Modeling the spread of influenza through a spatially-structured host population

Gregg Hartvigsen
Thursday, February 24, 2005
Posted: 1324 GMT (2124 HKT)

VATICAN CITY (CNN) -- Pope John Paul II has been rushed to hospital by ambulance after suffering a recurrence of the flu that forced him to be hospitalized for 10 days earlier this month.
Modeling the Spread of Influenza

Overview of the Problem
Structure of the Host Network
Modeling Influenza
Results
Conclusions
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Presentation from the 2000 Emerging Infectious Diseases Conference in Atlanta, Georgia
Emerging Infectious Diseases: A CDC Perspective. James M. Hughes, M.D.
Centers for Disease Control and Prevention, Atlanta, Georgia, USA
CDC’s Eight Priority Groups for Vaccination (All of Equal Importance)

2004 Vaccine Shortage

Who should get a flu vaccination?

People who are 65 years old or older —
Even if you’re in great health!

Children 6 to 23 months old —
Children younger than 2 years old have one of the highest rates of hospitalization from influenza

Adults and children with a chronic health condition —
Like heart disease, diabetes, kidney disease, asthma, cancer, or HIV/AIDS

Women who will be pregnant during flu season —
Flu season is typically November through March

Residents of nursing homes and long-term care facilities

Children aged 6 months to 18 years on chronic aspirin therapy

Healthcare workers involved in direct patient care

Out-of-home caregivers and household contacts of children younger than 6 months

If you’re not in one of these groups, you should not get vaccinated, to allow those at highest risk to get a shot.

http://www.cdc.gov/flu
November 12, 2004
The Progression of Diseases

Cholera

1348
Black Death
Modeling the Spread of Influenza

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Small-World Networks

\[ \text{swn-}P = 0.00 \]

\[ \text{swn-}P = \text{probability that each host’s edge is broken and rewired to a randomly chosen host from the population.} \]

Small-World Networks

Use Networks with 1K, 10K, and 100K Hosts begin with four neighbors (k) (transmission network)
One unlucky host gets inoculated
Structure of a Network

\[ k = \text{degree} \]

\[ \text{NCR} = \text{Neighbor Contact Rate} \]

\[ \text{Population Size} \]

\[ \text{swn-P} \]
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\[ \text{C.C.} = \frac{|E(T_v)|}{k_v^2} \]
Vaccination Strategies

1. Vaccinating Random Nodes
2. Vaccinating Hubs (nodes with the highest degree)
3. Vaccinating Nodes with Lowest Clustering Coefficient
4. Vaccinating Nodes with Highest Clustering Coefficient
5. Vaccinating Nodes Containing Cross-Cut Edges
Vaccination Strategies

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4. Vaccinating Nodes with Highest Clustering Coefficient
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Clustering Coefficient:

\[
C.C. = \frac{|E(T_v)|}{\binom{k_v}{2}}
\]

\(|E(T_v)| = \# \text{ of edges in the neighborhood of } v\)

\(\binom{k_v}{2} = \text{total } \# \text{ of possible edges in } T_v\)

Watts, 1999, *The Small-World Phenomenon*
Low clustering coefficient:
High clustering coefficient:
Vaccination Strategies

1. Vaccinating Random Nodes
2. Vaccinating Hubs (nodes with the highest degree)
3. Vaccinating Nodes with Lowest Clustering Coefficient
4. Vaccinating Nodes with Highest Clustering Coefficient
5. Vaccinating Nodes Containing Cross-Cut Edges
Vaccinating nodes with cross-cut edges
Design = 4-Way Factorial

<table>
<thead>
<tr>
<th>Factors</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWN – P</td>
<td>9</td>
</tr>
<tr>
<td>Vaccination Strategy</td>
<td>5</td>
</tr>
<tr>
<td>Percent Vaccinated</td>
<td>7</td>
</tr>
<tr>
<td>Population size</td>
<td>3</td>
</tr>
</tbody>
</table>

$9 \times 5 \times 7 \times 3 \times 10$ replicates = 9450 simulations
What do we measure?

- Peak #
- Time to Peak
- Peak #
- Duration
- Total # Infected
Modeling the Spread of Influenza

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Two experiments:

1. Test spread across network
2. Investigate vaccination rates and strategies on the slowing of influenza
Structure of the Transmission Network Influences the Extent of the Epidemic

Proportion of Population Infected

<table>
<thead>
<tr>
<th>Variable</th>
<th>Proportion Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>swnP</td>
<td>0.9%</td>
</tr>
<tr>
<td>k</td>
<td>17.6%</td>
</tr>
<tr>
<td>popsize</td>
<td>0.1%</td>
</tr>
<tr>
<td>NCR</td>
<td>57.9%</td>
</tr>
</tbody>
</table>
swnP = 0

