# Cost-Effectiveness of Screening and Vaccinating Asian and Pacific Islander Adults for Hepatitis B

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**Background:** As many as 10% of Asian and Pacific Islander adults in the United States are chronically infected with hepatitis B virus (HBV), and up to two thirds are unaware that they are infected. Without proper medical management and antiviral therapy, up to 25% of Asian and Pacific Islander persons with chronic HBV infection will die of liver disease.

**Objective:** To assess the cost-effectiveness of 4 HBV screening and vaccination programs for Asian and Pacific Islander adults in the United States.

**Design:** Markov model with costs and benefits discounted at 3%.

**Data Sources:** Published literature and expert opinion.

**Target Population:** Asian and Pacific Islander adults (base-case age, 40 years; sensitivity analysis conducted on ages 20 to 60 years).

**Time Horizon:** Lifetime.

**Perspective:** U.S. societal.

**Interventions:** A universal vaccination strategy in which all individuals are given a 3-dose vaccination series; a screen-and-treat strategy, in which individuals are given blood tests to determine whether they are chronically infected, and infected persons are monitored and treated; a screen, treat, and ring vaccinate strategy, in which all individuals are tested for chronic HBV infection and close contacts of infected persons are screened and vaccinated if needed; and a screen, treat, and vaccinate strategy, in which all individuals are tested and then vaccinated with a 3-dose series if needed. In all cases, persons found to be chronically infected are monitored and treated if indicated.

**Outcome Measures:** Costs (2006 U.S. dollars), quality-adjusted life-years (QALYs), and incremental cost-effectiveness.

**Results of Base-Case Analysis:** Compared with the status quo, the screen-and-treat strategy has an incremental cost-effectiveness ratio of $36 088 per QALY gained. The screen, treat, and ring vaccinate strategy gains more QALYs than the screen and treat strategy and incurs modest incremental costs, leading to incremental cost-effectiveness of $39 903 per QALY gained compared with the screen and treat strategy. The universal vaccination and screen, treat, and vaccinate strategies were weakly dominated by the other 2 strategies.

**Results of Sensitivity Analysis:** Over a wide range of variables, the incremental cost-effectiveness ratios of the screen and treat and screen, treat, and ring vaccinate strategies were less than $50 000 per QALY gained.

**Limitations:** Results depend on the accuracy of the underlying data and assumptions. The long-term effectiveness of new and future HBV treatments is uncertain.

**Conclusions:** Screening programs for HBV among Asian and Pacific Islander adults are likely to be cost effective. Clinically significant benefits accrue from identifying chronically infected persons for medical management and vaccinating their close contacts. Such efforts can greatly reduce the burden of HBV-associated liver cancer and chronic liver disease in the Asian and Pacific Islander population.

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Despite tremendous success in reducing the occurrence of acute and chronic hepatitis B virus (HBV) infection in U.S. children and adolescents (1), chronic HBV infection continues to be a serious health threat to Asian and Pacific Islander adults in the United States (defined here as persons having origins in East, South, and Southeast Asia or in the Pacific Islands [2]). Approximately 10% of Asian and Pacific Islander adults are chronically infected with HBV (3–7), compared with less than 0.5% of the overall U.S. population (8, 9). If unmonitored and untreated, chronic HBV infection results in death from liver failure or liver cancer in up to 1 in 4 people (10, 11); an estimated 3000 to 5000 such deaths occur annually in the United States (12). The striking racial and ethnic disparity in chronic HBV infection in the United States is largely ascribed to the fact that 67% of the Asian and Pacific Islander population is foreign born (13), originating from countries where HBV is endemic and the majority of chronic infections are acquired before adulthood (9). Because of the high prevalence of chronic HBV infection in this population, the incidence of liver cancer is more than 3 times higher among Asian and Pacific Islander males than among white males (14, 15), and 60% to 80% of cases of liver cancer in the Asian and Pacific Islander populations are attributable to HBV infection (16, 17).

To reduce their risk for dying of liver cancer, patients must first know that they are chronically infected with HBV and then be regularly screened for liver cancer (18).

*See also:*

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Recently developed antiviral therapies have been shown to be cost-effective in extending life and reducing morbidity for patients with HBV (19–22). However, as many as two thirds of chronically infected Asian and Pacific Islander adults are unaware of their infection and thus cannot benefit from treatment (6). Incomplete screening coverage also prevents unprotected persons from knowing that they should be vaccinated against HBV and leaves close contacts of chronically infected persons uninformed that they are at increased risk for infection (23).

To date, the national strategy for eliminating HBV transmission has largely focused on vaccinating newborns, children, and adolescents and screening pregnant women (24). The U.S. Advisory Committee on Immunization Practices first recommended HBV vaccination of all infants and children in 1982 (25). Subsequent recommendations were issued to implement catch-up vaccination in most Asian and Pacific Islander children (26) and, later, among all children and adolescents (27). However, a 1998 survey of Asian and Pacific Islander children in 6 major U.S. cities found that completion rates for the 3-dose series were only 14% to 67% (28). In addition, an estimated 40 000 legal immigrants who are chronically infected with HBV enter the United States each year; more than 50% of these individuals are Asian (29). The Advisory Committee on Immunization Practices recently issued screening recommendations that extend to all children and adults born in high-prevalence areas (for example, Asia and the Pacific Islands), regardless of previous HBV vaccination status (24, 30).

We conducted a cost-effectiveness analysis of HBV screening and vaccination strategies targeted to all (U.S.-born and foreign-born) Asian and Pacific Islander adults in the United States.

**Context**

About 10% of Asian and Pacific Islander adults in the United States are chronically infected with hepatitis B virus (HBV). Many are unaware of their infection and do not receive antiviral treatment.

**Contribution**

This analysis assesses the incremental cost-effectiveness of alternative strategies for voluntary screening for HBV in Asian and Pacific Islander adults. Compared with voluntary screening only, a strategy of screening and then treating infected persons and a strategy of screening and treating infected persons and ring vaccinating close contacts were cost-effective (about $36 000 to $40 000 per quality-adjusted life-year gained).

**Implication**

Programs to screen and treat Asian and Pacific Islander adults for HBV infection are probably cost-effective.

*—The Editors*

## METHODS

We used a Markov model of acute HBV infection and disease progression to assess the clinical and economic consequences of alternative HBV screening and vaccination strategies in a hypothetical cohort of 10 000 Asian and Pacific Islander adults 20 to 60 years of age (**Appendix**, available at www.annals.org).

We considered the status quo (voluntary screening only and no incremental screening or vaccination) and 4 incremental strategies: a universal vaccination strategy, in which all individuals are given a 3-dose vaccination series; a screen-and-treat strategy, in which individuals are given hepatitis B surface antigen (HBsAg) blood tests to determine whether they are chronically infected with HBV; a screen, treat, and ring vaccinate strategy, in which all individuals are given HBsAg blood tests to determine whether they are chronically infected, and close contacts of persons found to be infected are also screened with HBsAg and hepatitis B surface antibody blood tests and vaccinated if needed; and a screen, treat, and vaccinate strategy, in which all individuals are given HBsAg and hepatitis B surface antibody blood tests to determine whether they are chronically infected or should be vaccinated, and are then vaccinated with a 3-dose vaccination series if needed. In all cases, chronically infected persons are monitored and treated. We selected these 4 incremental strategies because they are the most clinically relevant. We did not consider all possible combinations of tests, vaccines, and treatments.

We took a societal perspective and included all health care costs and savings, regardless of payer or beneficiary. We estimated costs and benefits of the interventions (deaths averted and quality-adjusted life-years [QALYs] gained) over the lifetime of the cohort, including the lives of infants born to women in the cohort. We assumed that all interventions take place at the start of the time horizon. We discounted all future costs and benefits to the present at 3% (31).

### Decision Tree and Markov Model

We accounted for the dynamics of HBV infection, screening, and vaccination as follows. We start with a cohort of 10 000 persons who may be immune to, susceptible to, or chronically infected with HBV. For simplicity, all persons in the cohort are assumed to be the same age. We assumed age 40 years in the base case and varied age from 20 to 60 years in sensitivity analysis. At the beginning of the time horizon, individuals are screened and vaccinated, based on estimated rates of compliance with the intervention. They then progress through the Markov model on the basis of epidemiologic variables. Acute infections among newborns born to women in the cohort are modeled in a similar manner to that for adults, but with different disease progression variables (**Appendix**, available at www.annals.org).

The model was intended to capture the high-level costs and effectiveness of screening and treating a large cohort. We did not incorporate all clinical characteristics of disease progression and therapies (such as viral load and hepatitis B e antigen status) that would be important for a model focused on clinical treatment recommendations. In sensitivity analysis, we considered a range of values for treatment cost and effectiveness to account for the broad range of therapies (and hepatitis B e antigen status) mentioned in the literature (19–22, 30, 32–37). The model structure was based in part on other models in the literature (21, 22, 38–40) and was reviewed by clinicians involved in the care and treatment of patients with chronic HBV.

We implemented the model in Microsoft Excel (Microsoft Corp., Redmond, Washington), with the software add-in Sensit (Decision Support Services, San Francisco, California) to perform 1-way sensitivity analyses.

