Cost-Effectiveness of Nationwide Hepatitis B Catch-up Vaccination Among Children and Adolescents in China

David W. Hutton,[1] Samuel K. So,[2] and Margaret L. Brandeau[1]

Liver disease and liver cancer associated with childhood-acquired chronic hepatitis B are leading causes of death among adults in China. Despite expanded newborn hepatitis B vaccination programs, approximately 20% of children under age 5 years and 40% of children aged 5 to 19 years remain unprotected from hepatitis B. Although immunizing them will be beneficial, no studies have examined the cost-effectiveness of hepatitis B catch-up vaccination in an endemic country like China. We examined the cost-effectiveness of a hypothetical nationwide free hepatitis B catch-up vaccination program in China for unvaccinated children and adolescents aged 1 to 19 years. We used a Markov model for disease progression and infections. Cost variables were based on data published by the Chinese Ministry of Health, peer-reviewed Chinese and English publications, and the GAVI Alliance. We measured costs (2008 U.S. dollars and Chinese renminbi), quality-adjusted life years, and incremental cost-effectiveness from a societal perspective. Our results show that hepatitis B catch-up vaccination for children and adolescents in China is cost-saving across a range of parameters, even for adolescents aged 15 to 19 years old. We estimate that if all 150 million susceptible children under 19 were vaccinated, more than 8 million infections and 65,000 deaths due to hepatitis B would be prevented. *Conclusion*: The adoption of a nationwide free catch-up hepatitis B vaccination program for unvaccinated children and adolescents in China, in addition to ongoing efforts to improve birth dose and newborn vaccination coverage, will be cost-saving and can generate significant population-wide health benefits. The success of such a program in China could serve as a model for other endemic countries. (HEPATOLOGY 2010;51:405-414.)

China has the greatest burden of chronic hepatitis B virus (HBV) infection and liver cancer in the world, with an estimated 95 million people (7.3% of China's population) living with chronic HBV

infection and more than 40% of the worldwide deaths associated with HBV infection. Based on 2006 World Health Organization estimates, liver cancer and liver disease caused by acute and chronic HBV infection account for 263,000-300,000 deaths in China each year: a burden that exceeds the combined mortality from tuberculosis (200,000), HIV/AIDS (38,000), and malaria (37).[1-7]

In 1992, the Chinese government recommended HBV vaccination of all newborns; however, because of high vaccine prices and vaccination fees, many newborns were not vaccinated.[1] In 2002, the Chinese Ministry of Health partnered with the Global Alliance for Vaccines and Immunization (now known as the GAVI Alliance) to provide nationwide free HBV vaccines for all newborns and officially added infant HBV vaccination to China's National Immunization Program. These recent initiatives successfully increased newborn immunization nationwide, even in the poorer western provinces that traditionally had low vaccination rates.[1] The estimated three-dose vaccination coverage among infants increased from 70.7% among those born in 1997 to 89.8% among those born in 2003.[1](4)
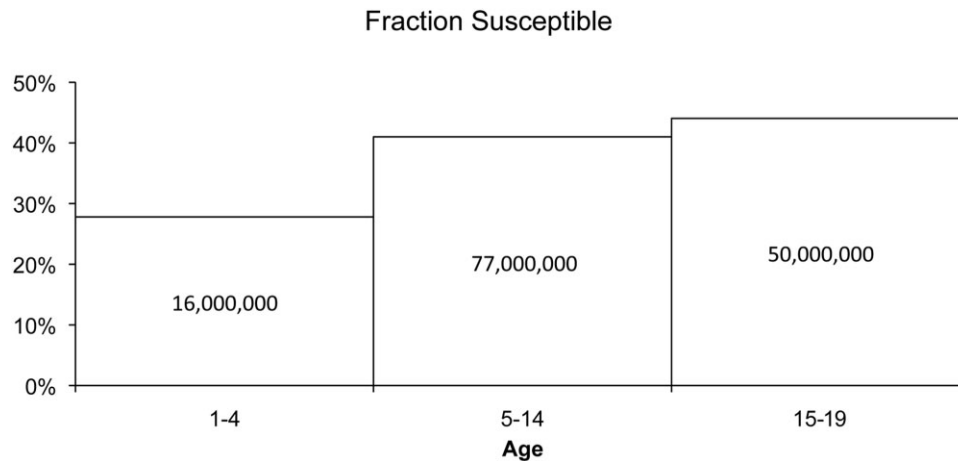
Fraction Susceptible

