Optimizing Influenza Vaccine Allocation

Jan Medlock

Department of Biomedical Sciences
Oregon State University
jan.medlock@oregonstate.edu

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Influenza

- Annual seasonal flu
- Rare epidemic or pandemic flu
Influenza in the US

- 30k deaths annually
- $90B in lost productivity annually
- 120M+ vaccine doses produced annually for seasonal flu
  - Around 85M typically used
- Vaccine production is poor for new pandemic flus
  - 2009 H1N1: less than 20M doses available prior to peak
- 300M population
Introduction

Basic Model

Uncertainty

Multiple Objectives

Conclusions

2009 H1N1 Influenza

WHO: Mexico swine flu deaths surpass 150
By Chris Honley, USA TODAY
MEXICO CITY — Mexico’s swine flu epidemic showed no signs of abating Monday, prompting residents to stock up on medicine and disinfectants and for the government to cancel school nationwide for a week.

The death toll from suspected swine flu cases in Mexico, the country at the center of the outbreak, continued to rise into the USA and

China quarantines U.S. school group over flu concerns

Updated 4:40 p.m. EDT, Thu, May 28, 2009

(CNN) - A group of students and teachers from a Maryland private school have been quarantined in China because of swine flu concerns, a school spokesman said Thursday.

The Chinese government has sent 21 students and three teachers to their hotel rooms in Kaili, China, because a passenger on their plane to China was suspected of having swine flu, or H1N1, said Udy Temple, director of communications for the Barte School in Silver Spring, Maryland.

Temple said the students and teachers are occupying two floors of a four-star hotel in the Guizhou province city in southern China.

The quarantine will end Friday, and the students are scheduled to return to the United States on Sunday, Temple said.

Mike Kennedy, the head of Barte School, said U.S. consulate officials have since told the school

Swine flu could kill hundreds of thousands in U.S. if vaccine fails, CDC says
As much as 40% of the workforce could be affected during the peak of a pandemic, health officials say, noting low resistance to the H1N1 virus and its persistence through the summer months

July 23, 2009 | Thomas H. Maugh II

Hundreds of thousands of Americans could die over the next two years if the vaccine and other control measures for the new H1N1 influenza are not effective, and, at the pandemic’s peak, as much as 40% of the workforce could be affected, according to new estimates from the Centers for Disease Control and Prevention.
H5N1 Bird Flu

447 cases and 263 deaths!
Optimizing Influenza Vaccine Distribution

Jan Medlock1,2* and Alison P. Galvani1

The criteria to assess public health policies are fundamental to policy optimization. Using a model parametrized with survey-based contact data and mortality data from influenza pandemics, we determined optimal vaccine allocation for five outcome measures: deaths, infections, years of life lost, contingent valuation, and economic costs. We find that optimal vaccination is achieved by prioritization of schoolchildren and adults aged 30 to 39 years. Schoolchildren are most responsible for transmission, and their parents serve as bridges to the rest of the population. Our results indicate that consideration of age-specific transmission dynamics is paramount to the optimal allocation of influenza vaccines. We also found that previous and new recommendations from the U.S. Centers for Disease Control and Prevention both for the novel swine-origin influenza and, particularly, for seasonal influenza, are suboptimal for all outcome measures.

Vaccination is the principal strategy for reducing the disease burden of many infectious diseases. The evaluation of the antigenic evolution of influenza. In addition, zoonosis can lead to the emergence of influenza subtypes, such as the novel swine-origin influenza virus. Consequently, manufacturing of influenza vaccine follows a tight schedule to achieve sufficient doses (24). This schedule is also vulnerable to disruptions, as evidenced by the vaccine contamination that left the United States short on doses in 2004 to 2005 (25). The World Health Organization recently announced that the unusually slow growth of swine-origin H1N1 in chicken eggs may cause shortfalls in current production of vaccine this year (26). When vaccine availability is limited or when vaccine efficacy is low, optimal allocation of vaccines is imperative. Nonetheless, vaccine allocation can also be improved when vaccine is plentiful and highly efficacious. We evaluated current vaccine allocation policies based on the optima derived from multiple outcome measures. We also compared the outcome measures with the 2007 U.S. population by age, and the shaded area is the proportion of each age group vaccinated under the optimal strategies for each outcome measure (labeled at the far left). YLL is the number of years of life lost.


- How to distribute limited vaccine doses?
- Age structure but not risk or occupation
Model

Age structured (0, 1–4, 5–9, 10–14, 15–19, ..., 70–74, 75+)
No birth or natural death
Model

\[
\begin{align*}
\frac{dU_{Sa}}{dt} & = -\lambda_a U_{Sa} \\
\frac{dU_{Ea}}{dt} & = \lambda_a U_{Sa} - \tau U_{Ea} \\
\frac{dU_{Ia}}{dt} & = \tau U_{Ea} - (\gamma + \nu_{Ua}) U_{Ia} \\
\frac{dU_{Ra}}{dt} & = \gamma U_{Ia} \\
\frac{dV_{Sa}}{dt} & = -(1 - \epsilon_a)\lambda_a V_{Sa} \\
\frac{dV_{Ea}}{dt} & = (1 - \epsilon_a)\lambda_a V_{Sa} - \tau V_{Ea} \\
\frac{dV_{Ia}}{dt} & = \tau V_{Ea} - (\gamma + \nu_{Va}) V_{Ia} \\
\frac{dV_{Ra}}{dt} & = \gamma V_{Ia}
\end{align*}
\]

\[
\lambda_a = \sum_{\alpha=1}^{17} \phi_{a\alpha} \sigma_{a\beta} \alpha \left( \frac{U_{I\alpha} + V_{I\alpha}}{N} \right)
\]

