# Epidemics, Networks, Interventions On Things I Learned About Very Recently

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https://www.bbc.com/news/business-51706225

Source: US Bureau of Labor Statistics

BBC

#### Data scientists Against Corona

#### **Mission Statement**

Without data, society cannot see. And if society cannot see, it cannot act wisely. Our mission is to make our skills as data scientists available to help society in its battle against the Coronavirus by improving its observations of the world. We do this by providing advice and assistance in the analysis of data, as well as initiating novel research projects designed to fully exploit tools of modern dat science.

To get an idea for what we can do for you, take a look at the Projects page.

Do you have a data task that you think we can help with? Then head over to the Data Consultancy Desk to let us know.



https://dataversuscorona.com/

# Outline

- 1) Basic Epidemiological Models
  - a) SIR and SIRS
  - b) SEIRS and SEIRS with Testing
  - c) Interventions
- 2) Epidemics on Networks
  - a) Spatial Structure
  - b) Interventions
- 3) How do the grown-ups model these things?
  - a) Modeling Interventions
  - b) Assessing Interventions

# **Basic Epidemiological Models**

# Preliminaries

- Suppose N is the size of a population
- How does this population change over time?

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \dot{N} = f(N)$$

- Let's look at 
$$\dot{N}=N$$
 and  $\dot{N}=N(1-N)$ 











# Model

 $\dot{S} = -\beta IS$  $I = \beta IS$ 

# $\dot{S} + \dot{I} = 0$ S(t) + I(t) = 1

### $\beta$ ... is the contact rate

(each individual has  $\beta$  contacts per unit time with a randomly chosen other)



Days

S Model R 

# $S = -\beta IS$ $I = \beta I S - \gamma I$ $R = \gamma I$

# $\dot{S} + \dot{I} + \dot{R} = 0$ S(t) + I(t) + R(t) = 1

### $\beta$ ... is the contact rate

(each individual has  $\beta$  contacts per unit time with a randomly chosen other)

#### $\gamma$ ... is the recovery rate

( $\gamma$  = 1/D where D is the time it takes an individual to recover)



https://fabiandablander.com/r/Nonlinear-Infection.html



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# Basic Reproduction Number: R<sub>0</sub>

- Average number of additional people an infected person infects before recovering
  - Assumes that everybody is susceptible (we are at the start of an epidemic)
  - $R_0 = \beta / \gamma$
- Averages might be a poor summary of the distribution
  - Fat tails, super-spreaders, requires different interventions



# Basic Reproduction Number: R<sub>0</sub>

- The probability of being infected until time  $\tau$  and then recovering is

$$p(\tau) = \gamma e^{-\gamma \tau}$$



- On average, one individual infects aueta others during time au

$$R_0 = \beta \tau \int_0^\infty \gamma e^{-\gamma \tau} d\tau = \beta \gamma \int_0^\infty \tau e^{-\gamma \tau} d\tau = \beta / \gamma$$

Newman (2018, p. 617)

# The Complexity of R<sub>0</sub>

- Variation in R<sub>o</sub>
  - 3 key influences: duration of infectiousness, likelihood of infection at contact, contact rate
  - 20 different  $R_0$  values have been reported for measles (ranging from 3.7 203.3)
  - "Limited evidence supports the applicability of R<sub>0</sub> outside the region where the value was calculated" (p. 2)
- R<sub>0</sub> is technically not influenced by vaccination campaigns
  - It assumes a completely susceptible population; R<sub>t</sub> is the right measure
- $R_0$  is very difficult to estimate
  - Nearly always retrospectively estimated
  - When estimated using mathematical models, highly dependent on assumptions

Delamater et al. (2019)



# $\dot{S} = -\beta IS + \mu R$

$$\dot{I} = \beta I S - \gamma I$$

$$\dot{R} = \gamma I - \mu R$$

#### $\beta$ ... is the contact rate

(each individual has  $\beta$  contacts per unit time with a randomly chosen other)

#### $\gamma$ ... is the recovery rate

( $\gamma$  = 1/D where D is the time it takes an individual to recover)

