

How modeling can help us prepare for an influenza pandemic: Vaccines

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Ira M. Longini, Jr.

Center for Statistical and Quantitative Infectious Diseases

University of Washington

Hutchinson Research Center

Seattle Washington

Epidemiologic Characteristics of Pandemic Influenza A(H1N1)

Strain Distribution

- Percent of Isolates that are Pandemic H1N1:

>98% US (since mid-June)

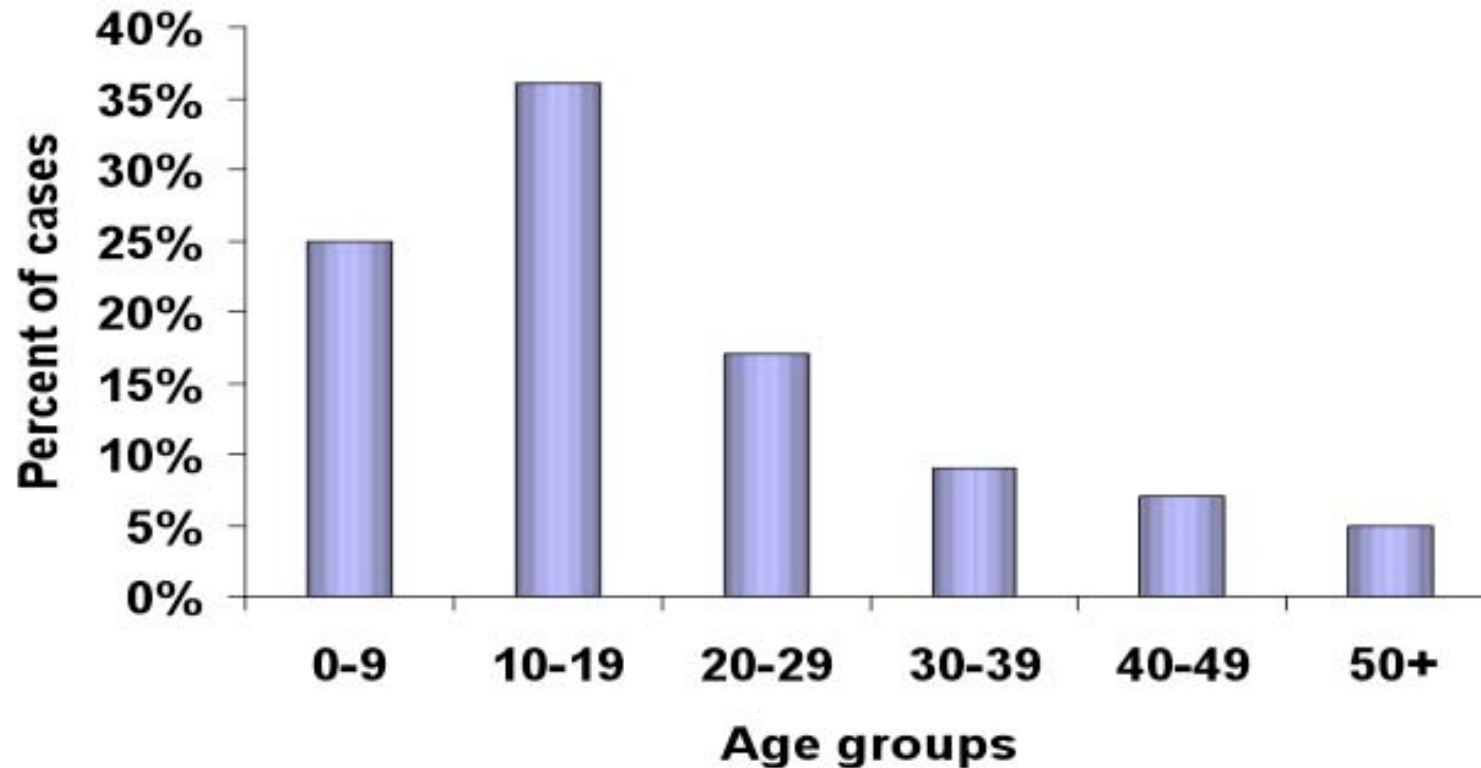
~90% Chile

~67% Victoria, Australia

<1% South Africa

Distribution of cases by age group

Laboratory-confirmed cases (Chile, EU and EFTA, Japan, Panama, Mexico)



SAR and R in US Households and NYC School

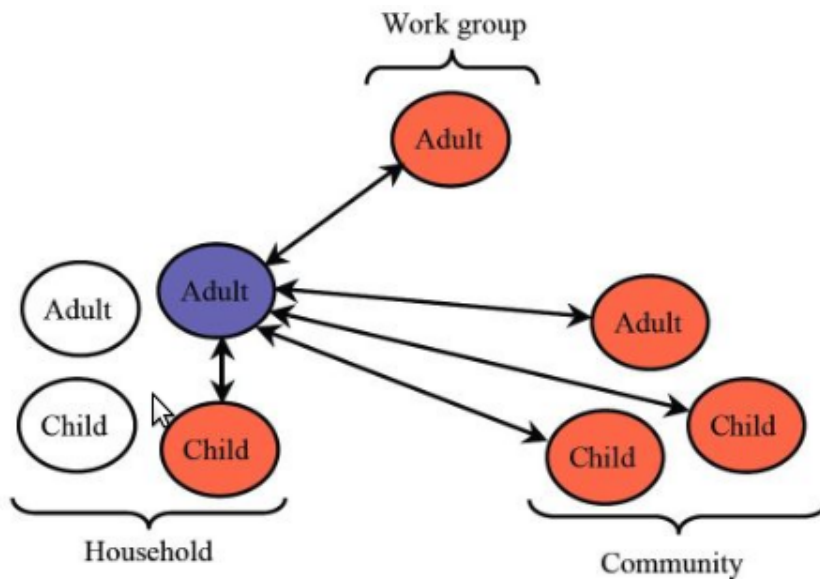
	Households		NYC School	
	Estimate	95% CI	Estimate	95% CI
SAR	24%	15%, 32%	0.09%	0.069%, 0.12%
<i>R</i>	-	-	2.42	1.84, 3.17

