Mathematical Modeling to Inform Early Outbreak Response

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Up front advertisement

I and other mathematical biologists around Australia are always interested in PhD students.

If you're interested, I can talk to you about opportunities here, or put you in touch with others.

Context/Background

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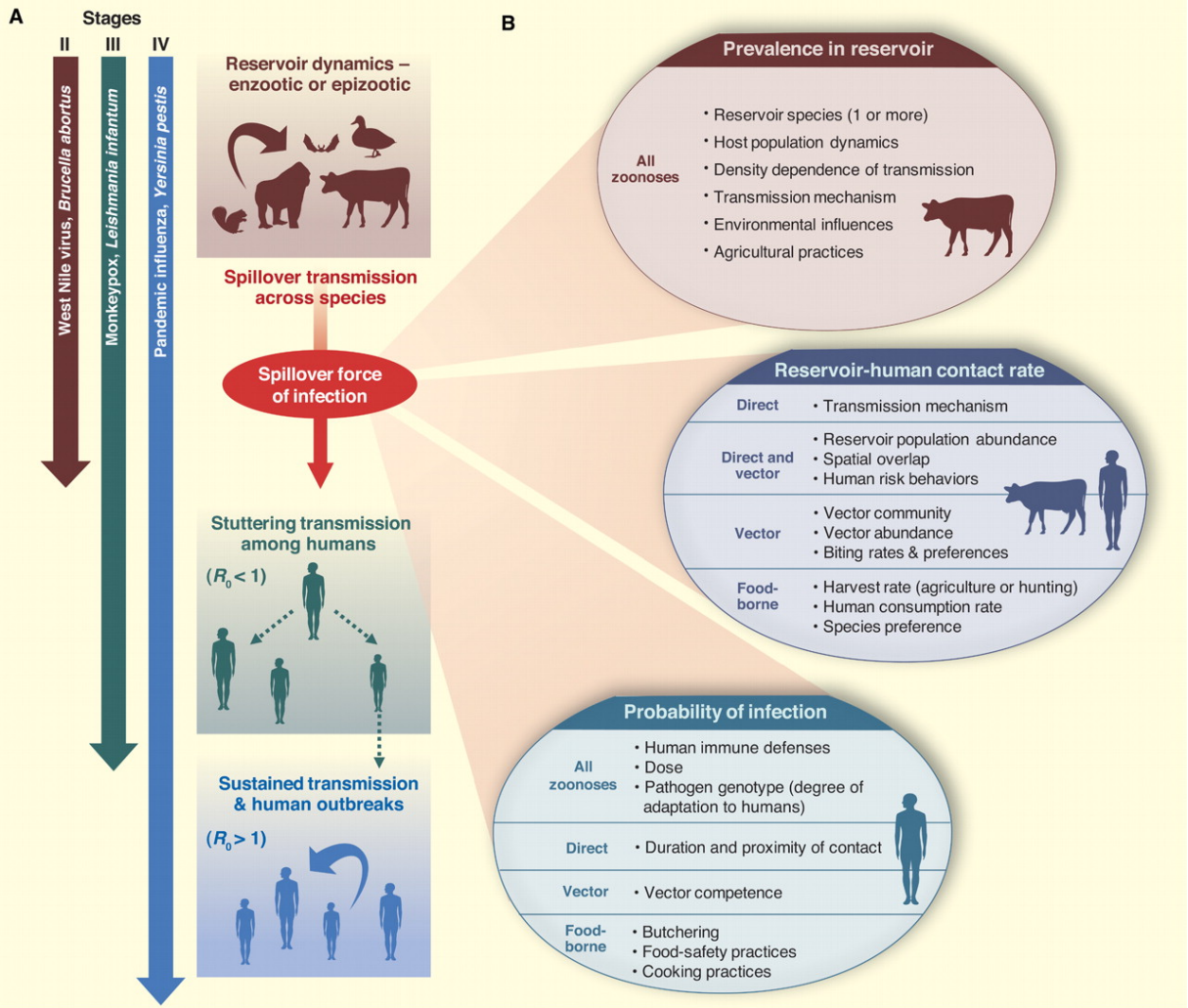
- 2019–Present La Trobe University
  - 2019-2020 Coronavirus — .

Many other small outbreaks have occurred in this time.

Zoonoses



Lloyd-Smith et al Epidemic dynamics at the human-animal interface

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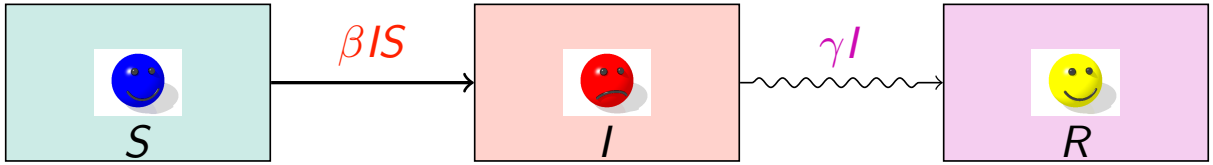
Common Problem in all stages:
Incomplete data and urgent policy choices.

