HHS Public Access

Author manuscript

Vaccine. Author manuscript; available in PMC 2017 September 04.

Published in final edited form as:

Vaccine. 2016 July 29; 34(35): 4243–4249. doi:10.1016/j.vaccine.2016.06.040.

Cost-effectiveness analysis of catch-up hepatitis A vaccination among unvaccinated/partially-vaccinated children

Abigail Hankin-Wei[a,*], **David B. Rein**[b], **Alfonso Hernandez-Romieu**[c], **Mallory J. Kennedy**[b], **Lisa Bulkow**[d], **Eli Rosenberg**[c], **Monica Trigg**[c], and **Noele P. Nelson**[e]

[a]Emory University School of Medicine, United States

[b]NORC, University of Chicago, United States

[c]Rollins School of Public Health, Emory University, United States

[d]Arctic Investigations Program, NCEZID, U.S. Centers for Disease Control and Prevention, United States

[e]Division of Viral Hepatitis, NCHHSTP, U.S. Centers for Disease Control and Prevention, United States

Abstract

Background—Since 2006, the US Centers for Disease Control and Prevention has recommended hepatitis A (HepA) vaccination routinely for children aged 12–23 months to prevent hepatitis A virus (HAV) infection. However, a substantial proportion of US children are unvaccinated and susceptible to infection. We present results of economic modeling to assess whether a one-time catch-up HepA vaccination recommendation would be cost-effective.

Methods—We developed a Markov model of HAV infection that followed a single cohort from birth through death (birth to age 95 years). The model compared the health and economic outcomes from catch-up vaccination interventions for children at target ages from two through 17 years vs. outcomes resulting from maintaining the current recommendation of routine vaccination at age one year with no catch-up intervention.

Results—Over the lifetime of the cohort, catch-up vaccination would reduce the total number of infections relative to the baseline by 741 while increasing doses of vaccine by 556,989. Catch-up vaccination would increase net costs by $10.2 million, or $2.38 per person. The incremental cost of HepA vaccine catch-up intervention at age 10 years, the midpoint of the ages modeled, was $452,239 per QALY gained. Across age-cohorts, the cost-effectiveness of catch-up vaccination is most favorable at age 12 years, resulting in an Incremental Cost-Effectiveness Ratio of $189,000 per QALY gained.

Conclusions—Given the low baseline of HAV disease incidence achieved by current vaccination recommendations, our economic model suggests that a catch-up vaccination recommendation would be less cost-effective than many other vaccine interventions, and that

*Corresponding author at: Emergency Medicine, Emory University, United States. ahankin@emory.edu (A. Hankin-Wei).

Conflict of interest

None.

HepA catch-up vaccination would become cost effective at a threshold of $50,000 per QALY only when incidence of HAV rises about 5.0 cases per 100,000 population.

Keywords

Hepatitis A; Vaccine recommendation; Economic modeling

1. Introduction

Over 100 million global hepatitis A virus (HAV) infections and 15,000 associated deaths are estimated to occur annually. Most hepatitis A-related morbidity and mortality occurs among low income, high endemic countries, where ≥90% of the population may be infected by age 10 years [1]. In high income, low endemic countries, such as the United States, the burden of HAV infections has decreased and most infections with a known risk factor are due to travel; although foodborne outbreaks are of increasing concern [2,3]. In the US in 2013, 1781 HAV cases were reported (0.6 cases per 100,000 population), including 518 hospitalizations and 9 deaths. Among children age 0–9 years, the group covered by routine vaccination, HAV infection rates were 0.14 cases per 100,000. Rates are slightly higher for older children and adults; 0.33 cases per 100,000 population among children age 10–19 years, and ranging from 0.64 to 0.74 cases per 100,000 population for adults age >19 years.[2]

The severity of hepatitis A disease typically increases with age. Children ≤5 years old often are asymptomatic, even when actively shedding HAV, thus placing household contacts at risk of HAV infection [4]. Conversely, infected older children and adults usually present with clinical symptoms including jaundice, nausea, abdominal pain, and poor appetite [4]. Serious complications of HAV infection are rare, but include liver failure and death, primarily in older adults. [5,6] Due to significant decreases in hepatitis A cases in the US, morbidity and mortality has decreased among children and adolescents, however, the average age of persons hospitalized for HAV has increased from 37.6 years to 45.5 years ($P < 0.0001$) during 2002–2011, and persons hospitalized for hepatitis A in recent are more likely to have liver disease and comorbid conditions [7,6]. Adults infected with HAV lose an average of 27 days of work [8]. In 2004, there were 5683 reported cases of HAV, with health care costs attributable to HAV infection totaling $9.3 million [9,2].

