

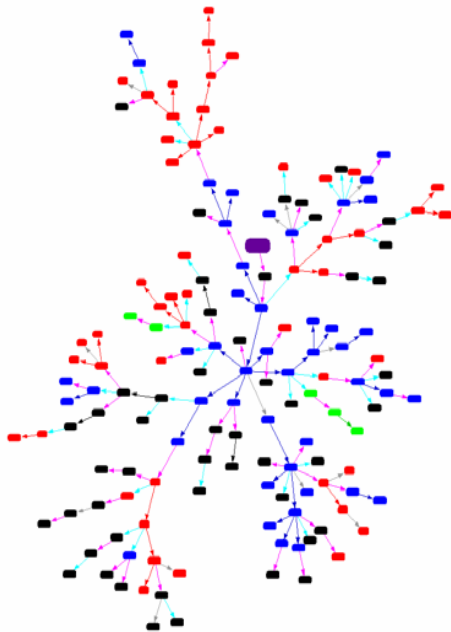


Design of Community Containment for Pandemic Influenza

Robert J Glass*, H Jason Min, Walter E Beyeler
Sandia National Laboratories

and

Laura M Glass
Albuquerque Public High School



*rjglass@sandia.gov





Design Process

- 1. Simulate spread** with networked agent-based approach:
 - explicit social contact network (current: stylized community of 10000)
 - influenza disease manifestation (current: scaled normal flu)
- 2. Implement containment strategies:**
 - modify contact network for social distancing or home quarantine
 - modify agent's disease response for antiviral influence
- 3. Define and run matrix** of containment strategy combinations (thousands of combinations, millions of simulations)
- 4. Weigh effectiveness of strategy combination** (e.g., attack rate, peak symptomatic) in context of constraints (e.g., antiviral courses available, days adults at home)
- 5. Evaluate results in light of model sensitivity and uncertainty** (e.g., disease manifestation, infectivity, virulence, social contact network...)

... a work in progress



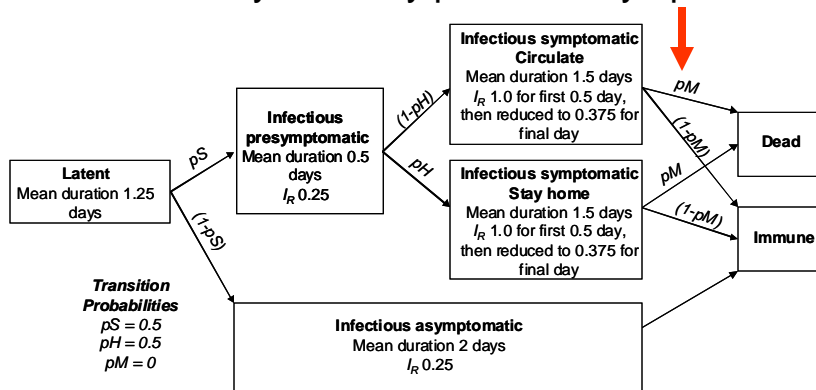
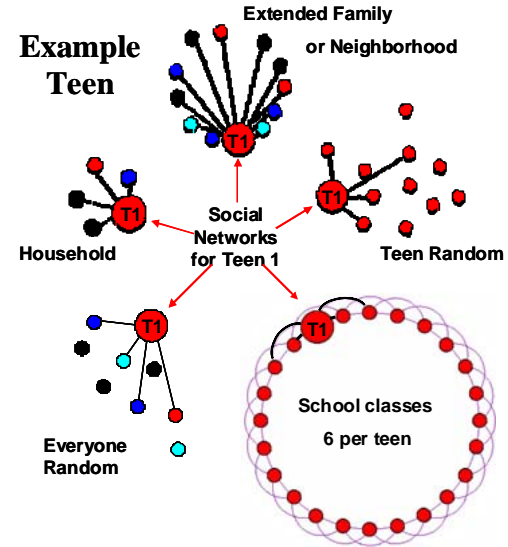
Outline

- **Brief Overview** of model assumptions, base case unmitigated results (see Glass et al (2005, 2006) for details), and strategy implementation.
- **Pull from current results to address:**
 - What community containment strategy combinations are effective?
 - How do constraints limit options?
 - What about Pre-pandemic vaccine?
 - Interaction with neighboring communities?
 - How sensitive are results to implementation threshold? Compliance? Disease manifestation (Ferguson vs Longini)?
 - Sensitivity of results to the infectious contact network?
- **Summary Points & Policy Implications**
- **Ongoing: Uncertainty Evaluation and Reduction**



