“The Role of Modeling in the COVID-19 Pandemic”

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Modeling the covid-19 pandemic

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HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

CENTER for COMMUNICABLE DISEASE DYNAMICS

MIDAS Models of Infectious Disease Agent Study

Funded by the National Institutes of Health

Disclaimer

- This talk will make almost no mention of data, big or small
- However data are important
- “Models are as good as their assumptions” Dr Anthony Fauci, March 2020

The range of possible futures

- Modeling has received a lot of attention

Sections

The Washington Post
Democracy Dies in Darkness

Gift Subscri

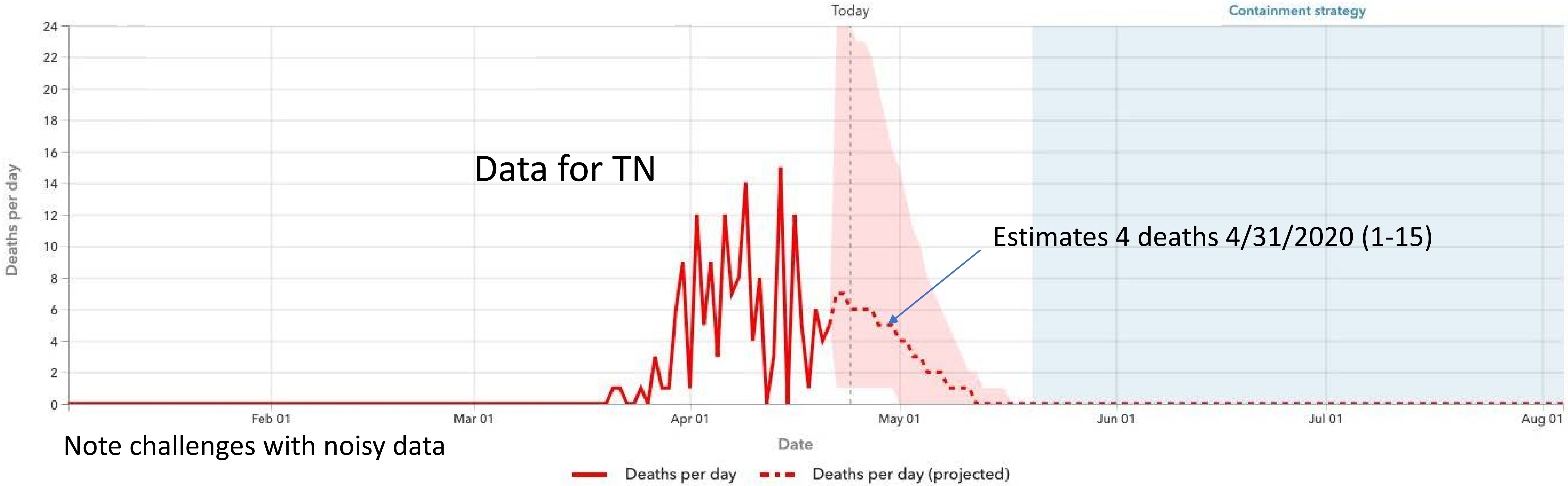
PostEverything • Perspective

Virus models predict possible outcomes. We can fight to stop the worst ones.

We don't need coronavirus projections to know we need to act to save lives.

