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This draft Recommendation Statement is based on an Evidence Report that is also available for public comment. To read the accompanying draft Evidence Report on Screening for Hepatitis B Virus Infection in Nonpregnant Adolescents and Adults and provide comments, go to http://www.uspreventiveservicestaskforce.org/draftrep.htm

The USPSTF makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service, and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decisionmaking to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

This draft Recommendation Statement is available for comment from February 11 until March 10, 2014, at 5:00 PM ET. You may wish to read the entire Recommendation Statement before you comment. A fact sheet that explains the draft recommendations in plain language is available here.

Screening for Hepatitis B Virus Infection in Nonpregnant Adolescents and Adults: U.S. Preventive Services Task Force Recommendation Statement DRAFT

Summary of Recommendation and Evidence

The U.S. Preventive Services Task Force (USPSTF) recommends screening for hepatitis B virus (HBV) infection in persons at high risk for infection.

This is a B recommendation.

Go to the Clinical Considerations section for additional information about risk factors for infection.

Table 3 describes the USPSTF grades, and Table 4 describes the USPSTF classification of levels of certainty about net benefit.

Rationale

Importance

It is estimated that about 700,000 to 1.4 million persons in the United States have chronic HBV infection (1, 2). In the United States, persons considered at high risk for HBV infection include persons from high-prevalence countries, persons who are HIV-positive, injection drug users, household contacts of persons with HBV infection, and men who have sex with men (2). The natural history of chronic HBV infection varies but can include the potential long-term sequelae of cirrhosis, hepatic decompensation, and hepatocellular carcinoma. An estimated 15% to 25% of persons with chronic HBV infection die from cirrhosis or hepatocellular carcinoma (2, 3). Individuals who are chronically infected also serve as a reservoir for person-to-person transmission of HBV infection. Screening for HBV infection could identify chronically infected individuals who may benefit from treatment or other interventions, such as surveillance for hepatocellular carcinoma.

Detection

Identification of chronic HBV infection based on serologic markers is considered accurate. Immunoassays for detecting hepatitis B surface antigen (HBsAg) have a reported sensitivity and specificity of greater than 98%.

Benefits of Detection and Early Intervention

DRAFT

The USPSTF found no randomized, controlled trials that provide direct evidence of the health benefits (i.e., reduction in morbidity, mortality, and disease transmission) of screening for HBV infection in asymptomatic adolescents and adults.

DRAFT

The USPSTF found adequate evidence that HBV vaccination is effective at decreasing disease acquisition.

DRAFT

The USPSTF found convincing evidence that antiviral treatment in patients with chronic HBV infection is effective at improving intermediate outcomes (i.e., virologic or histologic improvement or clearance of hepatitis B e antigen [HbeAg]) and adequate evidence that antiviral regimens improve health outcomes (such as reduced risk for hepatocellular carcinoma). The evidence showed an association between improvement in intermediate outcomes following antiviral therapy and improvement in clinical outcomes, but outcomes were heterogeneous and the studies had methodological limitations.

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The USPSTF found inadequate evidence that education or behavior change counseling reduces disease transmission.

DRAFT

Given the accuracy of the screening test and the effectiveness of antiviral treatment, the USPSTF concludes that screening is of moderate benefit for populations at high risk for HBV infection.

DRAFT

Harms of Detection and Early Intervention

DRAFT

The USPSTF found inadequate evidence on the harms of screening for HBV infection. Although evidence to determine the magnitude of harms of screening is limited, the USPSTF considers these harms to be small to none.

DRAFT

The USPSTF found adequate evidence that antiviral therapy regimens are associated with a higher risk for withdrawal due to adverse events than placebo. However, trials found no difference in the risk for serious adverse events or the number of participants who experienced any adverse event. In addition, most antiviral adverse events are self-limited with discontinuation of therapy. The USPSTF found adequate evidence that the magnitude of harms of treatment is small to none.

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USPSTF Assessment

DRAFT

The USPSTF concludes with moderate certainty that screening for HBV infection in adults at high risk for infection has moderate net benefit.

DRAFT

Clinical Considerations

DRAFT

Patient Population Under Consideration

DRAFT

This recommendation applies to asymptomatic, nonpregnant adolescents and adults who have not been vaccinated and other individuals at high risk for HBV infection.

