A Mathematical Model of Hepatitis A Transmission in the United States Indicates Value of Universal Childhood Immunization

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Roadmap

- Background
- Objectives
- The model
- Assumptions and sources of key parameters
- Outcomes
- Conclusions
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In 1999, the Advisory Committee for Immunization Practices (ACIP) recommended a regionally based immunization strategy against Hepatitis A (HA), depending on HA incidence rates prior to vaccination.
Background

The incidence rates decreased dramatically following the implementation of vaccination in 1995.

However, concerns have been raised that the regional approach might not be sufficient to control HA in the United States.

Source: CDC
Background

- We developed a mathematical model to evaluate population-level impact of different immunization strategies on future HA incidence in the U.S.

- We accounted for **herd protection effects**.
Background

• Model developed before re-evaluation of HA recommendations by the ACIP.

• In 2005: incidence rate in U.S = 1.5 per 100,000: lowest yet recorded.

• In late 2005, the ACIP recommended nationwide Universal Mass Vaccination at 1 year of age.
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Objectives

• Evaluate, using a dynamic model, impact of different immunization strategies on the evolution of future HA incidence in the U.S.

In particular, evaluate:

• Impact of herd protection effects
• Regional vs. nationwide immunization strategies
• Immunization at 1 year of age vs. 12 years of age
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The Model

• A dynamic “compartmental” model describing passage of hosts through the different “infectivity stages” of HAV.

• Stratified by:
  – Age: 0-1, 2-5, 6-11, 12-19, 20-39, 40+ (years)
  – Regions: as defined in ACIP 1999 recommendations

• Accounts for:
  – Indirect “herd protection” effects
  – HAV “importation”
Infectivity stages:

- **S**: Susceptible
- **i**: Infected & not yet infectious
- **I**: Infectious
- **R**: Recovered-Immune
- **V**: Vaccinated

Demography: 77 age classes
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Force of Infection

“Force of infection”
= rate of acquisition of the infection per-susceptible

- Age-dependent
- Baseline (pre-vaccination), estimated from:
  - Incidence at baseline
  - % symptomatic by age
  - under-reporting of symptomatic cases
  - % susceptible to HA infection
    [NHANES III seroprevalence]

Changes over time with prevalence of infectives.
Key Data

• Vaccine coverage:
  – In 2001 (cumulative coverage for 2-18 yr olds):
    ACIP regions 1, 2, 3= 30%, 20%, 1%  
    [Samandari, Bell, Armstrong (2004)]
  – After 2001 (for every vaccinated cohort): 70%  
    [model assumption]

• Assumed vaccine efficacy = 100% and lasts for at least 25 years
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Incidence rate for the whole U.S. with Different Immunization Strategies

Nationwide at 1 year of age

Regional (ACIP 1999) at 2 years of age

Nationwide at 12 years of age

Van Effelterre & Al, Clinical Infectious Diseases, 2006:43
Herd Protection Effects

Projection in the 17 Vaccinated States
Predicted Incidence rate per 100,000
Period 1995 - 2035

Not accounting for herd protection (static model)

Accounting for herd protection (dynamic model)

Van Effelterre & al, Clinical Infectious Diseases, 2006:43
Potential for HA Spread in the United States

- Evaluated by estimating the *basic reproduction number* \( R_0 \) = mean number of new infections generated by 1 primary infectious case during his (her) whole period of infectiousness when introduced in a fully susceptible population.

- \( R_0 \) estimated from the model:
  - from **1.11** in region with incidence rates < 10 / 100,000 pre-vaccination to **1.55** in region with incidence rates ≥ 20 / 100,000 pre-vaccination.

  \( \rightarrow \) In the absence of any HA importation, minimal immunization coverage of 1-year-olds needed to eliminate HA in the U.S. is **44%**.

  Somewhat higher coverage would be needed to also prevent these “imported” HA cases.
Now … what happened?

Model Projection vs. Observed Incidence rate / 100,000 in 17 Vaccinating States
Vaccinating States

- Important decrease of HA incidence over first 10 years of vaccination:
  - 88% in 2003 vs. 1990-1997 baseline.

- Model indicates HA decrease can be explained by herd protection effects induced by vaccination.

- Model predicts quite well observed incidence rates.
Now ... what happened?

Model Projection vs. Observed Incidence rate / 100,000 in 34 Non-Vaccinating States

Baseline 1990-1997

* * * Observed

- Model (mean)
- Model (different scenarios)
Non-Vaccinating States

• Model predicted that in the non-vaccinating states, HA incidence started to plateau around 2000.

• In reality, HA incidence steadily decreased in 2000-06 although estimated coverage 1% in 2003.

Possible causes of differences model vs. observed:
  – Some herd protection induced by vaccinating states
  – Natural negative trend of HA incidence
  – Part of natural cycles

• Model predicts possible longer-term moderate rise without vaccination.

UMV since late 2005.
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Conclusions

- Model indicates low potential for spread of HA in the U.S. This is very conducive to HA elimination in the U.S.
- Model indicates that U.M.V. of 1-year-olds = best strategy to control HA in the U.S.
- Model projects important herd protection effects induced by vaccination in early childhood (1 year of age), as observed over first 10 years vaccination.
- Model prediction:
  - close to observed incidence in vaccinated states
  - predicted plateau around 2000 and longer-term moderate rise without vaccination, while in reality, steadily decreased.
Conclusions (cont’d)

• Mathematical modelling allows to project population-level impact of vaccination under various vaccination strategies (schedule, population, …).

• Percent of HA cases related to international travels now increasing (18%, 38% in < 15 year-olds in 2005). Important to reduce travel-related HA (possible elimination in the U.S.?) Further modelling may be useful to investigate impact of travel-related HA on future epidemiology.

• Model could be adapted to epidemiology of other countries/regions to inform public health community about best vaccination strategy to decrease burden of HA disease.