

Economic Evaluation of Influenza Pandemic Mitigation Strategies in the US

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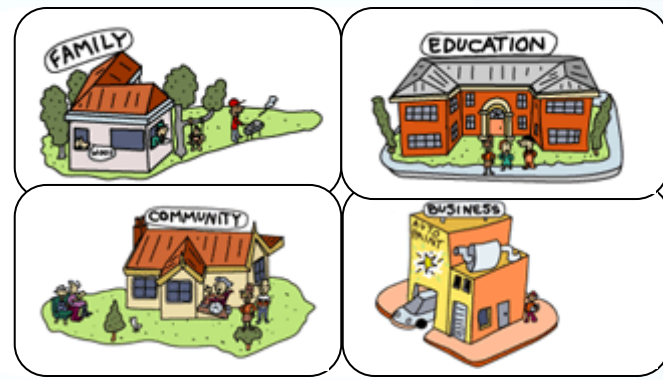
Background

- Recent epidemiological models
 - Show likely effectiveness of various interventions
 - Highlight the importance of targeted antiviral use and social distancing measures
- Missing: cost-effectiveness analysis of proposed strategies

Objective

To evaluate the cost-utility of alternative pandemic influenza mitigation strategies in the US from the societal perspective using a stochastic individual-level microsimulation model.

Methods

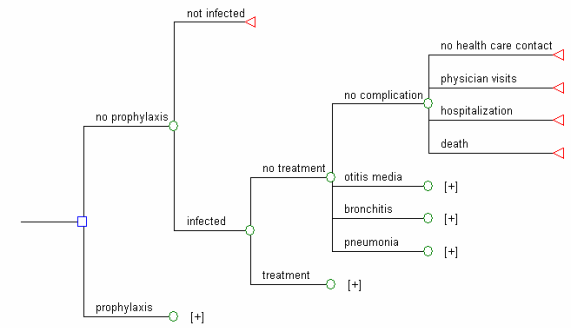


Agent-based stochastic influenza model* to predict influenza cases by intervention

- Structured population (1.6 million, 4 age groups)
- People interact in known contact groups and have daily contacts within
 - Households
 - Three closest households
 - Larger neighborhood and community
 - Play groups/daycare centers/schools (children) or workplaces (adults)

* Longini IM, Jr., Halloran ME, Nizam A, Yang Y. Containing pandemic influenza with antiviral agents. *Am J Epidemiol* 2004; 159: 623-633

Methods



- Cases follow clinical pathway:
 - May develop OM, bronchitis or pneumonia
 - May be hospitalized if illness is severe
 - May die
- Resource use and costs are attached to events to calculate incremental cost-effectiveness
- Incremental cost-effectiveness ratio:

$$ICER = \frac{\Delta Cost}{\Delta HealthOutcome} = \frac{Cost_{StrategyA} - Cost_{StrategyB}}{HealthOutcome_{StrategyA} - HealthOutcome_{StrategyB}}$$

Economic Evaluation

- Outcomes:
 - Cases, deaths, QALYs
 - Doses per capita needed
 - Total cost
- Time horizon: 6 months (until pandemic vaccine is available)
- Perspective: Society
 - i.e. costs incurred by health care provider, patient and society (productivity loss) are included

Interventions

- No intervention (baseline)
- Prophylaxis
 - HTAP 25/50/Unlimited
 - FTAP 25/50/Unlimited
 - Prevaccination
 - School closure
 - HTAP/FTAP/Vaccine + School closure
- Treatment of index cases



HTAP: Household Targeted Antiviral Prophylaxis
FTAP: Full Targeted Antiviral Prophylaxis

Data - Transmission



- $R_0 = 2.0$ (mean truncated normal distribution ranging from 1.5 to 2.6)
- Probability that infected individual is symptomatic: 0.67
- Asymptomatic infection 50% as infectious as symptomatic
- Contact probabilities:
 - Highest in HHs, daycare groups and HH clusters
 - Lower in schools and workgroups
 - Lowest in neighborhoods and communities at large

Data - Effectiveness

- Oseltamivir*:
 - Antiviral efficacy of reducing
 - Infection given exposure: 30%
 - Symptomatic disease given infection: 60%
 - Infectiousness to others: 62%
 - Also reduces incidence of complications, hospitalizations, and mortality and improves QoL
- Low efficacy vaccine: efficacy of reducing
 - Susceptibility to infection: 30%
 - Infectiousness to others: 50%