Fig. 1. Fraction and number of children and adolescents in China susceptible to HBV infection, by age group. The height of the bars represents the fraction of the population in that age group susceptible to HBV infection. Numbers inside the bars represent total numbers of people susceptible. Based on data from the 2006 China National Hepatitis Seroprevalence Survey.[8]

However, a substantial number of children and adolescents, particularly those born before 2002 in poorer rural provinces, are not protected from the virus. Data released by the Chinese Ministry of Health from its 2006 national seroepidemiologic study of more than 81,000 people showed that more than 20% of 1- to 4-year-olds and 40% of 5- to 19-year-olds remain unprotected from HBV (Fig. 1).[8] This equates to almost 150 million children and adolescents across all of China.[9] Although China encourages catch-up vaccination for unvaccinated children based on the observation of prior recommendations for newborn vaccination, compliance was poor until the vaccinations were made totally free.[1]

Traditionally, catch-up vaccination for unprotected children has not been included in the global strategy to control hepatitis B, primarily based on the assumption that without vaccination at birth, most children or adolescents will have been infected.[10,11] Very few studies have evaluated HBV vaccination in areas of high endemicity, and none have examined the cost-effectiveness of catch-up vaccination.[10] However, in light of the reduced vaccine costs and large numbers of unprotected individuals, it is important to reconsider the infant-only HBV vaccination paradigm and examine new programs to expand vaccination to children and adolescents in China who did not receive the HBV vaccine at birth.

We assessed the cost-effectiveness of a nationwide catch-up HBV vaccination program for children aged 1 to 19 years in China, taking a societal perspective and measuring all costs and health benefits (measured in quality-adjusted life years [QALYs]) of the vaccination programs.

Materials and Methods

We considered a strategy of catch-up vaccination for children and compared it with the status quo with current levels of vaccination coverage. The catch-up vaccination strategy provides hepatitis B vaccination immediately for children and adolescents who missed newborn vaccination. For children not participating in the intervention (and for all individuals under the status quo), we assumed that 0.5% would voluntarily seek the vaccine themselves each year in the future.

We developed a model to project costs and health impacts of both acute and chronic HBV infection. We developed a probability tree to evaluate the outcomes of acute HBV infection (new infection that is either asymptomatic or symptomatic) and a Markov model of disease progression to evaluate the health and economic impacts accruing from treated and untreated chronic HBV infection. The Markov model of disease progression captures the long-term effects of chronic HBV infection, which represent a much larger part of the overall disease burden of HBV than the effects of acute infection.[12] We modeled costs and health states for a hypothetical cohort of 10,000 children and adolescents aged 1 to 19 years throughout their lifetimes. We calculated costs and benefits for the overall cohort, and we examined individual cohorts of age 1 to 4 years, 5 to 10 years, 11 to 14 years, and 15 to 19 years. We measured costs and health outcomes in discrete time increments of 1 year, similar to other analyses.[13,14]

According to World Health Organization criteria,[15] an intervention is considered "very cost-effective" if the cost per disability-adjusted life year gained is less than the annual per capita gross domestic product, which in China is

approximately $2,500[16-18] (17,000 Chinese Yuan Renminbi [RMB]). An intervention is considered a good value if it costs less than three times the per capita gross domestic product. Because QALYs are roughly similar to disability-adjusted life years,[19] we use a threshold of 17,000 RMB ($2,500) per QALY gained for the intervention to be very cost-effective.

Data and Sources. To gather data needed for our model (Table 1, Supporting Tables 1 and 2), we performed a Medline search to review previous cost-effectiveness analyses of HBV vaccination in both China and the United States[1,20-22] and, more importantly, published Chinese government reports, national sero-epidemiologic surveys, and peer-reviewed articles published in Chinese. Values for model parameters were drawn from the existing literature when available. In most instances, Chinese data were used, although parameters that were less specific to China (e.g., those relating to the natural history of disease) were taken from international literature (Supporting Table 2). When no data were available, informed expert judgment was used (personal communication with the Chinese Center for Disease Control and Prevention (CDC), the China Foundation for Hepatitis Prevention and Control's national experts, and the World Health Organization's technical experts in China and the Western Pacific Region). In sensitivity analysis, we considered low and high values for all variables, using ranges to reflect values in the literature where available.

