University of Pittsburgh

Herd Immunity and the Benefits of Vaccination

Using Measles as an Example

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I have no conflicts of interest

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Outline of Talk

- Brief review of measles
- Brief review of vaccines
- The concept of community or herd immunity
- The Public Health Dynamics Laboratory (PHDL)
- Modeling infectious diseases
- The FRED Measles application
- FRED Measles – Texas version

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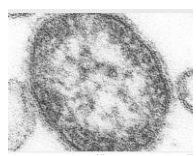
Measles



- Highly contagious viral disease that causes:
  – High fever
  – Cough
  – Runny nose
  – Watery eyes
  – Rash
- Potential Complications
  – Viral pneumonia (1:20)
  – Encephalitis (1:1000)
  – Death (1-2:1000)

https://en.wikipedia.org/wiki/Measles

https://www.cdc.gov/measles/about/signs-symptoms.html

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Measles infectious characteristics

- The Virus spreads ***through the air*** by coughing and sneezing of an infected person
- The virus can remain infectious for ***over 2 hours*** in the air
- It may take ***10-14 days*** to develop symptoms
  - A person can be infectious ***before they have symptoms***
  - Typically from ***4 days before*** the rash appears to ***4 days after*** the rash resolves

https://www.cdc.gov/measles/about/transmission.html

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Treatment

- There is no specific treatment for measles
- If complications (encephalitis, pneumonia) develop, therapy is supportive
  - There may be long term sequalae
  - There may be significant acute disability

https://www.cdc.gov/measles/downloads/MeaslesDataAndStatsSlideSet.pdf

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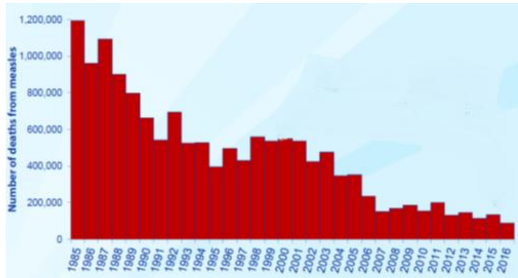
Outcomes

- Worldwide, there are still ***many deaths*** from measles, but mortality is declining



- Last death in the US was in 2015 – the first in a decade – and many initial cases in US outbreaks are found to originate in other countries

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No treatment but excellent prevention

- 1963 – Enders and colleagues created the first measles vaccine (live attenuated)
- Followed in 1968 a further modified version (Edmonston-Enders vaccine)

- The measles vaccine is a ***live attenuated*** vaccine

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Types of Vaccines

- attenuated (live) vaccines
  - The virus is still "viable" but has been altered to be less virulent (***MMR, chickenpox, smallpox***)
- inactivated vaccines
  - Vaccine made from virus particles that are not complete or have been damaged (***polio, rabies***)
- toxoid vaccines
  - Vaccine made from a pathogen's toxin (***tetanus, diphtheria***)

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Types of Vaccines (cont)

- subunit vaccines
  - Uses only a part of the virus to develop the immune response (***Hep B, HPV***)
- conjugate vaccine
  - Attaching a strong antigen to a poor antigen to improve immune response (***pneumococcal, meningococcal***)

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Prevention – the measles vaccine

- Current CDC recommendation is to have children received either:
  - MMR vaccine (Measles, Mumps, Rubella)
  - MMRV vaccine (Measles, Mumps, Rubella, Varicella)
- With respect to measles:
  - 1-dose is ~93% effective at preventing disease
  - 2-doses are ~97% effective at preventing disease

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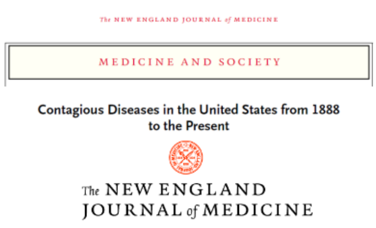
- For measles in the US, the vaccine had essentially eliminated the disease