Networked Agent-Based Model

- **Explicit social contact network, current:**
 - Stylized US community of 10000 (Census, 2000)
 - Agents: Child 18%, Teen 11%, Adult 59%, Senior 12%
 - Groups with explicit sub networks: Households, school classes, businesses, neighborhoods/extended families, clubs, senior gatherings, random
 - Household adult stays home to tend sick or sent home from school children in the family
- **Influenza disease manifestation, current:**
 - scaled normal flu, (Ferguson-like \sim viral shedding)
 - $p_{Symptomatic} = 0.5$, $p_{Home} = p_{Diagnosis} = 0.8$
 - Children 1.5 and Teens 1.25 times more infectious & susceptible than adults & seniors
 - Added 7 day recovery period for symptomatic (ill)



For Details see:

Local Mitigation Strategies for Pandemic Influenza, Robert J. Glass, Laura M. Glass, and Walter E. Beyeler, SAND-2005-7955J (December 21, 2005).

Targeted Social Distancing Design for Pandemic Influenza, Robert J. Glass, Laura M. Glass, Walter E. Beyeler, and H. Jason Min, *Emerging Infectious Diseases* November, 2006).



Transmission along network links

The probability that a contact will occur, p_c , in a small time interval, dt , along a link with contact frequency v_c is:

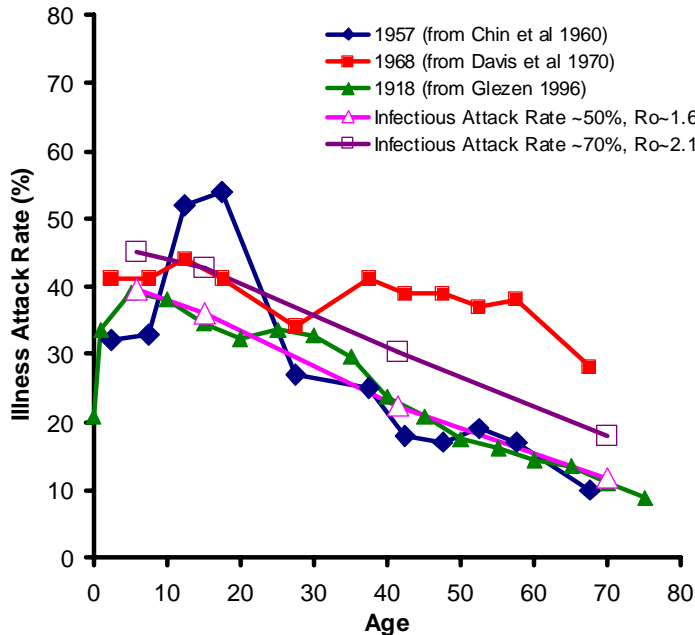
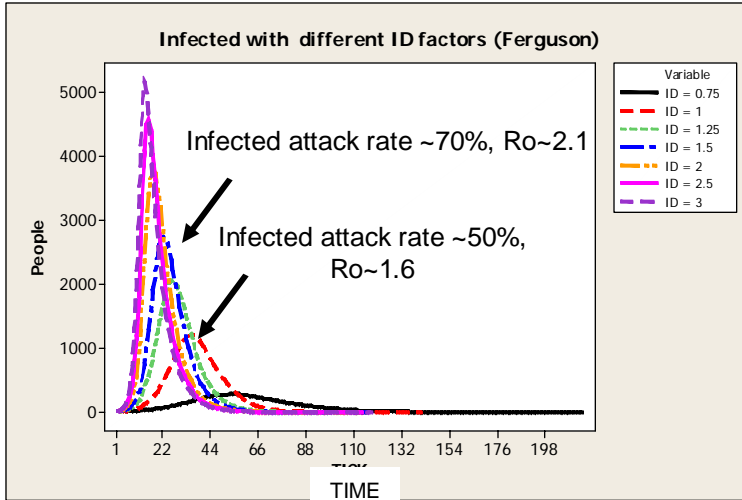
$$p_c = v_c dt$$

The fraction of total contacts between two linked individuals that actually result in transmission is given by $I_D * I_R * I_A * S_P * S_A$ where I_D is the infectivity of the disease, S_P is the susceptibility of people to the disease (here taken as 1.0), I_R is the relative infectivity of the infectious state that an agent is in, I_A is the relative infectivity of the agent who is transmitting, and S_A is the relative susceptibility of the agent receiving.

