CLINICAL GUIDELINE

ACP American College of Physicians®
Leading Internal Medicine, Improving Lives

Hepatitis B Vaccination, Screening, and Linkage to Care: Best Practice Advice From the American College of Physicians and the Centers for Disease Control and Prevention

Winston E. Abara, MD, PhD; Amir Qaseem, MD, PhD, MHA; Sarah Schillie, MD, MPH, MBA; Brian J. McMahon, MD; and Aaron M. Harris, MD, MPH*; for the High Value Care Task Force of the American College of Physicians and the Centers for Disease Control and Prevention

Background: Vaccination, screening, and linkage to care can reduce the burden of chronic hepatitis B virus (HBV) infection. However, recommendations vary among organizations, and their implementation has been suboptimal. The American College of Physicians' High Value Care Task Force and the Centers for Disease Control and Prevention developed this article to present best practice statements for hepatitis B vaccination, screening, and linkage to care.

Methods: A narrative literature review of clinical guidelines, systematic reviews, randomized trials, and intervention studies on hepatitis B vaccination, screening, and linkage to care published between January 2005 and June 2017 was conducted.

Best Practice Advice 1: *Clinicians should vaccinate against hepatitis B virus (HBV) in all unvaccinated adults (including pregnant women) at risk for infection due to sexual, percutaneous, or mucosal exposure; health care and public safety workers at risk for blood exposure; adults with chronic liver disease, end-stage renal disease (including hemodialysis patients), or HIV infection; travelers to HBV-endemic regions; and adults seeking protection from HBV infection.*

Best Practice Advice 2: *Clinicians should screen (hepatitis B surface antigen, antibody to hepatitis B core antigen, and antibody to hepatitis B surface antigen) for HBV in high-risk persons, including persons born in countries with 2% or higher HBV prevalence, men who have sex with men, persons who inject drugs, HIV-positive persons, household and sexual contacts of HBV-infected persons, persons requiring immunosuppressive therapy, persons with end-stage renal disease (including hemodialysis patients), blood and tissue donors, persons infected with hepatitis C virus, persons with elevated alanine aminotransferase levels (≥19 IU/L for women and ≥30 IU/L for men), incarcerated persons, pregnant women, and infants born to HBV-infected mothers.*

Best Practice Advice 3: *Clinicians should provide or refer all patients identified with HBV (HBsAg-positive) for posttest counseling and hepatitis B–directed care.*

Ann Intern Med. 2017;167:794-804. doi:10.7326/M17-1106 **Annals.org**
For author affiliations, see end of text.
This article was published at Annals.org on 21 November 2017.

In the United States, an estimated 847 000 persons are living with chronic hepatitis B virus (HBV) infection (1), and approximately 14 000 deaths that are attributable to it occur each year (2). About 2 of every 3 persons with chronic HBV infection are unaware of their infection, which contributes to ongoing transmission (3, 4). Approximately 70% of persons with chronic HBV infection in the United States are foreign-born (2, 5), and the prevalence among foreign-born persons is 3% to 5% (5) compared with 0.3% in the general population (1). Most cases in foreign-born persons occur among immigrants from Africa, Asia, and the Pacific Islands—regions with intermediate (2% to 7% prevalence of hepatitis B surface antigen [HBsAg]) or high (>7% prevalence of HBsAg) endemicity (6). Other high-burden populations include men who have sex with men (MSM), injection drug users, incarcerated populations, and sexual and household contacts of infected persons (7).

See also:

Summary for Patients I-22

Between 15% and 40% of persons with chronic HBV infection develop cirrhosis, hepatocellular carcinoma, or liver failure, and 25% die prematurely of these complications (8–10). Complications result in increased direct and indirect health care costs (4, 11) totaling approximately $1 billion (12). Vaccination and screening are cost-effective interventions to reduce the burden of chronic HBV infection, but their use remains low (7, 13). Only 24.6% of U.S. adults have received a complete hepatitis B vaccine series (13), and about 60% of HBV-

* This paper, written by Winston E. Abara, MD, PhD; Amir Qaseem, MD, PhD, MHA; Sarah Schillie, MD, MPH, MBA; Brian J. McMahon, MD; and Aaron M. Harris, MD, MPH, was developed for the High Value Care Task Force of the American College of Physicians and the Centers for Disease Control and Prevention. Individuals who served on the High Value Care Task Force from initiation of the project until its approval were Amir Qaseem, MD, PhD, MHA† (*Chair*); George M. Abraham, MD, MPH†; Robert Centor, MD†; Apostolos P. Dallas, MD‡; Nitin S. Damle, MD, MS‡; Douglas M. DeLong, MD†; Heather E. Gantzer, MD†; Lawrence Feinberg, MD‡; Carrie A. Horwitch, MD, MPH†; Linda L. Humphrey, MD, MPH†; Janet A. Jokela, MD, MPH†; Bruce Leff, MD‡; Joseph Ming Wah Li, MD†; Robert H. Lohr, MD†; Ana María López, MD, MPH†; Robert M. McLean, MD†; Thomas G. Tape, MD‡; William C. Taylor, MD‡; and Jeffrey Wiese, MD‡. Approved by the ACP Board of Regents on 24 April 2017.

† Author (participated in discussion and voting).

‡ Nonauthor contributor (participated in discussion but did not vote).

Figure. Summary of the American College of Physicians and Centers for Disease Control and Prevention best practice advice on hepatitis B vaccination, screening, and linkage to care for adults with chronic HBV infection.

Summary of the American College of Physicians and Centers for Disease Control and Prevention Best Practice Advice on Hepatitis B Vaccination, Screening, and Linkage to Care for Adults With Chronic HBV Infection

Disease/Condition	Chronic HBV infection
Target Audience	All clinicians
Target Patient Population	Adults who are at risk for or have HBV infection
Interventions Evaluated	Hepatitis B vaccination, hepatitis B screening tests (HBsAg, anti-HBs, anti-HBc), linkage to care, and treatment
Outcomes Evaluated	Vaccination coverage, HBV transmission, knowledge of HBV infection status, receipt of hepatitis B–directed care, complications of chronic HBV infection (cirrhosis, hepatocellular carcinoma, death), and health care costs
Benefits	Decreases in risk for continuous transmission of HBV infection, HBV-associated morbidity and mortality, and health care costs Increases in number of persons aware of their status, receiving hepatitis B–directed care, and receiving treatment and increases in care and treatment of HBV-infected mothers in order to reduce risk for perinatal transmission
Harms	Vaccination: Rare but can include mild fever, soreness at the injection site, anaphylaxis (1 case per 1.1 million doses), and adverse effects of treatment Screening: Potential emotional trauma from a rare false-positive test result; feelings of shame and depression in some HBV-infected persons Linkage to care: None
Talking Points for Providers	HBV is a serious cause of morbidity and mortality associated with liver disease. Vaccination of susceptible and unvaccinated adults is effective at preventing chronic HBV infection. Screening can easily identify susceptible and unvaccinated adults. Screening increases the number of persons who are aware that they have chronic HBV infection. Effective treatment can reduce complications, reduce morbidity and mortality, and help meet the goals of the national elimination strategy. HBV screening and vaccination are cost-effective and cost-saving.
Best Practice Advice	*Best Practice Advice 1: Clinicians should vaccinate against chronic hepatitis B virus (HBV) in all unvaccinated adults at risk for infection, including:* *a. Adults at risk by sexual exposure (sex partners of hepatitis B surface antigen [HBsAg]-positive persons, sexually active persons who are not in a mutually monogamous relationship, persons seeking evaluation or treatment for a sexually transmitted infection, and men who have sex with men).* *b. Adults at risk by percutaneous or mucosal exposure to blood (adults who are recent or current users of injection drugs; household contacts of HBsAg-positive persons; residents and staff of facilities for developmentally disabled persons; incarcerated, health care, and public safety workers at risk for exposure to blood or blood-contaminated body fluids).* *c. Adults with chronic liver disease, including but not limited to hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level greater than twice the upper limit of normal.* *d. Adults with end-stage renal disease, including those receiving predialysis care, hemodialysis, peritoneal dialysis, and home dialysis.* *e. Adults with HIV infection.* *f. Pregnant women who are at risk for hepatitis B virus infection during pregnancy (e.g., having more than 1 sex partner during the previous 6 months, having been evaluated or treated for a sexually transmitted infection, recent or current injection drug use, or having an HBsAg-positive sex partner).* *g. International travelers to regions with high or intermediate levels of endemic hepatitis B virus infection.* *h. Any adult seeking protection from HBV infection.* *Best Practice Advice 2: Clinicians should screen (hepatitis B surface antigen, antibody to hepatitis B core antigen, and antibody to hepatitis B surface antigen) for HBV in high-risk persons, including persons born in countries with 2% or higher HBV prevalence, men who have sex with men, persons who inject drugs, HIV-positive persons, household and sexual contacts of HBV-infected persons, persons requiring immunosuppressive therapy, persons with end-stage renal disease (including hemodialysis patients), blood and tissue donors, persons infected with hepatitis C virus persons with elevated alanine aminotransferase levels (≥19 IU/L for women and ≥30 IU/L for men), incarcerated persons, pregnant women, and infants born to HBV-infected mothers.* *Best Practice Advice 3: Clinicians should provide or refer all patients identified with HBV (HBsAg-positive) for posttest counseling and hepatitis B–directed care.*

anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus.