Basic Mathematical Model

Set S, I, and R to be the susceptible, infected, and recovered fractions.



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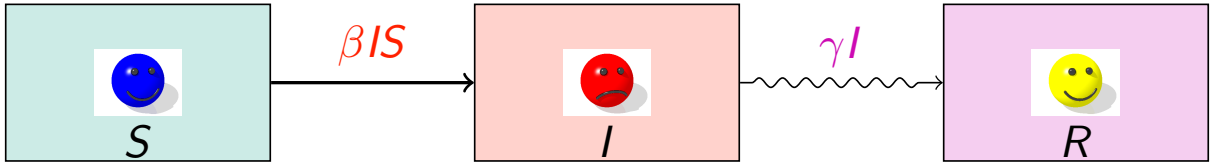

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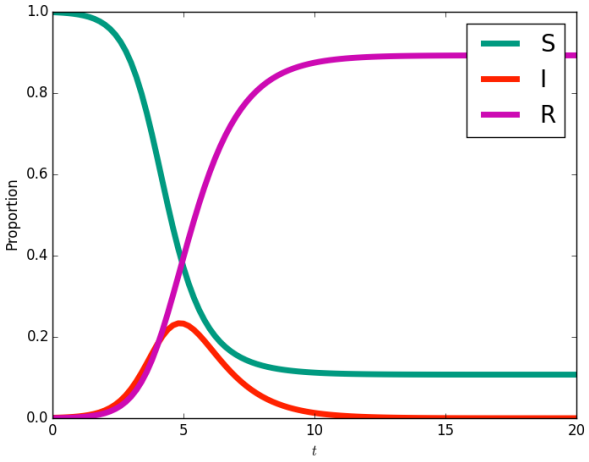

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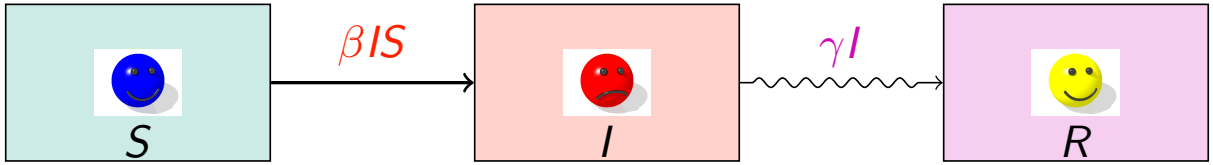

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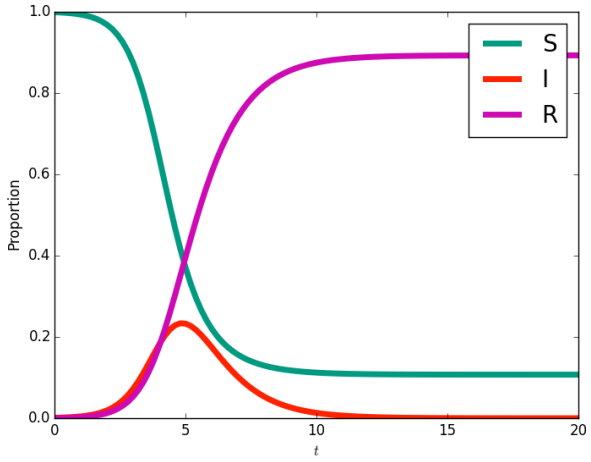

Note — early exponential growth: $\frac{d}{dt}I = (\beta S - \gamma)I \approx (\beta - \gamma)I$.

Topics for this talk

- How many Infected?
- Case Fatality Ratio?
- Asymptomatic Transmission?
- How will newly introduced clusters behave?
- Impact of one-off interventions?
- Not going to touch travel restrictions...

How many infections?

- One of the most critical things to know early on is how many cases have there been.
- The local health system is probably overwhelmed
  - Not testing mild cases.
  - Too busy treating cases to report data.
  - May not have the capacity to perform tests

Counting Exported Cases (H1N1)

Total number infected $\approx$ (Population size) $*$ (per-person risk)
Estimate per-person risk from people who travel.

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Table 1. Cases of novel influenza A/H1N1 among travelers to Mexico from three countries as of May 6, 2009 (Canada) or May 8, 2009 (US, UK, Spain) and associated estimates.