**Data from Welliver, et al. JAMA (2001); Hayden, et al. JID (2004);
Analysis by Yang, Longini, Halloran (2006)*

Data - Costs

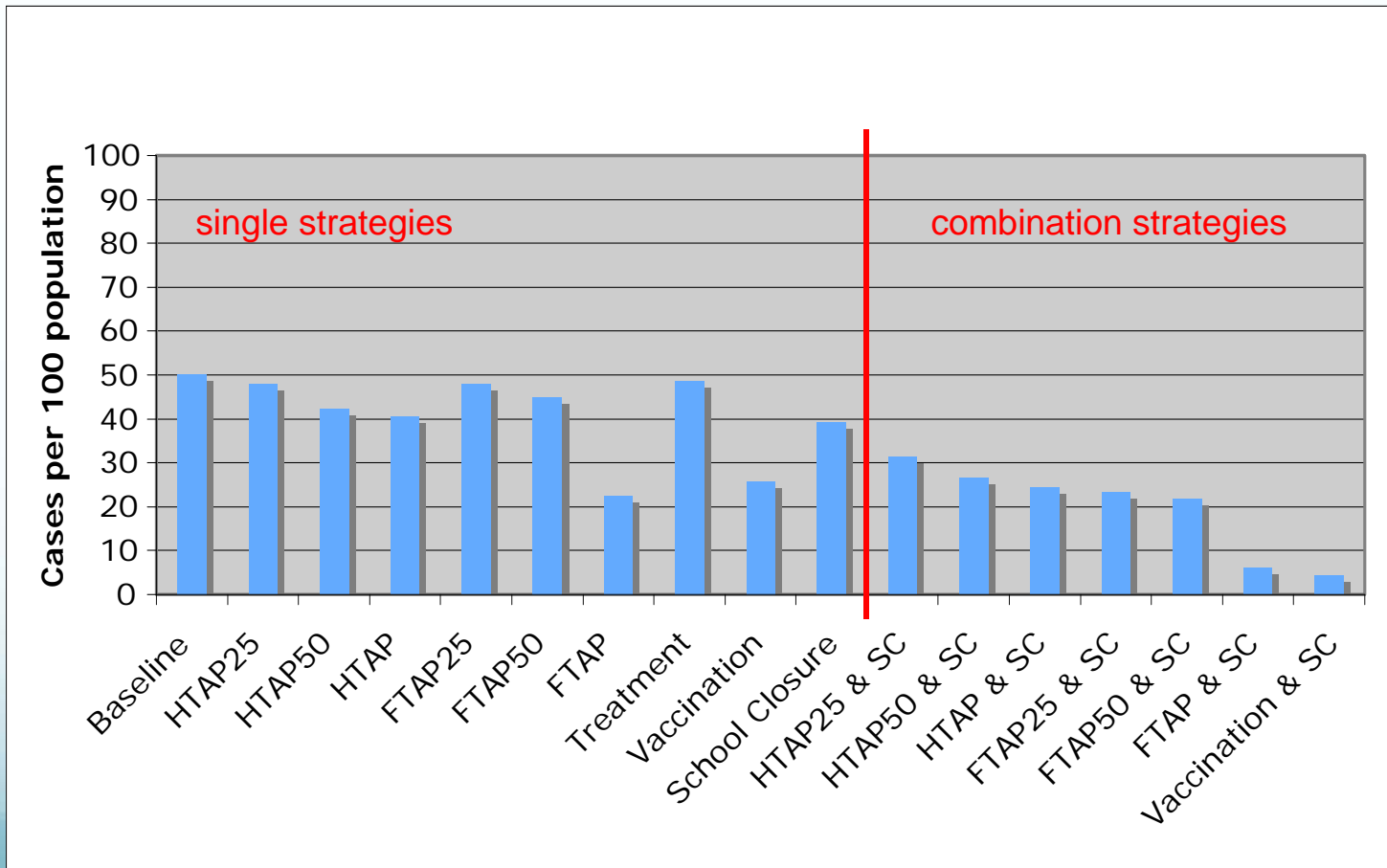


- Oseltamivir:
 - \$23.04 per course*
 - \$29.00 indirect cost per household
- Vaccine (for 2 doses):
 - \$13.32* (+ \$18.57 vaccine delivery) per person vaccinated
 - \$29.00 indirect cost per person vaccinated
- School closure: 2 700 per capita (productivity loss for parents, teachers, other staff) over duration of outbreak

**Including 20% storage & distribution cost*

***Indirect cost: travel cost and productivity loss to obtain prophylaxis/treatment*

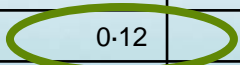
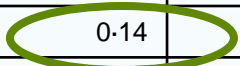
Results - Base Case I



