February 10, 2020
Coronavirus Forum
Center for Microbial Dynamics and Infection
Georgia Institute of Technology

Estimating the strength, speed, and final size of disease outbreaks: application to 2019-nCoV

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Technical References:
Sang Woo Park et al. (in review & available on medrxiv: 2020.01.30.20019877v3)
Sang Woo Park et al., *Epidemics* 27:12 (2019)
Taylor et al. J. Theor. Biol. 408: 145-154 (2016)
Weitz & Dushoff, *Scientific Reports* 5: 8751 (2015)

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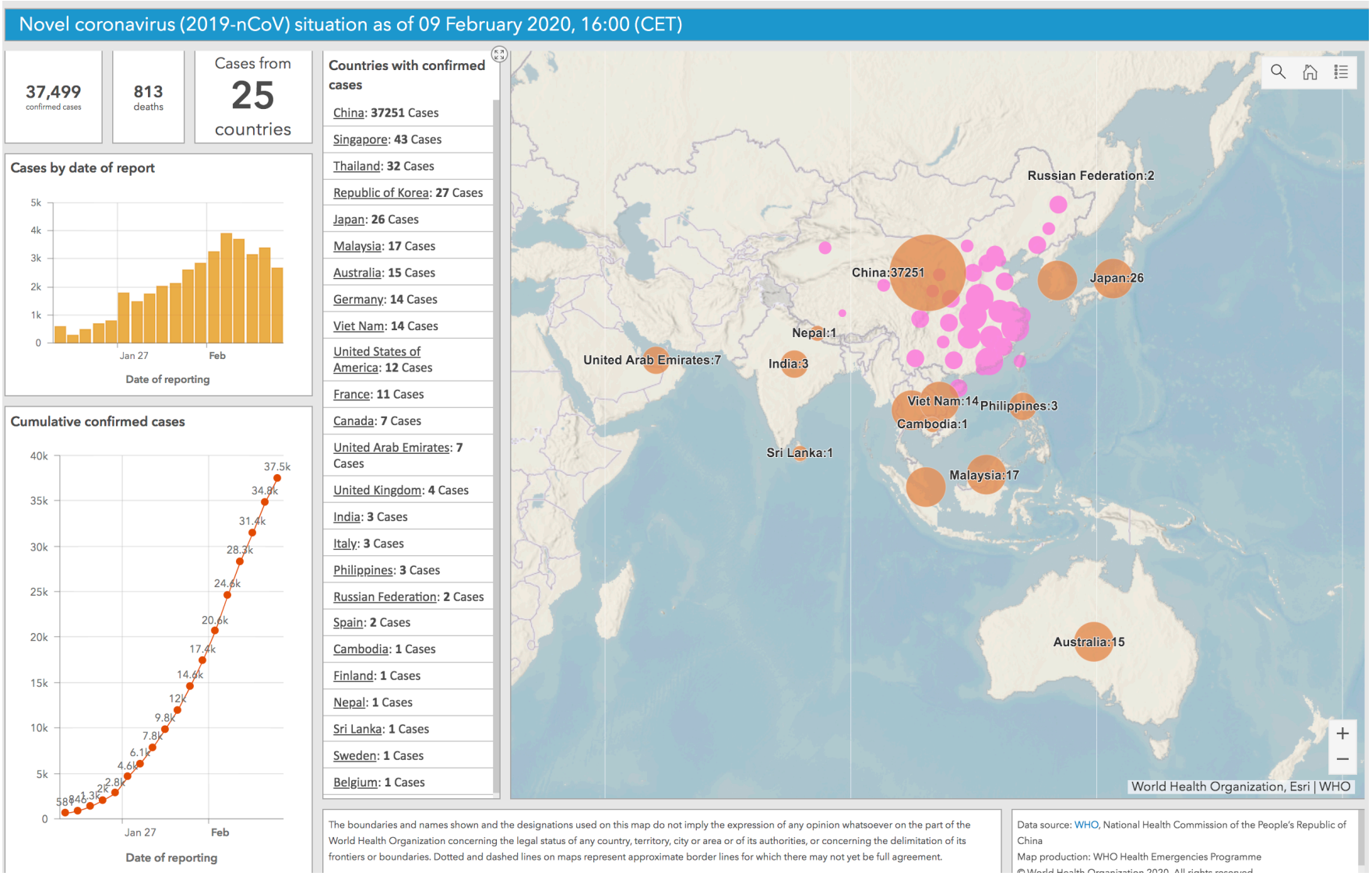
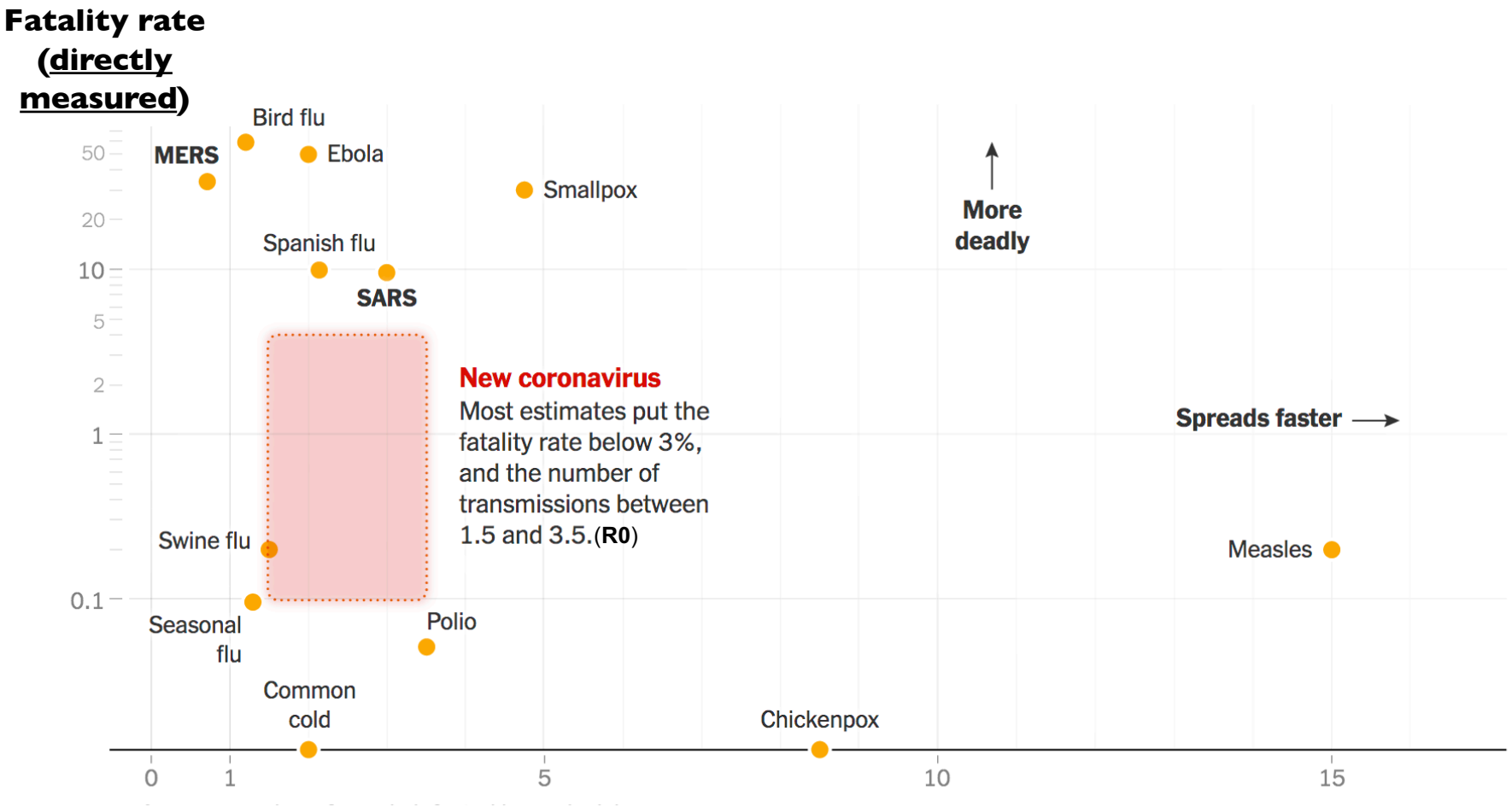