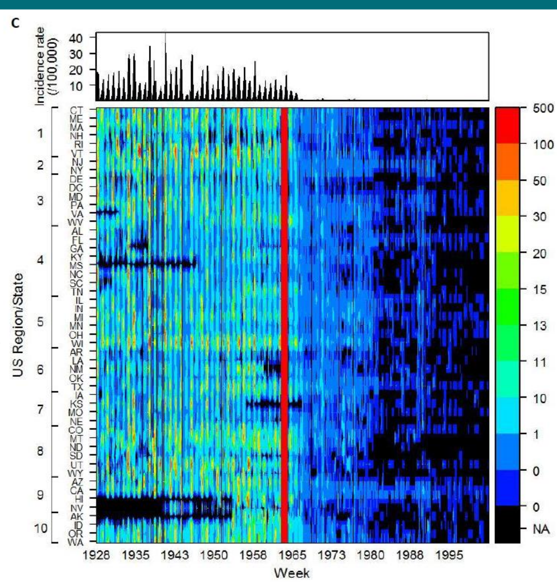

The NEW ENGLAND JOURNAL of MEDICINE

MEDICINE AND SOCIETY

Contagious Diseases in the United States from 1888 to the Present

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2013; 369:2152-2158



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Project Tycho

- Computerized the CDC mortality data from 1888 to the present

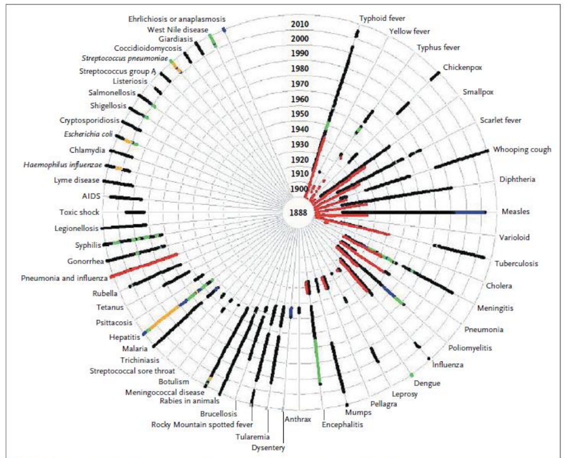

Figure 1. Availability of Weekly Counts of Reported Diseases from Any U.S. Location, 1888–2011.

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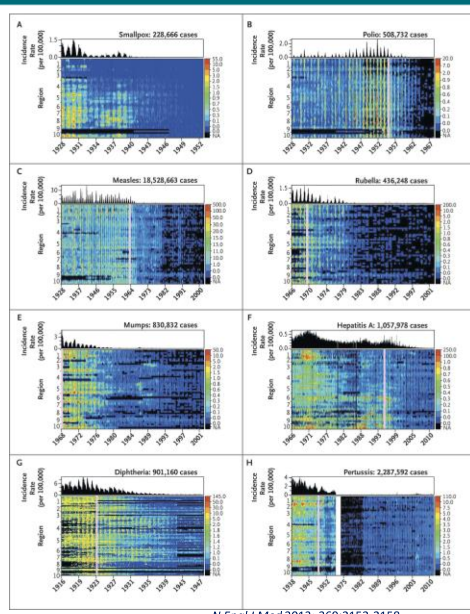
- Overall, between 1988 and 2012 – vaccines have prevented ***100,000,000*** cases of infectious disease



N Engl J Med 2013; 369:2152-2158

Who is protected – herd immunity

- Some ask:

  "Why should I have to vaccinate my child? If I am willing to accept the risk for my child, who does that hurt?"

