Optimizing Influenza Vaccine Allocation

Jan Medlock

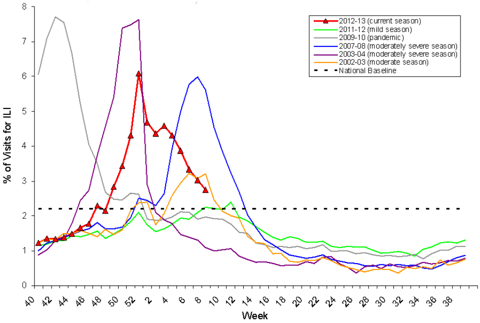
Department of Biomedical Sciences
Oregon State University
jan.medlock@oregonstate.edu

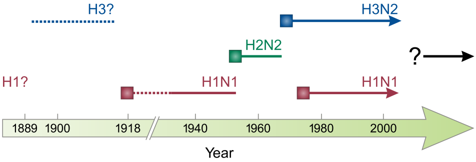
7 March 2013

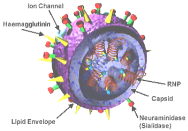
Oregon State UNIVERSITY OSU

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

2009 H1N1 Influenza

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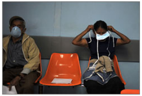

Enlarge By Eitan Abramovich, AFP/Getty Images

WHO: Mexico swine flu deaths surpass 150

By Chris Hawley, 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 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 spreading into the USA and

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China quarantines U.S. school group over flu concerns

updated 9:40 p.m. EDT, Thu May 28, 2009

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TEXT SIZE

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

Chinese health authorities prepare to take temperatures of passengers on a plane from Germany this week.

The Chinese government has confined 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 Vicky Temple, director of communications for the Barrie 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 Barrie School, said U.S. consular officials have since told the school

Los Angeles Times | ARTICLE COLLECTIONS

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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 25, 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!

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ORIGINAL ARTICLE

◄ Previous Volume 352:333-340 January 27, 2005 Number 4 Next ►

Probable Person-to-Person Transmission of Avian Influenza A (H5N1)

Kumnuan Ungchusak, M.D., M.P.H., Prasert Auewarakul, M.D., Scott F. Dowell, M.D., M.P.H., Rungrueng Kitphati, M.D., Wattana Auwanit, Ph.D., Pilaipan Puthavathana, Ph.D., Mongkol Uiprasertkul, M.D., Kobporn Boonnak, M.Sc., Chakrarat Pittayawonganon, M.D., Nancy J. Cox, Ph.D., Sherif R. Zaki, M.D., Ph.D., Pranee Thawatsupha, M.S., Malinee Chittaganpitch, B.Sc., Rotjana Khontong, M.D., James M. Simmerman, R.N., M.S., and Supamit Chunsutthiwat, M.D., M.P.H.

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GLOBAL UPDATE

Influenza: Deaths in Africa and Southeast Asia Add to Concerns Over Bird Flu

The New York Times

By ELISABETH ROSENTHAL
Published: May 4, 2009

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The New York Times **News**
Tuesday, April 13, 2010

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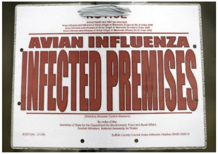
The Lede
The New York Times News Blog

February 5, 2007, 9:35 AM

Bird Flu Fight: 160,000 Turkeys Gassed and Burned in Britain

By TOM ZELLER JR.



A warning sign is displayed on a path leading towards a factory farm in eastern Britain yesterday. (Photo: Leon Neal/AFP Getty Images)

Problem Setup

Optimizing Influenza Vaccine Distribution

Jan Medlock[1,2]* and Alison P. Galvani[1]