Hepatitis A vaccine was approved by the US Food and Drug Administration in 1995, and was initially recommended (1996–1999) by the Advisory Committee on Immunization Practices (ACIP) for individuals at high risk or for children at age 2 years in communities with high rates of disease [10,11]. In 2006, the ACIP recommended routine HepA vaccination for children aged 12–23 months, for persons who are at increased risk for infection, and for any person wishing to obtain immunity. Children who are not vaccinated by age 2 years can be vaccinated at subsequent visits, and catch-up vaccination of unvaccinated children aged 2–18 years can be considered [8].

Following vaccine introduction, the number of reported hepatitis A cases decreased by greater than 95% from about 30,000 cases in 1996 to approximately 1400 cases in 2011 [2]. However, despite demonstrated safety and efficacy of HepA vaccine, 2-dose coverage is low. In 2014, vaccine coverage for children age 19–35 months for ≥1 and≥2 doses was 85.1%

and 57.5%, respectively [12]; coverage is lower for adolescents. [13]. Among adults aged 19–49 years in 2013 the total ≥2 dose coverage was only 12.3% [14].

Given the large population of adolescents and young adults who remain unvaccinated, decreasing rates of disease-acquired HAV immunity among the US adult population, and an ongoing threat of HAV outbreaks due to contaminated food [3], we sought to assess the cost-effectiveness of a one-time, age-cohort-based, catch-up vaccination campaign for US children aged 2–17 years.

2. Methods

2.1. Economic model

We adapted a previously-developed and described [12] Markov model of HepA vaccination to assess the cost-effectiveness of catch-up HepA vaccination among unvaccinated and partially-vaccinated children compared with unvaccinated children. “Catch-up” vaccination was defined as provision of two doses of HepA vaccination for children with no documentation of previous vaccination or administration of a second dose for children with documentation of only a single prior dose. The model compared lifetime clinical and economic outcomes for a single birth cohort over time, from birth to death or age 95 years.

The basic structure of the economic model is shown in Fig. 1. In the model, a cohort progressed between eight possible HAV-related states including HAV-susceptible but not infected, HAV-immune due to immunization or prior infection, post-transplant due to fulminant liver disease, and death due to either HAV or other causes. Progression between clinical states was based on the probability of related events, including vaccination, HAV infection, and health complications due to vaccination or infection [7,15,16]. Other transitions within the model included loss of vaccine-related immunity [17,18] and death due to non-HAV related causes.

Model inputs included vaccine costs, rates of HAV infection, probability of disease complications, and associated healthcare costs, gradual loss of immunity to HAV following infection, public health costs for an HAV-associated outbreak, costs of productivity loss, and all-cause probability of death due to non-HAV causes among the lifespan of the age cohort. These parameters are described in further detail below and in the article Supplement. Costs presented reflect 2015 US dollars. Each state/event was associated with potential costs for medical care and potential gains/losses in productivity and Quality-Adjusted Life Years (QALYs).

2.2. Background data for model inputs

We used a single average national incidence from 2008 to 2012 in our model, because 2008–2012 regional incidence was consistently low and homogeneous across US regions (Supplemental Table S-2). Based on published estimates, for each reported case of HAV infection we estimated 1.95 unreported symptomatic cases [16]. HAV-related clinical characteristics, disease progression, and assigned probability parameters are shown in Supplemental Table S-3. The probability of symptomatic disease of varying severity was assigned based on historical surveillance data [19–21]. In the model, vaccinated individuals

were assigned an initial HAV antibody (anti-HAV) geometric mean titer (GMT) level based on published data [18,22], with associated annual estimates of anti-HAV loss following immunization modeled using a random-effects linear spline model [22].

Baseline HepA vaccination coverage rates for children age 19–35 months and 13–19 years were obtained via public use data files from the U.S. Centers for Disease Control and Prevention's (CDC) National Immunization Surveys [23,24]. Because no comparable catch-up program existed to estimate the uptake of catch-up recommendations, we assumed that 50% of those unvaccinated and unaware of prior infection would receive the first dose of vaccine, and 50% of those who received the first dose would receive the second dose. Based on proprietary sales data provided by GlaxoSmithKline, we assumed that adults aged 18–64 years would receive adult vaccination at a rate of 0.5% per year [25]. The probability and costs of adverse events from HepA vaccination, and direct and indirect costs of HepA vaccination are shown in Supplemental Table S-4.

