Modeling Influenza Pandemic, Intervention Strategies, and Food Distribution

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Pandemic Flu

- “Epidemic over a wide geographic area and affecting a large proportion of the population.”
- Epidemiologists: “There is a high chance that a pandemic flu will hit the world in the near future”

<table>
<thead>
<tr>
<th>Pandemic cases in history</th>
<th>Excess Mortality</th>
<th>Populations Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918-19 (Spanish flu) (A/H1N1)</td>
<td>40-50 million (2.2-2.8%)</td>
<td>Persons &lt;65 years</td>
</tr>
<tr>
<td>1957-58 (Asian flu) (A/H2N2)</td>
<td>2 million (0.069%)</td>
<td>Infants, elderly</td>
</tr>
<tr>
<td>1968-69 (Hong Kong flu) (A/H3N2)</td>
<td>1 million (0.028%)</td>
<td>Infants, elderly</td>
</tr>
</tbody>
</table>

Swine Flu
http://www.cdc.gov/H1N1FLU/
Potential Impact of Pandemic Flu

- $71.3-165.5 billion economic impact in the U.S. (CDC)
- U.S. Department of Health & Human Services and U.S. Department of Commerce estimates
  - 20% of working adults will become ill
  - 40% workforce loss during peak outbreak periods

Preparedness and Response Plans

- Preparation efforts
  - Local governments
  - Federal government
  - NGOs
  - Companies
- Response plans focus on
  - How to treat ill people
  - Food, vaccine and medicine distribution
Focus of Analysis

- Modeling and understanding the disease spread geographically and over time
  - Impact of seasonality and mutation
- Analyzing the impact of intervention strategies
- Constructing a food distribution network
  - Estimating the food need
  - Number of facilities and their locations (over time)
  - Allocation of resources among the facilities

In collaboration with

GA Department of Education, and GA-DHR Department of Public Health

Disease Spread Model

- An individual-based stochastic model
- 5 age groups (0-5, 6-11, 12-18, 19-64, 65+)

\[ \begin{align*} 
S & \xrightarrow{p_A} A \\
E & \xrightarrow{1-p_A} S \\
P & \xrightarrow{1-p_D} D \\
A & \xrightarrow{p_D} L_H \\
R & \xrightarrow{1-p_R} S \\
I_S & \xrightarrow{p_I} I_A \\
I_A & \xrightarrow{p_I} I_P \\
D & \xrightarrow{p_H} S \\
H & \xrightarrow{p_H} I_S \\
D & \xrightarrow{p_D} S \\
I & \xrightarrow{1-p_I} S \\
\end{align*} \]

- \( p_A = 0.4 \) for adults (19-64) and 0.25 for others (1,2,3,4)
- \( p_R = 0.18 \) for children between 0 and 5, 0.12 for elderly (65+) and 0.06 for others (1,2,3)
- \( p_D = 0.344 \) for elderly and children between 0 and 5 and 0.172 for others (1,3,4)
- Duration of \( E + IP \sim \text{Weibull}(1.48, 0.47) \) (including an offset of 0.5 days) (1,5)
- Duration of \( IP = 0.5 \) days (1,5)
- Duration of \( IS \sim \text{Exponential}(2.7313) \) (1)
- Duration of \( IA \sim \text{Exponential}(1.63878) \) (1)
- Duration of \( I_H \sim \text{Exponential}(14) \) (1,5)

Disease Contact Network

- Households
- Peer groups (work place and schools)
- Community: Census tract-based
  - Population ~ (1500-8000)
- Test case: State of Georgia
  - Household statistics, work flow data, classroom sizes, age statistics

Flexible model, can be adapted to other states or the entire U.S.