Some parameters varied by age (Supporting Table 1). The initial prevalence of chronic HBV infection and of HBV immunity are different for different age groups. In addition, background mortality and the chance that an acute infection develops into a chronic infection vary by age. For example, an acute infection in a 1-year-old child has an 86% chance of becoming chronic, whereas an acute infection in a 5-year-old child has only a 30% chance of becoming chronic. As the model steps forward in time, these parameters are updated according to the aging of the children. We assumed that all other parameters relating to disease progression did not vary by age.

Compliance and Vaccine Effectiveness. We assumed that parents who knew of their children's infection or prior hepatitis B vaccination history would not have their children vaccinated. Of those unaware of their vaccination history or infection, we assumed that 70% complied with the intervention, regardless of the age of the children.

We assumed that the vaccination would consist of a three-dose series, and that the protection rate from three doses of the vaccine was 95%.[23-25] If the children complied with the intervention, we assumed that they all received all three doses, based on known high completion

rates in the target population.[1,26] We assumed that costs associated with program implementation would be similar to that of a recently completed 2-year, province-wide, school-based, pilot catch-up vaccination program that one of the authors (S. S.) helped to initiate in partnership with the Chinese CDC and Ministry of Health, the China Foundation for Hepatitis Prevention and Control, and the Qinghai provincial CDC and government.[27] The program provided free HBV catch-up vaccination and education for more than 500,000 children in kindergarten and primary school in the entire remote province of Qinghai between 2006 and 2008.[26] Vaccination at each school clinic was administered through the existing provincial CDC immunization offices that have branches to serve the immunization needs of the various districts in the province. We did not include program setup costs in the model, because such costs could be highly variable depending on the size and scope of a vaccination program. Setup cost for the recent Qinghai province catch-up vaccination program was approximately $0.40 (2.7 RMB) per child; we included this setup cost in our sensitivity analysis.

Epidemiologic Parameters. Epidemiological studies of HBV in China over the past 15 years have shown a reduction in the national estimates of HBV prevalence and incidence due to the expanded newborn immunization efforts. Estimates of the prevalence of chronic HBV infection in the general Chinese population dropped from 9.75% in a national survey conducted between 1992 and 1995, to 7.18% in a more recent 2006 national survey.[8,28] The prevalence of chronic HBV infection among young children is lower because children have had higher vaccination coverage than older members of the population. The latest national serological survey of more than 80,000 people conducted in 2006 in China estimated chronic HBV infection prevalence to be 0.96% among the almost 60 million children aged 1 to 4 years and 2.42% among the almost 190 million children aged 5 to 14 years.[8] Using prevalence data from this serological survey,[8] we estimated base case incidence of acute HBV infection to be 100/100,000 per year per unvaccinated person, regardless of age (see Supporting Information for calculations). Because estimates of incidence vary, we varied this parameter between 20/100,000 and 500/100,000 in sensitivity analysis.[6,8,20,21,29,30] We discuss incidence in terms of acute HBV infection per unvaccinated person because the policy affects unvaccinated persons and we wished to provide a comparable risk of infection across age groups. This incidence number is higher than published incidence numbers that are based on entire populations (for the latter, the denominator is larger and thus the reported incidence statistic is lower).

Table 1. Parameter Values: Base Value and Range Considered in Sensitivity Analysis