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

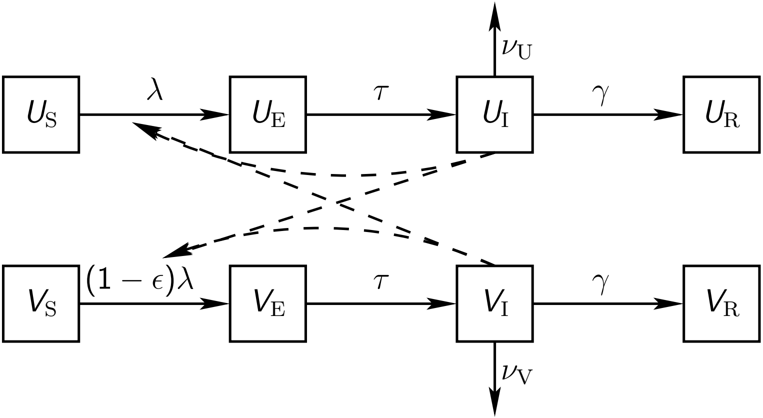
20% for those aged 5 to 19, 17% for those aged 20 to 49, 35% for those aged 50 to 64, and 63% for those older than 64 years (fig. S15), totaling

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

Medlock & Galvani, 2009, *Science*, 325: 1705–1708.

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

Model



Age structured $(0, 1\text{–}4, 5\text{–}9, 10\text{–}14, 15\text{–}19, \ldots, 70\text{–}74, 75+)$

No birth or natural death

Model

$$\frac{\mathrm{d}U_{\mathrm{S}a}}{\mathrm{d}t} = -\lambda_a U_{\mathrm{S}a} \qquad \frac{\mathrm{d}V_{\mathrm{S}a}}{\mathrm{d}t} = -(1-\epsilon_a)\lambda_a V_{\mathrm{S}a}$$

$$\frac{\mathrm{d}U_{\mathrm{E}a}}{\mathrm{d}t} = \lambda_a U_{\mathrm{S}a} - \tau U_{\mathrm{E}a} \qquad \frac{\mathrm{d}V_{\mathrm{E}a}}{\mathrm{d}t} = (1-\epsilon_a)\lambda_a V_{\mathrm{S}a} - \tau V_{\mathrm{E}a}$$

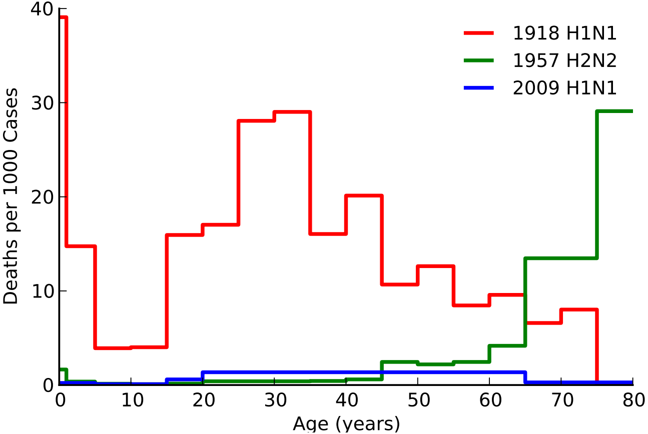
$$\frac{\mathrm{d}U_{\mathrm{I}a}}{\mathrm{d}t} = \tau U_{\mathrm{E}a} - (\gamma + \nu_{\mathrm{U}a}) U_{\mathrm{I}a} \qquad \frac{\mathrm{d}V_{\mathrm{I}a}}{\mathrm{d}t} = \tau V_{\mathrm{E}a} - (\gamma + \nu_{\mathrm{V}a}) V_{\mathrm{I}a}$$

$$\frac{\mathrm{d}U_{\mathrm{R}a}}{\mathrm{d}t} = \gamma U_{\mathrm{I}a} \qquad \frac{\mathrm{d}V_{\mathrm{R}a}}{\mathrm{d}t} = \gamma V_{\mathrm{I}a}$$

$$\lambda_a = \sum_{\alpha=1}^{17} \frac{\phi_{a\alpha}\sigma_a\beta_\alpha \left(U_{\mathrm{I}\alpha} + V_{\mathrm{I}\alpha}\right)}{N}$$