The probability of a disease transmission event along a given link between an infectious and a susceptible individual, p_i , is:

$$p_i = I_D I_R I_a S_D S_a v_c dt$$

↓ ↓



Unmitigated Results

Infectious Contact Fraction

Context	~50% ~Ro1.6	~70% ~Ro2.1
Households	40%	40%
Neighborhoods/extended families	22%	26%
School	23%	19%
Work	7%	6%
Senior Groups	1%	2%
All Extra & Clubs & Random	8%	8%

- Calibration only to disease infectivity I_D
- further calibration/specialization to social contexts of interest/ importance easy



Base Community Containment Strategies

Code		Description
S	Close Schools	Schools closed, all school contacts reduced by 90% , household contacts doubled
CTsd	Social Distance Children and Teenagers	Kids & Teens social distancing, all non-school and non-household contacts with or between children and teens reduced by 90% , household contacts doubled
ASsd	Social Distance Adults and Seniors	Adults & Seniors social distancing, all non-household non-work contacts with or between adults and seniors reduced by 90% , work contacts reduced by 50%, household contacts doubled
Q	Home Quarantine	Household Quarantine for 10 days once an individual is diagnosed, all non-household contacts for all household members reduced by 90% , household contacts doubled
T	Antiviral Treatment	Antiviral Treatment, 90% of people given antiviral course immediately after diagnosed, reduces infectivity by 60% (from Ferguson et al., 2006)
P	Home antiviral prophylaxis	Antiviral Prophylaxis, 90% of household members given antiviral for 10 days immediately after individual is diagnosed, reduces susceptibility by 30%, and if they are infected: reduces probability of symptomatic by 65%, reduces infectivity by 60% (from Ferguson et al., 2006)
Pex	Extended antiviral prophylaxis	Extended Antiviral Prophylaxis, 90% of linked persons within households, classes, work, and neighborhoods/extended families are given antiviral immediately for 10 days after person is diagnosed, reduces susceptibility by 30%, and if they are infected: reduces probability of symptomatic by 65%, reduces infectivity by 60% (from Ferguson et al., 2006)

Note that **P** necessarily contains **T**, and **Pex** necessarily contains **T** and **P**
When imposed, all mitigation strategies begin the day after 10 individuals are diagnosed within the community

64 combinations for one compliance, threshold ...



Base Simulation Matrix

- **2 disease manifestations:** (Ferguson-like, Longini-like)
- **7 disease infectivities** about a base case (yielding an infected attack rate of 50%) by factors of 0.75, 1.0 = basecase, 1.25, 1.5, 2.0, 2.5 and 3.0
- **2 boundary conditions** for external contact and instigation (open or closed)
- **8 community containment strategies** applied individually or in combination (64 combinations) with **4 vaccination strategies**
- **1 diagnosis rate** (80%) and **2 compliances** (60%, 90%) for social distancing, antiviral treatment and antiviral prophylaxis
- **2 implementation thresholds** (after 10 or 40 diagnosed)
- Each combination **run 100 times** with varying realizations of social contact network and initial adults infected (**2.86M runs**)
- For each, **measure** the number infected, symptomatic, their peaks, number antiviral courses, days adults are confined at home, who infects whom, etc, and put everything in a data base

Current: Expanding around base matrix for variation of **social contact network...**



Queries yield Lots and Lots of Tables...

Tens of thousands of scenarios can be queried by input or output values

TABLE 1: 90% compliance													TABLE 2: 90% compliance, trickle													TABLE 3: 60% compliance													TABLE 4: 60% compliance, trickle												
Green indicates those combinations that yielded an infected attack rate < 10%													Green indicates those combinations that yielded an infected attack rate < 10%													Green indicates those combinations that yielded an infected attack rate < 10%													Green indicates those combinations that yielded an infected attack rate < 10%												
IO Factor	Name	ASst	CEst	ICst	ICst	ICst	ICst	ICst	ICst	ICst	ICst	ICst	IO Factor	Name	ASst	CEst	ICst	ICst	ICst	ICst	ICst	ICst	ICst	ICst	IO Factor	Name	ASst	CEst	ICst	ICst	ICst	ICst	ICst	ICst	ICst	IO Factor	Name	ASst	CEst	ICst	ICst	ICst	ICst	ICst	ICst						
0.25	N	0	0	0	0	0	0	0	0	0	0	0	0.25	N	0	0	0	0	0	0	0	0	0	0	0.25	N	0	0	0	0	0	0	0	0	0	0	0.25	N	0	0	0	0	0	0	0	0	0				

