

Economic Benefits of Hepatitis B Vaccination at Sexually Transmitted Disease Clinics in the U.S.

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SYNOPSIS

Objective. This study assessed the long-term economic implications of a national program to vaccinate all adults treated at sexually transmitted disease (STD) clinics in a single year.

Methods. A model was developed to track the long-term disease outcomes and costs among a hypothetical cohort of 2 million STD clinic clients accessing services in one year, using data from published sources and demonstration projects at STD clinics in San Diego (California), Illinois, and Denver (Colorado). The model estimated net economic benefits of a routine hepatitis B vaccination policy at STD clinics nationwide compared with no vaccination.

Results. Without a vaccination program, an estimated 237,021 new hepatitis B virus (HBV) infections would occur over the lifetimes of the 2 million STD clinic clients seen in a single year. HBV-related medical costs and productivity losses would be \$1.6 billion. In a national program for routine vaccination at STD clinics, 1.3 million adults would be expected to receive at least one vaccine dose, and an estimated 45% of the new HBV infections expected without vaccination would be prevented. The vaccination program would cost \$138 million, HBV infections occurring despite the program would cost \$878 million, and clients' time and travel would cost \$45 million. The net economic benefit (savings) of routine vaccination would be \$526 million. If the indirect costs of lost productivity due to HBV infection are not considered, routine vaccination would have a net cost of \$28 million.

Conclusions. Estimates from this model suggest a national program for routine hepatitis B vaccination of adults at STD clinics would be a cost saving to society.

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In the U.S., a majority of adult hepatitis B virus (HBV) infections occur through sexual contact among men who have sex with men, heterosexual people with multiple sexual partners, and through the use of contaminated equipment among injection drug users.^{1,2} Since 1982, hepatitis B vaccination has been recommended for these high-risk groups, but vaccination coverage among them has been low.^{3,4} To overcome barriers to vaccination, the Advisory Committee on Immunization Practices (ACIP) has endorsed a strategy that includes routine vaccination of all adults at certain public-health venues where most clients are at high risk for HBV infection, including sexually transmitted disease (STD) clinics, human immunodeficiency virus counseling and testing sites, drug-abuse treatment facilities, and correctional facilities.⁵ Pilot programs in STD clinics demonstrated that hepatitis B vaccination can be feasibly integrated with other STD prevention services when vaccine was available and provided free of charge to clinic clients.⁶⁻⁹

Publicly funded STD programs operate clinic services for an estimated 1.8 million to 2.2 million individual clients annually (unpublished data, Centers for Disease Control and Prevention).⁹ Clinics in these programs have the physical infrastructure needed to provide hepatitis B vaccination, but most would require additional funds for vaccine purchase, vaccine administration, staff training, and vaccination record-keeping for a comprehensive vaccination program.⁷ The costs and benefits of financing such a program have not been adequately addressed, and could be key information for policy makers considering allocating funds for vaccination in these settings. In this study, we estimated the net economic benefits of a hepatitis B vaccination program at public STD clinics nationwide.

METHODS

Study design

We assumed a national program that would offer hepatitis B vaccine to a cohort of 2 million adult clients at STD clinics in one year and tracked the long-term disease outcomes and costs in a decision model (Figure 1). The model compared two scenarios: (1) no hepatitis B vaccination and (2) universal hepatitis B vaccination. In scenario 1, without vaccination, adults who did not have immunity from prior (resolved) infection or vaccination faced the risk of infection and a fraction of them became infected with HBV over their lifetimes. In scenario 2, vaccination was offered to all adults who did not report prior vaccination. Among adults who received vaccination and did not have immunity from prior infection or vaccination, immunity developed

based on the number of doses received and estimated vaccine efficacy after each dose. Adults who did not develop immunity from vaccination, or did not have immunity from prior infection, faced the risk of infection, and a fraction of them became infected. Routine vaccination was expected to lower infections in the client population and reduce cost of illness but add program costs. The net economic benefit of routine vaccination was estimated as the difference in expected societal costs under the two scenarios, discounted to 2005 dollars.¹⁰ Discounting accounts for differential timing of costs under the two scenarios.¹¹