### Data and Sources

We estimated values for the model variables (**Table 1** and **Appendix**, available at www.annals.org) on the basis of the medical literature and expert sources (1, 3–7, 10, 11, 19–22, 31–71). We examined 13 articles on the cost-effectiveness of HBV vaccination (38–40, 43, 57, 62, 72–78). Many of these studies focused on infants and children or high-risk groups. Few studies examined screening, and those that did focused on cost savings without examining the health benefits that could accrue from monitoring and treatment of previously unidentified disease (43, 75–77, 79). Many studies have examined the cost-effectiveness of interferon treatment for HBV infection, but few have examined the cost-effectiveness of more recent antiviral therapies (such as adefovir, entecavir, and telbivudine) (19–22, 32–36, 80–82). In sensitivity analysis, we considered low and high values for all variables. Where data were available, low and high values were chosen to reflect ranges in the literature.

### Compliance and Vaccine Effectiveness

We assumed 70% compliance with each intervention. We assumed that in the screen, treat, and vaccinate strategy, all persons who are tested and found to be already infected will accept medical management, and those who are tested and found to be uninfected will be vaccinated. Only persons tested and found to be susceptible are vaccinated. In the universal vaccination strategy, we assumed that all persons who complied were vaccinated, regardless of whether they were already infected or already immune. In the screen, treat, and ring vaccinate strategy, we assumed that public health officials could reach and test, and vaccinate if needed, 70% of an infected person's close contacts. We assumed that the HBV testing program would increase awareness of HBV and thus would increase the proportion of newborns who complete HBV prophylaxis compared with the status quo.

We assumed that all persons who are vaccinated would adhere to the full 3-dose vaccination series, and that vaccine protection lasts for a lifetime. The protection rate after all 3 doses was estimated to be 95% (10, 42, 62). We assumed that the vaccine did not cause any side effects that required medical care (83, 84) and that persons infected with HBV despite vaccination followed the same clinical course as those never vaccinated. For persons who did not comply with any intervention, as well as all persons under the status quo, we assumed that 0.5% would voluntarily vaccinate themselves each year in the future (about 5% over 10 years and 14% over 30 years); we varied this annual value from 0% to 2% in sensitivity analysis.

### Epidemiologic Variables

Recent serologic studies of Asian persons and Pacific Islanders in community settings have found chronic HBV prevalence ranging from 4.3% to 14.5% (3–7). We assumed that 10% of the cohort is chronically infected with HBV at the start of the time horizon and varied this value from 1% to 20% in sensitivity analysis. We assumed that 50% of the cohort is immune from previous resolved infection or vaccination (3, 6). Individuals not already infected or immune (the remaining 40% of the cohort) can become infected over the course of the time horizon (their remaining lifetime). We estimated the annual incidence of acute (that is, newly acquired) HBV infection among persons in the cohort to be 4.8 per 100 000 persons (46). One study suggests that passive surveillance may underreport HBV cases by 50% (44). In sensitivity analysis, we varied the annual incidence of acute HBV infection from 2.0 to 10.0 per 100 000 persons.

We modeled infant and adult acute infections in a manner similar to that in several published cost-effectiveness studies (38–40). We used data on perinatal transmission from a randomized, double-blinded, placebo-controlled trial (47). We modeled adult chronic infection in more detail, using information from a recent study of chronic HBV treatment and recent treatment guidelines (22, 30).

### Tests and Costs

We included costs of all testing, vaccination, and health care (**Table 1**). Test costs were obtained from the Centers for Medicare & Medicaid Services (55). The cost of each HBV vaccine dose was estimated to be $19.48 (56), and the cost to administer each vaccine dose or the blood tests was estimated to be $12.59 (40, 57). We estimated that tracking and contacting close contacts of infected persons (in the screen, treat, and ring vaccinate strategy) would cost $100 per contact (San Francisco Department of Public Health. Personal communication. 2007). We varied this cost from $0 to $500 in sensitivity analysis. We included annual normal health care costs for each person (61, 63).

Costs of medical care for chronic HBV infection were obtained from literature on the economics and cost-effectiveness of hepatitis treatment (19–22, 38, 58–60). Costs of treatment for acute HBV infection were obtained from the cost-effectiveness literature on HBV screening and vac-

*Table 1.* **Values for Model Variables***

| Variable | Base Value | Range | | Source† |
|---|---|---|---|---|
| | | Minimum Value | Maximum Value | |
| **Population** | | | | |
| Cohort age, *y* | 40 | 20 | 60 | Assumed |
| Women, % | 50 | 0 | 100 | Assumed |
| Prevalence | | | | |
| Already immune persons, %‡ | 50 | 30 | 70 | 3, 6 |
| Persons with chronic HBV infection, % | 10 | 1 | 20 | 3–7 |
| Persons with an elevated ALT level when identified as having chronic infection by the intervention, % | 15 | 10 | 30 | Assumed |
| Voluntary behaviors | | | | |
| Compliance with intervention, % | 70 | 10 | 95 | Assumed |
| Annual voluntary screening, % | 0.5 | 0.0 | 2.0 | Assumed |
| Annual voluntary vaccination, % | 0.5 | 0.0 | 2.0 | Assumed |
| Close contacts | | | | |
| Close contacts who are already HBsAg positive, % | 15 | 5 | 30 | 52, 53 |
| Close contacts who are already immune, % | 43 | 10 | 70 | 52, 53 |
| Household members of an HBsAg-positive Asian and Pacific Islander adult, *n* | 3 | 1 | 4 | 54 |
| Additional people in close contact, *n* | 1 | 0 | 2 | 52 |
| Effectiveness in vaccinating close contacts, % | 70 | 50 | 95 | 52 |
| **Annual transition probabilities related to chronic infection** | | | | |
| Normal ALT level transitions | | | | |
| To elevated ALT level, % | 1 | 0.5 | 3 | Assumed |
| To HCC, % | 0.34 | 0.1 | 0.5 | 37 |
| Elevated ALT level transitions | | | | |
| To compensated cirrhosis, % | 3.8 | 0.5 | 12.3 | 22 |
| To HCC, % | 1.5 | 0.5 | 9.5 | 22 |
| To durable virologic response if treated, %§ | 15 | 5 | 30 | 21, 22, 32–34 |
| Durable response transitions | | | | |
| Relapse to elevated ALT level, %§ | 7 | 2 | 15 | 21, 35, 36 |
| To HCC, % | 0.34 | 0.1 | 0.5 | 37 |
| Compensated cirrhosis transitions | | | | |
| To decompensated cirrhosis, % | 7.0 | 3.4 | 9.5 | 22 |
| To HCC, % | 3.3 | 1 | 11.3 | 22 |
| To death, % | 4.8 | 2 | 13.1 | 22 |
| Decompensated cirrhosis transitions | | | | |
| To ascites, %‖ | 35.5 | 26 | 47 | 22 |
| To variceal bleeding, %‖ | 7.6 | 3.7 | 16 | 22 |
| To encephalopathy, %‖ | 5.2 | 2.6 | 16 | 22 |
| To HCC, % | 3.3 | 1 | 11.3 | 22 |
| To liver transplantation, % | 5 | 0 | 40 | 19, 22, 64, 68 |
| To death, % | 17.3 | 5.8 | 22.1 | 22 |
| HCC transitions | | | | |
| To liver transplantation, % | 15 | 5 | 40 | 22, 65, 66, 68–71 |
| To death, % | 35.1 | 18.1 | 45.1 | 22, 50, 51 |
| To death while receiving medical management (because of early detection), % | 20 | 10 | 43.3 | 51 |
| Liver transplantation transition | | | | |
| To death, % | 6.7 | 2 | 11.3 | 22 |
| **Costs¶** | | | | |
| Discount rate, % | 3 | 0% | 5 | 31 |
| Test costs, $ | | | | |
| HBsAg testing (to identify infection)** | 14.43 | 10.00 | 20.00 | 55 |
| Anti-HBs testing (to identify immunity)** | 15.01 | 10.00 | 20.00 | 55 |
| Blood test administration | 12.59 | 5.00 | 15.00 | Assumed |
| Ring contact tracing (per person contacted)†† | 100.00 | 0.00 | 500.00 | Personal communication‡‡ |
| Vaccine costs, $ | | | | |
| Vaccine (per dose) | 19.48 | 15.00 | 25.00 | 56 |
| Vaccine administration | 12.59 | 5.00 | 15.00 | 40, 57 |
| Annual HBV medical management costs | | | | |
| Drugs to treat chronic HBV infection, $§§ | 5000 | 2000 | 12 000 | 19–22 |
| Patients receiving drug therapy while in durable response, %‖‖ | 50 | 0 | 100 | Assumed |
| Regular health monitoring, $ | 612 | 300 | 1200 | 22 |
| Cirrhosis, $ | 1046 | 500 | 5000 | 22 |
| Ascites, $ | 4404 | 1000 | 20 000 | 19, 22 |

