Summary of Recommendation and Evidence
The U.S. Preventive Services Task Force (USPSTF) recommends screening for hepatitis C virus (HCV) infection in persons at high risk of infection. The USPSTF also recommends offering one-time screening for HCV infection to adults born between 1945 and 1965 (Table 1). B recommendation.

Rationale
HCV is the most common chronic blood-borne pathogen in the United States and a leading cause of complications from chronic liver disease. The prevalence of the anti-HCV antibody in the United States is approximately 1.6% in noninstitutionalized persons. According to data from 1999 to 2008, about three-fourths of patients in the United States with HCV infection were born between 1945 and 1965, with a peak prevalence of 4.3% in persons 40 to 49 years of age from 1999 to 2002.1,2 The most important risk factor for HCV infection is past or current injection drug use, with most studies reporting a prevalence of 50% or more. The incidence of HCV infection was more than 200,000 cases per year in the 1980s but decreased to 25,000 cases per year by 2001. According to the Centers for Disease Control and Prevention, there were an estimated 16,000 new cases of HCV infection in 2009 and an estimated 15,000 deaths in 2007. Hepatitis C–related end-stage liver disease is the most common indication for liver transplants among U.S. adults, accounting for more than 30% of cases. Studies suggest that about one-half of the recently observed three-fold increase in incidence of hepatocellular carcinoma is related to acquisition of HCV infection two to four decades earlier.1

DETECTION
The USPSTF found adequate evidence that anti–HCV antibody testing followed by confirmatory polymerase chain reaction testing accurately detects chronic HCV infection. In screening strategies targeting persons with risk factors for HCV infection (such as past or present injection drug use, sex with an injection drug user, or blood transfusion before 1992), anti–HCV antibody testing is associated with high sensitivity (greater than 90%) and small numbers needed to screen to identify one case of HCV infection (fewer than 20 persons).1 Anti–HCV antibody testing remains highly accurate in low-prevalence populations, although the numbers needed to screen to detect one case of HCV infection are higher.

The USPSTF also found adequate evidence that various noninvasive tests have good to very good diagnostic accuracy in diagnosing fibrosis or cirrhosis.3

BENEFITS OF DETECTION AND EARLY INTERVENTION
The USPSTF found no direct evidence on the benefit of screening for HCV infection in asymptomatic adults in reducing morbidity and mortality. However, the USPSTF found adequate evidence that antiviral regimens result in sustained virologic response and improved clinical outcomes.

The USPSTF found inadequate evidence that counseling or immunization of patients with HCV infection against other infections improves health outcomes, reduces transmission of HCV, or changes high-risk behaviors. The USPSTF found inadequate evidence that knowledge of positive status for HCV infection reduces high-risk behaviors. The USPSTF also found inadequate evidence that labor management and breastfeeding strategies in HCV-positive women

See related Putting Prevention into Practice on page 405.
are effective at reducing the risk of mother-to-child transmission.

Given the accuracy of the screening test and the availability of effective interventions for HCV infection, the USPSTF concludes that screening is of moderate benefit for populations at high risk of infection. The USPSTF concludes that one-time screening in all adults in the United States born between 1945 and 1965 is also of moderate benefit.

HARMs OF DETECTION AND EARLY INTERVENTION

The USPSTF found limited evidence on the harms of screening for HCV. Potential harms of screening include anxiety, patient labeling, and feelings of stigmatization.

The USPSTF found adequate evidence on the harms associated with the diagnostic evaluation used to guide treatment decisions (liver biopsy). These harms include bleeding, infection, and severe pain in approximately 1% of persons who had a liver biopsy and death in less than 0.2%. However, the use of liver biopsy to guide treatment decisions is declining, and noninvasive tests have sufficient accuracy to diagnose fibrosis and cirrhosis. Thus, the absolute risk to persons who currently receive a diagnosis of HCV infection and subsequent treatment is probably declining.