Assessment of Risk

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A major risk factor for HBV infection is country of origin. The risk for HBV infection varies significantly by country of origin in U.S. foreign-born persons. Persons born in countries with an HBV prevalence of 2% or greater account for 47% to 95% of the chronically infected HBV population in the United States (2). Another important risk factor for HBV infection is lack of vaccination in infancy in U.S.-born persons with parents from a high-prevalence country (≥8%) (Table 1, Figure) (2).

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Table 1. Prevalence of Hepatitis B Virus Infection by Country of Origin

Prevalence	Region
High prevalence (≥8%)	China, subSaharan Africa, southeast Asia, countries of the Russian Federation, Bulgaria, Albania, equatorial South America, Greenland, Saudi Arabia, and Jordan
Moderately high prevalence (2% to 7%)	Eastern Europe, Alaska and northern Canada, eastern and northern regions of South America, north Africa, Russia, and south Asia
Low prevalence (<2%)	All others

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The Centers for Disease Control and Prevention (CDC) use a prevalence threshold of 2% or greater to define countries at high risk for HBV infection (2). Because this threshold is significantly higher than the estimated prevalence of HBV infection in the general U.S. population (0.3% to 0.5%) (2, 4), it is a reasonable threshold for deciding to screen in a patient population or risk group.

Studies of U.S. foreign-born persons have found a prevalence of chronic HBV infection of greater than 8% in foreign-born persons from the following countries: China, Vietnam, Laos, Cambodia, Myanmar, Afghanistan, Yemen, the Dominican Republic, Tonga, Micronesia, Ethiopia, Kenya, Somalia, Uganda, Eritrea, Zimbabwe, Cameroon, Sudan, western Africa (including Nigeria, Ghana, Liberia, Sierra Leone, Senegal, and Guinea), Albania, and Moldova (5).

Additional risk groups for HBV infection with a prevalence of 2% or greater include persons who are HIV-positive, injection drug users, household contacts of persons with HBV infection, and men who have sex with men (Table 2) (2).

Table 2. Prevalence of Hepatitis B Infection by Risk Group

Risk Group	% with HBV infection	Reference
HIV-positive persons*	6 to 14	2, 6
Men who have sex with men	9 to 17	6
Injection drug users	7 to 10	6
Heterosexual persons	4 to 6	6
Injection drug users	2.7 to 11	2, 7

Household contacts or sex partners of persons with HBV infection	3 to 20	2
Men who have sex with men	1.1 to 2.3	2

* Data from United States and western Europe.
Abbreviation: HBV = hepatitis B virus.

Persons who are immunosuppressed or undergoing hemodialysis have also been noted to have an increased risk for HBV infection. Black persons, males, and persons ages 30 to 39 years have a somewhat increased risk for acute HBV infection (2, 8).

Some persons with combinations of risk factors who do not fall into one of the above individual risk factor groups may also be at increased risk for HBV infection. However, reliable information about combinations of risk factors is not available. Clinicians should exercise their judgment in deciding whether these individuals are at high enough risk to warrant screening. For example, screening is probably appropriate in settings that treat a large proportion of individuals at increased risk, such as sexually transmitted infection clinics, HIV testing and treatment centers, health care settings that provide services for injection drug users or men who have sex with men, and correctional facilities (2).

The prevalence of HBV infection is low in the general U.S. population, and most infected individuals do not develop complications. Therefore, screening is not recommended in the general population.

Screening Tests

Screening for HBV infection is primarily done by testing for HBsAg. Testing for antibodies to HBsAg (anti-HBs) and hepatitis B core antigen (anti-HBc) may also be done as part of a screening panel to help distinguish between infection and immunity (2, 9). The CDC recommends screening for HBsAg with U.S. Food and Drug Administration (FDA)-approved tests, followed by a licensed, neutralizing confirmatory test for initially reactive results (2). Immunoassays for detecting HBsAg have a reported sensitivity and specificity of greater than 98% (10). Diagnosis of chronic HBV infection is characterized by persistence of HBsAg, HBV DNA, and total anti-HBc for at least 6 months (1, 2).

Treatment

Antiviral Regimens

The goals of antiviral treatment are to achieve sustained suppression of HBV replication and remission of liver disease in order to prevent cirrhosis, hepatic failure, and hepatocellular carcinoma. Interferons or nucleoside/nucleotide analogues are used to treat HBV infection. The FDA has approved seven antiviral drugs for treatment of chronic HBV infection: interferon alfa-2b, pegylated interferon alfa-2a, lamivudine, adefovir, entecavir, telbivudine, and tenofovir. Approved first-line treatments are pegylated interferon alfa-2a, entecavir, and tenofovir. Combination therapies have been evaluated but are not FDA-approved and are generally not used as first-line treatment because of tolerability, efficacy, and lower rates of resistance (1).

