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## Cost-Effectiveness of Testing Hepatitis B–Positive Pregnant Women for Hepatitis B e Antigen or Viral Load

Lin Fan, PhD, Kwame Owusu-Edusei Jr, PhD, Sarah F. Schillie, MD, MPH, and Trudy V. Murphy, MD

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

### Abstract

**OBJECTIVE**—To estimate the cost-effectiveness of testing pregnant women with hepatitis B (hepatitis B surface antigen [HBsAg]-positive) for hepatitis B e antigen (HBeAg) or hepatitis B virus (HBV) DNA, and administering maternal antiviral prophylaxis if indicated, to decrease breakthrough perinatal HBV transmission from the U.S. health care perspective.

**METHODS**—A Markov decision model was constructed for a 2010 birth cohort of 4 million neonates to estimate the cost-effectiveness of two strategies: testing HBsAg-positive pregnant women for 1) HBeAg or 2) HBV load. Maternal antiviral prophylaxis is given from 28 weeks of gestation through 4 weeks postpartum when HBeAg is positive or HBV load is high ( $10^8$  copies/mL or greater). These strategies were compared with the current recommendation. All neonates born to HBsAg-positive women received recommended active-passive immunoprophylaxis. Effects were measured in quality-adjusted life-years (QALYs) and all costs were in 2010 U.S. dollars.

**RESULTS**—The HBeAg testing strategy saved \$3.3 million and 3,080 QALYs and prevented 486 chronic HBV infections compared with the current recommendation. The HBV load testing strategy cost \$3 million more than current recommendation, saved 2,080 QALYs, and prevented 324 chronic infections with an incremental cost-effectiveness ratio of \$1,583 per QALY saved compared with the current recommendations. The results remained robust over a wide range of assumptions.

**CONCLUSION**—Testing HBsAg-positive pregnant women for HBeAg or HBV load followed by maternal antiviral prophylaxis if HBeAg-positive or high viral load to reduce perinatal hepatitis B transmission in the United States is cost-effective.

An estimated 5,000–8,000 persons who become infected with hepatitis B virus (HBV) develop chronic HBV annually.<sup>1</sup> Perinatal HBV exposure is an important source of chronic HBV. Approximately 24,000 neonates are born to mothers positive for hepatitis B surface

Corresponding author: Lin Fan, PhD, Centers for Disease Control and Prevention, 1600 Clifton Road, MS G-37, Atlanta, GA 30333; Wqm3@cdc.gov.

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antigen (HBsAg) annually in the United States.<sup>2,3</sup> Without intervention, more than 30% (approximately 7,200) of these neonates will become HBV-infected.<sup>4</sup> Approximately 90% of HBV-infected neonates will develop chronic HBV<sup>4</sup> and have a 25% risk of premature death from liver failure or hepatocellular carcinoma.<sup>1,3,4</sup> Active-passive immunoprophylaxis with hepatitis B vaccination and hepatitis B immune globulin potentially reduces chronic HBV infections to 5% or less (approximately 1,200) of perinatally exposed neonates. In this scenario, almost all of the neonates with HBV infection are born to pregnant women with high HBV load, the most important factor predicting breakthrough infections. High HBV load is measured in peripheral blood directly by quantifying the amount of HBV DNA in serum or is estimated by detecting hepatitis B e antigen (HBeAg), which strongly correlates with high HBV load.<sup>5-7</sup>

Maternal antiviral prophylaxis during pregnancy (eg, lamivudine, telbivudine, or tenofovir), in addition to active-passive immunoprophylaxis for neonates, might prevent 70% of perinatal breakthrough infections, possibly by suppressing HBV replication.<sup>8-11</sup> However, maternal antiviral prophylaxis is not currently the standard of care in the United States.<sup>1</sup> The objective of this study was to estimate the cost-effectiveness of testing for HBeAg or HBV load among HBsAg-positive pregnant women followed by maternal antiviral prophylaxis if indicated in addition to the recommended active-passive immunoprophylaxis for their neonates.

## MATERIAL AND METHODS

Based on the 2010 estimate of live births in the United States,<sup>12</sup> we used a birth cohort of 4 million neonates. We constructed a decision tree model to estimate the costs and effects of two sequential testing strategies:

1. Sequential HBeAg testing: among HBsAg-positive pregnant women, test for HBeAg followed by maternal antiviral prophylaxis if positive
2. Sequential HBV load testing: among HBsAg-positive pregnant women, determine HBV load followed by maternal antiviral prophylaxis if indicated for high HBV load.