Source: WHO, Feb 9, 2020

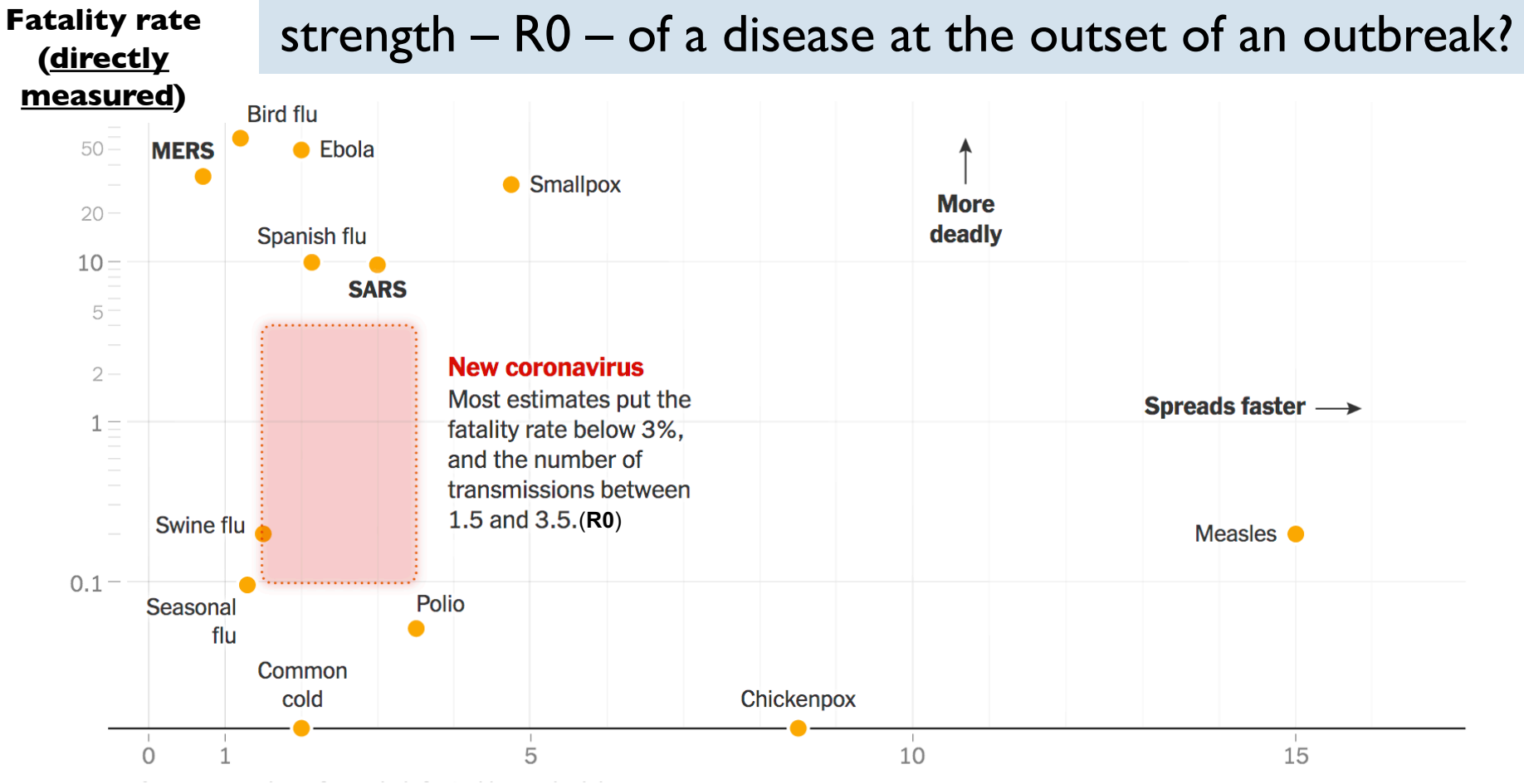


Basic reproductive number, "R0"
Equal to the average number of new infections per sick person
Indirectly measured

Source: NY Times, Feb 7, 2020

Question Motivating Today's Talk:

How certain should we be about estimates of the strength – R0 – of a disease at the outset of an outbreak?



