Webinar: The Role of Applied Math in Real-time Pandemic Response: How Basic Disease Models Work

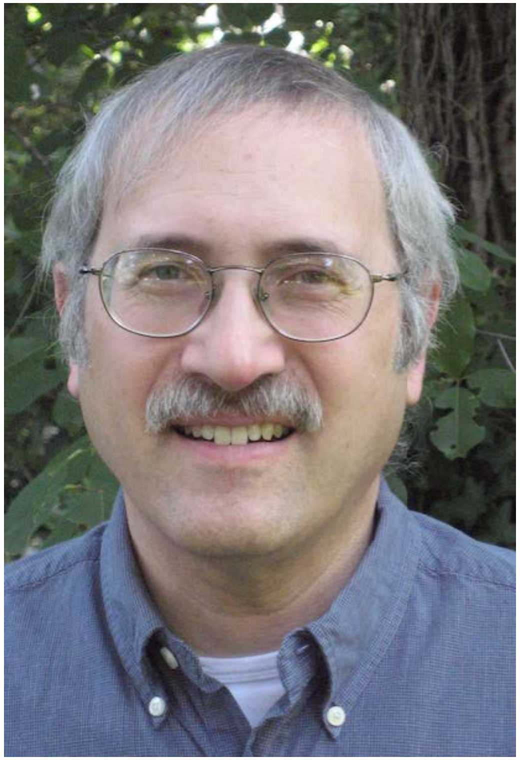
Presented by:

Professor Nina Fefferman

National Institute for Mathematical and Biological Synthesis, University of Tennessee, Knoxville

With support from the National Science Foundation (DBI-1300426)

MEET YOUR MODERATOR



Louis J. Gross, PhD

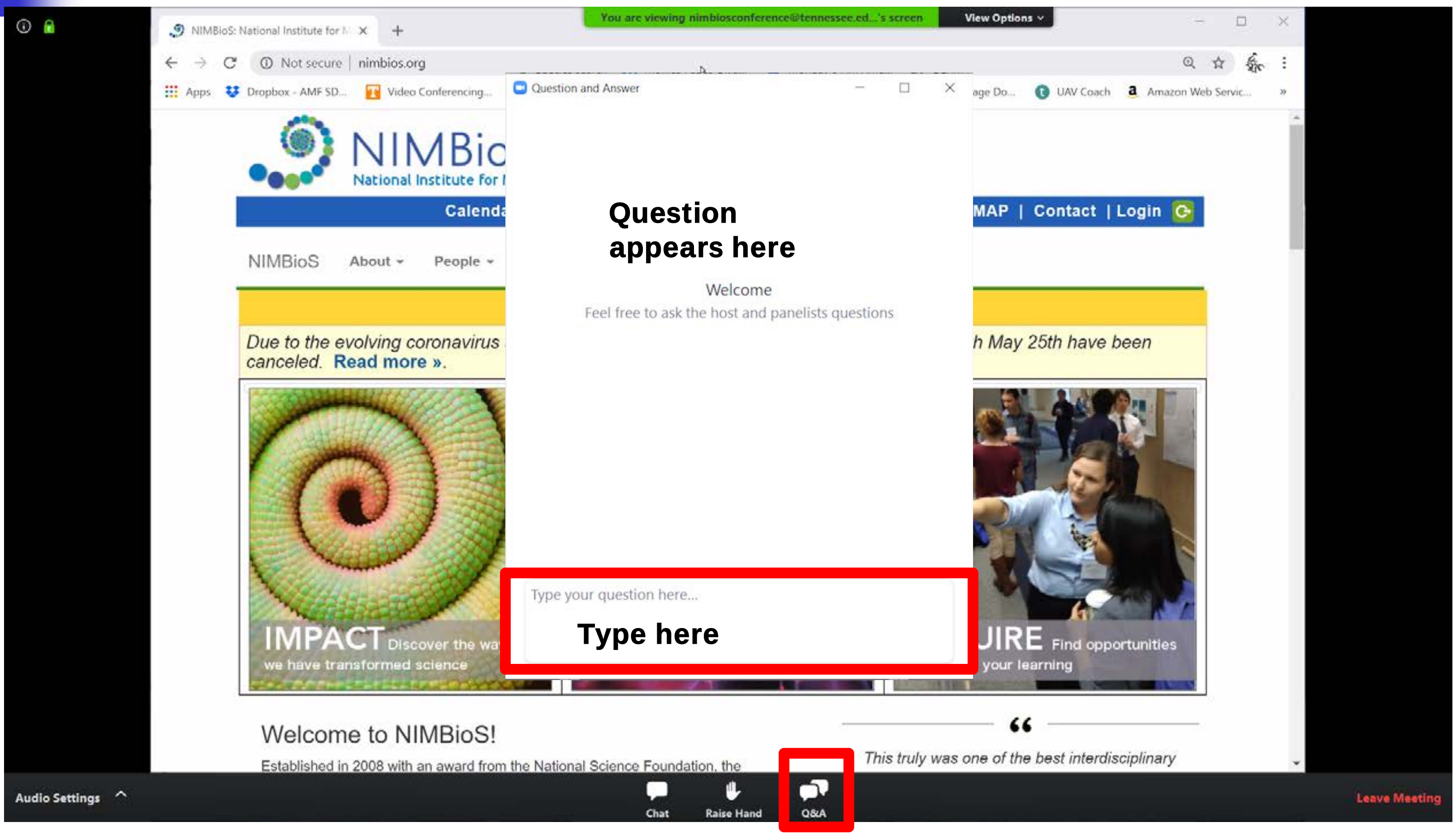
***Director,** National Institute for Mathematical and Biological Synthesis (NIMBioS)*

***Director,**, The Institute for Environmental Modeling, University of Tennessee*

***Chancellor’s Professor** of Ecology and Evolutionary Biology and Mathematics, University of Tennessee*

National Institute for Mathematical and Biological Synthesis

HOW TO INTERACT TODAY



www.nimbios.org/webinars

NIMBioS
National Institute for Mathematical and Biological Synthesis

NIMBioS Webinar Series

NIMBioS is hosting a series of webinars focusing on topics at the interface of mathematics and biology. Unable to attend the live presentation? That's ok! Register to attend, and you will receive a link to the webinar recording.

Upcoming Webinars

Costs and benefits of defending against viral infection: Lessons from natural ecosystems

Date: 3:30 EDT Tuesday, April 7, 2020

Speaker: Dr. David Talmy, Asst. Professor, Microbiology, University of Tennessee, Knoxville

Moderator: NIMBioS Director Louis Gross, NIMBioS Director and Chancellor's Professor of Ecology and Evolutionary Biology and Mathematics at the University of Tennessee

Abstract: The COVID-19 virus is shaping Earth in unprecedented ways, for example by changing the rate at which humans release greenhouse gasses into the atmosphere. Yet, through their activity in natural ecosystems, viruses have been shaping Earth as a system for millions of years. In this presentation, I will consider diverse ways viruses may have shaped Earth as a system, and discuss the value of mathematical models for understanding factors which govern the dynamics of viral infections globally.