In these two strategies, all women are routinely screened for HBsAg, and all neonates born to HBsAg-positive women receive recommended active-passive immunoprophylaxis with a hepatitis B vaccine dose and hepatitis B immune globulin starting within 12 hours of birth followed by completion of the hepatitis B vaccine series. We compared the costs and effects of the two sequential maternal testing strategies with those of the current recommendation<sup>13</sup>: HBsAg screening for all pregnant women. Neonates born to HBsAg-positive women receive active-passive immunoprophylaxis.<sup>13</sup> Neonates born to HBsAg-negative women receive a “birth dose” of hepatitis B vaccine before hospital discharge (within 72 hours of birth) followed by completion of the hepatitis B vaccine series.<sup>13</sup> We also estimated the costs and effects of two additional strategies:

1. No intervention: no HBsAg screening for pregnant women and no prophylaxis or hepatitis B vaccination for their neonates

2. Neonate vaccination only: no HBsAg screening for pregnant women and a complete hepatitis B vaccine series starting within 72 hours of birth without hepatitis B immune globulin.

We constructed a Markov model to estimate the lifetime cost (in 2010 U.S. dollars) and effects (quality-adjusted life-years [QALY]) associated with acquiring chronic HBV infection for neonates. The Markov model of chronic HBV infection includes a set of health states: inactive carrier, active chronic HBV infection, cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, and death.<sup>14</sup> Life expectancy is approximately 78 years in the United States; we used a life cycle of 80 years.<sup>15</sup> Like in previous studies, the natural history of chronic HBV in a general population is used to model the natural history of perinatally acquired chronic HBV, which is not well described.<sup>16</sup> Most perinatally infected neonates remain in the immune-tolerant stage during childhood; although significant complications can occur at a young age, most do not occur until adulthood. Therefore, we assumed that complications start at age 20 years, like in previous studies.<sup>17,18</sup>

The baseline parameter values (including plausible ranges) used in the decision tree and Markov model are summarized in Table 1. The overall prevalence of HBsAg among pregnant women was estimated at 0.6%.<sup>2,3,19</sup> Without intervention, we estimated an overall perinatal transmission rate of 35.7% for HBsAg-positive women combining the proportional transmission rates for HBeAg-positive and HBeAg-negative women.<sup>4,6,20</sup> We considered a three-dose hepatitis B vaccination series (without hepatitis B immune globulin) to be 72% efficacious for preventing perinatal infection.<sup>20</sup> The overall perinatal transmission rate was approximated at 5% with active-passive immunoprophylaxis.<sup>7,21,22</sup> We assumed 90% of HBV-infected neonates will develop chronic HBV.<sup>1,4,17</sup>

The prevalence of HBeAg and high viral load, and perinatal transmission rates among neonates, were based on ranges reported in the literature and the assumption that, without antiviral prophylaxis during pregnancy, transmission rates for sequential HBeAg testing and sequential HBV load testing had to equal the transmission rate with the current recommendation. For example, the transmission rate was estimated at 5% under the current recommendation. If the prevalence of HBeAg positivity among HBsAg-positive women is 30%, and the perinatal transmission rate for HBeAg-positive women is 15%,<sup>6,23–26</sup> then the prevalence of HBeAg negativity among HBsAg-positive women is 70%, and the perinatal transmission rate for neonates born to HBeAg-negative women would be 0.71%, because the overall perinatal transmission rate remains 5% ( $[30\% \times 15\%] + [70\% \times 0.71\%] = 5\%$ ).

We defined a high HBV load as  $10^8$  copies/mL or greater. The perinatal transmission rates start to increase as the HBV load reaches  $10^6$  copies/mL or greater.<sup>7</sup> Because prevalence data for women with HBV load higher or lower than  $10^6$  copies/mL are limited, we used  $10^6$  copies/mL or greater as the lower limit of value defined as high viral load for sensitivity analyses.<sup>7,18,25,27,28</sup> Approximately 10–30% of persons with chronic HBV have viral load  $10^8$  copies/mL or greater.<sup>7,25–27</sup> Consequently, we chose 20% prevalence as our base estimate. The estimated perinatal transmission rates for pregnant women with HBV load  $10^8$  copies/mL or greater ranges from 7 to 32%; we used 15% as the base estimate.<sup>7,25–27</sup>

Meta-analyses suggest that in addition to active-passive immunoprophylaxis, maternal antiviral prophylaxis can reduce perinatal transmission by 68% (range 37–85%).<sup>8,29</sup> We chose a 50% reduction rate as our base estimate. We assumed all pregnant women with HBeAg or high HBV load will accept antiviral prophylaxis (ie, a 4-month course of lamivudine, 100 mg orally once daily from 28 weeks of gestation through 4 weeks postdelivery<sup>18</sup>).