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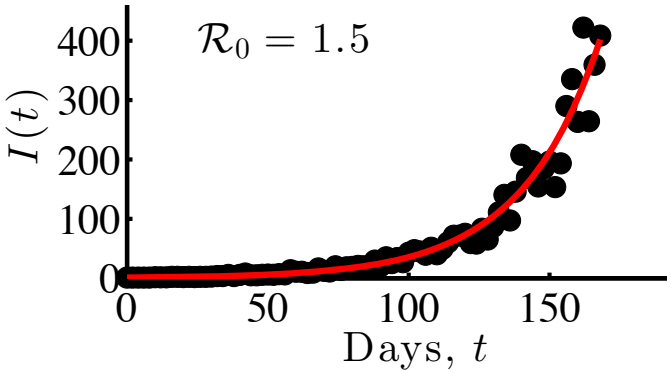
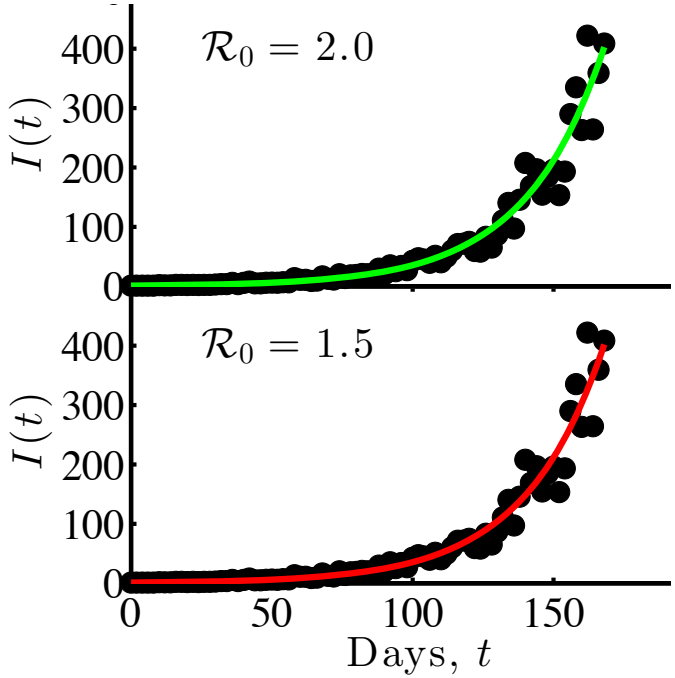
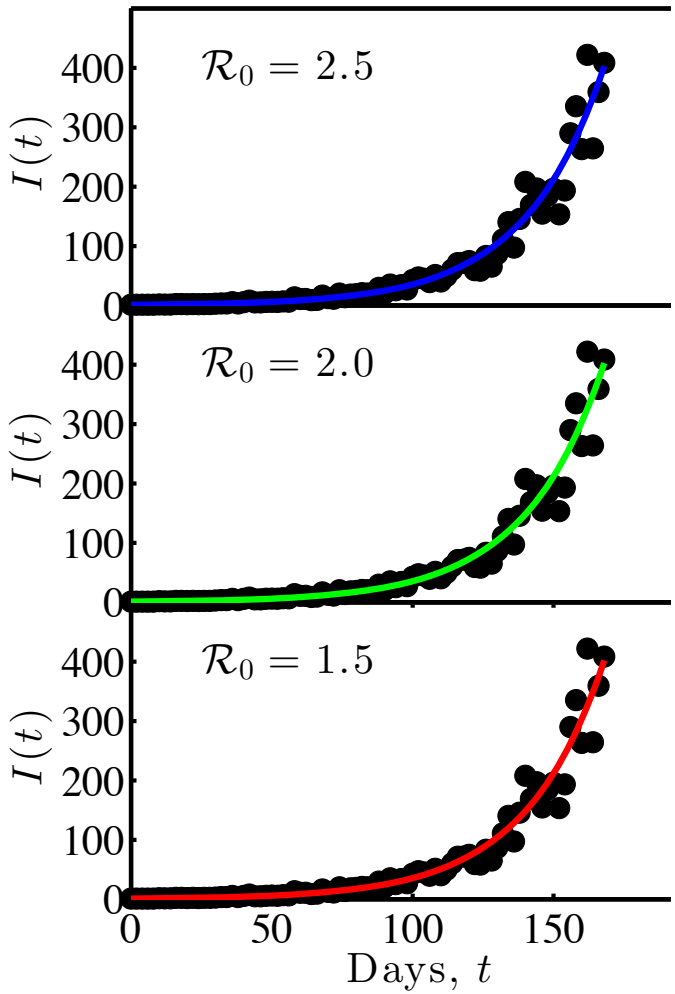

$\mathcal{R}_0 = 1.5$
400
300
200
100
0
$I(t)$
0
50
100
150
Days, t


$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
$I(t)$
400
300
200
100
0
400
300
200
100
0
0
50
100
150
Days, t