RESULTS: Mexico Outbreak – Generation interval

**Mean generation interval:
2.9 (95% CI: 2.8-3.0 days)**

Mathematical Model

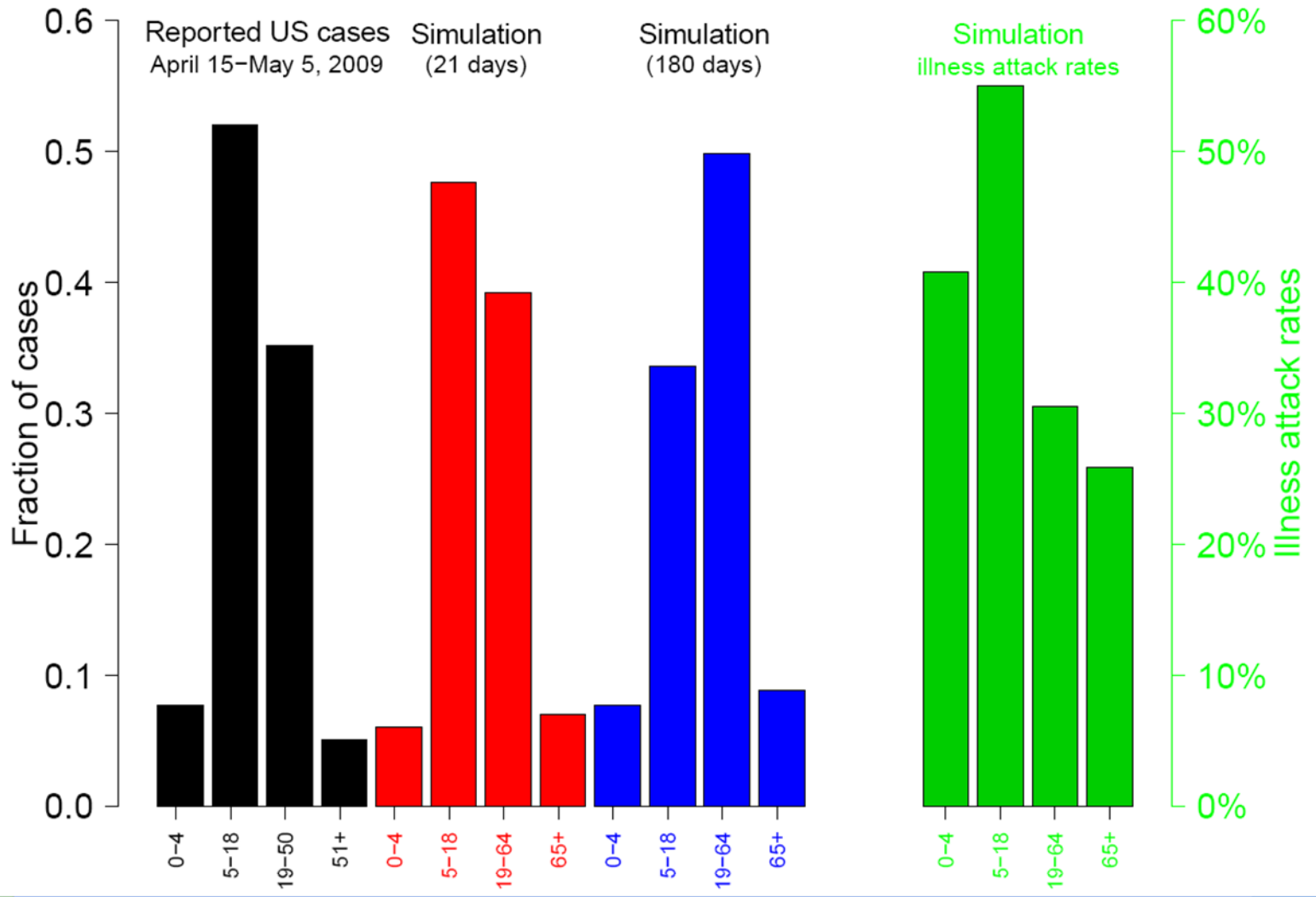
US epidemic simulator



Source: T. C. Germann, K. Kadau, I. M. Longini, Jr., and C. A. Macken. Mitigation strategies for pandemic influenza in the United States. *Proc Natl Acad Sci U S A*, 103:5935–40 (2006).