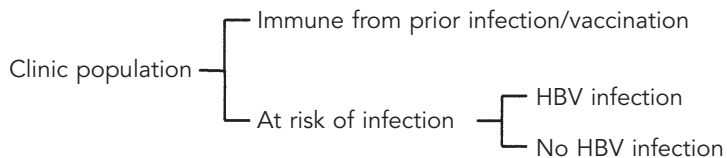
Disease progression and risk of HBV infection. Under both scenarios, people with newly acquired HBV infection were followed in a Markov model of natural history of HBV infection (Figure 1).¹² We assumed that the majority of adults with a new HBV infection would remain asymptomatic; about 30% would have acute illness that may include jaundice, hospitalization, and fulminant liver failure (FLF); and 6% would develop chronic infection.¹³⁻¹⁵ Of those who developed chronic HBV infection, we assumed the majority would remain asymptomatic, 0.06% would be hospitalized annually for acute exacerbation,¹⁶ and 0.5% would develop compensated cirrhosis or hepatocellular carcinoma (HCC) each year.¹⁷⁻²⁶ After each year, people with compensated cirrhosis would remain in the same health state or progress. Those whose disease progressed would develop either decompensated cirrhosis or HCC. Patients with FLF, cirrhosis, or HCC would have higher mortality rates compared with the general population. Patients with FLF, decompensated cirrhosis, and HCC were also candidates to receive liver transplantation. Those without infection, with resolved infection, and with chronic hepatitis B but no disease manifestations were assumed to have the same mortality rate as the general population.²⁷ Any of the transitions were permissible to a patient only once during follow-up. We used this model to estimate the long-term outcomes of HBV infection and their costs.

Based on a catalytic model of age-specific prevalence of antibody to hepatitis B-core antigen (anti-HBc) among 300 clients at an STD clinic in San Diego, we estimated the average risk of HBV infection during the remaining lifetime of clinic clients to be about 15%.^{13,28} Prevacination testing was not evaluated, as studies had already shown that in populations with HBV infection prevalence lower than 30%, routine vaccination without prevaccination testing was more cost-effective.²⁹⁻³²

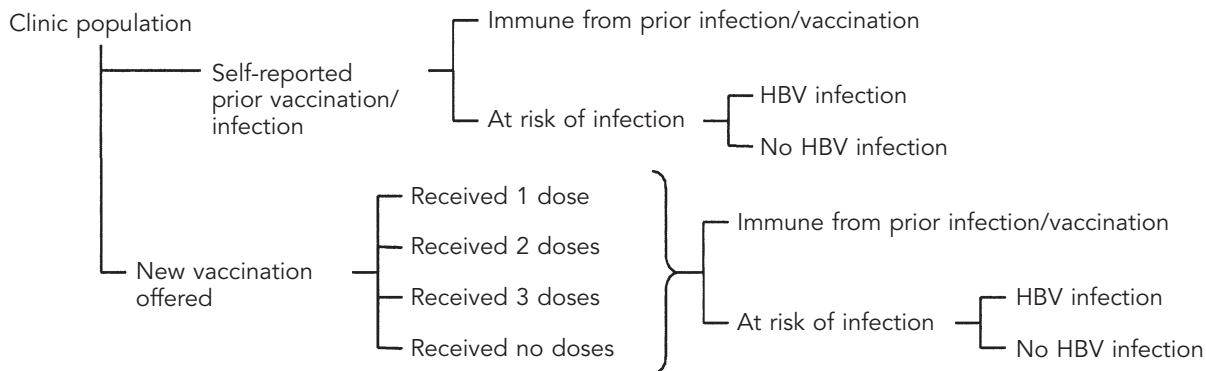
Routine vaccination at STD clinics. We assumed a three-dose series of monovalent adult hepatitis B vaccine