Infected attack rate of ~70%, Ro~2.1, ~1918-19



NLSAC



Strategy Combination Table

Network focused

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None								
T								
Q								
P	All measures shown will be averages of those simulations of 100 that yielded > 1% of the population infected							
Q,T								
Q,P								
Pex								
Q,Pex								

T: antiviral Treatment
 P: home antiviral Prophylaxis
 Pex: Extended antiviral Prophylaxis
 Q: home Quarantine

ASsd: Adult & Senior social distancing
 CTsd: Child & Teen social distancing
 S: School closure



Infected Attack Rate*

Network focused

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	71	56	65	53	62	50	17	5
T	66	50	57	45	51	39	4	3
Q	60	50	51	44	45	37	8	4
P	55	43	45	36	35	23	3	2
Q,T	53	43	43	35	33	23	3	2
Q,P	49	40	39	30	29	17	2	2
Pex	32	23	20	14	10	6	2	2
Q,Pex	26	18	12	8	6	4	2	2

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P: home antiviral Prophylaxis
Pex: Extended antiviral Prophylaxis
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S: School closure

*Infected attack rate is expressed as a percent of total population and is twice the illness attack rate



Constraining by Infected Attack Rate

Table colored for Infected Attack Rate < 10% and < 25%

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	71	56	65	53	62	50	17	5
T	66	50	57	45	51	39	4	3
Q	60	50	51	44	45	37	8	4
P	55	43	45	36	35	23	3	2
Q,T	53	43	43	35	33	23	3	2
Q,P	49	40	39	30	29	17	2	2
Pex	32	23	20	14	10	6	2	2
Q,Pex	26	18	12	8	6	4	2	2

T: antiviral Treatment
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S: School closure

■ Infected attack rate < 10% ■ Infected attack rate < 25%



Options without Antivirals

3 Options below 10%, 1 more below 25%

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	71	56	65	53	62	50	17	5
T	66	50	57	45	51	39	4	3
Q	60	50	51	44	45	37	8	4
P	55	43	45	30	35	23	3	2
Q,T	53	43	43	35	33	23	3	2
Q,P	49	40	39	30	29	17	2	2
Pex	32	23	20	14	10	6	2	2
Q,Pex	26	18	12	8	6	4	2	2

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S: School closure

Infected attack rate < 10% Infected attack rate < 25%



Adding Antivirals*

Segmenting by 4% antiviral coverage (today) and 25% (planned 3rd Q 2007)

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	0	0	0	0	0	0	0	0
T	24	18	21	16	18	14	2	1
Q	0	0	0	0	0	0	0	0
P	53	43	44	36	35	23	3	2
Q,T	19	15	16	12	12	8	1	1
Q,P	50	40	40	31	29	17	2	2
Pex	201	170	165	121	83	54	18	14
Q,Pex	184	143	106	75	51	36	16	14

T: antiviral Treatment
 P: home antiviral Prophylaxis
 Pex: Extended antiviral Prophylaxis
 Q: home Quarantine

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*percent coverage of population (# courses/10000)

Infected attack rate < 10%
 Infected attack rate < 25%

4% Antiviral coverage
 25% Antiviral coverage



Constraining Options

Intersecting tables for Infected Attack Rate and Antiviral Courses

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	0	0	0	0	0	0	0	0
T	24	18	21	16	18	14	2	1
Q	0	0	0	0	0	0	0	0
P	53	43	44	36	35	23	3	2
Q,T	19	15	16	12	12	8	1	1
Q,P	50	40	40	31	29	17	2	2
Pex	201	170	165	121	83	54	18	14
Q,Pex	184	143	106	75	51	36	16	14

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Infected attack rate < 10%
 Infected attack rate < 25%

4% Antiviral coverage
 25% Antiviral coverage



Superimposing Adult Days Home*

Adults stay home when sick, tending sick or sent home from school children

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	3	2	3	2	17	18	28	17
T	3	2	2	2	19	20	17	12
Q	6	5	5	4	22	23	21	15
P	3	2	2	2	24	25	13	11
Q,T	6	5	5	4	26	26	13	11
Q,P	6	5	5	3	27	25	13	11
Pex	2	1	1	1	23	19	12	11
Q,Pex	4	3	2	1	18	15	11	10

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*Averaged over entire adult population

- Infected attack rate < 10%
- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage



Pre-Pandemic Vaccine?