- Because the ability to stop epidemics requires a ***high level of immunity in the population***- and epidemics don't only effect those who fail to vaccinate

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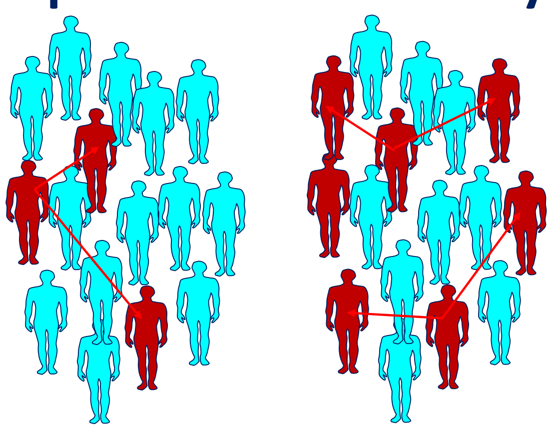
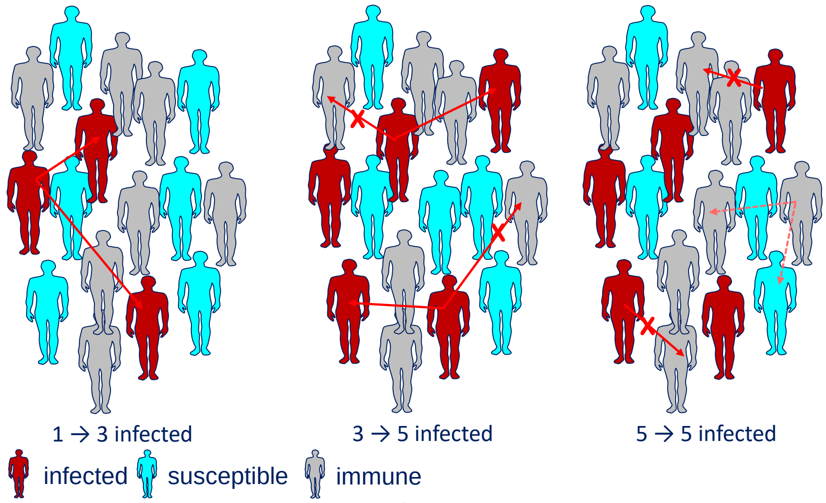
Epidemics – how they happen



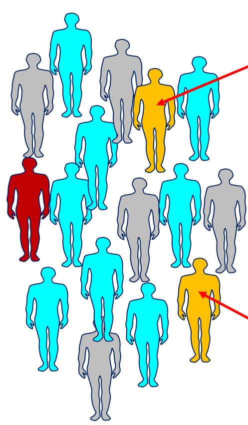
1 → 3 infected   3 → 7 infected   7 → 12 infected

infected susceptible

Epidemics – impact of immunity



There are "innocent bystanders"



The person cannot be vaccinated because of a specific medical condition (certain cancers, certain immunological diseases) usually just a few percent of people

The person was vaccinated, but vaccine did not produce sufficient immunity (~3-5% of people who are vaccinated against measles)

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Infectious diseases transmission

- Different diseases have different ability to transmit to others
- The ability is summarized in a characteristic called the "***Basic Reproductive Number***" or R_0
  - Represents (on average) the number of new cases of disease from each individual, in an ***unprotected*** population
  - $R_0 < 1$; the infection will ***die out***
  - $R_0 > 1$; the infection will ***spread***

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Herd (community) immunity

- *"…is a form of indirect protection from infectious disease that occurs when a large percentage of a population has become immune to an infection, thereby providing a measure of protection for individuals who are not immune."* -Wikipedia
- It makes it more likely that an infected individual will contact immune individuals during their infectious period

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Relative transmission

- Measles is a ***remarkably effective*** virus in an ***unprotected*** population
- It is ***6 times*** more infectious than influenza
- Herd immunity effectively changes the R_0 of the infection

Disease	R_0
Measles	**12-18**
Chicken Pox	10-12
Polio	5-7
Mumps	4-7
HIV/AIDS	2-5
Influenza	2-3
Ebola	1.5-2.5

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Public Health Dynamics Laboratory

The ***mission*** of the Public Health Dynamics Laboratory is to:

- Develop interdisciplinary approaches using computational models to advance the theory and practice of public health.
- Contribute to "Systems Thinking" in the training of the next generation of Public Health professionals.

