Case Study: Gerald

- Laboratory work performed 4 days prior to presentation was notable only for:
  - ALT: 131 U/L
  - AST: 115 U/L
- Three days prior to presentation, he had completed a 10-day course of amoxicillin for a tooth extraction
- Repeat laboratory work at time of presentation revealed:
  - ALT: 582 U/L
  - AST: 449 U/L
  - Alkaline phosphatase: 108 U/L
  - Total bilirubin: 0.2 mg/dL

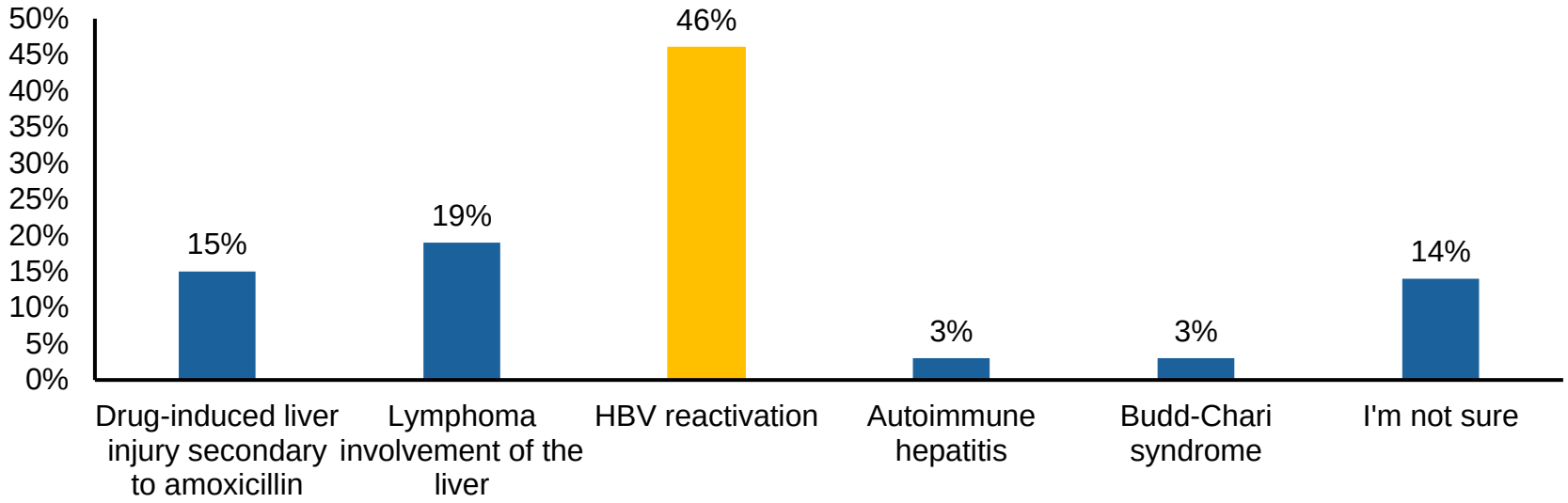
Saffo S, Lim JK. *Clin Liver Dis (Hoboken).* 2020;16(5):198-203.

Audience Response

What is the most likely diagnosis?

A. Drug-induced liver injury secondary to amoxicillin
B. Lymphoma involvement of the liver
C. HBV reactivation (HBVr)
D. Autoimmune hepatitis
E. Budd-Chiari syndrome
F. I’m not sure

What is the most likely diagnosis?



