

Review of Updated Hepatitis B Vaccine Recommendations and Potential Challenges With Implementation

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Abstract: Hepatitis B virus (HBV) infection is a vaccine-preventable disease associated with substantial morbidity and mortality. Although safe and effective hepatitis B vaccines are available, an increased number of adults must receive the hepatitis B vaccine in order to reach the goal of the US Department of Health and Human Services for HBV elimination. Previous guidelines from the US Centers for Disease Control and Prevention (CDC) for hepatitis B vaccination among adults utilized a risk-based approach that may have contributed to decreased uptake of the vaccine because the recommendations were difficult to adopt into clinical practice and assumed patients would recognize and disclose their risk factors. Based on review of epidemiologic and cost-effectiveness data, the CDC now recommends that all adults 19 to 59 years old receive the hepatitis B vaccine; however, a risk-based approach to hepatitis B vaccination was retained among adults age 60 years and older because universal vaccination in this age group would not lead to substantial reductions in acute HBV cases and be cost-effective. Implementation of these expanded hepatitis B vaccination recommendations in clinical and public health practice may pose challenges, including ensuring effective HBV screening practices, quality measures to track coverage of the hepatitis B vaccine, utilization of hepatitis B vaccines that have the highest completion rates for the vaccine series in a real-world setting, and sustained efforts to vaccinate high-risk groups such as individuals experiencing incarceration, utilizing sexually transmitted disease clinics, and injecting illicit drugs.

Keywords

Hepatitis B virus, vaccination, Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices, quality measures

Hepatitis B virus (HBV) infection is a vaccine-preventable disease. Despite the availability of effective vaccines and antiviral therapies, chronic HBV contributes to significant global morbidity and mortality, with an estimated 270 million adults infected and 820,000 deaths from causes related to HBV infection in 2019.¹⁻³ In the United States, chronic HBV prevalence is estimated to be as high

Table 1. Summary of Updated and Former Guidelines From the CDC for Hepatitis B Vaccination Among Adults²³

Updated CDC Guidelines	Former CDC Guidelines
<ul style="list-style-type: none"> • All adults 19-59 years old should receive the hepatitis B vaccine • Adults age 60 years and older should receive the hepatitis B vaccine only if they have an HBV risk factor defined in the former CDC guidelines 	<ul style="list-style-type: none"> • Adults who have any of the following HBV risk factors should receive the hepatitis B vaccine: <ul style="list-style-type: none"> – Infection by sexual exposure – History of current or recent injection drug use – Percutaneous or mucosal exposure to blood – Other risk factors for acquisition of HBV or developing complications as a result of HBV infection^a

CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus.

^aOther persons at risk for HBV infection defined as: those with HIV infection; those with chronic liver disease; those with hepatitis C virus infection; those with end-stage renal disease; those who have ever injected drugs; men who have sex with men; persons with elevated alanine aminotransferase or aspartate aminotransferase of unknown etiology; donors of blood, plasma, or organs; household or sexual contacts of hepatitis B surface antigen–positive patients; persons not in a long-term, mutually monogamous relationship (eg, >1 sex partner during the previous 6 months); those evaluated or treated for a sexually transmitted disease; health care and public safety workers at risk for occupational exposure to blood or blood-contaminated body fluids; residents and staff of facilities for developmentally disabled individuals; travelers to countries with intermediate or high prevalence of HBV infection; inmates of correctional facilities; and unvaccinated persons with diabetes who are 19 to 59 years old.

as 2.4 million adults.⁴ Although chronic HBV–related hospitalizations have remained stable at 1 per 100,000 hospitalizations,⁵ the mean costs associated with chronic HBV–related hospitalizations increased from \$15,203 in 2012 to \$16,970 in 2016.⁶ In addition, chronic HBV patients were associated with greater health care resource utilization and 3 times higher health care costs than patients without chronic HBV.⁷ Progress toward achieving the goal of HBV elimination has stalled as a result of suboptimal HBV screening and delays in linking chronic HBV patients to care and treatment.^{8–21} Implementing effective HBV screening and linking chronic HBV patients to treatment are both essential for reducing the risk of liver disease progression and development of hepatocellular carcinoma, as well as decreasing the reservoir of HBV that contributes to ongoing transmission.²²

Hepatitis B vaccination programs are also important in reducing the risk of acute HBV infection and the development of chronic HBV infection. Previous US guidelines for hepatitis B vaccination among adults were complex and involved a risk-based approach that included numerous risk factors that are not easily integrated into health care provider screening and assessments, assumed patients would recognize and disclose their risk factors, and contributed to HBV-related stigma and exacerbated health care disparities. In 2016, the US Centers for Disease Control and Prevention (CDC)'s Advisory Committee on Immunization Practices (ACIP) suggested that a work group examine revisions to hepatitis B vaccination recommendations.²³ The CDC ACIP Hepatitis Vaccines Work Group convened from September 2019 to May 2021, and in November 2021, the ACIP unanimously recommended the hepatitis B vaccine for all adults 19 to

59 years old but retained a risk-based approach to hepatitis B vaccination among adults age 60 years and older.²³ This article reviews the existing data and rationale for the CDC ACIP recommendations and discusses potential challenges in implementing the updated hepatitis B vaccination guidelines among adults in the United States.