infected persons are unaware of their infection (4). Screening among at-risk groups can mitigate the burden of chronic HBV infection by promptly identifying infected persons and linking them to care, but its implementation is suboptimal (7). Approximately 10% to 15% of eligible persons in the United States receive treatment (4). Linking HBV-infected patients to care facilitates timely treatment for eligible persons (14) and periodic surveillance (every 6 to 12 months) for hepatocellular carcinoma and monitoring of liver aminotransferase and HBV DNA levels, which are important in mitigating morbidity and mortality (8, 15).

Reducing the burden of chronic HBV infection by increasing vaccination, screening at-risk adults, and providing linkage to care is a public health priority (16, 17). Although clinical guidelines from the Centers for Disease Control and Prevention (CDC) (7, 18), the U.S. Preventive Services Task Force (USPSTF) (19), the American Association for the Study of Liver Diseases (AASLD) (8), and the Advisory Committee on Immunization Practices (ACIP) (20) have addressed these topics, their recommendations vary and implementation has been suboptimal (4, 7, 13). Most persons who are at risk for, are susceptible to, or have HBV infection are not screened, vaccinated, or linked to care (4, 7, 13). Recent studies have suggested additional at-risk groups that should receive HBV screening, treatment, or vaccination that were not in previously published clinical guidelines (21–27). This article by the American College of Physicians (ACP) and the CDC presents the best available evidence on hepatitis B vaccination, screening, and linkage to care. Using the ACP high-value care framework, we highlight consensus across guidelines and integrate this with current evidence for hepatitis B vaccination, screening, and linkage to care from the research literature to develop best practice advice statements. This evidence-based synthesis of current clinical guidelines and research findings is intended to amplify existing guidelines and promote high-value clinical practice. The target audience for this article includes all clinicians, and the target patient population is adults who are at risk for or have HBV infection.

METHODS

Literature Review

A narrative literature review of evidence on hepatitis B vaccination, screening, and linkage to care was conducted. We searched the published English-language literature from January 2005 (when highly potent hepatitis B drug treatment with low resistance rates became available) through June 2017 using the following Medical Subject Headings terms across MEDLINE, EMBASE, PubMed, CINAHL, Web of Science, and the Cochrane Library: *hepatitis B*, *hepatitis B screening*, *community-based hepatitis B screening*, *HBV screening*, *clinic-based hepatitis B screening*, *HBsAg testing*, *chronic hepatitis B*, *hepatitis B vaccination*, *hepatitis B linkage to care*, *hepatitis B continuum of care*, *hepatitis B cascade of care*, *hepatitis B vaccination cost-effectiveness*, and *hepatitis B treatment cost-effectiveness*. We selected current clinical guideline recommendations from the CDC, the USPSTF, the AASLD, and the ACIP and included systematic reviews, meta-analyses, and randomized and nonrandomized intervention studies from the research literature. Selected articles were further screened to include those that focused on the most recent guidelines on vaccination, screening, and treatment for chronic HBV infection; barriers to screening and linkage to care; adverse events associated with vaccination; and strategies to increase screening, vaccination, and linkage to an HBV-experienced provider among adults. Selected articles were reviewed by 2 persons to ensure that they met the selection criteria.

Consensus Process and Approval

This article was reviewed and approved by the CDC and the ACP High Value Care Task Force, whose members are physicians trained in internal medicine and its subspecialties and include experts in evidence synthesis who are familiar with the hepatitis literature. The CDC and the task force developed the best practice statements (summarized in the **Figure**) on the basis of the narrative review and approved them by consensus. All disclosures of interest were declared at each conference call. No individuals were recused from discussion or voting due to conflicts of interest.

VACCINATION

Vaccination is the most effective measure to prevent HBV infection and its complications (18). The vaccine confers protection in more than 90% of healthy adults younger than 40 years who receive the complete vaccine series (28, 29), and immunity lasts at least 3 decades (30–32). Recommendations for hepatitis B vaccination were introduced in 1982 and have since evolved into a comprehensive immunization strategy, although challenges remain (18). The ACIP recommends vaccination for all unvaccinated adults at risk for HBV infection, including sexual partners and household contacts of HBsAg-positive persons; sexually active persons who are not in a mutually monogamous relationship; persons seeking evaluation for a sexually transmitted infection; MSM; recent or current users of injection drugs; residents and staff at facilities for developmentally challenged persons; incarcerated persons; health care workers and public safety employees at risk for exposure to blood or blood-contaminated body fluids; adults aged 19 to 59 years with diabetes mellitus; persons with end-stage renal disease, including those receiving predialysis care, hemodialysis, peritoneal dialysis, or home dialysis; persons with chronic liver disease, including but not limited to hepatitis C virus infection, cirrhosis, nonalcoholic fatty liver disease, alcoholic liver disease, autoimmune liver disease, or an alanine aminotransferase (ALT) or aspartate aminotransferase level greater than twice the upper limit of normal; pregnant

Table 1. Risk Factors, Prevalence, and Testing Guidelines for Chronic HBV Infection

Risk Factor	Prevalence of HBsAg (95% CI), %*	Organizations Recommending Screening			Reference
		USPSTF, 2014	CDC, 2008	AASLD, 2009	
Born in region with intermediate-to-high prevalence (≥2%)	4.5–10.3 (2.5–12.9)	✓	✓	✓	2, 5
Men who have sex with men		✓	✓	✓	
Aged <30 y	1.1–2.3 (0–3.0)				7, 37–40
Co-infected with HIV	7 (5–10)				7
U.S.-born persons not vaccinated as infants whose parents were born in regions with high prevalence (≥8%)	–	✓	✓	✓	–
Injection drug users	11.8 (3.5–20)	✓	✓	✓	41
Co-infected with HIV	7 (6–8)				7
HIV-positive persons	4–17 (–)	✓	✓	✓	7
Household contacts or sexual partners of persons with known HBV infection	3–20 (–)	✓	✓	✓	7
Pregnant women†	0.38 (–)	✓	✓	✓	42
Persons requiring immunosuppressive therapy	–		✓	✓	–
Persons with end-stage renal disease, including those receiving hemodialysis	2.8 (2.3–3.3)		✓	✓	43
Elevated alanine aminotransferase or aspartate aminotransferase levels	–		✓	✓	–
Infants born to HBsAg-positive mothers†	1.1 (–)		✓		44
Donors of blood, plasma, organs, tissue, or semen	–		✓		–
Persons who are sources of blood or body fluids for exposures that might require postexposure prophylaxis‡	–		✓		–
Inmates of correctional facilities	1.0–3.7			✓	45
Persons with HCV infection	1.4 (1.3–1.5)			✓	46
Persons with multiple sexual partners or a history of sexually transmitted infections	–			✓	–

AASLD = American Association for the Study of Liver Diseases; CDC = Centers for Disease Control and Prevention; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; USPSTF = U.S. Preventive Services Task Force.
* Where available.
† HBsAg testing only is recommended for all pregnant women, and HBsAg and antibody to HBsAg testing are recommended for infants born to HBV-infected mothers.
‡ Screening should be done only if needed after exposure.

women who are at risk during pregnancy (>1 sex partner during the previous 6 months, previous evaluation or treatment for a sexually transmitted infection, recent or current injection drug use, or HBsAg-positive sex partner); HIV-infected persons; international travelers to regions with high or intermediate levels of endemic HBV infection; and any adult seeking protection from HBV infection (18, 20, 33). Adults in the following settings are also assumed to be at risk: sexually transmitted disease treatment facilities, HIV testing and treatment facilities, facilities providing drug abuse treatment and preventive services, health care settings targeting injection drug users and MSM, correctional facilities, hemodialysis facilities and end-stage renal disease programs, and institutions and nonresidential day care facilities for developmentally disabled persons (18).

