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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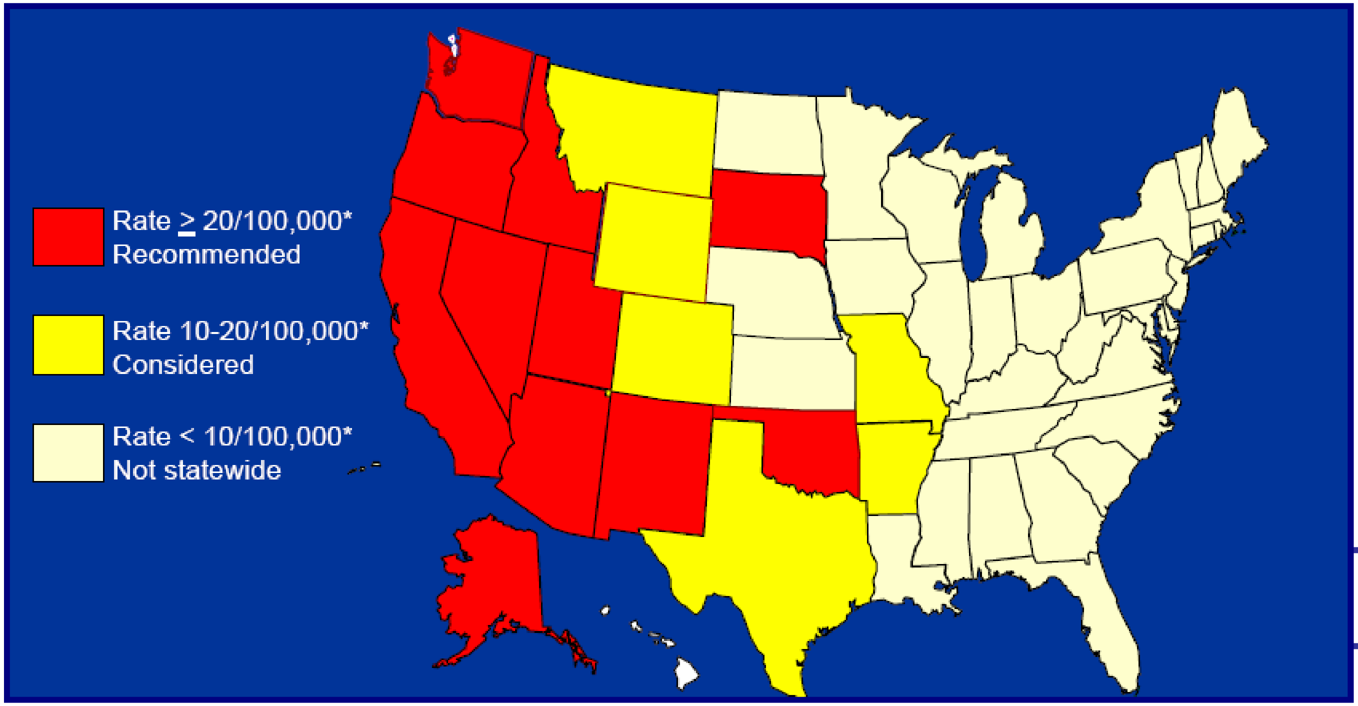
Background