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

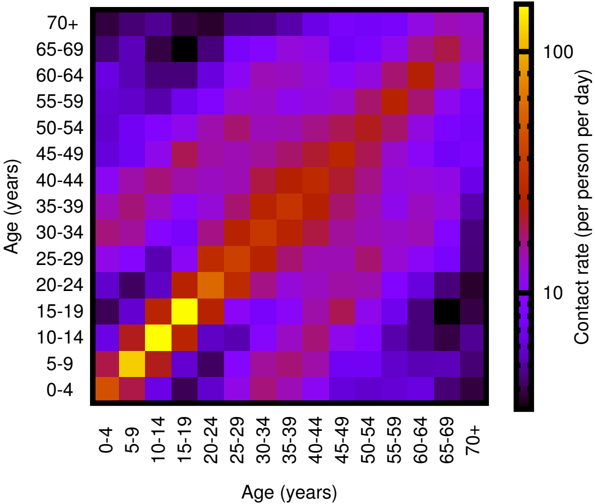
Case Mortality



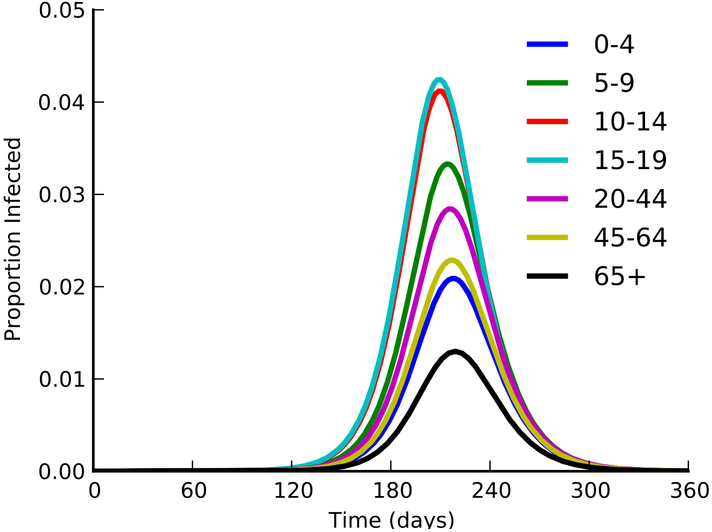
Sources: Serfling, Sherman, Houseworth, 1967, *Am J Epidemiol*; Luk, Gross, Thompson, 2001, *Clin Infect Dis*; Glezen, 1996, *Epidemiol Rev*; Presanis et al, 2009, *PLoS Med*.

Contacts

Mossong et al, 2008, *PLoS Med*

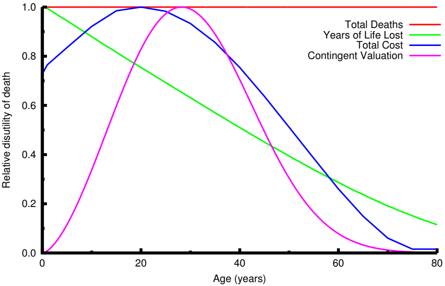


Model Infections without Vaccine



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

$$bN_{\mathrm{V}} + \sum_a \left(c_{\mathrm{U}a} N_{\mathrm{UI}a} + c_{\mathrm{V}a} N_{\mathrm{VI}a} + d_a N_{\mathrm{D}a} \right),$$

subject to

$$0 \le p_a \le 1, \qquad N_{\mathrm{V}} = \sum_a p_a N_a(0) \le Y,$$

$$U_{\mathrm{S}a}(0) = (1 - p_a) N_a(0), \qquad V_{\mathrm{S}a}(0) = p_a N_a(0),$$