David Talmy grew up in London, England. He was trained in mathematics as an undergraduate at the University of Sussex. Dr. Talmy is an assistant professor in the Department of Microbiology at the University of Tennessee, Knoxville. He is also an affiliate faculty member at the National Institute for Mathematical and Biological Synthesis. As a graduate, he transitioned into environmental research through a master's program at the University of York specifically tailored to train mathematicians in ecological research. His doctoral training was primarily at Plymouth Marine Laboratory in the UK, which houses one of the foremost European marine ecosystem modeli... hytoplankton. He spent ... coupling of autotro... acquisition and defens... ing, field, and laborat...

Regist...

NIMBioS.org/Webinars A recording of each webinar will be posted

MEET YOUR PRESENTER

Nina Fefferman, PhD

Professor *of Ecology and Evolutionary Biology and Mathematics, University of Tennessee*

Director, *The Mathematical Modeling Consulting Center, University of Tennessee*

Associate Director, *One Health Initiative, University of Tennessee*

NIMBioS
National Institute for Mathematical and Biological Synthesis

Webinar Objectives

- Understand how math models help us analyze and predict outbreaks
- Gain familiarity with concepts in the news about pandemics: R_0, "Flatten the Curve", etc.
- See how we can use models to design public health policy

The role of applied math in real-time pandemic response:

How basic disease models work

What Do Math Modelers Do?

Start with some problem in the world

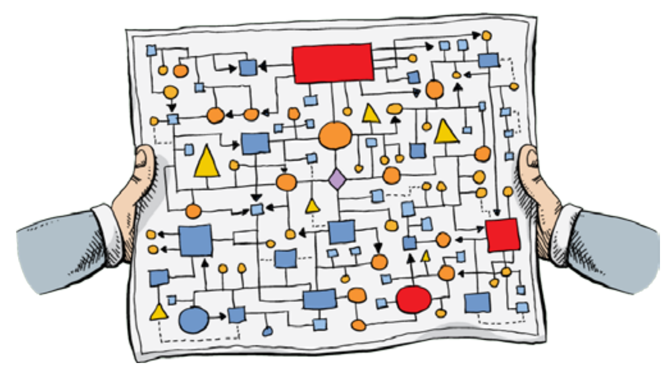
- Complicated Interactions
- Zillions of possible factors
- Lots of different possible measurements / observations
- Lots of things we can't measure

We can use math to explain!

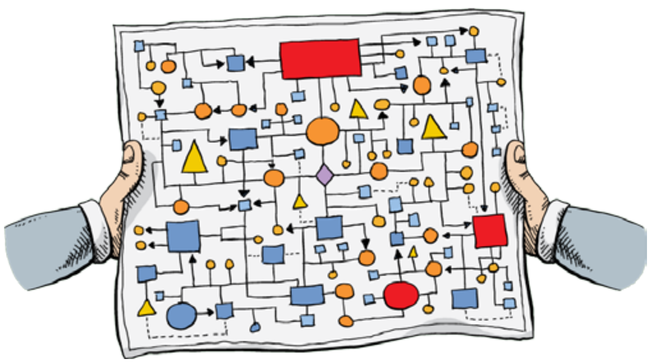
Start with some problem in the world

- Complicated Interactions
- Zillions of possible factors
- Lots of different possible measurements / observations
- Lots of things we can't measure

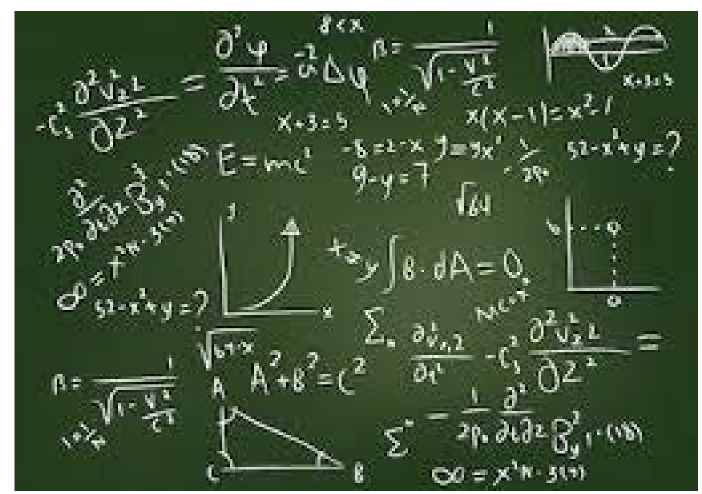
Distill the world to abstract logic



Turn logic into equations



Lets us turn conceptual logic into quantitative calculations and predictions: Numbers



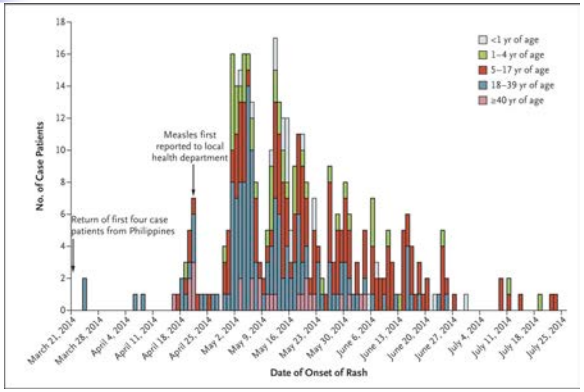
Lots of types of quantitative model methods

- Linear Algebra and Matrices
- Difference Equations
- Differential Equations
- Game Theory
- Networks
- Cellular Automata
- Agent Based Models
- Statistical Models

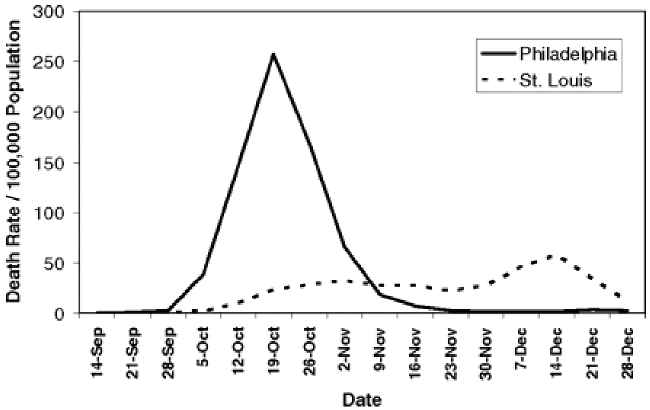
The **details** of what you do in each of these are different, but the basic idea is the same:

Logic → Equations → Predictions

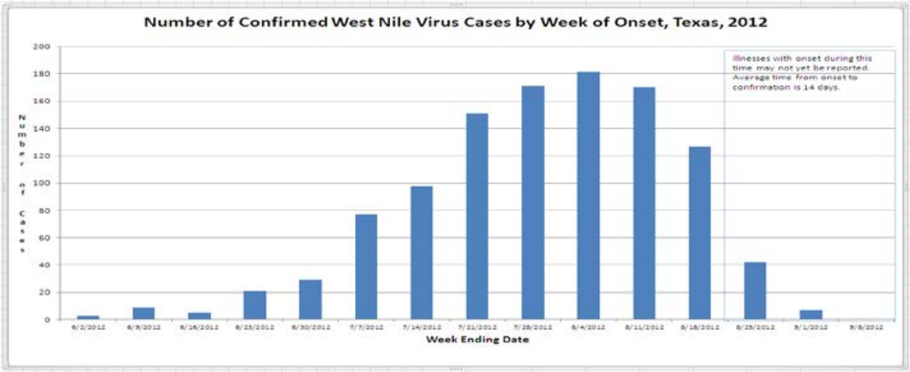
Let's Use Models to Understand Outbreaks



