The Meaning of the U.S. Preventive Services Task Force Grade I Recommendation: Screening for Hepatitis C Virus Infection

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The U.S. Preventive Services Task Force (USPSTF) formulates evidence-based recommendations for clinical preventive services. These recommendations are communicated by letter grades that reflect the quality of evidence and the magnitude of net health benefit expected from delivering the preventive service. When the USPSTF finds insufficient evidence to determine the balance of health benefits or harms of delivering a preventive service, because of a lack of studies, poor-quality studies, or good-quality studies with conflicting results, the USPSTF assigns the service an I letter grade. The USPSTF found insufficient evidence to recommend for or against screening for hepatitis C virus infection in high-risk individuals (I letter grade). This recommendation reflects the need for further research that would provide adequate evidence to assess the net health benefit for persons screened for hepatitis C virus infection.

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The USPSTF Grade I Recommendation and Screening for HCV Infection

IN THE BALANCE

and die as a result), the natural history of HCV infection is unclear. Only a minority of persons with chronic HCV infection (10% to 20%) develop cirrhosis after 20 to 30 years; there is currently no way to predict who will develop cirrhosis and who will not. Liver biopsy is commonly done as a part of diagnostic work-up and will cause major complications in 1% to 2% of patients. The evidence shows that only 30% to 40% of infected individuals referred for treatment are actually eligible to receive it and that 54% to 60% respond with sustained reduced viremia, although it is not known how long this lasts. In addition, the evidence shows that 50% to 60% of patients experience adverse effects as a result of treatment, and these adverse effects lead to many patients—up to 22% of those receiving combination therapy with pegylated interferon (2)—withdrawing from therapy.

It is not known whether current treatment will prevent severe liver disease such as cirrhosis or reduce progression to severe liver disease in HCV-infected persons. It is also not known whether counseling HCV-positive patients to change behavior decreases transmission of infection or improves intermediate or clinical outcomes. No evidence shows that counseling against alcohol use slows the progression to liver disease. There is also no evidence of the magnitude of harms associated with screening, such as psychological harms including anxiety, “labeling,” or impact on partner relationships. Because of these gaps in the chain of evidence needed to demonstrate improved health outcomes from screening for HCV infection in high-risk persons, the USPSTF gave a grade I recommendation to HCV screening for this group.

The USPSTF believes that the I recommendation, directed to the primary care clinician, reflects the lack of adequate evidence to make either a positive or a negative recommendation about screening for HCV infection. There may be other reasons to advocate for HCV testing—for example, disease surveillance, research, or disease management in a particular patient—and these may form the basis for other expert panels or organizations that may review the same evidence and arrive at a different recommendation. This does not change the fact that there is insufficient evidence to recommend screening on the basis of proven health benefits for the individual patient.

Practicing primary care clinicians have limited time and resources to deliver preventive services. The USPSTF believes that services with adequate evidence of substantial to moderate net health benefit (those with A and B recommendations) ought to receive the highest priority for delivery in the primary care setting. Once clinicians are able to deliver these services, they can decide how to prioritize services that have received C and I letter grades and, in rare cases, even those that have received grade D recommendations. This strategy would be expected to yield the greatest benefit to the health of individuals and the population with the most prudent use of time and resources. This USPSTF recommendation may not alter the practice of clinicians who already assess risk factors and screen high-risk patients for HCV infection. However, it is important to recognize that high-risk people are screened for HCV infection in the hope that treatment may improve health outcomes without causing substantial harms, not because of a proven, long-term net health benefit.

Finally, as mentioned earlier, a grade I recommendation reflects the need for more research. Hepatitis C virus infection is an important public health problem, and better treatment options and prevention strategies clearly are needed. The I letter grade should be viewed as representing the USPSTF conclusions based on the evidence available at this time. The USPSTF continually updates its recommendations, especially when there is new evidence of benefit, and looks forward to the time when its recommendation on screening for HCV infection can be reconsidered on the basis of new research.

Replication and iteration are hallmarks of science. Differences of opinion among independent experts regarding interpretation of current evidence are not unusual. An essential theme underlying all USPSTF recommendations is a commitment to evaluating the quality of scientific studies and synthesizing the results in a systematic and transparent fashion so that clinicians and patients can make informed decisions.

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