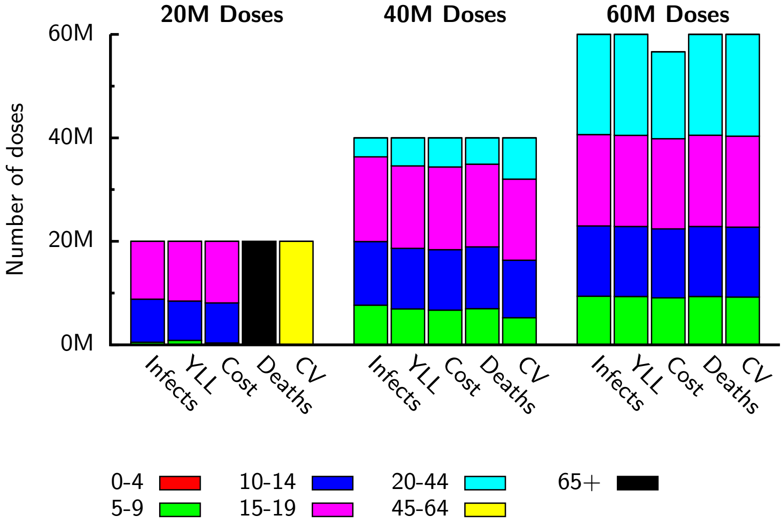
$$N_{\mathrm{UI}a} = U_{\mathrm{S}a}(0) - U_{\mathrm{S}a}(T), \quad N_{\mathrm{VI}a} = V_{\mathrm{S}a}(0) - V_{\mathrm{S}a}(T), \quad N_{\mathrm{D}a} = N_a(0) - N_a(T),$$

$$\frac{\mathrm{d}U_{\mathrm{S}a}}{\mathrm{d}t} = -\lambda_a U_{\mathrm{S}a}, \quad \frac{\mathrm{d}U_{\mathrm{E}a}}{\mathrm{d}t} = \lambda_a U_{\mathrm{S}a} - \tau U_{\mathrm{E}a}, \quad \frac{\mathrm{d}U_{\mathrm{I}a}}{\mathrm{d}t} = \tau U_{\mathrm{E}a} - (\gamma + \nu_{\mathrm{U}a}) U_{\mathrm{I}a}, \quad \frac{\mathrm{d}U_{\mathrm{R}a}}{\mathrm{d}t} = \gamma U_{\mathrm{I}a},$$

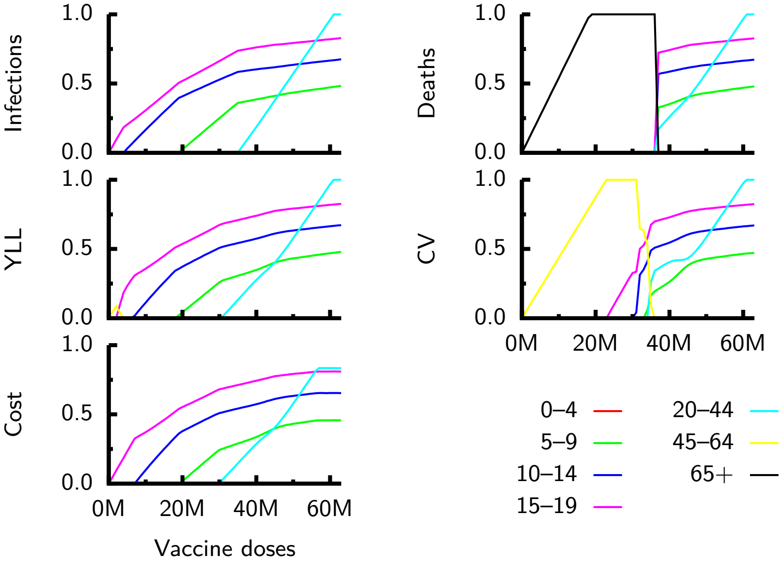
$$\frac{\mathrm{d}V_{\mathrm{S}a}}{\mathrm{d}t} = -(1 - \epsilon_a)\lambda_a V_{\mathrm{S}a}, \quad \frac{\mathrm{d}V_{\mathrm{E}a}}{\mathrm{d}t} = (1 - \epsilon_a)\lambda_a V_{\mathrm{S}a} - \tau V_{\mathrm{E}a}, \quad \frac{\mathrm{d}V_{\mathrm{I}a}}{\mathrm{d}t} = \tau V_{\mathrm{E}a} - (\gamma + \nu_{\mathrm{V}a}) V_{\mathrm{I}a}, \quad \frac{\mathrm{d}V_{\mathrm{R}a}}{\mathrm{d}t} = \gamma V_{\mathrm{I}a},$$

$$\lambda_a = \sum_\alpha \frac{\phi_{a\alpha} \sigma_a \beta_\alpha \left(U_{\mathrm{I}\alpha} + V_{\mathrm{I}\alpha} \right)}{N}.$$