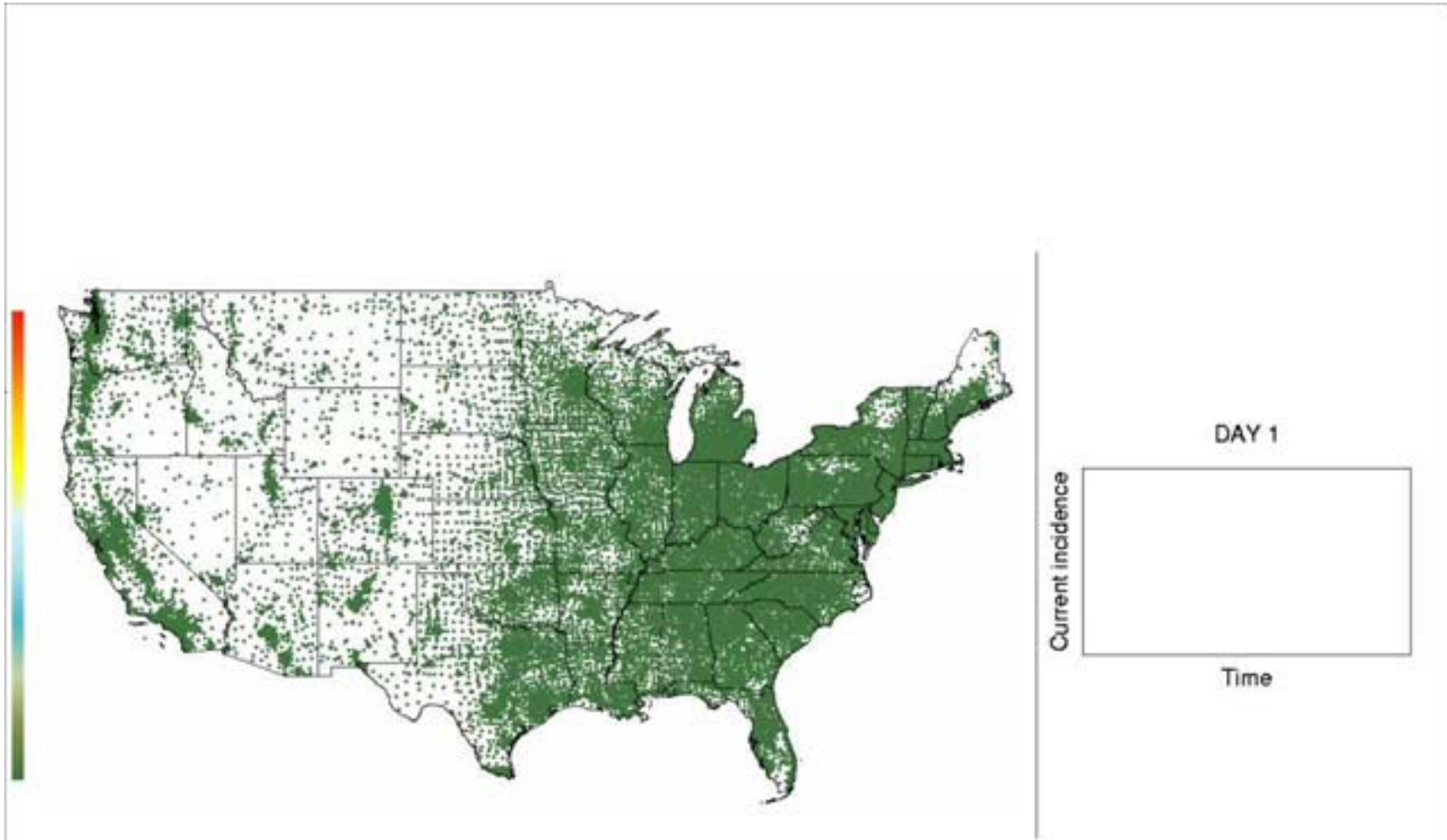
- All individuals in the US are represented
- Each individual interacts with others in various social groups
- Epidemic features based on earlier influenza pandemics

RESULTS: Simulation Studies, Single US Community



H1N1 in the US

10



Age-specific illness attack rates

	<i>average</i>	<i>0-4</i>	<i>5-18</i>	<i>19-29</i>	<i>30-64</i>	<i>65+</i>
$R_0=1.6$	32%	38%	53%	25%	27%	22%
$R_0=1.8$	38%	44%	57%	31%	33%	27%
$R_0=2.0$	42%	48%	60%	36%	38%	32%

We calibrated the simulation so that children have the highest attack rates, as in the 1957-1958 Asian Influenza pandemic and current pandemic H1N1.

What Could R_0 Mean?

Our estimates of R_0 from household SAR and school outbreaks is 1.3 - 1.7

Pandemic transmissibility

	<i>low</i>			<i>moderate</i>			<i>high</i>					
R_0	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4
Illness attack rate (%)	25	29	33	36	39	41	44	46	48	49	51	52
Cases (billions)	1.7	2.0	2.2	2.4	2.6	2.8	3.0	3.1	3.2	3.4	3.5	3.5

Pandemic Influenza A(H1N1) Vaccines

So far, pandemic H1N1 has been unstoppable without a vaccine when spreading in a country during the influenza season. Antiviral agents and NPI's have been moderately effective when used out of season.

Pandemic H1N1 Vaccines

- Both killed and live vaccines being developed.
- For killed vaccine, antigen-sparing adjuvanted vaccine could be used in emergency
 - No adjuvant: 15 μg per dose
 - With adjuvant: 7.5 μg per dose
- One or two doses in children and adults
 - How much protection after one dose
 - Kinetics of protection following each dose



ASPR

Total H1N1 Vaccine Output

Total Vaccine Manufacturing Output by Manufacturer



CSL 18.7%



sanofi pastuer 26.4%



MedImmune 5.84%



Novartis Vaccines 45.7%



GSK 3.4%

Source: Robin Robinson, DHHS

Expected vaccine efficacies (%) for inactivated seasonal influenza vaccine

	Homologous Good match	Heterologous Poor match
$VE_{S\text{-infection}}$	40	30
$VE_{P\text{-pathogenicity}}$	67	14
$VE_{SP\text{-disease}}$	80	40
$VE_{I\text{-infectiousness}}$	40	20