Healthcare costs associated with icteric infections were calculated using four case studies of hepatitis A outbreaks in the United States [25–28]. Because reported icteric cases are likely more severe than unreported cases, we used 33% reduction in medical costs for unreported relative to reported icteric infections, per prior HAV models [20]. Based on published case studies, we assumed separate inpatient costs for fulminant liver disease with and without liver transplant [26,29]. The direct and indirect costs of HAV infection are shown in Supplemental Table S-5.

Using the Human Capital Method, productivity losses were calculated by combining the age-specific labor participation rate and age-specific daily earnings with the duration of work loss attributable to HAV infection, stratified by disease severity, as well as work loss due to vaccine administration and adverse events [30]. For children aged 0–15 years, we applied the productivity losses of a parent or caregiver [20]. In the case of death attributable to HAV infection, we assumed work loss of 250 days per year (an established estimate that excludes weekends and absenteeism), adjusted for aged-based workforce participation [31,32]. Public health response costs per case are shown in Supplementary Table S-6. Public health response costs were classified into three major activities – surveillance, immune globulin coordination and administration, and public notification. All future costs and benefits were discounted at a 3% annual rate.

Vaccination costs were calculated based on vaccine cost, vaccine administration costs (adjusted, when appropriate for ages when multiple immunizations are given), rates of adverse events, and patient/caregiver workdays lost.

Parameters used in QALY calculations include background utilities, by age group and baseline relative utility values for HAV infection for symptomatic anicteric, non-fulminant icteric, and pre- and post-transplant liver failure, with values established by the Global Burden of Disease study [33]. Supplementary Table S-7 shows these values as compared to routine HepA vaccination without catch-up [34]. To calculate an infected individual's health utility, the relative value of their state was multiplied by their background utility. The QALY

input values were then converted to annualized values based on the duration of sickness experienced in a given year.

2.3. Summary measures

Summary measures included incremental cost-effectiveness ratios of baseline and intervention strategies and net cost per QALY gained. In the cost-effectiveness model, net costs were estimated as vaccine costs, vaccine administration costs, HAV infection and adverse event-related medical costs, productivity losses, and public health response costs. The net difference between the baseline and intervention scenarios was calculated as the sum of these costs in the intervention scenario minus the baseline scenario.

The model was designed to evaluate the cost-effectiveness among a single birth cohort, and therefore independent simulations were performed for each age at which catch-up vaccination was considered. Incremental cost-effectiveness ratios (ICER) represent quotients and cannot be averaged; therefore a restricted set of incremental outcomes (infections, discounted costs, QALYs, and life years) from each simulation were summed across age-groups to obtain the overall ICER across all ages. Population results, incremental differences, an expanded list of health outcomes, and univariate and probabilistic sensitivity analyses were performed for the 10 year-old cohort, the midpoint age for catch-up vaccination. Univariate sensitivity analyses were conducted for the scenario of catch-up vaccination at age 10 years. Threshold analyses were conducted for disease incidence.

3. Results

Over the lifetime of the cohort, catch-up vaccination at age 10 years would reduce total HAV infections relative to baseline by 741, with 556,989 additional vaccine doses administered. In total, for every 752 additional doses administered, one case of HAV infection would be averted. Table 1 displays the full set of outcomes for the baseline and the intervention scenario assuming a catch-up target age of 10 years.

Catch-up vaccination increased total discounted QALYs across the 10 year-old cohort by 23, or 0.000006 QALYs per person. Catch-up vaccination increased net costs by $10.2 million or $2.38 per person. The catch-up vaccination intervention increased vaccine and administration costs for children, but decreased these costs for adults, as individuals vaccinated by the catch-up campaign would not require HepA vaccination in adulthood. Catch-up vaccination decreased costs of treatment due to HAV infections and decreased cost of public health surveillance given the lower number of total reported cases (Supplemental Table S-6). The incremental cost of the HepA vaccine catch-up at age 10 years was $452,239 per QALY gained.