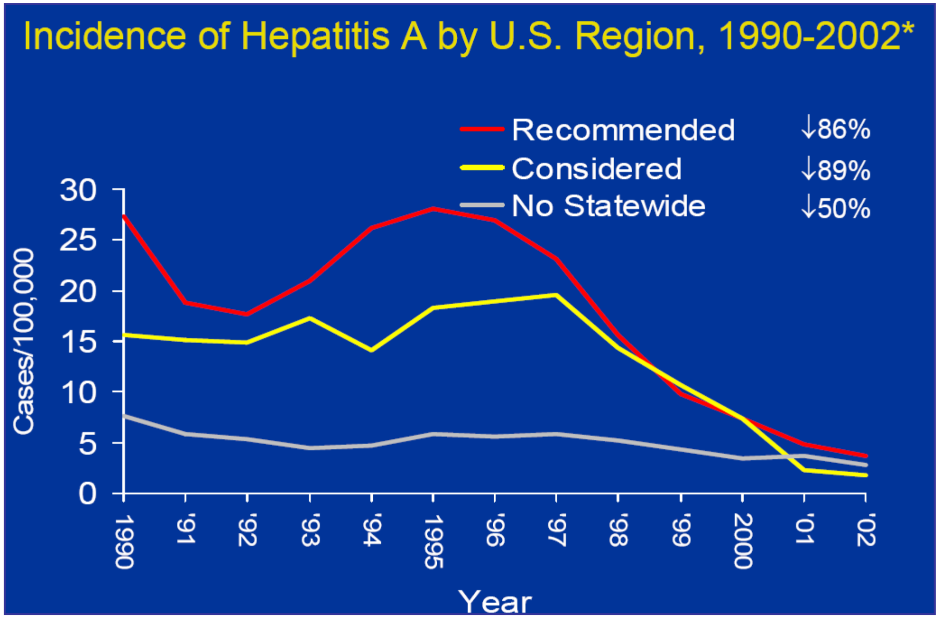
In 1999, the *Advisory Committee for Immunization Practices* (*ACIP*) recommended a regionally based immunization strategy against Hepatitis A (HA), depending on HA incidence rates prior to vaccination.



Source: CDC

Background

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



Source: CDC

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

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”

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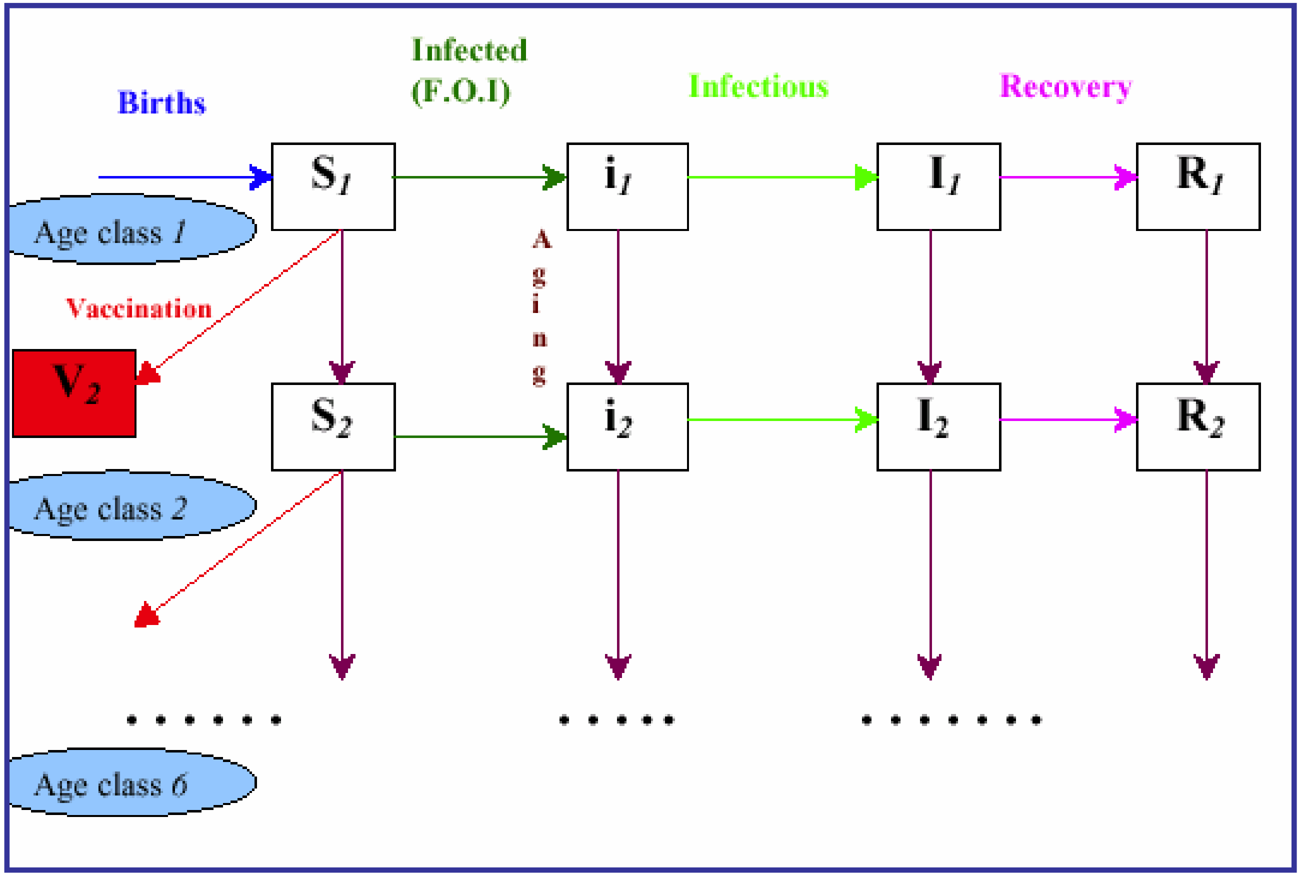
The model