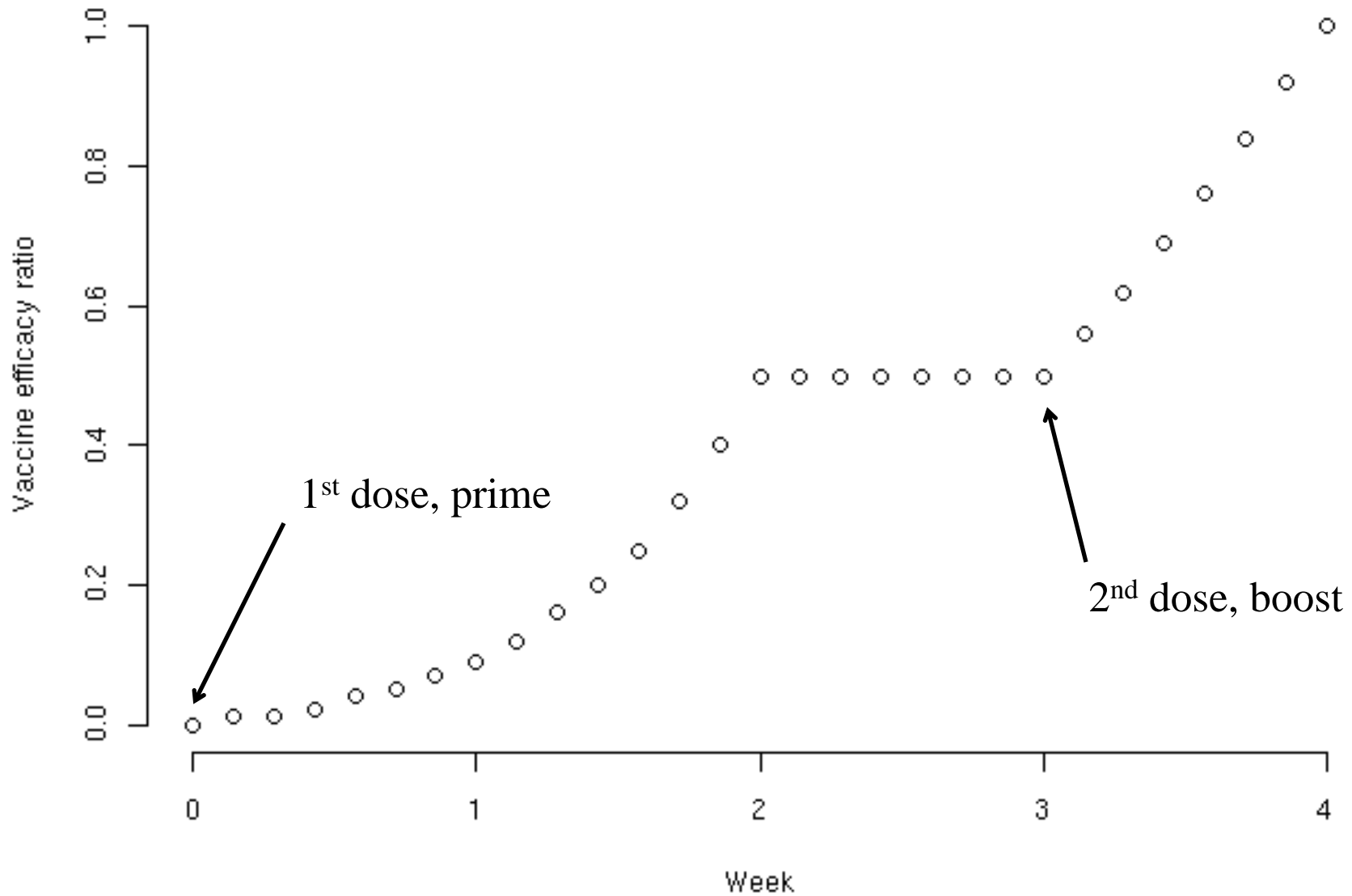
Basta NE, Halloran ME, Matrajt L, Longini IM. *AJE* (2008)

Expected vaccine efficacies (%) for live attenuated seasonal influenza vaccine

	Homologous Good match	Heterologous Poor match
$VE_{S\text{-infection}}$	40	30
$VE_{P\text{-pathogenicity}}$	83	57
$VE_{SP\text{-disease}}$	90	70
$VE_{I\text{-infectiousness}}$	50	30

Basta NE, Halloran ME, Matrajt L, Longini IM. *AJE* (2008)