	US (confirmed+probable)	Canada (confirmed)	UK (confirmed)	Spain (confirmed)	Total
Cases with Mexico travel history	132	62	19	70	283
Cases with travel history known/total cases	928/1890	86/179	37/38	93/93	
With only one case per possible cluster, and near border cases removed	85	56	17	no data to assess clusters; 70 assumed	228
Travel volume for April	526,861	119,473	22,013	20,903	668,347
Inferred incidence rate (/million person-days)	72	148	246	957	117
Inferred cases in Mexico	229,000	475,000	789,000	3,062,000	375,000
Inferred incidence rate (/million person-days)*	18	44	55	241	35
Inferred cases in Mexico*	*59,000*	*142,000*	*178,000*	*771,000*	*113,000*

doi:10.1371/journal.pone.0006895.t001

Lipsitch et al 2009

Counting Exported Cases (nCoV)

Table 1: Estimated case numbers based on the baseline assumptions and alternative scenarios explored.

	Baseline[1]	**Smaller catchment[1]**	**Shorter detection window[1]**	**6 exported cases**	**8 exported cases**
Exported number of confirmed cases[2]	7	7	7	6	8
Daily international passengers travelling out of Wuhan International Airport[3]	3,301	3,301	3,301	3,301	3,301
Effective catchment population of Wuhan International Airport	19 million	11 million	19 million	19 million	19 million
Detection window (days)	10 days	10 days	8 days	10 days	10 days
Estimated total number of cases (95% CI)	4,000 (1,700 – 7,800)	2,300 (1,000 – 4,500)	5,000 (2,200 – 9,700)	3,400 (1,400 – 7,000)	4,600 (2,100 – 8,600)

Case Fatality Ratio

From The Conversation:

> Up to January 22, 17 deaths have tragically occurred from 582 cases (about 3%). This is lower than the proportion who die from influenza-associated pneumonia, which one study estimated to be 10%. It's a crude comparison, but one we can at least mull over for now.

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and in another article:

- **It's not yet severe**. Fewer than 100 people have died so far. The mortality rate is just under 3%. China has moved aggressively to contain the virus meaning it should have have less impact on gross domestic product than earlier pandemics.

Potential Bias

Potential Biases in Estimating Absolute and Relative Case-Fatality Risks during Outbreaks – Lipsitch et al

- We may underestimate total number of cases (because less severe cases missed)
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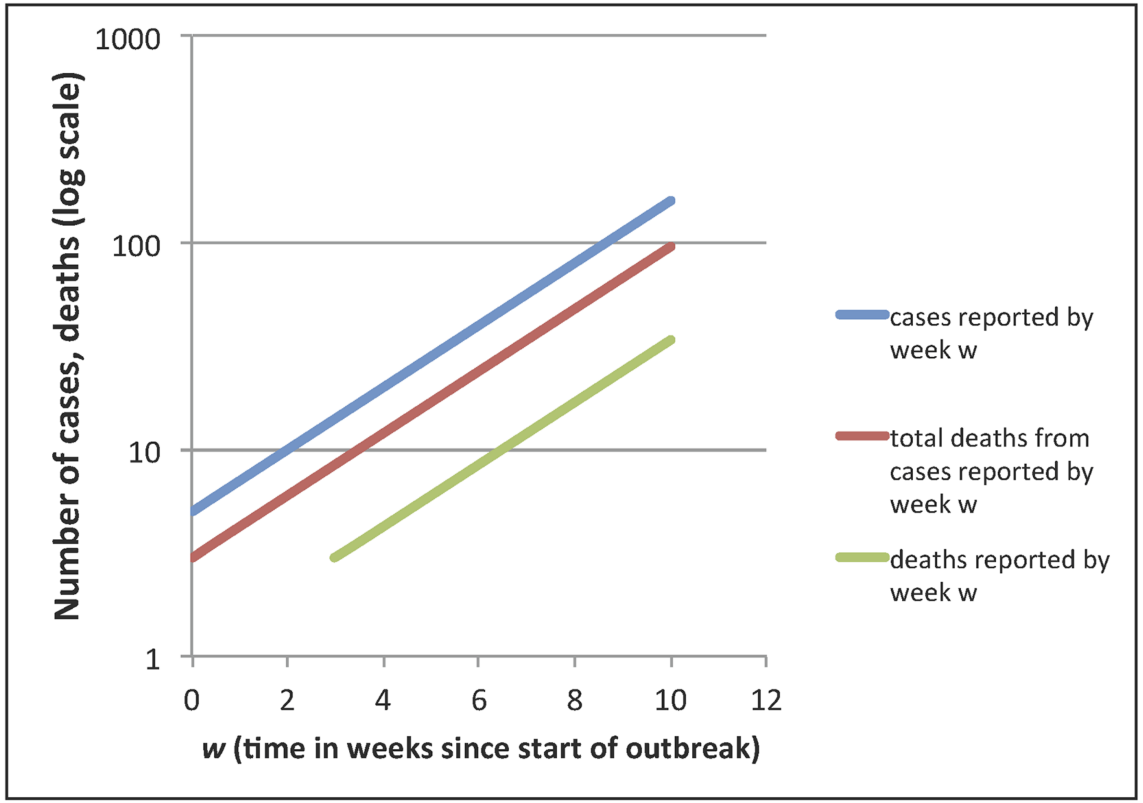