*Continued on following page*

*Table 1*—Continued

| Variable | Base Value | Range | | Source† |
|---|---|---|---|---|
| | | Minimum Value | Maximum Value | |
| Encephalopathy, $ | 6024 | 3000 | 20 000 | 19, 22 |
| Variceal hemorrhage, $ | 8686 | 4000 | 24 000 | 19, 22 |
| HCC, $ | 42 018 | 20 000 | 75 000 | 19, 22 |
| Liver transplantation (1-time cost), $ | 192 641 | 80 000 | 350 000 | 19, 22, 58–60 |
| Transplantation follow-up, $ | 24 166 | 10 000 | 50 000 | 19, 22 |
| Annual normal health care, $ | 3403 | 1500 | 4000 | 61, 63 |
| **Quality multipliers** | | | | |
| Acute HBV infection | 0.94 | 0.90 | 1.00 | 40 |
| Chronic HBV, normal ALT level | 1.00 | 0.95 | 1.00 | 21, 40 |
| Chronic HBV, elevated ALT level | 0.99 | 0.90 | 1.00 | 21, 40 |
| Durable response to treatment | 1.00 | 0.90 | 1.00 | 22 |
| Compensated cirrhosis | 0.80 | 0.70 | 0.93 | 21, 22 |
| Decompensated cirrhosis | 0.60 | 0.50 | 0.70 | 21, 22 |
| Hepatocellular carcinoma | 0.73 | 0.50 | 0.80 | 21, 22 |
| Liver transplantation | 0.86 | 0.70 | 0.90 | 21, 22 |

* ALT = alanine aminotransferase; anti-HBs = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCC = hepatocellular carcinoma.
† Numbers are reference numbers.
‡ Recent studies suggest that 31% to 45% of Asian and Pacific Islander adults lack protective antibodies to HBV (3, 6). Given our base assumption that 10% of the cohort is already infected, the remaining 40% of the cohort lacks immunity.
§ We used estimates of the effectiveness of therapies in creating a durable response in persons with chronic HBV infection (21, 22, 32–36) to generate a plausible average effectiveness of therapy across the range of patients that a screening program would be likely to identify.
|| Patients remain in these states of health, with risks for HCC, liver transplantation, and death.
¶ Expressed in 2006 dollars. Costs were converted to 2006 dollars by using the medical care component of the Consumer Price Index.
** Strategies using HBV core antigen testing or aminotransferase screening could also be considered, but HBsAg and anti-HBs are more likely to be considered the most appropriate tests for HBV screening in Asian and Pacific Islander adults, on the basis of experience in large screening programs (3–5). We assumed that the HBsAg and anti-HBs tests had perfect sensitivity and specificity, and testing was therefore not repeated.
†† We assumed a single round of contact tracing (that is, the close contacts of a newly identified chronically infected person would be traced, but the contacts of those close contacts would not be traced).
‡‡ San Francisco Department of Public Health, 2007.
§§ We estimated the annual cost of HBV drug therapy by averaging values found in the literature (19–22). The range of values considered in sensitivity analysis was chosen to reflect the range of costs of different treatments.
|||| Treatments for chronic HBV infection may involve continuous drug therapy, or drug therapy for a given period and then no therapy. To account for possible treatment regimens, we assumed that 50% of individuals who achieve a durable response with therapy will continue to receive drug therapy. The range for this value reflects the possibility of different drug regimens.

cination (38–40). We used costs and effectiveness measures to reflect "average drug therapy" among a heterogeneous patient population. Because of uncertainty about the costs and effectiveness of current and future drug therapies, we used wide ranges for these variables in sensitivity analysis. The lowest range of costs was chosen to be similar to annual costs for lamivudine (20, 21), and the high end of the range was chosen to be similar to higher estimates of annual costs for interferon (21, 22).

### Health Outcomes

We measured discounted QALYs experienced by persons in the cohort and their newborns, as well as the number of HBV-related deaths and the number of children born with HBV. We assumed that each life-year lost as a result of fatal hepatitis represents 1 lost QALY. The utility losses resulting from nonfatal HBV were based on published reports: A utility decrement of 0.06 was assumed for acute infections (40), and utility decrements of 0.01, 0.20, 0.40, 0.27, and 0.14 were assumed for chronic hepatitis with an elevated alanine aminotransferase level, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and liver transplantation, respectively (21, 22, 40). We assumed no utility loss for chronic hepatitis with a normal alanine aminotransferase level (21, 40).

### Role of the Funding Source

We received no funding for this study.

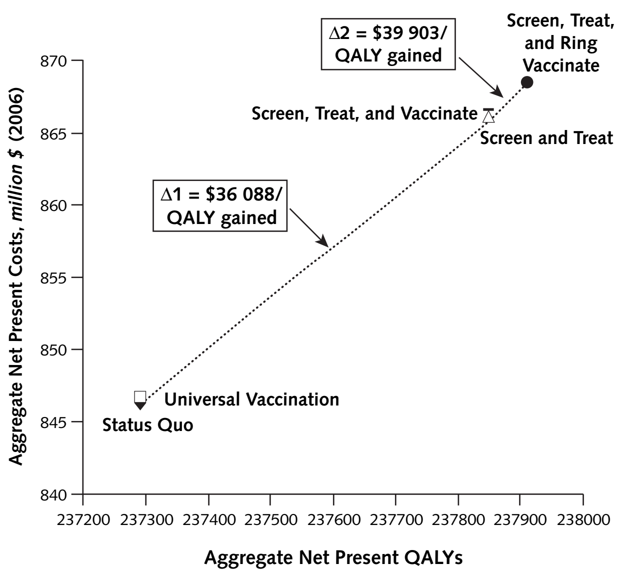
## RESULTS

### Base Case

We calculated the costs incurred and health benefits attained for each intervention and the status quo (**Figure 1**). The universal vaccination and screen, treat, and vaccinate strategies are weakly dominated (**Figure 1**) because they generate higher costs and only slightly higher QALYs compared with the next cheaper alternative strategy and are therefore not as cost-effective (or cost-efficient) as the nondominated strategies. The status quo, the screen-and-treat strategy, and the screen, treat, and ring vaccinate strategy were undominated. The screen-and-treat strategy has an incremental cost-effectiveness ratio of $36 088 per QALY gained compared with the status quo. The screen, treat, and ring vaccinate strategy is slightly more expensive and generates more QALYs than the screen-and-treat strategy. It has a cost-effectiveness ratio of $39 903 per QALY gained compared with the screen-and-treat strategy.

Our analyses show that the main health benefits accrue from screening and subsequent treatment of HBV-infected individuals. Screening identifies persons who are chronically infected but asymptomatic. These individuals can then receive medical management to avoid illness and death from chronic HBV infection. Few neonatal cases are prevented by any of the strategies (**Table 2**). The main costs of strategies that involve screening accrue not from screening but from treatment of newly identified individuals with chronic HBV infection. The strategies that involve vaccination of broad groups (the screen, treat, and vaccinate and universal vaccination strategies) are not cost-effective compared with the other strategies because such vaccination provides little incremental health benefit for the additional vaccination costs (9). Ring vaccination is part of a cost-effective strategy, however, because it identifies and protects individuals who have a much higher chance of acquiring chronic HBV infection than the average person in the cohort.

*Figure 1.* **Total costs incurred and quality-adjusted life-years (*QALYs*) experienced by a cohort of 10 000 persons for each intervention and the status quo.**




### Sensitivity Analysis

We performed 1-way sensitivity analysis over estimated data ranges for all variables (**Appendix**, available at www.annals.org). In almost all cases, the screen and treat and screen, treat, and ring vaccinate strategies had an incremental cost-effectiveness ratio of less than $50 000 per QALY gained.

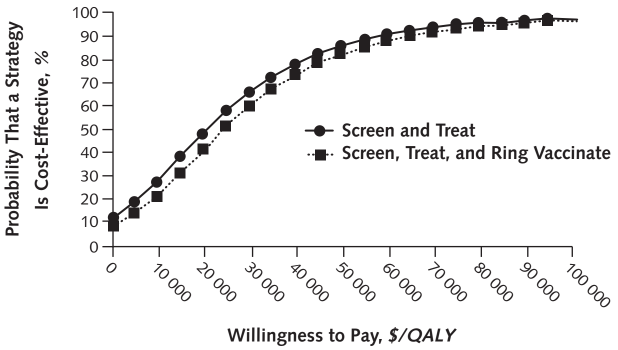
The results were sensitive to several variables, including cohort age, rates of disease progression, effectiveness of therapy, and costs of antiviral drugs to treat chronic HBV infection. For a cohort of older persons (age 60 years), the cost-effectiveness of the screen-and-treat and screen, treat, and ring vaccinate strategies is approximately $58 000 and $67 000 per QALY gained, respectively. The main benefits of the screen-and-treat and screen, treat, and ring vaccinate strategies accrue from medical management of chronic HBV infection in patients found to be infected. If disease progression rates are lower than estimated in the base case, the 2 interventions are less cost-effective than in the base case. For example, if chronic HBV infection is less likely to lead to cirrhosis, the cost-effectiveness of these interventions is around $65 000 per QALY gained. If the cost of drugs to treat chronic HBV infection is half the value assumed in the base case, the cost-effectiveness of the 2 strategies is close to $28 000 per QALY gained; if the drug cost is twice as high as in the base case, the cost-effectiveness is approximately $60 000 per QALY gained. Results were most sensitive to the effectiveness of antiviral drugs in cre-

*Table 2.* **Costs and Health Outcomes of Vaccination Strategies by a Cohort of 10 000 Persons***

| Outcome | Strategy | | | | |
|---|---|---|---|---|---|
| | Status Quo | Universal Vaccination | Screen and Treat | Screen, Treat, and Vaccinate | Screen, Treat, and Ring Vaccinate |
| **Cost, *$1000*** | | | | | |
| Program | – | 673 | 189 | 597 | 467 |
| Health care | 846 008 | 845 965 | 866 015 | 865 995 | 868 145 |
| Total | 846 008 | 846 638 | 866 204 | 866 592 | 868 612 |
| **Outcomes** | | | | | |
| Infected people identified by screening, *n* | – | – | 700 | 700 | 775 |
| HBV-related deaths, *n* | 288.12 | 288.00 | 230.52 | 230.47 | 224.30 |
| Children born with HBV, *n* | 13.06 | 13.06 | 12.03 | 12.03 | 11.91 |
| QALYs experienced | 237 289 | 237 290 | 237 849 | 237 850 | 237 909 |

* HBV = hepatitis B virus; QALY = quality-adjusted life-year.
† All costs and QALYs were discounted to the present at 3%. Costs are expressed in 2006 dollars. Costs and QALYs for HBV-infected children born to women in the cohort were calculated on the basis of newborn life expectancy and other newborn variables and are included in this table in total costs and QALYs experienced.