### Table 1. Screening for Hepatitis C Virus Infection in Adults: Clinical Summary of the USPSTF Recommendation

<table>
<thead>
<tr>
<th>Population</th>
<th>Persons at high risk of infection, and adults born between 1945 and 1965</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td>Screen for HCV infection</td>
</tr>
<tr>
<td>Grade: B</td>
<td></td>
</tr>
<tr>
<td>Risk assessment</td>
<td>The most important risk factor for HCV infection is past or current injection drug use. Additional risk factors include receiving a blood transfusion before 1992, long-term hemodialysis, being born to a mother with HCV infection, incarceration, intranasal drug use, getting an unregulated tattoo, and other percutaneous exposures. Adults born between 1945 and 1965 are more likely to be diagnosed with HCV infection, because they received a blood transfusion before the introduction of screening in 1992 or because they have a history of other risk factors for exposure decades earlier.</td>
</tr>
<tr>
<td>Screening tests</td>
<td>Anti–HCV antibody testing followed by confirmatory polymerase chain reaction testing accurately identifies patients with chronic HCV infection. Various noninvasive tests with good diagnostic accuracy are possible alternatives to liver biopsy for diagnosing fibrosis or cirrhosis.</td>
</tr>
<tr>
<td>Screening interval</td>
<td>Persons with continued risk of HCV infection (such as injection drug users) should be screened periodically. Evidence on how often screening should occur in these persons is lacking. Adults born between 1945 and 1965 and persons who are at risk because of potential exposure before universal blood screening need to be screened only once.</td>
</tr>
<tr>
<td>Treatment</td>
<td>Antiviral treatment prevents long-term health complications of HCV infection (e.g., cirrhosis, liver failure, hepatocellular carcinoma). The combination of pegylated interferon (alfa-2a or alfa-2b) and ribavirin is the standard treatment for HCV infection. In 2011, the U.S. Food and Drug Administration approved the protease inhibitors boceprevir and telaprevir for the treatment of HCV genotype 1 infection (the predominant genotype in the United States).</td>
</tr>
<tr>
<td>Balance of benefits and harms</td>
<td>On the basis of the accuracy of HCV antibody testing and the availability of effective interventions for persons with HCV infection, the USPSTF concludes that there is a moderate net benefit to screening in populations at high risk of infection. The USPSTF concludes that there is also a moderate net benefit to one-time screening in all adults in the United States born between 1945 and 1965.</td>
</tr>
<tr>
<td>Other relevant USPSTF recommendations</td>
<td>The USPSTF has made recommendations on screening for hepatitis B virus infection in adolescents, adults, and pregnant women. These recommendations are available at <a href="http://www.uspreventiveservicestaskforce.org/">http://www.uspreventiveservicestaskforce.org/</a>.</td>
</tr>
</tbody>
</table>

**NOTE:** For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, go to http://www.uspreventiveservicestaskforce.org/.

HCV = hepatitis C virus; USPSTF = U.S. Preventive Services Task Force.
The USPSTF found adequate evidence that antiviral therapy regimens are associated with a high rate of harms, such as fatigue, headache, influenza-like symptoms, hematologic events, and rash. However, antiviral therapy is given for a defined duration, serious adverse events are uncommon, and adverse events are self-limited and typically resolve after treatment is discontinued. The USPSTF found adequate evidence that these harms of treatment are small.

USPSTF ASSESSMENT
The USPSTF concludes with moderate certainty that screening for HCV infection in adults at increased risk of infection and one-time screening in adults in the 1945-1965 birth cohort have moderate net benefit.

Clinical Considerations
PATIENT POPULATION
This recommendation applies to all asymptomatic adults without known liver disease or functional abnormalities.

ASSESSMENT OF RISK
The most important risk factor for HCV infection is past or current injection drug use. Another established risk factor for HCV infection is receipt of a blood transfusion before 1992. Because of the implementation of screening programs for donated blood, blood transfusions are no longer an important source of HCV infection. In contrast, 60% of new HCV infections occur in persons who report injection drug use within the past six months.

Additional risk factors include long-term hemodialysis, being born to a mother with HCV infection, incarceration, intranasal drug use, getting an unregulated tattoo, and other percutaneous exposures (such as in health care professionals or from having surgery before the implementation of universal precautions). Evidence on tattoos and other percutaneous exposures as risk factors for HCV infection is limited. The relative importance of these additional risk factors may differ on the basis of geographic location and other factors.

Large population-based studies report an independent association between high-risk sexual behaviors (multiple sex partners, unprotected sex, or sex with a person who has HCV infection or with an injection drug user) and HCV infection. However, HCV seems to be inefficiently transmitted through sexual contact, and observed associations may have been confounded by other high-risk behaviors.

In 1998, the highest prevalence rates of the anti-HCV antibody occurred in persons with significant direct percutaneous exposures, such as injection drug users and persons with hemophilia (60% to 90%); persons with less significant percutaneous exposures involving smaller amounts of blood, such as patients receiving hemodialysis (10% to 30%), had more moderate prevalence rates. Persons engaging in high-risk sexual behaviors (1% to 10%); recipients of blood transfusions (6%); and persons with infrequent percutaneous exposures, such as health care professionals (1% to 2%), had the lowest prevalence rates.

Among patients with abnormal results on liver function tests (measurement of aspartate transaminase, alanine transaminase, or bilirubin) who were tested for reasons other than HCV screening, finding the cause of the abnormality often includes testing for HCV infection and is considered case finding rather than screening; therefore, it is outside the scope of this recommendation.