Rationale for Expanding Hepatitis B Vaccination Recommendations

A summary of the updated and former CDC ACIP recommendations for hepatitis B vaccination is provided in Table 1. The CDC ACIP Hepatitis Vaccines Work Group used 2 guiding principles when considering expansion of hepatitis B vaccination recommendations.²³ First, a risk-based strategy for hepatitis B vaccination may not be successful in meeting the goal of the US Department of Health and Human Services for elimination of viral hepatitis by 2030. Notably, incident cases of acute HBV infection have plateaued at 20,000 cases annually over the past 10 years, and among all cases, only one-third had an identifiable risk factor. Rates of acute HBV infection are highest among individuals 30 to 59 years old, and rates have increased among individuals age 40 years and older. Hepatitis B vaccination coverage, defined as 3 or more doses of a hepatitis B vaccine, among adults age 19 years and older was low at 30% overall, and only 33% to 39% among individuals with risk factors, including travelers and patients with chronic liver diseases or diabetes. Expansion and simplification of adult hepatitis B vaccination recommendations as outlined by the National Academies of Sciences, Engineering, and Medicine also may improve health care access, as a risk-based approach

Table 2. Potential Challenges With Implementing Updated Guidelines From the CDC for Hepatitis B Vaccination Among Adults

Challenges With Implementing Updated CDC Guidelines
<ul style="list-style-type: none"> • Ensuring effective HBV screening practices and recommendations • Promoting quality measures, such as HEDIS measures, to track coverage of the hepatitis B vaccine among adults • Selecting a hepatitis B vaccine that has the highest completion rate for the vaccine series in real-world settings • Sustaining efforts to vaccinate individuals at high risk for HBV exposure, including those experiencing incarceration, utilizing sexually transmitted disease clinics, and injecting illicit drugs

CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus; HEDIS, Healthcare Effectiveness Data and Information Set.

to vaccination may favor individuals with access to health care, who trust to disclose stigmatizing risk factors, who are aware of their risk, and who have a higher health literacy.

Second, the CDC ACIP Hepatitis Vaccines Work Group reviewed available evidence to determine whether universal vaccine recommendations would increase hepatitis B vaccine uptake among individuals with risk factors, be an effective use of resources, and include adults of all ages.²³ When vaccine uptake for influenza, pneumococcal, and hepatitis B vaccines among cohorts that utilized a risk-based approach to vaccines was compared with cohorts that included universal vaccination, the vaccination coverage increased from 23% to 36%. Increased hepatitis B vaccine coverage that may result from universal recommendations also may reduce patient stigma to disclose risk factors, make it easier for providers to implement recommendations in practice, and advance health equity goals. Using a cost-effectiveness model, the CDC ACIP Hepatitis Vaccines Work Group estimated that a universal hepatitis B vaccine for all adults would result in an incremental cost-effectiveness ratio per quality-adjusted life year gained of \$153,000 and would require 352 million doses of hepatitis B vaccine be administered to result in a 24% reduction in acute HBV cases. In contrast, when the cost-effectiveness model evaluated a policy of universal hepatitis B vaccination only for adults 19 to 59 years old, the incremental cost-effectiveness ratio per quality-adjusted life year gained was \$117,000 and would require 298 million doses to be administered to result in a 23% reduction in acute HBV cases. Although a majority of the CDC ACIP Hepatitis Vaccines Work Group voted in favor of a universal hepatitis

B vaccination recommendation among all adults, the overall ACIP committee voted for universal vaccination among adults 19 to 59 years old and retained a risk-based approach among adults aged 60 years and older. Several members of the ACIP committee noted increasing costs and diminishing returns in preventing acute HBV cases as the primary reasons for recommending universal vaccination only among adults 19 to 59 years old.