*Figure 2.* **Results of sensitivity analysis: cost-effectiveness acceptability curves.**




The incremental cost-effectiveness of the screen-and-treat strategy was calculated compared with the status quo, and the incremental cost-effectiveness ratio of the screen, treat, and ring vaccinate strategy was calculated compared with the screen-and-treat strategy. Results are based on 10 000 Monte Carlo simulations. All variables were varied simultaneously. We assumed that each variable was uniformly distributed between the high and low estimates shown in **Table 1**, and that variable values were independent. QALY = quality-adjusted life-year.

ating a durable response: If the effectiveness of antiviral treatment in creating a durable response is only one third the value estimated in the base case, the cost per QALY gained increases to approximately $74 000 and $80 000 for the screen-and-treat and screen, treat, and ring vaccinate strategies, respectively.

The results were not sensitive to the inclusion of infants. Even if the cohort age is fixed to 20 years (the age group most likely to bear children in the future), changing the cohort from all-male (no childbirths) to all-female decreases the cost-effectiveness ratio by less than $10 000 per QALY gained. This is probably because levels of prophylaxis and vaccination for infants are already high.

Over all variable ranges considered, the screen-and-treat and the screen, treat, and ring vaccinate strategies have similar incremental cost-effectiveness ratios compared with the status quo and with each other. Given the relatively small difference in the cost-effectiveness ratios of the 2 strategies, policymakers would probably wish to screen Asian and Pacific Islander adults for chronic HBV infection and also perform ring vaccination.

We conducted probabilistic sensitivity analysis by using Monte Carlo simulation, examining the screen-and-treat and screen, treat, and ring vaccinate strategies (**Figure 2**). Both strategies had similar cost-effectiveness ratios and were likely to be cost-effective. The screen, treat, and ring vaccinate strategy had an 8% chance of being cost-saving, an 82% chance of having an incremental cost-effectiveness ratio of less than $50 000 per QALY gained, and a 97% chance of having an incremental cost-effectiveness ratio of less than $100 000 per QALY gained.

## DISCUSSION

We assessed the cost-effectiveness of 4 strategies for HBV testing and catch-up vaccination among Asian and Pacific Islander adults. Compared with the status quo, the screen-and-treat and screen, treat, and ring vaccinate strategies are highly cost-effective, with incremental cost-effectiveness ratios of approximately $38 000 per QALY gained. This level of cost-effectiveness is similar to that for HIV screening in the general U.S. population, which has been estimated to cost $15 000 per QALY gained (85, 86) and was recently recommended by the Centers for Disease Control and Prevention (87). Medical interventions that cost less than $50 000 per QALY gained are generally considered acceptable (88).

The screen-and-treat and screen, treat, and ring vaccinate strategies are a good health value because they allow infected persons to get proper follow-up and clinical treatment for a disease that can be managed to avoid substantial morbidity and mortality. Vaccination for HBV without screening (the universal vaccination strategy) is not cost-effective precisely because it does not improve the health outcomes of infected persons. The screen, treat, and ring vaccinate strategy is cost-effective because it identifies additional people who need medical management and vaccinates the people who are most likely to become infected. The screen, treat, and vaccinate strategy also identifies people who need medical management and vaccinates individuals who are not protected. This strategy is cost-effective compared with the status quo but is weakly dominated by the screen-and-treat and screen, treat, and ring vaccinate strategies.

We did not include the costs of lost earnings for persons who become ill from HBV infection. This cost is implicitly captured by the quality multipliers for health states (31). Changes in the quality multipliers in sensitivity analysis had little effect on the cost-effectiveness ratios, and in all cases, the screen-and-treat and screen, treat, and ring vaccinate remained the preferred strategies.

Sensitivity analysis shows that the screen-and-treat and screen, treat, and ring vaccinate strategies are cost-effective even if the prevalence of chronic HBV infection is only 1%. The cost of screening is small compared with the costs and benefits of treating persons who are identified by a screening program, so such strategies are cost-effective even at low prevalence. Thus, these strategies may be cost-effective in other populations, such as immigrants from countries with intermediate levels of endemic HBV infection (for example, an HBsAg prevalence of 2% to 7%).

Our analysis has several limitations. We assumed that individuals have a constant annual chance of acquiring HBV infection. Reducing the prevalence of chronic HBV infection through vaccination can have the secondary effect of reducing the incidence of acute HBV infection. However, this reduction may be offset by the high numbers of chronically infected immigrants who enter the United

States each year. We assumed that all individuals identified as having chronic HBV infection would receive treatment if indicated. If fewer persons received treatment, the screening strategies would become less cost effective. Finally, we did not examine all possible screening, vaccination, and treatment combinations. Combinations we did not consider could be cost-effective in certain groups of Asian persons and Pacific Islanders: For example, in elderly persons, ring screening might be appropriate, but ring vaccination might not (because of the slow progression of chronic HBV).

The National Hepatitis B Act, introduced to the U.S. Congress on 15 December 2005 and to the U.S. Senate in June 2006, acknowledged the heavy burden of chronic infection among the Asian and Pacific Islander population and recognized the need for a comprehensive public education and awareness campaign designed to help patients and their physicians identify and manage the illness, as well as the need for government funding and advocacy for HBV prevention, education, research, and medical management (89, 90).

Our analysis shows that HBV screening programs for Asian and Pacific Islander adults are likely to be highly cost effective, but that a broad catch-up vaccination program without screening is unlikely to be cost-effective in this cohort. Clinically significant benefits accrue from identifying chronically infected persons (whose HBV infection can then be managed) and from vaccinating their close contacts. Thus, it is particularly important to focus HBV screening efforts on high-prevalence groups, such as foreign-born Asians and Pacific Islanders (particularly individuals from China and East Asia, where the prevalence of chronic HBV infection is high) and those who have a foreign-born parent.

The Asian and Pacific Islander community is one of the fastest-growing and most diverse populations in the United States (91), but knowledge about HBV in this community is low (6, 92–94). Strong collaboration between the public health system and organizations that provide culturally and linguistically appropriate education and outreach to educate Asians and Pacific Islanders about HBV and its risks (72, 95) is needed to address the high prevalence of chronic HBV infection and the high rate of liver cancer in these populations. Screening adults, along with continued newborn, childhood, and adolescent vaccination efforts, can greatly reduce the large disparity in the disease burden of chronic HBV infection between the Asian and Pacific Islander population and the general population in the United States.

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## APPENDIX

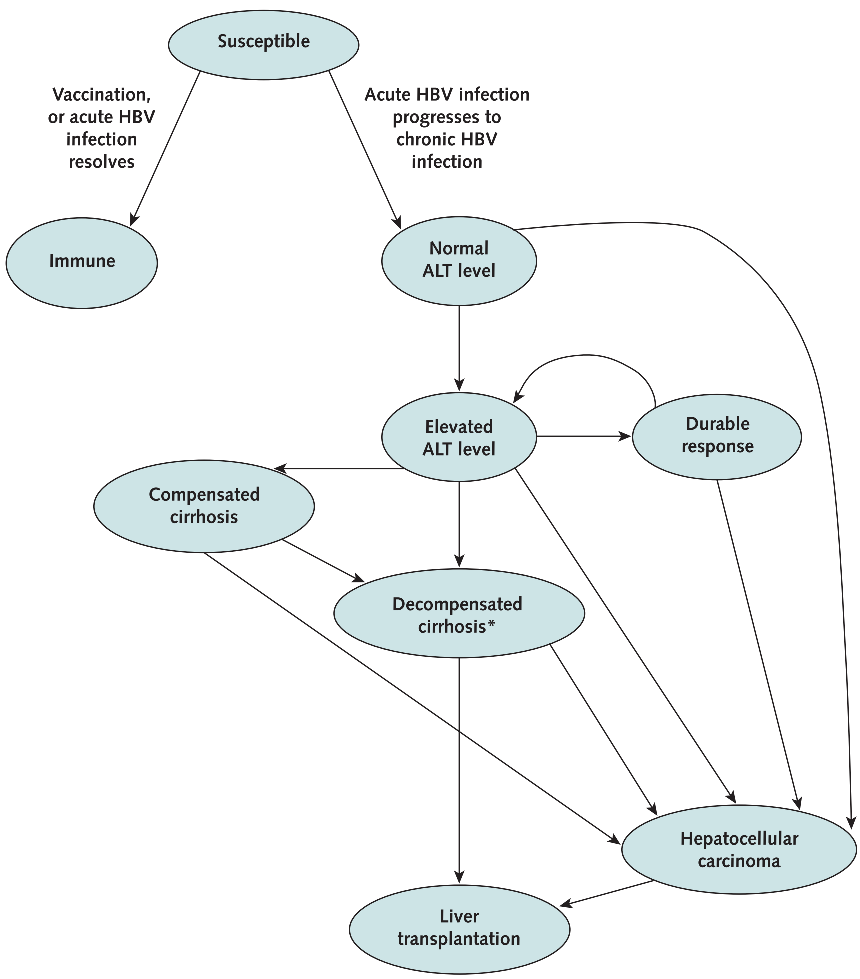
### Model Structure

**Appendix Figure 1** shows our Markov model of HBV infection and progression. **Appendix Figure 2** shows how we modeled acute HBV infection.