Table 2 presents summary outcome measures for each age cohort, 2–17 years. Across cohorts, cost of catch-up vaccination produced a range of ICER values from $269,000 per QALY gained at age 17 years to $725,000 per QALY gained at age 4 years, excluding age 12. Across all cohorts, the costs of catch-up were $147.8 million with an increase in QALYs of 342, and an ICER of $432,159.

We found that the cost-effectiveness of catch-up vaccination tracked with the age of the cohort targeted for vaccination, with catch-up becoming more cost-effective when targeting children in late adolescence. This effect was due to several factors, (a) the population coverage of HepA vaccination at the time that this analysis was performed, with coverage due to routine vaccination decreasing as age increased (b) higher rates of symptomatic disease among older children infected with HAV as compared with younger children infected, and (c) vaccination of older children averting the need for higher-cost adult vaccination. With the exception of age 12 years, the per-person costs of catch-up increases to $2.55 per person at age 7 years and then decreases to $1.81 per person. The cost-effectiveness of catch-up vaccination is most favorable at age 12 years, resulting in an ICER of $189,000 per QALY gained. This is because the model assumes that the administration costs of HepA vaccination are split with other vaccines routinely administered at age 12 years, thus lowering the cost.

Table 3 shows variables tested in the univariate sensitivity analysis. The results show that the impact of vaccination on ICER was most sensitive to the discount rate, followed by the rate of adult vaccination. Catch-up vaccination was also highly sensitive to large variations in incidence, and was moderately sensitive to the price of vaccination. Catch-up vaccination was largely insensitive to univariate shifts in the rate of catch-up adoption, QALY values assigned to HAV disease states, and the long-term effectiveness of the vaccine.

Threshold analyses that increased disease incidence to rates far higher than presently observed found that the ICER of hepatitis A catch-up vaccination at age 10 years fell below $100,000 per QALY at an incidence of 3.0–4.0 per 100,000, fell below $50,000 per QALY at an incidence of approximately 5.0 per 100,000, and was cost-saving at incidence levels above 9.0 per 100,000 (Supplemental Table S-8).

4. Discussion

Our findings suggest that, given the current US HAV disease incidence, a catch-up vaccination program would not be cost effective at a threshold of $50,000 per QALY, and would cross this threshold only if incidence of HAV were greater than 5.0/100,000. The incremental cost per QALY given current US HAV disease incidence ranged from a low of $190,000 per QALY gained at age 12 years to a high of $725,000 per QALY gained at age 4 years.

Relative to the cost per QALY projected for hepatitis A catch-up vaccination, studies assessing the economic impact of catch-up interventions for other vaccinations show lower cost per QALY. For example, a simulation model of a five-year catch-up program for human papilloma virus vaccination in the US for females aged 13–18 years cost $97,300 per QALY [35], and a catch-up meningococcal conjugate vaccine intervention followed by a routine vaccination program would cost $127,000 per year of life saved [36]. The improved cost-effectiveness of these catch-up vaccination interventions relative to hepatitis A are driven by higher baseline disease incidence, higher case-fatality ratio, and increased cost of care for complications.

Changing patterns of vaccine acceptance in the US may impact future calculations of the cost-effectiveness of catch-up HepA vaccination. If rates of parental refusal of childhood vaccination increase, then rising incidence of vaccine-preventable infections might alter the cost-effectiveness of a catch-up campaign, reducing cost per QALY gained [37]. The effect of vaccine refusal on disease resurgence has been noted in recent outbreaks of measles and pertussis, with individuals with non-medical vaccine exemptions making up a majority of unvaccinated individuals infected in these outbreaks [38,39].

5. Limitations

The results are limited in several respects. First, the values of certain parameters used in the model are uncertain; the most important among these are the rates of HepA vaccine catch-up uptake and adult vaccination. Sensitivity analyses indicate that the ICER of catch-up is insensitive to uptake, but is sensitive to adult vaccination rate. In the model, catch-up vaccination is assumed to replace adult vaccinations. Consequently, as the annual rate of adult vaccination increases, the cost-savings associated with replacing more expensive adult vaccine with less expensive children's formulations increases. Our annual rate of adult vaccination might be underestimated because we were only able to obtain data from GlaxoSmithKlein, additional vaccine is distributed in the US by other manufacturers.

Second, the model output is based on hepatitis A incidence from 2008 to 2012 and the cost effectiveness conclusions are strongly tied to factors such as vaccine uptake and disease transmission patterns which may change over time, altering future cost.