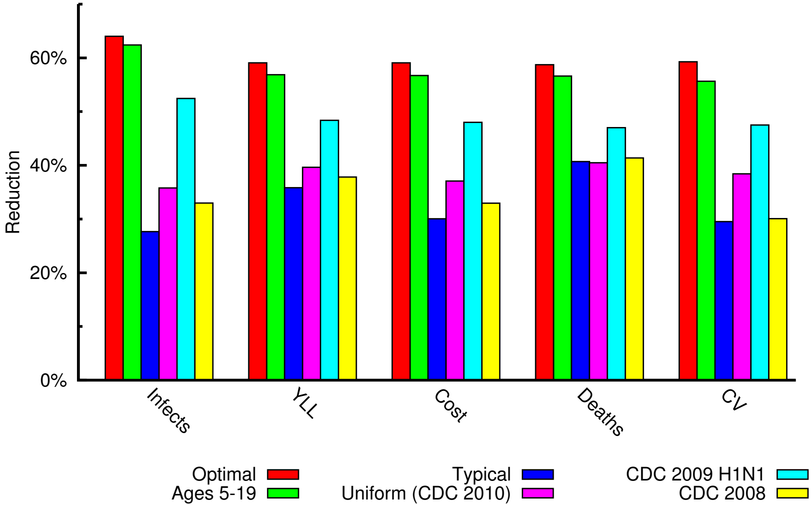
Whom to Vaccinate?



Whom to Vaccinate?



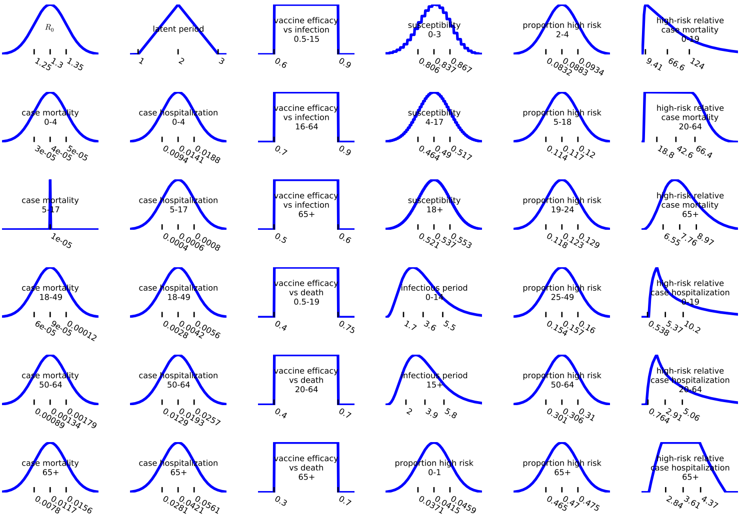
Much Better than Other Strategies



Uncertainty & Sensitivity Analysis

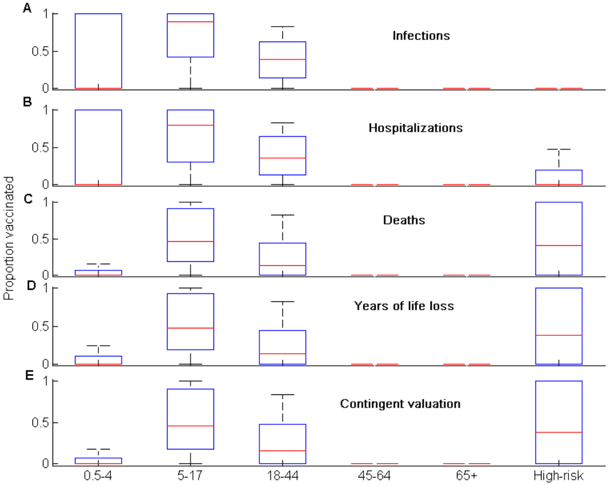
- Same model, with risk groups
- Build parameter distributions from literature
- Sample from these distributions and then optimize
- Analyze...