Figure 1. Hepatitis B vaccination at STD clinics: decision and Markov models

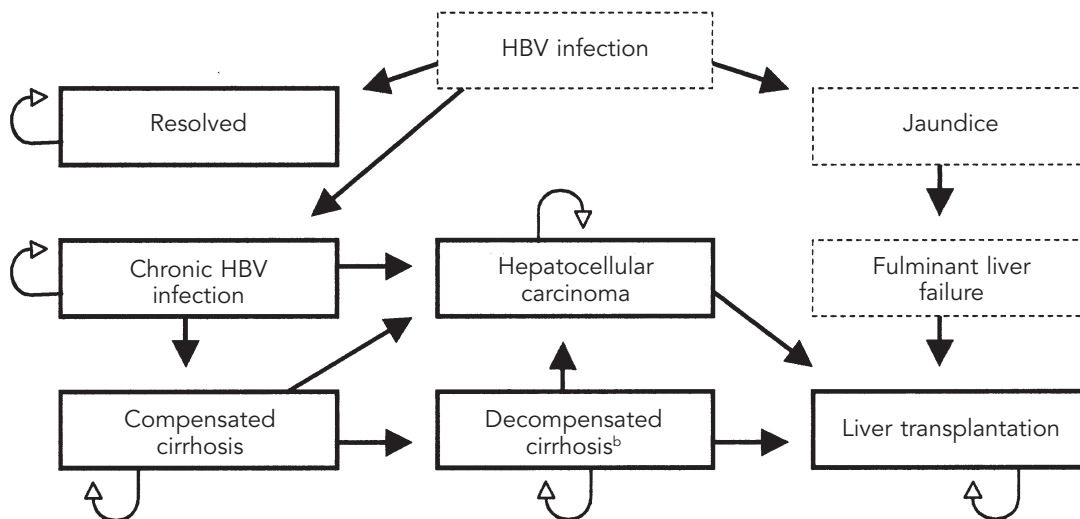
Scenario 1: no vaccination



Scenario 2: routine vaccination



Markov model of hepatitis B disease progression^a



^aBox with solid borders represents an annual health state, arrows indicate allowed transitions; death from each state not shown separately. Box with dashed borders represents health state only allowed in the first year of the model.

^bDecompensated cirrhosis includes ascites, variceal hemorrhage, and encephalopathy.

STD = sexually transmitted disease

HBV = hepatitis B virus

administered following the recommended schedule would be offered in one year to all clients who did not report prior vaccination.²⁹ Protective immunity would develop among 90% who completed the series, 75% who received two doses, and 40% who received a single dose.^{33–35} We assumed vaccine protection would be lifelong and adverse effects would be negligible.

Based on self-reported prior vaccination, we assumed 90% of adults would be eligible for vaccination, and based on the vaccine acceptance in demonstration projects (Viral Hepatitis Integration Projects, VHIPs) in San Diego, Denver, and Illinois, we assumed 50% to 75% would receive at least one dose of vaccine. Among those who received one dose, 40% to 55% would receive a second dose, and 20% to 30% would complete the series.^{6–8,36} Among those who would be offered vaccine, we assumed 16% would be immune from prior infection (based on anti-HBc positivity).²⁸ We assumed that 10% of vaccine would be wasted due to storage and handling.³⁷

Cost of illness. Lifetime medical cost and productivity loss from HBV infection was estimated from outputs of the Markov model. The model used updated medical cost data for acute and chronic hepatitis B adjusted for inflation (Table 1). Productivity losses from hepatitis B-related excess mortality, adjusted for unemployment rate and inflation, were estimated from median daily wages of the U.S. population.³⁸ All costs were discounted at a 3% annual rate, a standard rate established by the U.S. Panel on Cost-Effectiveness in Health and Medicine.¹¹

Program costs. We assumed vaccines would be offered at no charge to clients; the program would purchase vaccine at the U.S. federal contract price (Table 1);³⁹ and the vaccine administration costs would be similar to those incurred in the VHIPs.^{6–8,36} Also based on the VHIPs, we included infrastructure costs associated with staff training, supervision, protocol development, and record-keeping associated with vaccination, but excluded the physical infrastructure cost associated with establishing and maintaining clinic facilities.⁷ All program costs were assumed to occur in the initial year, and, hence, were not discounted. We also included clients' cost of time and travel for the second and third doses of vaccine. We assumed patients would spend a mean of one hour at the clinic at each vaccination visit—the typical time recorded for visits in the San Diego pilot study.²⁸ We also assumed that preparation for a clinic visit would take one hour, and another hour would be spent traveling each way, to and from the clinic. We valued patient time at an average \$8.50 per hour, for a total of \$34.00 per clinic visit. To estimate

the mean cost of patients' time, we assumed 30% of patients at STD clinics are competitive employees, earning \$16.13 per hour as estimated from the national monthly data of private average hourly earnings of production workers,⁴⁰ while 70% earn the minimum wage (\$5.15 per hour in 2005).