#### $\mu$ ... is the reinfection rate

( $\mu$  = 1/D where D is the time it takes an individual to lose immunity)



https://fabiandablander.com/r/Nonlinear-Infection.html



https://fabiandablander.com/r/Nonlinear-Infection.html



$$\begin{split} \dot{S} &= \frac{-\beta SI}{N} + \xi R \\ \dot{E} &= \frac{\beta SI}{N} - \sigma E \\ \dot{I} &= \sigma E - \gamma I - \mu_I I \\ \dot{R} &= \gamma I - \xi R \\ \dot{F} &= \mu_I I \\ N &= S + E + I + R \end{split}$$

### Interventions

#### **Epidemic Calculator**



https://gabgoh.github.io/COVID/index.html

# Limitations

- Interventions change R<sub>0</sub> by magic, leading to no mechanistic insight
- All these models assume uniform mixing
- Every person is equally likely to have contact with every other person
- One way to incorporate spatial structure is with networks



# **Epidemics on Networks**

# Adding Network Structure

- Relax the assumption of a fully connected graph
- Nodes need to be connected for disease to transmit
  - Epidemic depends on network structure and position of initially infected people



# Size of the Outbreak

- Use bond percolation to calculate the expected size of the outbreak
  - A fraction of  $\phi$  edges is occupied at random
  - Disease starts at a randomly chosen node

$$\phi = 1 - e^{-\beta\tau}$$



Newman (2018, p. 628)

## **Dynamics on Networks**

$$\Pr(X_{i} = S \to E) = \left[ p \frac{\beta I}{N} + (1-p) \frac{\beta \sum_{j \in C_{G}(i)} \delta_{X_{j}=I}}{|C_{G}(i)|} \right] \delta_{X_{i}=S}$$

$$\Pr(X_{i} = E \to I) = \sigma \delta_{X_{i}=E}$$

$$\Pr(X_{i} = I \to R) = \gamma \delta_{X_{i}=I}$$

$$\Pr(X_{i} = I \to F) = \mu_{I} \delta_{X_{i}=I}$$

$$\Pr(X_{i} = R \to S) = \xi \delta_{X_{i}=R}$$

Dottori et al. (2015) and https://github.com/ryansmcgee/seirsplus



The effect of network locality on total infections

https://bit.ly/3bFDshk





https://bit.ly/3bFDshk



$$\begin{split} \dot{S} &= -\frac{\beta SI}{N} - q \frac{\beta_D SD_I}{N} + \xi R \\ \dot{E} &= \frac{\beta SI}{N} + q \frac{\beta_D SD_I}{N} - \sigma E - \theta_E \psi_E E \\ \dot{I} &= \sigma E - \gamma I - \mu_I I - \theta_I \psi_I I \\ \dot{D}_E &= \theta_E \psi_E E - \sigma_D D_E \\ \dot{D}_I &= \theta_I \psi_I I + \sigma_D D_E - \gamma_D D_I - \mu_D D_I \\ \dot{R} &= \gamma I + \gamma_D D_I - \xi R \\ \dot{F} &= \mu_I I + \mu_D D_I \\ N &= S + E + I + D_E + D_I + R \end{split}$$