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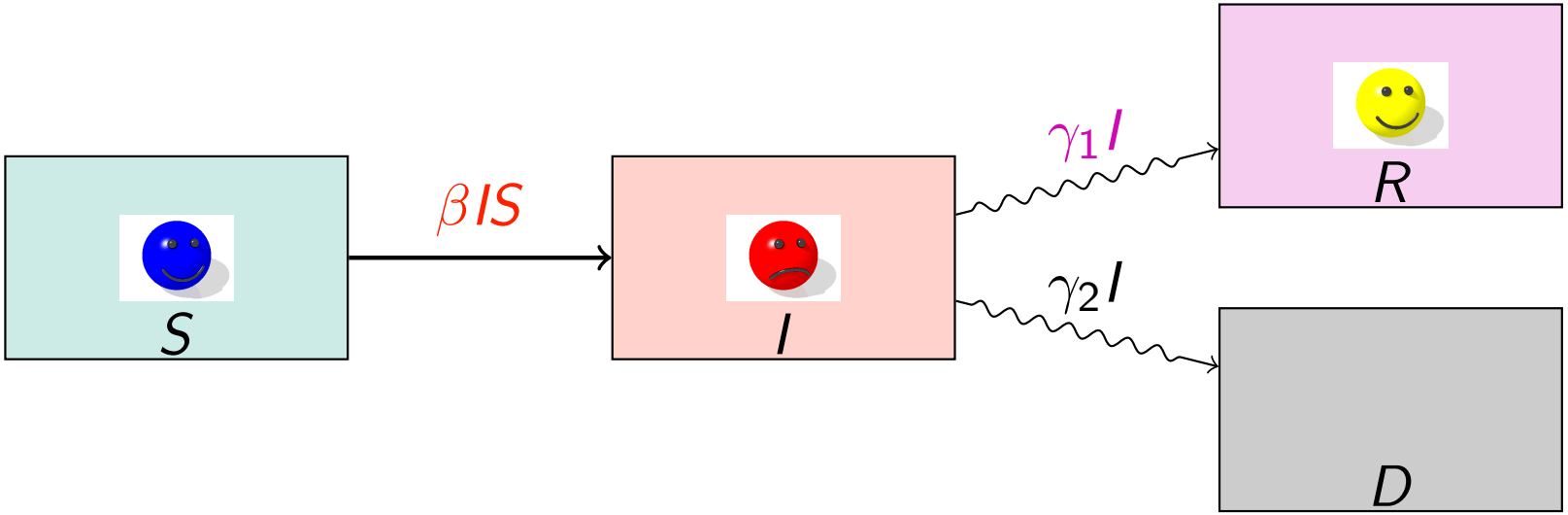

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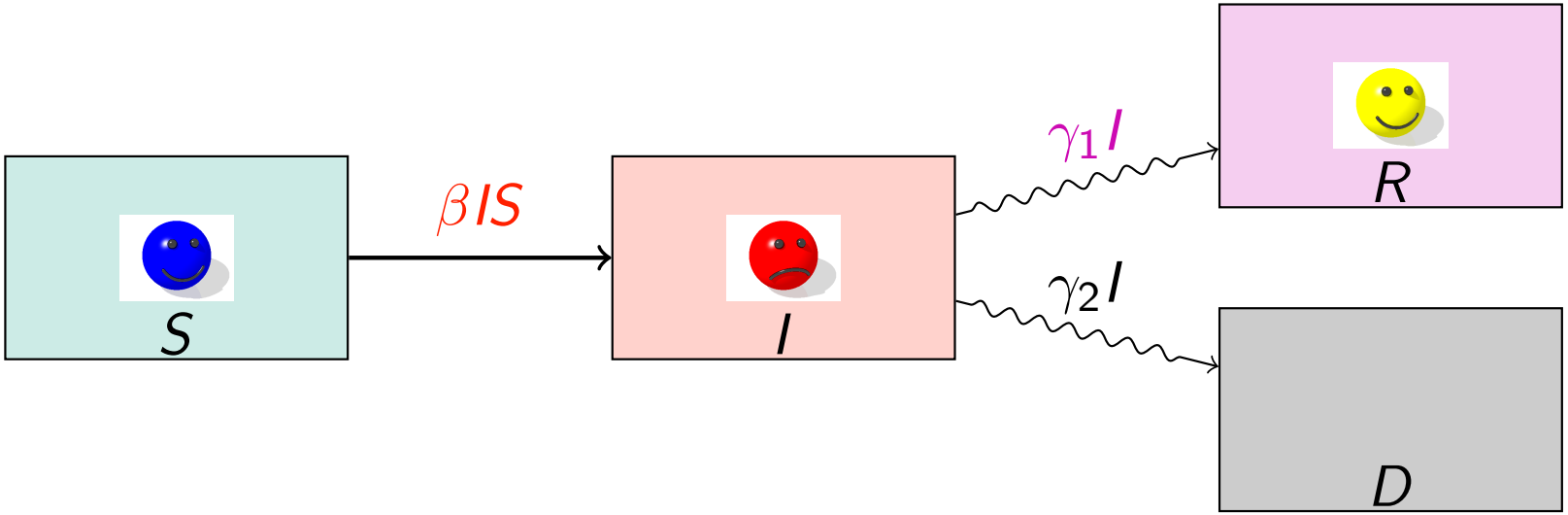