Vaccine efficacy buildup assumption ¹⁹

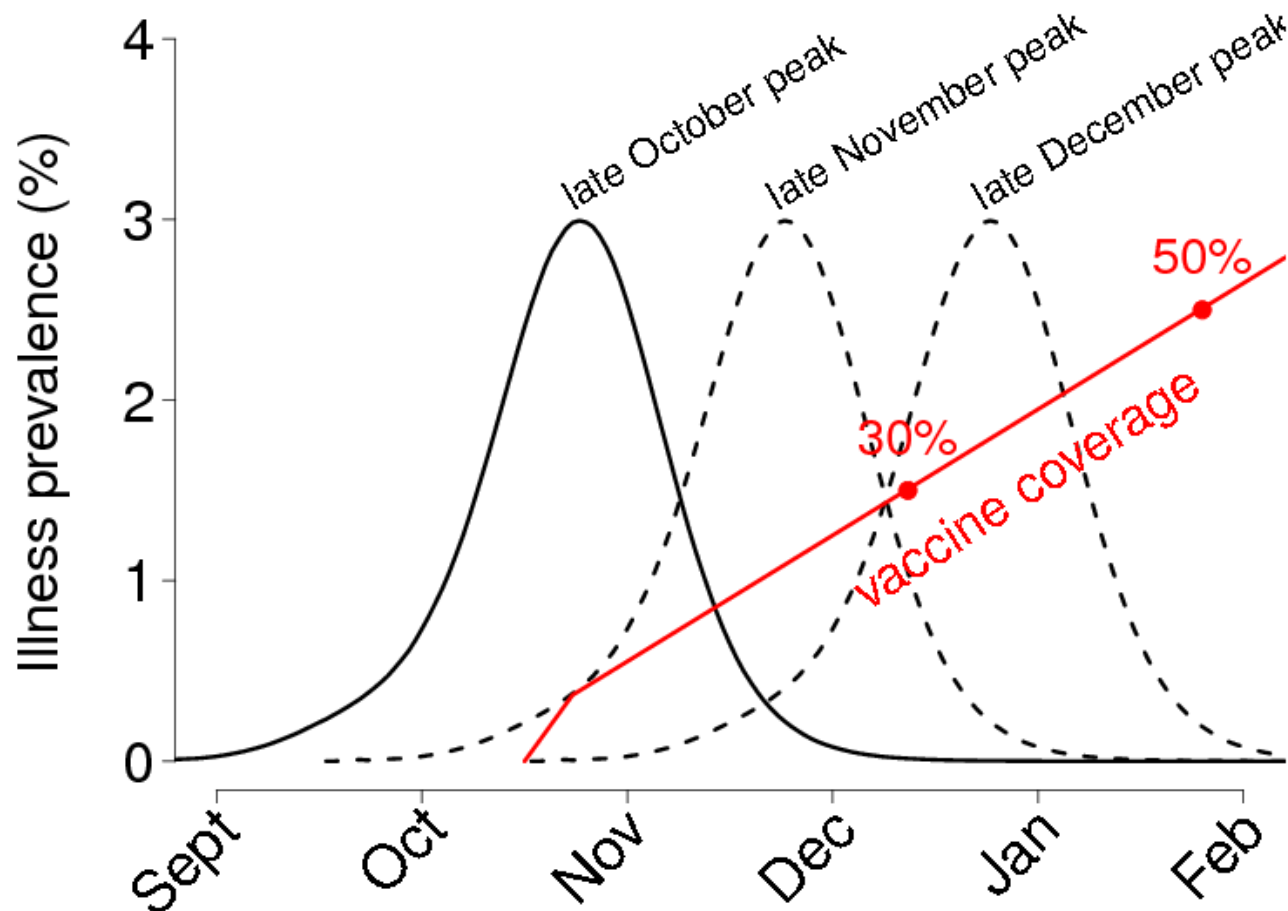


Vaccine production schedule

Month	US doses	Percent Coverage (2 doses)	Cumulative Percent
Oct 15-22	45 M	7.3	7.3
Oct 23-31	20 M	3.3	10.6
November	80 M	13.0	23.6
December	80 M	13.0	36.6
January	80 M	13.0	49.6
February	80 M	13.0	62.6

Information taken from NBSB teleconference on Aug.14, 2009.

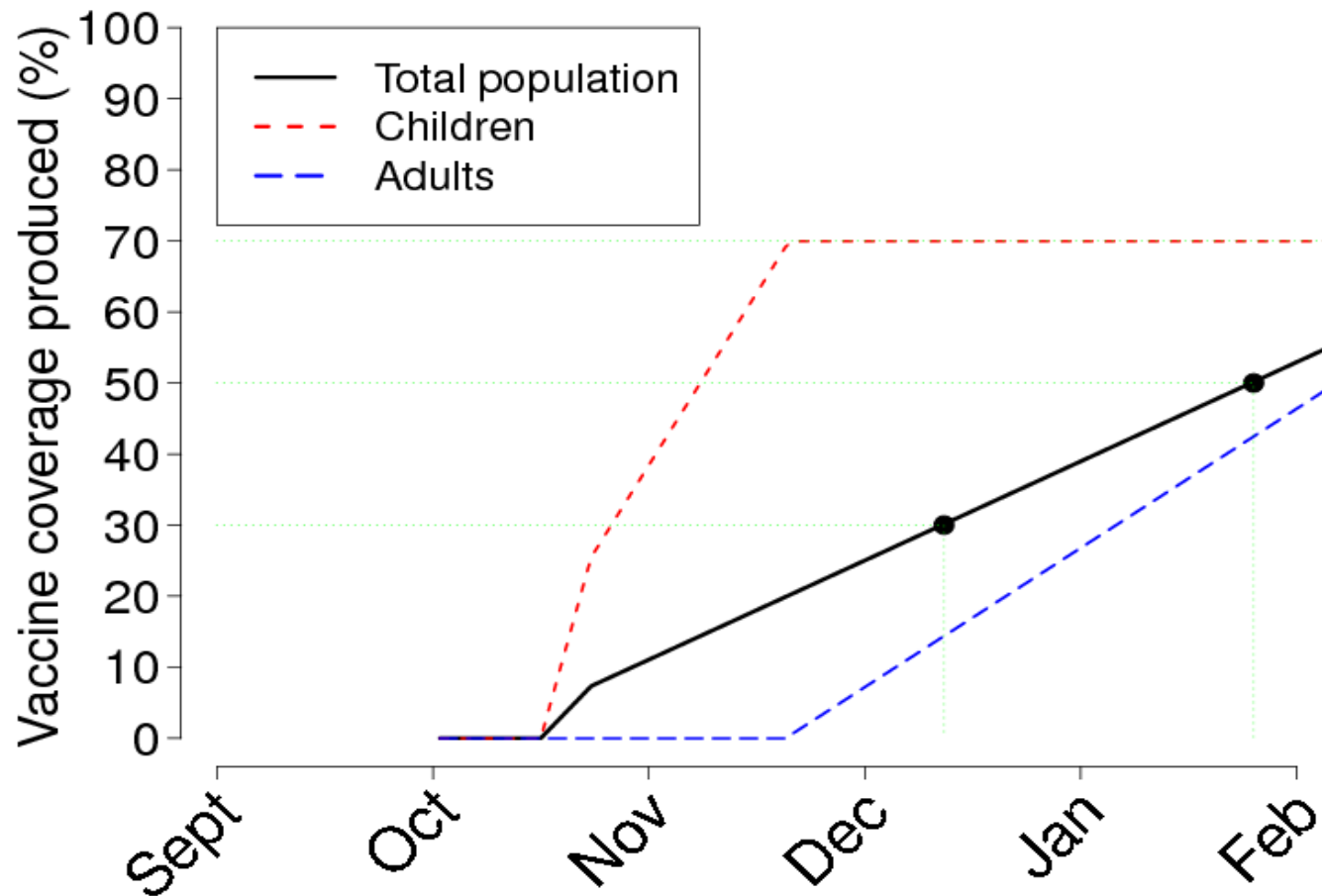
Timing: epidemic peak and vaccine supply