Parameter	Base Value	Range Minimum Value	Range Maximum Value	References
Population				
Discount rate	3%	0%	5%	35
Probabilities				
Starting population				
Compliance with vaccine intervention	70%	10%	95%	–
Percent chronically infected who are aware of infection*	50%	33%	95%	45,46
Percent aware who receive medical management	50%	0%	100%	–
Chronic infections that have elevated ALT	2.0%	0.5%	5.0%	–
Already immune (given no chronic infection)	50%	33%	75%	–
Aware of immunity (previous vaccination)	75%	50%	100%	–
Protected by three doses of HBV vaccine	95%	92%	99%	23-25
Annual voluntary vaccination	0.5%	0.0%	2.0%	–
Acute infection				
Annual acute HBV infection incidence	100/100,000	20/100,000	500/100,000	6,8,20,21,29,30
Asymptomatic acute infections	90%	40%	99%	31,32,37,47,48
Symptomatic acute infections that require hospitalization	12%	2%	50%	31,32,37
Hospitalized cases that are fulminant	4%	1%	51%	31,32,37
Fulminant cases that result in death	70%	10%	100%	31,32,37
Disease progression parameters (annual probabilities)				
Normal ALT to elevated ALT†	0.15%	0.10%	0.20%	49
Normal ALT to HCC	0.34%	0.15%	0.50%	51
Durable virologic response while on treatment	15%	5%	30%	13,38,52-54
Chronic HBV infection with elevated ALT to compensated cirrhosis	3.8%	0.5%	12.3%	13,36
Chronic HBV infection with elevated ALT to HCC	1.5%	0.5%	9.5%	13,36
Durable response relapse to elevated ALT	7%	2%	15%	13,55,56
Durable response to HCC	0.34%	0.15%	0.50%	51
Compensated cirrhosis to decompensated cirrhosis	7%	3%	10%	13,36
Mortality from compensated cirrhosis	4.8%	2.0%	13.1%	13,36
Mortality from decompensated cirrhosis	17.3%	5.8%	22.1%	13,36
Cirrhosis to HCC	3.3%	1.0%	11.3%	13,36,57
Cirrhosis to cirrhosis with ascites	68%	50%	90%	13
Cirrhosis to cirrhosis with variceal bleeding	14.6%	7.0%	30.0%	13
Cirrhosis to cirrhosis with encephalopathy	10%	5%	30%	13
Receiving a liver transplant while in decompensated cirrhosis	1.5%	0%	40%	13,36,58-60
Mortality from HCC	40.0%	32.0%	47.3%	13,36,61,62
Mortality from HCC while on medical management (due to early detection)	20%	10%	40%	62
Receiving a liver transplant while in HCC	0.1%	0%	40%	13,36,60,63-67
Mortality first year after liver transplantation	15%	7.5%	30%	13,36
Mortality second and subsequent years after liver transplantation	1.5%	0.75%	3.0%	13,36
Cost (USD)				
Vaccine				
Vaccine (per dose)	0.34	0.26	0.43	68–70‡
Vaccine administration (per dose)	0.60	0.35	7.66	69§
Liver transplantation	30,000	7,500	120,000	36,71
Annual treatment				
Fraction of patients on drug therapy while in durable response§	50%	0%	100%	–
Drugs	2,000	500	8,000	36,72
Regular health monitoring	250	62.50	1,000	22,71
Cirrhosis	2,000	500	8,000	22,36,71
Ascites	2,500	625	10,000	22,36,71
Encephalopathy	2,500	625	10,000	22,36,71
Variceal hemorrhage	2,500	625	10,000	22,36,71
HCC	5,000	1250	20,000	22,36,71
Transplantation follow-up	3,000	750	12,000	36
Annual normal health care costs	118	30	472	17
Quality multipliers				
Acute HBV infection	0.94	0.90	1.00	37
Chronic HBV infection, normal ALT	1.00	0.95	1.00	37,38
Chronic HBV infection, elevated ALT	0.99	0.90	1.00	36–38
Durable response	1.00	0.90	1.00	13
Compensated cirrhosis	0.80	0.70	0.93	13,36,38
Decompensated cirrhosis	0.60	0.50	0.70	13,36,38
HCC	0.73	0.50	0.80	13,36,38
Liver transplantation	0.86	0.70	0.90	13,36,38

*Percentage of all chronically infected individuals who are aware of their infection.

†This value was estimated from Lin et al.[49] and then calibrated to yield approximately 25% mortality from untreated liver disease.[23,50]

‡Personal communication (Dr. S. So with physicians in China).

§Some therapies are discontinued if the therapy suppresses the virus. This parameter is the fraction of patients who continue on drug therapy after the therapy has suppressed the virus into a "durable response."

Abbreviations: ALT, alanine aminotransferase; anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBsAg+, hepatitis B surface antigen-positive; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; USD, U.S. dollars.

Acute HBV infections were modeled in a similar manner to those of other published cost-effectiveness studies.[31,32] The likelihood of an acute HBV infection becoming chronic varies by age. We used a data from a meta-analysis[33] to relate this likelihood with age (see Supporting Table 1 for estimated values). There are differences of opinion about this likelihood, especially at older ages,[34] so we performed sensitivity analysis on this probability.