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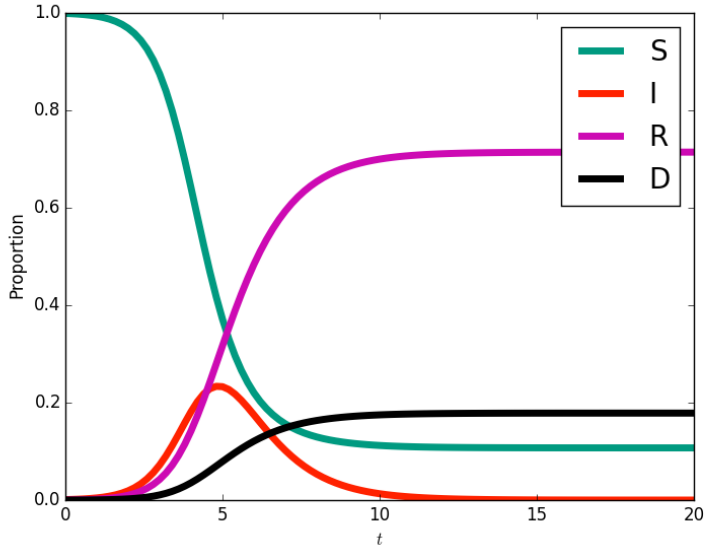
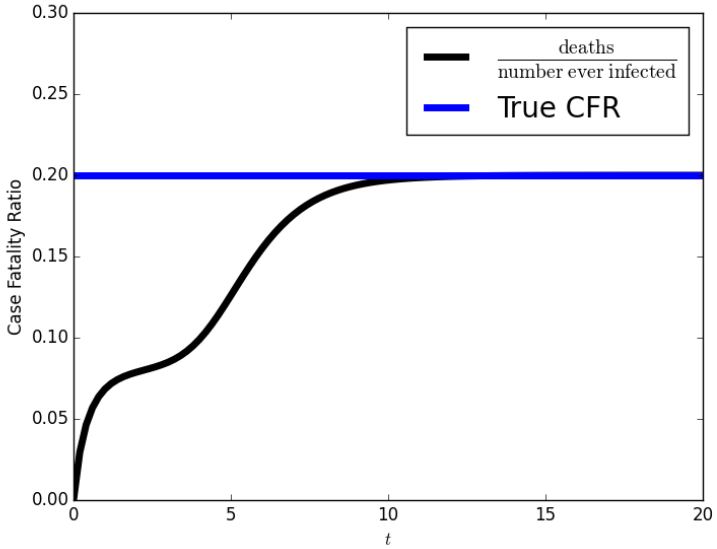
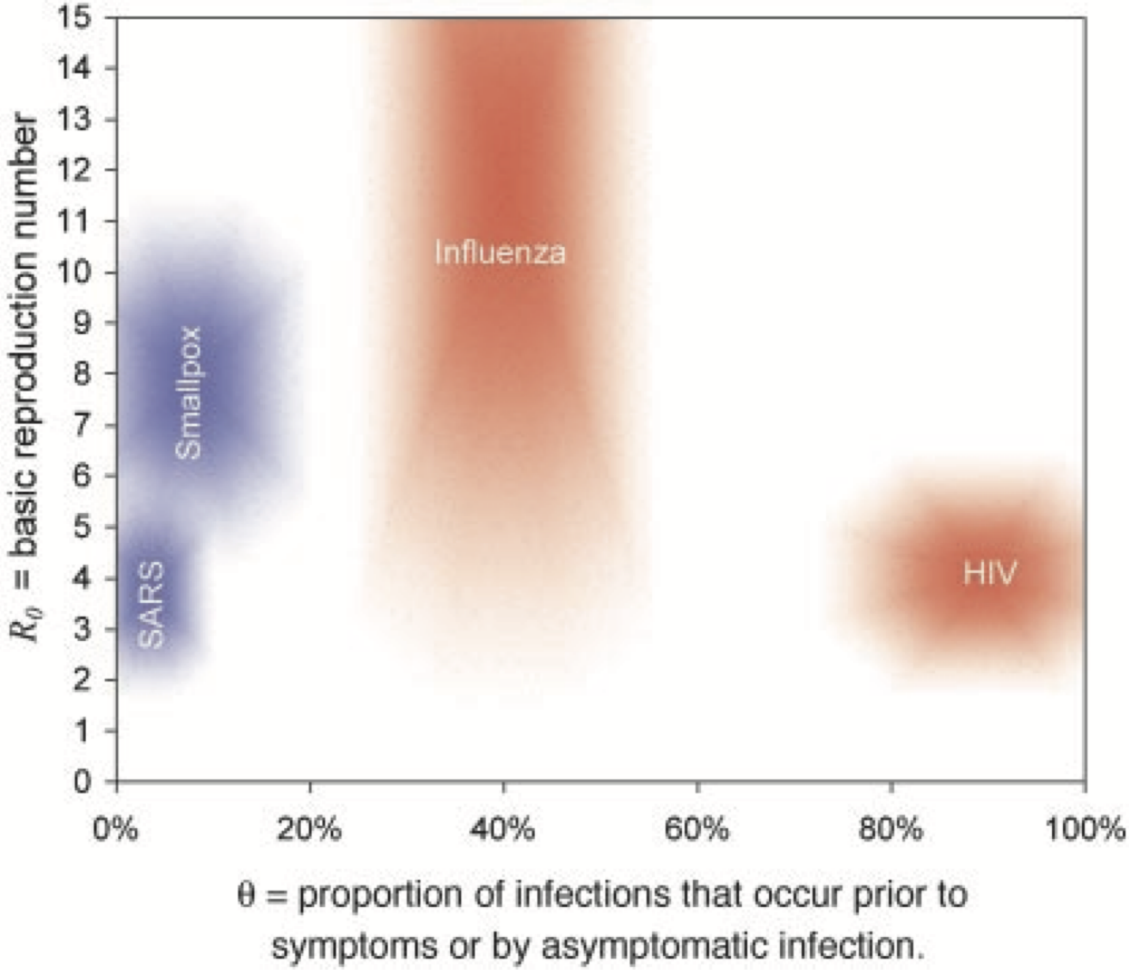




