The Contribution of Mathematical Models to Our Understanding of Influenza Dynamics

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tell.fil.purdue.edu

Outline:

I. What is the flu?

II. Why should we model the flu?

III. Things to know before modeling…

IV. Types of Models

- A. Differential Equation Model
- B. Agent-based (Small-World Network) Model

-Common respiratory illness caused by an influenza virus

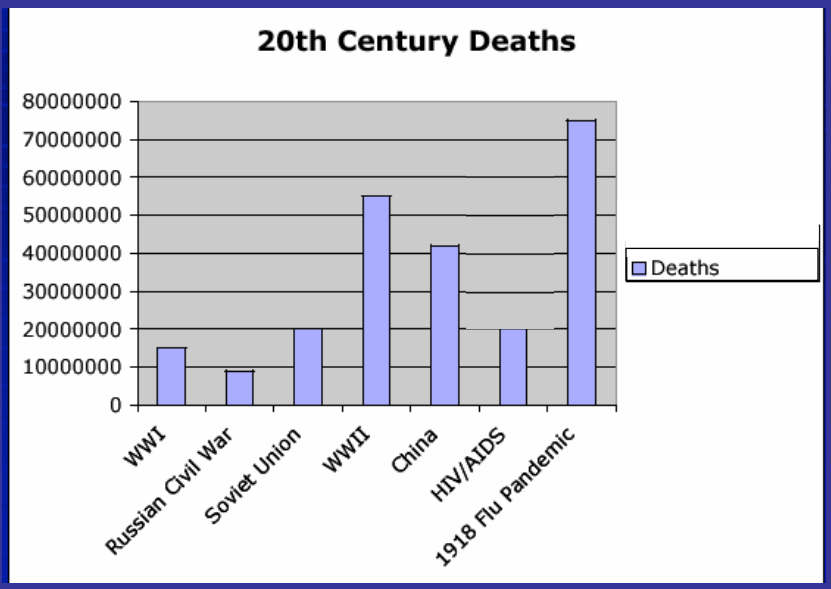
-Each year in U.S.:

- 5 – 20% of the population gets sick
- 200,000 individuals hospitalized
- 36,000 die (elderly and chronically ill)

-1918 pandemic

- 50-100 million die (all ages)

www.wagt.com/news/health/922332.html



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Problems with epidemic data:

1. Many do not visit a doctor when sick
2. Many doctors do not report cases
3. Wrong diagnoses
   - secondary infections
   - were already chronically ill
4. Data that are available are hard to find!

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Things to know before making a model:

1. details concerning causal agent
2. evolution
3. transmission

- contact networks

1. The causal agent

Influenza A virion consists of:

-Host-derived lipid bilayer

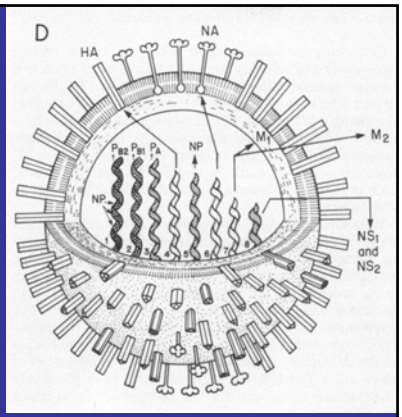
- protein matrix

- 8 single-stranded RNA segments

  - polymerases

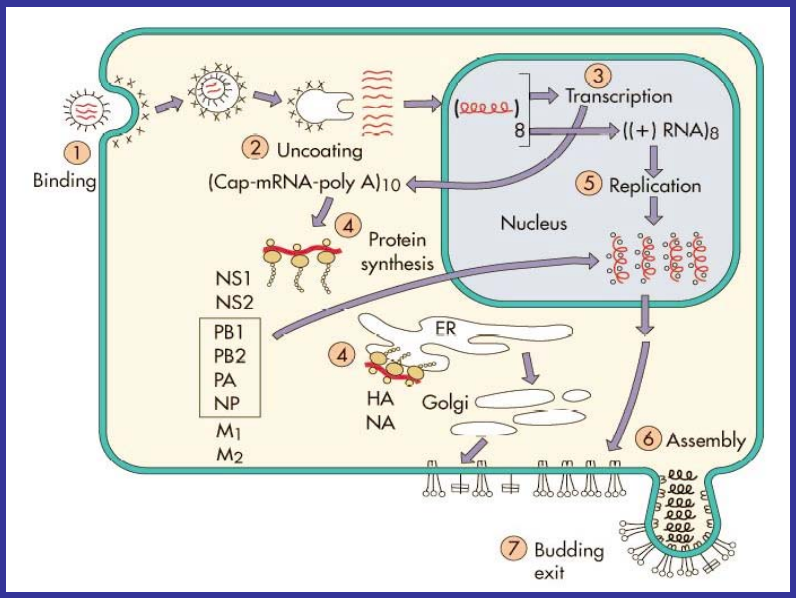
  - hemagglutinin (HA)