The disease-specific mortality rate and annual transition rates among chronic HBV infection health states were estimated from the natural history of hepatitis B in the general population.<sup>1,27,30–35</sup> We assumed all cases of cirrhosis come from chronic HBV, and all decompensated cirrhosis come from cirrhosis (Table 1).

Costs and QALYs were derived from the literature.<sup>1,18,27,30–34,36</sup> The cost was adjusted to reflect 2010 U. S. dollars using the medical care component of the consumer price index for All Urban Consumers.<sup>37</sup> We conducted the analyses from the health care system's perspective. Data describing the societal costs such as productivity loss and caregivers' costs were not available. Therefore, we used the health care system's costs to estimate the cost to save 1 QALY. The base cost for antiviral prophylaxis was for a 4-month course of lamivudine. Depending on the choice of antiviral drugs, the cost for a 4-month course ranges from \$1,000 to \$4,000.<sup>1,18,30,32</sup> We assumed a \$100 cost for annual monitoring (ie, office visits, HBsAg, and HBeAg tests)<sup>30</sup> for chronic HBV in the first 20 years for those infected through perinatal transmission (Table 1).

We performed one-way sensitivity analyses on each variable and ranked the range of incremental cost-effectiveness ratios to determine the most influential variables. We then used these variables to conduct a multiway probabilistic sensitivity analysis (ie, a Monte Carlo analysis with 10,000 simulations) to investigate how changes in these variables would affect the estimated incremental cost-effectiveness ratio (measured in dollars per QALY saved). Parameters of the distribution for the variables (such as  $\alpha$  and  $\beta$  for  $\beta$  distribution and  $\mu$  and  $\lambda$  for lognormal distribution) are not available; therefore, we used a triangular distribution, which requires the minimum, likeliest, and maximum values for all variables.

Both outcomes (costs and QALYs) were discounted at a 3% annual rate.<sup>38</sup> We calculated the incremental cost-effectiveness ratio for each strategy compared with the current recommendation. TreeAge Pro 2012 was used to build the decision tree and Markov model. Institutional review board approval was not required because we used secondary data for this study.

## RESULTS

We determined the number of neonates with perinatal HBV infection and their lifetime complications for each of the interventions compared with the base case (Table 2). The no intervention strategy had the highest number of children (7,711) who developed chronic HBV. Among the 7,711 children, 1,316 would develop hepatocellular carcinoma, 1,227 would develop decompensated cirrhosis, and 251 would need a liver transplant. The infant vaccination only strategy had the second highest number of infants who developed chronic

HBV and the sequential HBV load testing strategy using  $10^6$  copies/mL or greater as the cutoff for high viral load had the lowest number of children who developed chronic HBV (Table 2). Compared with no intervention and infant vaccination only, the current recommendation was cost-effective with an incremental cost-effectiveness ratio of \$7,146 and \$6,358 per QALY saved, respectively (Table 3). Compared with the current recommendation, sequential HBeAg testing saved 3,080 QALYs and \$3.3 million (cost-saving), and the sequential HBV load testing using  $10^8$  copies/mL or greater saved 2,080 QALYs with a cost of \$3.3 million (incremental cost-effectiveness ratio: \$1,583 per QALY saved). Sequential HBeAg testing dominated sequential HBV load testing using  $10^8$  copies/mL or greater with 1,000 QALYs and \$6.6 million saved.

Results for the one-way sensitivity analyses are presented in Table 4. Both strategies remained cost-effective throughout the range of values used in the sensitivity analyses. The most influential variables were the cost and efficacy of antiviral prophylaxis. When the cost of antiviral prophylaxis increased from \$800 to \$4,000, the incremental cost-effectiveness ratios for sequential HBeAg testing and sequential HBV load testing using  $10^8$  copies/mL or greater increased to \$4,540 and \$7,172 per QALY saved, respectively. When the antiviral-associated reduction of perinatal transmission decreased from 80% to 20%, the incremental cost-effectiveness ratios for sequential HBeAg testing and sequential HBV load testing increased to \$4,708 and \$11,167 per QALY saved, respectively. Other influential variables affecting the incremental cost-effectiveness ratios included lifetime chronic HBV costs and QALY, perinatal transmission rate, the cost of HBV load testing, and the proportion of women receiving antiviral prophylaxis when this strategy is applied.