Third, though some entities, including the World Health Organization Strategic Advisory Group of Experts have advised that national immunization programs may consider inclusion of single-dose HepA vaccine in immunization schedules, this study utilized the current US ACIP two-dose recommendation only [40,41].

Finally, the model excluded herd immunity effects of vaccination. However, previous analyses indicate that herd immunity associated with routine vaccination would result in even lower incidence and less favorable cost-effectiveness for catch-up [20].

6. Conclusions

In this paper, we presented findings of an economic model designed to evaluate the cost effectiveness of a one-time catch up campaign for children aged 2–17 years who are partially or not vaccinated against HAV. This model found that catch-up vaccination is not cost-effective at the current disease incidence of less than one infection annually per 100,000 population, with a projected cost per QALY gained of $269,000–$725,000, varying with age at catch-up vaccination. Sensitivity analyses showed that cost-effectiveness of vaccination was primarily sensitive to disease incidence and the degree to which catch-up vaccination averted later adult vaccination in the model cohort.

Decreasing hepatitis A incidence in the US and reduced exposure to HAV has resulted in decreasing anti-HAV seroprevalence among adults, and an increasing proportion of susceptible adults. This decrease in US adult immunity to HAV may result in greater risk for

infection among adults relative to prior generations, when most adult Americans would have reached adulthood with natural acquired immunity [6,8].

The 2006 ACIP hepatitis A vaccine recommendations state that catch-up vaccination of unvaccinated children aged 2–18 years can be considered. Such considerations are based on individual clinical decision making. Despite lack of cost-effectiveness of routine hepatitis A catch-up vaccination, health care providers should be cognizant of the increasing susceptibility to HAV and increased severity of disease among older adults. As such, since HepA vaccine provides long-term protection against HAV, providers should consider offering vaccine to any unvaccinated child.

This study illustrates the important role that economic modeling can have on public health decision-making, especially in understanding the impact that different epidemiological parameters may have on the cost effectiveness and societal impact of a given intervention. In the future, economic modeling could be helpful for assessing the cost-effectiveness of adult hepatitis A catch-up vaccination, as well as the cost-effectiveness of single-dose hepatitis A catch-up vaccine at any age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors wish to acknowledge and thank Katherine A. Hicks of RTI-Health Solutions for her prior contributions to the development of the model used in this analysis.

This works was supported by Cooperative Agreement Number 5U38PS004646 by the National Center for HIV, Viral Hepatitis, STD and TB Prevention (NCHHSTP), Centers for Disease Control and Prevention, as part of the NCHHSTP Epidemiologic and Economic Modeling Cooperative Agreement. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

Abbreviations

HepA	hepatitis A
HAV	hepatitis A virus
QALY	Quality adjusted life years
ACIP	Advisory Committee on Immunization Practices

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2016.06.040.

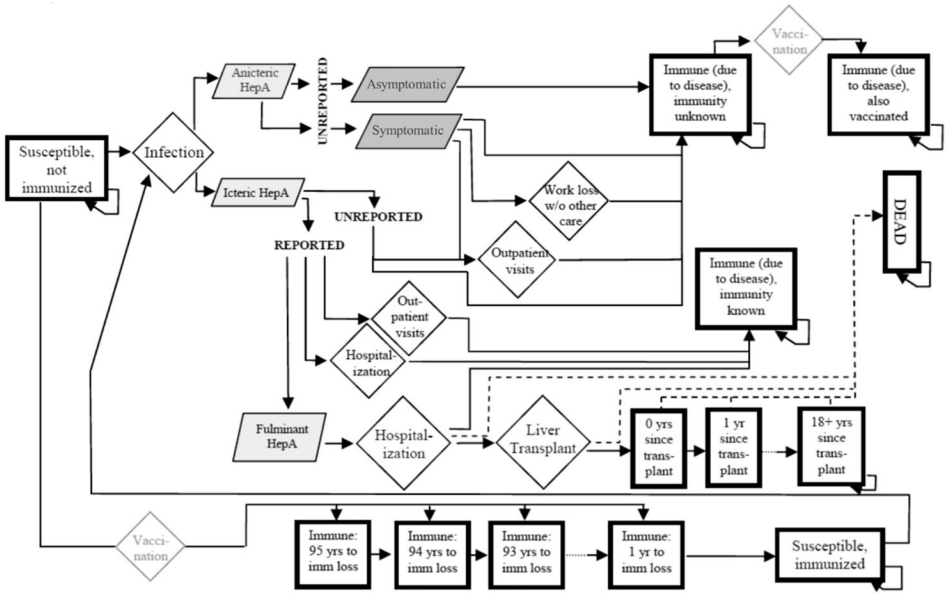

Fig. 1.