Demography: 77 age classes

Infectivity stages:

S: Susceptible **i**: Infected & not yet infectious **I**: Infectious
R: Recovered-Immune **V**: Vaccinated (index 1-6: age class)

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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.

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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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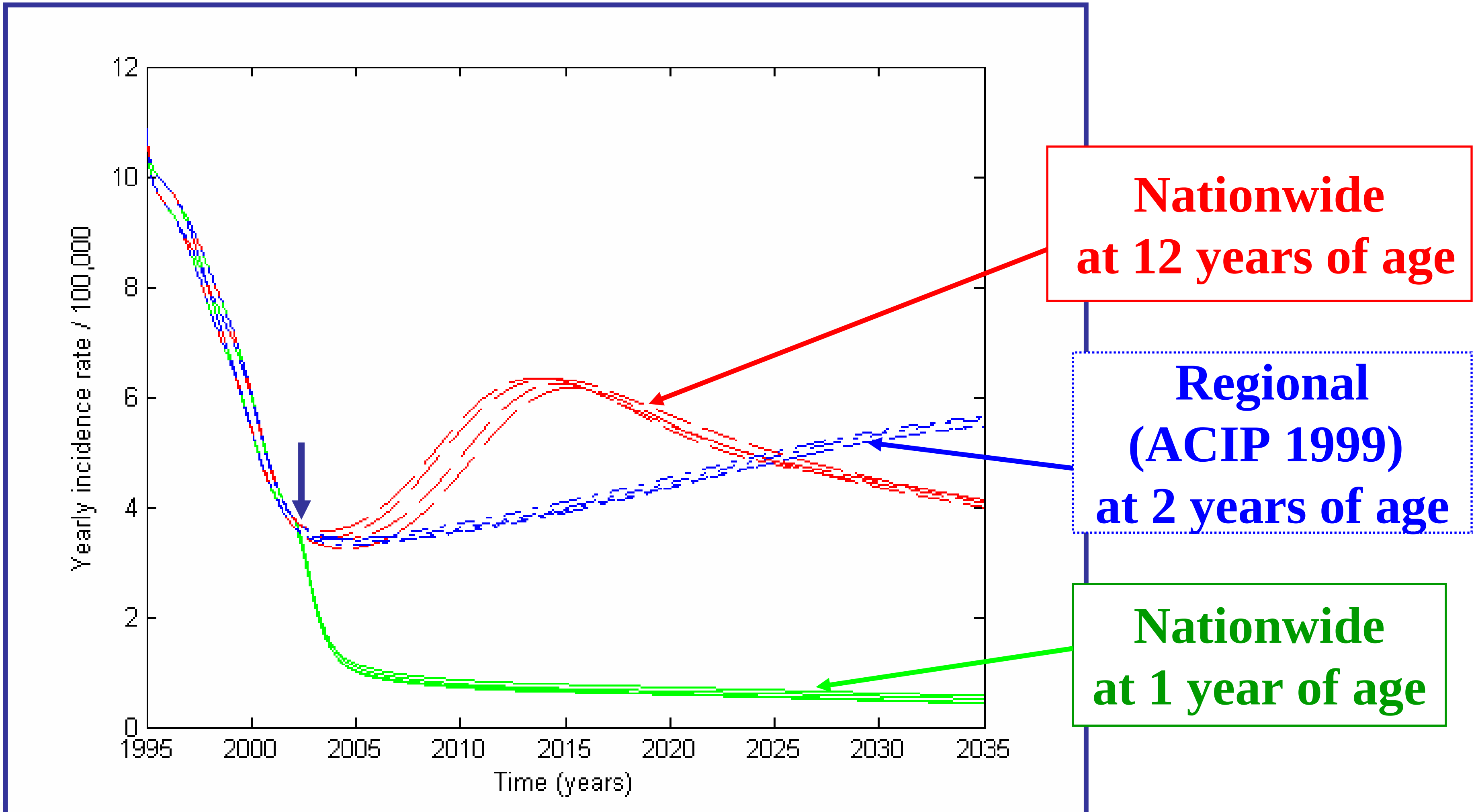
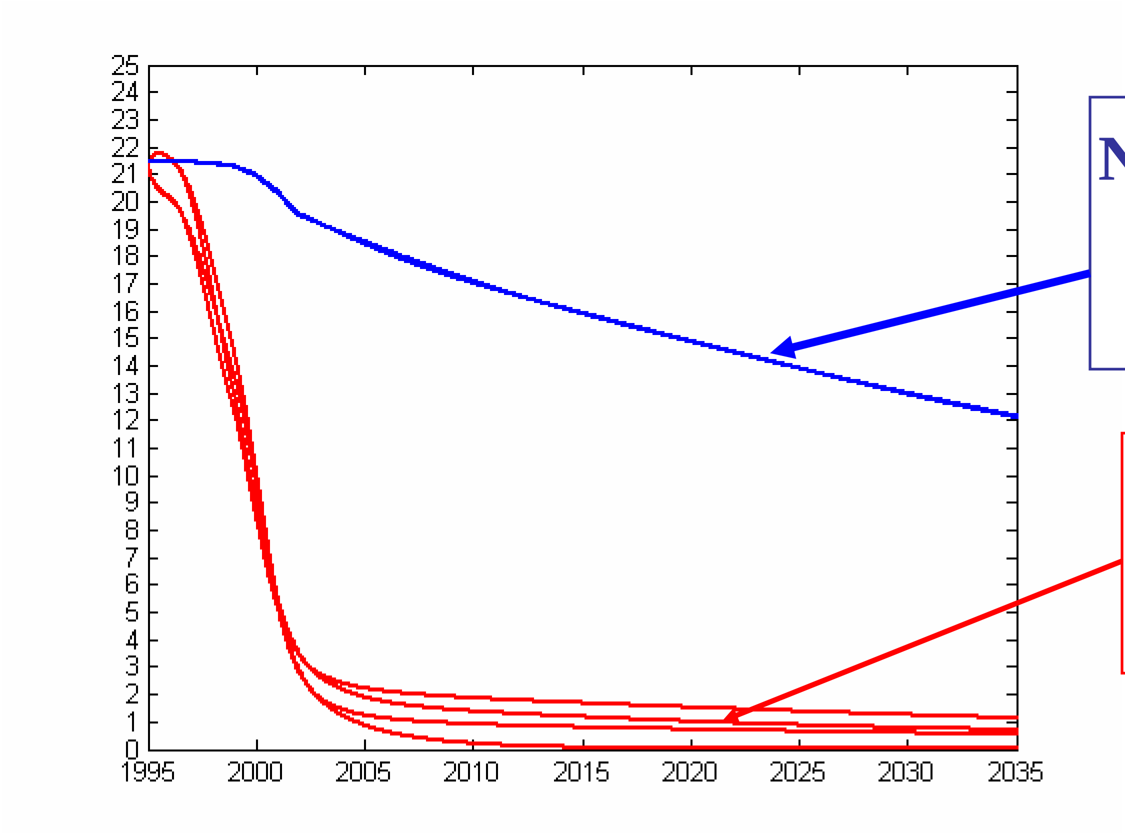
Incidence rate for the whole U.S. with Different Immunization Strategies



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)

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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.