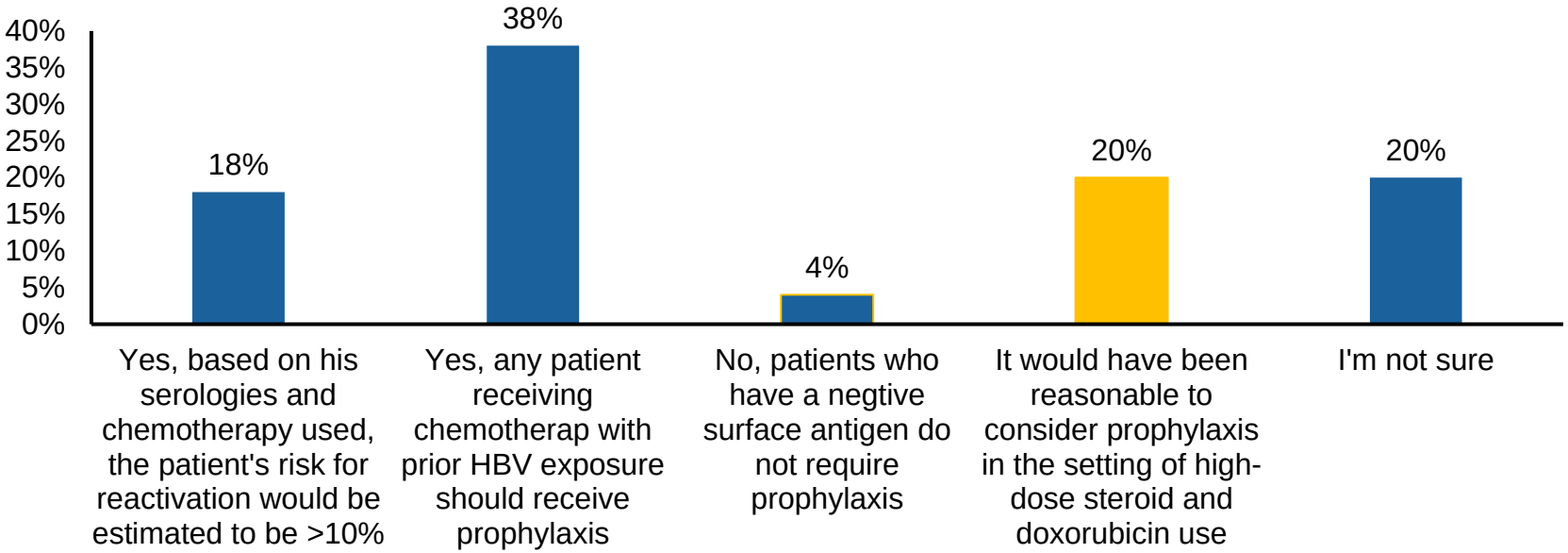
Results recorded on April 7, 2021

Audience Response

Should Gerald have received antiviral prophylaxis prior to the initiation of chemotherapy?

A. Yes, based on his serologies and chemotherapy used, the patient's risk for reactivation would be estimated to be > 10%
B. Yes, any patient receiving chemotherapy with prior HBV exposure should receive prophylaxis
C. No, patients who have a negative surface antigen do not require prophylaxis
D. It would have been reasonable to consider prophylaxis in the setting of high-dose steroid and doxorubicin use
E. I'm not sure

Should Gerald have received antiviral prophylaxis prior to the initiation of chemotherapy?



Results recorded on April 7, 2021

Case Study: Gerald

- After admission, chemotherapy was withheld in the context of his hepatitis
- Serologies were performed
- Notable findings included:
  - HBsAg+
  - HBeAg+
  - HBeAb-
  - Hepatitis B viral load: 6.28 log values
- Ultrasound of the abdomen revealed an echogenic liver with no evidence of portal or hepatic vein thrombosis