Results of the probabilistic sensitivity analysis focusing on the influential variables (from Table 4) are presented in Table 5. Both strategies remained cost-effective compared with the current recommendation. The maximum incremental cost-effectiveness ratios were \$20,796 and \$29,708 per QALY saved for sequential HBeAg testing and sequential HBV load testing, respectively.

We also examined  $10^6$  copies/mL or greater as the value defining high HBV load. Compared with the current recommendation, sequential HBV load testing with  $10^6$  copies/mL or greater HBV load prevented 551 chronic HBV infections, 94 hepatocellular carcinoma cases, 83 decompensated cirrhosis cases, 18 liver transplants, and saved 3,440 QALYs at a cost of \$8.0 million. Applying  $10^6$  copies/mL or greater to define a high HBV load saved 360 more QALYs with approximately \$11.3 million in costs compared with sequential HBeAg testing (incremental cost-effectiveness ratio: \$31,389 per QALY) and saved 1,360 more QALYs with approximately \$4.7 million in costs compared with sequential HBV load testing with  $10^8$  copies/mL or greater defining high viral load (incremental cost-effectiveness ratio: \$3,456 per QALY). In the one-way and multiway probabilistic sensitivity analyses, sequential HBV load testing with  $10^6$  copies/mL or greater remained cost-effective compared with the current recommendation (Tables 2–5).

## DISCUSSION

Our study demonstrated that either sequential HBeAg testing or sequential HBV load testing was cost-effective under a wide range of assumptions compared with the current recommendation. The cost-effectiveness of sequential HBeAg testing and sequential HBV load testing relies on several factors, including the cost and efficacy of maternal antiviral prophylaxis and lifetime costs associated with chronic HBV infection.

Several studies have concluded that maternal antiviral prophylaxis among HBsAg-positive women during pregnancy, in addition to active-passive immunoprophylaxis for the neonate, is cost-effective or cost-saving.<sup>1,18,27</sup> The purpose of sequential HBeAg testing and HBV load testing is to identify HBsAg-positive women whose neonates have the highest risk for perinatal transmission. If maternal antiviral prophylaxis is cost-effective in preventing perinatal HBV infection among the general population of HBsAg-positive women, identification of the highest risk population using HBeAg testing or HBV load testing is likely to be cost-effective, because the cost of testing for HBeAg or DNA is small compared with the cost of antiviral prophylaxis during pregnancy.

Several antivirals (ie, lamivudine, tenofovir, and telbivudine) reduce HBV viral load and might reduce perinatal HBV transmission.<sup>9–11</sup> Although lamivudine is the most studied maternal antiviral for preventing HBV perinatal transmission, tenofovir or telbivudine has been considered because they effectively reduce HBV load with lower rates of drug resistance than lamivudine.<sup>18,39,40</sup> We do not expect the choice of antiviral agent alone to change the cost-effectiveness given the results from sensitivity analyses.

Although HBeAg testing is less expensive than HBV load testing, HBeAg testing can miss a small proportion of women with negative HBeAg but high HBV load.<sup>41</sup> In our baseline assumption, sequential HBeAg testing dominated sequential HBV load testing using  $10^8$  copies/mL or greater as the cutoff value for high viral load (lower cost, higher QALY saved for HBeAg testing). However, results of a comparison between the two strategies depends on the cutoff for high HBV load, the costs of HBeAg and HBV load testing, the prevalence of HBeAg and high HBV load among HBsAg-positive pregnant women, and the perinatal transmission rates. Sequential HBV load testing using  $10^6$  copies/mL or greater has an incremental cost-effectiveness ratio of \$31,389 per QALY saved compared with sequential HBeAg testing.