Simulation Model Details-1

- Events
  - 3 main type of events
    - Disease progress within an individual
    - Close type of infection (in a household or peer group)
    - Nonclose type of infection (in the community or as an import)
  - Compare time of next infection with the disease progress type of event
  - Start the simulation with 30 initial seeds
Simulation Model Details-2

- Assumed parameters
  - Probability of developing symptoms, hospitalization and death (age based)
  - Duration of the disease stages
  - $R_0$: the average number of secondary cases generated by an infectious individual
  - $\theta$: the proportion of transmission that occurs at either presymptomatic or asymptomatic stage
  - $\omega$: the proportion of infections generated by individuals who are never symptomatic
  - $\gamma$: the proportion of transmission which occurs outside the households
  - $\delta$: the proportion of transmission outside the home that occurs in the community
  - $N$: size of the community
  - $n_{HA}$: active household size (excluding dead)
  - $\delta_{ij}$: indicator function which is 1 if individuals $i$ and $j$ share the same household or 0 otherwise
  - $\delta_{PG}$: indicator function which is 1 if individuals $i$ and $j$ share the same peer group or 0 otherwise
  - $\epsilon_A$: probability that a symptomatic adult withdraws from peer group
  - $\epsilon_C$: probability that a symptomatic child withdraws from peer group

- Parameters calculated based on the assumed parameters
  - $\beta$: coefficient of transmission
  - $h_{PS}$: relative hazard of presymptomatic with respect to symptomatic
  - $h_{AS}$: relative hazard of asymptomatic with respect to symptomatic
  - $h_{PH}$: relative hazard of peer group with respect to household
  - $h_{CH}$: relative hazard of community with respect to household

- Other parameters
  - Probability of compliance to a quarantine (Base case = 0.5)
Expected number of secondary infections by Stage X
(Asymptomatic, Symptomatic, Presymptomatic)
(Household, Peer Group, Community)

\( \Phi_P (h) \) is the probability that an infection does not occur between two individuals during the stage \( P \) for a constant hazard of infection \( h \)

Average number of secondary cases generated by a Presymptomatic individual in the Household

\[
R_{PH} = \sum_{i=1}^{n} p_h(n-1) \left(1 - \Phi_P \left( \frac{h_{PH}}{n} \right) \right)
\]

Calculation of Parameters-2

\[
\phi_X (h) = E(e^{-hD_X}) = \int_0^\infty e^{-ht} f_X(t) \, dt
\]

\[
R_0 = \sum_{X \in \{P,A,S\}} \sum_{Y \in \{H,P,C\}} r_{XY}
\]

\[
\theta = \frac{\sum_{X \in \{P,A\}} \sum_{Y \in \{H,P,C\}} r_{XYP}}{R_0}
\]

\[
\omega = \frac{\sum_{Y \in \{H,P,C\}} r_{AY} + p_A \sum_{Y \in \{H,P,C\}} r_{YP}}{R_0}
\]

\[
\gamma = \frac{\sum_{X \in \{P,A,S\}} \sum_{Y \in \{P,C\}} r_{XY}}{R_0}
\]

\[
\delta = \frac{\sum_{X \in \{P,A,S\}} \sum_{Y \in \{P,C\}} r_{XY}}{\sum_{X \in \{P,A,S\}} \sum_{Y \in \{P,C\}} r_{XY}}
\]
The force of infection for individual $i$ is calculated as follows:

$$\lambda_i = \sum_{j=1}^{N} \left\{ \delta^{H}_{ij} \frac{m_{ij} \beta}{n_{ij}} + \delta^{P}_{ij} m_{ij} \epsilon_{ij} h_{ij} \beta + \frac{m_{ij} h_{ij} \beta}{N} \right\}$$

where

$$\epsilon_{ij} = \begin{cases} 0 & \text{with probability } \epsilon_{a} \text{ if } j \text{ was an adult and was symptomatic} \\ 0 & \text{with probability } \epsilon_{c} \text{ if } j \text{ was a child and was symptomatic} \\ 1 & \text{otherwise} \end{cases}$$

$$m_{ij} = \begin{cases} 1 & \text{if } j \text{ was symptomatic} \\ h_{ij} & \text{if } j \text{ was presymptomatic} \\ 0 & \text{if } j \text{ was asymptomatic} \end{cases}$$