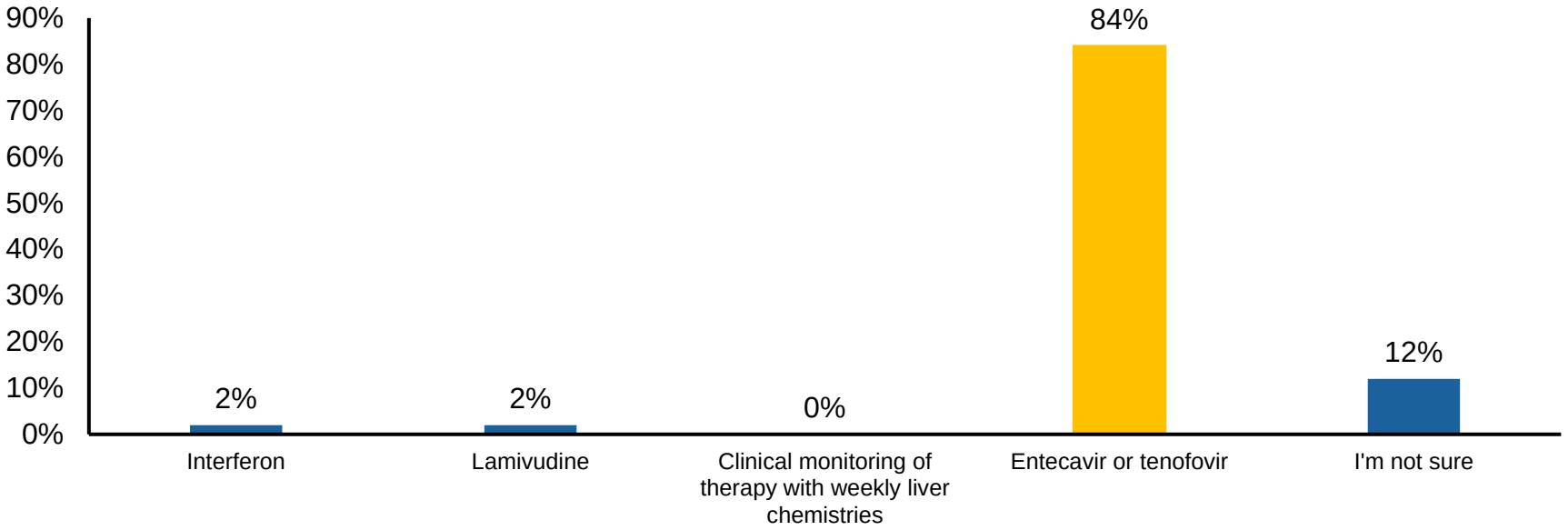
Saffo S, Lim JK. *Clin Liver Dis (Hoboken).* 2020;16(5):198-203.

Audience Response

Which of the following is the best choice treatment of HBVr in this patient?

A. Interferon
B. Lamivudine
C. Clinical monitor of therapy with weekly liver chemistries
D. Entecavir or tenofovir
E. I’m not sure

Which of the following is the best choice treatment of HBVr in this patient?



Results recorded on April 7, 2021

CME OUTFITTERS

Managing Patients at Risk for HBVr

- All patients undergoing immunosuppressive treatment should be considered for HBV screening (HBsAg, anti-HBc, HBsAb) for appropriate risk stratification for HBVr
- Risk of HBVr depends on both the serological status of the patient and the immunosuppressive agents used
- Patients who experience HBVr in the context of immunosuppression or require preemptive antiviral prophylaxis should be treated with high-potency oral nucleos(t)ide analogue such as entecavir or tenofovir

Saffo S, Lim JK. *Clin Liver Dis (Hoboken).* 2020;16(5):198-203.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Identify at-risk individuals in your practice and screen for HBV
- Share resources for dealing with stigma and discrimination with patients and the health care team
- Most patients with HBV **CAN** be treated and managed in the primary care setting
- Initiate regular monitoring and surveillance for HCC
- Heighten awareness of HBVr in patients receiving immunosuppression

CME OUTFITTERS

AFTER THE SHOW

Questions & Answers
Recorded on April 7, 2021

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Participants can print their certificate or statement of credit immediately.

CME OUTFITTERS

Visit the

Liver Disease Hub

After the live webcast, this activity will be available on the Liver Disease Hub where you'll find free resources and education for health care providers on hepatitis B

https://www.cmeoutfitters.com/liver-hub/

CME OUTFITTERS

Hepatitis B Patient Education Hub

A robust hub of patient education and resources for your patients to learn more about hepatitis B

https://www.cmeoutfitters.com/hbv-patient-education-hub/