Several factors affect the choice of antiviral drug, including patient characteristics, HBV DNA level, serum transaminase levels, and HBeAg status. Biopsy is sometimes performed to determine the extent of liver inflammation and fibrosis (1). Surrogate endpoints of antiviral treatment include loss of HBeAg, loss of HBsAg, HBeAg seroconversion in HBeAg-positive patients, and suppression of HBV DNA to undetectable levels by polymerase chain reaction in HBeAg-negative and anti-HBe–positive patients (2). Duration of treatment varies depending on time required to achieve HBV DNA suppression and alanine aminotransferase (ALT) normalization, presence of HBeAg, presence of coinfection, presence of cirrhosis, and choice of drug (1).

Vaccination

Current U.S. policy is for universal vaccination of all infants at birth, catchup vaccination of adolescents, and vaccination of high-risk adults, such as health care workers, injection drug users, and household contacts of patients with HBV infection (1). Vaccination results in greater than 90% protective antibody response after the third dose in adults and greater than 95% protective antibody response in adolescents (1). The CDC recommends that persons who are tested for HBV infection receive the first dose of the vaccine at the same medical visit as screening (2).

Other Considerations

Research Needs and Gaps

The development and validation of clinical decision support or other tools to help clinicians efficiently and accurately identify populations at high risk for HBV infection are needed. Available clinical trials largely report intermediate or surrogate outcomes and are of relatively short duration. Clinical trials of adequate duration and power to evaluate long-term health outcomes (e.g., cirrhosis, end-stage liver disease, disease-specific mortality, quality of life, and all-cause mortality) are needed. In the absence of such randomized, controlled trials, registries to assess treatment efficacy are also needed.

Discussion

Burden of Disease

The epidemiology of HBV infection has been evolving in the United States, probably because of implementation of vaccination programs beginning in 1991. The number of reported acute symptomatic cases of HBV infection decreased from more than 20,000 cases annually in the mid-1980s to 2,890 cases in 2011 (11). However, the actual estimated number of new cases in the United States is approximately 6.5 times the number of reported cases because of underreporting (11). The burden of HBV infection disproportionately affects foreign-born persons from high-prevalence countries and their unvaccinated offspring, persons who are HIV-positive, men who have sex with men, and injection drug users (Table 2). Cases of acute HBV infection are also more likely to occur in persons ages 30 to 39 years (2.33 cases per 100,000 in 2010), men, and black persons (8).

An estimated 704,000 persons in the United States had chronic HBV infection in 2008 (1, 12). Persons born in countries with an HBV infection prevalence of 2% or greater, such as Africa, Asia, and parts of South America, account for 47% to 95% of chronically infected persons in the United States (2). The death rate of HBV infection in the United States in 2010 was an estimated 0.5 deaths per 100,000 persons (13). The highest death rates occurred in persons ages 55 to 64 years, males, and persons of nonwhite, nonblack race (13).

Scope of Review

This is an update of the 2004 USPSTF recommendation on screening for chronic HBV infection in asymptomatic, nonpregnant persons in the general population (14). The USPSTF commissioned a systematic review with a focus on evidence gaps identified in the previous USPSTF recommendation and new studies published since 2004. New key questions focused on the benefits and harms of antiviral treatment, benefits of education or behavior change counseling, and the association between improvements in intermediate and clinical outcomes after antiviral therapy. Key questions related to the immunization of children were excluded. In 2009, the USPSTF published a separate recommendation that addresses prenatal screening for HBV infection (10). The USPSTF will update its recommendation on prenatal screening in the future; therefore, it is not a focus of this recommendation.

Accuracy of Tests

The USPSTF previously reviewed HBV serological testing and found it to be accurate (sensitivity and specificity >98%) (10).

Effectiveness of Early Detection and Treatment

No randomized, controlled trials compared screening with no screening to provide direct evidence of the benefit of screening.

No trials examined the effectiveness of education or behavior change counseling in patients with chronic HBV infection for reducing transmission or improving health outcomes.