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Models of Infectious Disease Agent Study (MIDAS)
National Center of Excellence
- PI: Burke
- Sponsor: NIGMS/NIH

Vaccine Modeling Initiative
- PI Burke
- Sponsor: Bill and Melinda Gates Foundation

Public Health Adaptive Systems Studies
- PI: Potter
- Sponsor: CDC

Public Health International Modeling Fellows Program
- PI: Grefenstette/Burke
- Sponsor: Benter Foundation

Data Across Sectors for Health (DASH)
- PI: Roberts (Hacker)
- Sponsor: Roberts Wood Johnson Foundation

Collaborators:

MIDAS
www.midas.pitt.edu

VMI Vaccine Modeling Initiative
www.vaccinemodeling.org

PHASYS
www.phasys.pitt.edu

Benter Foundation

Robert Wood Johnson Foundation

Allegheny County ACHD Health Department

Carnegie-Mellon University

Johns Hopkins Medicine

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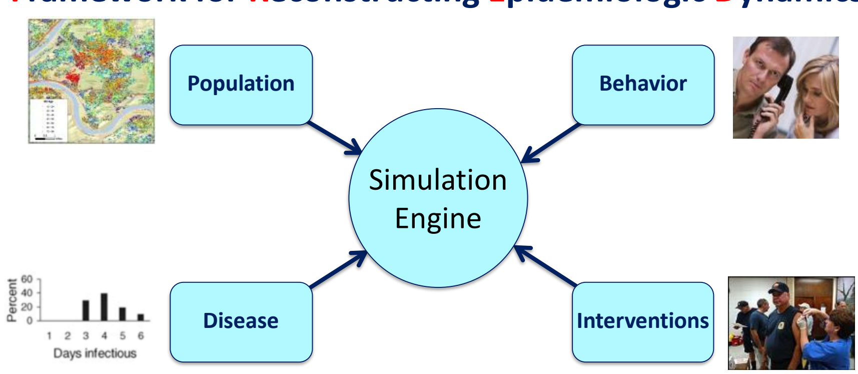
Framework for Reconstructing Epidemiologic Dynamics



Grefenstette JJ, Brown ST, Rosenfeld R, et al.
FRED (A Framework for Reconstructing Epidemic Dynamics): An open-source software system for modeling infectious diseases and control strategies using census-based populations.
BMC Public Health, 2013 Oct;13(1), 940.

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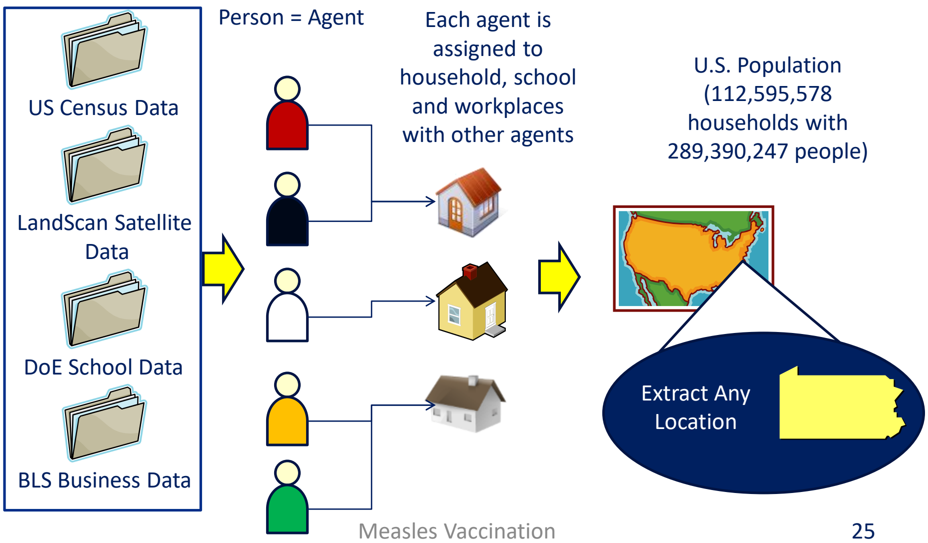
Census-matched synthetic population