Results - Base Case II (per 1,000 pop)

Intervention	Total cost (m \$)	QALYs	Deaths	Courses
No intervention	0.19	21 141	13	-
FTAP25	0.18	21 157	12	246
FTAP50	0.18	21 175	11	481
HTAP25	0.19	21 181	11	250
School closure	2.72	21 210	10	-
HTAP50	0.17	21 239	8	498
Treatment only	0.19	21 241	8	243
HTAP	0.17	21 264	7	651
Prevaccination	0.14	21 271	6	-
HTAP25 and school closure	2.70	21 273	7	204
FTAP25 and school closure	2.66	21 300	6	150
FTAP50 and school closure	2.66	21 310	5	279
HTAP50 and school closure	2.68	21 316	5	374
HTAP and school closure	2.67	21 330	4	395
FTAP	0.12	21 351	5	2,447
FTAP and school closure	2.61	21 403	1	640
Prevaccination and school closure	2.62	21 403	1	-

increasing



Results - Base Case II (per 1,000 pop)

Scenario	Total cost in million \$ per 1000	Incremental cost in million \$ per 1000	QALYs per 1000	Incremental QALYs per 1000	Incremental cost-utility ratio (\$)
FTAP	0.12		21 352		
FTAP & SC	2.61	2.48	21 403	51	48 472
Prevaccination & SC	2.62	2.50	21 403	51	48 638

Results - Sensitivity Analysis

- Basic reproductive number
 - R_0 2.0:
 - Most effective single strategy/lowest cost: FTAP
 - ICER for combination strategies < \$25,000/QALY
 - R_0 1.6: pandemic controlled with FTAP25
- Mortality / School closure
 - Ranking unaffected
 - ICER for combination strategies < \$45,000/QALY
- Chance of pandemic 1/33
 - Very similar to base case

Limitations

- Characteristics of pandemic strain unknown
- Current feasibility of some strategies
 - Pre-Pandemic vaccine
 - In principle, very effective intervention
 - Limitations: degree of strain match, production capacity and shelf life
 - Oseltamivir
 - Not strain-dependent, longer shelf life
 - Limitation: potential emergence of antiviral-resistant pandemic strains

Conclusions

- All interventions reduce illness attack rate, morbidity and mortality.
- Many interventions are also cost saving.
- Stockpiling antivirals/low-efficacy vaccine is cost-saving to society and avoids loss of life.
- Adding school closure provides the greatest benefit and is likely to be an attractive strategy if transmission and mortality is high.

Economic Evaluation of Influenza Pandemic Mitigation Strategies in the United States Using a Stochastic Microsimulation Transmission Model

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Maarten J. Postma, MSc, PhD,⁴ M. Elizabeth Halloran, BSc, MD, MPH, DSc,³ Ira M. Longini, Jr., MS, PhD³

SOH1N1 2009

Pre-Pandemic

- Pandemic Plans: Canada advocated vaccine, if not available treatment with antivirals
- Stockpile: Canada has an antiviral stockpile for approximately 20% of population
- Research:
 - CIHR operating grants for pandemic preparedness since 2006
 - All areas, e.g. ethics (prioritization), vaccine development, mathematical modeling

Interaction OAHPP – Mathematical Modelers

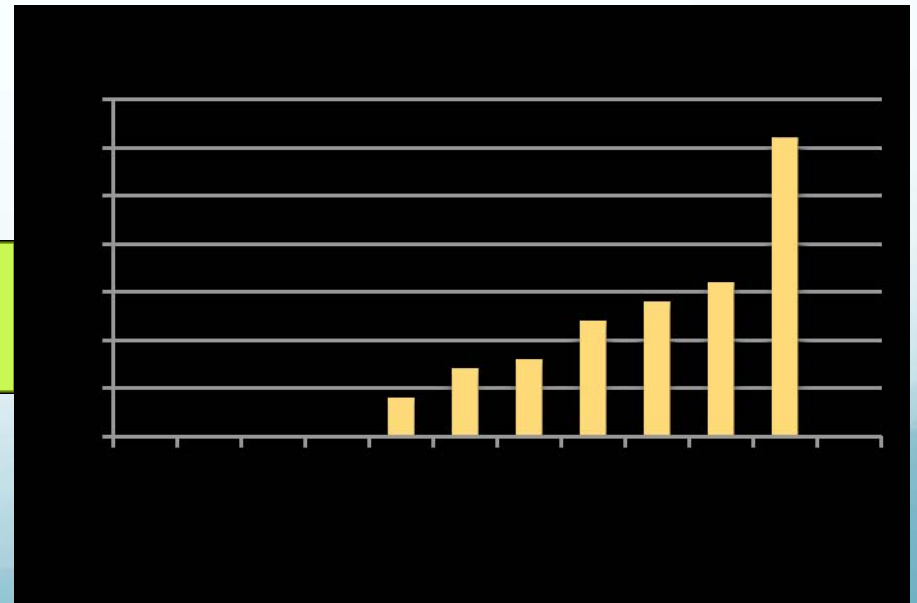
- Friday, April 24 first news of Swine Flu
- Sunday, April 26, invitation to all Ontario influenza modelers to attend TC with OAHPP