Hepatitis B vaccine is usually given as a 3- or 4-dose series, but higher dosages may be required for immunocompromised persons and those with end-stage renal disease (18, 34, 35). These persons should receive postvaccination testing, and those with suboptimal response (antibody to HBsAg level <10 mIU/mL) should be revaccinated (18, 34, 35).

Since the implementation of universal hepatitis B vaccination among infants and the ACIP's recommendations, there has been a significant decrease in the rate of acute HBV infection in adults (9.6 per 100 000 persons in 1982 vs. 1.1 per 100 000 persons in 2015) (18, 36) and the proportion of noninstitutionalized persons who have ever been infected with HBV (5.5% during 1988 to 1994 vs. 3.7% during 2007 to 2012) (1). Because of the low vaccination coverage and the risk for HBV transmission (13), increasing coverage among unvaccinated adults is essential.

Best Practice Advice 1

Clinicians should vaccinate against chronic hepatitis B virus (HBV) in all unvaccinated adults at risk for infection, including:

a. Adults at risk by sexual exposure (sex partners of hepatitis B surface antigen [HBsAg]-positive persons, sexually active persons who are not in a mutually monogamous relationship, persons seeking evaluation or treatment for a sexually transmitted infection, and men who have sex with men).

b. Adults at risk by percutaneous or mucosal exposure to blood (adults who are recent or current users of injection drugs; household contacts of HBsAg-positive persons; residents and staff of facilities for developmentally disabled persons; incarcerated, health care, and public safety workers at risk for exposure to blood or blood-contaminated body fluids).

c. Adults with chronic liver disease, including but not limited to hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level greater than twice the upper limit of normal.

d. Adults with end-stage renal disease, including those receiving predialysis care, hemodialysis, peritoneal dialysis, and home dialysis.

e. Adults with HIV infection.

f. Pregnant women who are at risk for hepatitis B virus infection during pregnancy (e.g., having more than 1 sex partner during the previous 6 months, having been evaluated or treated for a sexually transmitted infection, recent or current injection drug use, or having an HBsAg-positive sex partner).

g. International travelers to regions with high or intermediate levels of endemic hepatitis B virus infection.

h. Any adult seeking protection from HBV infection.

SCREENING

Current guidelines from the CDC (7), the USPSTF (19), and the AASLD (8) recommend screening for specific populations and persons at increased risk for chronic HBV infection. Table 1 summarizes these populations and at-risk groups, the prevalence of HBV infection among them, and screening recommendations. Although recommendations for some groups vary, all 3 organizations recommend screening for persons born in regions with intermediate-to-high prevalence of HBV infection (Table 2) or with other known HBV-related risks. In addition, prevaccination testing is recommended for health care personnel at increased risk for HBV infection and those who perform exposure-prone procedures (47). Despite these recommendations, screening in these groups is suboptimal (4, 11, 48, 49). Table 3 shows HBV screening seromarkers (HBsAg, antibody to HBsAg, and antibody to hepatitis B core antigen), associated clinical states, and recommended clinical management. Screening for HBV with HBsAg testing is only recommended for pregnant women.

Persons receiving chemotherapy or immunosuppressive therapy should be screened for HBV because of the risk for virus reactivation (21, 22, 26). Cases of HBV reactivation have also been reported among patients receiving direct-acting antivirals for hepatitis C virus infection (23–25). Reactivation can result in hepatocellular injury, fulminant hepatitis, liver failure, and death (21–26). Clinicians should therefore screen all patients receiving chemotherapy, immunosuppressive therapy, or direct-acting antivirals.

Table 2. Regions and Countries With HBV Prevalence of 2% or Higher

Region	HBV Prevalence ≥2%
Africa	All countries
Asia	All countries
Caribbean	Antigua and Barbuda, Dominica, Grenada, Haiti, Jamaica, St. Kitts, St. Lucia, and Turks and Caicos Islands
Central America	Guatemala and Honduras
Eastern Europe	All countries except Hungary
Middle East	All countries except Cyprus and Israel
North America	Indigenous populations in northern Canada
South America	Bolivia, Brazil, Colombia, Ecuador, Guyana, Suriname, and Venezuela
South Pacific	All countries except nonindigenous populations of Australia and New Zealand
Western Europe	Malta and indigenous populations of Greenland

HBV = hepatitis B virus.

Best Practice Advice 2

Clinicians should screen (hepatitis B surface antigen, antibody to hepatitis B core antigen, and antibody to hepatitis B surface antigen) for HBV in high-risk persons, including persons born in countries with 2% or higher HBV prevalence, men who have sex with men, persons who inject drugs, HIV-positive persons, household and sexual contacts of HBV-infected persons, persons requiring immunosuppressive therapy, persons with end-stage renal disease (including hemodialysis patients), blood and tissue donors, persons infected with hepatitis C virus, persons with elevated alanine aminotransferase levels (≥19 IU/L for women and ≥30 IU/L for men), incarcerated persons, pregnant women, and infants born to HBV-infected mothers.

LINKAGE TO CARE

Linkage to care is the process of referring patients with chronic HBV infection to medical care and ensuring that they receive directed care and treatment. Although not all patients with chronic HBV infection require treatment, they all should be routinely evaluated for hepatocellular carcinoma and treatment eligibility through history and physical examination (50, 51). Patients who are linked to care can achieve significant reductions in HBV-associated morbidity and mortality (4, 11, 52, 53). However, most persons with chronic HBV infection are not linked to care because they are unaware of their infection (4) or are not referred despite their diagnosis (54). Between 20% and 40% of persons with chronic HBV infection require treatment; however, all require monitoring of liver aminotransferase and HBV DNA levels (4, 8). Only 10% to 15% of eligible persons receive antiviral therapy, demonstrating that many who could benefit from therapy do not receive it (4). Linkage to care ensures that patients with chronic HBV infection receive treatment when they become eligible (elevated HBV DNA and liver aminotransferase levels), hepatocellular carcinoma surveillance, behavioral risk reduction counseling, and vaccination of susceptible sexual and household contacts (8, 18, 55).

Best Practice Advice 3

Clinicians should provide or refer all patients identified with HBV (HBsAg-positive) for posttest counseling and hepatitis B–directed care.

HARMS OF VACCINATION, SCREENING, AND LINKAGE TO CARE

Adverse effects from hepatitis B vaccination are rare and mild; the most common are soreness at the injection site (3% to 29%) and mild fever (1% to 6%) (18). Anaphylaxis after vaccine administration has been reported (56) but is rare, occurring once per 1.1 million doses (57). The vaccine is contraindicated in persons

Table 3. Antibody and Antigen Biomarkers for HBV Infection

Clinical State	HBsAg	Total Anti-HBs	Total Anti-HBc	Action
Chronic infection	Positive	Negative	Positive	Link to hepatitis B–directed care
Acute infection	Positive	Negative	Positive (IgM anti-HBc)	Link to hepatitis B–directed care
Resolved infection	Negative	Positive	Positive	Counseling, reassurance
Immune (vaccinated)	Negative	Positive	Negative	Reassurance
Susceptible (never infected and no evidence of vaccination)	Negative	Negative	Negative	Vaccination
Isolated core antibody*	Negative	Negative	Positive	Depends on situation

anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus.
* Can be the result of a false-positive result, which requires repeated testing; past infection or passive transfer to an infant born to an HBsAg-positive mother, which requires no action; or occult HBV infection, which needs to be known if the patient ever becomes immunosuppressed, receives chemotherapy, or is treated with antiviral therapy for hepatitis C virus infection and warrants consideration of monitoring of HBV DNA levels.

with yeast allergies because yeast is a component of the vaccine (58). Other harms of HBV screening and linkage to care include fear of a positive test result, stigma associated with HBV screening, feelings of shame and depression in infected persons, and treatment costs (16, 50).