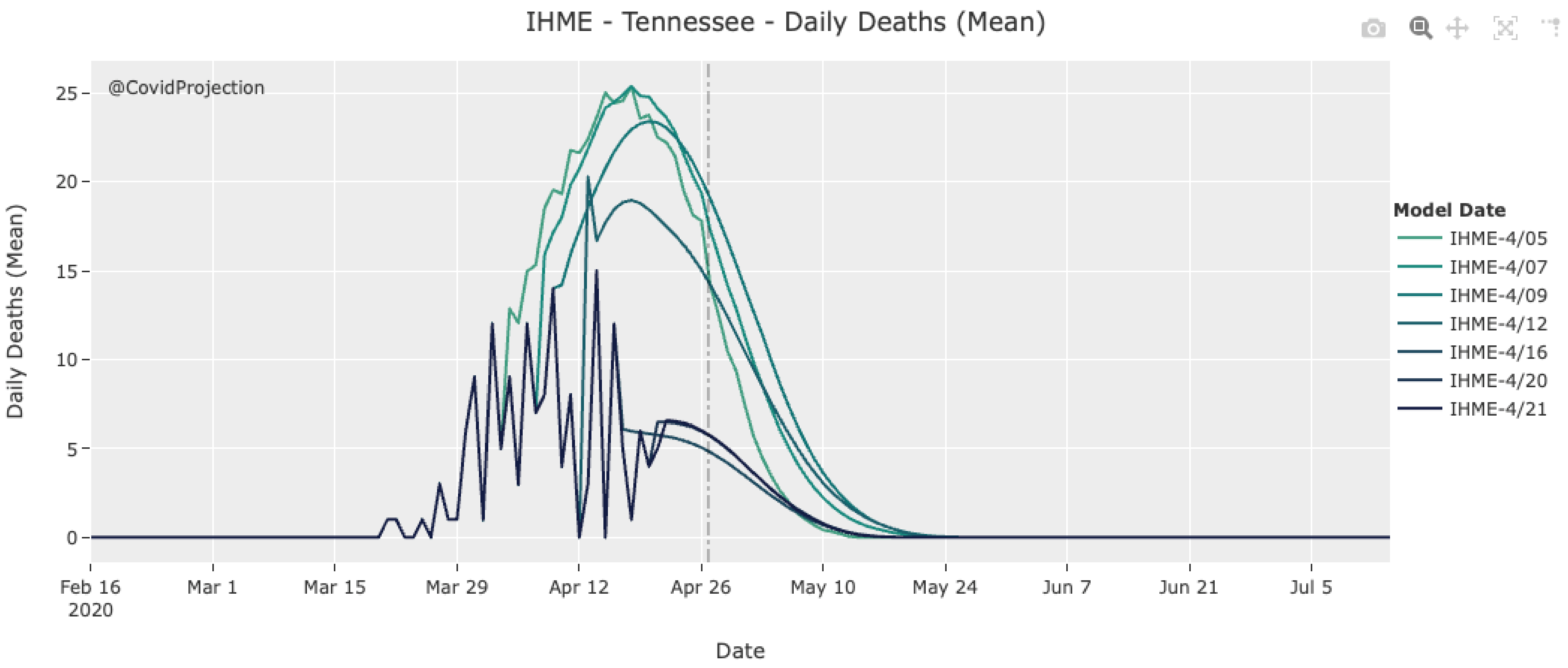
An example of a model

- This is from the Institute for Health Metrics and Evaluation at the University of Washington
- It assumes cases climb and then decline along a curve and then fit the data to that curve in order to estimate the shape of it



Note challenges with noisy data

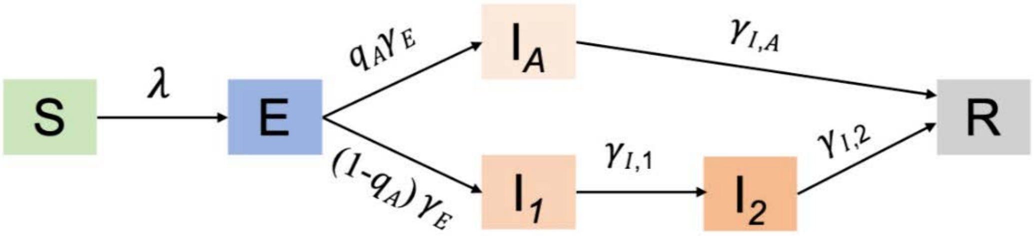
Estimates can change over time



From covidprojections.org

Another sort of model

- A compartmental mechanistic model
- You specify parameters for the rates with which people move through the different compartments
- And write down the equations
- Can also run simulations



Force of Infection $\lambda = \lambda_1 I_1 + \lambda_2 I_2 + \lambda_A I_A$

An example of a mechanistic model

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY FEBRUARY 2016, VOL. 37, NO. 2

