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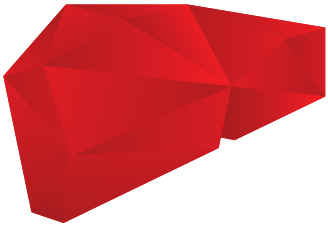

Simplifying the Approach to Chronic Hepatitis B Screening and Management

Includes the Simplified Approach Hepatitis B Algorithm (SABA), recommendations to simplify management and improve care of chronic hepatitis B patients

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CHB is underdiagnosed in the US

>2 MILLION

individuals have chronic hepatitis B virus (HBV) infection in the US[1]

ONLY 1 out of 3

people are diagnosed or aware of their CHB in the US[2]

Those who are unaware of their HBV infection are at risk for[3]:

- **Transmitting the virus** to others
- Developing **serious liver disease such as HCC**

Vaccination without prior screening can give a **dangerous perception of prevention** among contagious HBV carriers[4]

CHB=chronic hepatitis B; HCC=hepatocellular carcinoma.

CDC recommends universal screening for HBV infection for all adults in the US[3]

With 1 blood draw, you can measure 3 potential markers of infection[5]

1

HBsAg
Hepatitis B surface antigen

Hallmark of infection

2

Anti-HBs
Hepatitis B surface antibody

Marker of immunity[a]

3

Anti-HBc
Hepatitis B core antibody

Marker of prior exposure

Possible test results[3,5]				
HBsAg	+	–	–	–
Anti-HBs	–	+/-	+	–
Anti-HBc[b]	+	+	–	–
Interpretation	Acute or chronic infection[c]	Exposure to HBV At risk for reactivation[d]	Immunity from vaccination	At risk for HBV infection
Action	Evaluation and further testing	Follow up as appropriate[e]	No further action required	Vaccinate

> "Tests for HBV infection are **widely available, cheap, and accurate**" [6]
>
> R. Rajbhandari and R.T. Chung, *Annals of Internal Medicine*

HCV=hepatitis C virus; IgM=immunoglobulin M.
[a]Through vaccination.
[b]Anti-HBc refers to total anti-HBc.
[c]Patient is chronically infected if HBsAg+ for ≥6 months; patients with acute infection will be positive for anti-HBc IgM.
[d]Patients undergoing immunosuppressive therapy or treatment with direct-acting antivirals for HCV coinfection should be monitored for HBV reactivation.
[e]Patients with cirrhosis may need to be monitored for HCC per American Association for the Study of Liver Diseases (AASLD)/European Association for the Study of the Liver (EASL) guidelines.[5,7]

CHB is undermanaged and undertreated in the US, which could lead to increased risk of HCC

~2 out of 3
patients diagnosed with CHB:

- Do not receive regular monitoring of CHB or HCC surveillance[8,9,a]
- Do not receive antiviral treatment[10,b]

~1 out of 4
patients diagnosed with CHB:

- Develop serious complications such as cirrhosis or HCC[11]

Routine surveillance for HCC has resulted in a 37% reduction of HCC-related mortality in patients with CHB[12,c]

For patients who developed HCC during the study (153/18,816), screening for HCC was associated with identification of a higher percentage of early-stage HCC, greater utilization of treatment with curative intent (ie, resection), and improved survival at every year during the study period.[12,c]

For patients who developed HCC, 5-year survival was[12,c]

46% in the routine surveillance group

0% in the control group

AFP=alpha-fetoprotein.

[a]Based on a study of 2338 CHB patients followed during 2006–2013 in the Chronic Hepatitis Cohort Study, in which 62% received less than annual HBV DNA assessment, and a study of 55,317 patients with CHB from the US Truven MarketScan Databases of commercially insured and Medicare patients with private insurance supplement (2007-2014), in which <40% received annual HCC surveillance.

[b]Based on an analysis of 57,847 patients diagnosed with CHB from the commercial US Truven Health MarketScan Database (2007-2014). In this analysis, treatment rates were 30.7% in the overall population of patients diagnosed with CHB and 34.8% in patients diagnosed with CHB and cirrhosis.