Evidence on different screening strategies for identifying persons with HBV infection is limited to one fair-quality, cross-sectional study (n=6,194) conducted in France in a sexually transmitted diseases clinic (15). The study found that an HBV screening strategy focused on testing persons born in higher-prevalence countries missed about two thirds of patients with HBV infection (sensitivity, 31%; number needed to screen, 16). An alternative screening strategy that tested men and the unemployed identified 98% (48/49) of patients with HBV infection after screening about two thirds of the population (number needed to screen, 82) (15). Well-established risk factors, such as injection drug use and high-risk sexual behaviors, were not predictive. Applicability of this study to U.S. primary care settings may be limited (15).

Intermediate Outcomes

Twenty-two placebo-controlled trials (n=35 to 515; duration, 8 weeks to 3 years) of antiviral therapy reported intermediate outcomes (e.g., histologic improvement, HBeAg loss or seroconversion, HBsAg loss or seroconversion, or virologic response) (1). Two trials were rated as good quality; most of the remaining trials were rated as fair quality. Methodological issues in the other trials included unclear or inadequate methods of randomization, allocation concealment, and blinding. Nine trials were conducted in the United States or Europe. Fifteen trials enrolled patients who were entirely or largely HBeAg-positive. Trials evaluated adefovir (k=4), interferon alfa-2b (k=8), lamivudine (k=9), and tenofovir (k=1). Trials reported baseline rates of prevalence of cirrhosis from 5% to 44% (1).

Pooled estimates showed that antiviral therapy was statistically significantly more effective than placebo or no treatment in achieving histologic improvement (k=7; risk ratio [RR], 2.1 [95% CI, 1.8 to 2.6]; I^2=0%), HBeAg loss or seroconversion (k=10; RR, 2.1 [95% CI, 1.6 to 2.9]; I^2=4%), HBsAg loss or seroconversion (k=12; RR, 2.4 [95% CI, 1.2 to 4.9]; I^2=0%), virologic response (k=9; RR, 7.2 [95% CI, 3.2 to 16]; I^2=58%), and ALT normalization (k=12; RR, 2.5 [95% CI, 2.1 to 3.0]; I^2=27%) (1). Results remained consistent when stratified by individual drug and in sensitivity and subgroup analyses based on outcomes, study quality, duration of treatment, and HBeAg-positive status. Evidence on the first-line drugs pegylated interferon, entecavir, and tenofovir is limited (1).

Eight fair- to good-quality trials (n=42 to 638; duration, 48 to 96 weeks) compared first-line antiviral drugs with lamivudine or adefovir. Entecavir (four trials) and pegylated interferon (two trials) were associated with an increased likelihood of intermediate outcomes (virologic and histologic improvement) compared with lamivudine (1). Analyses were limited by small numbers of trials. Entecavir was associated with an increased likelihood of virologic (k=4; RR, 1.6 [95% CI, 1.1 to 2.5]; I^2=94%) and histologic (k=2; RR, 1.2 [95% CI, 1.1 to 1.3]; I^2=0%) improvements compared with lamivudine. Compared with lamivudine, pegylated interferon alfa-2b was associated with an increased likelihood of HBeAg loss or seroconversion (k=1; RR, 1.6 [95% CI, 1.2 to 2.1]), HBsAg loss or seroconversion (k=2; RR, 16 [95% CI, 2.2 to 121]; I^2=0%), ALT normalization (k=2; RR, 1.4 [95% CI, 1.2 to 1.6]; I^2=0), virologic improvement (k=2; RR, 2.8 [95% CI, 1.9 to 4.4]; I^2=0%), and histologic improvement (k=2; RR, 1.2 [95% CI, 1.0 to 1.4]; I^2=0%). Head-to-head trials of entecavir versus lamivudine were heterogeneous for virologic response (k=4; RR, 1.6 [95% CI, 1.1 to 2.5]; I^2=94%) (1). Estimates from all trials favored entecavir over lamivudine (RR range, 1.3 to 2.1), including the two largest good-quality trials (RR, 2.1 [95% CI, 1.8 to 2.4] and 1.3 [95% CI, 1.2 to 1.4]). Studies comparing tenofovir with adefovir (two trials) showed no clear differences in effect on intermediate outcomes (1).

Clinical Outcomes

Eleven randomized trials (n=40 to 651; duration, 10 months to 7.5 years) of antiviral therapy versus placebo or no treatment reported clinical outcomes (e.g., cirrhosis, hepatocellular carcinoma, mortality). One trial was rated as good quality and the remaining trials were fair-quality (1). Methodological issues included inadequate details about method of randomization, allocation concealment, and blinding. Five trials took place in the United States or Europe. Two trials enrolled mostly HBeAg-negative patients. Trials evaluated adefovir (k=2), interferon alfa-2a (k=2), and lamivudine (k=4). Trials reported baseline rates of prevalence of cirrhosis from 5% to 40% (1).