What makes a disease controllable?

Factors that make an infectious disease outbreak controllable
C. Fraser et al



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- If a proportion θ of these occur before symptom onset, then completely effective targeting of symptomatic people could reduce the average number of infections to $\mathcal{R}_0\theta$.

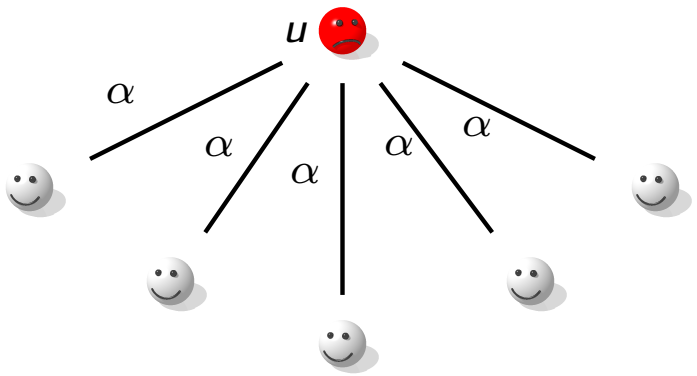
Early behavior of new clusters

Once the disease is spreading in one location there will be travel-related spread.

- How likely is a new cluster to go extinct (on its own)?
- If it doesn't go extinct, what happens?
- Let's assume an infected individual transmits to k individuals with probability p_k (the <u>offspring distribution</u>).

Extinction Probability

(assuming the same offspring distribution for all individuals).