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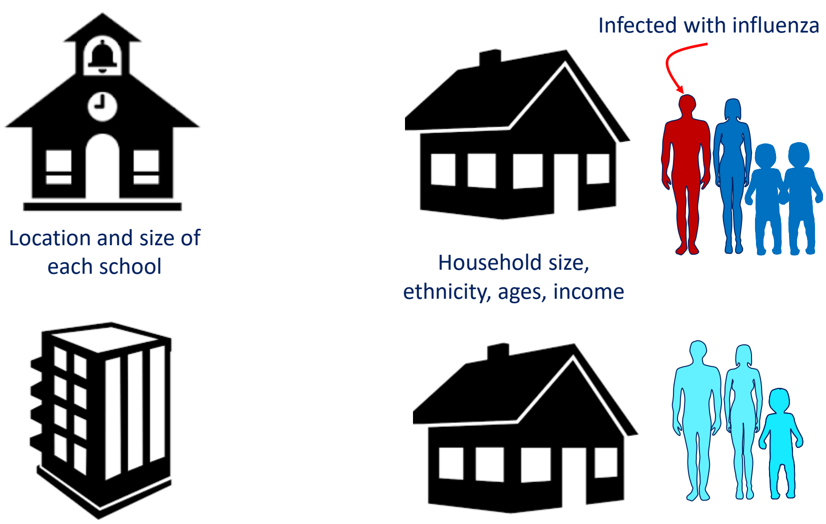
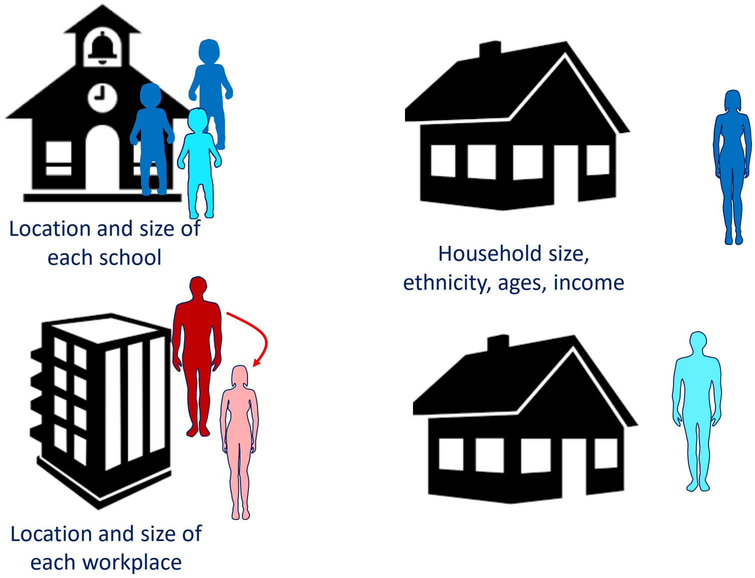
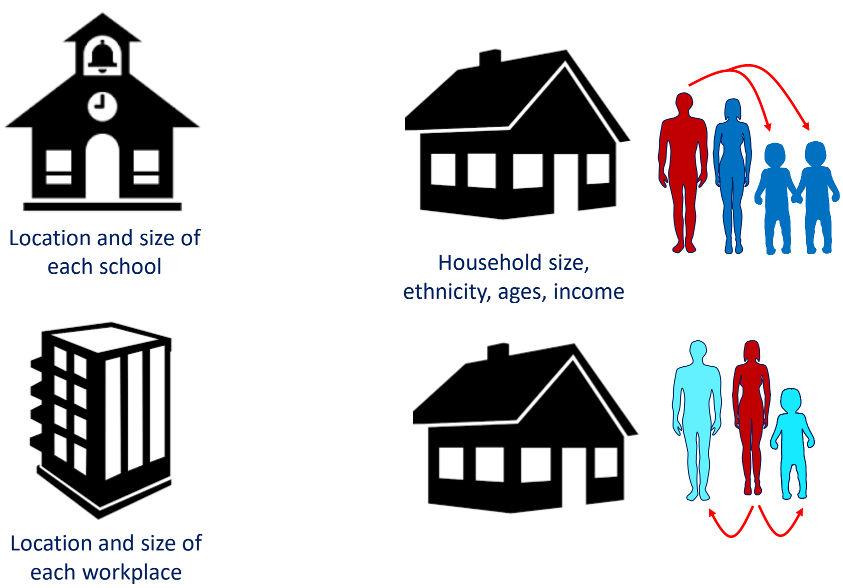