Pooled estimates for incident cirrhosis (k=3; RR, 0.70 [95% CI, 0.33 to 1.46]; I^2=0%), hepatocellular carcinoma (k=5; RR, 0.57 [95% CI, 0.32 to 1.04]; I^2=2%), and mortality (k=5; RR, 0.55 [95% CI, 0.18 to 1.71]; I^2=43%) had trends that favored antiviral therapy over placebo but were likely underpowered for these outcomes (1).

The largest trial, the CALM (Cirrhosis Asian Lamivudine Multicentre) study, had a large effect on the pooled estimate for hepatocellular carcinoma (1, 16). Forty-one sites across Australia, China, Hong Kong, Malaysia, New Zealand, the Philippines, Singapore, Taiwan, and Thailand participated in the trial. Eighty-five percent of patients were men and 98% were Asian (16). This fair-quality study enrolled 651 patients with advanced liver disease who were randomized to lamivudine or placebo. The trial was discontinued early after a median duration of 32.4 months because it reached a prespecified stopping threshold for a composite outcome (hepatic decompensation, hepatocellular carcinoma, spontaneous bacterial peritonitis, bleeding gastroesophageal varices, or liver-related mortality) (1, 16). Results were adjusted for country, sex, baseline ALT, Child-Pugh score, and Ishak fibrosis score. Lamivudine was associated with decreased risk for hepatocellular carcinoma (adjusted hazard ratio [HR], 0.49 [95% CI, 0.25 to 0.9]), disease progression (adjusted HR, 0.5 [95% CI, 0.6 to 0.7]), and worsening of liver disease (adjusted HR, 0.5 [95% CI, 0.2 to 0.9]) compared with placebo (16).

There were too few clinical events in head-to-head trials of entecavir or pegylated interferon alfa-2a versus pegylated and nonpegylated interferon to determine effects on clinical outcomes (1).

Association Between Intermediate and Clinical Outcomes

Seven fair-quality and three poor-quality observational studies evaluated the link between intermediate and clinical health outcomes after antiviral therapy (1). These 10 observational studies (n=22 to 818; duration of followup, 4 to 9.9 years) assessed various intermediate (virologic or biochemical remission, histologic improvement, HBeAg loss, or composite intermediate outcomes) and clinical outcomes (death, hepatocellular carcinoma, or a composite clinical outcome) (1). Patient populations (e.g., presence of cirrhosis, HBeAg status) and antiviral therapy administered (lamivudine vs. interferon) also varied. Methodological issues included unclear blinding status of outcome assessors, failure to report loss to followup, and not addressing key confounders (age, sex, fibrosis stage, HBV viral load, HBeAg status) (1).

Observational studies found that improvements in various intermediate outcomes were associated with improved clinical outcomes (1). One fair-quality study in HBeAg-negative patients found that maintenance of virologic remission (no virologic breakthrough) was associated with a reduced risk for hepatocellular carcinoma (adjusted HR, 0.10 [95% CI, 0.01 to 0.77]) (17). One fair-quality study evaluated achieving virologic remission with lamivudine therapy in HBeAg-negative patients and found no significant benefit (adjusted HR, 0.77 [95% CI, 0.35 to 1.69]) in the reduction of hepatocellular carcinoma (18).

HBV Vaccination

No studies evaluated the effects of HBV vaccination on long-term clinical outcomes. Vaccination was associated with decreased risk for HBV acquisition in health care workers (k=4; RR, 0.5 [95% CI, 0.4 to 0.7]; I^2=18%) based on the presence of serological markers (HBsAg or anti-HBc) (19). Pooled analyses from three fair- to good-quality trials demonstrated that vaccination was also associated with a decreased risk for HBV acquisition compared with placebo in men who have sex with men based on HBsAg seroconversion (RR, 0.2 [95% CI, 0.1 to 0.4]; I^2=45%) or elevated ALT (RR, 0.2 [95% CI, 0.2 to 0.3]; I^2=2%) (3, 20–22).

Harms of Screening and Treatment

Pooled estimates showed no statistically significant difference between antiviral therapy and placebo or no treatment in risk for serious adverse events (k=12; RR, 0.8 [95% CI, 0.6 to 1.1]; I^2=0%) or any adverse event (k=7; RR, 0.96 [95% CI, 0.9 to 1.0]; I^2=0%) (1). Studies did show an increased risk for withdrawal due to adverse events (k=9; RR, 4.0 [95% CI, 1.4 to 11]; I^2=0%). Results for harms were largely consistent when stratified according to individual drugs (1).