Parameter Distributions

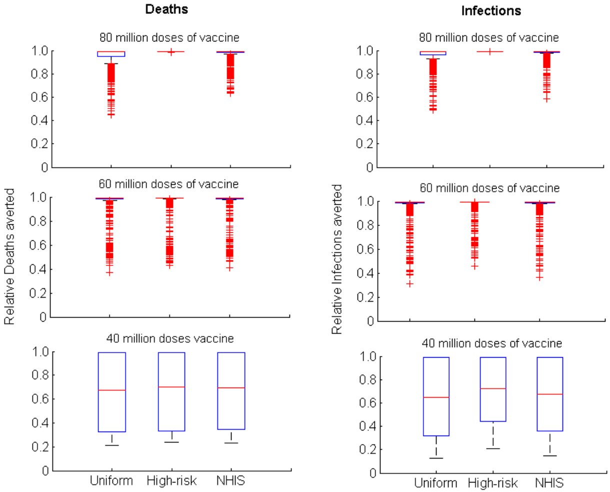


80M Vaccine Doses

No Vaccine for Ages 45+!



Big Improvement



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

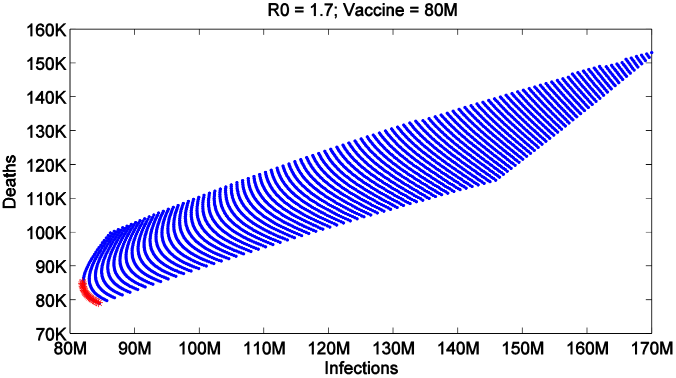
3. Vaccine efficacy vs. infection

from both Sensitivity Index and Partial Rank Correlation Coefficient.

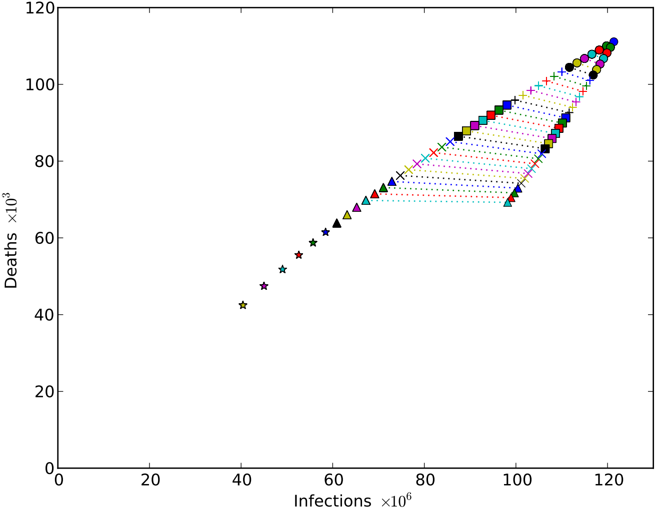
Multi-Objective Optimization

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

Minimizing Infections & Deaths



Minimizing Infections & Deaths



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!

- Collaborators
  - Alison P. Galvani, Martial L. Ndeffo Mbah, Jeffrey P. Townsend (Yale University)
  - Lauren A. Meyers (University of Texas at Austin)
- Funding
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