Location and size of each school
Household size, ethnicity, ages, income
Location and size of each workplace


Location and size of each school
Household size, ethnicity, ages, income
Location and size of each workplace

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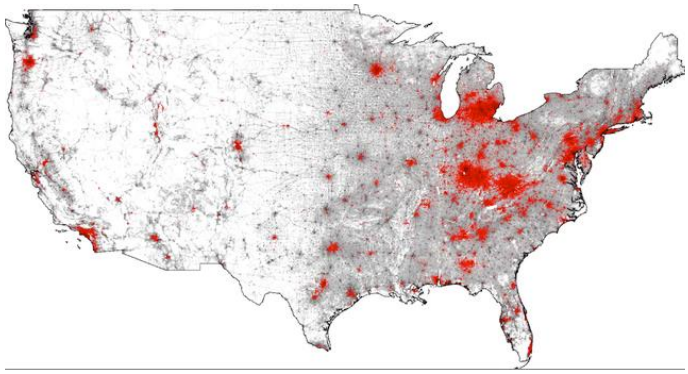
- Model of the introduction of avian influenza into a population with little or no immunity



Ferguson NM, Cummings DA, Fraser C, Cajka JC, Cooley PC, Burke DS.
Strategies for mitigating an influenza epidemic
Nature July 27, 2006; 442: 448-52

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FRED Measles

- Prompted by the publicity of the resurgence of measles in the public media (after the Disneyland outbreak of 2014-15)
- Calibrated FRED (built for influenza) to the disease characteristics for Measles
  - More infectious
  - Infection spreads by close contact
- Created an application that can describe the expected number of cases when an infected person is placed in a county

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Initial FRED Measles

http://fred.publichealth.pitt.edu/

- Important assumptions:
  - All schools in county have the ***same vaccination rate***
  - We compare 80% vaccination rates among those <16 to 95% vaccination among those same children
  - Randomly insert a new case into the county
  - Run the model multiple times, show the ***median number of cases***

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Impact -Use as a policy tool

FiveThirtyEight

Politics Sports Science & Health Economics Culture

JUN. 12, 2017 AT 9:11 AM

Facts Alone Won't Convince People To Vaccinate Their Kids

It took an outbreak, a mathematical model and a new law to get immunization rates up in California.

By Erin Hare

Filed under Public Health

"The FRED Measles model can be used to visualize infectious disease dynamics in any county, so Pan could show his fellow senators exactly how an outbreak would play out in their own backyards."

Erin Hare, 538.com

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Impact – use as a policy tool


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AP

California, 11 other states introduce vaccine bills

By Andis Robeznieks | April 22, 2015

Health officials have declared California's measles outbreak over, but the legislative response is just getting rolling.

The outbreak started at the Disneyland theme park and sickened 131 Californians and another 16 people from other states.

Dr. Richard Pan, a pediatrician and California state legislator, used FRED measles to explain herd immunity to colleagues in the California Legislature

"... Sen. Marty Block, a San Diego Democrat, said he was convinced to vote “yes” after Pan showed him a computer modeling program [from the University of Pittsburgh] that simulates how quickly a measles outbreak could spread depending on a community's vaccination rate."