Measles (Gastañaduy *et al.* 2016)



1918 Flu (Hatchett *et al.* 2007)

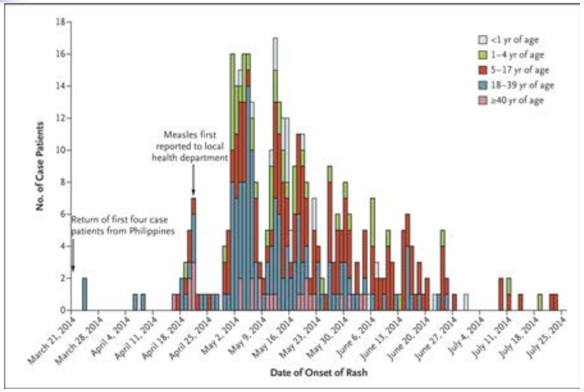


West Nile virus (TX Dept of SHS, 2012)

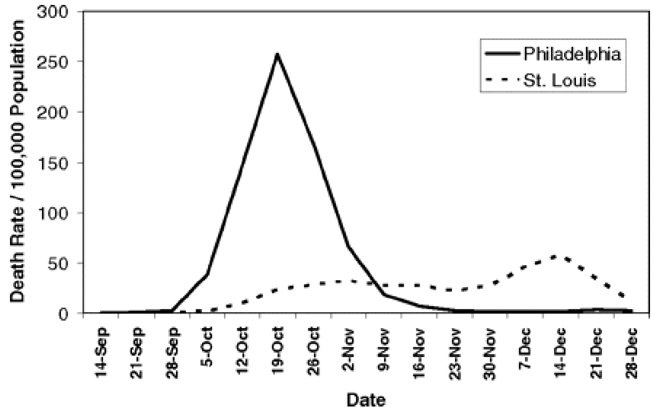
Let’s try to explain the pattern:

Why do outbreaks end?

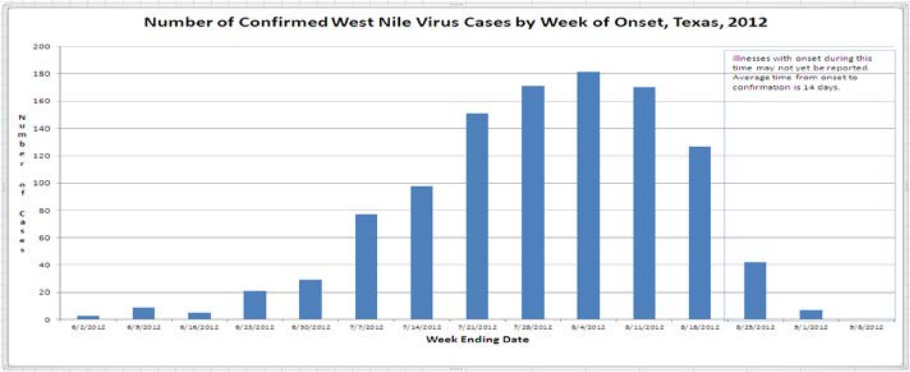
(even if we don’t have a vaccine)



Measles (Gastañaduy *et al.* 2016)



1918 Flu (Hatchett *et al.* 2007)



West Nile virus (TX Dept of SHS, 2012)

Let’s Abstract the Logic of Infections Together

What do we know about infectious diseases and how they work?

Healthy, Susceptible People

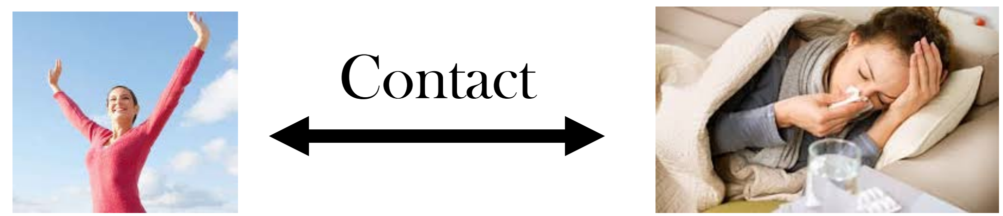
Catch Infections From

Sick, Infectious People

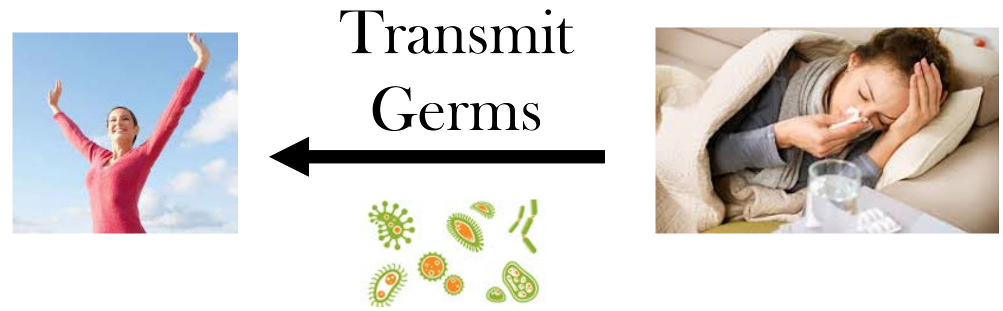
What happens to Susceptible People?

A couple of steps:

1)



2)



3)

Mathy things about what happens to Susceptible People

Contact

Transmit Germs

We need both

Together this gives a **rate** of  becoming 

Let's call it Rate 1 and keep it for later

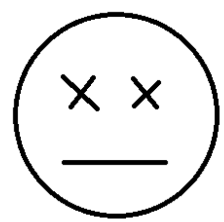
What happens to Infectious People?

Simpler:

Recover

Good

Die



Not Good

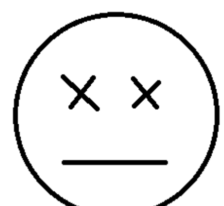
Mathy things about what happens to Infectious People?

Still simpler:

Rate

Good

Rate



Not Good

Mathy things about what happens to Infectious People?

Still simpler:

Rate

Good

This option is depressing – let's ignore it

Mathy things about what happens to Infectious People?

Still simpler:

Rate

Good

Let's call this one Rate 2

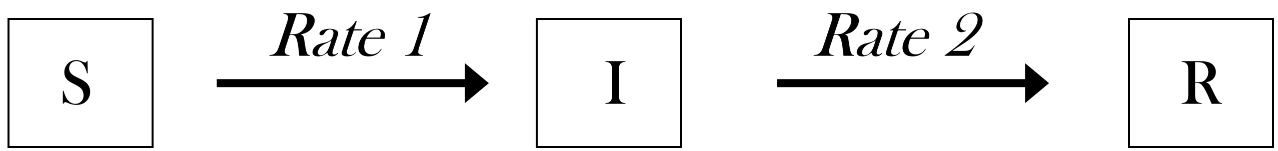
Let's Put it All Together

Susceptible People become Infectious at Rate1 and Recover at Rate 2

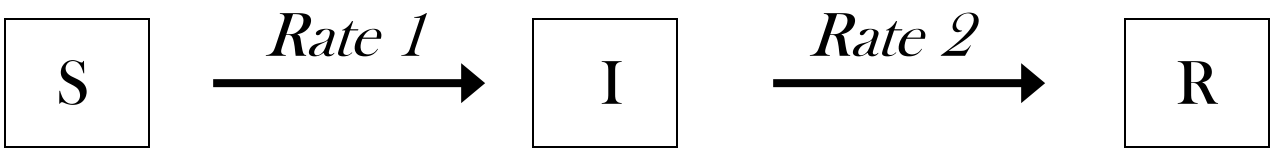
Abstract logic of our system is:

S —*Rate 1*→ I —*Rate 2*→ R

Now let's make our logic into equations

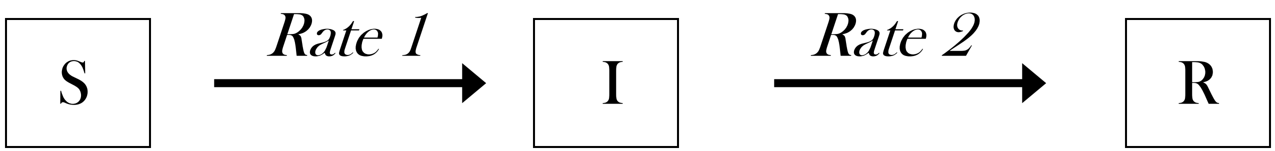


How many people will still be Susceptible tomorrow?



$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

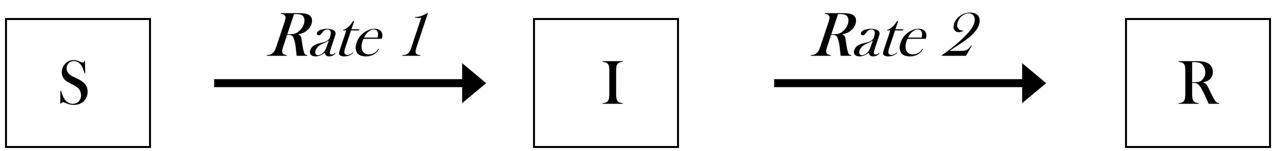
How many people will be Infectious tomorrow?



$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

How many people will be Recovered tomorrow?

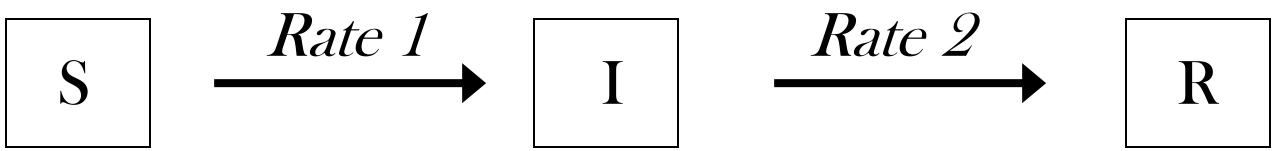


$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

$$R_{tomorrow} = R_{today} + (Rate2) * I_{today}$$

The Complete Math!



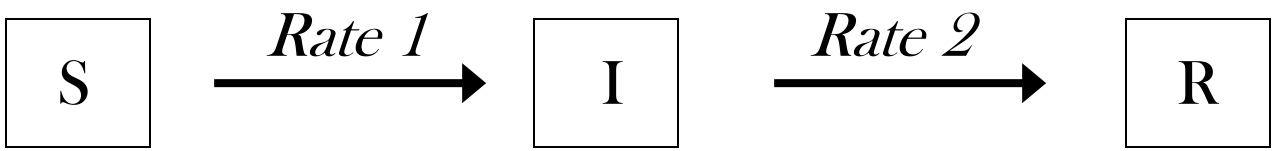
$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

$$R_{tomorrow} = R_{today} + (Rate2) * I_{today}$$

This is really simple – Is it useful?

YES



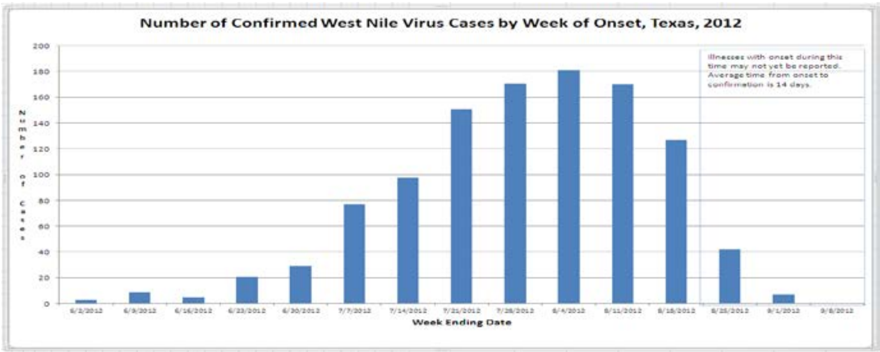
$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

$$R_{tomorrow} = R_{today} + (Rate2) * I_{today}$$

Let's go back to the question:

Why do outbreaks end?



West Nile virus (TX Dept of SHS, 2012)

What is the pattern to explain?

- First the number of Infectious people goes up
- Then it goes down

Why?

Why do outbreaks end?

- First the number of Infectious people goes up
- Then it goes down

Notice:

This is a question just about the numbers of **Infectious People** over time

When will the number of Infectious people fit that pattern?

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) I_{today}$$

$I_{tomorrow}$ is **increasing** when

$$(Rate1) * S_{today} * I_{today} - (Rate2) I_{today} > 0$$

the parts we add are bigger than the parts we subtract

Why you actually took algebra:

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) I_{today}$$

This means:

$$(Rate1) I_{today} S_{today} - (Rate2) I_{today} > 0$$

$$(Rate1) I_{today} S_{today} > (Rate2) I_{today}$$

$$(Rate1) S_{today} > (Rate2)$$

Aha!

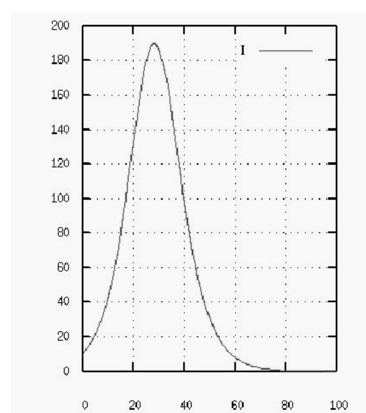
I is increasing when $(Rate1)S_{today} > (Rate2)$

So what happens?
Remember:

$$S_{tomorrow} = S_{today} - (Rate1)I_{today}S_{today}$$

S can only decrease!