Base-case and sensitivity analyses

In the U.S., more than 80% of the adults attending STD clinics are 30 years of age or younger.⁹ To reflect this statistic, we ran the base-case analysis for a cohort aged 25 years. For the Markov model, long-term disease progression rates from published studies were converted to annual rates using the formula $p=1-\exp(-rt)$; where p is the long-term rate, r is the annual rate, and t is the time between two health states.⁴¹ All base-case parameter values are reported in Table 1. We used univariate sensitivity analysis to examine the impact on model outcomes of changes in the uncertain model parameters. We also carried out threshold analyses of the two variables to which model outcomes were most sensitive, to determine the respective input levels at which medical cost savings alone would just compensate for program costs.

RESULTS

Baseline estimation

In scenario 1, without a vaccination program, the model estimated 237,021 new HBV infections would occur over the lifetime of the 2 million annual STD clinic clients. These new infections would result in 71,106 acute hepatitis B cases and 14,221 cases of chronic HBV infection. Among people with acute hepatitis B, 1,138 would develop FLF, 137 would require liver transplantation, and 848 would die. Among those with chronic HBV infection 2,933 would develop cirrhosis, 917 would develop HCC, 121 would require liver transplantation, and 3,060 would die. The societal cost of HBV infections would be \$1,587 million: \$346 million in medical costs and \$1,241 million in productivity losses (Table 2).

In the first year of a national vaccination program (scenario 2), a total of 1.3 million clients would receive vaccination: 626,040 clients would receive a single dose, 306,360 clients would receive two doses, and 399,600 clients would receive three doses of vaccine. This level of vaccine coverage would prevent 105,828 of the new HBV infections expected without vaccination, a 45% reduction. Reduction in infection would avert 31,748 acute hepatitis B cases and resultant complications, including 508 FLF cases, 61 liver transplantations, and 378 deaths. In addition, 6,350 chronic HBV infections

Table 1. Base-case parameter estimates of vaccination, and HBV infection and disease, among people treated at STD clinics at age 25

<i>Parameter</i>	<i>Base-case value</i>
Self-reported prior vaccination or infection (percent)	10.0
Immune from prior infection (percent)	16.0
Immune from prior vaccination (percent) ^a	5.0
Risk of infection in remaining lifetime (percent)	15.0
Vaccine dose completion rates (percent)	
First dose	74.0
Second dose among recipients of first dose	53.0
Third dose among recipients of first dose	30.0
Vaccine efficacy by dosage (percent)	
1 dose	40.0
2 doses	75.0
3 doses	90.0
Outcomes of new HBV infection (percent)	
Symptomatic acute hepatitis B	30.0
Asymptomatic acute hepatitis B	70.0
Outcomes of symptomatic acute hepatitis B (percent) ^b	
Jaundice	83.0
Hospitalization	22.0
FLF	1.6
Death	1.0
Liver transplantation among patients with FLF (percent) ^c	12.0
Chronic HBV infection among new infections (percent)	6.0
Annual disease progression rates from chronic hepatitis B	
Hospitalization for acute exacerbation ^d	0.0006
Compensated cirrhosis	0.0050
HCC	0.0002
Annual disease progression rates from compensated cirrhosis	
Hospitalization	0.2243
Decompensated cirrhosis	0.0338
HCC	0.0246
Death	0.0380
Annual disease progression rates from decompensated cirrhosis	
HCC ^e	0.0246
Liver transplantation by age (in years) ^f	
20–29	0.0098
30–39	0.0228
40–49	0.0324
50+	0.0200
Death	0.2639
Annual disease progression rates from HCC	
Liver transplantation by age (in years) ^g	
20–29	0.0195
30–39	0.0457
40–49	0.0649
50+	0.0399
Death ^h	0.7110
Annual mortality rate from liver transplantation ⁱ	0.1390

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Table 1 (continued). Base-case parameter estimates of vaccination, and HBV infection and disease, among people treated at STD clinics at age 25

<i>Parameter</i>	<i>Base-case value</i>
Annual medical costs per case (in 2005 U.S. dollars)	
Jaundice, no hospitalization	\$367
Jaundice, hospitalized ^d	\$8,081
FLF ^e	\$17,407
Chronic hepatitis B, hospitalized ^d	\$13,980
Compensated cirrhosis, no hospitalization	\$1,321
Compensated cirrhosis, hospitalized	\$24,567
Decompensated cirrhosis	\$45,593
HCC	\$38,381
Liver transplantation, first year	\$272,420
Liver transplantation, follow-up years	\$26,676
Mean daily productivity loss (in 2005 U.S. dollars) ^k	\$145
Program costs (in 2005 U.S. dollars)	
Vaccine price per dose ^l	\$24.25
Vaccine administration cost per dose ^m	\$12.00
Protocol development and record-keeping per dose	\$5.00
Staff training and supervision per 10,000 doses	\$125,000.00
Client's travel cost for vaccination per visit ⁿ	\$6.00
Client's time cost for vaccination per visit ⁿ	\$34.00

^aIn San Diego, California, 10% of the clients reported prior vaccination or infection; we assumed that only half of them would have prior immunity.