This study has several limitations. First, all limitations associated generally with models are applicable because our model is a simplification of real-world events. Second, the validity of models and the results depend largely on the availability and reliability of the data. We used parameter values that varied substantially. As a result of lack of data on the parameters of the distribution for each variable, we used a triangular distribution for all variables. Using different distributions might change the results of the probabilistic sensitivity analyses. However, it is difficult to determine the magnitude or direction of any change. We assumed that the rates of adverse events for pregnant women and children from maternal antiviral prophylaxis were similar to those without maternal antiviral prophylaxis. Had we included complications attributable to antiviral therapy, the cost-effectiveness estimates for the



strategies that included antiviral therapy would be higher (less favorable). An increasing body of evidence shows that the incidences of adverse events and birth defects among pregnant women and children associated with antiviral prophylaxis are comparable to those without antiviral prophylaxis.<sup>8,10,11,39,40,42</sup> Our results might be conservative because we did not include the potential benefit of identifying women who should be treated or monitored for liver disease during pregnancy.

Drug resistance from long-term use of lamivudine has been a concern; however, the rate of drug resistance after a 3-month course of lamivudine is reported to be no higher than no antiviral prophylaxis.<sup>1,8,18</sup> Tenofovir and telbivudine have low rates or no documented drug resistance when used in other settings.<sup>10,11,43</sup> Another safety concern is postpartum flare.<sup>18,44,45</sup> Studies report mixed results regarding change in the rate of postpartum flares after maternal antiviral prophylaxis.<sup>45,46</sup> Because evidence for the safety of antiviral prophylaxis during pregnancy is still accumulating, antiviral prophylaxis for maternal liver disease during pregnancy has generally been postponed.<sup>16,47</sup>

Despite these limitations, our results suggest that health care providers might wish to consider HBeAg or HBV load sequential testing for HBsAg-positive pregnant women to identify women whose neonates are at increased risk for perinatal HBV infection and to ensure evaluation and monitoring of the pregnant women for the complications of chronic HBV infection, including during pregnancy and in the postpartum period.

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Table 1

## Parameter Inputs

Parameter	Base Assumption	Range*	Reference
Prevalence of HBsAg among pregnant women	0.6%	0.4–0.8%	3,19,48
Risk of perinatal transmission without vaccination	35.7%	Calculated	4,6,20,49
Vaccine efficacy (three-dose)	72%		20,49
Risk of perinatal transmission with active-passive immunoprophylaxis	5%	2–8%	1,7,21,22
Likelihood of symptoms after perinatal infection	1%		4
Risk of fulminant hepatitis after symptomatic infection	0.1%		4
Risk of chronic HBV infection after perinatal infection	90%		1,4,17
Risk of chronic HBV infection after fulminant hepatitis	33.3%		4
Risk of death from fulminant hepatitis	70%		4
Prevalence of HBeAg among HBsAg-positive persons	30%	13.5–45%	6,23,25,27,30
Risk of perinatal transmission among HBeAg-positive women with active-passive immunoprophylaxis	15%	7–23%	6,23–26
Risk of perinatal transmission among HBeAg-negative women with active-passive immunoprophylaxis	0.71%	Calculated	
Prevalence of HBsAg-positive women with viral load $10^8$ copies/mL or greater	20%	8–34%	7,25,27
Risk of perinatal transmission among women with viral load $10^8$ copies/mL or greater with active-passive immunoprophylaxis	15%	8–36%	7,25–27
Risk of perinatal transmission among women with viral load less than $10^8$ copies/mL with active-passive immunoprophylaxis	2.5%	Calculated	
Prevalence of HBsAg-positive women with viral load $10^6$ copies/mL or greater	50%	31–51%	7,25,34
Risk of perinatal transmission among women with viral load $10^6$ copies/mL or greater with active-passive immunoprophylaxis	10%	6–15%	7,26
Risk of perinatal transmission among women with viral load less than $10^6$ copies/mL with active-passive immunoprophylaxis	0%	Calculated	
Reduction from lamivudine	50%	37–85%	8,29
Transitional probabilities, disease-specific mortality			
Inactive carrier			
Chronic hepatitis B	7.3%	0.3–7.3%	27,33,35
Mortality	0		Assumption
Chronic hepatitis B			
Inactive carrier	17%	10.5–42%	33,35
Cirrhosis	5%	0.4–15.3%	1,33,35
Hepatocellular carcinoma	0.5%	0.2–0.7%	33,35
Mortality	2.5%	1.8–3.6%	31
Cirrhosis			
Decompensated cirrhosis	5.4%	2.8–10%	1,27,31–33
Hepatocellular carcinoma	2.4%	0.5–3%	1,27,31–33
Mortality	3.7%	3–4.4%	31,33,35
Decompensated cirrhosis			
Hepatocellular carcinoma	2.4%	1–10%	1,27,31–33
Transplant	1.8%	1–10%	1,27,31–33,35