[c]Results from a randomized, controlled trial of 18,816 patients (35-59 years old) with CHB in China who were randomized to either a routine surveillance group (ultrasound and AFP screening every 6 months), or a control group, who had regular access to healthcare but did not receive routine screening for HCC. During this 5-year study, 86 out of 9373 patients in the screening group and 67 out of 9443 patients in the control group developed HCC. This trial was published in 2004 and helped to establish the rationale for routine HCC screening in patients with CHB.[13] Limitations of the study include that adherence to surveillance was suboptimal (<60%) and that it was conducted in only 1 geographical area; additional data to confirm the benefits of screening for HCC would add to the evidence base.[12,13]

Patients with chronic HBV infection are at more risk for comorbidities than uninfected people

Some comorbidities that are more prevalent in CHB patients include[14]:

Chronic kidney disease

Bone disease (eg, osteoporosis)

Metabolic disorders (eg, diabetes)

Cardiovascular disease (eg, hypertension)

Burden of renal impairment in CHB infection

1.7×–3.5×

higher prevalence of **chronic kidney disease is seen in CHB patients** vs uninfected population[14,a]

Burden of bone-related comorbidities in CHB infection

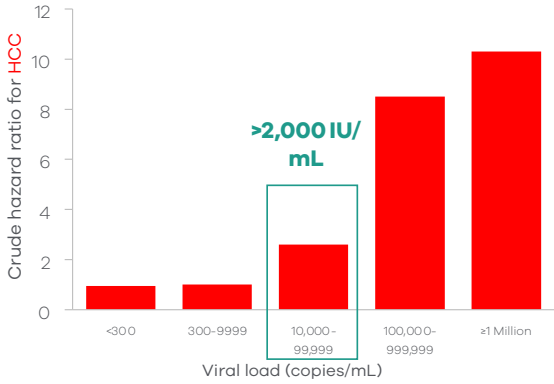
Up to 1.7×

higher prevalence of **osteoporosis and/or bone fracture is seen in CHB patients** vs uninfected population[14,a]

[a]Retrospective, observational study with case matching of CHB patients without HDV coinfection, based on U.S. administrative healthcare claims from Commercial/Medicare (n=32,523) and Medicaid (n=11,503) databases from 2006 to 2015.

HBV is the leading cause of HCC globally and antiviral treatment may decrease the risk of HCC[11]

Higher HBV DNA Levels Are Associated With Increased Risk of Cirrhosis and HCC[15,16]



Risk for HCC was significantly higher in those with baseline HBV DNA >2,000 IU/mL (>10,000 copies/mL)

HCC can develop in patients with CHB with or without cirrhosis[17]

~20% of HCC in HBV develops <u>without</u> cirrhosis

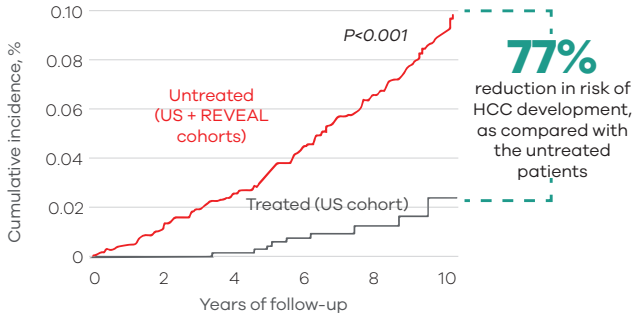
CHB-infected liver → Inflammation → Fibrosis → Cirrhosis → **HCC**

Both pathways to HCC can occur simultaneously

Antiviral therapy has shown a significant reduction in cumulative incidence of HCC[18,a]

Cumulative Incidence of HCC

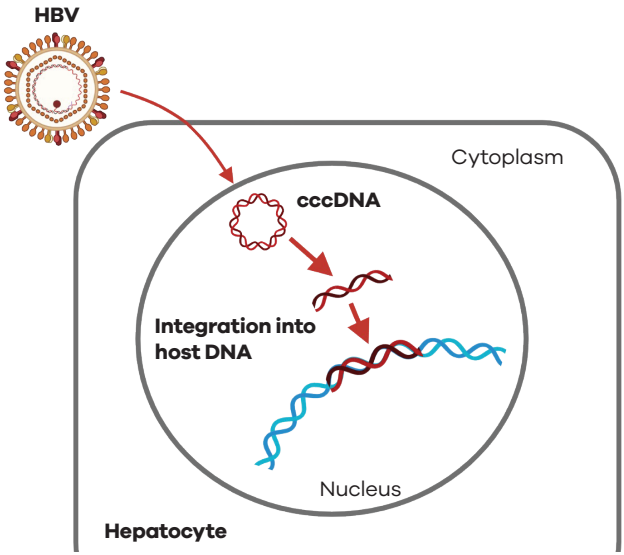
(Study with a retrospective and US cohort and a Taiwanese REVEAL-HBV cohort)



[a]A study that included a retrospective US cohort (N=2255 patients with CHB of whom 973 received antiviral treatment) and the community-based Taiwanese REVEAL-HBV study cohort (N=3653; 1991-2014). Figure adapted with permission from Lin D, et al.