Two head-to-head trials demonstrated that pegylated interferon alfa-2a was associated with greater risk for serious adverse events (RR, 2.1 [95% CI, 1.0 to 4.5]; I^2=0%), withdrawals due to adverse events (RR, 7.6 [95% CI, 1.1 to 52]; I^2=38%), and any adverse event (RR, 1.7 [95% CI, 1.5 to 2.0]; I^2=55%) versus lamivudine. There were no statistically significant differences between entecavir and lamivudine or tenofovir and adefovir (1).

No placebo-controlled trials of pegylated interferon alfa-2a or entecavir reported harms, and only one trial each of telbivudine and tenofovir reported harms data (1).

Estimate of Magnitude of Net Benefit

The USPSTF found adequate evidence that HBV vaccination is effective at decreasing disease acquisition. The USPSTF also found convincing evidence that antiviral treatment in patients with chronic HBV infection is effective at improving intermediate outcomes (virologic or histologic improvement or clearance of HBeAg).

The USPSTF concludes with moderate certainty that antiviral treatment results in an important improved clinical outcome (reduced hepatocellular carcinoma) and that antiviral therapy regimens have small harms. As a result, the USPSTF concludes that the net benefit of screening for HBV infection in high-risk populations is moderate.

How Does Evidence Fit With Biological Understanding?

Acute HBV infections are usually self-limited. Risk for chronic infection varies with age, with about 5% of acute infections in adults developing into chronic HBV infection (3). HBV infection that persists for at least 6 months is considered chronic. Although most infected individuals do not develop chronic infection, potential long-term sequelae include cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Increased viral load is associated with greater risk for cirrhosis, hepatocellular carcinoma, liver-related mortality, and disease transmission. Death from cirrhosis or hepatocellular carcinoma occurs in about 15% to 25% of persons who are chronically infected with HBV (3).

Update of the Previous USPSTF Recommendation

In 2004, the USPSTF recommended against screening for chronic HBV infection in asymptomatic persons in the general population (D recommendation) (14). The USPSTF found that screening for HBV infection in the general population does not improve long-term health outcomes, such as cirrhosis, hepatocellular carcinoma, or mortality; that the prevalence of HBV infection is low in the general population; and that the majority of infected individuals do not develop chronic infection, cirrhosis, or HBV-related liver disease. The USPSTF found limited evidence on the effectiveness of treatment interventions on clinical outcomes and on potential harms related to screening (e.g., labeling, anxiety) (1, 14). As a result, the USPSTF concluded that the potential harms of screening for HBV infection in the general population likely exceeded the potential benefits (14).

Recommendations of Others

The CDC and the American Association for the Study of Liver Diseases recommend screening for HBV infection in high-risk individuals, including all foreign-born persons from regions with an HBsAg prevalence of greater than 2%, regardless of vaccination history; U.S.-born persons not vaccinated as infants whose parents were born in regions with an HBsAg prevalence of 8% or greater; injection drug users; men who have sex with men; household contacts and sex partners of HBsAg-positive persons; hemodialysis patients; immunosuppressed persons; and persons who are HIV-positive (2, 9). The CDC also recommends screening for HBV infection in blood, organ, or tissue donors; persons with occupational or other exposures to infectious blood or body fluids; and persons who received HBV vaccination as adolescents or adults with high-risk behaviors (2). In addition, the American Association for the Study of Liver Diseases recommends that individuals with multiple sex partners or a history of sexually transmitted diseases, inmates of correctional facilities, and individuals with hepatitis C virus infection be screened (9). The Institute of Medicine endorses screening for HBV infection in high-risk groups similar to those recommended by the CDC (23). The American Academy of Family Physicians is currently reviewing its recommendation on screening for HBV infection.

Table 3: What the Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Table 4: Levels of Certainty Regarding Net Benefit

Level of Certainty*	Description

High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: • The number, size, or quality of individual studies. • Inconsistency of findings across individual studies. • Limited generalizability of findings to routine primary care practice. • Lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies. • Important flaws in study design or methods. • Inconsistency of findings across individual studies. • Gaps in the chain of evidence. • Findings not generalizable to routine primary care practice. • A lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

*The U.S. Preventive Services Task Force defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

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