swnP = 0.5

swnP = 0.05

swnP = 1.0
Response Variable = ArcSin Proportion of Population Infected

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>MS</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>swnP</td>
<td>8</td>
<td>72.053</td>
<td>996.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>vacstrat</td>
<td>4</td>
<td>46.822</td>
<td>647.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>per_vacc</td>
<td>6</td>
<td>253.705</td>
<td>3508.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>popsize</td>
<td>2</td>
<td>12.832</td>
<td>177.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>swnP*vacstrat</td>
<td>32</td>
<td>2.663</td>
<td>36.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>swnP*per_vacc</td>
<td>48</td>
<td>4.035</td>
<td>55.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>swnP*popsize</td>
<td>16</td>
<td>0.640</td>
<td>8.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>vacstrat*per_vacc</td>
<td>24</td>
<td>2.359</td>
<td>32.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>vacstrat*popsize</td>
<td>8</td>
<td>3.035</td>
<td>41.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>per_vacc*popsize</td>
<td>12</td>
<td>0.160</td>
<td>2.22</td>
<td>0.009</td>
</tr>
<tr>
<td>swnP<em>vacstrat</em>per_vacc</td>
<td>192</td>
<td>0.555</td>
<td>7.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>swnP<em>vacstrat</em>popsize</td>
<td>64</td>
<td>0.261</td>
<td>3.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>swnP<em>per_vacc</em>popsize</td>
<td>96</td>
<td>0.325</td>
<td>4.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>vacstrat<em>per_vacc</em>popsize</td>
<td>48</td>
<td>0.227</td>
<td>3.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>swnP<em>vacstrat</em>per_vacc*popsize</td>
<td>384</td>
<td>0.092</td>
<td>1.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Error</td>
<td>8504</td>
<td>0.072</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>9448</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[ r^2 = 93.9 \]
Main Effect of swnP

24.3% Variance, P < 0.001

Percent Infected

swnP

0.00 0.01 0.02 0.03 0.04 0.05 0.10 0.50 1.00
Main Effect of Vaccination Strategy

6.7% Variance, P < 0.001

Vaccination Strategy:
- Random
- Hubs
- Low C.C.
- High C.C.
- Cross-cuts

Percent Infected:
- Random: 50% (c)
- Hubs: 30% (a)
- Low C.C.: 40% (b)
- High C.C.: 60% (d)
- Cross-cuts: 30% (b)
Vaccinate 10% Low Clustering Coefficient

Vaccinate 10% High Clustering Coefficient
Main Effect of Percent Vaccinated

41.4 % Variance, P < 0.001
Main Effect of Population Size

![Bar chart showing the main effect of population size on the percentage of infected. The x-axis represents population size (100, 1000, 10000, 100000, 1000000), and the y-axis represents the percent infected (0, 10, 20, 30, 40, 50, 60). The bars are labeled 'c', 'b', and 'a', and the variance is 0.7%, P < 0.001.](image)
Vaccination Strategy x swnP

3.1% Variance, P < 0.001

Percent Infected

Vaccination Strategy

- swnP = 0.0
- swnP = 0.01
- swnP = 0.02
- swnP = 0.03
- swnP = 0.04
- swnP = 0.05
- swnP = 0.1
- swnP = 0.5
- swnP = 1.0

Random hubs low c.c. high c.c. cross-cuts
Antigenetic Evolution

Host 1
Day t

00101

00001

Host 2
Day t+1
Cross Immunity

Vaccine Circulating Flu Strain

1 1 1 1 + 1 1 1 1 = Total Immunity

1 1 1 1 + 1 0 1 0 = Partial Immunity

1 1 1 1 + 0 0 0 0 = No Immunity

• The percent match between flu strains determines the degree of cross immunity observed
Closer matches of vaccine to circulating flu reduces epidemic

20 % population (N=10,000) vaccinated
Fig. 1. Overall structure of the most parsimonious trees. The thick line running from the lower left (*=root) to the upper right (open square) is called the trunk and represents the successful H3N2 lineage. The vertical lines indicate the range of isolates from the flu years (October 1 to September 30).

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Conclusions (5)

1. Structure of the transmission network influences the extent of the epidemic

- **Proportion of Population Infected**
  - *swnP* and *k*:
    - **0.9%** when *swnP* is low and *k* is high.
    - **17.6%** when *swnP* is high and *k* is low.
  - *popsize* and **NCR**:
    - **0.1%** when *popsize* is low and NCR is high.
    - **57.9%** when *popsize* is high and NCR is low.
Conclusions (5)

2. Model appears to simulate both the dynamics and evolution of influenza.
Conclusions (5)

3. Best to vaccinate hubs. And this gets better as population size increases.
Conclusions (5)

4. It’s good to vaccinate people whose friends don’t know each other.
Conclusions (5)

5. Worst (worse than random) - vaccinate people whose friends all know each other (high clustering coef.)
CDC’s Eight Priority Groups for Vaccination (All of Equal Importance)

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Even if you’re in great health!

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Out-of-home caregivers and household contacts of children younger than 6 months

If you’re not in one of these groups, you should not get vaccinated, to allow those at highest risk to get a shot.
Modeling Other Systems?

Rinderpest

FAO - UN

1997

WORLDWIDE HIV PREVALENCE RATES

KEY:
% of adults infected
UNAVAILABLE
0.0 - 0.1%
0.1 - 0.5%
0.5 - 1%
1 - 5%
5 - 15%
15 - 39%

SARS (work by Sarah Olscamp)

Homma Farian
Matthew Haas et al.
23 of 34 (68%) patients died.

Epidemic curve showing the dates of onset for 12 confirmed and 21 suspected human cases of avian influenza A (H5N1) infection, Thailand, 2004.

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