We **HAVE** to get **this** picture for I over time



This is also how we compare outbreaks

I is increasing when $(Rate1) * S_{today} > (Rate2)$

We can re-write as a ratio $\frac{(Rate1) * S_{today}}{(Rate2)} > 1$

This ratio at the start of an outbreak (when most people are Susceptible) is called R_0 for this model

The **bigger** the R_0 for a disease, the **worse** we expect the outbreak to be

Some R_0 values for our favorite diseases

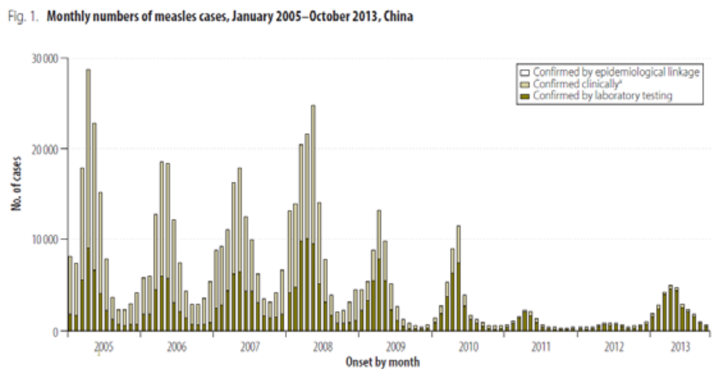
Disease	$\boldsymbol{R_0}$
Measles	12–18
Smallpox	3.5–6
HIV/AIDS	2–5
COVID-19	1.4–3.9 ???
Influenza 1918	1.4–2.8
Ebola 2014	1.5–2.5
Influenza (seasonal)	0.9–2.1

Shamelessly copied from Wikipedia.org for this talk

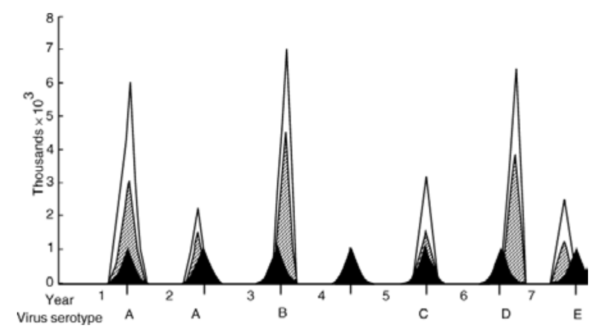
We can estimate R_0 from equations or from observations of outbreak curves

But wait, we know diseases don't just go away permanently – What's going on?

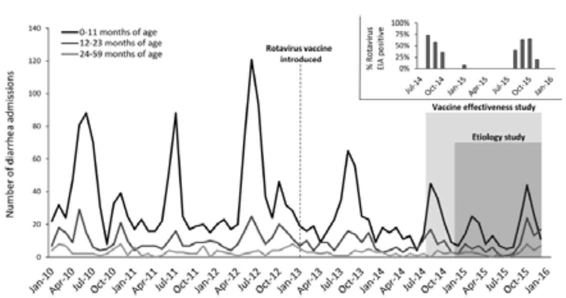
Measles in China: Chao Ma et al. 2014



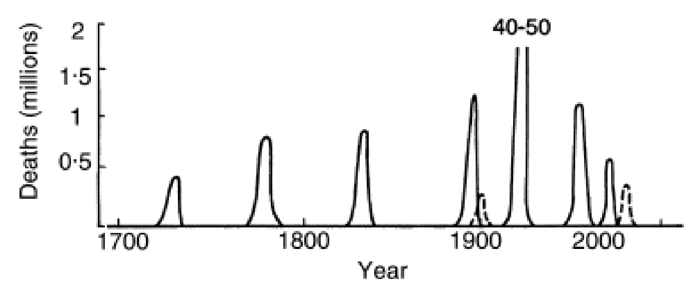
Annual Flu Outbreaks: Potter 2008



Rotavirus in Africa: Platts-Mills et al. 2017



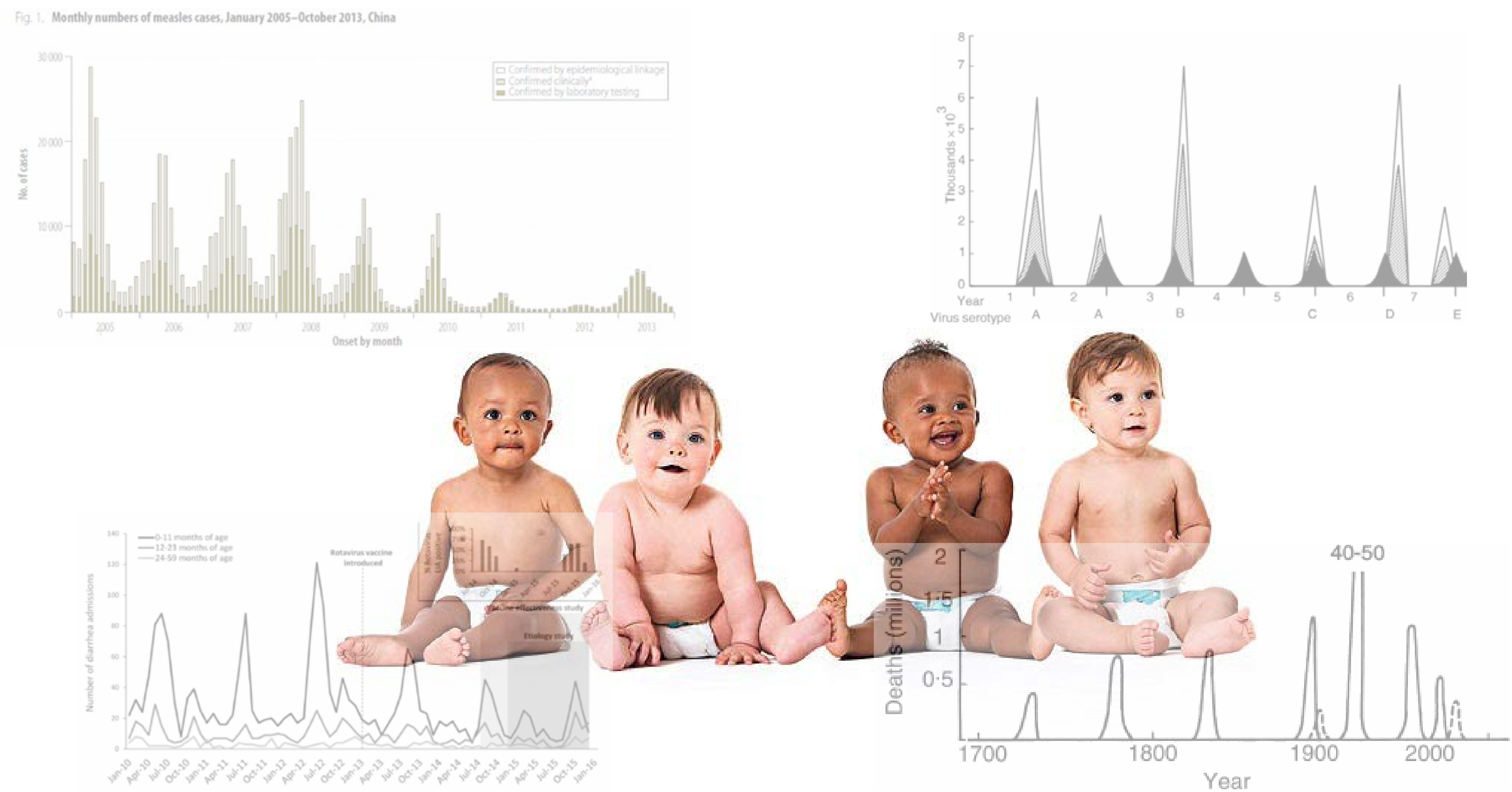
Global Flu Pandemics: Potter 2008



Babies!