# **Incorporating Interventions**

$$\begin{split} \Pr(X_i = S \to E) &= \left[ p\left(\frac{\beta I + q\beta_D D_I}{N}\right) + (1-p) \left( \frac{\beta \left[\sum_{j \in C_G(i)} \delta_{X_j = I}\right] + \beta_D \left[\sum_{k \in C_Q(i)} \delta_{X_k = D_I}\right]}{|C_G(i)|} \right) \right] \delta_{X_i = S} \\ \Pr(X_i = E \to I) &= \sigma \delta_{X_i = I} \\ \Pr(X_i = I \to R) &= \gamma \delta_{X_i = I} \\ \Pr(X_i = I \to F) &= \mu_I \delta_{X_i = I} \\ \Pr(X_i = E \to D_E) &= \left( \theta_E + \phi_E \left[ \sum_{j \in C_G(i)} \delta_{X_k = D_E} + \delta_{X_k = D_I} \right] \right) \psi_E \delta_{X_i = E} \\ \Pr(X_i = I \to D_I) &= \left( \theta_I + \phi_I \left[ \sum_{j \in C_G(i)} \delta_{X_k = D_E} + \delta_{X_k = D_I} \right] \right) \psi_I \delta_{X_i = I} \\ \Pr(X_i = D_E \to D_I) &= \sigma_D \delta_{X_i = D_E} \\ \Pr(X_i = D_I \to R) &= \gamma_D \delta_{X_i = D_I} \\ \Pr(X_i = D_I \to F) &= \mu_D \delta_{X_i = D_I} \\ \Pr(X_i = R \to S) &= \xi \delta_{X_i = R} \\ \Pr(X_i = any \to S) &= \nu \delta_{X_i \neq F} \end{split}$$

https://github.com/ryansmcgee/seirsplus





https://bit.ly/3bFDshk

# **Modeling in the Real-world**

# Modeling in the Real-world Modeling Interventions

### Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand

Neil M Ferguson, Daniel Laydon, Gemma Nedjati-Gilani, Natsuko Imai, Kylie Ainslie, Marc Baguelin, et al.

- Two Strategies: Mitigation and Suppression
  - Mitigation: Slowing but not necessarily stopping epidemic growth
  - Suppression: Reversing epidemic growth (i.e.,  $R_0 < 1$ )
- Authors used an individual-based transmission model developed for influenza
  - Individuals reside in areas defined by high-resolution population density data
  - Contacts are made within households, schools, at work, etc.
  - Age and household size defined by census data
  - Schools defined by data on schools (average class-sizes, staff-student ratios)
  - Workplace size and commuting distance between them was also calibrated
  - Individuals start at locations and then move around
  - ½ of transmission occur in households, ¼ in schools & workplace, ¼ in community (match social mixing surveys)

Ferguson et al. (<u>2020</u>)

16th March

# Imperial College Report: Modeling Interventions

- Parameters (among others)
  - Incubation period 5.1 days
  - 6.5 days mean duration of infectiousness (50% more infectious than asymptomatic)
  - R<sub>0</sub> = 2.4 [2.0, 2.6]
  - Infection seeded early January to reach cumulative number of deaths (14th March)
  - <sup>2</sup>/<sub>3</sub> assumed to be sufficiently symptomatic to self-isolate within 1 day of symptom onset
  - 5 days mean duration from infection to hospitalization
  - Bed demand
    - 8 days if no critical care
    - 16 if critical care (10 days ICU)

Age-group	% symptomatic cases	% hospitalised cases	Infection Fatality Ratio	
(years) requiring hospitalisation rec		requiring critical care		
0 to 9	0.1%	5.0%	0.002%	
10 to 19	0.3%	5.0%	0.006%	
20 to 29	1.2%	5.0%	0.03%	
30 to 39	3.2%	5.0%	0.08%	
40 to 49	4.9%	6.3%	0.15%	
50 to 59	10.2%	12.2%	0.60%	
60 to 69	16.6%	27.4%	2.2%	
70 to 79	24.3%	43.2%	5.1%	
80+	27.3%	70.9%	9.3%	

# Type of Interventions

Label	Policy	Description	
CI	Case isolation in the home	Symptomatic cases stay at home for 7 days, reducing non-	
		household contacts by 75% for this period. Household	
		contacts remain unchanged. Assume 70% of household	
		comply with the policy.	
HQ	Voluntary home	Following identification of a symptomatic case in the	
	quarantine	household, all household members remain at home for 14	
		days. Household contact rates double during this	
		quarantine period, contacts in the community reduce by	
		75%. Assume 50% of household comply with the policy.	
SDO	Social distancing of those	Reduce contacts by 50% in workplaces, increase household	
	over 70 years of age	contacts by 25% and reduce other contacts by 75%.	
		Assume 75% compliance with policy.	
SD	Social distancing of entire	All households reduce contact outside household, school or	
	population	workplace by 75%. School contact rates unchanged,	
		workplace contact rates reduced by 25%. Household	
		contact rates assumed to increase by 25%.	
PC	Closure of schools and	Closure of all schools, 25% of universities remain open.	
	universities	Household contact rates for student families increase by	
		50% during closure. Contacts in the community increase by	
		25% during closure.	



