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

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Overview

• Motivation
• Timeline
• Methods
• Results
• Limitations
• Conclusions
Motivation

- Large population of adolescents and young adults who remain unvaccinated against hepatitis A

- Due to lower rates of incident infection in childhood, lower rates of disease-acquired HAV immunity among the US adult population
  - Increased vulnerability to outbreaks
  - Several HAV outbreaks due to contaminated food observed

- Severity of HAV symptoms increases with age of infection
  - Decreased incidence → Older average age of infection → More severe outcomes when infection occurs
  - Catch-up vaccination may be necessary due to decreasing population anti-HAV seroprevalence
Motivation, cont.

• Hepatitis A vaccine is the only vaccine on the childhood vaccination schedule without a catch-up recommendation

• In order to contemplate a recommendation change regarding catch-up, the cost-effectiveness of catch up vaccination needed to be assessed

• This study assessed the cost-effectiveness of a one-time, age-cohort-based, catch-up vaccination campaign for US children aged 2–17 years
Timeline

• February - April 2015
  • ACIP Hepatitis Vaccines Work Group discussed HAV vaccination including the methods and results of this study

• July 2016
  • Results published*

• The ACIP Hepatitis Vaccines Work Group resumed discussing the findings in the context of Hepatitis A catch-up vaccination from March to May 2017

Methods: Economic model

• Previously published Markov model of HAV vaccination*
  • Same model used for 2005 ACIP HAV vaccination discussions

• Tested the cost-effectiveness of a policy of catch-up HAV vaccination of unvaccinated and partially vaccinated children as compared to no catch-up, with catch-up defined as:
  • A probability and cost of two doses of HAV vaccine for children with no documentation of previous vaccination
  • A probability and cost of a second dose for children with documentation of only a single prior dose

Methods: Economic model, cont.

• Simulated outcomes in succession for each age from 2 to 17 and summed outcomes and costs in excel to calculate final results

• The model simulates patient progression between eight possible HAV-related states based on the probability of vaccination, HAV infection, and health complications due to vaccination or infection

• Model parameters include
  • Vaccine costs
  • Rates of HAV infection
  • Probability of disease complications, and associated healthcare costs
  • Gradual loss of vaccine acquired immunity
  • Public health costs for an HAV-associated outbreak
  • Costs of productivity loss
  • All-cause probability of death due to non-HAV causes among the lifespan of the age cohort

• Costs and Quality-Adjusted Life Years (QALYs) assigned by state annually
Methods: Parameters

• Incidence: 1 case per 100,000 persons.
  • Average national incidence from 2008 to 2012
  • No evidence of regional variation; very different from earlier analyses

• Adjustment for under-reporting: 1:1.95 reported to unreported cases. Lower than previous analyses

• Probability of symptomatic disease increased with age according to published estimates

• Distribution of disease severity based on surveillance data

• Loss of vaccine acquired immunity by year estimated based on new data

Methods: Parameters, cont.

• Existing Coverage: NIS for children age 19–35 months and 13–17 years
  • Age-specific coverage estimated linearly based on two estimates

• Catch-up adoption: Assumed rate
  • No comparable catch-up program to estimate vaccine uptake
  • 50% of those unvaccinated and unaware of prior infection would receive the first dose of vaccine
  • 50% of those who received the first dose would receive the second dose

• Adult vaccination: Adults aged 18–64 years vaccinated at a rate of 0.5% per year
  • Estimated from GlaxoSmithKline proprietary sales data

Trofa A, personal communication, 2 April 2015
Methods: Parameters, cont.