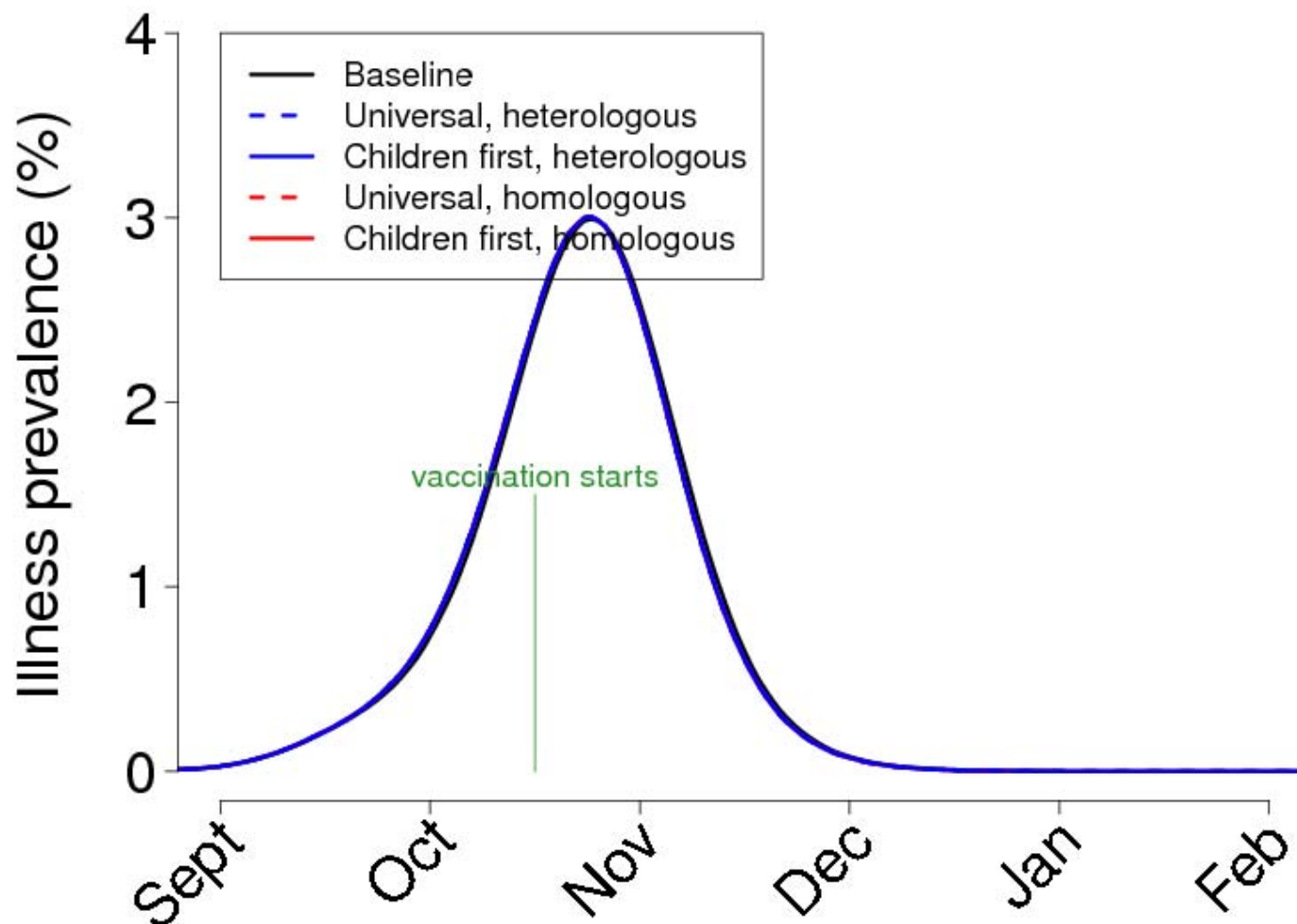
Information taken from NBSB teleconference August 14, 2009 assuming 2 doses per person

Strategy: children first vs universal ²²

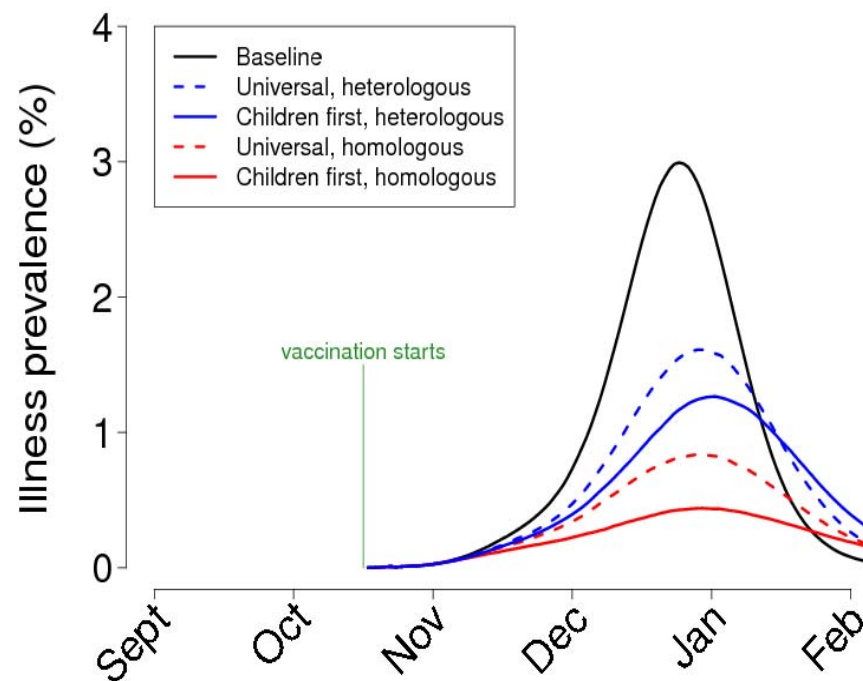
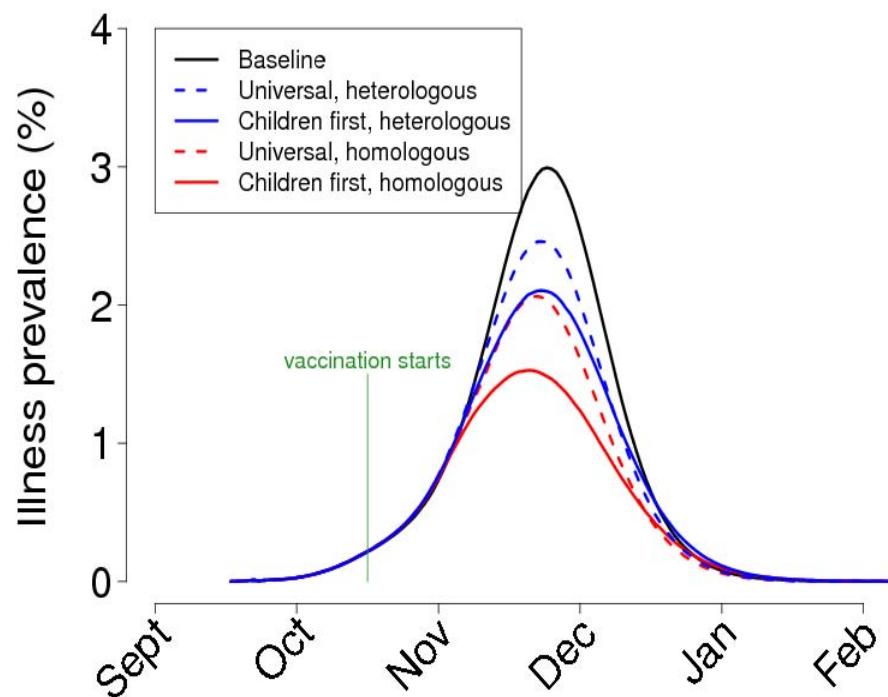
One dose followed by second dose