$\mathcal{R}_0 = 2.5$
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$I(t)$
0
100
200
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400
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100
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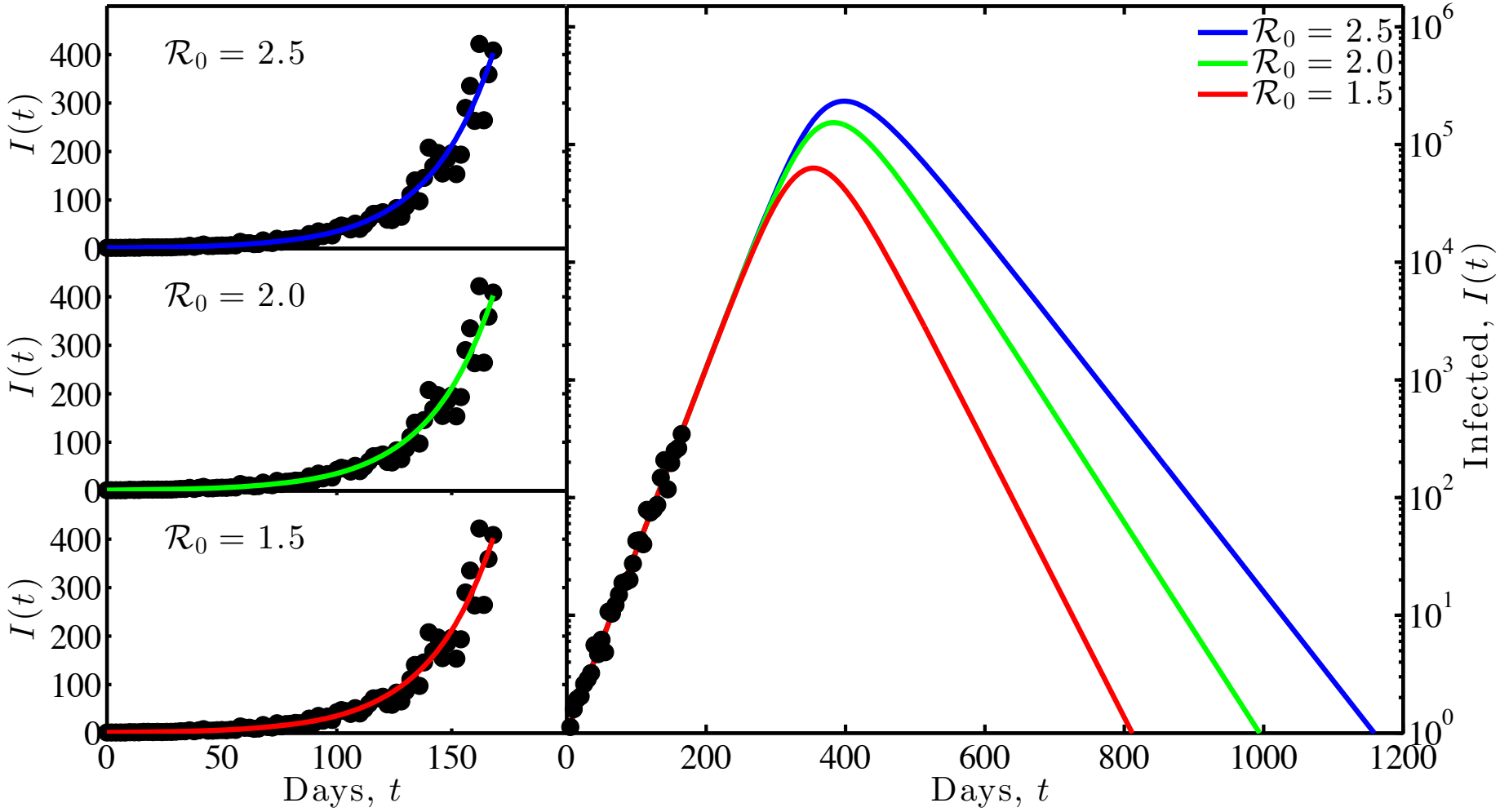
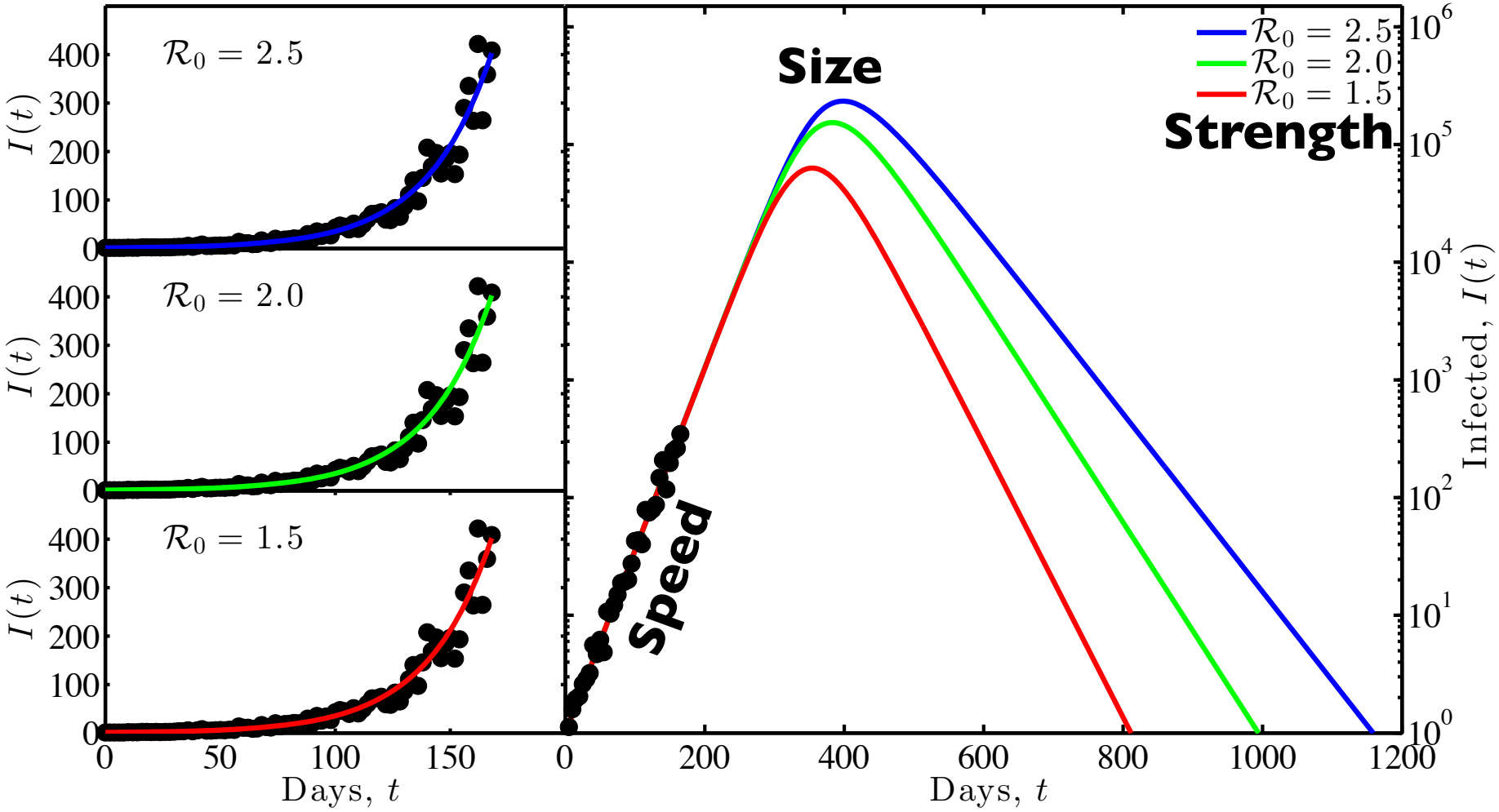
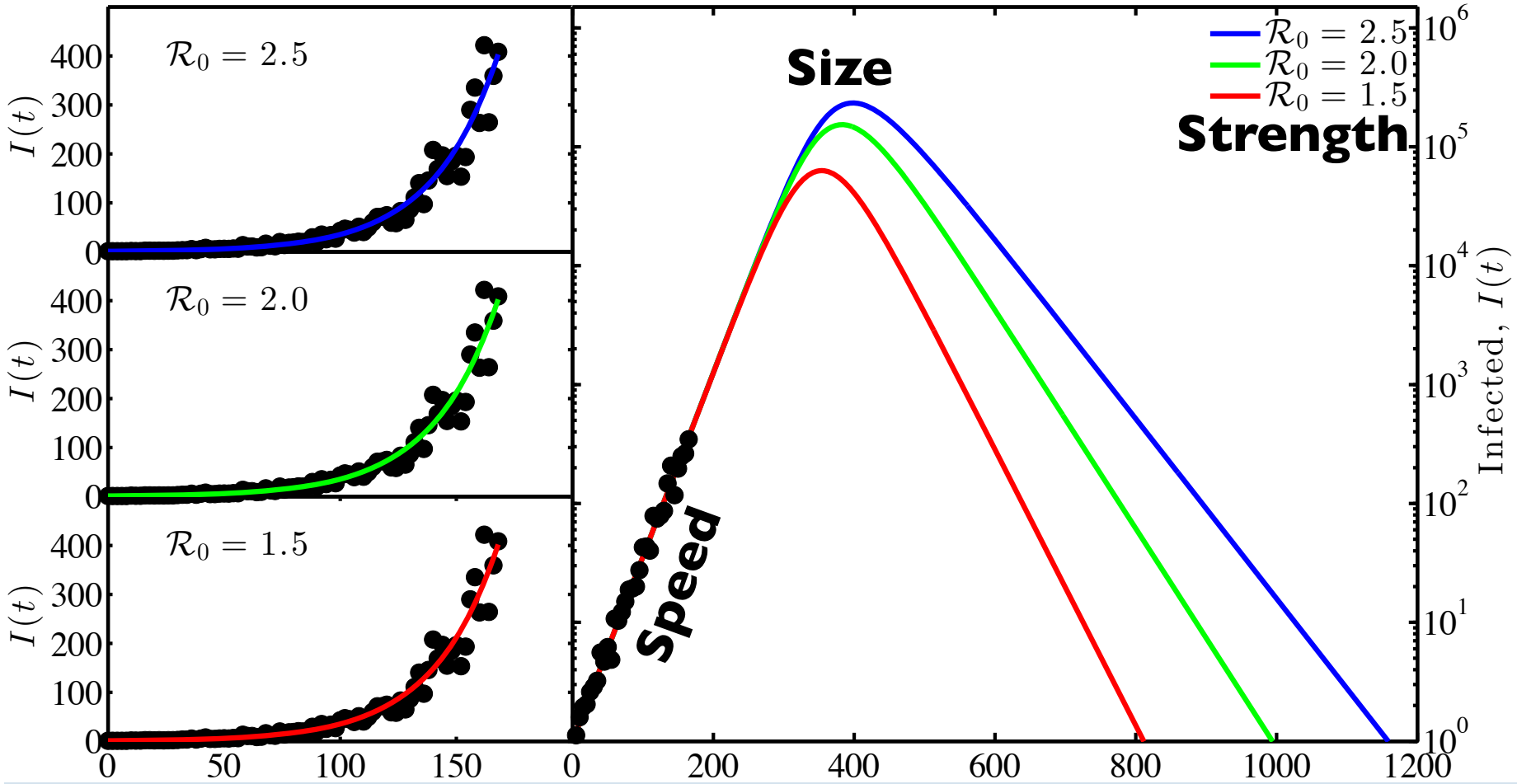
Days, t