Measles in China: Chao Ma et al. 2014

Annual Flu Outbreaks: Potter 2008



In reality, the number of Susceptibles ISN'T only decreasing

$$S_{tomorrow} =$$

$$S_{today} + S_{babies} - (Rate1) I_{today} S_{today}$$

How much disease we can keep around the population is directly tied to the birth rate *(and if people lose immunity over time)*

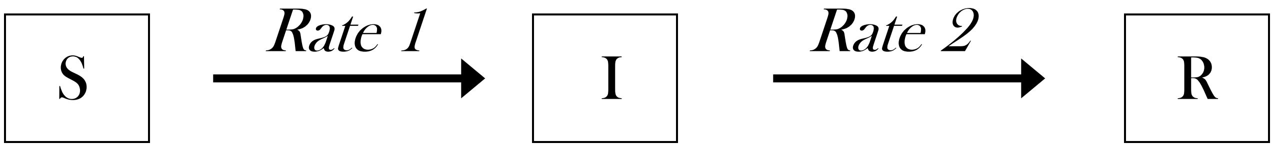
This is also why Vaccines can protect people who aren't even vaccinated

$$S_{tomorrow} = S_{today} - S_{vacc} - (Rate1) I_{today} S_{today}$$

Taking out enough Susceptibles so that $(Rate1) S_{today} \ngtr (Rate2)$ is the goal!

Called the "herd immunity threshold"

This really simple model is so powerful!

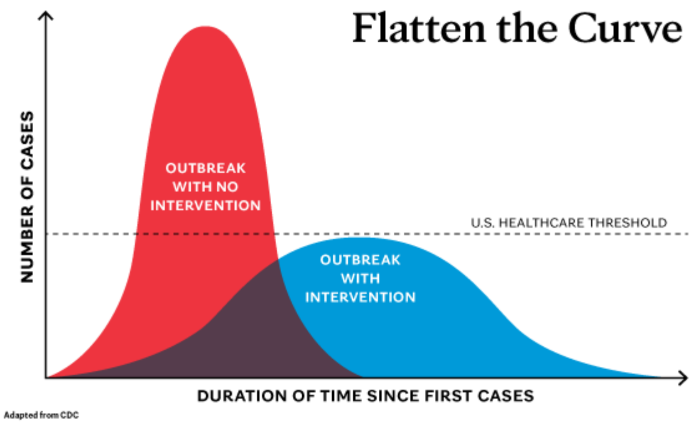


$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

$$R_{tomorrow} = R_{today} + (Rate2) * I_{today}$$

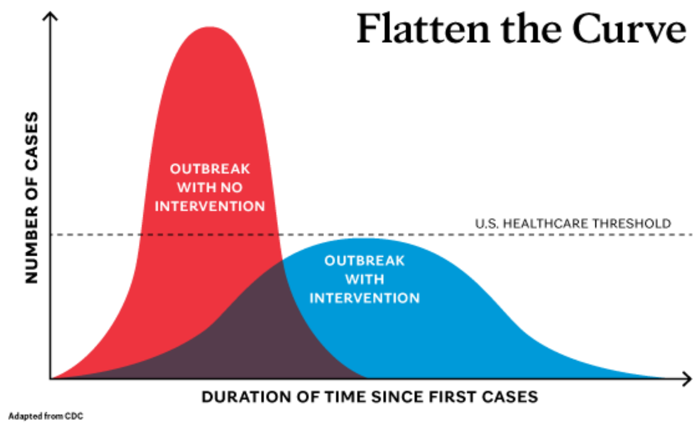
Let's use it to understand what we mean by "flatten the curve"



$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

It's all about Rate 1



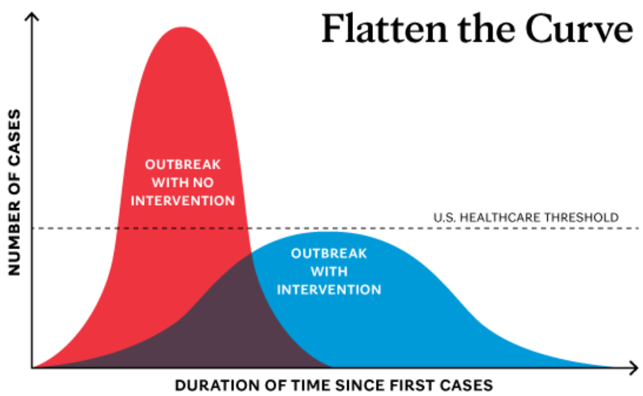
$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

If we can slow down Rate 1

$$S_{tomorrow} = S_{today} - (Rate1) * S_{today} * I_{today}$$

$$I_{tomorrow} = I_{today} + (Rate1) * S_{today} * I_{today} - (Rate2) * I_{today}$$

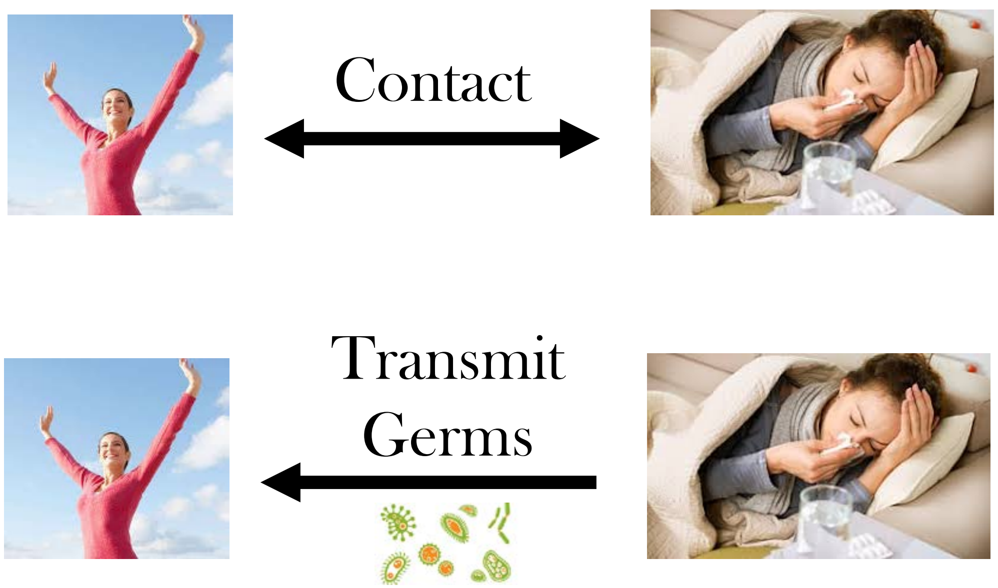


- People move out of S more slowly
- I increases more slowly
- It takes **longer** to run out of S, but we **never** build up as many I at once

Keeps people alive – never run out of hospital beds

Remember how we got Rate 1?