7% coverage, 50% efficacy, superposition on Adult Days Home*

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	3	2	3	2	17	18	25	15
T	3	2	2	2	20	22	14	11
Q	6	5	5	4	23	23	18	14
P	3	2	2	2	26	25	13	11
Q,T	5	4	4	3	27	26	13	11
Q,P	5	4	4	3	26	23	12	10
Pex	2	1	1	1	21	17	11	10
Q,Pex	4	2	1	1	17	14	11	10

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*Averaged over entire adult population

- Infected attack rate < 10%
- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage



Interaction with Neighbor Communities?

1 person/day for 120 day period, superposition on Adult Days Home*

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	3	3	3	2	22	23	33	33
T	3	2	3	2	24	26	35	33
Q	6	5	5	5	27	28	35	34
P	3	2	2	2	29	30	34	32
Q,T	6	5	5	4	30	31	34	33
Q,P	6	5	5	4	32	32	34	33
Pex	2	2	2	1	35	35	33	32
Q,Pex	5	3	3	2	36	35	34	32

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- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage



Sensitivity to Implementation Threshold?

Increase from 10 to 40 diagnosed people, superposition on Adult Days Home*

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	3	2	3	2	15	15	20	16
T	3	2	3	2	17	17	17	13
Q	6	5	5	4	19	19	20	17
P	3	2	2	2	20	19	15	12
Q,T	6	5	5	4	21	20	16	14
Q,P	6	5	5	4	22	21	14	12
Pex	2	2	1	1	21	17	13	12
Q,Pex	4	3	2	2	18	16	13	12

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- Infected attack rate < 10%
- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage



Sensitivity to Compliance?

Decrease from 90% to 60% compliance, superposition on Adult Days Home*

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	3	3	3	3	16	17	20	22
T	3	3	3	3	18	19	26	29
Q	7	6	7	6	20	20	23	24
P	3	3	3	3	21	22	28	25
Q,T	6	6	6	6	23	23	29	30
Q,P	6	6	6	6	24	25	30	25
Pex	2	2	2	2	31	29	21	18
Q,Pex	5	5	5	5	32	26	19	17



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- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage



Sensitivity to Disease Manifestation?

Longini-like influenza manifestation, superposition on Adult Days Home*

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	5	4	5	4	25	26	46	24
T	4	3	4	3	30	32	23	15
Q	8	6	7	6	33	34	34	23
P	4	3	3	3	39	38	18	14
Q,T	7	6	5	4	42	37	18	15
Q,P	7	6	5	4	42	35	18	13
Pex	3	2	2	1	32	25	15	13
Q,Pex	5	3	2	1	25	20	15	13