In 2010, the overall incidence rate of acute HCV infection was 0.3 cases per 100,000 persons and varied by race or ethnicity. The incidence rate for acute hepatitis C was lowest among persons of Asian or Pacific Islander descent and highest among American Indians and Alaska Natives. Blacks had the highest mortality rates from HCV, at 6.5 to 7.8 deaths per 100,000 persons, according to data from 2004 to 2008.

BIRTH-COHORT SCREENING
Persons born between 1945 and 1965 are more likely to be diagnosed with HCV infection, possibly because they received blood transfusions before the introduction of screening in 1992 or have a history of other risk factors for exposure decades earlier. Many persons with chronic HCV infection are unaware of their condition. A risk-based approach may miss detection of a substantial proportion of persons with HCV infection in the birth cohort because of a lack of patient disclosure or knowledge about prior risk status. As a result, one-time screening for HCV infection in the birth cohort may identify infected patients at earlier stages of disease who could benefit from treatment before developing complications from liver damage.

The USPSTF concluded that the benefit of screening for HCV infection in persons in the birth cohort is probably similar to that in persons at higher risk of infection. Birth-cohort screening is probably less efficient than risk-based screening, meaning more persons will need to be screened to identify one patient with HCV infection. Nevertheless, the overall number of Americans who will probably benefit from birth-cohort screening is greater than the number who will benefit from risk-based screening.

The USPSTF recognizes that increased screening and the resulting increased diagnoses and treatment could result in increased overall harms because not all treated persons will benefit from treatment, including those who will never develop signs or symptoms of disease.
(overdiagnosis). The USPSTF weighed this potential harm against the potential harm of undertreatment attributable to underdiagnosis. It is hoped that future research will reduce overtreatment by clarifying which persons are most likely to benefit from early diagnosis and treatment. However, given that persons in the birth cohort have been living with HCV infection for 20 or more years, the potential benefit of screening and early treatment will probably be at its highest now and in the near future before decreasing. After weighing the competing harms of overtreatment and underdiagnosis, the USPSTF recommends one-time screening for this cohort.

SCREENING TESTS

Anti–HCV antibody testing followed by polymerase chain reaction testing for viremia is accurate for identifying patients with chronic HCV infection. Various noninvasive tests with good diagnostic accuracy are possible alternatives to liver biopsy for diagnosing fibrosis or cirrhosis.

SCREENING INTERVALS

Persons in the birth cohort and those who are at risk because of potential exposure before universal blood screening and are not otherwise at increased risk need only be screened once. Persons with continued risk for HCV infection (injection drug users) should be screened periodically. The USPSTF found no evidence about how often screening should occur in persons who continue to be at risk of new HCV infection.

SCREENING IMPLEMENTATION

The USPSTF believes that screening should be voluntary and undertaken only with the patient’s knowledge and understanding that HCV testing is planned. Patients should be informed orally or in writing that HCV testing will be performed unless they decline (opt-out screening). The USPSTF further believes that before HCV screening, patients should receive an explanation of HCV infection, how it can (and cannot) be acquired, the meaning of positive and negative test results, and the benefits and harms of treatment. Patients should also be offered the opportunity to ask questions and to decline testing.

TREATMENT

The purpose of antiviral treatment regimens is to prevent long-term health complications of chronic HCV infection (e.g., cirrhosis, liver failure, hepatocellular carcinoma). The combination of pegylated interferon (alfa-2a or alfa-2b) and ribavirin is the standard treatment for HCV infection. In 2011, the U.S. Food and Drug Administration approved the protease inhibitors boceprevir and telaprevir for the treatment of HCV genotype 1 infection (the predominant genotype in the United States). Trials have found increased sustained virologic response rates in patients with HCV genotype 1 infection who received triple therapy consisting of pegylated interferon, ribavirin, and boceprevir or telaprevir compared with dual therapy consisting of pegylated interferon and ribavirin. Evidence is lacking on the comparative effects of current antiviral treatments on long-term clinical outcomes. Regimens with protease inhibitors are usually of shorter duration than dual therapy (24 or 28 weeks vs. 48 weeks). Triple therapy with protease inhibitors is associated with an increased risk of hematologic events (e.g., anemia; neutropenia; thrombocytopenia, particularly with boceprevir) and rash (telaprevir) compared with dual therapy. These adverse events are self-limited and typically resolve after the discontinuation of treatment.7

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The U.S. Preventive Services Task Force recommendations are independent of the U.S. government. They do not represent the views of the Agency for Healthcare Research and Quality, the U.S. Department of Health and Human Services, or the U.S. Public Health Service.

REFERENCES