### Acute and Neonatal Infection

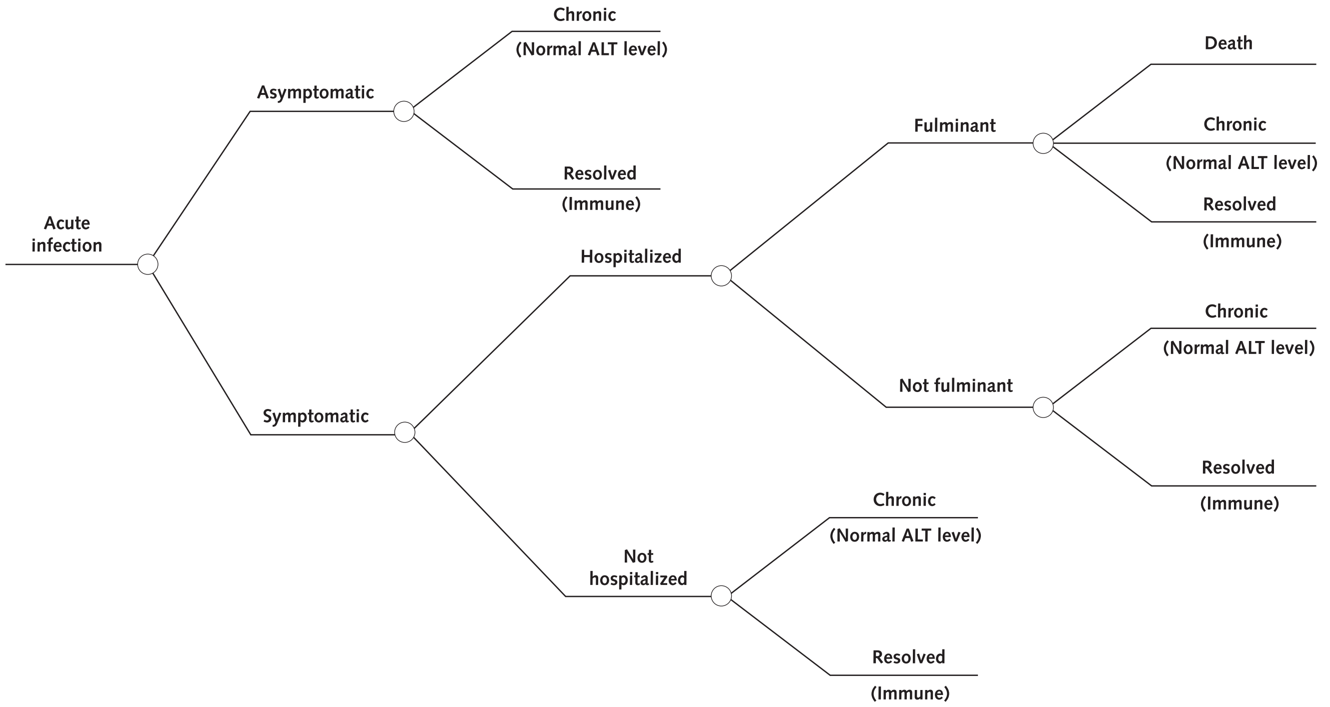
**Appendix Table 1** shows the values for all variables we used in modeling acute HBV infection and neonatal HBV infection. We estimated that 60% of adult HBV acute infections are asymptomatic, 99% of infant HBV acute infections are asymptomatic, and 12% of symptomatic acute infections require hospitalization (38). For both age groups, we estimated that 4% of hospitalized cases are fulminant, with 70% of such cases resulting in death, and that 6% of all adult infections and 90% of infant

*Appendix Figure 1.* **Markov model of hepatitis B virus (*HBV*) infection and progression.**




Circles represent health states, and lines represent transitions. At the start of the time horizon, individuals in the cohort can be in 1 of 4 states: susceptible, immune, normal ALT [alanine aminotransferase] level, or elevated ALT level. For clarity, the state "death" is not shown, although all states can transition to it. Transition rates between chronic HBV states may differ depending on whether the patient is aware of his or her status (and under medical management and treatment). The model was implemented with annual transition probabilities. *The model assumes that individuals in the decompensated cirrhosis state also have ascites, variceal hemorrhage, or encephalopathy.

*Appendix Figure 2.* **Process of acute hepatitis B virus (*HBV*) infection.**




A person who acquires acute HBV infection is assumed to traverse this tree in the span of 1 year. A patient who starts in the susceptible state (see **Appendix Figure 1**) and acquires an acute HBV infection will end in the immune state (if the infection resolves), the normal ALT [alanine aminotransferase] level state (if the infection is chronic), or the death state.

infections become chronic (10, 11, 38, 40). We estimated that 25% of chronic infections in infants eventually progress to liver disease (38, 47). Lifetime costs and QALYs among infants were calculated on the basis of data from the literature and an assumption that symptoms of liver disease would present at age 45 years (38–40).

## Evidence Searches and Summaries

We performed a MEDLINE search in May 2007 to identify relevant data for our model. We found 310 articles using combinations of Medical Subject Heading search terms of *hepatitis B/prevention and control* and *cost-benefit analysis*; *hepatitis B, "immunization"* and *economics*; *and mass screening, hepatitis B,* and *cost-benefit analysis.* We reviewed all studies that assessed cost-effectiveness of interventions to screen and vaccinate individuals for HBV and examined references to articles not found in our search. We supplemented the articles found in this manner with other papers known to the authors (for example, articles in press but not yet published). To find information relevant to current treatment for chronic HBV, we searched for articles published since 2000 by using the Medical Subject Heading search terms *hepatitis B, chronic/therapy* and *cost-benefit analysis*. This search returned 24 articles. We focused on studies that had information relevant to treatment effectiveness and societal-level costs. **Appendix Table 2** shows the relevant studies that we identified. For each key variable in **Table 1**, **Appendix Table 3** shows the range of values provided by the studies described in **Appendix Table 2**.

## Sensitivity Analysis

For the upper and lower limit of each variable range, **Appendix Table 4** shows the incremental cost-effectiveness of the screen and treat strategy compared with the status quo and the incremental cost-effectiveness of the screen, treat, and ring vaccinate strategy compared with the screen and treat strategy. The table does not show results for the universal vaccination or screen, treat, and vaccinate strategies because they were always weakly dominated.

*Appendix Table 1.* **Variable Values Relating to Acute and Neonatal Infection***

| Variable | Base Value | Range | | Source† |
|---|---|---|---|---|
| | | Minimum Value | Maximum Value | |
| **Adult acute HBV infection** | | | | |
| Annual incidence, % | 0.0048 | 0.002 | 0.010 | 1, 43–46 |
| Annual incidence among close contacts, % | 0.038 | 0.005 | 0.154 | Assumed |
| Persons protected by 3 doses of vaccine, % | 95 | 80 | 100 | 10, 42, 62 |
| Asymptomatic adult acute infections, % | 60 | 40 | 80 | 38–40 |
| Symptomatic acute infections that require hospitalization, % | 12 | 2 | 50 | 38–40 |
| Hospitalized cases that are fulminant, % | 4 | 1 | 51 | 38–40 |
| Fulminant cases that result in death, % | 70 | 10 | 100 | 38–40 |
| Infections that become chronic (per acute infection), % | 6 | 3 | 15 | 38–40 |
| **Neonatal infection‡** | | | | |
| Transmission from HBsAg-positive mother | | | | |
| Base HBV transmission from HBsAg-positive mother, % | 92.0 | 80 | 95 | 47 |
| Baseline prophylaxis completion (birth doses), % | 50.0 | 40 | 95 | 38, 48 |
| Effect of testing program on prophylaxis completion, % | 85.0 | 0 | 100 | Assumed |
| Prophylaxis effectiveness, % | 95.0 | 85 | 100 | 49 |
| Infection | | | | |
| Asymptomatic infant infections, % | 99 | 92 | 100 | 47 |
| Probability of becoming a chronic carrier given vertical infection, % | 90.0 | 50 | 95 | 10, 11 |
| Chronic infections that progress to liver disease, % | 25 | 10 | 30 | 38, 47 |
| Infant life expectancy, *y* | 77.5 | 1 | 85 | 41 |
| Age at onset of HBV complications of infant infections, *y* | 45 | 30 | 65 | Assumed |
| **Costs§** | | | | |
| Vaccine costs, $ | | | | |
| Infant vaccination (3 doses + administration) | 56.22 | 40 | 75 | 38 |
| HBIG infant immunoprophylaxis | 48.69 | 40 | 75 | 38 |
| Net present lifetime treatment costs (infant infection), $ | | | | |
| Symptomatic/hospitalized/fulminant/death | 16 465 | 12 000 | 20 000 | 38, 40 |
| Symptomatic/hospitalized/fulminant/no death | 36 549 | 30 000 | 45 000 | 38, 40 |
| Symptomatic/hospitalized/not fulminant | 13 893 | 8000 | 15 000 | 38, 40 |
| Symptomatic/not hospitalized | 468 | 300 | 700 | 38, 40 |
| Liver disease | 114 052 | 87 500 | 130 000 | 38, 40 |