  → 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.

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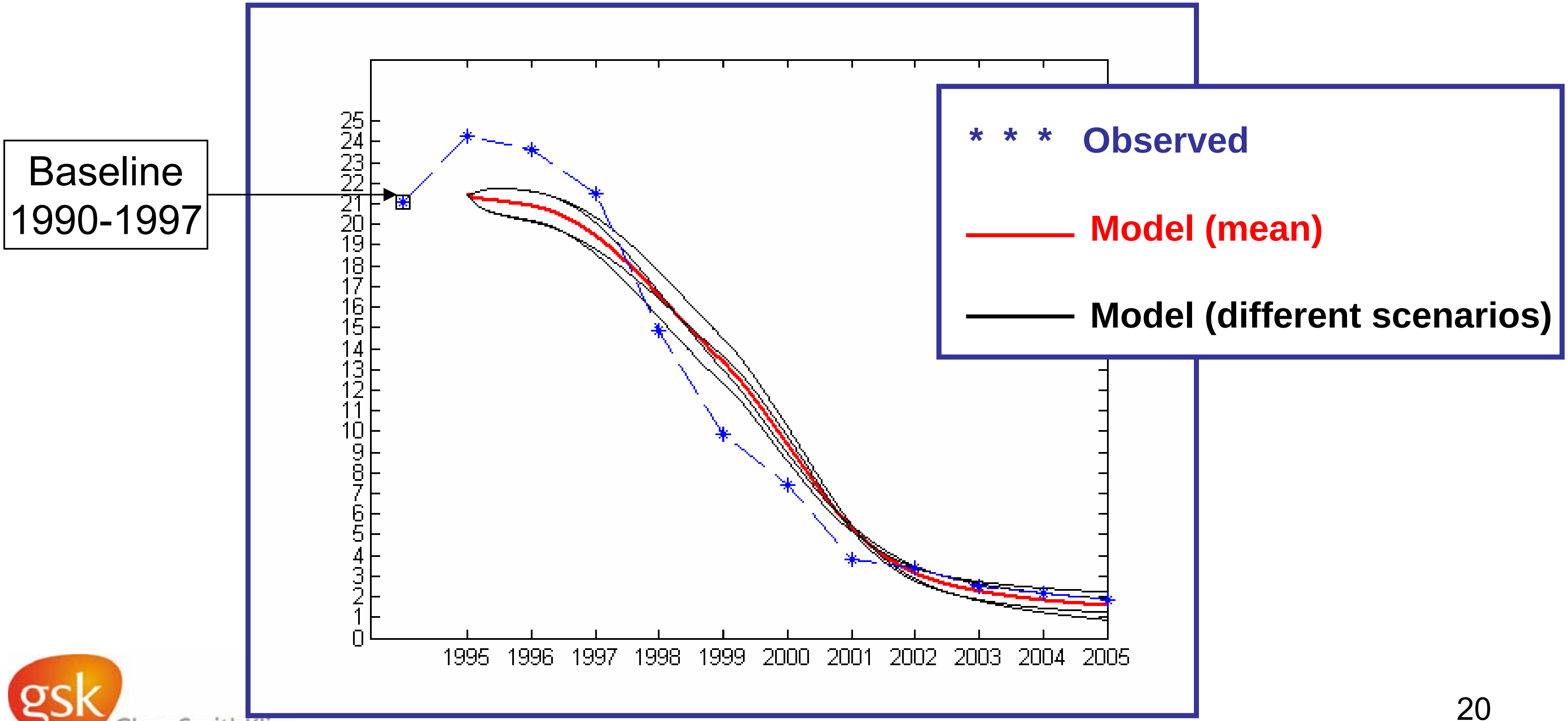
Now … what happened?