Costs of Vaccination, Screening, and Linkage to Care

Hepatitis B vaccination, screening, and linkage to care are cost-effective (59–65). A study examined the cost-effectiveness of routine vaccination compared with no vaccination at a sexually transmitted infection clinic and showed that the incremental cost-effectiveness ratio (ICER) associated with routine vaccination was $3500 per quality-adjusted life-year (QALY) gained (66). Another analysis showed that screening of immigrants from HBV-endemic countries was cost-effective (<$50 000 per QALY gained) (63).

A study comparing the cost-effectiveness of 2 HBV screening strategies (screening and treatment, or screening and treatment of the index case patient and vaccination of their close contacts) versus voluntary screening among Asian or Pacific Island–born persons in the United States found ICERs of $36 088 per QALY gained for the first strategy and $39 903 per QALY gained for the second strategy (59). Similarly, a cost-effectiveness analysis of screening and treatment programs among Asian-born persons in the United States found that screening and treatment were cost-effective ($46 489 per QALY gained) compared with no screening (62). Another study compared the cost-effectiveness of early- versus late-stage treatment over a 20-year period. The study found an ICER of $19 505 per QALY gained at 10 years that progressively decreased to $5184 per QALY gained at 20 years among persons in the early-stage treatment group (61). More recent models have demonstrated the cost-effectiveness of screening and treatment or vaccination among groups with ICERs less than $18 009 (Centers for Disease Control and Prevention. Unpublished data).

Hepatitis B vaccination and screening are also cost-saving (7, 67). The price per vaccine dose ($24 to $62) is substantially lower than the medical costs associated with treatment of chronic HBV infection ($4000 to $26 000), decompensated cirrhosis ($38 932 to $153 110), and liver transplantation ($343 241 to $514 862) in the first year (60, 66–68). Furthermore, the cost of screening in populations with an HBsAg prevalence of at least 2% is $750 to $3752 per case of chronic HBV infection identified (7), significantly lower than the annual medical costs.

Discussion

What Is the Current State of Practice in the United States?

There are gaps in vaccination and screening of persons at risk for HBV infection. Current estimates show that vaccination coverage (≥3 doses) is 24.6% among adults aged 19 years or older (13) and is lower for black persons (29.4%) and Hispanic persons (22.5%) than white persons (34.9%) (13). Vaccination coverage among high-risk adults (MSM, injection drug users, and persons at risk for HIV and other sexually transmitted infections) is approximately 45% (69). In addition, coverage is approximately 20.7% among foreign-born adults in the United States compared with 25.5% among U.S.-born adults, 25.3% among adults with health insurance compared with 19.4% among those without, 27.4% among adults with chronic liver conditions, and 64.7% among health care personnel (13).

Prevalence of HBV screening is 11% to 67% among foreign-born persons (48, 70), 28% to 52% among MSM (49, 71), and approximately 28% among patients receiving chemotherapy (72). The prevalence of guideline-adherent treatment and care among persons with chronic HBV infection is low (4, 73, 74). Between 10% and 15% of eligible persons in the United States receive treatment (4), 40% to 78% of patients with chronic HBV infection receive recommended ALT monitoring (54, 73, 75), and fewer than 40% are monitored for HBV DNA (54, 73). Periodic assessment of ALT and HBV DNA levels is important to evaluate disease progression and treatment eligibility.

Why Does Practice Not Follow the Evidence?

Many barriers contribute to low rates of hepatitis B vaccination, screening, and linkage to care, especially in foreign-born populations (76–80). Patient-level barriers include lack of knowledge about chronic HBV in-

Table 4. Barriers to Evidence-Based Practice of Vaccination, Screening, and Linkage to Care for Chronic HBV Infection and Approaches to Overcome Them

Level	Barriers to Evidence-Based Practice	Approaches to Overcome Barriers
Patient	Lack of awareness about chronic HBV infection and the health benefits of the hepatitis B vaccine Low educational and socioeconomic levels Lack of health insurance coverage and difficulty navigating the health care system Stigma associated with chronic HBV infection and fear of a positive test result	Increase patients' knowledge about risk for and severity of chronic HBV infection and benefits of screening, vaccination, and treatment.
Clinician	Lack of awareness about risk for chronic HBV infection in high-risk populations Lack of routine assessment of adult vaccine needs and HBV risk during clinical encounters Low level of awareness of guideline-based recommendations on treatment and monitoring of chronic HBV infection Some clinical practices may not routinely store hepatitis B vaccine	Routinely assess HBV risk and vaccine needs during clinical encounters. Increase clinicians' awareness about groups at risk for chronic HBV infection. Vaccinate all patients at risk for HBV infection. Screen all patients at high risk for chronic HBV infection. Monitor patients with chronic HBV infection periodically to determine disease progression and initiate treatment when indicated. Refer to a liver specialist or hepatitis B–experienced health care provider when patients with chronic HBV infection become eligible for treatment. Clinical practices that do not stock the hepatitis B vaccine can refer susceptible patients to the local health department or to larger clinical practices that do.
System	A complex health care system that may require referral to a liver specialist can present challenges to persons who lack knowledge about how the health care system works.	Use EMR prompts and reminders, standing orders, and patient reminder systems to improve hepatitis B vaccination and screening. Use culturally and linguistically competent peer navigators in health care settings to increase the number of patients who receive hepatitis B–directed care and to facilitate continuity of care.

EMR = electronic medical record; HBV = hepatitis B virus.

fection, ignorance about the hepatitis B vaccine and its health benefits, misinformation about vaccines, low levels of English language proficiency, cultural and language differences, lack of health insurance or access to health care resources, and difficulty navigating the health care system (76, 77). In some communities, stigma associated with chronic HBV infection and fear of a positive test result can present challenges to screening and care (80, 81).

Clinician-level barriers include a lack of awareness about clinical care guidelines and the risk for chronic HBV infection in certain populations (76, 82, 83), resulting in missed opportunities for vaccination or screening (79). Failure to screen for HBV infection or monitor liver aminotransferase and HBV DNA levels and lack of awareness of current treatment guidelines among physicians are some reasons that many treatment-eligible patients are missed (4, 79). The hepatitis B vaccine may also not be routinely stored in some clinical practices, and this can present challenges to vaccination in the clinical setting (84).

System-level barriers include limited hepatitis B funding for programs for uninsured adults (74) and the complexities surrounding payments for adult vaccines by insurers (85). The complex health care system, which may require referral to a liver specialist or an HBV-experienced health care provider, may present a barrier to persons who lack knowledge about the way the health care system works (77).

Evidence-Based Strategies to Increase Hepatitis B Vaccination, Screening, and Linkage to Care

Various strategies have been implemented in clinical and community settings to increase hepatitis B vaccination, screening, and linkage to care (86–92). Partnerships between community-based programs and local health centers with culturally and linguistically competent patient navigators have proved effective in increasing patient awareness of chronic HBV infection, identifying infected adults, vaccinating susceptible persons, linking infected persons to care and complementary resources, and overcoming cultural and linguistic barriers to high-quality care (87–90, 92). The provisions of the Patient Protection and Affordable Care Act can increase vaccination coverage because they enable uninsured susceptible adults to receive the vaccine without cost sharing (93).

Clinicians should routinely assess HBV risk and vaccine needs, discuss health benefits of vaccination and screening during clinical encounters, and offer vaccination and screening when indicated (84). When a patient is infected with HBV, household and sexual contacts should be screened, susceptible contacts should be vaccinated, and infected contacts should be linked to care. Increasing clinicians' awareness of the importance of HBV screening, monitoring liver aminotransferase and HBV DNA levels, and adherence to treatment guidelines can increase the number of eligible patients receiving treatment (4, 79). Clinical practices that do not stock the hepatitis B vaccine can coordinate with local health departments or large practices that stock the vaccine to refer susceptible patients and ensure they are vaccinated (94).