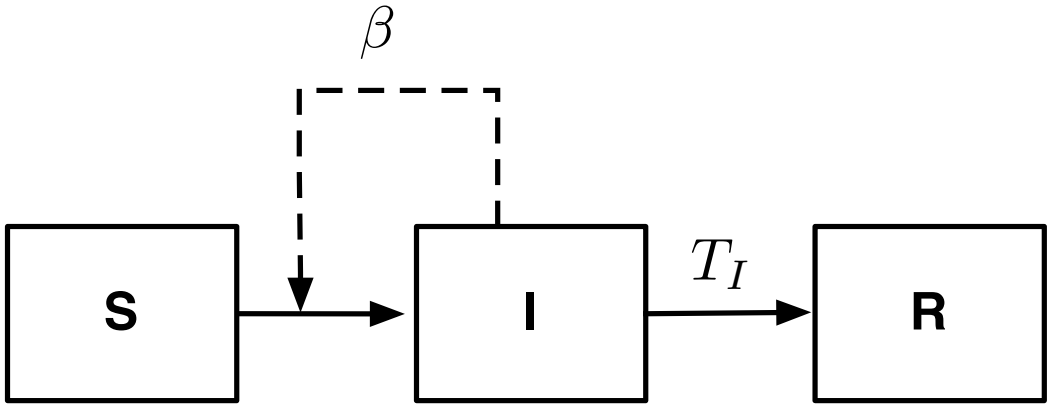

$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
0
100
200
300
400
0
50
100
150
Days, t
0
200
400
600
800
1000
1200
Days, t
10^0
10^1
10^2
10^3
10^4
10^5
10^6
Infected, $I(t)$


$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
0
100
200
300
400
0
50
100
150
Days, t
Size
Strength
Speed
0
200
400
600
800
1000
1200
Days, t
10^0
10^1
10^2
10^3
10^4
10^5
10^6
Infected, $I(t)$



Tentative conclusion: Many values of R0 can be compatible with the same observed rate of increase in cases – even if projected outbreak sizes are different.

SIR Model - Basics



Population "Classes"

S – The number of susceptible individuals

I – The number of infectious individuals

R – The number of "removed" individuals (through recovery or, possibly, death)

Mechanisms

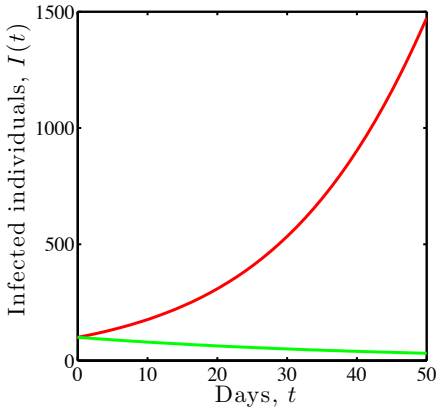
Infection: Requiring contact between a ***S*** and a ***I*** individual at rate β.

Recovery: After a period of infectiousness of average duration T_I.

SIR Model – Initial Dynamics Depend on Basic Reproductive Number, R_0

The expected number of cases, initially changes like:

$$\dot{I} = \frac{I}{T_I}\left(\mathcal{R}_0 - 1\right)$$



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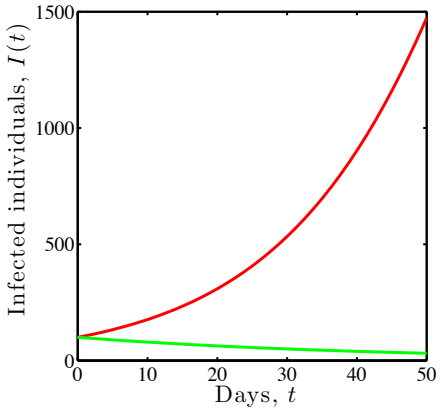

where

$$\mathcal{R}_0 \equiv \overbrace{\beta}^{\text{infections per time}} \times \overbrace{T_I}^{\text{infectious period}}$$