Ferguson et al. (2020)

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#### Mitigation Strategies



Deaths (Best case): 250,000 GB and 1.1-1.2 Million US

Ferguson et al. (2020)

# Modeling Interventions





# Modeling Interventions: Conclusions

- Mitigation is not feasible (healthcare system overloaded many times over)
- Need population-wide social distancing + other interventions (home case isolation, school and university closure) to suppress  $R_0$  below 1
- These measures need to be in place for a long time (could be 18 months or more) to avoid rebound
  - Adaptive population-wide social distancing is an idea, but in place still <sup>2</sup>/<sub>3</sub> of the time



# Critique

#### Italy and Spain's daily death tolls are plateauing, but in the UK and US every day brings more new deaths than the last

Daily deaths with coronavirus (7-day rolling average), by number of days since 3 daily deaths first recorded Stars represent national lockdowns 🖈



### Review of Ferguson et al "Impact of non-pharmaceutical interventions..."

Chen Shen<sup>†</sup>, Nassim Nicholas Taleb<sup>\*</sup>, Yaneer Bar-Yam<sup>†</sup> <sup>†</sup>New England Complex Systems Institute, \*School of Engineering, New York University

#### First version, March 17, 2020. Corresponding author: yaneer@necsi.edu allows for relaxing restrictions in areas earlier that are less affected, enables unifected areas to assist in response in the

Neil Ferguson and an Imperial College team perform detailed simulations of outbreak response [1]. This is an important work because they model social/government response, not just contagion. They show suppression (lockdown so that  $R_0 < 1$ ) is essential because mitigation ( $R_0 > 1$ ), "fattening the curve") necessarily results in massive overload of hospitals and many dead. This is an important conclusion that should inform policy makers.

However, they make structural mistakes in analyzing outbreak response. They ignore standard Contact Tracing [2] allowing isolation of infected prior to symptoms. They also ignore door-to-door monitoring to identify cases with symptoms [3]. Their conclusions that there will be resurgent outbreaks are wrong. After a few weeks of lockdown almost all infectious people are identified and their contacts are isolated prior to symptoms and cannot infect others [4]. The outbreak can be stopped completely with no resurgence as in China, where new cases were down to one yesterday, after excluding imported international travelers that are ouraantined.

Their assumptions are equivalent to ergodicity, as they consider new infections to be a function of infected fraction and immunity, and not influenced by where in the trajectory of the outbreak they are, distinguishing going up from going down.

They also don't specify whether achieving less than one case (extinction of the virus) is possible in their model. The actual minimal number for resurgence is larger than 1 because (1) a significant percentage of infected individuals do not infect others, indeed only 5% of close contacts of infected individuals traced in China subsequently tested positive [2], and (2) small outbreaks can be stopped by contact tracing, which is enhanced by the availability of testing [5]. The availability of testing is also not included in their analysis. These interventions imply the exponential growth they report after relaxing restrictions would require a significant number of initial cases.

Since lockdowns result in exponentially decreasing numbers of cases, a comparatively short amount of time can be sufficient to achieve pathogen extinction, after which relaxing restrictions can be done without resurgence. Since the exponential decay is highly sensitive to the interventions made by both government and social action, simulating their effects is less helpful than the advice to 'go all out' and refine the effort over time with improved tracing, testing, and other protocols. Finally, the use of geographic boundaries and travel restrictions allows for effective and comparatively low cost imposition and relaxation of interventions. Such a multiscale approach accelerates response efforts, reduces social impacts.

afforder, enables unifected areas to assist in response in the ares that are infected, and is a much more practical and effective may to stop otherwise devastating outbreaks [6]. If actions had been taken earlier, successful local lockdowns, as performed in China in Hubei province, would have been possible instead of national lockdowns.