Health Outcomes and Costs. We measured health and economic outcomes for all children and adolescents in the cohort over their lifetimes. Because newborn vaccination coverage is rapidly increasing in China,[1] we excluded the effects of infection on future children born to girls currently in the cohort. We took a societal perspective and included all costs and savings, regardless of source or beneficiary, and we discounted all costs and health outcomes to the present at 3%.[35]

We included the costs of vaccination, treatment, and all other health care costs for HBV-infected and uninfected individuals in the cohort over their lifetimes. We did not count time from work or school due to disease, because that morbidity is accounted for in quality-of-life adjustments.[35] We gathered treatment cost data from several recent studies of the cost of chronic HBV infection in China[22,36] and then converted them to U.S. dollars. Because costs vary significantly for different regions of China, we conducted sensitivity analysis on all cost parameters.

We measured several health outcomes including deaths, HBV infections averted, and QALYs gained. Quality adjustments for health states were taken from published literature.[13,36-38]

Results

Base Case. Base case results for the entire cohort of children and adolescents aged 1 to 19 years, and for individual age cohorts, are shown in Table 2. In all cases, catch-up vaccination is cost-saving: it increases QALYs and saves costs compared with the status quo.

Sensitivity Analysis. We performed two-way sensitivity analysis on the incidence of acute HBV infection and the age of the cohort (Fig. 2). In areas where annual incidence of acute HBV infection is 100/100,000 or higher among susceptible children (base case), it is cost-saving to vaccinate all children aged 1 to 19 years. If annual incidence is 20/100,000 (one-fifth as high as estimated in the base case), catch-up vaccination is still cost-saving for children aged 2 years and younger, and would be highly cost-effective for children aged 3 to 10 years, costing less than $2,500 (17,000 RMB) per QALY gained. The catch-up vaccination program becomes less cost-effective as acute HBV infection incidence decreases and as the age of the children vaccinated increases.

We performed one-way sensitivity analysis across the ranges of all parameters (Supporting Table 3). In almost all cases, catch-up vaccination was cost-saving. In addition to cohort age and incidence of acute HBV infection (discussed above), the cost-effectiveness ratio was most sensitive to the costs of administering the vaccine. If the total cost of vaccine and administration is at the high end of our range ($8 [55 RMB] per child vaccinated), then the intervention costs $5,800 (40,000 RMB) per QALY gained for a cohort of 10-year-olds.

Table 2. Costs and Health Outcomes by Age Group

	Ages 1–4		Ages 5–10		Ages 11–14		Ages 15–19		Ages 1–19	
	Status Quo	Catch-up Vaccination	Status Quo	Catch-up Vaccination	Status Quo	Catch-up Vaccination	Status Quo	Catch-up Vaccination	Status Quo	Catch-up Vaccination
Cost (USD)*										
Program cost	0	12,000	0	12,000	0	12,000	0	12,000	0	12,000
Health care costs	35,706,000	35,650,000	35,777,000	35,738,000	34,815,000	34,786,000	36,849,000	36,828,000	35,819,000	35,786,000
Total costs	35,706,000	35,662,000	35,777,000	35,751,000	34,815,000	34,799,000	36,849,000	36,840,000	35,819,000	35,798,000
Outcomes										
Vaccinations	0	4,367	0	4,354	0	4,354	0	4,300	0	4,339
Acute infections	339	113	314	105	292	98	252	85	292	98
New chronic infections	23.1	7.7	16.3	5.4	12.0	4.0	8.6	2.9	13.7	4.6
HBV-related deaths†	29	26	61	59	56	55	178	177	91	90
QALYs experienced	297,126	297,147	291,048	291,061	283,391	283,400	273,524	273,530	284,228	284,239
Incremental cost-effectiveness ratio		Cost-saving		Cost-saving		Cost-saving		Cost-saving		Cost-saving

Each case assumes a cohort of 10,000 children. All costs and QALYs were discounted to the present at 3%.

Abbreviations: HBV, hepatitis B virus; QALY, quality-adjusted life year; USD, U.S. dollars.

*Costs are expressed in 2008 USD.