Model structure diagram. In this diagram rectangular boxes represent states between which the cohort is distributed at the end of every year based on the transitions and events that occur. Diamonds represent events that affect costs and the end-of-year state. Disease development stages are represented by shaded parallelograms. Dotted lines indicate death from HAV-related causes.

Table 1

Lifetime health, utilization, and economic outcomes associated with routine vaccination and universal vaccination with 'Catch-Up' vaccination opportunities at Age 10.

Parameter	Base scenario	Intervention scenario	Difference
Number of HAV infections	8976	8235	−741
Number of symptomatic anicteric cases	1934	1863	−71
Number of icteric cases	5107	4509	−598
Number of reported cases	1731	1528	−203
Number of HAV-related outpatient visits	12,405	11,029	−1376
Number of cases with HAV-related hospitalizations	978	868	−110
Number of cases with HAV-related liver transplants	53.91	50.87	−3.04
Number of HAV-related deaths	35.51	33.24	−2.27
Number of life years lost due to HAV-related deaths	989	900	−90
Days of caregiver work loss due to HAV complications	7937	7124	−813
Days of patient work loss due to HAV complications	23,352	19,704	−3648
Days of work loss due to HAV-related death	34,416	29,054	−5363
Total days of work loss due to HAV	65,705	55,882	−9823
Number of doses of HAV vaccinations administered	5,740,643	6,297,626	556,984
Days of work loss due to childhood immunizations	0	0	0
Days of work loss due to adult immunizations	0	0	0
Days of work loss due to all immunizations	0	0	0
Number of HAV vaccination-related mild adverse events	26,946	30,952	4006
Number of HAV vaccination-related severe adverse events	5.28	6.07	0.79
Medical cost of HAV-related outpatient visits	$952,866	$803,837	$ −149,029
Medical cost of HAV-related hospitalizations	$2,880,525	$2,414,507	$ −466,018
Medical cost of HAV-related liver transplants	$5,752,379	$5,199,289	$ −553,090
Total medical cost of treating HAV complications	$9,585,770	$8,417,633	$ −1,139,888
Cost of caregiver work loss due to HAV complications	$814,072	$746,465	$ −67,608
Cost of patient work loss due to HAV complications	$881,768	$727,664	$ −154,104
Cost of work loss due to HAV-related death	$1,063,562	$886,349	$ −177,213
Total cost of work loss due to HAV	$2,759,402	$3,350,185	$353,047
Cost of administration of child HAV vaccination	$38,096,164	$45,616,035	$7,519,871
Cost of acquisition of child HAV vaccination	$130,408,364	$137,089,884	$6,681,520
Cost of adverse events/work loss due to child HAV immunization	$2,997,138	$3,350,185	$353,047
Total cost of childhood HAV vaccination	$171,501,666	$186,056,104	$14,554,438
Cost of work loss due to adult HAV vaccination	$0	$0	$0
Cost of administration of adult HAV vaccination	$1,079,684	$540,064	$ −539,620
Cost of acquisition of adult HAV vaccination	$4,998,762	$2,500,407	$ −2,498,355
Cost of adverse events/work loss from adult HAV immunization	$46,323	$23,172	$ −23,151
Total cost of adult HAV immunization	$6,124,769	$3,063,642	$ −3,061,126
Cost of work loss due to all HAV immunizations	$0	$0	$0
Cost of administration, acquisition, and adverse events from HAV immunizations	$177,626,435	$189,119,747	$11,493,312

Parameter	Base scenario	Intervention scenario	Difference
Cost of surveillance of HAV cases	$15,790	$13,151	$ −2640
Cost of coordination and administration of IG shots for contacts	$329,446	$274,376	$ −55,070
Cost of public notification of HAV cases	$3,683	$3,044	$ −639
Total HAV-related cost to public health system	$348,920	$290,571	$ −58,349
Total HAV-related cost	$190,320,527	$200,188,429	$9,867,902
Total HAV-related cost excluding cost of patient work loss of due to HAV	$188,375,197	$198,574,415	$10,199,218
Quality-adjusted life years – undiscounted	274,623,573	274,623,658	85
Quality-adjusted life years – discounted	112,269,493	112,269,516	23
Number of life years – undiscounted	318,408,233	318,408,293	60
Number of life years – discounted	124,363,127	124,363,137	10
Incremental cost per quality-adjusted life year (excluding cost of work loss of afflicted due to HAV)			$452,239
Incremental cost per life year			$164,208
Incremental cost per discounted life year			$969,744

Vaccine. Author manuscript; available in PMC 2017 September 04.