  - neuraminidase (NA)



Reproduced from Webster et al's *Evolution and Ecology of Influenza A Viruses*

1. The causal agent



Reproduced from Medical Microbiology 4th edition Fig. 56-2

2. Evolution

1. Antigenic drift

- polymerases lack proofreading capability = mutations

- cause of seasonal outbreaks

AGCUAAGGCGA → AGGUAAGGCGA

- 30% difference in amino acid sequence of HA or NA = new subtype

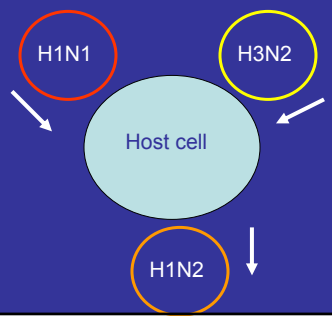
- 16 different HA (H1, H2..), 9 different NA (N1, N2..)

2. Evolution

2. Antigenic shift

- gene segments integrated into progeny virions relatively randomly

- occurs when one is infected with 2 different parent viruses at once



- often cause of pandemics

2. Transmission

-Virus spreads from one host to another in airborne respiratory droplets

-latency period = 1-3 days

-Infectious period = up to 6 days

- Symptoms appear 1-4 days after infection

- Can spread disease when you don't know you have it!

www.coolquiz.com

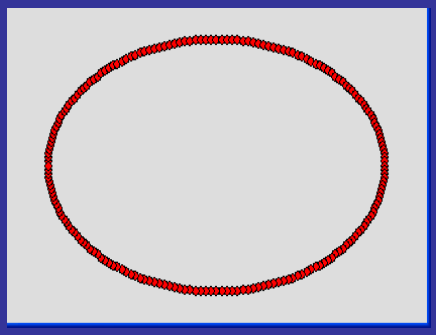
2. Transmission

R_o = average # of secondary infections caused by a primary infection in a completely susceptible population

$R_o > 1$ but < 3

Christina Mills et al, 2004, *Nature*

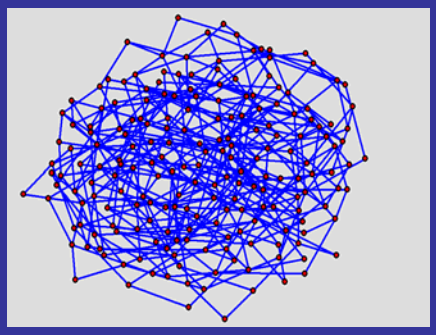
2. Transmission



Regular *k*-circulant

High clustering coefficient

High average path length



Random

Low clustering coefficient

Low average path length

Clustering Coefficient:

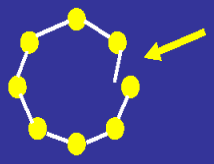
$$C.C. = \frac{|E(T_v)|}{\binom{k_v}{2}}$$

$|E(T_v)|$ = # of edges in the neighborhood of v

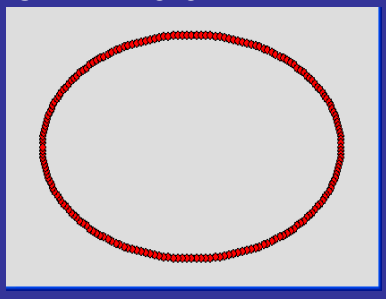
$\binom{k_v}{2}$ = total # of possible edges in T_v