Potential Challenges With Implementing Updated Hepatitis B Vaccination Guidelines

Potential challenges with implementing the updated CDC ACIP guidelines for hepatitis B vaccination are summarized in Table 2. Ensuring effective HBV screening is essential for expanding hepatitis B vaccine coverage. Although current HBV screening guidance remains risk-based,⁵ cost-effectiveness models have found that universal one-time testing of adults 18 to 69 years old with hepatitis B surface antigen, compared with current practice, would prevent an additional 7 cases of compensated cirrhosis, 3 cases of decompensated cirrhosis, 5 cases of hepatocellular carcinoma, 2 liver transplants, and 10 HBV-related deaths, with a savings of \$263,000 per 100,000 adults screened.²⁴ Although universal one-time testing with hepatitis B surface antigen may be effective in identifying cases of chronic HBV,²⁴ the additional tests of antibody to hepatitis B surface antigen and immunoglobulin G antibody to the hepatitis B core antigen will identify individuals who may benefit from receiving the hepatitis B vaccine, require additional testing to determine whether they are infected, or may need education regarding potential risk for HBV reactivation in the future.²⁵

Quality measures can monitor changes in performance and improve the quality of care at a population level. These quality measures can be tied to reimbursement, and health care insurance plans also use these measures to evaluate the quality of care of health plans and inform consumer selection of health plans. Healthcare Effectiveness Data and Information Set measures are used to evaluate the quality of private health plans and can inform consumer selection of health plans. The National Adult and Influenza Immunization Summit developed and tested a new adult immunization status measure that was incorporated into the 2019 Healthcare Effectiveness Data and Information Set measures.²⁶ The adult immunization status measure included the percentage of members 19 years and older who were up-to-date on annual influenza, tetanus, diphtheria, and/or tetanus toxoid, reduced diphtheria toxoid and acellular pertussis, herpes zoster, and 13- and 23-valent pneumococcal vaccines.²⁶ Although this specific measure did not include

the hepatitis B vaccine, the National Adult and Influenza Immunization Summit recommended that the Medicare End Stage Renal Disease Program measure the extent to which beneficiaries receive recommended influenza, pneumococcal, and hepatitis B vaccines.²⁶ Incorporation of hepatitis B vaccination into quality measures may be an effective way to ensure that progress toward implementing the updated CDC ACIP hepatitis B vaccination guidelines is monitored.

Although several safe and effective hepatitis B vaccines have been approved by the US Food and Drug Administration,²² implementing expanded hepatitis B vaccination recommendations into clinical and public health practice must consider 3 important factors. First, real-world data comparing completion of the hepatitis B vaccine series among the approved vaccines should be an important factor for health care systems and public health organizations to consider when selecting a specific hepatitis B vaccine. When evaluating hepatitis B vaccination completion in the Kaiser Permanente Southern California health care system, individuals who initiated a 2-dose hepatitis B vaccine were 1.8 times more likely to complete the recommended series compared with those who initiated a 3-dose hepatitis B vaccine.²⁷ Although there are limited real-world data comparing the various hepatitis B vaccines, cost-effectiveness analyses have revealed that the 2-dose hepatitis B vaccine was cost-saving across multiple adult populations.^{28,29} Second, when attempting to vaccinate a greater proportion of the population with the hepatitis B vaccine as a strategy to decrease occurrence of acute cases of HBV infection, health care systems and public health organizations must continue to focus vaccination efforts on populations at highest risk for HBV exposure. These populations include individuals who experience incarceration,³⁰ utilize clinical services at sexually transmitted disease clinics,³¹ or inject illicit drugs and obtain care at sites such as syringe exchange programs.³² Third, creative strategies will be needed to vaccinate the increased number of individuals who are now eligible for the hepatitis B vaccine. Attempts to vaccinate a large portion of the US population with the COVID-19 vaccine may provide insight into attempts to scale up administration of the hepatitis B vaccine. For instance, strategies such as vaccinating hospitalized patients at time of discharge from the hospital and linking these patients to vaccine clinics for a second dose of the COVID-19 vaccine were successfully utilized by the Priscilla Chan and Mark Zuckerberg San Francisco General Hospital.³³ This strategy of vaccinating patients at the time of discharge from hospitalization with linkage to care for additional doses of vaccine may also be needed to increase the number of individuals who receive the hepatitis B vaccine.

Conclusion

An increased number of adults must receive the hepatitis B vaccine in order to reduce HBV-associated morbidity and mortality and to reach the goal of the US Department of Health and Human Services for HBV elimination. Previous US guidelines for hepatitis B vaccination among adults utilized a risk-based approach for identifying those who should receive a vaccine. In developing updated guidelines for hepatitis B vaccination among adults, the CDC ACIP reviewed epidemiologic and cost-effectiveness data and recommended the hepatitis B vaccine for all adults 19 to 59 years old; however, the CDC ACIP retained a risk-based approach for hepatitis B vaccination among adults age 60 years and older because universal vaccination in this age group would not lead to substantial reductions in acute HBV cases and be cost-effective. Implementation of these expanded hepatitis B vaccination recommendations into clinical and public health practice may pose several challenges, including ensuring effective HBV screening practices, quality measures to track coverage of the hepatitis B vaccine, utilization of hepatitis B vaccines that have the highest completion rates for the vaccine series in a real-world setting, and sustained efforts to vaccinate high-risk groups such as individuals experiencing incarceration, utilizing sexually transmitted disease clinics, and injecting illicit drugs.

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