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Impact of SB 277 in California

Dr. Richard Pan at California Department of Public Health

Vaccination rate, pre SB 277: 92.9%
Vaccination rate, post SB 277: 95.6%
(~168,000 more children vaccinated)

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Caveats related to FRED Measles

- Original measles simulation assumes either 80% vaccination or 95% vaccination
- Assumes a ***uniform vaccination rate*** within each county (all schools in the county were considered the same)
- This is obviously not correct

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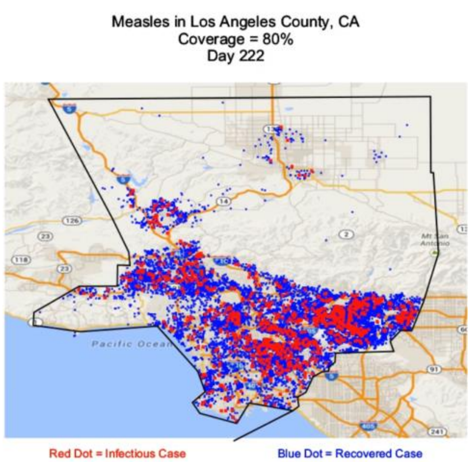
The scenario would never happen



- People would ***respond*** to what they saw
  - Keep children home from school
  - Vaccinate their children
  - Change group behaviors

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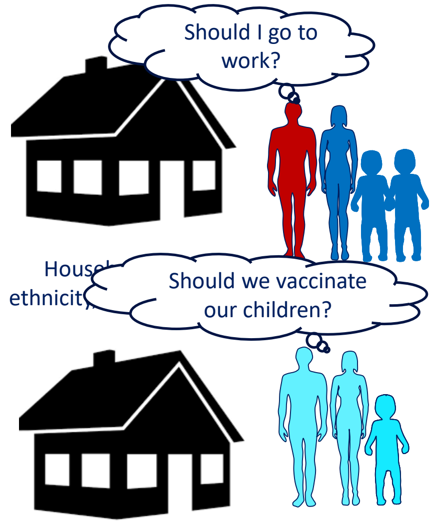
Location and size of each school

When a school (or workplace) develops a lot of cases of measles – people mat change their behavior



Location and size of each workplace

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Improvements – actual vaccination

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FRED Measles Texas

- Obtained data from the Texas Department of State Health Services on vaccination rates ***by school for private schools*** and by ***district for public schools***.

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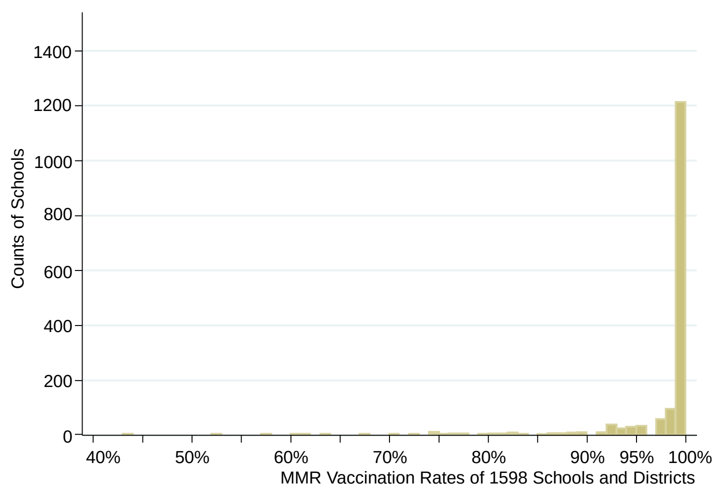
Texas has variable vaccination rates