†Deaths are HBV-related deaths for the entire cohort, including deaths of persons who were chronically infected prior to the intervention.
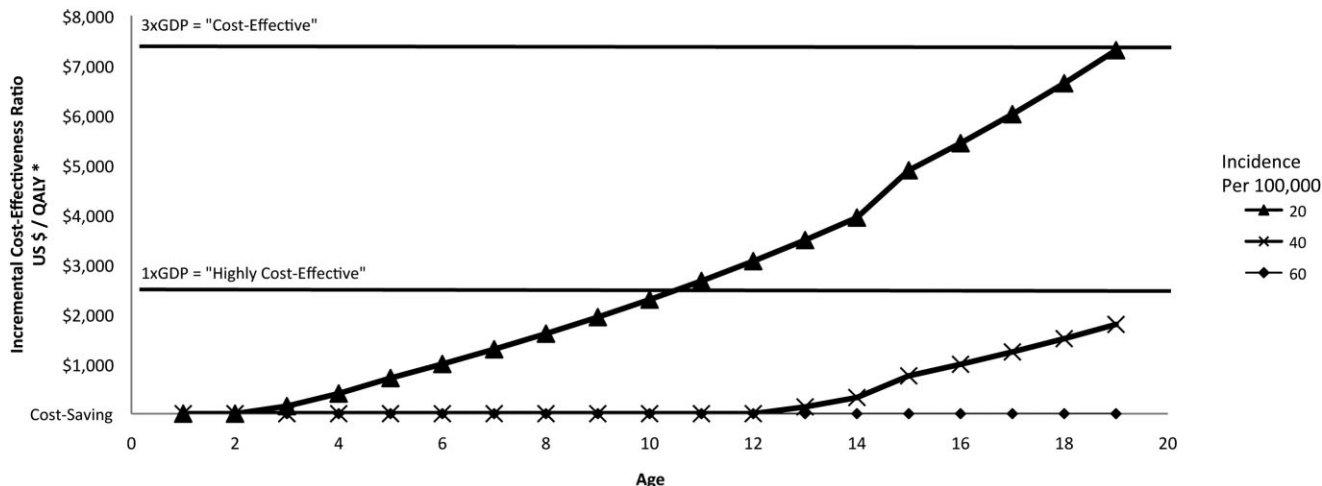
Fig. 2. Cost-effectiveness of catch-up HBV vaccination in China (incremental cost in U.S. dollars per QALY gained) as a function of cohort age and annual incidence of acute HBV infection (base case incidence 100/100,000 per year). When the line intersects the horizontal axis, the intervention is cost-saving. *Incremental cost-effectiveness ratio of vaccination versus no vaccination.

In our base case analysis, the chance an acute infection becomes chronic is based on a meta-analysis.[33] One previous study that was not included in that meta-analysis found a lower likelihood.[34] Reflecting that study, we lowered the chance of an acute infection becoming chronic (see Supporting Information for calculations) and found that vaccination is still cost-saving for children up to age 10 years and costs less than $2,500 per QALY gained up until age 15 years (Supporting Fig. 3).

In the base case, we did not include setup costs because they can be highly variable depending on the size and scope of the program. When we included setup costs similar to those in a recent catch-up vaccination program in Qinghai province (about $0.40 [2.7 RMB] per child), the catch-up vaccination program was still cost-effective.

China has recently experienced rapid economic growth and increased prosperity. This economic growth may lead to higher costs for HBV treatment, and for health care in general. In addition, rural areas in China may have lower health care costs and higher HBV incidence (due to lower vaccination coverage) than urban areas. Thus, we conducted two-way sensitivity analysis on health care costs and incidence (Fig. 3). We varied annual incidence of
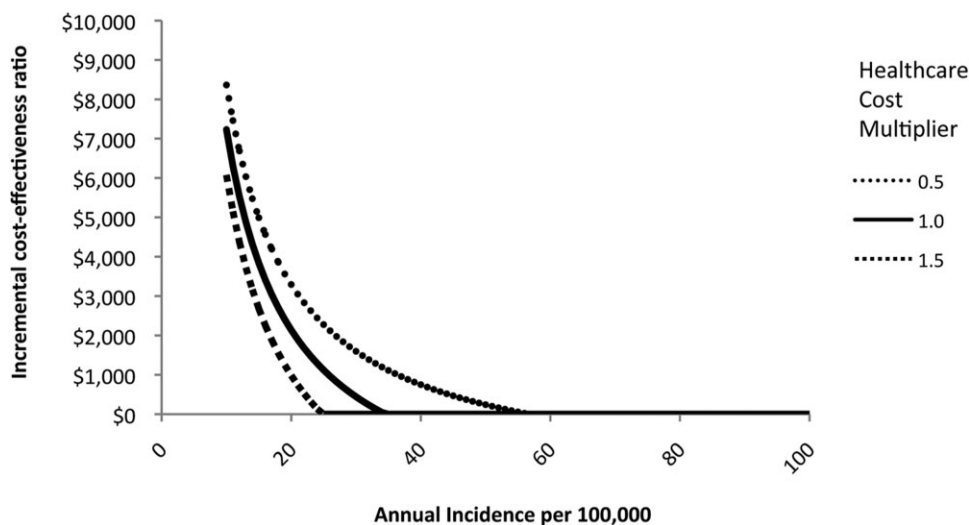