Parameter	Base Assumption	Range*	Reference
Mortality	39%	22.5–50%	31,33,35
Hepatocellular carcinoma			
Transplant	4.6%	3.6–40%	1,27,31–33,35
Mortality	56%	26–70%	31,33,35
Transplant			
First year mortality	15%		1,33,35
Second year mortality	1.5%		14,35
Cost (U.S. dollars)			
Antiviral prophylaxis for 4 mo	1,600	800–4,000	1,18,30,32
HBV load test	240	50–500	18,30,34,36
Hepatitis B immunoglobulin	731	60–731	4,18,32
HBeAg test	30		30,36
Infant acute	468	208–12,304	4,30,33
Infant fulminant	19,000	13,000–52,322	4,30,33
Inactive carrier	100	60–2,130	33
Chronic HBV	1,170	761–6,980	1,18,30–33,50
Cirrhosis	1,519	227–37,380	1,18,30–33,50
Decompensated cirrhosis	17,623	11,459–102,800	1,18,30–33,50
Hepatocellular carcinoma	11,585	7,533–108,950	1,18,30–33,50
Transplant	133,117	86,552–328,407	1,18,30–33,50
Posttransplant	19,317	12,560–31,681	1,18,30–33,50
Effectiveness (QALY)			
Carrier	1	0.95–1	1,27,30
Chronic	0.99	0.9–1	1,27,30
Compensated	0.8	0.7–0.9	1,27,30
Decompensated cirrhosis	0.6	0.5–0.7	1,27,30
Hepatocellular carcinoma	0.73	0.5–0.8	1,27,30
Transplant	0.86	0.7–0.9	1,27,30

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HBeAg, hepatitis B e antigen; QALY, quality-adjusted life-years.

\*The specified ranges were used in one-way sensitivity analyses and Monte Carlo simulations.

**Table 2**  
**Number of Infants With Lifetime Complications From Perinatal Hepatitis B Virus Infection\***

Strategy	Chronic HBV Infection		Hepatocellular Carcinoma		Decompensated Cirrhosis		Liver Transplant	
	Expected	Prevented	Expected	Prevented	Expected	Prevented	Expected	Prevented
No intervention <sup>†</sup>	7,711	-6,631	1,316	-1,131	1,227	-1,055	251	-215
Infant vaccination only	2,160	-1,080	369	-184	344	-172	71	-35
Current recommendation	1,080	Reference	185	Reference	172	Reference	36	Reference
Sequential HBeAg testing	594	486	101	84	95	77	20	16
Sequential HBV load testing 10 <sup>8</sup> copies/mL or greater as cutoff	756	324	129	56	121	51	25	11
Sequential HBV load testing 10 <sup>6</sup> copies/mL or greater as cutoff	529	551	91	94	85	87	18	18

HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.

\* Results based on a hypothetical 2010 birth cohort of 4 million neonates.

<sup>†</sup> Of 7,711 infants with chronic HBV, 1316 develop hepatocellular carcinoma, 1227 develop decompensated cirrhosis, and 251 receive a liver transplant.

**Table 3**

**Baseline Cost-Effectiveness Results\***

Strategy	Total Cost (Millions)	Incremental Cost (Millions)	Total QALY (Life-Years)	Incremental QALY	Incremental Cost-Effectiveness Ratio
No intervention	246.1	-301.8	187,750,960	-42,240	7,146.0
Infant vaccination only	504.9	-43.0	187,786,320	-6,880	6,250.0
Sequential HBeAg testing	544.6	-3.3	187,796,280	3,080	Cost-saving
Current recommendation	547.9		187,793,200		Reference
Sequential HBV load testing, 10 <sup>8</sup> copies/mL or greater as cutoff	551.2	3.3	187,795,280	2,080	1,582.7
Sequential HBV load testing, 10 <sup>6</sup> copies/mL or greater as cutoff	555.9	8.0	187,796,640	3,440	2,339.2

QALY, quality-adjusted life years; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.

A negative incremental cost means less cost; a negative incremental QALY saved means fewer QALYs gained.