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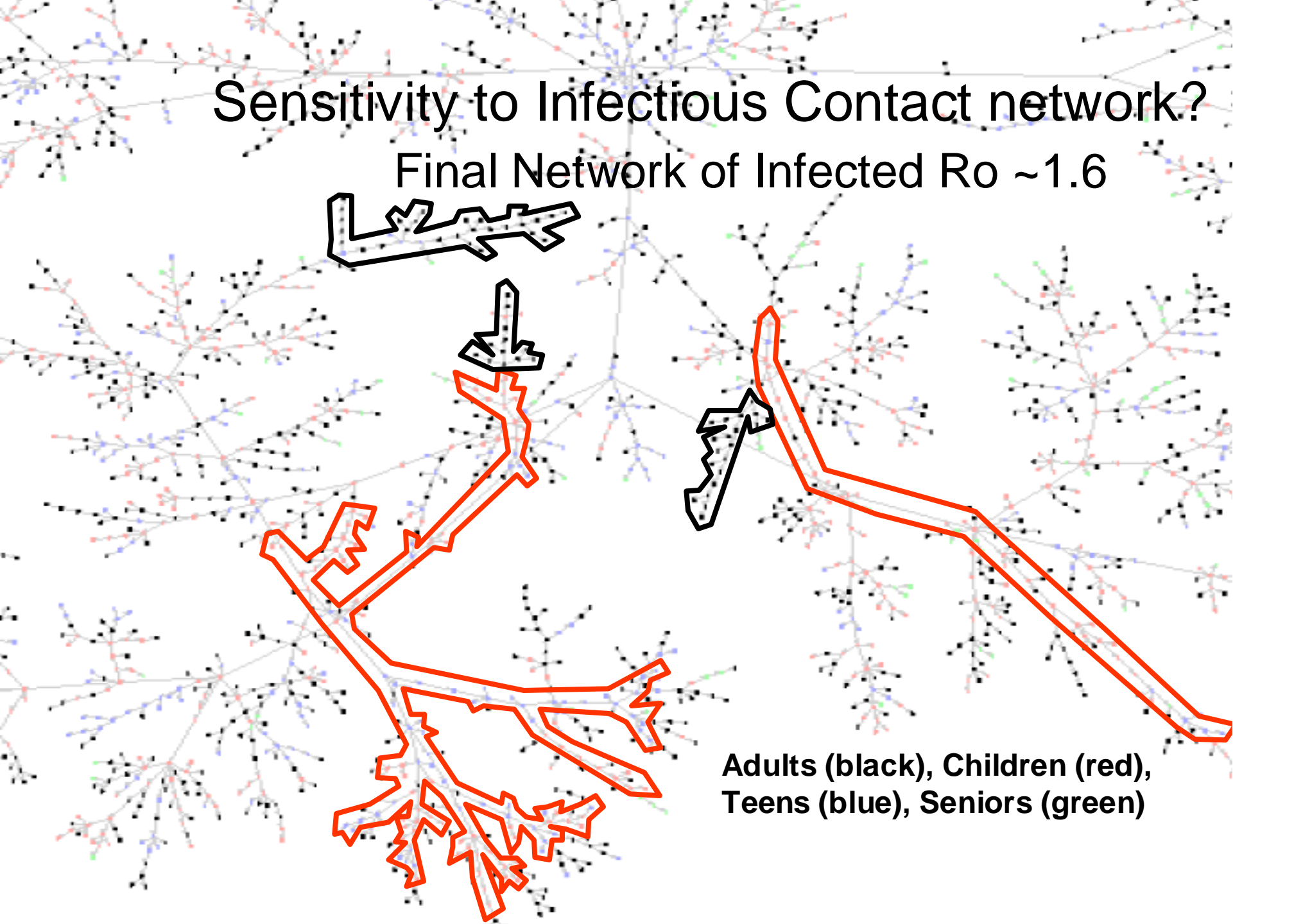
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- Infected attack rate < 10%
- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage

Sensitivity to Infectious Contact network?

Final Network of Infected $R_0 \sim 1.6$



Adults (black), Children (red),
Teens (blue), Seniors (green)



Adults, Children & Teens on Par?

Identical Infectivity/susceptibility and contacts/day, on Adult Days Home*

Case based

	None	ASsd	CTsd	CTsd ASsd	S	S ASsd	S CTsd	S CTsd ASsd
None	4	3	3	2	18	23	23	20
T	3	2	3	2	21	30	29	13
Q	6	4	6	3	25	30	29	17
P	3	2	3	1	26	22	29	12
Q,T	6	3	6	2	28	22	28	12
Q,P	6	3	6	2	29	19	25	11
Pex	2	1	2	0	26	14	17	11
Q,Pex	4	1	3	1	22	13	15	11

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- Infected attack rate < 10%
- Infected attack rate < 25%
- 4% Antiviral coverage
- 25% Antiviral coverage



Summary Points & Policy Implications

From Current Model Results:

- **Social distancing forms a foundation** for effective community containment
 - Alone it may be able to hold a pandemic at bay
 - In combination with case based strategies (all of which are less effective alone) lost work days can be decreased
 - But strategies must be implemented **quickly** and with **high compliance**

Policy Implication: Planning, education, and training must be designed for the effective implementation of social distancing measures *first* and case based strategies *second*.

- **Pre-pandemic vaccination** at current levels (7% coverage and 50% efficacy) does not significantly influence the spread.

Policy Implication: Pre-pandemic vaccine at such low levels should be used to keep critical people on the job. *Caveat: Targeted vaccination scenarios in progress

- **Influx from neighboring communities** reduces effectiveness of community containment strategies and increases the time strategies must be vigilantly applied.

Policy Implication: A uniform national policy could reduce this time for all.



Ongoing: Uncertainty Evaluation & Reduction

- **Disease manifestation**
 - Infectivity relation, visible vs invisible infected
 - Aerosol? Surfaces? (influences contact network definition too)
- **Social contact network**
 - Sub group network: structured to fully mixed
 - Groups: augmented and relative importance (households, neighborhoods/extended families, schools, work, clubs, church, public transportation, etc)
 - Consider situations of critical interest (College campuses, military reservations, high rises...)
 - Collect & incorporate contact network data
 - Instantiation from community data (refined Ferguson & Longini)
- **Incorporate Reactive Agent Behavior** (social modeling)
- **Refine analysis** in response to evolving constraints, new information, and changes in uncertainty