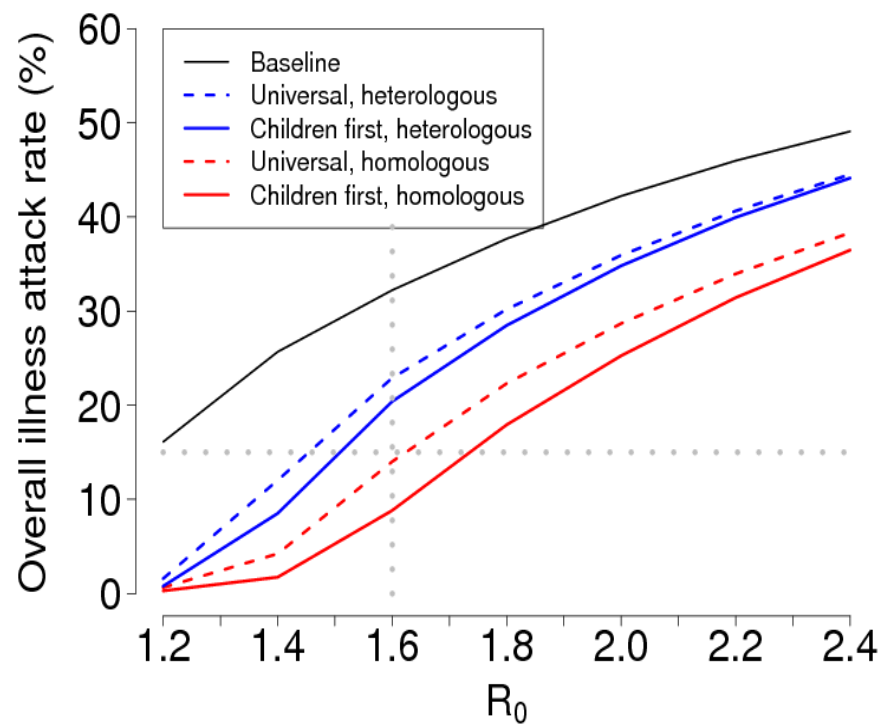
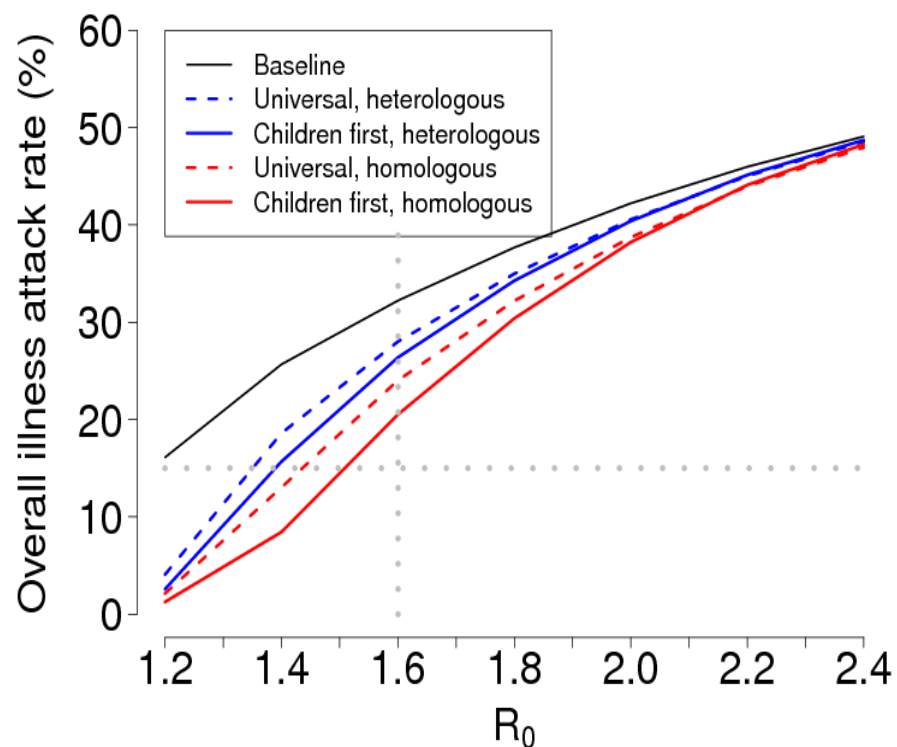
Epidemic curves: late October peak, $R_0=1.6$