The Community Preventive Services Task Force has recommended clinician-based or health care system–based interventions, including electronic medical record (EMR) prompts, provider education, vaccine recommendation by a provider, standing orders or protocols for HBV screening and vaccination, and patient reminders and recall systems when vaccines are due (91). In the Indian Health Service, EMR prompts

and standing orders resulted in substantially higher vaccination coverage than national estimates (95). A randomized study also showed that health care providers who received EMR prompts ordered significantly more screening tests than those who did not (40.9% vs. 1.1% [$P < 0.001$]) (86).

Including hepatitis B vaccination as part of routine preventive services to all unvaccinated adults in settings with a high proportion of adults with risk factors for HBV infection (sexually transmitted infection clinics, health care facilities that serve injection drug users and MSM, and correctional health care facilities) is another useful strategy (66). Software algorithms have been successfully used to identify names associated with foreign birth so that EMR reminders can prompt the provider to assess HBV screening and vaccination status (96, 97). This system can complement existing strategies to identify patients at risk for chronic HBV infection. Culturally competent peer navigators can also mitigate system-level barriers that a complex health care system may present to patients with chronic HBV infection (98, 99). Table 4 summarizes barriers at the patient, clinician, and system level and strategies to overcome them.

The current low hepatitis B vaccination coverage among adults necessitates reconsideration of the existing risk-based vaccination strategy. Because the administration schedule typically includes 3 vaccine doses over 6 months, the vaccine series needs to be started and completed before exposure to the risk factor to protect persons at greatest risk. Furthermore, the multitude of factors constituting an indication for adult hepatitis B vaccination can create implementation challenges for vaccine providers. An adult vaccination strategy that is not based on risk may be the next step toward achieving elimination.

The burden and costs associated with chronic HBV infection in the United States are high. Vaccination of susceptible adults is important to prevent infection and reduce ongoing transmission. Screening in high-risk populations is the first step in the care cascade to identify persons with chronic HBV infection, and vaccination and linkage to care are effective at reducing HBV-associated morbidity and mortality. The best practice advice statements in this article amplify and complement existing clinical guidelines by reiterating the importance of hepatitis B vaccination and screening in at-risk persons and linking infected persons to care. Evidence-based strategies that effectively implement this advice are critical to accomplishing the goals of the national hepatitis B elimination plan.

From Centers for Disease Control and Prevention, Atlanta, Georgia; American College of Physicians, Philadelphia, Pennsylvania; and Alaska Native Tribal Health Consortium and Centers for Disease Control and Prevention, Anchorage, Alaska.

Disclaimer: The conclusions, findings, and opinions expressed by the authors do not necessarily reflect the official position of the Centers for Disease Control and Prevention.

Financial Support: Financial support for the development of this paper comes exclusively from the ACP operating budget.

Disclosures: Dr. McMahon reports that the program he works in, the Alaska Native Tribal Health Consortium Liver Disease and Hepatitis Program (a nonprofit managed care system serving American Indians and Alaska Natives), has 2 research grants from Gilead Sciences for hepatitis C treatment. Dr. McMahon is not an investigator listed on these grants but does see patients who receive free hepatitis C medications supplied by Gilead Sciences in the course of his patient care duties. Dr. Lohr reports that he is the Treasurer of the American College of Physicians. Dr. McLean reports personal fees from Takeda Pharmaceuticals outside the submitted work and is a member of the American College of Physicians Clinical Guidelines Committee and the American College of Rheumatology Quality of Care Committee. Authors not named here have disclosed no conflicts of interest. Authors followed the policy regarding conflicts of interest described at www.annals.org/article.aspx?articleid=745942. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M17-1106. All financial and intellectual disclosures of interest were declared and potential conflicts were discussed and managed. No individuals were recused from discussion or voting due to conflicts of interest. A record of disclosures of interest is kept for each High Value Care Task Force meeting and conference call and can be viewed at www.acponline.org/clinical-information/high-value-care.

Requests for Single Reprints: Amir Qaseem, MD, PhD, MHA, American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106; e-mail, aqaseem@acponline.org.

Current author addresses and author contributions are available at Annals.org.

References

1. **Roberts H, Kruszon-Moran D, Ly KN, Hughes E, Iqbal K, Jiles RB, et al.** Prevalence of chronic hepatitis B virus (HBV) infection in U.S. households: National Health and Nutrition Examination Survey (NHANES), 1988–2012. Hepatology. 2016;63:388-97. [PMID: 26251317] doi:10.1002/hep.28109

2. **Mitchell T, Armstrong GL, Hu DJ, Wasley A, Painter JA.** The increasing burden of imported chronic hepatitis B–United States, 1974–2008. PLoS One. 2011;6:e27717. [PMID: 22163270] doi:10.1371/journal.pone.0027717

3. **Lin SY, Chang ET, So SK.** Why we should routinely screen Asian American adults for hepatitis B: a cross-sectional study of Asians in California. Hepatology. 2007;46:1034-40. [PMID: 17654490]

4. **Cohen C, Holmberg SD, McMahon BJ, Block JM, Brosgart CL, Gish RG, et al.** Is chronic hepatitis B being undertreated in the United States? J Viral Hepat. 2011;18:377-83. [PMID: 21143343] doi:10.1111/j.1365-2893.2010.01401.x

5. **Kowdley KV, Wang CC, Welch S, Roberts H, Brosgart CL.** Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. Hepatology. 2012;56:422-33. [PMID: 22105832] doi:10.1002/hep.24804

6. **Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ.** Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet. 2015;386:1546-55. [PMID: 26231459] doi:10.1016/S0140-6736(15)61412-X

