

Screening for Hepatitis C Virus Infection in Adults

Research Focus for Clinicians

In response to a request from the public, the Agency for Healthcare Research and Quality (AHRQ) provided support to the Oregon Evidence-based Practice Center to perform a systematic review to evaluate the evidence about the effects of screening for hepatitis C virus (HCV) infection on clinical outcomes in asymptomatic adults without known liver enzyme abnormalities, including pregnant women. In addition, the authors of the review evaluated the relative effectiveness of various screening strategies for HCV infection and the potential harms of screening. The authors of this review did not address screening for HCV infection in children, patients with occupational exposure, and post-transplant, HIV-infected, and hemodialysis patients. The systematic review included 162 reports of eligible studies published from 1947 through May 2012. An online version of this summary provides links directly to the sections of the full report with references for individual findings, inclusion criteria for the studies, and an explanation of the methods for rating the studies and determining the strength of evidence for individual findings. The online version of this summary and the full report are available at www.effectivehealthcare.ahrq.gov/hepatitis-c-screening.cfm. This summary is provided to inform discussions with patients of options and to assist in decisionmaking along with consideration of a patient's values and preferences. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines.

Background

HCV is the most common chronic blood-borne pathogen in the United States. About 78 percent of individuals who test positive for anti-HCV antibody have detectable hepatitis C virus in their blood, indicating chronic HCV infection. The Centers for Disease Control and Prevention (CDC) estimated that there were 16,000 new cases of acute HCV infection in 2009. HCV infection was associated with an estimated 15,000 deaths in 2007. The greatest risk factors for HCV infection are injection drug use and transfusions before 1992. About 75 percent of patients with HCV infection were born between the years of 1945 and 1965, with the highest prevalence (4.3%) in people 40 to 49 years of age in 1999–2002.

HCV is a leading cause of complications from liver disease including cirrhosis, hepatic failure, hepatocellular cancer, and death. Although the yearly incidence of HCV infection has been declining over the last two decades, the rates of cirrhosis, hepatic failure, and hepatocellular cancer are expected to rise in the next 10 to 20 years. This contradiction in the rates is due to the long lag time between infection and development of complications. Screening for HCV infection in asymptomatic adults without a history of liver disease or known liver enzyme abnormalities may identify infected patients early, before they develop serious or irreversible liver damage. Data from the CDC suggest that out of every 100 people infected with HCV, about 75–85 people will develop chronic HCV infection. About 5–20 people will develop cirrhosis over a period of 20–30 years, with the rates of cirrhosis increasing after 30 years.¹

¹ www.cdc.gov. Accessed November 1, 2012.

HCV antibody testing with subsequent polymerase chain reaction (PCR) testing for circulating virus was found to be accurate for identifying patients with HCV infection in a previous systematic review.²

This review, together with a complementary review on the effectiveness of antiviral HCV treatments, has been used by the U.S. Preventive Services Task Force (USPSTF) to update its recommendations on HCV screening.

Conclusions

No direct evidence comparing clinical outcomes in patients who were screened with outcomes in patients who were not screened was available, and no long-term studies that followed patients from screening through diagnosis and treatment to determine clinical outcomes were identified. However, several studies provided indirect evidence about the potential benefits of screening. Studies have shown that screening tests (HCV antibody testing with subsequent PCR testing for circulating virus) can accurately identify adults with chronic HCV infection. Targeted screening strategies based on the presence of multiple risk factors resulted in numbers needed to screen to identify one case of HCV infection of less than 20; however, targeted screening strategies miss about 10–67 percent of infected patients, depending on how narrowly the screening is targeted. Furthermore, in HCV-positive patients, treatment with antiviral regimens resulted in sustained virologic response (SVR) rates of 43–80 percent, which was associated with a reduction in hepatocellular carcinoma and all-cause mortality. However, these antiviral regimens were also associated with adverse effects.

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² U.S. Preventive Services Task Force. *Ann Intern Med.* 2004;140(6):462-4. PMID: 15023712.

Conclusions (Continued)

The USPSTF used this systematic review to inform their recommendations about population screening for hepatitis C. The USPSTF concluded that screening is of moderate benefit for populations at high risk for HCV infection. The USPSTF also concluded that there is a moderate net benefit to one-time screening in all adults in the United States born between 1945 and 1965. The updated USPSTF recommendations for screening for HCV infection are outlined below.

Screening Recommendations for HCV Infection

U.S. Preventive Services Task Force 2013 Recommendations*

The USPSTF recommends screening for HCV infection in adults at high risk, including those with any history of intravenous drug use or blood transfusions before 1992.

The USPSTF recommends that clinicians offer screening for HCV infection in adults born between 1945 and 1965.

The USPSTF classified this as a Grade B recommendation (the USPSTF recommends the service; there is moderate certainty that the net benefit is moderate).

* Source: www.uspreventiveservicestaskforce.org. Accessed June 26, 2013.

The evidence was insufficient to determine the effectiveness of counseling in patients who were HCV positive or the effectiveness of immunizations for hepatitis A and B infections on clinical outcomes. Limited evidence suggests that for some patients, knowledge of hepatitis C status may be associated with reduction in high-risk behaviors such as alcohol use in the short term. Additional research is needed to understand effective interventions for preventing vertical transmission.

Centers for Disease Control and Prevention 2012 Recommendation†

In addition to their 1998 guidelines† for testing for chronic HCV infection, the CDC published the following recommendation in August 2012.