A few other issues are of importance: They ignore the possibility of superspreader events in gatherings by not including the fat tail distribution of contagion in their model. This leads them to deny the importance of banning them, which has been shown to be incorrect, including in South Korea [7]. Cutting the fat tail of the infection distribution is critical to reducing  $P_0$  [8].

The model they use appears to be in the general class of SIR differential equations used in epidemiology and is therefore not well suited for incorporating real world conditions at fine or large scale. These include (1) significant interactive local dynamics and travel restrictions that cannot be seen from aggregate quantities or averages across geographic locations, (2) non-normal distributions of the number of infections per person (superspreader events) as well as the infection period, and (3) dynamic or stochastic values of parameters that arise from variations in sampling of distributions as well as the impact of changing social response epitors, their model is several degrees of abstraction away from what is warranted by the simation

While the efforts to model social response are important, leaving out critical aspects of the response yields incorrect answers. Focusing on details but using incorrect assumptions makes for bad policy advice. Where lives are at stake, it is essential for science to adhere to higher standards.

#### REFERENCES

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#### https://www.ft.com/coronavirus-latest





#### Chart 12.b: New Daily Cases in South Korea

https://github.com/CSSEGISandData/COVID-19/blob/master/csse\_covid\_19\_data/csse\_covid\_19\_time\_series/time\_series\_19-covid-Confirmed.csv



# Ferguson et al. (2020) on South Korea

"The measures used to achieve suppression might also evolve over time. As case numbers fall, it becomes more feasible to adopt intensive testing, contact tracing and quarantine measures akin to the strategies being employed in South Korea today. Technology – such as mobile phone apps that track an individual's interactions with other people in society – might allow such a policy to be more effective and scalable if the associated privacy concerns can be overcome. However, if intensive NPI packages aimed at suppression are not maintained, our analysis suggests that transmission will rapidly rebound, potentially producing an epidemic comparable in scale to what would have been seen had no interventions been adopted."

- Ferguson et al. (2020, p. 15)

# **Contact Tracing**

- Ferretti et al. (2020)
- Transmission can be
  - Pre-symptomatic
  - Symptomatic
  - Environmental
  - Asymptomatic





# **Contact Tracing**

- Ferretti et al. (2020)
- Transmission can be
  - Pre-symptomatic
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# Modeling in the Real-world Assessing the Effect of Interventions

### Estimating the number of infections and the impact of nonpharmaceutical interventions on COVID-19 in 11 European countries

Seth Flaxman<sup>\*</sup>, Swapnil Mishra<sup>\*</sup>, Axel Gandy<sup>\*</sup>, H Juliette T Unwin, Helen Coupland, Thomas A Mellan, Harrison et al.

- Interventions influence the basic reproductive number R,
- Difficulties in estimating R<sub>t</sub>:
  - High proportion of infections not detected
  - Different proportions of infections being detected over time due to changes in testing policies
  - Most countries measure only severely ill patients or high-risk groups



#### Chart 7: Timeline of Events in Hubei



# Estimating Number of Infections: Hack

- Case data is unreliable
- Alternative way: back-calculate infections from observed deaths (Pueyo, 2020a)
- Germany has 85,025 reported cases and 1,111 reported deaths (Wikipedia, 3rd of April, 09:51)



# **Imperial College Model**





Flaxman et al. (2020)

# Imperial College Death Model

$$D_{tm} \sim \text{Negative-Binomial}\left(d_{t,m}, d_{t,m} + \frac{d_{t,m}^2}{\psi}\right)$$

 $\psi \sim \text{Half-Normal}(0, 5)$ 

 $\pi_m \sim ifr_m \cdot (\text{Gamma}(5.1, 0.86) + \text{Gamma}(18.8, 0.45))$ 

$$d_{t,m} = \sum_{ au=0}^{t-1} c_{ au,m} \cdot \pi_{t- au,m}$$

 $D_{tm}$  ... deaths for day t and country m  $\pi_m$  ... time from infection to death  $ifr_m$  ... infection-fatality ratio per country  $C_{\tau m}$  ... number of new infections

