

Economic Analysis of Hepatitis B Screening and Treatment

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(See the article by Eckman et al, on pages 1294–1306.)

Approximately 350 million people worldwide are living with chronic hepatitis B virus (HBV) infection, and an estimated 620,000 die annually from complications of HBV-related liver disease [1]. In the United States, the incidence of acute HBV infection has declined substantially since 1985 as a result of the availability of effective HBV vaccines and widespread immunization of infants and high-risk populations [2]. Nevertheless, approximately 43,000 new cases of acute HBV infection occur each year in the United States [3]. Further, although vaccination programs have successfully reduced the incidence, the prevalence of chronic HBV infection has not declined, primarily because of the immigration of chronically infected persons from countries with high or intermediate HBV endemicity [4]. National surveys indicate that approximately 1.25 million US residents have chronic HBV infection (prevalence, 0.3%–0.5%) [5], and many are likely unaware of their infection status [6].

The public health impact of chronic HBV infection is almost entirely related to its long-term effects on liver-related complications [7, 8]. Specifically, chronic HBV infection is a major cause of cirrhosis, hepatic decompensation, and hepatocellular carcinoma, and the risk of these complications increases with higher HBV DNA levels [9, 10]. The number of hospitalizations, outpatient visits, and expenditures associated with chronic HBV infection has persistently increased over the past 20 years [4, 11], and as the influx of patients with chronic HBV infection in the United States continues, utilization of HBV-related health care services is expected to increase further.

Given the prevalence of chronic HBV infection and its public health impact, screening the members of at-risk groups for HBV infection with HBV surface antigen (HBsAg) has the potential to identify chronically infected patients before long-term complications manifest. Identification of chronic HBV infection by means of screening enables the implementation of a number of important interventions that could decrease the risk of subsequent liver-related complications and help to reduce transmission of infection, including (1) counseling to encourage the adoption of behaviors that reduce the risk of HBV transmission; (2) determination of close contacts who require HBsAg testing and subsequent vaccination (if HBsAg-negative); (3) avoidance of excessive alcohol; (4) clinical evaluation to detect

hepatic decompensation; (5) screening for viral coinfections (eg, human immunodeficiency virus, hepatitis C, and hepatitis D); (6) periodic surveillance for hepatocellular carcinoma; (7) immunization against hepatitis A; and (8) initiation of antiviral therapy, if warranted, to delay or reverse the progression of liver disease. The Centers for Disease Control and Prevention released comprehensive HBV testing recommendations in 2008 (Table 1) [12]. In particular, these guidelines recommend screening for HBV infection for persons born in regions where the HBV prevalence is $\geq 2\%$, but it has been unclear whether this 2% screening threshold is cost-effective. Very few data have evaluated the cost-effectiveness of screening for active HBV infection. Such economic analyses are important, however, to help clinicians and health policymakers determine whether current HBV screening strategies constitute an effective use of health care resources [13, 14].

In this issue of *Clinical Infectious Diseases*, Eckman and colleagues address the important and relevant question of the cost-effectiveness of screening for HBV infection with HBsAg in the United States and treating eligible patients [15]. The investigators conducted a cost-effectiveness analysis using a Markov model, a repetitive decision tree that models health outcomes occurring over time [16]. The investigators determined the probabilities associated with transitions to these outcomes and the distributions of

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Table 1. Groups Recommended for Screening for Hepatitis B Virus (HBV) Infection

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| Persons born in regions of intermediate and high HBV endemicity (hepatitis B surface antigen prevalence, $\geq 2\%$) |
| US-born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (hepatitis B surface antigen prevalence, $\geq 8\%$) |
| Other high-risk groups recommended for screening |
| Donors of blood, plasma, organs, or tissues |
| Hemodialysis patients |
| Hepatitis C virus–infected persons |
| Human immunodeficiency virus–infected persons |
| Household, needle-sharing, or sex contacts of persons known to be HBsAg-positive |
| Infants born to HBsAg-positive mothers |
| Injection drug users |
| Inmates of correctional facilities |
| Men who have sex with men |
| Persons who are the sources of blood or body fluids for exposures that might require postexposure prophylaxis (eg, needlestick injuries) |
| Persons with elevated liver aminotransferases of unknown etiology |
| Persons needing immunosuppressive therapy |
| Pregnant women |