It was a combination of:



This is how to slow down Rate 1

Social Distancing

Contact

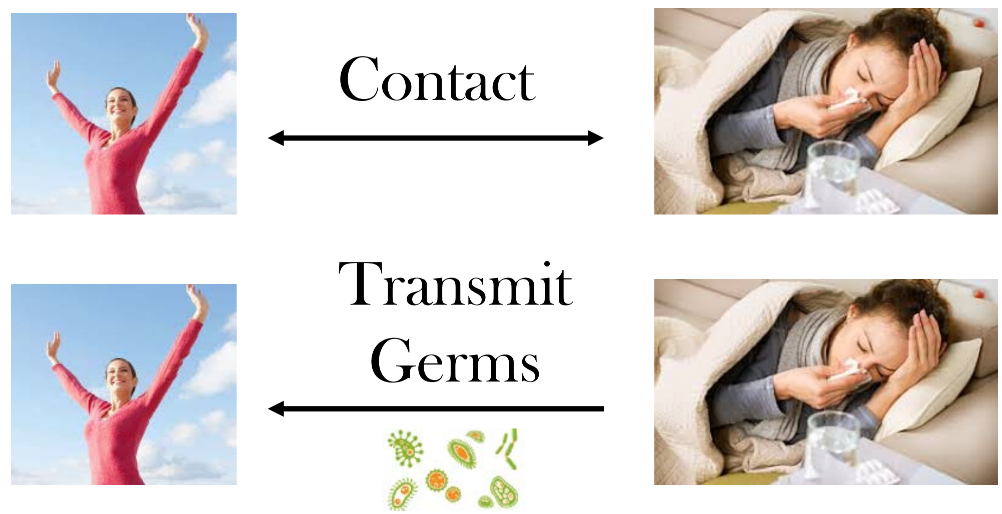
Better Hygiene

Transmit
Germs

This is how to slow down Rate 1

Social Distancing

Better Hygiene



Using just this, we can **predict:**

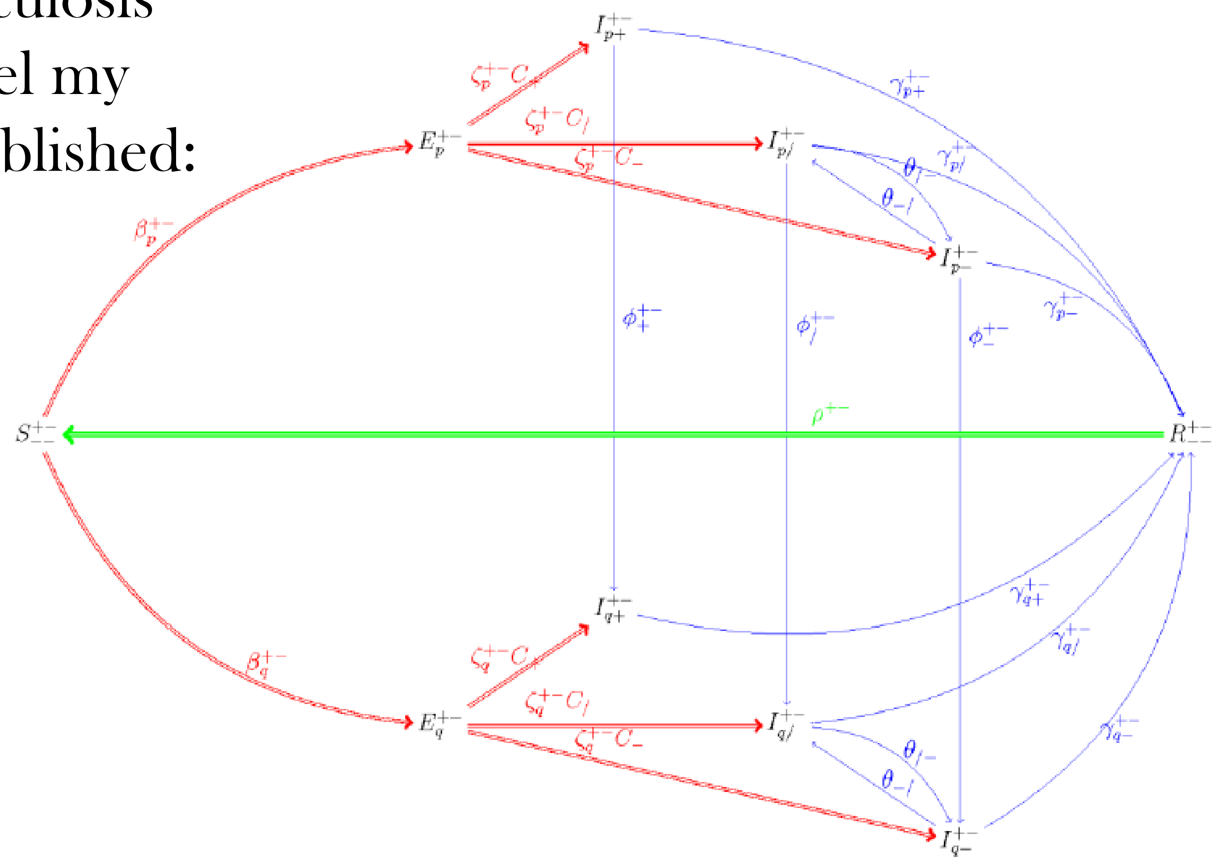
- How effective is shelter-in-place?
- How long do we need to continue sheltering?
- What percent of people have to shelter to shut down the outbreak?

Not all the answers can be obtained this easily…

- We usually use continuous averages instead
- Many diseases are more logically complicated
  - Different ways of being transmitted
    - Insect bites
    - Sexual contact
    - Contamination of an environment (fomite)
    - Mother to fetus
    - etc.
  - Delay between being infected and becoming infectious
  - Immunity can go away over time
  - Age-based differences
  - Seasonal/Climatological differences
  - Opportunistic infection
  - etc.

The logic and the math can look complicated

The logic of a Tuberculosis and HIV/AIDS model my students and I just published:



DeNegre, Myers, Fefferman. *Antibiotics* 2020

The logic and the math can look complicated

The equations were worse:

The first 12 equations (out of 40) from a model to understand how different strains of TB would circulate in parts of Africa where there is already a high prevalence of AIDS in the population

$$
\begin{aligned}
\frac{dS^{--}_{--}}{dt} = \; & -\beta^{--}_{p} S^{--}_{--} I_{all,p} - \beta^{--}_{q} S^{--}_{--} I_{all,q} + \rho^{--} R^{--}_{--} \\
& + \alpha (S^{--}_{--} + E^{--}_{p} + E^{--}_{q} + I^{--}_{p+} + R^{--}_{--} + S^{++}_{--} \\
& \quad + E^{++}_{p} + E^{++}_{q} + I^{++}_{p+} + R^{++}_{--} + S^{++}_{-+} + E^{++}_{q2} + R^{++}_{-+}) \\
& - \omega S^{--}_{--}
\end{aligned}
$$

$$
\begin{aligned}
\frac{dS^{+-}_{--}}{dt} = \; & -\beta^{+-}_{p} S^{+-}_{--} I_{all,p} - \beta^{+-}_{q} S^{+-}_{--} I_{all,q} + \rho^{+-} R^{+-}_{--} \\
& + \alpha (S^{+-}_{--} + E^{+-}_{p} + E^{+-}_{q} + I^{+-}_{p+} + R^{+-}_{--} + S^{+-}_{-+} + E^{+-}_{q2} + R^{+-}_{--}) \\
& - (\omega + \omega_{v}) S^{+-}_{--}
\end{aligned}
$$

$$\frac{dS^{+-}_{-+}}{dt} = -\beta^{+-}_{q} S^{+-}_{-+} I_{all,q} + \rho^{+-} R^{+-}_{-+} + \alpha (S^{+-}_{-+} + E^{+-}_{q2} + I^{+-}_{q2} + R^{+-}_{-+}) - (\omega + \omega_{v}) S^{+-}_{-+}$$

$$\frac{dS^{++}_{--}}{dt} = -\beta^{++}_{p} S^{++}_{--} I_{all,p} - \beta^{++}_{q} S^{++}_{--} I_{all,q} + \rho^{++} R^{++}_{--} - \omega S^{++}_{--}$$