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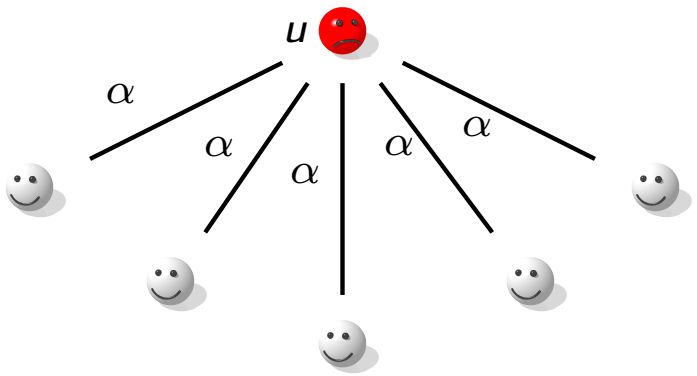

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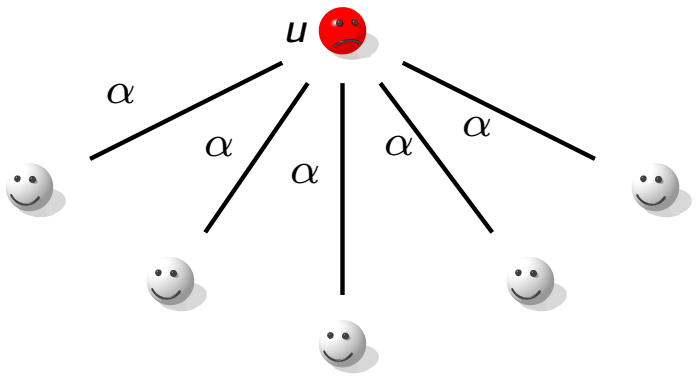

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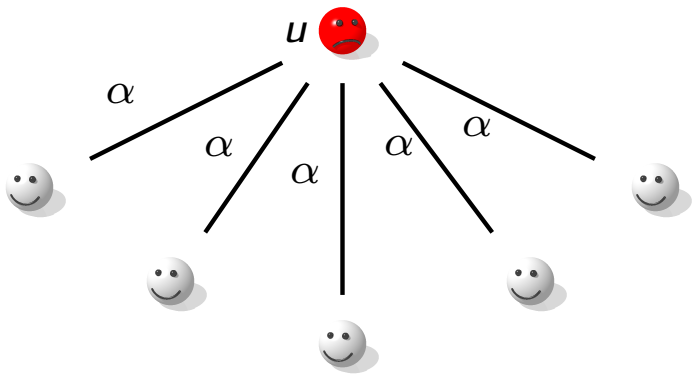

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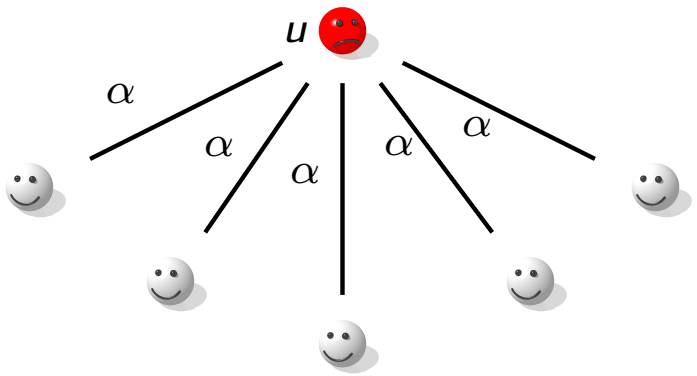

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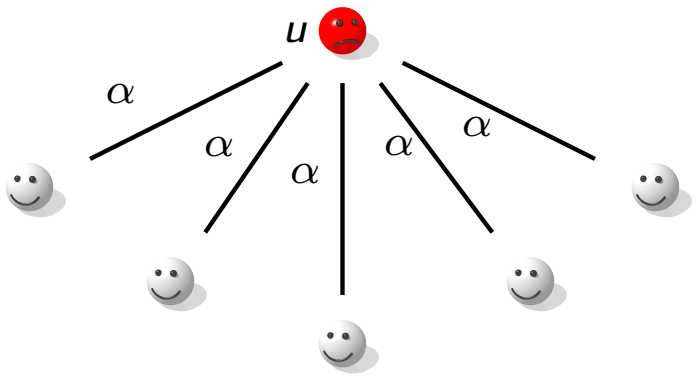

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We can calculate α iteratively by solving $\alpha_{g_1} = \psi(\alpha_g)$ starting from $\alpha_0 = 0$.