April 26, 2009 **11:38:36** AM GMT-04:00

Hi, guys; I have received permission from XXX to invite you all to join the OAHPP pandemic response team, effective tomorrow. Our team will help organize and coordinate modeling, systematic review, and clinical epidemiological efforts under the broader umbrella of YYY and the surveillance and epidemiology team.

April 26, 2009 **11:53:29** AM GMT-04:00

Hi, all; Please find attached instructions for the 1 pm teleconference on modeling and H1N1 swine flu:



Decision-Maker Needs

- April 27:
 - Look at how this might look over the next 1-2 weeks in Ontario
 - Start synthesizing data from available models around antiviral use and social distancing
- April 28:
 - antiviral use (treatment, prophylaxis, or both),
 - "economically intensive" social distancing measures as school closure

Our Dilemma

- Specific requests from OAHPP
- Literature on pandemic planning not entirely suitable to answer all those questions
 - Hypothetical virus
 - Focus on severe pandemic with high R_0
 - Focus to inform pandemic planning (e.g. size of ideal stockpile)
 - Strategies not quite realistic (school closure, vaccination)
 - Choice of strategies depends on R_0
- No understanding of H1N1 (natural history)

Mathematical Models Support Decision-Making

- Specific guidance derived from existing and rapidly created models included
 - Policy decisions to recommend against widespread early use of antiviral drugs (due to potential resistance)
 - Non-closure of schools with single case imports
 - Emphasis on the use of vaccine production resources to generate SOH1N1 vaccine rather than seasonal influenza vaccine
 - Guidance around likely trends in age-specific illness rates, case-fatality rates, and the importance of seasonality in the genesis of “second waves”

Lessons learnt

- What worked well
 - Infrastructure in place (modeler network, many personal contacts, nationally and internationally)
 - Collaborative environment
 - Willingness to share information by many players
 - Informality of requests
- What didn't work that well
 - Disconnect from other disciplines
 - Funding and manpower
 - Proprietary attitudes among some participants

Other Slides

Review of MIDAS Models

- Broad agreement in their predictions.
- Most strategies assessed are combined strategies including both “non-pharmaceutical interventions” (NPIs: school closure, quarantine, travel restriction) and medical interventions (antivirals, including targeted prophylaxis of contacts).
- Overall conclusion: “... at the expected transmissibility of a pandemic strain, **timely implementation of a combination of targeted household antiviral prophylaxis, and social distancing measures could substantially lower the illness attack rate** before a highly efficacious vaccine could become available.”

Modeling targeted layered containment of an influenza pandemic in the United States

M. Elizabeth Halloran^{††}, Neil M. Ferguson[§], Stephen Eubank[¶], Ira M. Longini, Jr.^{††}, Derek A. T. Cummings[§], Bryan Lewis[¶], Shufu Xu[†], Christophe Fraser[§], Anil Vullikanti[¶], Timothy C. Germann[¶], Diane Wagener^{**}, Richard Beckman[¶], Kai Kadaul, Chris Barrett[¶], Catherine A. Macken[¶], Donald S. Burke^{††}, and Philip Cooley^{**}

Sander et al 2008

- Analyzed a range of mitigation strategies, single and in combination, for pandemic flu mitigation in the United States using the agent-based transmission model of Longini et al.
- Full Targeted Antiviral Prophylaxis (FTAP) with an unlimited stockpile, whereby contacts of infected persons are prophylaxed, is the most effective single strategy, but adding school closure provides the greatest benefit and is likely to be an attractive strategy if transmission and mortality rates are high.
- There is a strong R_0 threshold just under 2.0, below which interventions aimed at the population at large (prevaccination, school closure) are less valuable.

Challenges

- Manpower
- Funding
- Disconnect with other disciplines and decision makers
- Vast body of non-published knowledge – how to tap into it