^bBased on data from Sentinel Counties' Surveillance for acute viral hepatitis, Division of Viral Hepatitis, Centers for Disease Control and Prevention, 2000–2003.

^cRate of liver transplantation among FLF was the mean ratio of the estimated number of liver transplants for hepatitis B-related acute FLF cases among adults provided by United Network for Organ Sharing to the estimated number of hepatitis B-related acute FLF cases among adults from surveillance data.

^dBased on the National Inpatient Sample, Healthcare Utilization Project. Agency for Healthcare Research and Quality, Department of Health and Human Services (US), 2003.

^eAnnual progression rate from decompensated cirrhosis to HCC was the same as the annual rate of HCC from compensated cirrhosis.

^fAnnual rates of liver transplantation among decompensated cirrhosis patients were assumed to be half the rates of liver transplantation for HCC.

^gEstimated ratios of age-specific liver transplantation for HCC from United Network for Organ Sharing, to annual age-specific U.S. HCC incidence from National Program of Cancer Registries, Centers for Disease Control and Prevention, and Surveillance Epidemiology and End Results, National Cancer Institute for the years 1998–2001 (Personal communication, F. Ahmed, National Center for Chronic Disease Prevention and Health Promotion, November 2005).

^hMortality rate among HCC patients was estimated from mean annual survival data for patients with liver and intrahepatic bile duct cancer, 1997–2001.

ⁱBased on the survival rates of liver transplant for malignant neoplasm, United Network for Organ Sharing as of August 19, 2005.

^jEstimated by applying Medicare mean national cost to charge ratios to the mean hospitalization charges culled from the National Inpatient Sample, Healthcare Utilization Project, Agency for Healthcare Research and Quality, Department of Health and Human Services (US), 2003.

^kAnnual productivity loss was estimated by multiplying the daily loss by 260 annual workdays times 0.95 for 5% unemployment adjustment. No productivity loss was included for adults >65 years of age.

^lVaccine price includes \$0.75 per dose Federal Excise Tax that covers compensation for vaccine-related injuries.

^mThe estimated vaccine administration cost was the mean cost from 10,048 records of private sector reimbursement for one dose of adult hepatitis vaccination, estimated from MarketScan[®] less average private sector vaccine price. This is higher than the administration cost estimated from STD clinics' operations data, and closer to the true cost of vaccine administration.

ⁿTransportation cost based on mean per-mile cost of \$0.40 and mean round-trip travel of 15 miles. Time cost calculated at \$8.50 per hour; mean time spent in preparation, transit, and clinic visit is four hours.

HBV = hepatitis B virus

STD = sexually transmitted disease

FLF = fulminant liver failure

HCC = hepatocellular carcinoma

would be prevented, which would avert 1,309 cirrhosis cases, 410 HCC cases, 54 liver transplantations, and 1,366 deaths.

The first year of the vaccination program would require 2,708,400 doses of vaccine (including an estimated 10% wastage) and cost \$138 million, including \$95 million for vaccine and administration, \$30.5 million for staff training and supervision, and \$12.2 million for protocol development and vaccination record-keeping. In addition, clients' travel and time for vaccination would cost \$45 million. HBV infections that occur despite the vaccination program would cost \$879 million, including \$192 million in medical costs

and \$687 million in productivity losses. The total cost of HBV infection and management with a vaccination program is \$1,061 million (compared with \$1,587 million without vaccination), yielding a net economic benefit of \$526 million. If indirect costs of potential productivity losses were excluded from the analysis, the vaccination program would have a net cost of \$28 million, or \$263 per new HBV infection averted.