\* Based on a hypothetical 2010 birth cohort of 4 million neonates and 2010 U.S. dollars, both costs and QALYs were discounted at a 3% annual rate. A negative incremental cost means less cost; a negative incremental QALY saved means fewer QALYs gained.



**Table 4**

Most Influential Variables\* for Cost-Effectiveness of Sequential Testing Strategies Compared With the Current Strategy

Variable	Range	Incremental Cost-Effectiveness Ratio Range (\$/QALY saved)	
		Sequential HBeAg Testing	Sequential HBV Load Testing*
Use 10 <sup>8</sup> copies/mL or greater as cutoff value for high viral load			
Cost of antiviral prophylaxis	\$800–4,000 for 4 mo	Cost saving–4,540	Cost saving–7,172
Reduction of perinatal transmission rates from antiviral prophylaxis	20–80% reduction	Cost saving–4,708	Cost saving–11,167
Lifetime cost for chronic hepatitis B	\$26,800–48,400	Cost saving	Cost saving–2,285
Lifetime QALYs for chronic hepatitis B <sup>†</sup>	37.78–43.21	Cost saving	1,093–2,743
Perinatal transmission rate	2–8%	Cost saving–2,316	Cost saving–7,167
Cost for HBV load test	\$50–500	Cost saving <sup>‡</sup>	Cost saving–4,582
HBV prevalence among pregnant women	0.4–0.8%	Cost saving	1,567–1,590
Proportion of women receiving antiviral prophylaxis	50–100%	Cost saving	1,582–7,209
Use 10 <sup>6</sup> copies/mL or greater as cutoff value for high viral load			
Cost of antiviral prophylaxis	\$800–4,000 for 4 mo	Cost saving–4,540	Cost saving–10,711
Reduction of perinatal transmission rates from antiviral prophylaxis	20–80% reduction	Cost saving–4,708	Cost saving–13,378
Lifetime cost for chronic hepatitis B <sup>†</sup>	\$26,800–48,400	Cost saving	Cost saving–3,047
Lifetime QALY for chronic hepatitis B <sup>†</sup>	37.78–43.21	Cost saving	1,622–3,944
Perinatal transmission rate	2–8%	Cost saving–2,316	Cost saving–6,138
Cost for HBV load test	\$50–500	Cost saving <sup>‡</sup>	1,013–4,153
HBV prevalence among pregnant women	0.4–0.8%	Cost saving	2,312–2,352
Proportion of women receiving antiviral prophylaxis	50–100%	Cost saving	2,339–6,005

QALY, quality-adjusted life years; HBeAG, hepatitis B e antigen; HBV, hepatitis B virus.

\* The influential variables were determined by ranking the cost-effectiveness ratio range in the one-way sensitivity analyses for the model variable input, both costs and QALYs were discounted at a 3% annual rate.

<sup>†</sup> Discounted at 3% annual rate; low-end lifetime cost and QALYs from chronic hepatitis B infection are 10% percentile cost and QALYs from Markov model; high-end lifetime cost and QALYs from chronic hepatitis B infection are 90% percentile cost and QALYs from Markov model.

<sup>‡</sup> Remains unchanged because HBV DNA testing does not apply to current recommendation or sequential HBeAg testing.

**Table 5**

Multiway Probabilistic Sensitivity Analysis\* of Sequential Testing Strategies Compared With the Current Recommendation

	Incremental Cost-Effectiveness Ratio (\$/QALY saved)			
	10 <sup>8</sup> Copies/mL or Greater for High Viral Load		10 <sup>6</sup> Copies/mL or Greater for High Viral Load	
	HBeAg Test	HBV Load Test	HBeAg Test	HBV Load Test
Mean	Cost-saving	3,151	Cost-saving	4,500.1
2.5% <sup>†</sup>	Cost-saving	Cost-saving	Cost-saving	Cost-saving
10%	Cost-saving	Cost-saving	Cost-saving	81
50%	Cost-saving	2,519	Cost-saving	3,587
90%	3,172	7,642	3,178	10,055
97.5%	6,120	12,108	6,092	15,374
Maximum	20,796	29,708	15,188	30,760

QALY, quality-adjusted life years; HBeAG, hepatitis B e antigen; HBV, hepatitis B virus.

\* Based on Monte Carlo analysis with 10,000 simulations. Costs and QALYs were discounted at a 3% annual rate.

<sup>†</sup> Represents 2.5 percentile of the cost-effectiveness ratio.