7. **Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, et al; Centers for Disease Control and Prevention (CDC).** Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. MMWR Recomm Rep. 2008;57:1-20. [PMID: 18802412]
8. **Lok AS, McMahon BJ.** Chronic hepatitis B. Hepatology. 2007;45: 507-39. [PMID: 17256718]
9. **McMahon BJ.** The natural history of chronic hepatitis B virus infection. Hepatology. 2009;49:S45-55. [PMID: 19399792] doi:10.1002 /hep.22898
10. **McMahon BJ.** Natural history of chronic hepatitis B. Clin Liver Dis. 2010;14:381-96. [PMID: 20638020] doi:10.1016/j.cld.2010.05.007
11. **Ward JW, Lok AS, Thomas DL, El-Serag HB, Kim WR.** Report on a single-topic conference on "Chronic viral hepatitis–strategies to improve effectiveness of screening and treatment." Hepatology. 2012;55:307-15. [PMID: 22105599] doi:10.1002/hep.24797
12. **Cohen C, Evans AA, London WT, Block J, Conti M, Block T.** Underestimation of chronic hepatitis B virus infection in the United States of America [Letter]. J Viral Hepat. 2008;15:12-3. [PMID: 18088239]
13. **Williams WW, Lu PJ, O'Halloran A, Kim DK, Grohskopf LA, Pilishvili T, et al.** Surveillance of vaccination coverage among adult populations–United States, 2015. MMWR Surveill Summ. 2017;66:1-28. [PMID: 28472027] doi:10.15585/mmwr.ss6611a1
14. **Kim CH, Um SH, Seo YS, Jung JY, Kim JD, Yim HJ, et al.** Prognosis of hepatitis B-related liver cirrhosis in the era of oral nucleos(t)ide analog antiviral agents. J Gastroenterol Hepatol. 2012;27: 1589-95. [PMID: 22554121] doi:10.1111/j.1440-1746.2012.07167.x
15. **McMahon BJ.** Chronic hepatitis B virus infection. Med Clin North Am. 2014;98:39-54. [PMID: 24266913] doi:10.1016/j.mcna.2013.08 .004
16. **National Academies of Sciences, Engineering, and Medicine.** Eliminating the Public Health Problem of Hepatitis B and C in the United States: Phase One Report. Washington, DC: National Academies Pr; 2016. doi:10.17226/23407
17. **U.S. Department of Health and Human Services.** Viral Hepatitis Action Plan Overview. 2016. Accessed at www.hhs.gov/hepatitis /action-plan/u-s-viral-hepatitis-action-plan-overview/index.html on 2 June 2016.
18. **Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al; Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC).** A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. MMWR Recomm Rep. 2006;55:1-33. [PMID: 17159833]
19. **LeFevre ML; U.S. Preventive Services Task Force.** Screening for hepatitis B virus infection in nonpregnant adolescents and adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2014;161:58-66. [PMID: 24863637] doi:10.7326/M14 -1018
20. **Kim DK, Riley LE, Harriman KH, Hunter P, Bridges CB; Advisory Committee on Immunization Practices.** Recommended immunization schedule for adults aged 19 years or older, United States, 2017. Ann Intern Med. 2017;166:209-19. [PMID: 28166560] doi:10.7326/ M16-2936
21. **Lok AS, Ward JW, Perrillo RP, McMahon BJ, Liang TJ.** Reactivation of hepatitis B during immunosuppressive therapy: potentially fatal yet preventable. Ann Intern Med. 2012;156:743-5. [PMID: 22586011] doi:10.7326/0003-4819-156-10-201205150-00013
22. **Lalazar G, Rund D, Shouval D.** Screening, prevention and treatment of viral hepatitis B reactivation in patients with haematological malignancies. Br J Haematol. 2007;136:699-712. [PMID: 17338776]
23. **Collins JM, Raphael KL, Terry C, Cartwright EJ, Pillai A, Anania FA, et al.** Hepatitis B virus reactivation during successful treatment of hepatitis C virus with sofosbuvir and simeprevir. Clin Infect Dis. 2015; 61:1304-6. [PMID: 26082511] doi:10.1093/cid/civ474
24. **Wang C, Ji D, Chen J, Shao Q, Li B, Liu J, et al.** Hepatitis due to reactivation of hepatitis B virus in endemic areas among patients with hepatitis C treated with direct-acting antiviral agents. Clin Gastroenterol Hepatol. 2017;15:132-6. [PMID: 27392759] doi:10.1016/j.cgh .2016.06.023
25. **Bersoff-Matcha SJ, Cao K, Jason M, Ajao A, Jones SC, Meyer T, et al.** Hepatitis B virus reactivation associated with direct-acting antiviral therapy for chronic hepatitis C virus: a review of cases reported to the U.S. Food and Drug Administration Adverse Event Reporting System. Ann Intern Med. 2017;166:792-8. [PMID: 28437794] doi:10 .7326/M17-0377
26. **Paul S, Saxena A, Terrin N, Viveiros K, Balk EM, Wong JB.** Hepatitis B virus reactivation and prophylaxis during solid tumor chemotherapy: a systematic review and meta-analysis. Ann Intern Med. 2016;164:30-40. [PMID: 26595058] doi:10.7326/M15-1121
27. **American Association for the Study of Liver Diseases; Infectious Diseases Society of America.** HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. 2017. Accessed at www.hcvguidelines.org/sites/default/files/full-guidance-pdf/HCV Guidance_April_12_2017_b.pdf on 17 October 2017.
28. **Assad S, Francis A.** Over a decade of experience with a yeast recombinant hepatitis B vaccine. Vaccine. 1999;18:57-67. [PMID: 10501235]
29. **Venters C, Graham W, Cassidy W.** Recombivax-HB: perspectives past, present and future. Expert Rev Vaccines. 2004;3:119-29. [PMID: 15056038]
30. **McMahon BJ, Bulkow LR, Singleton RJ, Williams J, Snowball M, Homan C, et al.** Elimination of hepatocellular carcinoma and acute hepatitis B in children 25 years after a hepatitis B newborn and catch-up immunization program. Hepatology. 2011;54:801-7. [PMID: 21618565] doi:10.1002/hep.24442
31. **Bruce MG, Bruden D, Hurlburt D, Zanis C, Thompson G, Rea L, et al.** Antibody levels and protection after hepatitis B vaccine: results of a 30-year follow-up study and response to a booster dose. J Infect Dis. 2016;214:16-22. [PMID: 26802139] doi:10.1093/infdis/jiv748
32. **Simons BC, Spradling PR, Bruden DJ, Zanis C, Case S, Choromanski TL, et al.** A longitudinal hepatitis B vaccine cohort demonstrates long-lasting hepatitis B virus (HBV) cellular immunity despite loss of antibody against HBV surface antigen. J Infect Dis. 2016;214: 273-80. [PMID: 27056956] doi:10.1093/infdis/jiw142
33. **Centers for Disease Control and Prevention (CDC).** Use of hepatitis B vaccination for adults with diabetes mellitus: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 2011;60:1709-11. [PMID: 22189894]
34. **Centers for Disease Control and Prevention.** Guidelines for Vaccinating Kidney Dialysis Patients and Patients with Chronic Kidney Disease. July 2015. Accessed at www.cdc.gov/vaccines/pubs/down loads/dialysis-guide-2012.pdf on 2 June 2016.
35. **Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al; Infectious Diseases Society of America.** 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis. 2014;58:e44-100. [PMID: 24311479] doi:10.1093 /cid/cit684
36. **Centers for Disease Control and Prevention.** Viral Hepatitis Surveillance: United States, 2015. Accessed at www.cdc.gov/hepatitis /statistics/2015surveillance/pdfs/2015HepSurveillanceRpt.pdf on 2 June 2017.
37. **Seage GR 3rd, Mayer KH, Lenderking WR, Wold C, Gross M, Goldstein R, et al.** HIV and hepatitis B infection and risk behavior in young gay and bisexual men. Public Health Rep. 1997;112:158-67. [PMID: 9071279]
38. **MacKellar DA, Valleroy LA, Secura GM, McFarland W, Shehan D, Ford W, et al; Young Men's Survey Study Group.** Two decades after vaccine license: hepatitis B immunization and infection among young men who have sex with men. Am J Public Health. 2001;91: 965-71. [PMID: 11392942]
39. **Weinbaum CM, Lyerla R, Mackellar DA, Valleroy LA, Secura GM, Behel SK, et al; Young Men's Survey Study Group.** The Young Men's Survey phase II: hepatitis B immunization and infection among young men who have sex with men. Am J Public Health. 2008;98: 839-45. [PMID: 18382012] doi:10.2105/AJPH.2006.101915
40. **Wilkins T, Zimmerman D, Schade RR.** Hepatitis B: diagnosis and treatment. Am Fam Physician. 2010;81:965-72. [PMID: 20387772]