Disease Spread in Georgia

<table>
<thead>
<tr>
<th>$R_0$ Value</th>
<th>Peak Infectivity</th>
<th>Peak Day</th>
<th>CAR</th>
<th>IAR</th>
<th>Death Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>2.48%</td>
<td>70</td>
<td>32.50%</td>
<td>49.05%</td>
<td>0.57%</td>
</tr>
<tr>
<td>1.8</td>
<td>5.27%</td>
<td>50</td>
<td>44.20%</td>
<td>67.49%</td>
<td>0.80%</td>
</tr>
<tr>
<td>2.1</td>
<td>8.01%</td>
<td>40</td>
<td>51.27%</td>
<td>78.27%</td>
<td>0.93%</td>
</tr>
</tbody>
</table>


Swine flu peak ~1%
Peak day ~100
Hospitalization & Mortality Curves using 2009 adjusted parameters

- Influenza weekly report shows till now (around 140 days after the initial case) 193 hospitalization, 5 deaths in GA

Comparison between Hospitalization & Mortality Curves using two sets of parameters
Disease Spread in Georgia

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<tr>
<td>1.5</td>
<td>2.4%</td>
<td>70</td>
<td>32.6%</td>
<td>49.6%</td>
<td>0.5%</td>
</tr>
<tr>
<td>1.8</td>
<td>5.2%</td>
<td>50</td>
<td>44.2%</td>
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<td>40</td>
<td>51.2%</td>
<td>78.2%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

How does the disease spread geographically over time?

Seed Atkinson

Seed Fulton

Day 10

Day 10
Infections over Time

- Peak infection rate is similar regardless of starting location
- Time of peak depends on the starting locations
  - Similar for densely populated areas
  - Different for less dense areas
# Seasonality

- Strength and mechanisms of seasonality can alter the spread and persistence of infectious diseases (Ferrari 2008, Stone 2007)
- Transmission rate changes over time
  - “there is an enhancement of 10% of the transmission parameter during the influenza season (November-February in the Northern hemisphere) and a reduction to as low as 10% during the non-influenza season (June-July in the Northern hemisphere)” (Colizza 2007, Grais 2004)
- Model $R_0$ as a sinusoidal function of time $t$
  - (Casagrandi 2006, Stone 2007):
  $$ R_0(t) = R_0^*(1 + \epsilon \cos(2\pi t)) $$

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## Seasonality Experimental Setting

- Nine pairs of combination for $(R_0^*, \epsilon)$
- 4 different starting times (January, April, July and October)
- Impact of
  - Start time
  - Seasonality factor $\epsilon$
  - $R_0^*$
Preliminary Results on Seasonality

- Two peaks if the pandemic starts in April
- As $R_0^*$ increases, second peak decreases
- As $\epsilon$ increases
  - Second peak increases
  - Time between two peaks decreases

Discussion (Seasonality)

- Why pandemics starting in April will have a second wave?
  - Herd Immunity:
    - When Susceptible population reaches a threshold an outbreak won’t happen in the remaining population
Mutation

- Antigenic “Drift” and “Shift”
  - Drift causes annual flu. Frequency: ~every 2-3 years
  - Shift results in a new subtype and is likely to cause a pandemic. Frequency: irregular

- Use SIRS model to describe the mutation process
  - A new dominant strain causes individuals who have recovered from the original strain become susceptible again with a positive probability $\delta$

- Time $t^*$ when mutant emerges

Combination of seasonality and mutation can lead to three peaks

Results (Mutation)

- $(R_0=1.5, \delta=5\% \text{ and } 8\%)$
- $(R_0=1.5, \delta=10\% \text{ and } 20\%)$
Results (3 Waves)

- \( R_0^* = 1.5 \)
- \( \varepsilon = 0.3 \)
- \( \delta = 0.015 \)
- Start in April
- Mutant strain emerged at 275 days

1918 Pandemic Flu

Deaths per 1,000 persons
Discussion on Mutation

- Why a viral mutation that emerges during the downward slope of an initial wave may cause a severe second wave?
  - Force of infection: the rate at which susceptible persons are infected by the virus
  - The prevalence of infections depends on the value of the force of infection (# of infected persons) as well as the # of susceptible persons

Public Policy Indication

- Public health officials need to determine what data to be collected to facilitate forecasting and planning
  - Early characterization and the emerging viral characteristics may help predict
  - Importance of active surveillance and virus typing during the course of an epidemic
- If a second wave is possible
  - Plan medical supplies, personnel staffing, and education of the public accordingly, and the time gained for vaccine development
- Reproducing a 3-wave epidemic may help shed additional light on the 1918 pandemic
**Intervention Strategy: Voluntary Quarantine**