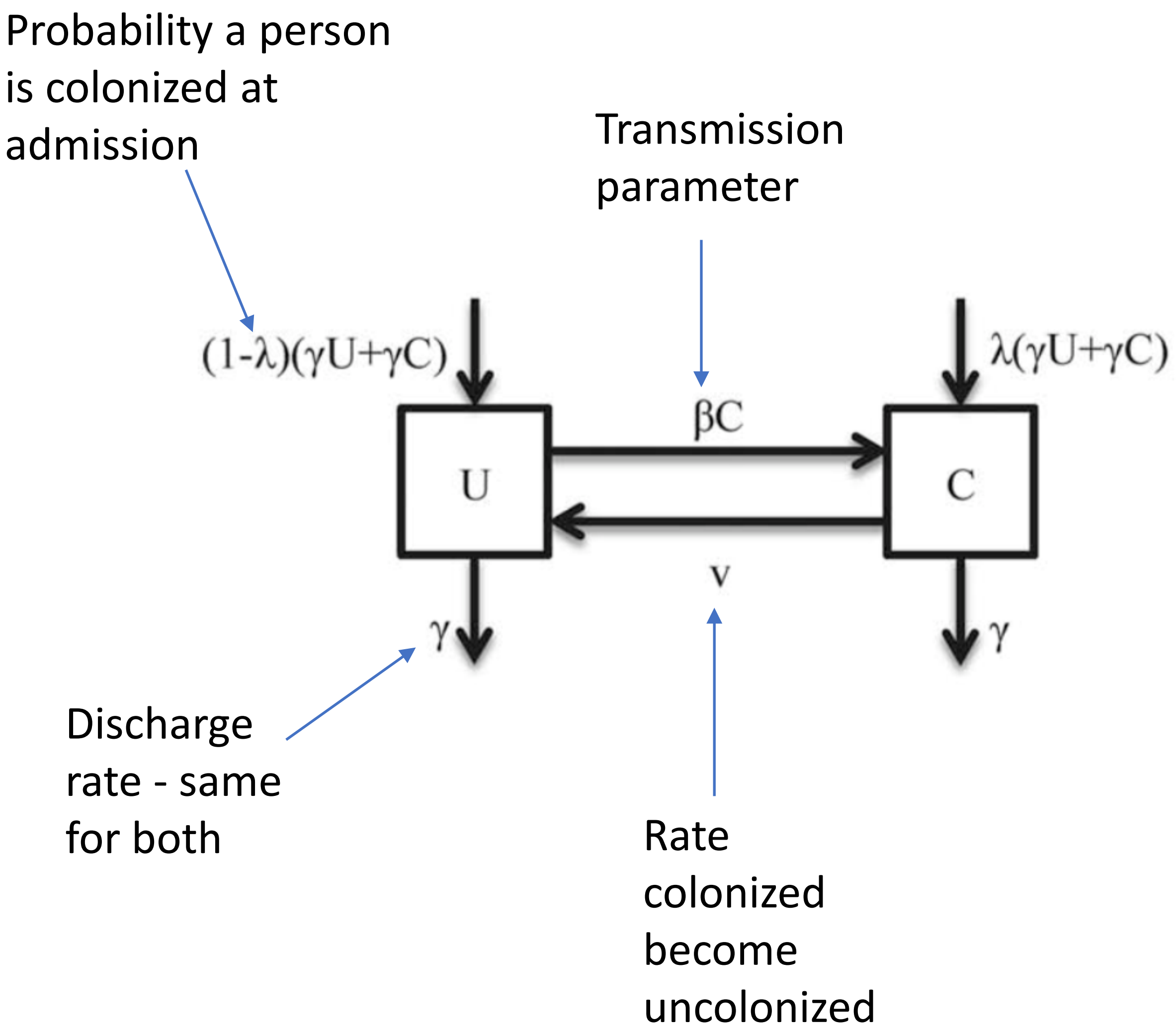
ORIGINAL ARTICLE

Impact of Host Heterogeneity on the Efficacy of Interventions to Reduce *Staphylococcus aureus* Carriage

Qiuzhi Chang, MSPH; Marc Lipsitch, DPhil;* William P. Hanage, PhD*

- As you may know, for some reason some people (as much as 30%) are more likely to persistently carry *S. aureus* than others
- This has implications for how easy we expect it to be to control