Watts, 1999, *The Small-World Phenomenon*

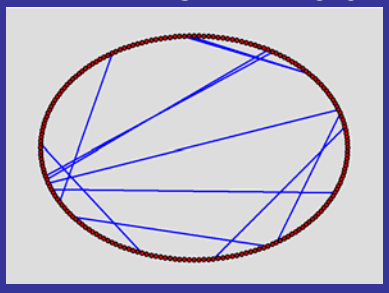
2. Transmission



swnP = 0.0



swnP = 0.02



Small-World Network

swnP = probability each host's edge is broken and rewired to a randomly chosen host from the population

Watts and Strogatz, 1998, *Nature*

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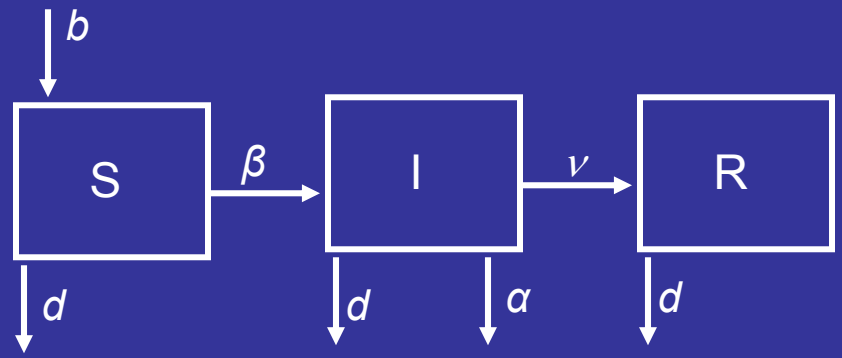
1. Differential Equation Models = SIR Models

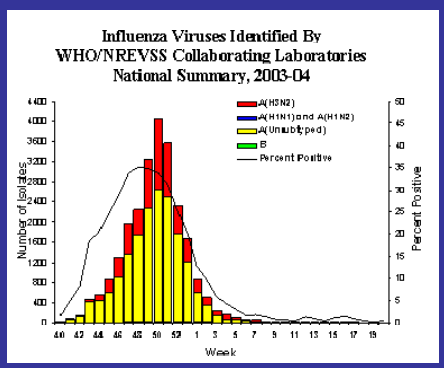
$$dS/dt = b\,(S + I + R) - dS - \beta SI$$
$$dI/dt = \beta SI - (\alpha I + dI + \nu I)$$
$$dR/dt = \nu I - dR$$



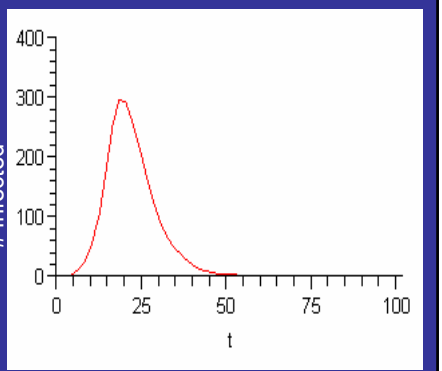
$\beta = 0.0006$ $\quad b = 0$

$\nu = 0.2$ $\quad d = 0$

$\alpha = 0$



www.cdc.gov/flu



Predicting whether an epidemic will occur:

$R_o = ßS / \nu$

$R_o > 1$ epidemic will occur

$R_o < 1$ epidemic will not occur

What else can we do with them?