Sensitivity analysis

The net economic benefit was most sensitive to changes in the cohort age, risk of infection, proportion of clients receiving at least one dose, and mean daily

Table 2. Hepatitis B vaccination at STD clinics: expected outcomes and economic implications among 2 million clients

	Scenario 1: no vaccination	Scenario 2: routine vaccination	Difference ^a
Clinical outcomes (number of cases)			
New HBV infection	237,021	131,194	105,828
Acute infections	71,106	39,358	31,748
Jaundice	59,018	32,667	26,351
FLF	1,138	630	508
Chronic HBV infection	14,221	7,872	6,350
Cirrhosis	2,933	1,623	1,309
HCC	917	508	410
Liver transplantation:			
For acute hepatitis B	137	76	61
For chronic hepatitis B	121	67	54
Death			
From FLF	848	469	378
From cirrhosis and HCC	3,060	1,694	1,366
Cost outcomes			
Medical costs	\$345,976,333	\$191,501,439	\$154,474,894
Productivity loss	\$1,240,941,712	\$686,873,930	\$554,067,782
Total	\$1,586,918,045	\$878,375,369	\$708,542,676
Program costs			
Vaccine and administration	N/A	\$94,929,420	N/A
Staff training and supervision	N/A	\$30,469,500	N/A
Protocol development and immunization records	N/A	\$12,187,800	N/A
Total	N/A	\$137,586,720	N/A
Clients' travel cost for vaccination	N/A	\$6,633,360	N/A
Clients' time cost for vaccination	N/A	\$38,075,486	N/A
Total cost	\$1,586,918,045	\$1,060,670,935	\$526,247,110
Cost without productivity losses	\$345,976,333	\$373,797,005	-\$27,820,672
Net economic benefit ^b	N/A	N/A	\$526,247,110
Net economic benefit without productivity loss	N/A	N/A	-\$27,820,672

^aSome differences are inexact due to rounding errors.

^bNet economic benefit is the difference between the two scenarios of the sum of cost of illness, program costs, and clients' travel and time costs for vaccination.

STD = sexually transmitted disease

HBV = hepatitis B virus

FLF = fulminant liver failure

HCC = hepatocellular carcinoma

N/A = not applicable

wage—changing 11% to 17%, with a 10% change from base-case value of any of the parameters. Net economic benefit was relatively less sensitive to changes in vaccine efficacy, rates of receiving dose two and dose three among patients receiving dose one, prevalence of immunity from prior infection (anti-HBc prevalence), proportion of new infections with acute hepatitis B, lifetime risk of chronic HBV infection, annual rate of compensated cirrhosis among people with chronic HBV infection, and the annual discount rate; changing 1% to 9%, with a 10% change in each parameter (Figure 2). Net economic benefit changed less than 1%, with a 10% change in each of the other parameters.

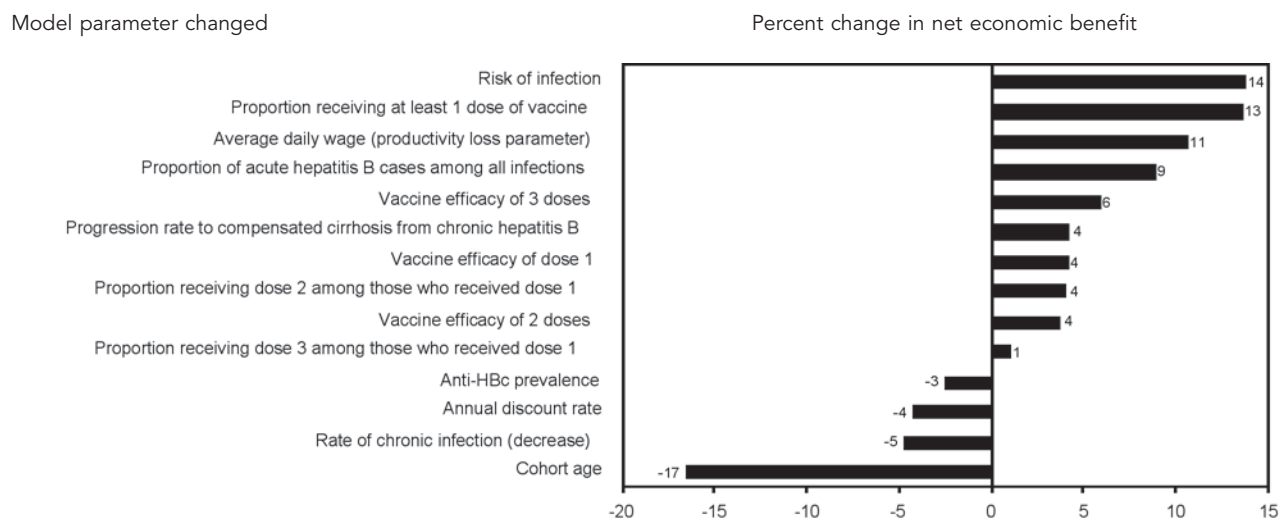
The net economic benefit without productivity losses was relatively more sensitive to all parameter values, with the lifetime risk of HBV infection, and the proportion of STD clients who accept the first dose of vaccine, as the most influential inputs. In a scenario in which lost productivity due to illness was not considered, the net economic benefits increased by 56%, with a 10% increase of either parameter from baseline levels. We determined that medical cost savings alone would be sufficient to compensate for program-related costs if either the lifetime risk of infection among susceptible patients increased by 3% (to 17.7%) or the proportion of STD clinic clients who accept the first dose of vaccine increased by 13% (to 87.3%).