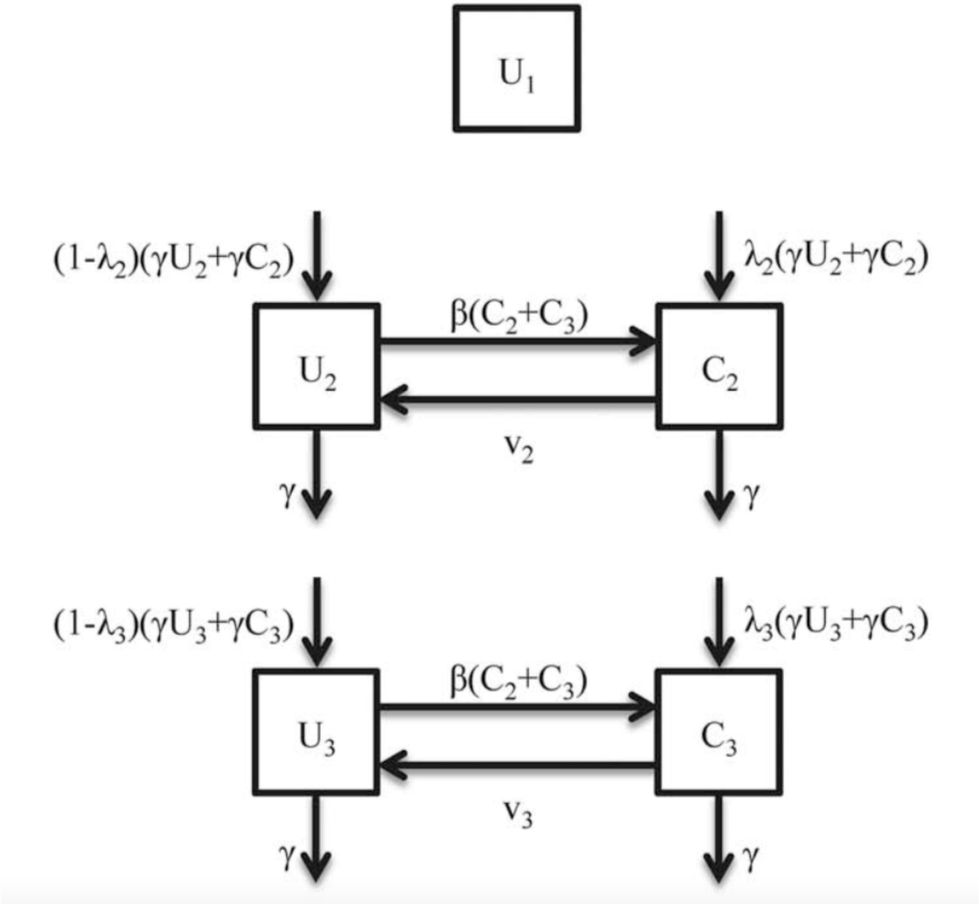
A really really simple model for a hospital



- There are just two compartments – uncolonized and colonized

$$\dot{U} = (1-\lambda)(\gamma U + \gamma C) - \beta UC + vC - \gamma U$$
$$\dot{C} = \lambda(\gamma U + \gamma C) + \beta UC - vC - \gamma C \text{ or } C = 1 - U$$

Making it more complicated – a heterogeneous model



- Now you have three groups of people
- 1 are refractory to colonization
- 2 are intermittent carriers
- 3 are persistent carriers

$$\dot{U}_2 = (1-\lambda_2)(\gamma U_2 + \gamma C_2) - \beta U_2 (C_2 + C_3) + v_2 C_2 - \gamma U_2$$
$$\dot{C}_2 = \lambda_2 (\gamma U_2 + \gamma C_2) + \beta U_2 (C_2 + C_3) - v_2 C_2 - \gamma C_2$$
$$\dot{U}_3 = (1-\lambda_3)(\gamma U_3 + \gamma C_3) - \beta U_3 (C_2 + C_3) + v_3 C_3 - \gamma U_3$$
$$\dot{C}_3 = \lambda_3 (\gamma U_3 + \gamma C_3) + \beta U_3 (C_2 + C_3) - v_3 C_3 - \gamma C_3$$