Fig. 3. Cost-effectiveness of catch-up HBV vaccination in China (incremental cost in U.S. dollars per quality-adjusted life year gained) as a function of acute HBV incidence and health care cost. Assumes a cohort age of 10 years old. Incidence represents acute (symptomatic and asymptomatic) HBV infections per 100,000 persons per year. All health care costs except for those related to vaccination were varied proportionally; thus, for example, 1.0 represents the base case, and 1.5 represents all costs (except for vaccination cost) being 150% of the value assumed in the base case. The base case incidence was 100/100,000 persons per year. All scenarios with incidence higher than 60/100,000 persons per year were cost-saving.
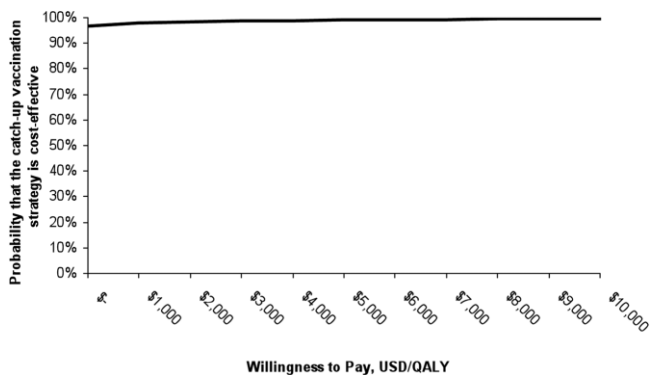
Fig. 4. Results of Monte Carlo sensitivity analysis: cost-effectiveness acceptability curve. Results are based on 10,000 Monte Carlo simulations in which all parameters were varied simultaneously. Each parameter was uniformly distributed between the high and low estimates shown in Table 1, and parameter values were chosen independently.

acute HBV infection between 10/100,000, a rate similar to that among vaccinated individuals,[20,21] and 100/100,000 (the base case incidence). We varied all costs of health care and HBV treatment simultaneously from 50% to 150% of the base case values. If incidence is lower than in the base case, there is less benefit from the vaccination program. Similarly, if the costs of treating HBV and its complications are lower, then the program has less benefit. However, treatment costs must be significantly lower and incidence significantly lower than in the base case before catch-up vaccination is not cost-effective.

We performed probabilistic sensitivity analysis in which we varied all parameters simultaneously in a Monte Carlo simulation (Fig. 4). Parameters were drawn from a uniform probability distribution between the low and high values (Table 1) and were assumed to be uncorrelated. With these assumptions, the catch-up vaccination program has a 97% chance of being cost-saving and a 98% chance of having an incremental cost-effectiveness ratio of less than $2,500 (17,000 RMB) per QALY gained.

Discussion

In recent years, China has made great strides in protecting newborns from HBV infection, but many children and adolescents still remain unprotected, particularly those born before 2003. Incomplete vaccination coverage is particularly acute in rural areas,[8] so catch-up vaccination efforts in such areas could be especially cost-effective, and could help reduce regional disparities in the burden of disease caused by HBV.

Our study is the first cost-effectiveness analysis of catch-up HBV vaccination for children in an endemic country. We found that free nationwide catch-up vaccination for children and adolescents in China is likely to be cost-saving,

or to cost less than $2,500 (17,000 RMB) per QALY gained for many combinations of parameter values.