HBV infection influences the risk of HCC through a variety of mechanisms

HBV-related oncogenesis may occur at any phase of infection, even during the early stages of CHB[19]



~90%

of HBV-associated HCC includes HBV DNA integration into the host DNA[20]

Immune-tolerant patients can also have oncogenic transformation due to integration early after infection[21]

Immune-tolerant patients who are not receiving antiviral therapy have a **2.5× higher 10-year risk of HCC** than immune active patients who are receiving antiviral therapy[22]

It Is Time for a Simplified Approach to Hepatitis B Elimination

The Simplified Approach Hepatitis B Algorithm (SABA)

The goal of the SABA panel was to **provide a simplified approach to HBV care that increases HBV screening and treatment**[23]

Members of the SABA expert panel[23]

Douglas Dieterich, MD, *Gastroenterologist*

Su Wang, MD, MPH, *Primary Care Physician*

Young-Suk Lim, MD, PhD, *Gastroenterologist*

Kosh Agarwal, MD, *Hepatologist*

Camilla Graham, MD, MPH, *Infectious Disease*

Paul Kwo, MD, *Hepatologist*

Chun-Jen Liu, MD, PhD, *Primary Care Physician*

Mark Sulkowski, MD, *Infectious Disease*

Scan here to learn more about the SABA expert panel recommendations.

The 2022 SABA guideline was funded by Gilead Sciences, Inc., and developed independently by the SABA panel. Gilead Sciences did not review the content of the manuscript.

SABA seeks to address CHB treatment gaps and increase treatment rates

The expert panel recommends utilizing 3 objective factors, severity of liver disease, age, and HBV DNA level, as criteria for treatment. The expert panel's approach was to assume that **all patients with CHB require treatment except those who do not "qualify" for treatment**[23]

Treatment Criteria Recommendations[23,a]

Age	HBV DNA	ALT
≥30	>2000 IU/mL	Regardless of ALT
<30	>2000 IU/mL	>ULN

ALT ULN defined as >30 U/L for males and >19 U/L for females

Irrespective of ALT levels, treat all chronic hepatitis B patients with cirrhosis and detectable HBV DNA levels[23]

"There is clinical evidence demonstrating that **HBV DNA levels of >2000 IU/mL** are associated with an **increased risk of HCC or progression to cirrhosis**, regardless of HBeAg status or ALT level"[23]

ALT=Alanine transaminase; HBeAg=hepatitis B e antigen; ULN=Upper limit normal.
[a]If HBV DNA <2000 IU/mL OR if less than age 30 and HBV DNA >2000 IU/mL and ALT ≤ULN, then reevaluate for treatment eligibility in 6 months. Use clinical judgment and shared decision-making to determine if patient would benefit from or prefer treatment.

CHB care via recommendations for monitoring and patient education

Recommendations for monitoring patients with CHB starting on treatment[23]:

Assess **ALT and HBV DNA** every 3 months until viral suppression is achieved, and every 6 months thereafter

Ultrasound with AFP every 6 months

Assess **HBsAg and fibrosis** (testing consistent with cirrhosis) annually

Guidance for education of patients with CHB[23]:

Discuss **side effects**, challenges with **adherence**, and other issues

Promote maintenance of **health and well-being**; counsel the patient on a healthy lifestyle and assess risk factors for metabolic-associated fatty liver disease

Connect the patient to **support services** (eg, patient assistance programs, copay cards, peer support)

Identifying and overcoming barriers to optimal HBV management

Barriers to treatment may include[23-26]:

- Patients not wanting to start therapy
- Potential challenges with compliance to treatment in younger patients
- Lack of knowledge about HBV transmission and its consequences
- Limited proficiency in English and linguistic isolation
- Social stigma

Recommendations to overcome barriers include[19,22,24,25]:

- Educate all patients with elevated HBV DNA that they could have an increased risk of HCC and that HBV-related oncogenesis may occur even during the early stages of CHB
- Provide targeted educational materials on screening and prevention of disease
- Educate and provide testing and linkage to care at no or low cost
- Educate that CHB is transmissible but treatable

These recommendations are intended to be **realistic, implementable** in diverse settings, and **sensitive to resource limitations** and cost burdens within the US healthcare system[23]

Find educational materials for patients on HepB.com

hepB.com™

HCP=healthcare professional.

Leverage the Simplified Algorithm to increase treatment rates and help close CHB treatment gaps

Clinical takeaways from SABA[23]

"The goals of antiviral therapy are to suppress viral replication and to reduce the risk of mortality, HCC, progression of liver disease, and transmission to others..."

"Educating patients and soliciting their treatment preferences are also part of ensuring that care has a meaningful impact on their lives"

To learn more about care of patients with CHB, please visit:

hepBMD.com

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