Parameters

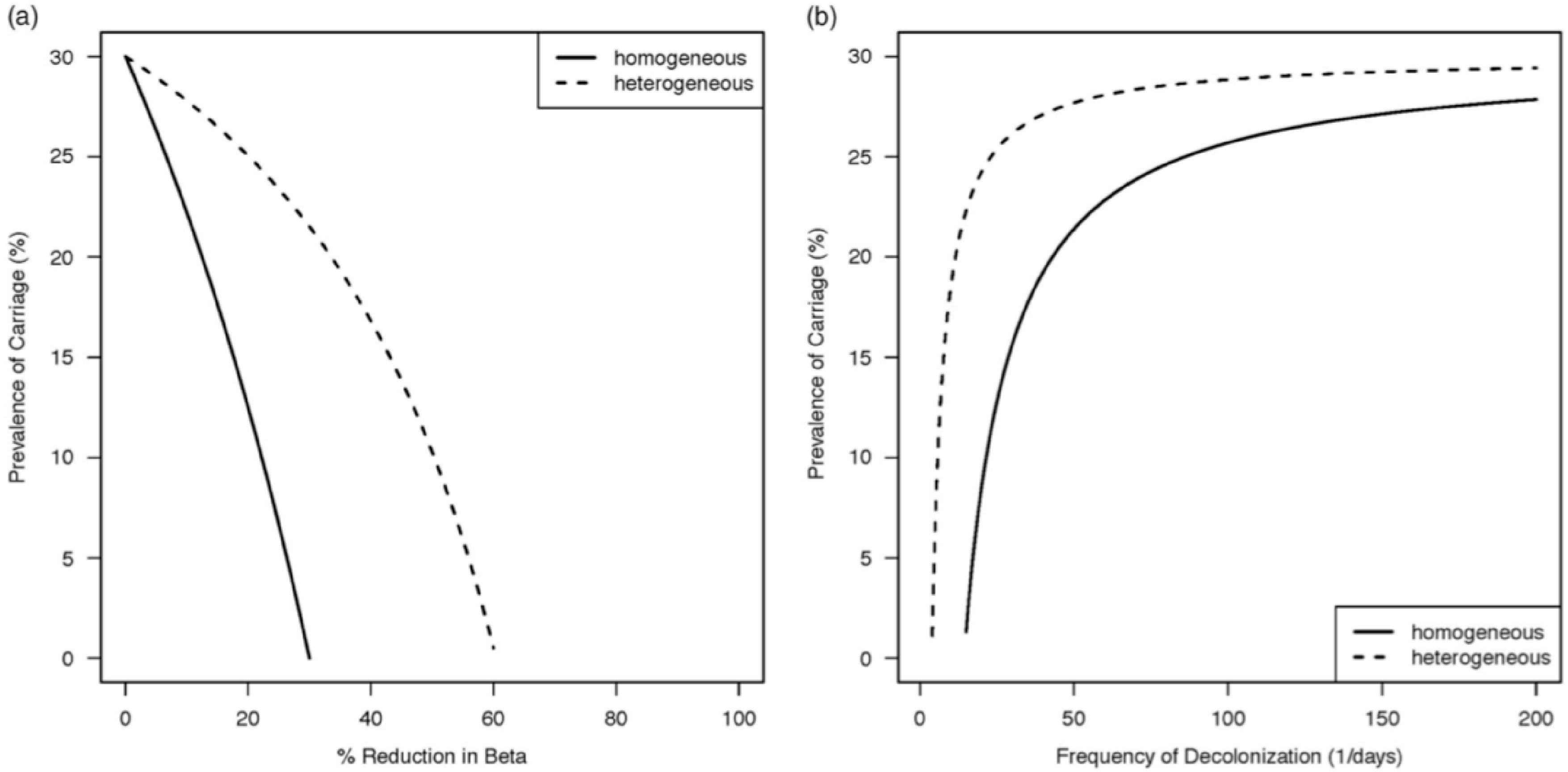
Model	Parameter	Value	Description
Homogeneous	β	$\lambda = \frac{C}{U+C} : 0.028\ \text{day}^{-1}$ $\lambda = 0 : 0.232\ \text{day}^{-1}$	Transmission parameter
	v	$\ln(2)/35\ \text{day}^{-1}$	Natural clearance rate
	γ	$7\ \text{days}^{-1}$	Discharge rate
Heterogeneous	β	$\lambda_i = \frac{C_i}{U_i+C_i} : 0.115\ \text{day}^{-1}$ $\lambda_i = 0 : 0.866\ \text{day}^{-1}$	Transmission parameter assuming 20% persistent, 30% intermittent, and 50% non-carriers (Figure 2)
	β^*	$\lambda_i = \frac{C_i}{U_i+C_i} : \frac{x_2\beta^*}{0.3\beta^*+v_2} + \frac{x_3\beta^*}{0.3\beta^*+v_3}$ $\lambda_i = 0 : 1 = \frac{x_2\beta^*}{0.3\beta^*+v_2+\gamma} + \frac{x_3\beta^*}{0.3\beta^*+v_3+\gamma}$ (x_2 and x_3 are the proportions of intermittent and persistent carriers)	Transmission parameter for 30% overall carriage prevalence in populations with varying proportions of carrier classes (Figure 3)
	v_2	$\ln(2)/14\ \text{day}^{-1}$	Natural clearance rate for intermittent carriers
	v_3	$\ln(2)/154\ \text{day}^{-1}$	Natural clearance rate for persistent carriers
	γ	$7\ \text{days}^{-1}$	Discharge rate

Why are we doing this?