Age groups \( a = 1, 2, 3, 4, 5, \ldots, 16, 17 \)
are ages 0, 1–4, 5–9, 10–14, 15–19, \ldots, 70–74, 75+. 
Case Mortality

Contacts


![Contact rate map](image)
Model Infections without Vaccine

- 0-4
- 5-9
- 10-14
- 15-19
- 20-44
- 45-64
- 65+

Time (days)
Proportion Infected
Objective Functions

- Total Infections
- Total Deaths
- Years of Life Lost
- Total Cost
- Contingent Valuation
Nonlinear Constrained Optimization

Find \( p_1, p_2, \cdots, p_{17} \) that minimizes

\[
bN_V + \sum_a \left( c_{Ua} N_{UIa} + c_{Va} N_{VIa} + d_a N_{Da} \right),
\]

subject to

\[
0 \leq p_a \leq 1, \quad N_V = \sum_a p_a N_a(0) \leq Y,
\]

\[
U_{Sa}(0) = (1 - p_a) N_a(0), \quad V_{Sa}(0) = p_a N_a(0),
\]

\[
N_{UIa} = U_{Sa}(0) - U_{Sa}(T), \quad N_{VIa} = V_{Sa}(0) - V_{Sa}(T), \quad N_{Da} = N_a(0) - N_a(T),
\]

\[
\frac{dU_{Sa}}{dt} = -\lambda_a U_{Sa}, \quad \frac{dU_{Ea}}{dt} = \lambda_a U_{Sa} - \tau U_{Ea}, \quad \frac{dU_{Ia}}{dt} = \tau U_{Ea} - (\gamma + \nu U_a) U_{Ia}, \quad \frac{dU_{Ra}}{dt} = \gamma U_{Ia},
\]

\[
\frac{dV_{Sa}}{dt} = -(1 - \epsilon_a) \lambda_a V_{Sa}, \quad \frac{dV_{Ea}}{dt} = (1 - \epsilon_a) \lambda_a V_{Sa} - \tau V_{Ea}, \quad \frac{dV_{Ia}}{dt} = \tau V_{Ea} - (\gamma + \nu V_a) V_{Ia}, \quad \frac{dV_{Ra}}{dt} = \gamma V_{Ia},
\]

\[
\lambda_a = \sum \phi_{a\alpha} s_{a\beta} \gamma \left( \frac{U_I \alpha + V_I \alpha}{N} \right).
\]
Whom to Vaccinate?

- **20M Doses**
- **40M Doses**
- **60M Doses**

<table>
<thead>
<tr>
<th>Number of doses</th>
<th>Infects</th>
<th>YLL</th>
<th>Cost</th>
<th>Deaths</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0M</td>
<td>0-4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20M</td>
<td>5-9</td>
<td>10-14</td>
<td>20-44</td>
<td>45-64</td>
<td>65+</td>
</tr>
</tbody>
</table>

- **0-4**  
- **5-9**  
- **10-14**  
- **15-19**  
- **20-44**  
- **45-64**  
- **65+**
Whom to Vaccinate?

Infections

Deaths

YLL

CV

Cost

Vaccine doses

0M 20M 40M 60M

0–4 20–44

5–9 45–64

10–14 65+

15–19
Much Better than Other Strategies
Uncertainty & Sensitivity Analysis

- Same model, with risk groups
- Build parameter distributions from literature
- Sample from these distributions and then optimize
- Analyze...
Parameter Distributions
80M Vaccine Doses
No Vaccine for Ages 45+!

Infections

Hospitalizations

Deaths

Years of life loss

Contingent valuation

Proportion vaccinated
Big Improvement

Deaths
- 80 million doses of vaccine
- 60 million doses of vaccine
- 40 million doses of vaccine

Infections
- 80 million doses of vaccine
- 60 million doses of vaccine
- 40 million doses of vaccine

Uniform is CDC 2010. High-risk is CDC 2006 (ages 0–4, 50+, & high-risk people). NHIS is typical use.
Importance of Parameters

Most important determinants of vaccine allocation:

1a. Recovery rate in ages 0–14
1b. Recovery rate in ages 15+
2. $R_0$
3. Vaccine efficacy vs. infection from both Sensitivity Index and Partial Rank Correlation Coefficient.
Multi-Objective Optimization

- Policymakers not just interested in one objective
- Multi-Objective Optimization finds Pareto sets
  - No objective can be improved without worsening another
Minimizing Infections & Deaths

R0 = 1.7; Vaccine = 80M
Minimizing Infections & Deaths

![Graph showing the relationship between infections and deaths, with multiple objectives represented by different symbols and colors.]
Multi-Objective Optimization

- Very slowly working up to 6 objectives
- Probably lots of similarity will reduce complexity
Optimization Under Uncertainty

- For a fixed vaccine allocation
  - Sample from parameter distributions
  - Run model
  - Aggregate for a distribution of outcomes
- Simultaneously optimize multiple statistics of outcomes:
  - Median outcome
  - Worst case (e.g. upper 95% quantile)
- Another multi-objective problem!
Conclusions

- Can improve vaccination policies substantially
- Can incorporate uncertainty & multiple objectives
- Also working with NDSSL at Virginia Tech to understand differences in optimal distribution in network models
- Problems:
  - Huge uncertainty for pandemic influenza
  - Timing of vaccine availability
  - Societal optimum vs. Individual optimum
  - Parental resistance to vaccination
Thanks!

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