Table 2

Incremental summary outcome measures per age cohort included in the analysis and for all age-cohorts pooled together.

Cohort			Incremental Results						
Age	**Year of birth**	**Starting population**	**Infections**	**Discounted QALYs**	**Discounted life years**	**Discounted costs**	**$/person**	**QALY/person**	**ICER***
2	2012	3,952,841	−772	13	4	$9,172,919	$2.32	0.0000033	$694,240
3	2011	3,953,590	−679	13	3	$9,522,024	$2.41	0.0000033	$717,691
4	2010	3,999,386	−652	14	4	$9,896,821	$2.47	0.0000035	$724,814
5	2009	4,130,665	−665	17	6	$10,414,199	$2.52	0.0000041	$627,967
6	2008	4,247,694	−685	19	7	$10,775,540	$2.54	0.0000045	$569,416
7	2007	4,316,233	−710	21	9	$10,992,191	$2.55	0.0000049	$512,475
8	2006	4,265,555	−699	21	9	$10,834,800	$2.54	0.0000049	$511,802
9	2005	4,138,349	−721	22	11	$10,418,910	$2.52	0.0000053	$476,165
10	2004	4,112,052	−741	23	10	$10,199,218	$2.48	0.0000056	$452,239
11	2003	4,089,950	−762	23	11	$9,933,351	$2.43	0.0000056	$436,144
12	2002	4,021,726	−774	25	13	$4,679,302	$1.16	0.0000062	$189,782
13	2001	4,025,933	−802	24	12	$9,174,316	$2.28	0.0000060	$386,316
14	2000	4,058,814	−837	26	14	$8,884,981	$2.19	0.0000064	$338,425
15	1999	3,959,417	−852	27	14	$8,265,037	$2.09	0.0000068	$307,849
16	1998	3,941,553	−876	27	15	$7,618,023	$1.93	0.0000069	$294,083
17	1997	3,880,894	−889	27	15	$7,016,799	$1.81	0.0000070	$268,626
All years		61,141,811	−12,116	342	157	$147,798,431	$2.42	0.0000056	$432,159

* ICER is not exactly equal to discounted costs divided by discounted QALYs due to rounding.

Table 3

Sensitivity of the ICER of catch-up vaccination at age 10 years to univariate changes in key model parameters.

Category	Variable	Baseline	Low	High	ICER at low parameter value	ICER at high parameter value
Coverage	Catchup, 1st dose | never vaccinated	0.500	0.375	0.625	$446,427	$454,308
Costs	Child vaccine purchase cost – public	$16.18	$12.14	$20.23	$385,554	$519,089
	Child vaccine purchase cost – private	$31.49	$23.62	$39.36	$347,235	$557,242
	Percentage of child vaccine purchased at the public price	0.550	0.413	0.688	$516,216	$390,547
	Annual rate of adult vaccination	0.005	0.0038	0.0063	$591,433	$319,517
Risk	Incidence	1 per 100,000	n/a	1.5/100,000	n/a	$295,183
				3.0/100,000		$118,020
				4.0/100,000		$73,997
				5.0/100,000		$47,540
				6.0/100,000		$30,316
				9.0/100,000		$1666
				12.0/100,000		Cost – saving
Health impacts (QALY decrements)	Mild	0.005	0.005	0.007	$588,726	$437,977
	Moderate	0.053	0.039	0.053		
	Severe	0.210	0.076	0.210		
Effectiveness (rate of decline in antibody titers)	Years 1–4	0.166	0.166	0.200	$424,630	$501,217
	Years 5–9	0.065	0.050	0.650		
	Years 10+	0.054	0.050	0.540		
Value of future benefits	Discount Rate	0.030	0.000	0.050	$24,855	$935,801