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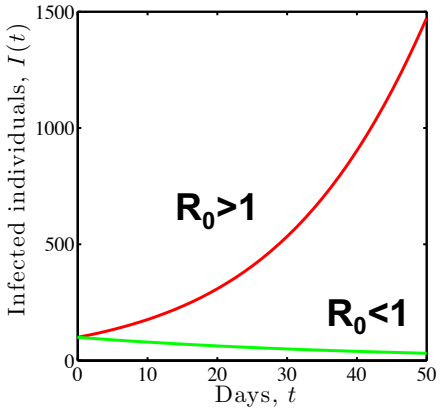


where

$$\mathcal{R}_0 \equiv \overbrace{\beta}^{\text{infections per time}} \times \overbrace{T_I}^{\text{infectious period}}$$

such that

- Disease spreads whenever the average number of new cases exceeds unity, i.e: $\mathcal{R}_0 > 1$
- The increase is exponential

Estimating, R_0, for 2019-nCoV

	Basic reproductive number $\mathcal{R}_0$
Study 1	1.5–3.5
Study 2	2.5 (1.5–3.5)*
Study 3	2.92 (95% CI: 2.28–3.67)
Study 4	3.8 (95% CI: 3.6–4.0)
Study 5	2.2 (90% CI: 1.4–3.8)
Study 6	5.47 (95% CI: 4.16–7.10)‡
Study 7	2.0–3.1

Bedford *et al.* [4]
Imai *et al.* [5]
Liu *et al.* [6]
Read *et al.* [8]
Riou and Althaus [10]
Zhao *et al.* [9]
Majumder and Mandl [7]

Many model choices:

Branching process

SEIR model (like SIR but with an asymptomatic class)

Exponential growth…

Estimating, R_0, for 2019-nCoV

	Basic reproductive number $\mathcal{R}_0$	Mean generation interval $\bar{G}$ (days)	Generation-interval dispersion κ	
Study 1	1.5–3.5	10	1	Bedford *et al.* [4]
Study 2	2.5 (1.5–3.5)*	8.4	unspecified†	Imai *et al.* [5]
Study 3	2.92 (95% CI: 2.28–3.67)	8.4	0.2	Liu *et al.* [6]
Study 4	3.8 (95% CI: 3.6–4.0)	7.6	0.5	Read *et al.* [8]
Study 5	2.2 (90% CI: 1.4–3.8)	7–14	0.5	Riou and Althaus [10]
Study 6	5.47 (95% CI: 4.16–7.10)‡	7.6–8.4	0.2	Zhao *et al.* [9]
Study 7	2.0–3.1	6–10	0	Majumder and Mandl [7]

Many model choices & latent assumptions:

Branching process

SEIR model (like SIR but with an asymptomatic class)

Exponential growth…

How to reconcile and weight different models to get a pooled estimate and uncertainty in R0?

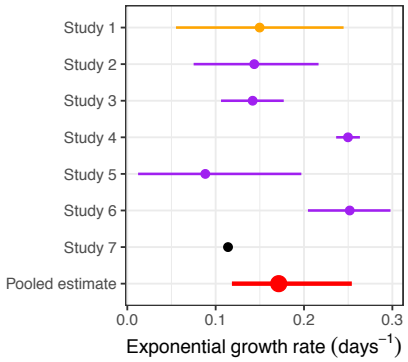
Pooled estimates via a speed-strength relationship

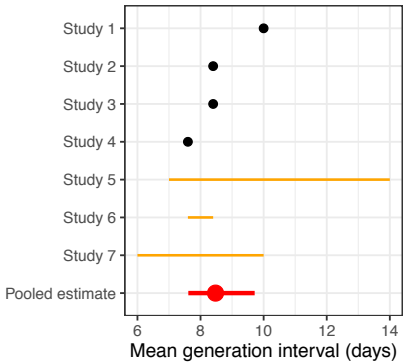
(technically using generation intervals)

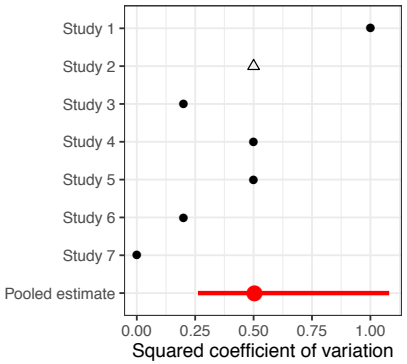
Sang Woo Park

Jonathan Dushoff

Step 1: estimate latent uncertainty in 'parameters'.







Pooled estimates via a speed-strength relationship

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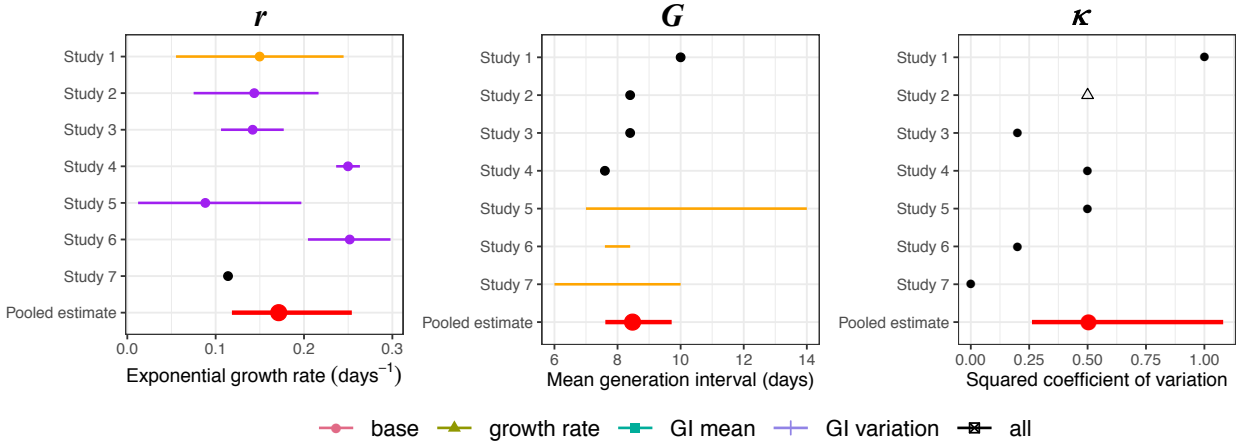
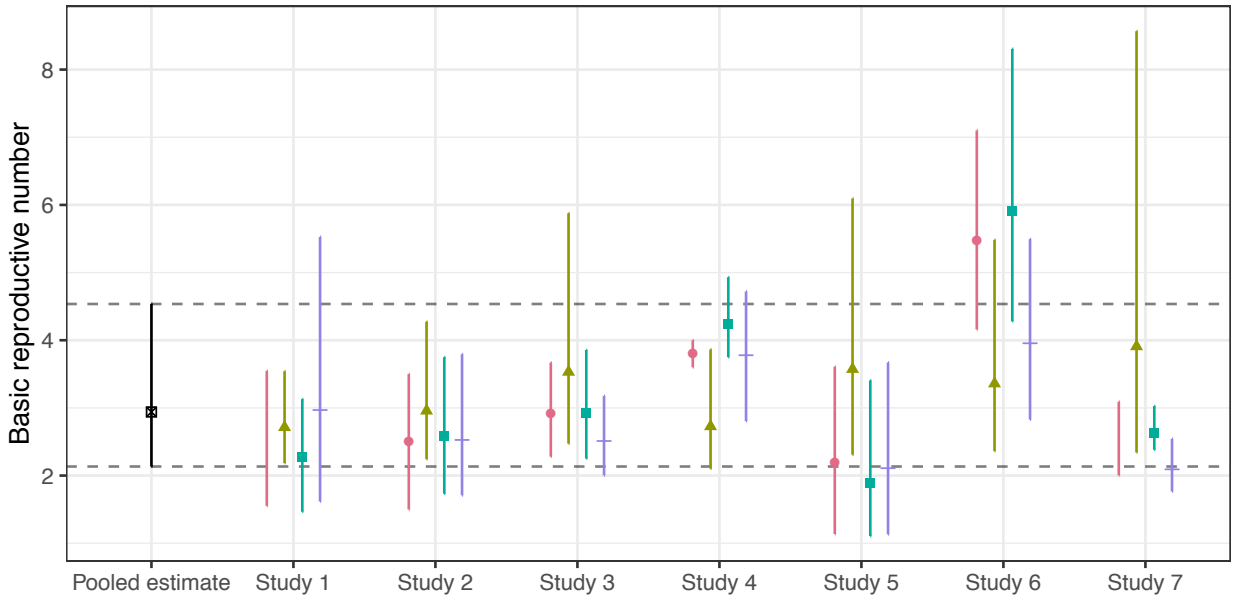