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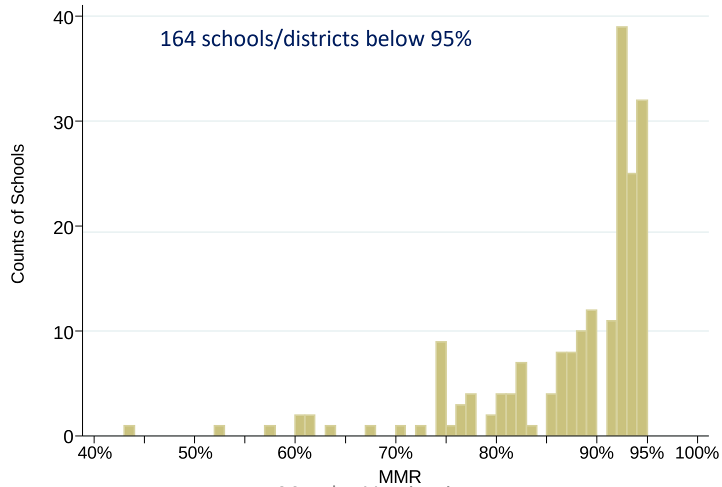
Schools less than 95%



Measles Vaccination 41

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FRED Measles Texas: definitions

- **Refusers**: when vaccination rates are below 95%, those children are ***assumed*** to have declined to be vaccinated
- **Innocent bystanders**: There is a small percentage of children who:
  - Cannot be vaccinated for health reasons
  - Receive the vaccination but it does not provide immunity (~3% of those vaccinated)
- ***Metropolitan Statistical Area (MSA)*** – high population areas that are typically large cities

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FRED Measles Texas - Assumptions

- Where we had district data, we assumed all schools in the district had the same vaccination rate
- For schools with over 95% vaccination, we assumed that there were no refusers, only innocent bystanders

FRED Measles Texas: scenarios

- ***Non-targeted***: a child infected with measles is randomly placed in ***any school*** in the county or Metropolitan Statistical Area (large city)
- ***Targeted***: a child infected with measles is specifically placed into a ***school that has refusers*** (has a vaccination rate less than 95%)

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FRED Measles Texas: Display

Median predicted cases under current vaccine conditions and the area experiences a non-targeted measles introduction	Median predicted cases under current vaccine conditions and the area experiences a targeted measles introduction (a school <95%)
Median predicted cases under current vaccine conditions and the area experiences a non-targeted measles introduction with a 10% lower vaccination rate	Graph of the number of cases (both in ***refusers*** and ***innocent bystanders***) that would occur in a targeted measles introduction under current vaccine conditions

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Web tool:

http://fred.publichealth.pitt.edu/texas_measles

The website if open to anyone

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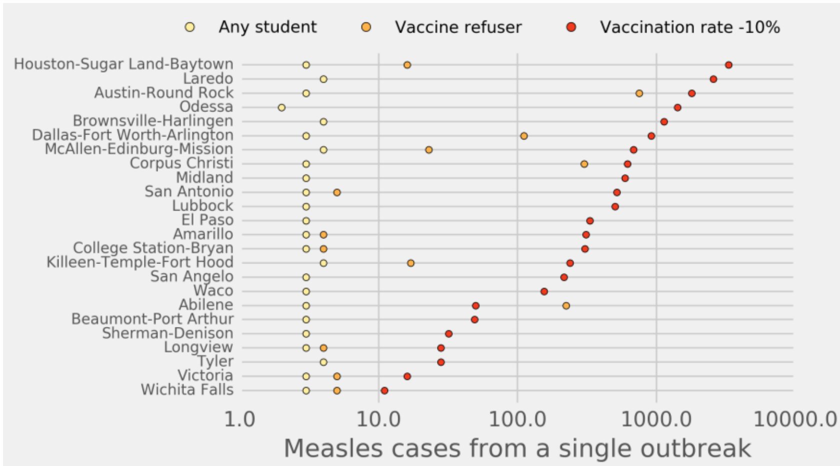
Summary of expected cases



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Conclusions:

- Even under current vaccination conditions, there is a ***reasonable risk*** that the introduction of a case of measles into many Texas counties and cities would result in ***large numbers of measles cases***
- Families who refuse vaccination put others at risk as well, in many simulations the number of ***innocent bystander*** infections was nearly equal to the number of infections among ***refusers***

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Conclusions

- ***Herd (community) Immunity*** protects not only vaccinated individuals, but prevents the development of epidemics in situations where they might otherwise occur

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Questions?