41. **Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al.** Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet. 2011; 378:571-83. [PMID: 21802134] doi:10.1016/S0140-6736(11) 61097-0
42. **Walker TY, Smith EA, Fenlon N, Lazaroff JE, Dusek C, Fineis P, et al.** Characteristics of pregnant women with hepatitis B virus infection in 5 US public health jurisdictions, 2008–2012. Public Health Rep. 2016; 131(5):685-694. [PMID: 28123209]
43. **Burdick RA, Bragg-Gresham JL, Woods JD, Hedderwick SA, Kurokawa K, Combe C, et al.** Patterns of hepatitis B prevalence and seroconversion in hemodialysis units from three continents: the DOPPS. Kidney Int. 2003;63:2222-9. [PMID: 12753311]
44. **Schillie S, Walker T, Veselsky S, Crowley S, Dusek C, Lazaroff J, et al.** Outcomes of infants born to women infected with hepatitis B. Pediatrics. 2015;135:e1141-7. [PMID: 25896839] doi:10.1542/peds .2014-3213
45. **Weinbaum C, Lyerla R, Margolis HS.** Prevention and Control of Infections with Hepatitis Viruses in Correctional Settings. Waltham, MA: Massachusetts Medical Society; 2003.
46. **Tyson GL, Kramer JR, Duan Z, Davila JA, Richardson PA, El-Serag HB.** Prevalence and predictors of hepatitis B virus coinfection in a United States cohort of hepatitis C virus-infected patients. Hepatology. 2013;58:538-45. [PMID: 23505059] doi:10.1002/hep.26400
47. **Centers for Disease Control and Prevention (CDC).** Updated CDC recommendations for the management of hepatitis B virus-infected health-care providers and students. MMWR Recomm Rep. 2012;61:1-12. [PMID: 22763928]
48. **Waldorf B, Gill C, Crosby SS.** Assessing adherence to accepted national guidelines for immigrant and refugee screening and vaccines in an urban primary care practice: a retrospective chart review. J Immigr Minor Health. 2014;16:839-45. [PMID: 23512323] doi:10 .1007/s10903-013-9808-6
49. **Hechter RC, Jacobsen SJ, Luo Y, Nomura JH, Towner WJ, Tartof SY, et al.** Hepatitis B testing and vaccination among adults with sexually transmitted infections in a large managed care organization. Clin Infect Dis. 2014;58:1739-45. [PMID: 24571863] doi:10 .1093/cid/ciu103
50. **Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH; American Association for the Study of Liver Diseases.** AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2016;63:261-83. [PMID: 26566064] doi:10.1002/hep.28156
51. **Bruix J, Sherman M; American Association for the Study of Liver Diseases.** Management of hepatocellular carcinoma: an update. Hepatology. 2011;53:1020-2. [PMID: 21374666] doi:10.1002/hep .24199
52. **Lai CL, Yuen MF.** Prevention of hepatitis B virus-related hepatocellular carcinoma with antiviral therapy. Hepatology. 2013;57:399-408. [PMID: 22806323] doi:10.1002/hep.25937
53. **Gordon SC, Lamerato LE, Rupp LB, Li J, Holmberg SD, Moorman AC, et al; CHeCS Investigators.** Antiviral therapy for chronic hepatitis B virus infection and development of hepatocellular carcinoma in a US population. Clin Gastroenterol Hepatol. 2014;12:885-93. [PMID: 24107395] doi:10.1016/j.cgh.2013.09.062
54. **Spradling PR, Xing J, Rupp LB, Moorman AC, Gordon SC, Teshale ET, et al; Chronic Hepatitis Cohort Study (CHeCS) Investigators.** Infrequent clinical assessment of chronic hepatitis B patients in United States general healthcare settings. Clin Infect Dis. 2016;63: 1205-8. [PMID: 27486115]
55. **Lok AS, McMahon BJ, Brown RS Jr, Wong JB, Ahmed AT, Farah W, et al.** Antiviral therapy for chronic hepatitis B viral infection in adults: a systematic review and meta-analysis. Hepatology. 2016;63: 284-306. [PMID: 26566246] doi:10.1002/hep.28280
56. **Stratton KR, Howe CJ, Johnston RB Jr.** Adverse events associated with childhood vaccines other than pertussis and rubella. Summary of a report from the Institute of Medicine. JAMA. 1994;271: 1602-5. [PMID: 8182813]
57. **Bohlke K, Davis RL, Marcy SM, Braun MM, DeStefano F, Black SB, et al; Vaccine Safety Datalink Team.** Risk of anaphylaxis after vaccination of children and adolescents. Pediatrics. 2003;112:815-20. [PMID: 14523172]
58. **André FE.** Summary of safety and efficacy data on a yeast-derived hepatitis B vaccine. Am J Med. 1989;87:14S-20S. [PMID: 2528292]
59. **Hutton DW, Tan D, So SK, Brandeau ML.** Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B. Ann Intern Med. 2007;147:460-9. [PMID: 17909207]
60. **Eckman MH, Kaiser TE, Sherman KE.** The cost-effectiveness of screening for chronic hepatitis B infection in the United States. Clin Infect Dis. 2011;52:1294-306. [PMID: 21540206] doi:10.1093 /cid/cir199
61. **Post SE, Sodhi NK, Peng CH, Wan K, Pollack HJ.** A simulation shows that early treatment of chronic hepatitis B infection can cut deaths and be cost-effective. Health Aff (Millwood). 2011;30:340-8. [PMID: 21289356] doi:10.1377/hlthaff.2008.0905
62. **Li F, Hutton DW, Abdel-Rasoul M, Kirkpatrick RB, Hanje AJ.** A cost effectiveness analysis of a community-based HBV screening and treatment program conducted among an Asian population in Central Ohio. Hepatology. 2012;56(Suppl 1):93A.
63. **Rossi C, Schwartzman K, Oxlade O, Klein MB, Greenaway C.** Hepatitis B screening and vaccination strategies for newly arrived adult Canadian immigrants and refugees: a cost-effectiveness analysis. PLoS One. 2013;8:e78548. [PMID: 24205255] doi:10.1371/journal .pone.0078548
64. **Veldhuijzen IK, Toy M, Hahné SJ, De Wit GA, Schalm SW, de Man RA, et al.** Screening and early treatment of migrants for chronic hepatitis B virus infection is cost-effective. Gastroenterology. 2010; 138:522-30. [PMID: 19879275] doi:10.1053/j.gastro.2009.10.039
65. **Barbosa C, Smith EA, Hoerger TJ, Fenlon N, Schillie SF, Bradley C, et al.** Cost-effectiveness analysis of the national Perinatal Hepatitis B Prevention Program. Pediatrics. 2014;133:243-53. [PMID: 24394684] doi:10.1542/peds.2013-0718
66. **Kim SY, Billah K, Lieu TA, Weinstein MC.** Cost effectiveness of hepatitis B vaccination at HIV counseling and testing sites. Am J Prev Med. 2006;30:498-506. [PMID: 16704944]
67. **Centers for Disease Control and Prevention.** CDC Vaccine Price List. 2016. Accessed at www.cdc.gov/vaccines/programs/vfc /awardees/vaccine-management/price-list on 1 June 2016.
68. **Hoerger TJ, Schillie S, Wittenborn JS, Bradley CL, Zhou F, Byrd K, et al.** Cost-effectiveness of hepatitis B vaccination in adults with diagnosed diabetes. Diabetes Care. 2013;36:63-9. [PMID: 22933435] doi:10.2337/dc12-0759
69. **Centers for Disease Control and Prevention (CDC).** Hepatitis B vaccination coverage among adults–United States, 2004. MMWR Morb Mortal Wkly Rep. 2006;55:509-11. [PMID: 16691181]
70. **Vijayadeva V, Spradling PR, Moorman AC, Rupp LB, Lu M, Gordon SC, et al.** Hepatitis B virus infection testing and prevalence among Asian and Pacific Islanders. Am J Manag Care. 2014;20:e98-e104. [PMID: 24884958]
71. **Hoover KW, Butler M, Workowski KA, Follansbee S, Gratzer B, Hare CB, et al; Evaluation Group for Adherence to STD and Hepatitis Screening.** Low rates of hepatitis screening and vaccination of HIV-infected MSM in HIV clinics. Sex Transm Dis. 2012;39:349-53. [PMID: 22504597] doi:10.1097/OLQ.0b013e318244a923
72. **Hwang JP, Somerfield MR, Alston-Johnson DE, Cryer DR, Feld JJ, Kramer BS, et al.** Hepatitis B virus screening for patients with cancer before therapy: American Society of Clinical Oncology provisional clinical opinion update. J Clin Oncol. 2015;33:2212-20. [PMID: 25964247] doi:10.1200/JCO.2015.61.3745
73. **Juday T, Tang H, Harris M, Powers AZ, Kim E, Hanna GJ.** Adherence to chronic hepatitis B treatment guideline recommendations for laboratory monitoring of patients who are not receiving antiviral treatment. J Gen Intern Med. 2011;26:239-44. [PMID: 20978862] doi: 10.1007/s11606-010-1549-9
74. **Wong CR, Garcia RT, Trinh HN, Lam KD, Ha NB, Nguyen HA, et al.** Adherence to screening for hepatocellular carcinoma among patients with cirrhosis or chronic hepatitis B in a community setting. Dig Dis Sci. 2009;54:2712-21. [PMID: 19876735] doi:10.1007 /s10620-009-1015-x