* HBIG = hepatitis B immune globulin; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus.
† Numbers are reference numbers.
‡ The birth rate per woman was calculated as a function of cohort age based on U.S. Census data for Asian and Pacific Islander women (96). We estimated the following annual birth rates per 1000 women: age 20 to 24 years, 83.7; age 25 to 29 years, 134.5; age 30 to 34 years, 128.2; age 35 to 39 years, 59.0; age 40 to 44 years, 13.8; age 45 to 49 years, 0.9; age ≥50 years, 0.0.
§ Expressed in 2006 dollars. Costs were converted to 2006 dollars by using the medical care component of the Consumer Price Index.

*Appendix Table 2.* **Evidence from Selected Studies Related to Key Model Variables***

| Author, Year (Reference) | Intervention Studied | Type of Evidence† | Information Used in Models |
|---|---|---|---|
| Guane et al., 2004 (3) | Screening | III | Proportion of persons with chronic HBV infection |
| Chao et al., 2004 (4) | Screening | III | Proportion of persons already immune; proportion of persons with chronic HBV infection |
| CDC, 2006 (5) | Screening | III | Proportion of persons with chronic HBV infection |
| Lin et al., 2007 (6) | Screening | III | Proportion of persons already immune; proportion of persons with chronic HBV infection |
| Lee et al., 2005 (7) | Screening | III | Proportion of persons with chronic HBV infection |
| van Steenbergen et al., 2004 (52) | Screening, ring vaccination | III | Effectiveness in vaccinating close contacts; number of members in the household of an HBsAg-positive Asian or Pacific Islander; proportion of close contacts who are already HBsAg positive; proportion of close contacts who are already immune |
| Lok et al., 1987 (53) | Screening | III | Proportion of close contacts who are already HBsAg positive; proportion of close contacts who are already immune |
| Chen et al., 2006 (37) | Screening | II-2 | Normal ALT level to HCC; durable response to HCC |
| Kanwal et al., 2005 (22) | Treatment | V | Durable virologic response while receiving treatment; chronic HBV infection with elevated ALT level to compensated cirrhosis; chronic HBV infection with elevated ALT level to HCC; compensated cirrhosis to decompensated cirrhosis; death from compensated cirrhosis; death from decompensated cirrhosis; cirrhosis to HCC; cirrhosis to cirrhosis with ascites; cirrhosis to cirrhosis with variceal bleeding; cirrhosis to cirrhosis with encephalopathy; death from HCC; receiving a liver transplant while in decompensated cirrhosis; receiving a liver transplant while in HCC; death after liver transplantation; costs of HBV drugs, regular HBV health monitoring, cirrhosis, ascites, encephalopathy, variceal hemorrhage, HCC, liver transplantation, and transplantation follow-up; QALY multipliers for durable response to treatment, compensated cirrhosis, decompensated cirrhosis, HCC, and liver transplantation |
| Perrillo et al., 2004 (32) | Treatment | I | Durable virologic response while receiving treatment |
| Peters et al., 2004 (33) | Treatment | I | Durable virologic response while receiving treatment |
| Chan et al., 2005 (34) | Treatment | I | Durable virologic response while receiving treatment |
| Shepherd et al., 2006 (21) | Treatment | IV | Durable virologic response while receiving treatment; durable response relapse to elevated ALT; drug costs; QALY multipliers for chronic HBV with normal ALT level, chronic HBV with elevated ALT level, compensated cirrhosis, decompensated cirrhosis, HCC, and liver transplantation |
| Cooksley, 2004 (35) | Treatment | V | Durable response relapse to elevated ALT level |
| Krogsgaard et al., 1998 (36) | Treatment | I | Durable response relapse to elevated ALT level |
| Wong et al., 2000 (64) | Treatment | V | Receiving a liver transplant while in decompensated cirrhosis; receiving a liver transplant while in HCC |
| Salomon et al., 2003 (50) | Treatment | V | Death from HCC |
| Yuen et al., 2000 (51) | Screening, treatment | II-3 | Death from HCC; death from HCC while receiving medical management |
| Krahn et al., 1998 (57) | Vaccination | V | Vaccine administration (per dose); QALY multipliers for acute HBV infection, chronic HBV with normal ALT level, and chronic HBV with elevated ALT level |
| Brooks et al., 2001 (20) | Treatment | V | Drug costs |
| Bennett et al., 1997 (19) | Treatment | V | Costs of HBV treatment drugs, ascites, encephalopathy, variceal hemorrhage, HCC, liver transplantation, and transplantation follow-up |
| Nath et al., 2006 (58) | Treatment | III | Liver transplantation costs |
| Han et al., 2000 (59) | Treatment | III | Liver transplantation costs |
| Yao et al., 1999 (60) | Treatment | III | Liver transplantation costs |
| CDC, 2004 (1) | Screening | III | Annual acute HBV incidence |
| Kim et al., 2006 (43) | Vaccination | III | Annual acute HBV incidence |
| Alter et al., 1987 (44) | Screening | III | Annual acute HBV incidence |
| Wasley et al., 2007 (45) | Screening | III | Annual acute HBV incidence |
| CDC, 2005 (46) | Screening | III | Annual acute HBV incidence |
| Shivananda et al., 2006 (42) | Vaccination | I | Protected by 3 doses of vaccine |
| Alimonos et al., 1998 (62) | Vaccination | II-1 | Protected by 3 doses of vaccine |
| Jacobs et al., 2003 (40) | Vaccination | V | Asymptomatic acute infections; symptomatic acute infections that require hospitalization; hospitalized cases that are fulminant; fulminant cases that result in death; acute infections that become chronic; net present lifetime treatment costs (infant infection); QALY multipliers for acute HBV infection, chronic HBV with normal ALT level, and chronic HBV with elevated ALT level |

*Appendix Table 2*—**Continued**

| Author, Year (Reference) | Intervention Studied | Type of Evidence† | Information Used in Models |
|---|---|---|---|
| Margolis et al., 1995 (38) | Vaccination | V | Asymptomatic acute infections; symptomatic acute infections that require hospitalization; hospitalized cases that are fulminant; fulminant cases that result in death; acute infections that become chronic; chronic newborn infections that progress to liver disease; baseline prophylaxis completion (birth doses); net present lifetime treatment costs (infant infection) |
| Pisu et al., 2002 (39) | Vaccination | V | Asymptomatic acute infections; symptomatic acute infections that require hospitalization; hospitalized cases that are fulminant; fulminant cases that result in death; acute infections that become chronic |
| Beasley et al., 1983 (47) | Vaccination | I | Base HBV transmission from an HBsAg-positive mother; proportion of infant infections that are asymptomatic; chronic newborn infections that progress to liver disease |
| CDC, 2004 (48) | Vaccination | III | Baseline prophylaxis completion (birth doses) |
| André and Zuckerman, 1994 (49) | Vaccination | IV | Prophylaxis effectiveness |

* ALT = alanine aminotransferase; CDC = Centers for Disease Control and Prevention; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; QALY = quality-adjusted life-year.
† I = randomized, controlled trial; II-1 = controlled trial without randomization; II-2 = cohort or case–control analysis; II-3 = multiple time series, uncontrolled experiment; III = opinions of respected authorities, descriptive epidemiology; IV = systematic review or meta-analysis; V = cost-effectiveness analysis. Adapted from reference 30.