People who should be tested once for HCV infection without prior ascertainment of HCV risk factors include:

- Adults born during 1945 through 1965

† Source: www.cdc.gov/hepatitis/hcv/guidelinesc.htm. Accessed August 8, 2013.

Clinical Bottom Line

Clinical Benefits and Harms of Screening for HCV in Nonpregnant and Pregnant Asymptomatic Adults**

There was no direct evidence of clinical benefits and limited evidence on harms associated with screening, when compared with no screening or between different screening approaches, in nonpregnant and pregnant adults. ○○○

Sensitivity of Different Methods for HCV Screening

Retrospective analyses showed that targeted screening strategies based on multiple risk factors were associated with sensitivities greater than 90 percent and with numbers needed to screen to identify one case of HCV infection of less than 20. More narrowly targeted screening strategies were associated with numbers needed to screen of less than two, but with the trade-off of missing up to two-thirds of infected patients. ●○○

Clinical Benefits and Harms Associated With Detection and Treatment of HCV Infection

Biopsy-related adverse effects appeared to be small, with a risk of death of less than 0.2 percent and a risk of serious complications (primarily bleeding and severe pain) of about 1 percent. ●●○

From 15 to 33 percent of patients with screen-detected chronic HCV infection received treatment; however, depending on the population assessed and the criteria used to determine treatment eligibility, this was likely to vary. ●●○

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Clinical Benefits and Harms Associated With Detection and Treatment of HCV Infection (Continued)

Treatment of HCV genotype 1 infection with triple and dual antiviral therapy regimens resulted in sustained virologic response (SVR) rates of 66–80 percent and 43–52 percent, respectively. § ●●○

Evidence from cohort studies and meta-analyses suggests that achieving an SVR after antiviral therapy is associated with a lower risk of all-cause mortality, hepatocellular carcinoma, and cirrhosis when compared with not achieving an SVR; however, the smaller supporting studies had some methodological shortcomings. ●●○

Dual and triple antiviral therapy regimens have been shown to be associated with harms such as fatigue, headache, flu-like symptoms, hematologic events, and rash. ●●○

Impact of Awareness of HCV Status and Counseling on Health Outcomes and Reduction in Spread of HCV or High-Risk Behaviors in HCV-Positive Patients‡

Knowledge of HCV status may reduce alcohol use in the short term. ●○○

Evidence on the effects of counseling or immunizations for hepatitis A and B infections on health outcomes, reduction in the spread of HCV, or decrease in high-risk behaviors was limited. ○○○

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Clinical Bottom Line (Continued)

Risk of Vertical HCV Transmission During Delivery or the Perinatal Period

The risk of vertical transmission of HCV infection did not differ significantly between cesarean (elective or emergent) delivery and vaginal delivery. ●●○

Prolonged labor (>6 hours based on one study) after membrane rupture was associated with increased risk of vertical transmission of HCV infection. ●○○

No significant association was found between breastfeeding and risk of transmitting HCV infection. ●●○

**Assessments of the benefits and harms of screening are likely to be contingent on the effectiveness of antiviral regimens, which are the subject of a complementary review that is available at www.effectivehealthcare.ahrq.gov/hepctreatment.cfm.

‡For information on the effectiveness of antiviral regimens in patients infected with HCV of other genotypes, please refer to the complementary review on treatment of HCV infection available at www.effectivehealthcare.ahrq.gov/hepctreatment.cfm.

§The general effectiveness of counseling and risk-prevention interventions in non-HCV-infected people was not assessed in this review.

Strength of Evidence Scale

High: ●●● High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.

Moderate: ●●○ Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

Low: ●○○ Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.

Insufficient: ○○○ Evidence either is unavailable or does not permit a conclusion.

Additional Information

- New oral agents, some of which do not require the use of interferon in the treatment regimen, are under development and have obtained fast-track status from the U.S. Food and Drug Administration for review in the next few years. Preliminary studies suggest that these agents are more tolerable than currently available therapies.
- Clinical practice has evolved toward less routine use of biopsy. However, the review found no studies reporting current estimates of the proportion of patients who undergo biopsy before treatment.
- Noninvasive tests are being developed for diagnosing fibrosis and cirrhosis and for guiding treatment decisions in HCV-positive patients (see the full report at www.effectivehealthcare.ahrq.gov/hepatitis-c-screening.cfm.)

What To Discuss With Your Patients

- The patient's risk status for HCV infection
- That HCV infection is potentially curable
- What the USPSTF recommendations say about screening for HCV infection based on population prevalence and the patient's risk status
- The available diagnostic tests for HCV infection and their accuracy
- The potential emotional and social impact of being screened for HCV infection
- The potential benefits and harms of diagnostic tests for HCV infection
- If the patient tests positive for HCV infection, the possibility that he/she might be referred to a liver specialist
- For HCV-positive patients:
 - The available tests and workup strategies to guide treatment decisions and the accuracy of the various tests
 - The importance of monitoring for liver fibrosis, cirrhosis, and cancer
 - The impact of various interventions for preventing vertical transmission of HCV during delivery or in the perinatal period

Resource for Patients



Testing for the Hepatitis C Virus, Why Testing May Be Important for You is a free companion to this clinician research summary. It can help adults talk with their health care professionals about screening for HCV infection.

Ordering Information

For electronic copies of *Testing for the Hepatitis C Virus, Why Testing May Be Important for You*, this clinician research summary, and the full systematic review, visit www.effectivehealthcare.ahrq.gov/hepatitis-c-screening.cfm. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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