• QALYs, updated using Global Burden of Disease study values

• Updated costs using four case studies of U.S. hepatitis A outbreaks
  • Mild symptomatic disease
  • Unreported icteric infection
  • Reported icteric infection
  • Hospitalization
  • Fulminant liver failure
    • With Transplant
    • Without Transplant

• Productivity losses for parents/caregivers and death from HAV

• Lifetime time horizon using a 3% annual rate

Methods: Summary measures

• Incremental difference in costs and QALYs
  • Intervention scenario (catch-up) minus the baseline scenario (no catch-up)
  • Difference in vaccine costs, vaccine administration costs, HAV infection and adverse event-related medical costs, productivity losses, and public health response costs

• Sensitivity analyses were performed for the 10 year-old cohort, the midpoint age for catch-up vaccination

• Threshold analyses were conducted for disease incidence
Incremental summary outcome measures per age cohort included in the analysis and for all age-cohorts pooled together.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Age</th>
<th>Year of birth</th>
<th>Starting population</th>
<th>Infections</th>
<th>Discounted QALYs</th>
<th>Discounted life years</th>
<th>Discounted costs</th>
<th>$/person</th>
<th>QALY/person</th>
<th>ICER*</th>
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</table>

* ICER is not exactly equal to discounted costs divided by discounted QALYs due to rounding.
Comparison of Top-line Results (ages 2 to 17)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
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<tbody>
<tr>
<td>Incremental Costs</td>
<td>$147 million</td>
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<tr>
<td>Incremental QALYs</td>
<td>342</td>
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<tr>
<td>Overall ICER</td>
<td>$432,159</td>
</tr>
<tr>
<td>ICER Range by age</td>
<td>$190,000-$724,000</td>
</tr>
</tbody>
</table>

Results by Age Compared

Created from draft results.
Example Results for Age 10 Cohort

• Catch-up vaccination reduced total HAV infections by 741, with 556,989 additional vaccine doses administered

• For every 752 additional doses administered, one case of HAV infection would be averted

• 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 HAV vaccination in adulthood

• The incremental cost of the HAV vaccine catch-up at age 10 years was $452,239 per QALY gained
Results All Cohorts, cont.

• Cost-effectiveness of catch-up vaccination decreased 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:
  • Higher probability of symptomatic disease among older children
  • Less discounting of future costs of disease
  • Vaccination of older children averted the need for higher-cost adult vaccination with less delay in averting these costs

• The cost-effectiveness of catch-up vaccination was most favorable at age 12 years, resulting in an ICER of $190,000 per QALY gained
  • Model assumes that the administration costs of HAV vaccination were split with other vaccines routinely administered at age 12 years, thus lowering the cost of vaccination
Results, Sensitivity Analysis

• Results were most sensitive to
  • Discount rate. ICER = $24,000/QALY when the discount rate is 0%
  • Cost of child vaccine in the public and private market
  • Annual rate of adult vaccination. Catch-up more cost-effective when it is assumed to replace more adult vaccination
  • Incidence, Baseline = 1/100,000
    • ICER = $47,000 at an incidence of 5/100,000
    • Cost-saving at an incidence of 12/100,000

• Results were insensitive to rate of catch-up adoption, QALY decrements and rate of loss of vaccine acquired immunity
Limitations

• The values of certain parameters used in the model are uncertain; the most important among these are the rates of HAV 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
  • Since catch-up vaccination is assumed to replace adult vaccinations, 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 at the time of the study

• The model output is based on hepatitis A incidence from 2008 to 2012 and the cost-effectiveness conclusions are tied to factors disease transmission patterns which may change over time, altering future cost
Limitations, cont.

• Utilized the current US ACIP two-dose recommendation only
  • World Health Organization Strategic Advisory Group of Experts have advised that national immunization programs may consider inclusion of single dose HAV vaccine in immunization schedules

• Herd immunity effects of vaccination were excluded from the model; 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
Conclusions

• Our findings suggest that, given the current US HAV disease incidence, a catch-up vaccination program would not be cost-effective at thresholds of $50,000, $100,000 or $200,000 per QALY saved.

• The ICER of vaccination falls below $50,000/QALY saved at an HAV incidence of 5.0 cases per 100,000 persons.

• 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.
Conclusions, cont.

• 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.

• The improved cost-effectiveness of these catch-up vaccination interventions (e.g., HPV vaccine, meningococcal conjugate vaccine) relative to hepatitis A are driven by higher baseline disease incidence, higher case-fatality ratio, and higher costs of care for complications.

• Because incidence is so low the cost-effectiveness of catch-up vaccination is poor; however, catch-up vaccination could be justified based on offsets to adult vaccination if such substitution occurs.