*Appendix Table 3.* **Values from the Literature***

| Variable | Value [Range] (Reference) |
|---|---|
| **Population** | |
| Prevalence | |
| Already immune persons, % | 42.7 (3); 50.3 (6) |
| Persons with chronic HBV infection, % | 10.4 (3); 11.5 (4); 14.8 [12.5–17.1] (5); 8.9 [8.0–10.0] (6); 4.3 (7) |
| Close contacts | |
| Close contacts who are already HBsAg positive, % | 11 (52); 28.3 (53) |
| Close contacts who are already immune, % | 43 (52); 43.1 (53) |
| Additional persons in close contact, *n* | 1.7 (52) |
| Effectiveness in vaccinating close contacts, % | 90 (52) |
| **Probability of chronic infection** | |
| Normal ALT level transition | |
| To HCC | 0.00337 (37) |
| Elevated ALT level transitions | |
| To compensated cirrhosis, % | 3.0, 4.6 [0.5–15] (22) |
| To HCC, %† | 1.5 [0–10] (22) |
| To durable virologic response if treated, % | 25 (interferon), 32 (pegylated interferon), 18 (lamivudine), 18 (adefovir) (HBeAg seroconversion for HBeAg-positive persons), 14 (overall "response" for HBeAg-negative persons) (21); 0, 7 20, 33 [0–40] (interferon) , 0, 4.5, 10, 24, 10, 20 [0–30] (lamivudine), 10, 12, 17.5 [0–20] (adefovir) (22); 11 (lamivudine), 85 (adefovir/lamivudine), 92 (adefovir/lamivudine) (virologic response), 6 (lamivudine), 31 (adefovir/lamivudine) (normalization of ALT) (32); 5 (lamivudine), 47 (adefovir), 53 (adefovir/lamivudine) (normalization of ALT), 0 (lamivudine), 26 (adefovir), 35 (adefovir/lamivudine) (undetectable HBV DNA) (33); 14 (lamivudine), 36 (pegylated interferon/lamivudine) (sustained virologic response after half a year) (34) |
| Durable response transitions | |
| Relapse to elevated ALT level, % | 9 (21); 10–15 (to interferon, mostly within the first year) (35); 10 (relapse after median 4.7 years) (36) |
| To HCC† | 0.00337 (37) |
| Compensated cirrhosis transitions | |
| To decompensated cirrhosis, %† | 7.3 [3.5–10] (22) |
| To HCC, %† | 3.4 [1–12] (22) |
| To death, %† | 4.9 [2–14] (22) |
| Decompensated cirrhosis transitions | |
| To ascites (probability), % | 68 [50–90] (22) |
| To variceal bleeding (probability), % | 14.6 [7–30] (22) |
| To encephalopathy (probability), % | 10 [5–30] (22) |
| To HCC, % | 3.4 [1–12] (22) |
| To liver transplantation, % | 3.1 (19); 25 [0–40] (22); 1.5 (64); 26 of patients put on waiting list, 45 of those received transplant within 2–4 years (65); 16 eligible for transplant (67); 2 of patients with HBV–related cirrhosis per year‡ |
| To death, % | 19 [6–25] (22) |
| HCC transitions | |
| To liver transplantation (probability), % | 30 [0–40] (22); 26 of patients put on waiting list, 45 of patients on waiting list received transplant within 2–4 years (65); 16 eligible for transplant (67); 75 eligible for transplant (69); 11 of patients put on waiting list, 67 of those received transplant (70); 30 eligible for transplant (71); 14 of HCC patients per year§ |
| To death, %§ | 43.3 [20–60] (22); 43.3 [31.9–49.9] (50); 65 (symptomatic HCC) (51) |
| To death while receiving medical management (due to early detection), % | 30 (with detection) (51) |
| Liver transplantation transition | |
| To death, %§ | 6.9 [2–12] (22) |
| **Annual HBV medical management costs** | |
| Drugs | 2361 for interferon-α (1997 USD) (19); 1580.80 for lamivudine, 5589.10 for interferon-α (1999 USD) (20); 158 [50–500] for lamivudine, 528 [100–1000] for adefovir, 750 [500–1000] for interferon (monthly, 2004 USD) (22); 3254.40 for interferon, 6338.88 for pegylated interferon, 1095.36 for lamivudine, 3835.13 for adefovir (2005 GBP) (21) |
| Regular health monitoring | 52 [25–100] per physician visit, 80 [50–150] per laboratory test, 150 [50–250] per ultrasonography (2004 USD) (22) |
| Cirrhosis | 964 [500–5000] (2004 USD) (22) |
| Ascites | 4058 [1000–10 000] (2004 USD) (22); 1633–16 480 (1997 USD) (19) |
| Encephalopathy | 3337, 14 406 [1000–25 000] (2004 USD) (22); 2503–15 700 (1997 USD) (19) |
| Variceal hemorrhage | 4393, 22 444 [2000–30 000] (2004 USD) (22); 3293–17 889 (1997 USD) (19) |
| HCC | 38 715 [20 000–70 000] (2004 USD) (22); 13 037–29 032 (1997 USD) (19) |
| Liver transplantation (1-time cost) | 127 499 [50 000–100 000] (2004 USD) (22); 95 608–243 504 (1997 USD) (19); 35 000–59 600 for HBIG only (58); 10 000 [5000–20 000] per dose of HBIG, 7–19 doses/y (2000 USD) (59); 18 560–58 240 for HBIG only (1999 USD)(60) |
| Transplantation follow-up | 16 697–23 488 (1997 USD) (19); 22 266 [10 000–50 000] (2004 USD) (22) |
| Annual normal health care | 2888 among persons age 6–64 y (2002 USD) (61) |

*Appendix Table 3*—**Continued**

| Variable | Value [Range] (Reference) |
|---|---|
| **Quality multipliers** | |
| Acute HBV infection | 0.94 (40) |
| Chronic HBV, normal ALT level | 1.00 (21); 1.00 (40) |
| Chronic HBV, elevated ALT level | 0.96 (21); 1.00 (40) |
| Durable response to treatment | 1.00 [0.90–1.00] (22) |
| Compensated cirrhosis | 0.56 (21); 0.80 [0.70–0.90] (22) |
| Decompensated cirrhosis | 0.44 (21); 0.60 [0.50–0.70] (22) |
| Hepatocellular carcinoma | 0.44 (21); 0.73 [0.50–0.80] (22) |
| Liver transplantation | 0.68 (21); 0.86 [0.70–0.90] (22) |
| **Adult acute infection** | |
| Annual acute HBV incidence among Asian and Pacific Islanders in the United States, % | 0.00055 in children and adolescents (1); 0.64 [0.47–0.61] in high-risk persons (43); 0.0054 (44); 0.00120 (45); 0.0048 (46) |
| Persons protected by 3 doses of vaccine, % | 95 (10); 98–99 (42); 92 (62) |
| Asymptomatic acute infections, % | 60 (38); 60 (39); 48.9 (40) |
| Symptomatic acute infections that require hospitalization, % | 12 (38); 12 (39); 16.3–19 (40) |
| Hospitalized cases that are fulminant, % | 1 (38); 4 (39); 0.73 (40) |
| Fulminant cases that result in death, % | 70 (38); 70 (39); 55 (40) |
| Infections that become chronic (per acute infection), % | 6 (38); 6 (39); 5.74–8.24 (40) |
| **Neonatal infection** | |
| Transmission from HBsAg-positive mother | |
| Base HBV transmission from HBsAg-positive mother, % | 92 from HBeAg-positive mothers (47) |
| Baseline prophylaxis completion (birth doses), % | 95 for first dose, 76 for all 3 doses (38); 46.0 (48) |
| Prophylaxis effectiveness, % | >90 (49) |
| Infection | |
| Infant infections that are asymptomatic, *n* | 108 of 109 (58 infected placebo recipients and 51 persistently infected HBIG-treated infants) (47) |
| Probability of becoming a chronic carrier given vertical infection, % | 90 (10); 90 (11) |
| Chronic infections that progress to liver disease, % | 25 (38); 25–30 (47) |
| **Costs of vaccination and treatment** | |
| Vaccine | |
| Infant vaccination (3 doses + administration) | 35.01 (1993 USD) (38) |
| HBIG infant immunoprophylaxis | 32.01 (1993 USD) (38) |
| Vaccine administration (per dose) | 11.13 (2002 USD) (40); 24 (1994 CAD) (57) |
| Net present lifetime treatment (infant infection) | |
| Symptomatic/hospitalized/fulminant/death | 16 340 (1993 USD) (38); 21 080 (2002 USD) (40) |
| Symptomatic/hospitalized/fulminant/no death | 16 340 (1993 USD) (38); 21 080 (2002 USD) (40) |
| Symptomatic/hospitalized/not fulminant | 6240 (1993 USD) (38); 8927 (2003 USD) (40) |
| Symptomatic/not hospitalized | 210 (1993 USD) (38); 314 (2002 USD) (40) |
| Liver disease | 20 285, 46 750, 87 000, 96 500 (1993 USD) (38); 2452, 18 337, 26 093 (annual 2002 USD) (40) |

* ALT = alanine aminotransferase; CAD = Canadian dollars; GBP = Great Britain pound; HBeAg = hepatitis B e antigen; HBIG = hepatitis B immune globulin; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; USD = U.S. dollars.

† Annual rate.

‡ We estimated 2%, on the basis of approximately 450 patients with hepatitis B–related cirrhosis receiving liver transplants (68) of 20 000 persons with decompensated cirrhosis (based on about 3500 deaths annually [66] and 17.3% of persons dying each year [22]).

§ We estimated 14%, on the basis of approximately 500 patients with HCC receiving liver transplants (68) of 3500 persons with HCC (based on about 1250 deaths annually [66] and 35.1% of persons dying each year [22]).