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- Yet we've seen that the extinction probability is α.
- The non-extinct outbreaks must get all of the missing cases.
- So setting the average size of non-extinct outbreaks to X, we find $\alpha \cdot 0 + (1-\alpha)X = \mathcal{R}_0^g$.

$$X = \frac{\mathcal{R}_0^g}{1-\alpha}$$

One-shot interventions

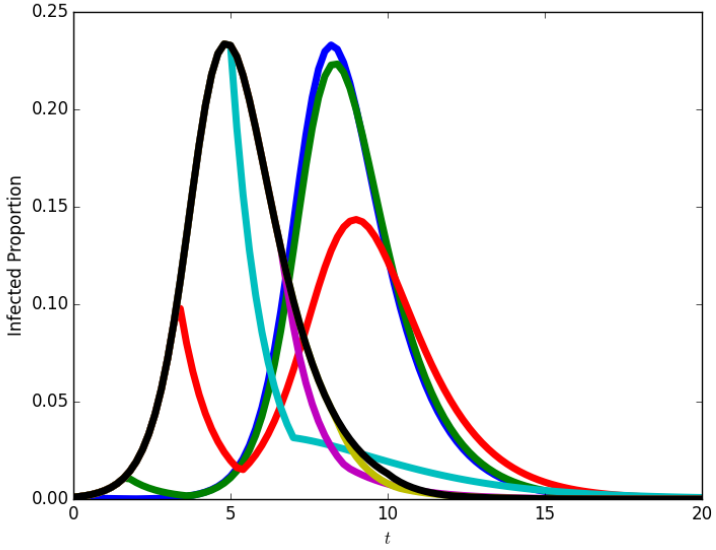
Imagine we have an intervention (say a school closing) which is too expensive to maintain long-term. We have one chance to implement it.
Should we use it as soon as there are any cases?

One-shot interventions

This corresponds to a temporary reduction in β:

$$\frac{d}{dt}S = -\beta IS$$
$$\frac{d}{dt}I = \beta IS - \gamma I$$
$$\frac{d}{dt}R = \gamma I$$

sample solutions



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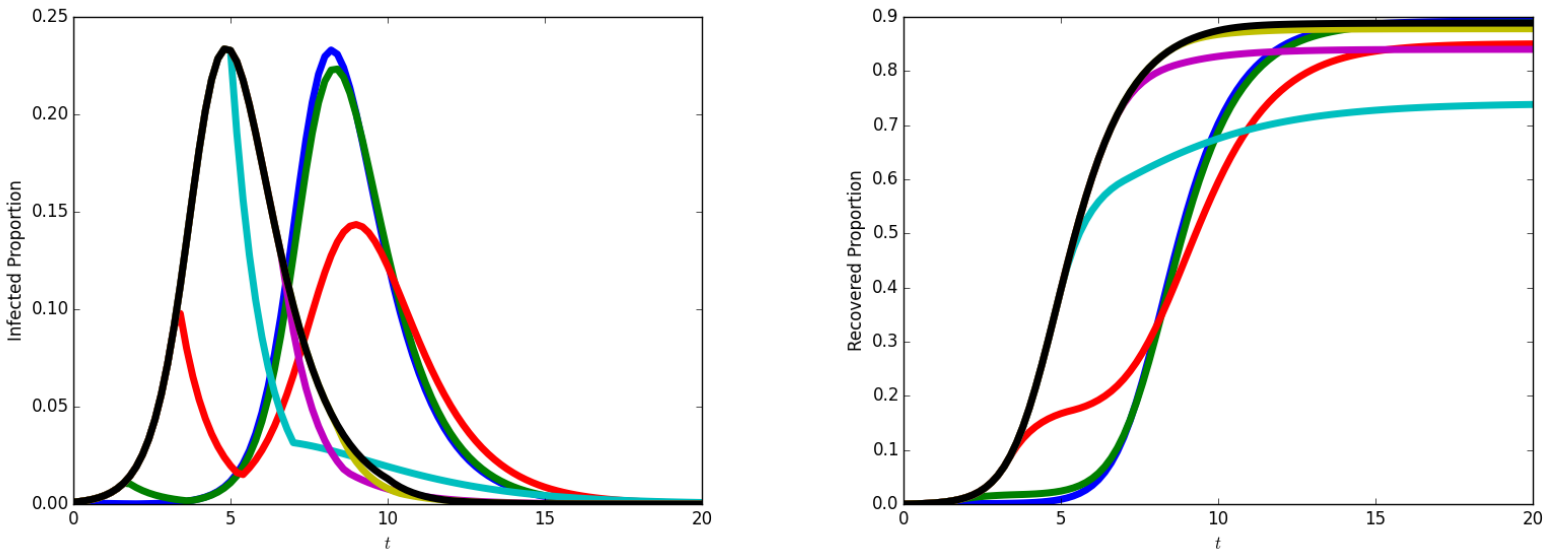

So if the disease is later reintroduced intervening too early won't accomplish anything except delay the peak. But intervening too late also won't accomplish anything.

Discussion

Hopefully I've given a taste of some common questions that policy makers face when responding to an emerging epidemic, and how mathematics can give insights.