Step 2: incorporate different types of uncertainty into R0 estimates by study or as part of a 'pooled' estimate (using a Bayesian multi-level model)

$$\mathcal{R}_0 = \left(1 + \kappa r \bar{G}\right)^{1/\kappa}$$



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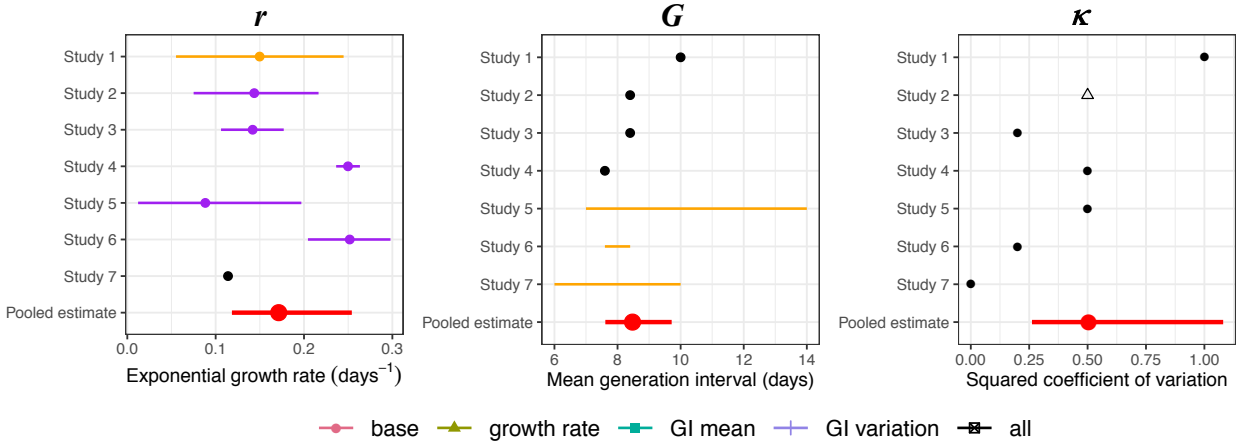

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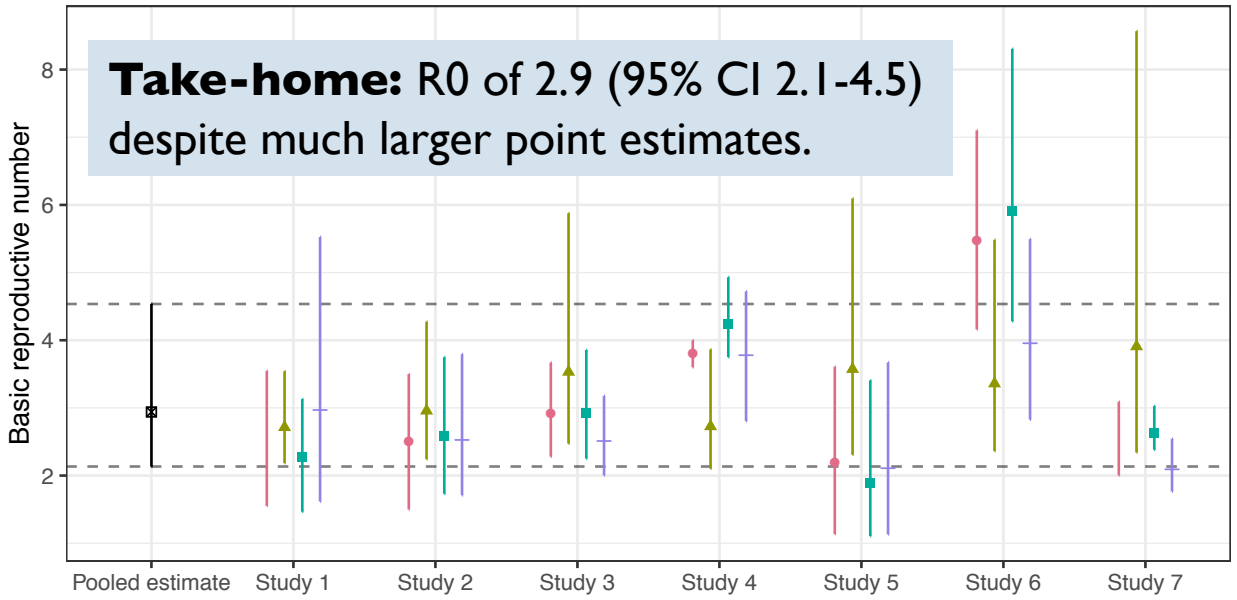


Conditions for epidemic growth

$$\mathcal{R}_0 \equiv \overbrace{\beta}^{\text{infections per time}} \times \overbrace{T_I}^{\text{infectious period}}$$