Previous studies of childhood vaccination for other diseases in Asia have reported a wide range of cost-effectiveness estimates. Some vaccinations, such as those for Japanese encephalitis, are estimated to be cost-saving.[39] Vaccination of infants and children for rotavirus is estimated to be cost-saving or to cost less than $10,000 (68,000 RMB) per disability-adjusted life year gained.[40-42] Catch-up vaccination for HBV compares very favorably with these programs.

Our analysis has several limitations. Because of limited quality-of-life studies in China, we used health-related quality-of-life data from several international studies. However, sensitivity analysis revealed that catch-up vaccination is cost-saving even with significantly different quality-of-life estimates. We did not include the costs of time spent by vaccine recipients or their parents. We did not include the effects of catch-up vaccination on future hepatitis B incidence (as more people are vaccinated, there will be fewer infectious people to transmit the disease). Because our model ignores this effect, our analysis underestimates the value of the catch-up program. Our analysis is based on current treatment options and current costs. However, chronic HBV infection is a disease that individuals may live with for many years. As treatments for chronic HBV infection evolve, the costs and health benefits of HBV treatment may change. Our sensitivity analysis revealed that higher HBV treatment costs make catch-up vaccination even more economically attractive because vaccination helps avert those costs.

A free, nationwide catch-up vaccination program for children and adolescents in China is likely to be cost-saving—and feasible. Recent pilot programs for HBV catch-up vaccination in China, including an aggressive vaccination program in Beijing,[20,21,43] have been successful in increasing vaccination coverage. In addition, a demonstration program in the remote, rural province of Qinghai provided HBV education and free vaccination to 54,680 grade school students at 331 schools between September 2006 and April 2007[26] (unpublished data). The program led to an unprecedented 99.4% three-dose HBV vaccine coverage. The program was expanded in 2007-2008 to educate and provide free vaccination to the remaining 500,000 kindergarteners and grade school children in the province.[26] Replication of such school-based catch-up vaccination efforts implemented by existing provincial health department staff nationwide is likely to be both feasible and highly cost-effective, and can disseminate vaccination programs even to isolated regions of China, where the need for catch-up vaccination is particularly urgent.
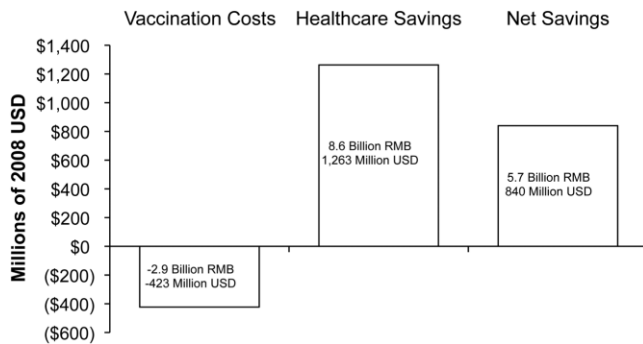
Fig. 5. Estimated vaccination program costs, health care savings, and net savings for a hypothetical free catch-up vaccination program for children and adolescents aged 1 to 19 years in China. Negative numbers represent costs; positive numbers are net savings. All numbers are expressed in net present 2008 currency. RMB, Chinese Yuan Renminbi; USD, U.S. dollars.

The overall health and economic impacts of catch-up vaccination could be immense. Approximately 150 million children and adolescents in China aged 19 years and younger are unprotected from HBV.[8,9,44] We estimate that the cost to vaccinate these children against HBV would be on the order of $423 million (2.9 billion RMB) ($2.82 [19 RMB] per three-dose vaccination series × 150 million vaccinations), and would lead to net present cost savings of almost $840 million (5.7 billion RMB) (calculated using our model) (Fig. 5). Even if some HBV-infected or immune children were vaccinated in such a program (thus leading to cost for extra vaccination), and even if such a one-time vaccination program incurred significant setup costs, it would still be highly cost-saving. Such catch-up vaccination could prevent as many as 8.2 million people from becoming HBV-infected, 390,000 from developing chronic HBV infection, and 65,000 from dying of HBV-related liver disease and liver cancer. This study provides strong support for the new national program introduced by China in 2009 to immunize all children under 15 years of age who have not received hepatitis B vaccination.

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