- Efforts to control *S. aureus* have had mixed results
- Not clear the role of compliance, among other things
- We wanted to ask about the impact of heterogeneity on the effort needed to control

- Considered hand hygiene (reduces transmission rate)
- And decontamination (moves people from C back to U at a higher rate)

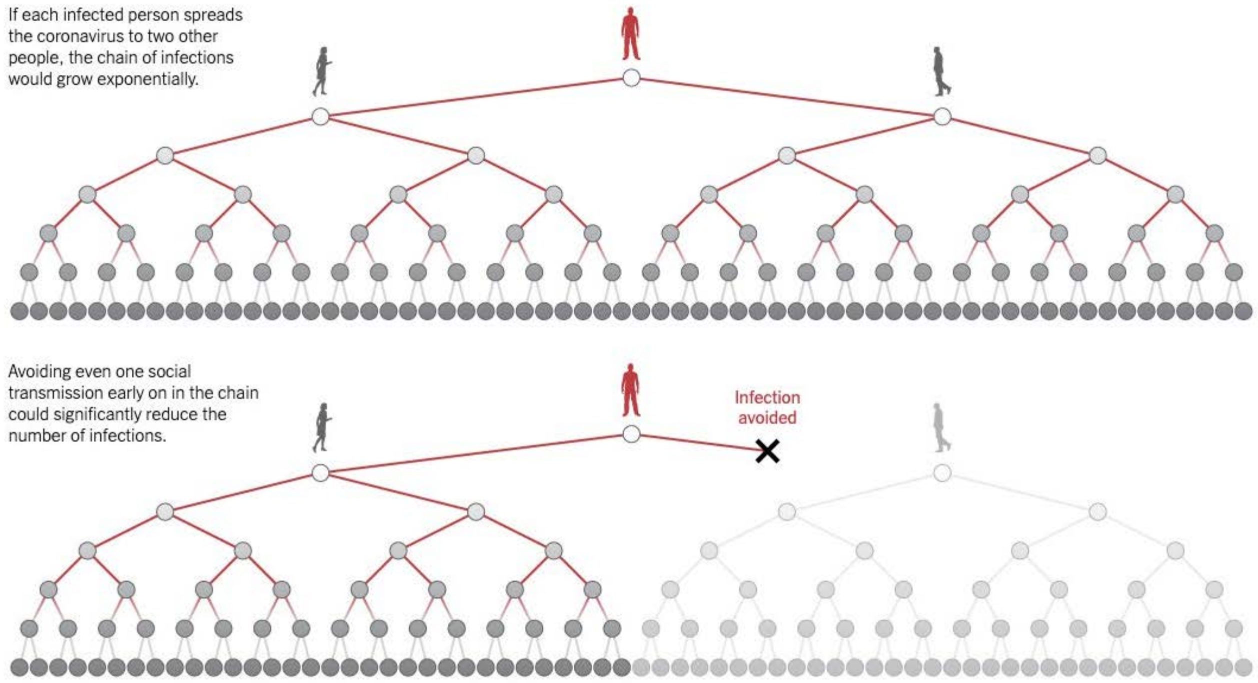
Heterogeneity makes it harder to control



This is assuming that each of the groups in the heterogeneous model are uncolonized on admission

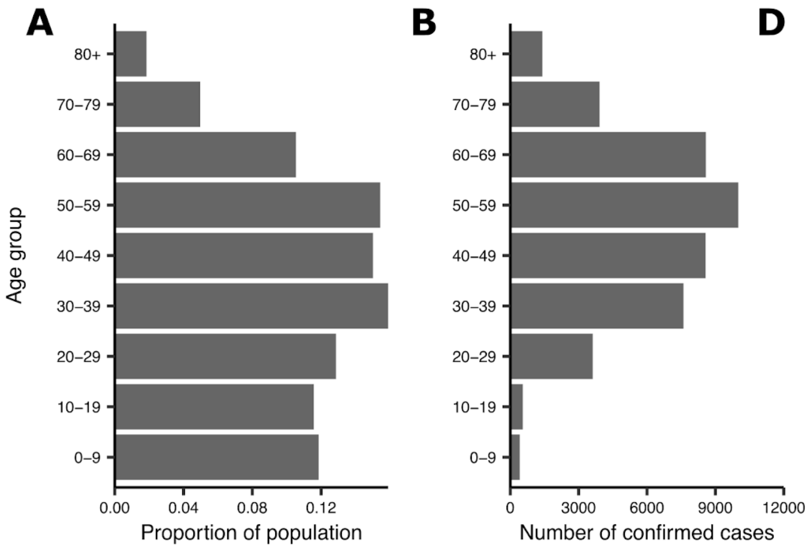
Why is that? The top line answer is intuitive