NOTE. Table adapted from Weinbaum et al [12]. HBsAg, HBV surface antigen.

patients within each health state on the basis of a detailed literature review of clinical and epidemiologic studies. Five screening and treatment strategies were then considered. Cost estimates were obtained from average Medicare reimbursement rates and the 2008 *Red Book* [17]. Outcome values, which represented quality-of-life measures for various conditions, were based on prior published literature. After iteration of the model, a number of sensitivity analyses were performed to determine the stability of the results over a range of plausible estimates of HBV prevalence, costs, and rates of relevant conditions.

The investigators found that screening for HBV infection among persons from regions where the HBsAg prevalence is at least 2%, followed by antiviral treatment for those identified with chronic HBV infection using a low-cost, high-resistance nucleoside or nucleoside analog (eg, lamivudine), was cost-effective, compared with no screening (marginal cost-effectiveness ratio, \$29,230 per quality-adjusted life year [QALY], which is below the societal willingness-to-pay threshold of \$50,000 per QALY). In addition, sensitivity analyses revealed that the marginal cost-effectiveness

ratio remained below \$50,000 per QALY when screening persons from areas where the HBsAg prevalence was at least 0.3%. These results provide evidence for the cost-effectiveness of current HBV screening recommendations and should stimulate discussions to consider extending screening for HBV infection to patients from areas where the HBsAg prevalence is as low as 0.3%.

The results of this economic analysis support current HBV screening guidelines, but they also emphasize that it is the implementation of these recommendations that will decrease the morbidity and mortality associated with chronic HBV infection. Implementation of HBV testing recommendations is high among some subgroups, such as pregnant women and hemodialysis patients [12, 18], but is low in other settings. One study conducted among primary care clinics within an urban hospital system in New York City between 2005 and 2006 found that HBsAg screening was performed for only 56% of persons born in countries with a high rate of HBV infection ($\geq 8\%$ HBsAg prevalence) and in 40% of persons born in regions with intermediate HBV endemicity (2%–7% HBsAg

prevalence) [19]. Low rates of adherence to HBV screening recommendations might be due to a lack of awareness of the guidelines among health care providers [20]. In addition, competing issues often arise during an office visit that may preclude HBV testing, and patients might be reluctant to acknowledge behaviors that increase their risk for HBV infection. The precise barriers to HBV screening during routine care will need to be evaluated in order to develop appropriate interventions to improve screening rates.

The Institute of Medicine's 2010 report, "Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C," highlights the lack of knowledge and awareness about HBV infection and screening among health care and social-service providers, policymakers, and members of the public, and notes that resources being allocated for HBV surveillance, prevention, and control remain inadequate [21]. Improvements in these areas for all involved parties are necessary to increase rates of identification of HBV-infected persons in the United States. The report recommends the implementation of educational programs

in HBV infection for health care and social service providers and the development of effective outreach programs to target at-risk populations and increase awareness of HBV infection among the general public. Programs to improve viral hepatitis surveillance are also recommended. Whether these interventions will result in higher rates of screening will need to be evaluated if they are implemented.

Economic analyses, such as those by Eckman and colleagues, complement HBV clinical studies by translating health outcomes into standard health economic metrics. Eckman and colleagues demonstrate that surveillance of active HBV infection can be cost-effective. However, surveillance is only effective if undertaken. The challenge remains to raise awareness of HBV infection among health care providers and patients and to then implement hepatitis B screening strategies in the appropriate settings.

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