Where infections per time, β, is a product of:

- Contacts by infectious individuals per unit time
- Probability of contact with a susceptible (S_0/N)
- Probability that the contact transmits the disease

Conditions for epidemic growth also suggest opportunities for **control**

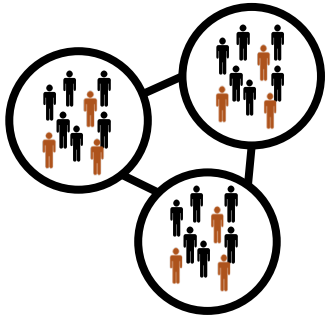
$$\mathcal{R}_0 \equiv \overbrace{\beta}^{\text{infections per time}} \times \overbrace{T_I}^{\text{infectious period}}$$

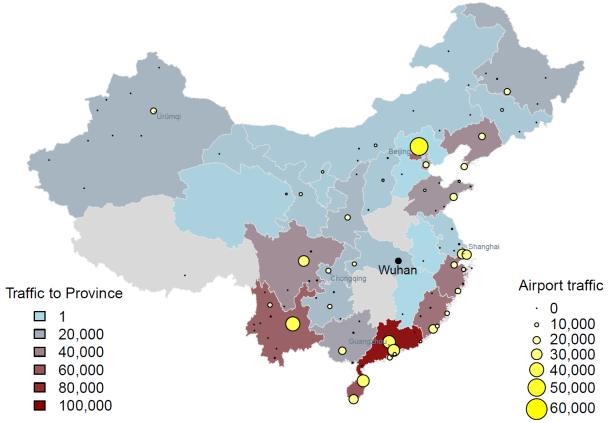
Hospitalization & treatment

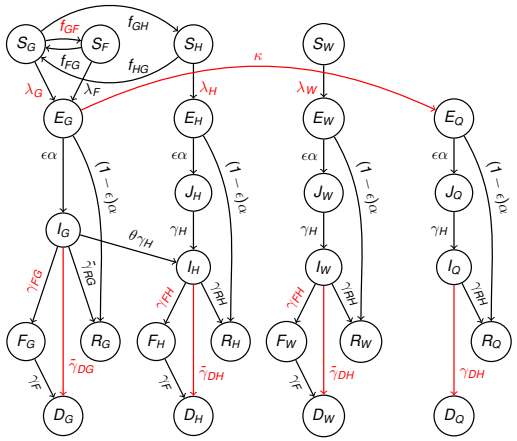
Where infections per time, β, is a product of:

- Contacts by infectious individuals per unit time — **Contact tracing & targeted isolation**
- Probability of contact with a susceptible (S_0/N) — **Vaccination (herd or ring)**
- Probability that the contact transmits the disease — **Process engineering & PPE (masks)**

Next-stage models (and efforts to control)







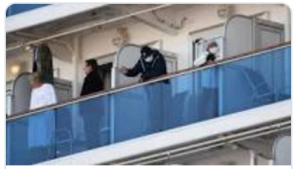
SEIR Metapopulation Model
As per Read et al., medRxiv 2020.01.23.20018549v2

Control (and consequences):
Limiting travel (but also has negative consequences for limiting medical supplies, increasing anxiety, and co-localizing infected patients).

Cruise Ship's Coronavirus Outbreak Leaves Crew Nowhere to Hide

The New York Times

4 hours ago



Diamond Princess Cruise Ship Has 65 More Coronavirus Cases : Goats and…

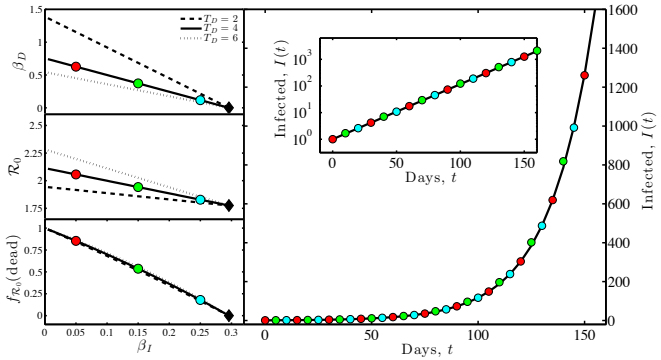
NPR

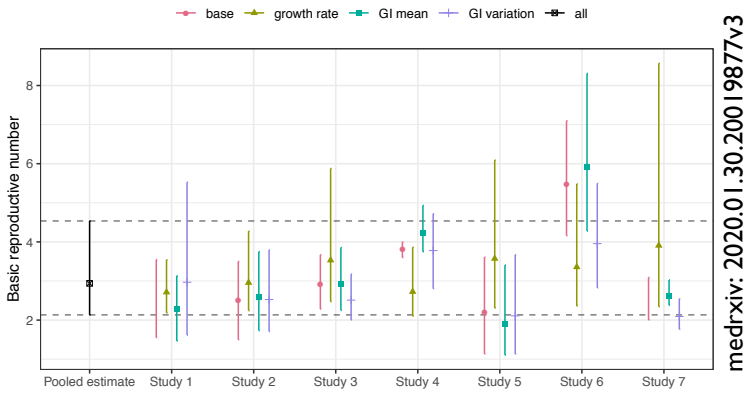
4 hours ago

Category based SEIR model
As per Pandey et al. Science (2014)

Control (and consequences):
Focuses on risk groups, challenging to differentially target accurately given complexity of model.

Estimating the strength, speed, and final size of disease outbreaks: application to 2019-nCoV





medrxiv: 2020.01.30.20019877v3

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Questions?

Acknowledgements
Sang Woo Park, Princeton
Jonathan Dushoff, McMaster
Bradford Taylor, GT (now MSKCC)

Technical References

Park, S W., Bolker, B. M., Champredon, D. Earn, D.J., Li, M., Weitz, J.S., Grenfelll, B.T., and Dushoff, J.D. Reconciling early-outbreak preliminary estimates of the basic reproductive number and its uncertainty: framework and applications to the novel coronavirus (2019-nCoV) outbreak. *Eurosurveillance* in review & medrxiv.

Park, S.W., Champredon, D., Weitz, J.S., and Dushoff, J. (2019) Exploring how generation intervals link strength and speed of epidemics. *Epidemics.* 27: 12-18.

Taylor, B.P., Dushoff, J. and Weitz, J.S. (2016) Stochasticity and the limits to confidence when estimating R0 of Ebola and other emerging infectious diseases. *J. Theor. Biol.* 408: 145-154.

J.S. Weitz and J. Dushoff (2015). Modeling post-death transmission of Ebola: challenges for inference and opportunities for control. Scientific Reports 5: 8751