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



Vaccinating States

- Important decrease of HA incidence over first 10 years 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.

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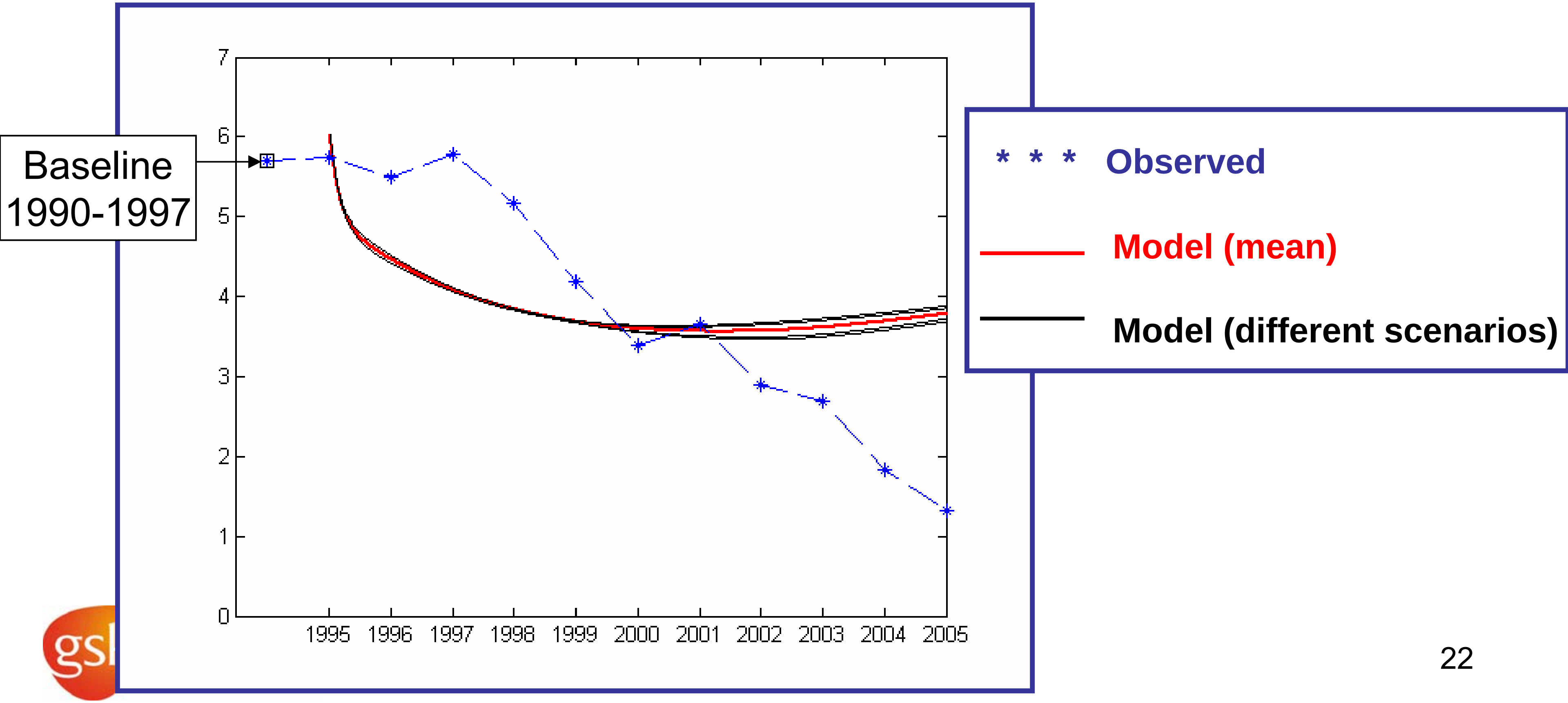
Now … what happened?

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



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.

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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.