*Appendix Table 4.* **Results of One-Way Sensitivity Analysis***

| Variable | Incremental Cost per QALY Gained, $ | | | |
|---|---|---|---|---|
| | Screen and Treat vs. Status Quo | | Screen, Treat, and Ring Vaccinate vs. Screen and Treat | |
| | At Minimum Value | At Maximum Value | At Minimum Value | At Maximum Value |
| **Population** | | | | |
| Cohort age | 23 640 | 58 255 | 25 518 | 67 605 |
| Women | 36 174 | 36 003 | 39 999 | 39 808 |
| Prevalence | | | | |
| Already immune persons | 36 088 | 36 088 | 39 903 | 39 903 |
| Persons with chronic HBV infection | 39 130 | 35 919 | 39 903 | 39 903 |
| Persons with an elevated ALT level when identified as having chronic infection by the intervention | 40 710 | 28 352 | 45 237 | 30 943 |
| Voluntary behaviors | | | | |
| Compliance with intervention | 36 089 | 36 088 | 37 077 | 59 981 |
| Annual voluntary screening | 36 556 | 34 926 | 40 159 | 39 403 |
| Annual voluntary vaccination | 36 096 | 36 065 | 39 995 | 39 633 |
| Close contacts | | | | |
| Close contacts who are already HBsAg positive | 36 088 | 36 088 | 48 041 | 37 834 |
| Close contacts who are already immune | 36 088 | 36 088 | 40 254 | 39 652 |
| Household members of an HBsAg-positive Asian and Pacific Islander adult | 36 088 | 36 088 | 39 903 | 39 903 |
| Number of additional people in close contact | 36 088 | 36 088 | 39 903 | 39 903 |
| Effectiveness in vaccinating close contacts | 36 088 | 36 088 | 39 903 | 39 903 |
| **Annual transition probabilities related to chronic infection** | | | | |
| Normal ALT level transitions | | | | |
| To elevated ALT level | 39 710 | 29 228 | 44 281 | 31 689 |
| To HCC | 34 684 | 36 908 | 38 803 | 40 543 |
| Elevated ALT level transitions | | | | |
| To compensated cirrhosis | 63 745 | 28 219 | 69 443 | 31 680 |
| To HCC | 43 025 | 26 468 | 47 412 | 29 251 |
| To durable virologic response if treated | 73 834 | 23 871 | 80 178 | 26 766 |
| Durable response transitions | | | | |
| Relapse to elevated ALT level | 27 512 | 48 542 | 30 733 | 53 202 |
| To HCC | 32 879 | 38 374 | 36 492 | 42 332 |
| Compensated cirrhosis transitions | | | | |
| To decompensated cirrhosis | 37 365 | 35 462 | 41 275 | 39 230 |
| To HCC | 37 161 | 34 017 | 41 103 | 37 585 |
| To death | 36 898 | 34 799 | 40 910 | 38 297 |
| Decompensated cirrhosis transitions | | | | |
| To ascites | 36 100 | 36 078 | 39 915 | 39 893 |
| To variceal bleeding | 36 118 | 36 038 | 39 932 | 39 853 |
| To encephalopathy | 36 097 | 36 058 | 39 912 | 39 873 |
| To HCC | 37 161 | 34 017 | 41 103 | 37 585 |
| To liver transplantation | 36 827 | 33 936 | 40 584 | 37 924 |
| To death | 35 881 | 36 135 | 39 847 | 39 916 |
| HCC transitions | | | | |
| To liver transplantation | 36 813 | 34 260 | 40 554 | 38 302 |
| To death | 27 438 | 38 217 | 32 393 | 41 752 |
| To death while receiving medical management (because of early detection) | 40 913 | 28 119 | 44 098 | 33 011 |
| Liver transplantation transition | | | | |
| To death | 36 113 | 36 076 | 39 890 | 39 910 |
| **Costs** | | | | |
| Discount rate | 26 517 | 44 835 | 27 920 | 51 356 |
| Test costs | | | | |
| HBsAg testing (to identify infection) | 36 033 | 36 157 | 39 867 | 39 949 |
| Anti-HBs testing (to identify immunity) | 36 088 | 36 088 | 39 765 | 40 041 |
| Blood test administration | 35 994 | 36 118 | 39 694 | 39 969 |
| Ring contact tracing (per person contacted) | 36 088 | 36 088 | 37 142 | 50 946 |
| Vaccine costs | | | | |
| Vaccine (per dose) | 36 090 | 36 086 | 39 786 | 40 048 |
| Vaccine administration | 36 089 | 36 088 | 39 685 | 39 972 |
| Annual HBV medical management costs | | | | |
| Drugs to treat chronic HBV infection | 26 135 | 59 312 | 30 028 | 62 946 |
| Patients receiving drug therapy while in durable response | 29 207 | 42 969 | 33 070 | 46 736 |
| Regular health monitoring | 28 838 | 49 745 | 32 705 | 53 462 |

## *Appendix Table 4*—Continued

| Variable | Incremental Cost per QALY Gained, $ | | | |
|---|---|---|---|---|
| | Screen and Treat vs. Status Quo | | Screen, Treat, and Ring Vaccinate vs. Screen and Treat | |
| | At Minimum Value | At Maximum Value | At Minimum Value | At Maximum Value |
| Cirrhosis | 36 288 | 34 644 | 40 102 | 38 465 |
| Ascites | 36 255 | 35 323 | 40 070 | 39 140 |
| Encephalopathy | 36 110 | 35 987 | 39 925 | 39 803 |
| Variceal hemorrhage | 36 138 | 35 927 | 39 952 | 39 742 |
| HCC | 35 227 | 37 379 | 39 062 | 41 163 |
| Liver transplantation (1-time cost) | 35 826 | 36 454 | 39 655 | 40 250 |
| Transplantation follow-up | 35 799 | 36 616 | 39 627 | 40 408 |
| Annual normal health care | 34 355 | 36 632 | 38 171 | 40 447 |
| **Quality multipliers** | | | | |
| Acute HBV infection | 36 088 | 36 088 | 39 897 | 39 913 |
| Chronic HBV, normal ALT level | 36 088 | 36 088 | 39 757 | 39 903 |
| Chronic HBV, elevated ALT level | 31 700 | 36 652 | 35 065 | 40 524 |
| Durable response to treatment | 49 793 | 36 088 | 54 911 | 39 903 |
| Compensated cirrhosis | 35 048 | 37 537 | 38 757 | 41 498 |
| Decompensated cirrhosis | 35 843 | 36 337 | 39 633 | 40 177 |
| Hepatocellular carcinoma | 36 416 | 35 990 | 40 257 | 39 797 |
| Liver transplantation | 36 207 | 36 059 | 40 028 | 39 872 |
| **Adult acute HBV infection** | | | | |
| Annual incidence | 36 088 | 36 088 | 39 903 | 39 903 |
| Annual incidence among close contacts | 36 088 | 36 088 | 40 253 | 38 754 |
| Persons protected by 3 doses of vaccine | 36 088 | 36 088 | 39 903 | 39 903 |
| Asymptomatic adult acute infections | 36 088 | 36 088 | 39 835 | 39 972 |
| Symptomatic acute infections that require hospitalization | 36 088 | 36 088 | 40 017 | 39 473 |
| Hospitalized cases that are fulminant | 36 088 | 36 088 | 39 956 | 39 096 |
| Fulminant cases that result in death | 36 088 | 36 088 | 39 960 | 39 875 |
| Infections that become chronic (per acute infection) | 36 088 | 36 088 | 40 034 | 39 514 |
| **Neonatal infection** | | | | |
| Transmission from HBsAg-positive mother | | | | |
| Base HBV transmission from HBsAg-positive mother | 36 091 | 36 088 | 39 907 | 39 902 |
| Baseline prophylaxis completion (birth doses) | 36 084 | 36 109 | 39 898 | 39 927 |
| Effect of testing program on prophylaxis completion | 36 084 | 36 066 | 39 929 | 39 878 |
| Prophylaxis effectiveness | 36 091 | 36 087 | 39 906 | 39 902 |
| Infection | | | | |
| Asymptomatic infant infections | 36 088 | 36 088 | 39 902 | 39 903 |
| Probability of becoming a chronic carrier given vertical infection | 36 099 | 36 087 | 39 915 | 39 902 |
| Chronic infections that progress to liver disease | 36 102 | 36 084 | 39 919 | 39 898 |
| Infant life expectancy | 36 174 | 36 084 | 39 998 | 39 898 |
| Age at onset of HBV complications of infant infections | 36 067 | 36 105 | 39 880 | 39 922 |
| **Costs** | | | | |
| Vaccine costs | | | | |
| Infant vaccination (3 doses + administration) | 36 088 | 36 089 | 39 903 | 39 903 |
| HBIG infant immunoprophylaxis | 36 088 | 36 089 | 39 903 | 39 904 |
| Net present lifetime treatment costs (infant infection) | | | | |
| Symptomatic/hospitalized/fulminant/death | 36 088 | 36 088 | 39 904 | 39 903 |
| Symptomatic/hospitalized/fulminant/no death | 36 088 | 36 088 | 39 903 | 39 903 |
| Symptomatic/hospitalized/not fulminant | 36 088 | 36 088 | 39 926 | 39 899 |
| Symptomatic/not hospitalized | 36 088 | 36 088 | 39 903 | 39 903 |
| Liver disease | 36 088 | 36 088 | 39 903 | 39 903 |

* Expressed in 2006 dollars. ALT = alanine aminotransferase; anti-HBs = hepatitis B surface antibody; HBIG = hepatitis B immune globulin; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCC = hepatocellular carcinoma.