- Infected individuals and their family members stay home until recovered
- Compliance rate <100%
- Start time and duration of voluntary quarantine (education/promotion)
  - Prolonged quarantine
    - May increases ignorance and negatively impact public morale
  - Limited (2-12 weeks) quarantine
  - Effect on peak infectivity and infection attack rate

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**Disease Spread under Voluntary Quarantine**

- Quarantine leads to two peaks
**When to start the voluntary quarantine?**

- To minimize the peak, or maximum "capacity" needed
  - Start sometime during weeks 4-6
  - If shorter quarantine → start later
  - Diminishing returns as the duration increases

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**Results based on 50% compliance rate**

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**When to start the voluntary quarantine?**

- To minimize the total % of infected population, i.e., the total "capacity" needed
  - Start sometime between weeks 5-7
  - If shorter quarantine → start later
How long to impose quarantine?

- A longer quarantine
  - delays the timing and reduces the magnitude of the second peak
  - does not significantly impact the first peak
  - reduces the percentage affected at the maximum peak

Effect of Compliance Rate on the Attack Rate

- Base case: 50%
Summary of results for an 8-week quarantine

<table>
<thead>
<tr>
<th>$R_0$ Value</th>
<th>Quarantine Start</th>
<th>Peak Infectivity</th>
<th>Peak Day</th>
<th>CAR</th>
<th>IAR</th>
<th>Death Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>7</td>
<td>0.80%</td>
<td>52</td>
<td>26.52%</td>
<td>40.46%</td>
<td>0.47%</td>
</tr>
<tr>
<td>1.8</td>
<td>4</td>
<td>1.88%</td>
<td>63</td>
<td>36.82%</td>
<td>56.14%</td>
<td>0.66%</td>
</tr>
<tr>
<td>2.1</td>
<td>3</td>
<td>3.9%</td>
<td>49</td>
<td>41.20%</td>
<td>62.81%</td>
<td>0.75%</td>
</tr>
</tbody>
</table>

The reduction in peak infectivity, CAR, IAR, and death ratio

<table>
<thead>
<tr>
<th>$R_0$ Value</th>
<th>Peak Infectivity</th>
<th>CAR</th>
<th>IAR</th>
<th>Death Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>67.74%</td>
<td>18.40%</td>
<td>18.51%</td>
<td>18.22%</td>
</tr>
<tr>
<td>1.8</td>
<td>64.71%</td>
<td>16.70%</td>
<td>16.82%</td>
<td>17.22%</td>
</tr>
<tr>
<td>2.1</td>
<td>50.44%</td>
<td>19.52%</td>
<td>19.68%</td>
<td>19.68%</td>
</tr>
</tbody>
</table>

For $R_0 = 1.5$, a voluntary 4-week quarantine with 50% percent compliance rate is at least as effective as a 6-week school closure both in terms of IAR and peak activity.

Estimating the food need (Metropolitan Atlanta Area)

- 3-meals per day
- Several alternatives to calculate the food need
  - Serve the households with
    - An infected (symptomatic or hospitalized) individual
      - All, or only those below 25K income, or below the poverty level
    - All adults infected (symptomatic or hospitalized)
      - All, or only those below 25K income, or below the poverty level
  - Serve the quarantined households
- Depending on who we serve, the total food need changes dramatically
  - From 250K (all adults infected, below poverty level) to 35 Million (an individual infected, all income levels)
The impact of voluntary quarantine on food need (Metropolitan Atlanta Area)

- Serve the households with all adults infected (symptomatic or hospitalized), $R_0 = 1.8$
- No intervention vs. 8-week quarantine

Food Distribution Network

- S: Supply point
- MF: Major facility
- POD: Point of Distribution
- D: Demand point
Decisions (in each time period)

- Which facilities to open/close
- How much food to send:
  - from the suppliers to each of the major facilities
  - from the major facilities to each of the PODs
- Subject to
  - Capacity constraints
  - Potential locations
- To minimize
  - Opening/closing, operating, and distribution costs