Epidemic curves: late November and December peaks, $R_0=1.6$



Illness attack rate vs R_0 : late November and December peaks



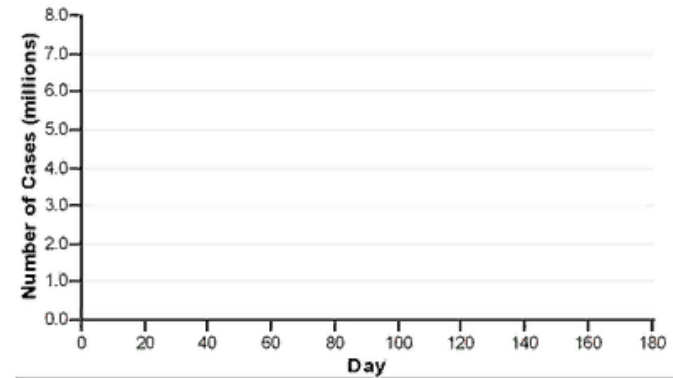
Universal Vaccination, Late December Peak



$R_0 = 1.6$

Day 001

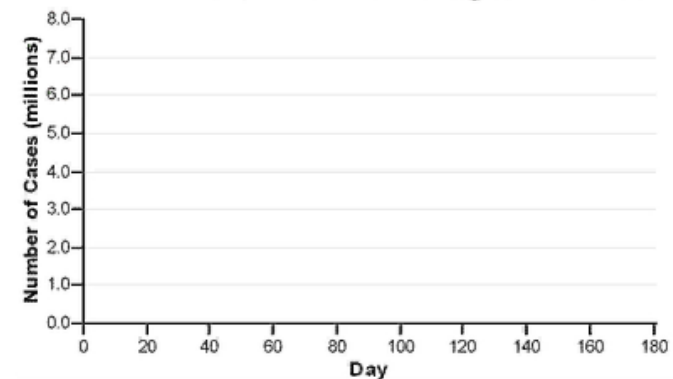
Intervention(s): None



Illness Prevalence (%): 0.01 - 1.00 1.01 - 2.00 2.01 - 3.00 3.01 - 4.00 4.01 - 5.00



Intervention(s): 70% coverage, universal



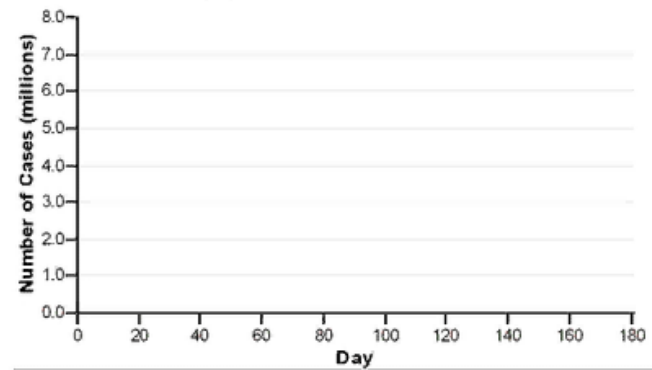
Child First, Late December Peak



$R_0 = 1.6$

Day 001

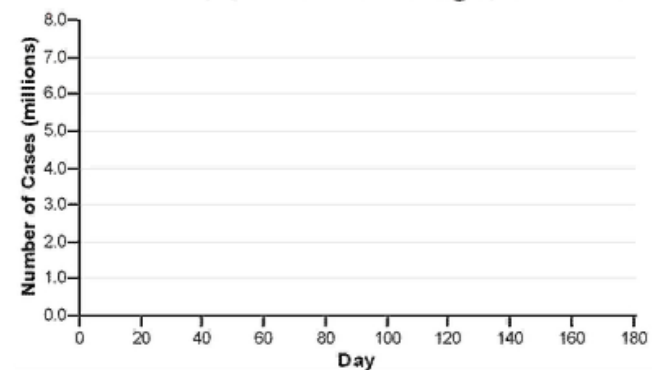
Intervention(s): None



Illness Prevalence (%): 0.01 - 1.00 1.01 - 2.00 2.01 - 3.00 3.01 - 4.00 4.01 - 5.00



Intervention(s): 70% coverage, child first



Illness attack rates (%)

$R_0 = 1.6$

Strategy	baseline	Oct peak	Nov peak	Dec peak
Baseline	32.2			
Universal, good match		32.2	24.0	14.0
Children first, good match		32.2	20.5	8.8
Universal, poor match		32.2	28.0	22.9
Children first, poor match		32.2	26.4	20.4

CDC Group Recommendations

- School children (grades K-12th) and staff;
- Children (≥ 6 months) and staff in child care centers;
- Pregnant women;
- Children 6 months-4 years of age;
- New parents and household contacts of children < 6 months of age;
- Non-elderly adults (age < 65 years) with high-risk medical conditions;
- Health care and emergency services personnel (regardless of age).

http://www.who.int/csr/disease/swineflu/notes/h1n1_vaccine_20090713/en/index.html

<http://www.cdc.gov/h1n1flu/vaccination/statelocal/planning.htm>

Summary

- **Timing:**
 - The later the epidemic peak, the more effective current planned vaccine supply will be on reducing cases.
 - If epidemic peak is late October, planned vaccine supply will have little effect.
- **Strategy:**
 - Children first is better than universal vaccination in reducing cases

Further Research

- Vaccinating groups at high risk of death with mortality as outcome
- Vaccinating other high priority groups: will use up vaccine likely with little effect on main transmission
- Age- and risk-group indications for specific vaccines
- Immunogenicity data to inform vaccine efficacy inputs
- Sensitivity analyses

Open Questions

- Policy for first and second dose?
- Plans for evaluating efficacy in the field?
- Plans to use adjuvanted, antigen-sparing vaccines?

Our Flu Research Group

Betz Halloran, Ira Longini

Yang Yang

Dennis Chao

Eben Kenah

Valerie Obenchain

Jonathan Sugimoto

Laura Matrajt

Nicole Basta

Gail Potter

Rebecca Allen

The End