DISCUSSION

Enhanced disease surveillance in four U.S. counties indicated that 36% of those reported with acute hepatitis B between 1996 and 1998 had been previously treated for an STD.² This finding provides a strong rationale for vaccinating adults who are provided with health care at STD clinics. Integrating routine hepatitis B vaccination in public STD clinics would require developing a program that provides vaccine, pays for vaccine administration, and trains professionals to administer vaccination. Our estimates indicate that such an undertaking would be economically beneficial to the country. Expenditures on vaccination would decrease long-term disease incidence and avert costs, with a net savings to society of more than \$500 million in the program's first year.

Despite the anticipated economic benefit, funding for routine vaccination for adults who are un- or underinsured has been inadequate. Over the past decade, in the absence of a national program, state and local STD programs have developed hepatitis B vaccination programs and sought financing from existing sources with limited success. A 2001 survey of STD programs found that 33% of programs had a policy for hepatitis B vaccination and about 65% of clinics in these program areas offered vaccine.⁴² However, only 26% offered vaccine to all STD clinic clients, and the

Figure 2. Sensitivity analyses: change in net economic benefit in response to 10% change in model parameter values from base case^a



^aParameter change is an increment unless otherwise indicated.

Anti-HBc = antibody to hepatitis B core antigen

lack of vaccine funding was cited as the major barrier to program implementation.⁴³ Thus, STD programs nationwide require substantial additional financing to implement ACIP recommendations for adult hepatitis B vaccination.⁷

Limitations

Our analysis has several limitations. First, the model assumes that scale-up vaccination for the target population in one year is feasible. Although the model estimates were based on pilot programs, if program activities could not be scaled up during this time frame, our model may overestimate the benefits of a vaccination program. Second, we expect that sufficient funds would be available in a national program to achieve the level of vaccine compliance assumed in the base case; if lower vaccine completion rates were allowed, both costs and net savings would be lower.⁴⁴ Our estimated cost of illnesses was conservative because we included productivity loss from mortality only, and excluded antiviral treatment costs for chronic hepatitis B. Both acute and chronic hepatitis B-related illnesses could lead to a patient's inability to work at least in the short term and increase the cost of illness. Also, antiviral treatment costs are likely to increase the costs of illness.⁴⁵ With higher costs of illness, the net economic benefit of vaccination would be higher. In the absence of a more exact measurement, we also assumed a constant rate of development of both HCC and cirrhosis, likely overestimating the cost of disease by increasing the burden at younger ages. Finally, we did not consider the potential herd-immunity effects of routine vaccination within or outside the cohort, which is likely to make vaccination more cost-effective.⁴⁶

CONCLUSION

In the U.S., programs providing routine infant vaccination since 1991 and catch-up adolescent vaccination since 1995 have led to dramatic declines in hepatitis B incidence.^{1,5,47} Currently, more than 90% of new infections occur among adults, and many of those infected have previously sought health care in venues such as STD clinics, HIV counseling and testing sites, drug abuse treatment facilities, and correctional facilities.^{1,2,5} National programs that would finance hepatitis B vaccination in these settings can improve vaccination coverage among people at risk for HBV infection, and reduce the burden of hepatitis B among adults in the U.S. As highly immunized cohorts age, vaccinating adults will become a less essential strategy; however, implementing these programs can accelerate elimination of HBV infection among adults until highly immunized cohorts

vaccinated through routine infant and adolescent vaccination programs reach adulthood.

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