-Analyze data from real outbreaks

- Incorporate Evolution

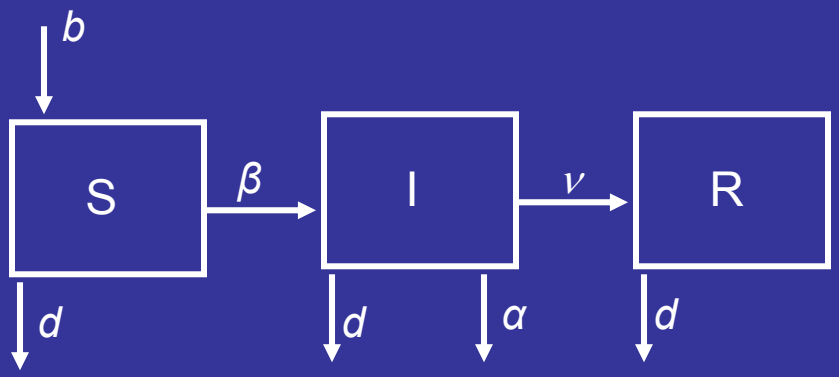
-Vaccinate

Vaccination

$dS/dt = b(S + I + R) - dS - \beta SI - \lambda S$

$dI/dt = \beta SI - (\alpha I + dI + \nu I)$

$dR/dt = \nu I - dR + \lambda S$

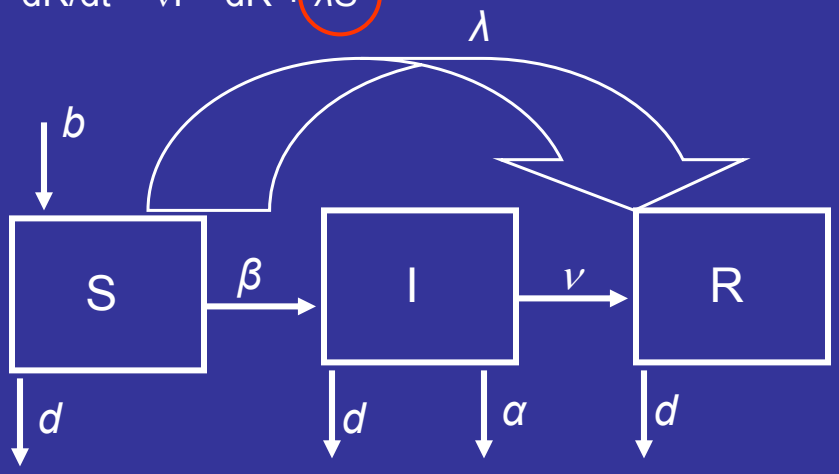


Vaccination

$dS/dt = b(S + I + R) - dS - \beta SI - \lambda S$

$dI/dt = \beta SI - (\alpha I + dI + \nu I)$

$dR/dt = \nu I - dR + \lambda S$

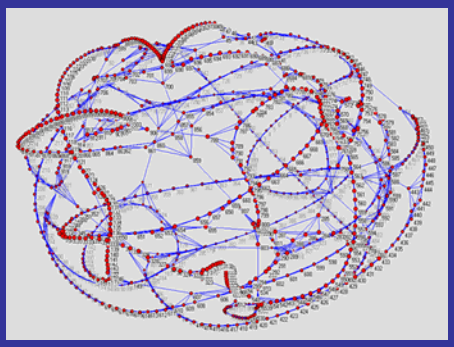


2. Agent-based Models

Our Small-World Network Model:

Parameters

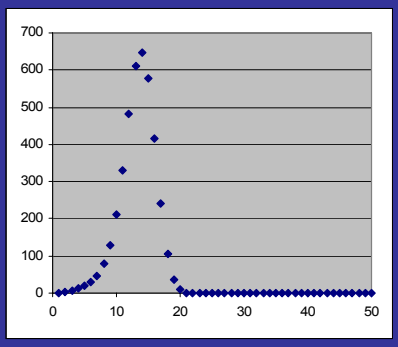
- *k*
- *swnP*
- *NCR*
- latency period
- infectious period (*d*)

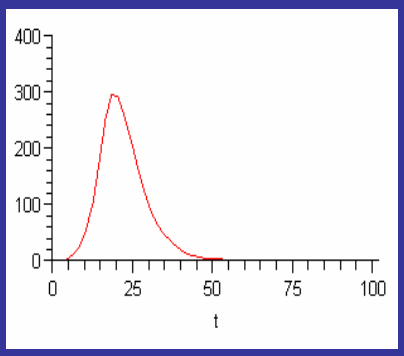


k = 4 lat period = 1

swnP = 0.05 inf period = 3

NCR =0.5





(SIR model)

Predicting whether an epidemic will occur:

$$R_o = k * (1 - (1 - NCR)^d)$$

Ex:

$R_o = 2$ when:

$k = 4$

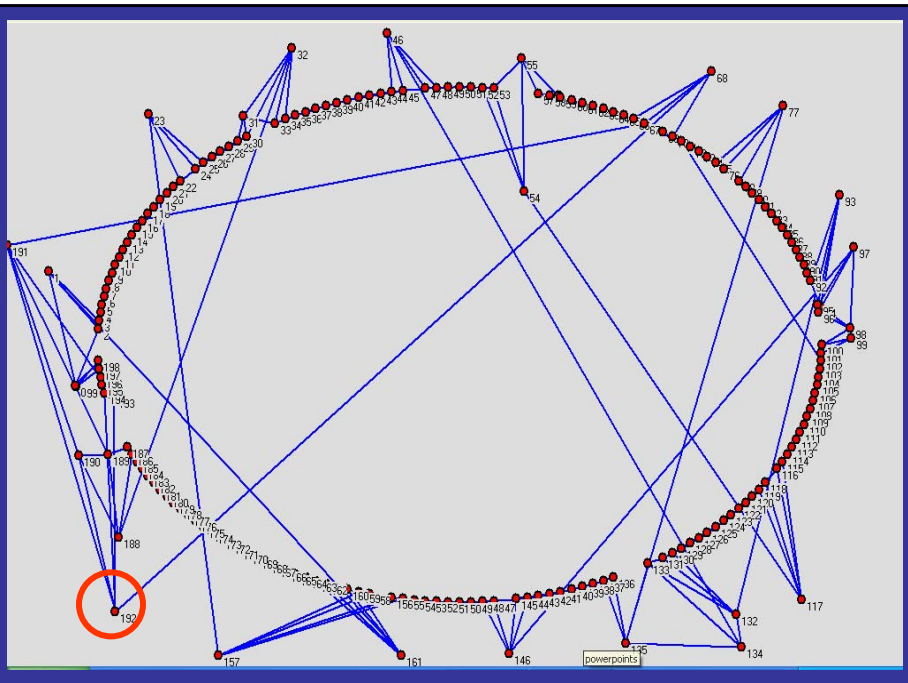
$NCR = \sim 0.2$

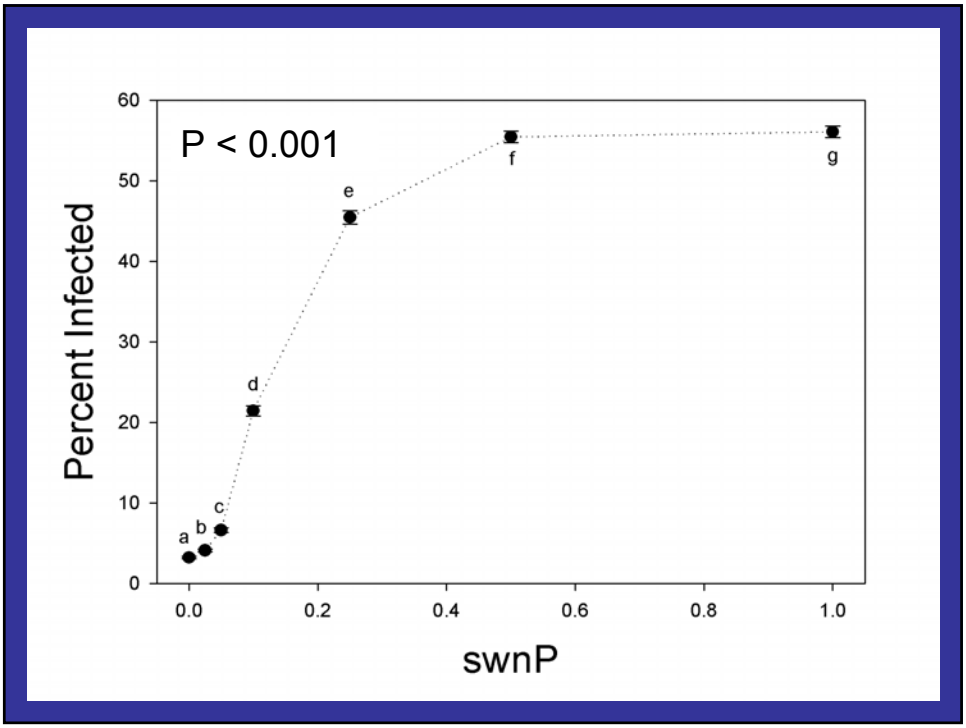
$d = 3$

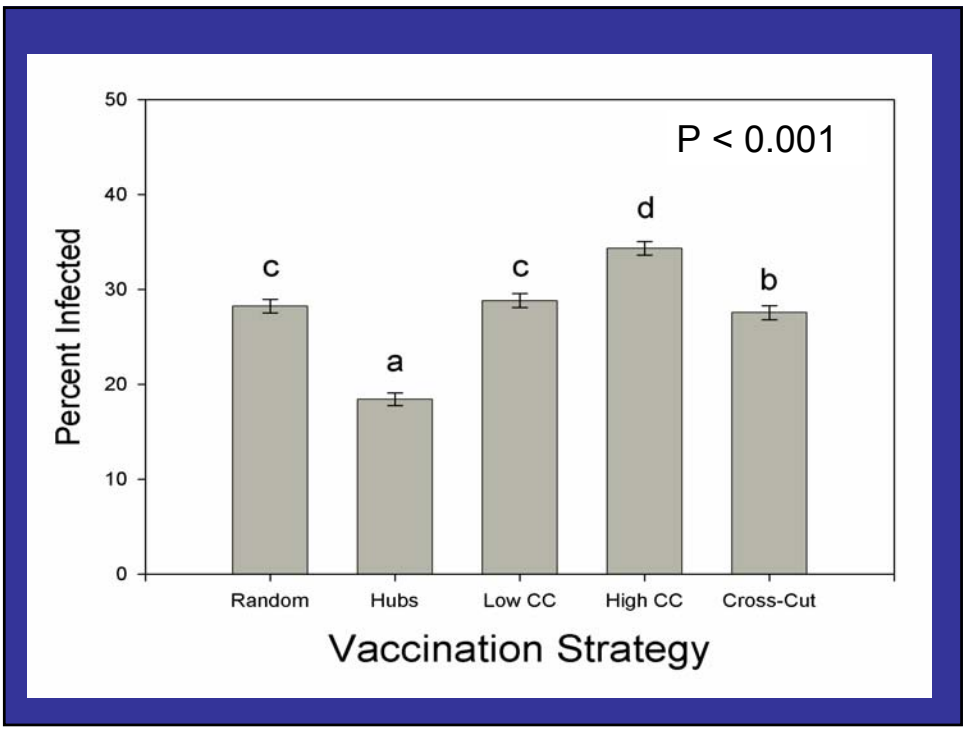
k	4
R_o	2
Latency period	1
Infectious period	3
swnP	0.0, 0.025, 0.05, 0.1, 0.25, 0.5, 1.0
Population size	1000, 10000, 100000
Vaccination effort	0 – 30%

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

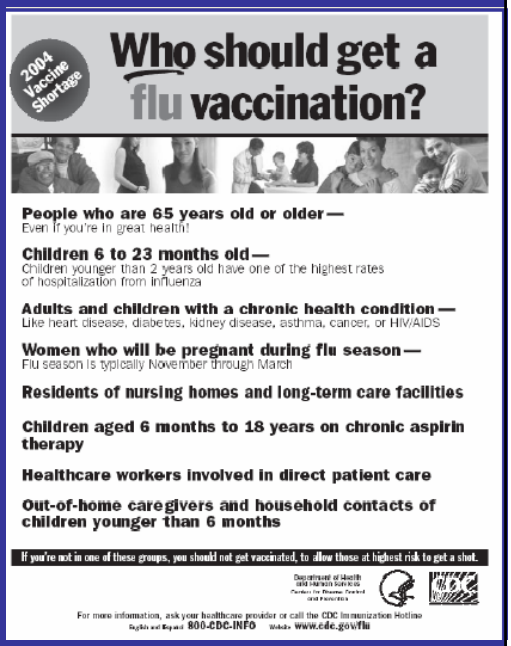



P < 0.001
Percent Infected
swnP
0
10
20
30
40
50
60
0.0
0.2
0.4
0.6
0.8
1.0
a
b
c
d
e
f
g


P < 0.001
Percent Infected
Vaccination Strategy
0
10
20
30
40
50
c
a
c
d
b
Random
Hubs
Low CC
High CC
Cross-Cut

CDC's 8 priority groups

(all of equal importance)



www.cdc.gov (2004)

Conclusions:

1. Mathematical models have increased our understanding of influenza and allow us to predict/prepare.
2. SIR models are very simple and a vast amount can be learned from them.
3. Agent-based models are both more realistic and more complex. Still, they allow you to do things that SIR models do not (targeted vaccinations!).

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