75. **Sarkar M, Shvachko VA, Ready JB, Pauly MP, Terrault NA, Peters MG, et al.** Characteristics and management of patients with chronic hepatitis B in an integrated care setting. Dig Dis Sci. 2014;59:2100-8. [PMID: 24728968] doi:10.1007/s10620-014-3142-2
76. **Hu KQ, Pan CQ, Goodwin D.** Barriers to screening for hepatitis B virus infection in Asian Americans. Dig Dis Sci. 2011;56:3163-71. [PMID: 21861105] doi:10.1007/s10620-011-1840-6
77. **Sriphanlop P, Jandorf L, Kairouz C, Thelemaque L, Shankar H, Perumalswami P.** Factors related to hepatitis B screening among Africans in New York City. Am J Health Behav. 2014;38:745-54. [PMID: 24933144] doi:10.5993/AJHB.38.5.12
78. **Upadhyaya N, Chang R, Davis C, Conti MC, Salinas-Garcia D, Tang H.** Chronic hepatitis B: perceptions in Asian American communities and diagnosis and management practices among primary care physicians. Postgrad Med. 2010;122:165-75. [PMID: 20861600] doi:10.3810/pgm.2010.09.2213
79. **Ferrante JM, Winston DG, Chen PH, de la Torre AN.** Family physicians' knowledge and screening of chronic hepatitis and liver cancer. Fam Med. 2008;40:345-51. [PMID: 18465284]
80. **Yoo GJ, Fang T, Zola J, Dariotis WM.** Destigmatizing hepatitis B in the Asian American community: lessons learned from the San Francisco Hep B Free Campaign. J Cancer Educ. 2012;27:138-44. [PMID: 21748476] doi:10.1007/s13187-011-0252-9
81. **Hu KQ.** Hepatitis B virus (HBV) infection in Asian and Pacific Islander Americans (APIAs): how can we do better for this special population? Am J Gastroenterol. 2008;103:1824-33. [PMID: 18479498] doi:10.1111/j.1572-0241.2008.01878.x
82. **Caballero JB, Martin M, Weir RC, Agbayani N, Soon NA, Chen K.** Hepatitis B prevention and care for Asian Americans, Native Hawaiians and Pacific Islanders at community health centers. J Health Care Poor Underserved. 2012;23:1547-57. [PMID: 23698669] doi:10.1353/hpu.2012.0186
83. **Burman BE, Mukhtar NA, Toy BC, Nguyen TT, Chen AH, Yu A, et al.** Hepatitis B management in vulnerable populations: gaps in disease monitoring and opportunities for improved care. Dig Dis Sci. 2014;59:46-56. [PMID: 24052195] doi:10.1007/s10620-013-2870-z
84. **McHugh JA, Cullison S, Apuzzio J, Block JM, Cohen C, Leong SL, et al.** Chronic hepatitis B infection: a workshop consensus statement and algorithm. J Fam Pract. 2011;60:E1-8. [PMID: 21901174]
85. **Williams WW, Lu PJ, O'Halloran A, Kim DK, Grohskopf LA, Pilishvili T, et al; Centers for Disease Control and Prevention (CDC).** Surveillance of vaccination coverage among adult populations–United States, 2014. MMWR Surveill Summ. 2016;65:1-36. [PMID: 26844596] doi:10.15585/mmwr.ss6501a1
86. **Hsu L, Bowlus CL, Stewart SL, Nguyen TT, Dang J, Chan B, et al.** Electronic messages increase hepatitis B screening in at-risk Asian American patients: a randomized, controlled trial. Dig Dis Sci. 2013;58:807-14. [PMID: 23073671] doi:10.1007/s10620-012-2396-9
87. **Rein DB, Lesesne SB, Smith BD, Weinbaum CM.** Models of community-based hepatitis B surface antigen screening programs in the U.S. and their estimated outcomes and costs. Public Health Rep. 2011;126:560-7. [PMID: 21800750]
88. **Chandrasekar E, Kaur R, Song S, Kim KE.** A comparison of effectiveness of hepatitis B screening and linkage to care among foreign-born populations in clinical and nonclinical settings. J Multidiscip Healthc. 2015;8:1-9. [PMID: 25609976] doi:10.2147/JMDH.S75239
89. **Beckett GA, Ramirez G, Vanderhoff A, Nichols K, Chute SM, Wyles DL, et al; Centers for Disease Control and Prevention (CDC).** Early identification and linkage to care of persons with chronic hepatitis B virus infection–three U.S. sites, 2012–2014. MMWR Morb Mortal Wkly Rep. 2014;63:399-401. [PMID: 24807238]
90. **Perumalswami PV, Factor SH, Kapelusznik L, Friedman SL, Pan CQ, Chang C, et al.** Hepatitis Outreach Network: a practical strategy for hepatitis screening with linkage to care in foreign-born communities. J Hepatol. 2013;58:890-7. [PMID: 23333446] doi:10.1016/j.jhep.2013.01.004
91. **The Community Guide.** Increasing appropriate vaccination. 2016. Accessed at www.thecommunityguide.org/vaccines/index.html on 2 June 2016.
92. **Harris AM, Schoenbachler BT, Ramirez G, Vellozzi C, Beckett GA.** Testing and linking foreign-born people with chronic hepatitis B virus infection to care at nine U.S. programs, 2012–2014. Public Health Rep. 2016;131 Suppl 2:20-8. [PMID: 27168657]
93. **U.S. Department of Health and Human Services.** Affordable Care Act and Immunization. 2010. Accessed at www.hhs.gov/healthcare/facts-and-features/fact-sheets/aca-and-immunization/index.html on 2 June 2016.
94. **Association of Immunization Managers.** Immunization Program Manager Contacts. Rockville, MD: Association of Immunization Managers; 2016. Accessed at www.immunizationmanagers.org/?MemPage on 2 June 2016.
95. **Bridges CB, Hurley LP, Williams WW, Ramakrishnan A, Dean AK, Groom AV.** Meeting the challenges of immunizing adults. Vaccine. 2015;33 Suppl 4:D114-20. [PMID: 26615170] doi:10.1016/j.vaccine.2015.09.054
96. **van Gemert C, Wang J, Simmons J, Cowie B, Boyle D, Stoove M, et al.** Improving the identification of priority populations to increase hepatitis B testing rates, 2012. BMC Public Health. 2016;16:95. [PMID: 26832144] doi:10.1186/s12889-016-2716-7
97. **MacLachlan JH, Wang YJ, Cowie BC.** A validation of the use of names to screen for risk of chronic hepatitis B in Victoria, Australia, 2001 to 2010. Euro Surveill. 2013;18. [PMID: 24300885]
98. **Ramirez G, Cabral R, Patterson M, Schoenbachler BT, Bedell D, Smith BD, et al.** Early identification and linkage to care for people with chronic HBV and HCV infection: the HepTLC Initiative. Public Health Rep. 2016;131 Suppl 2:5-11. [PMID: 27168655]
99. **Ward JW.** Strategies for expanding access to HBV and HCV testing and care in the United States: the CDC Hepatitis Testing and Linkage to Care Initiative, 2012–2014. Public Health Rep. 2016;131:1-4. doi:10.1177/00333549161310S201

Current Author Addresses: Drs. Abara, Schillie, and Harris: Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, MS G-37, Atlanta, GA 30333.
Dr. Qaseem: American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.
Dr. McMahon: Arctic Investigations Program, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, 4055 Tudor Center Drive, Anchorage, AK 99508.

Author Contributions: Conception and design: W.E. Abara, A. Qaseem, B.J. McMahon, A.M. Harris, D.M. DeLong, A.M. López, R.M. McLean.
Analysis and interpretation of the data: W.E. Abara, A. Qaseem, B.J. McMahon, A.M. Harris, R. Centor, J.A. Jokela, A.M. López, R.M. McLean.
Drafting of the article: W.E. Abara, A. Qaseem, B.J. McMahon, A.M. Harris.
Critical revision of the article for important intellectual content: W.E. Abara, S. Schillie, B.J. McMahon, A.M. Harris, G.M. Abraham, R. Centor, D.M. DeLong, L.L. Humphrey, J.A. Jokela, R.H. Lohr, A.M. López, R.M. McLean.
Final approval of the article: W.E. Abara, A. Qaseem, S. Schillie, B.J. McMahon, A.M. Harris, G.M. Abraham, R. Centor, D.M. DeLong, H.E. Gantzer, C.A. Horwitch, L.L. Humphrey, J.A. Jokela, J.M.W. Li, R.H. Lohr, A.M. López, R.M. McLean.
Statistical expertise: A. Qaseem.
Obtaining of funding: A. Qaseem.
Administrative, technical, or logistic support: W.E. Abara, A. Qaseem, A.M. Harris.
Collection and assembly of data: W.E. Abara, A.M. Harris.