$$\frac{dS^{++}_{-+}}{dt} = -\beta^{++}_{q} S^{++}_{-+} I_{all,q} + \rho^{++} R^{++}_{-+} - \omega S^{++}_{-+}$$

$$I_{all,p} = I^{--}_{p+} + I^{--}_{p/} + I^{--}_{p-} + I^{+-}_{p+} + I^{+-}_{p/} + I^{+-}_{p-} + I^{++}_{p+} + I^{++}_{p/} + I^{++}_{p-}$$

$$I_{all,q} = I^{--}_{q+} + I^{--}_{q/} + I^{--}_{q-} + I^{+-}_{q+} + I^{+-}_{q/} + I^{+-}_{q-} + I^{++}_{q+} + I^{++}_{q/} + I^{++}_{q-} + I^{+-}_{q2} + I^{++}_{q2}$$

$$\frac{dE^{--}_{p}}{dt} = \beta^{--}_{p} S^{--}_{--} I_{all,p} - \zeta^{--}_{p} E^{--}_{p} - \omega E^{--}_{p}$$

$$\frac{dE^{--}_{q}}{dt} = \beta^{--}_{q} S^{--}_{--} I_{all,q} - \zeta^{--}_{q} E^{--}_{q} - \omega E^{--}_{q}$$

$$\frac{dE^{+-}_{p}}{dt} = \beta^{+-}_{p} S^{+-}_{--} I_{all,p} - \zeta^{+-}_{p} E^{+-}_{p} - (\omega - \omega_{v}) E^{+-}_{p}$$

$$\frac{dE^{+-}_{q}}{dt} = \beta^{+-}_{q} S^{+-}_{--} I_{all,q} - \zeta^{+-}_{q} E^{+-}_{q} - (\omega - \omega_{v}) E^{+-}_{q}$$

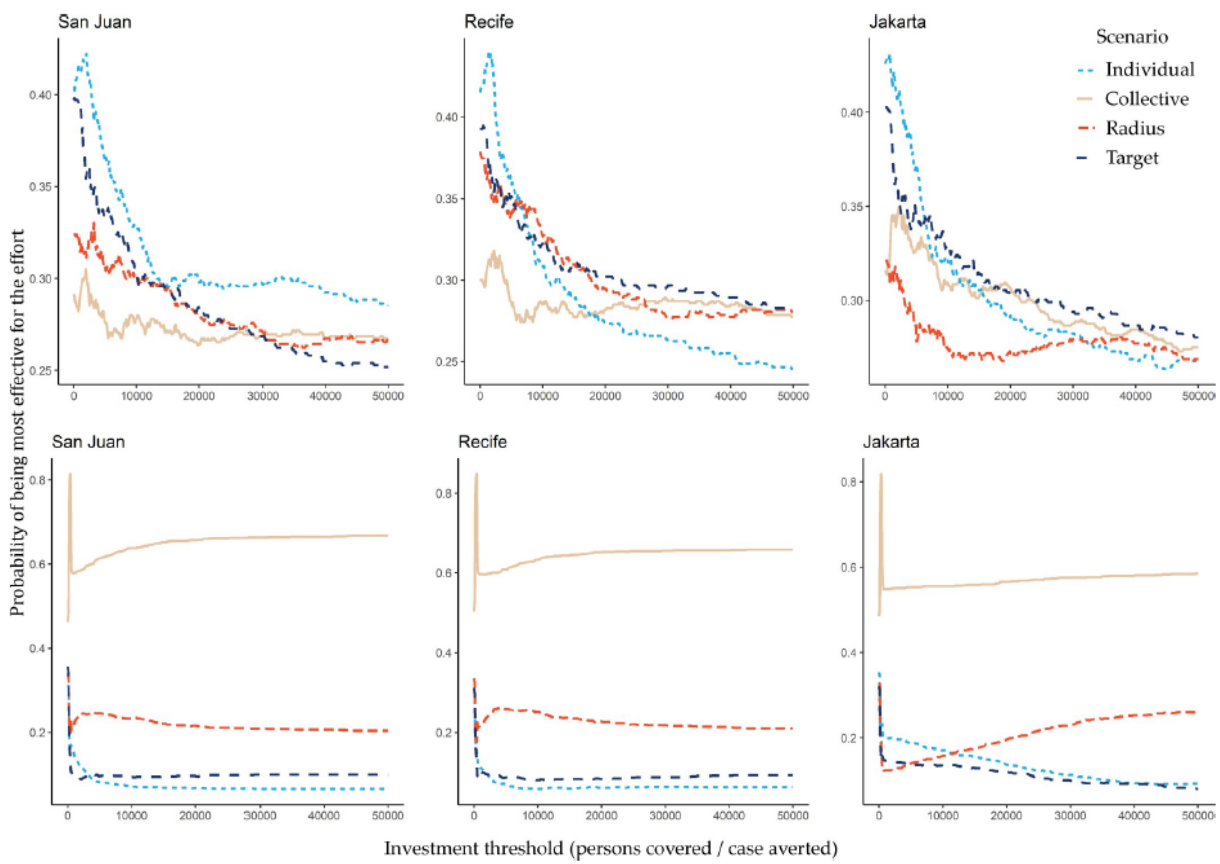
$$\frac{dE^{++}_{p}}{dt} = \beta^{++}_{p} S^{++}_{--} I_{all,p} - \zeta^{++}_{p} E^{++}_{p} - \omega E^{++}_{p}$$

DeNegre, Myers, Fefferman. *Antibiotics* 2020

But the basic ideas are EXACTLY THE SAME

The predictions our models make allow us to compare interventions

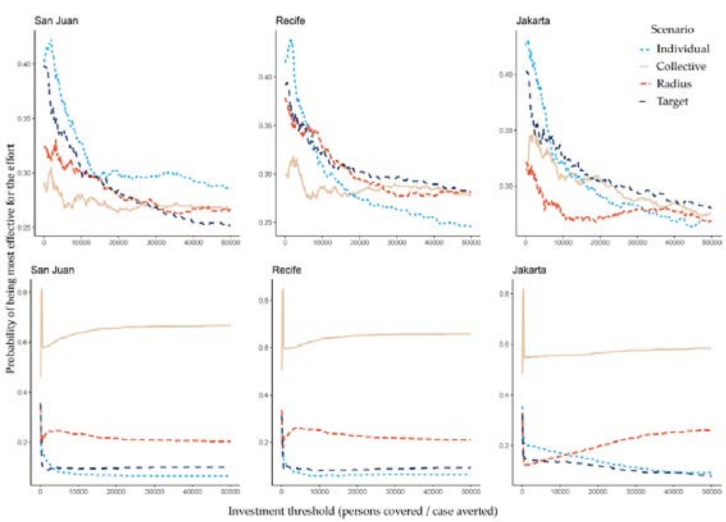
Model outcomes comparing mosquito control strategies to combat Zika virus in different cities



Stone, Schwab, Fonseca, Fefferman. *PLoS NTD* 2020

Sometimes we use predicted curves, sometimes we use theoretical thresholds

Together, these are the critical tools of mathematical epidemiology



$$R_0 = \frac{(Rate1) * S_{today}}{(Rate2)}$$

Moral: Math Models Keep Us All Safer

- **Thank you for your participation!**

Questions? Please use the Question button on Zoom to post these

NIMBioS
National Institute for Mathematical and Biological Synthesis