Models

- Dynamic model
  - Decisions made and updated in each time period
    - 5 scenarios are generated in each time period for the remaining time horizon and the average is used as an estimate
- Static model
  - Decisions about opening the facilities is done at the beginning of the planning horizon
  - Resource allocation decisions are made in each time period

Tradeoffs?
Solution Approaches

- Basic (Add-Drop type) heuristic
- Single period heuristic
  - Instead of using the basic heuristic, solve the single period problem optimally for the weighted average demand and current period’s demand
- Single period heuristic with basic heuristic
  - Use the basic heuristic to solve the problem for the weighted average demand case
  - Then, solve the single period problem optimally for the current demand
- Solve the problem optimally
Computational Results: Georgia Case

- 1615 census tracts in Georgia (for disease spread model)
- 603 census tracts (15 counties) in Metropolitan Atlanta Area
  - Distances between census tracts
- Estimated data
  - Cost figures
  - Supply amount
  - Potential facility locations and capacities
- Three different setting for the shipment costs:
  - Low (Facility related costs dominate)
  - Comparable (Shipment and facility costs are comparable)
  - High (Shipment costs dominate)

Heuristics vs. Optimal Solution

- 8-hour time limit on the CPLEX 9.0
  - Longer time limits result in memory problems in finding the optimal solution
- Gwinnett and Fulton counties
  - The number of MF’s is the most important factor in making the problem hard
- Large instances: Single period heuristic with basic heuristic outperforms best integer solution found within time limits
Food distribution under no Intervention vs. 8-Week Quarantine (for $R_0 = 1.8$)

- Number of PODs, locations, open duration
- Food distribution problem setting (metro Atlanta)
  - 603 demand points
  - 151 PODs
  - 10 MFs
  - 20 supply points
- Quarantine
  - start at the beginning of fourth week
  - serve the households with all adults infected
- Food distribution starts when the number of infected individuals at a given time is greater than 0.5% of the total population
  - Weeks 5-12 for no intervention (8 weeks period)
  - Weeks 6-18 for 8-week quarantine case (13 weeks period)

<table>
<thead>
<tr>
<th>Shipment Cost</th>
<th>Demand</th>
<th>Quarantine</th>
<th>No Intervention</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Cost</td>
<td>2629980</td>
<td>3594185</td>
<td>26.83%</td>
<td></td>
</tr>
<tr>
<td>Demand within 10</td>
<td>603</td>
<td>151</td>
<td>10</td>
<td>20 supply points</td>
</tr>
<tr>
<td>Comparable Cost</td>
<td>1756733.73</td>
<td>22016751.71</td>
<td>23.34%</td>
<td></td>
</tr>
<tr>
<td>Demand within 10</td>
<td>97.00%</td>
<td>98.87%</td>
<td>9.12%</td>
<td></td>
</tr>
<tr>
<td>High Cost</td>
<td>27207118.24</td>
<td>36044412.99</td>
<td>24.27%</td>
<td></td>
</tr>
<tr>
<td>Demand within 10</td>
<td>98.50%</td>
<td>99.18%</td>
<td>9.68%</td>
<td></td>
</tr>
</tbody>
</table>

- Under quarantine, reduction in total demand (26.83%) is greater than the reduction in IAR (16.82%)
- As the shipment costs increase
  - The demand served within 10 miles increases
  - The reduction in total cost gets closer to the reduction in total demand
Number of Open PODs over Time (No Intervention vs. Quarantine)

- Both in quarantine and no intervention case
  - Number of open PODs peak earlier when compared to demand

Open Duration of Open POD’s (No Intervention vs. 8-week Quarantine)

- Under quarantine
  - the duration of open PODs in less populated areas decreases most
  - the variation in the duration of open PODs decreases
Conclusions and Next steps

- Modeling of pandemic flu spread, intervention strategies, and food distribution logistics
- Modeling
  - Seasonality and virus mutation
- Intervention strategies
  - School closures
  - Antiviral and vaccine allocation
- Food distribution
  - Additional heuristics
  - New runs with new data from Red Cross on potential suppliers

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Questions/Discussions?

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