Flaxman et al. (<u>2020</u>)

# Imperial College Death Model



# Imperial College Death Model

Time from Infection to Death Survival Function 0.06 1.000 0.05 0.998 0.04 Probability Density 0.996 0.03 0.994 0.02 0.992 0.01 0.00 0.990 20 30 50 60 20 30 50 60 0 10 40 10 40 0 Days Days

# Imperial College Infection Model

 $g \sim \text{Gamma}(6.5, 0.62)$ 

$$c_{t,m} = R_{t,m} \sum_{\tau=0}^{t-1} c_{\tau,m} \cdot g_{t-\tau}$$
$$R_{t,m} = R_{0,m} \exp\left(-\sum_{k=1}^{6} \alpha_k \cdot I_{k,t,m}\right)$$

 $\alpha_k \sim \text{Gamma}(0.50, 1)$ 

- $R_{0,m} \sim \text{Normal}(2.4, |\kappa|)$ 
  - $\kappa \sim \text{Normal}(0, 0.50)$

 $c_{1,m}, \dots, c_{6,m} \sim \text{Exponential}(\tau)$  $\tau \sim \text{Exponential}(0.03)$ 

#### Serial Interval Distribution



g ... serial interval distribution

(time between when a person gets infected and subsequently infects others)

 $C_{tm}$  ... number of new infections

 $R_{\rm tm}$  ... Reproduction number

 $\mathbf{I}_{\rm ktm}$  ... Indicator variable for Intervention

 $\alpha_{\mathbf{k}}$  ... coefficient for intervention  $\mathbf{k}$ 

# Imperial College Modeling Results

Table 1: Posterior model estimates of percentage of total population infected as of 28th March 2020.

Country	% of total population infected (mean [95%	Reported Cases	
Austria	1.1% [0.36%-3.1%]		
Belgium	3.7% [1.3%-9.7%]	~ 832,000	~ 15,000
Denmark	1.1% [0.40%-3.1%]		
France	3.0% [1.1%-7.4%]	~ 2.1 Million	~ 59,000
Germany	0.72% [0.28%-1.8%]	~ 600,000	~ 85,000
Italy	9.8% [3.2%-26%]	~ 5.9 Million	~ 115,000
Norway	0.41% [0.09%-1.2%]		
Spain	15% [3.7%-41%]	~ 7 Million	~ 112,000
Sweden	3.1% [0.85%-8.4%]		
Switzerland	3.2% [1.3%-7.6%]		
United Kingdom	2.7% [1.2%-5.4%]	~ 4.8 Million	~ 34,000

(B) Belgium



(E) Germany







Figure 15: Effects of different interventions when used as the only covariate in the model.

Flaxman et al. (2020)





Figure 10: 7-day-ahead forecast for Italy. Figure 11: 7

Figure 11: 7-day-ahead forecast for Spain.



Flaxman et al. (2020)

# **Assessing Interventions: Conclusions**

- Interventions have drastically reduced R<sub>t</sub> and saved lives
  - Too little data to estimate effect of intervention per country
  - Difficult to disentangle individual intervention effects due to correlation in time
- Substantially more infections than currently reported
  - Yet still only about 4.9% [1.1% 11%] of people have been infected
  - To few to get herd immunity (which is ~ 50 75% for an  $R_0 = 2-4$ )
  - Interventions reduce rate of herd immunity drastically
    - Virus will be able to spread quickly after they are lifted
  - Estimates of the attack rate need to be validated using newly developed antibody tests

- Seriously cool modeling, all code publicly available



Fatal flaws

### Covid-19's death toll appears higher than official figures suggest

Measuring the total number of deaths tells a grimmer tale

#### Deaths per 100,000 people per week, selected regions

Region's normal death rate

Confirmed covid-19 deaths

#### Excess deaths not attributed to covid-19



Spain, confirmed covid-19 deaths per 100,000 people per week\*



https://econ.st/3bMfQaL



Italy, confirmed covid-19 deaths per 100,000 people per week\*



https://econ.st/3bMfQaL

# Thank you for your attention!