- Population prevalence of *S. aureus* colonization is ~ 30%
- If fully half the population is naturally resistant to being colonized, the pathogen has to be more transmissible overall to achieve the same prevalence in the fraction it *can* colonize.



What can we learn from this for the pandemic?

- The uncertain role of children in transmission
- Children get less sick. But they can become infected



Epidemiology and Transmission of COVID-19 in Shenzhen China: Analysis of 391 cases and 1,286 of their close contacts

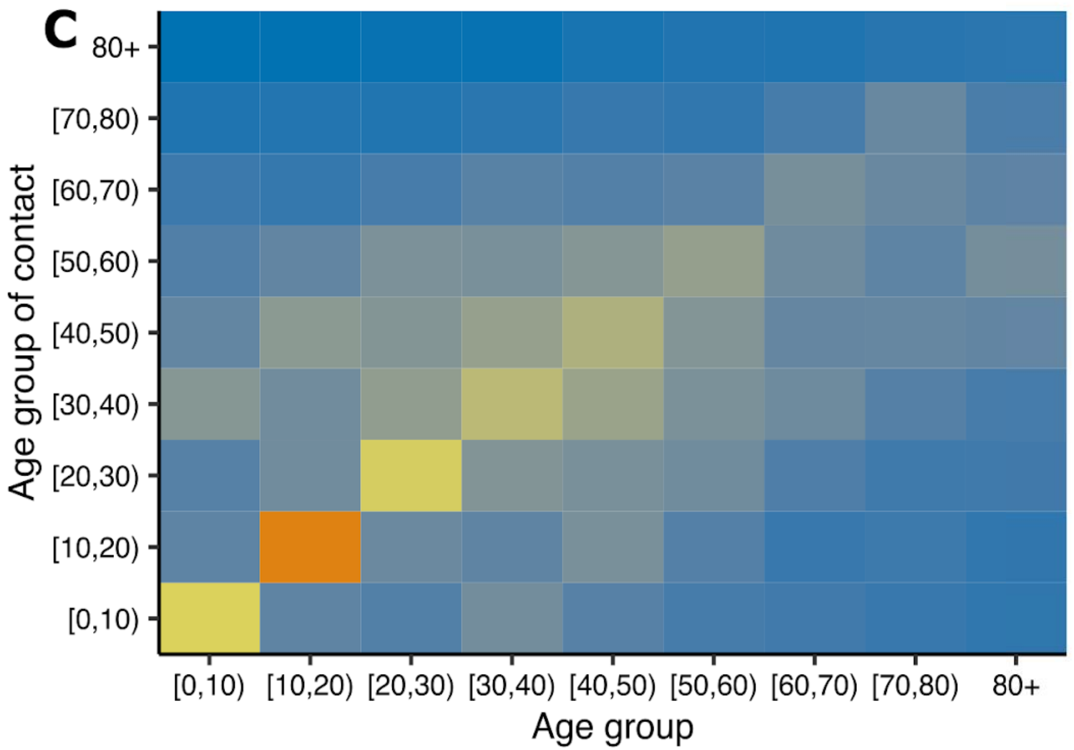
Qifang Bi, Yongsheng Wu, Shujiang Mei, Chenfei Ye, Xuan Zou, Zhen Zhang, Xiaojian Liu, Lan Wei, Shaun A Truelove, Tong Zhang, Wei Gao, Cong Cheng, Xiujuan Tang, Xiaoliang Wu, Yu Wu, Binbin Sun, Suli Huang, Yu Sun, Juncen Zhang, Ting Ma, Justin Lessler, Teijian Feng

doi: https://doi.org/10.1101/2020.03.03.20028423

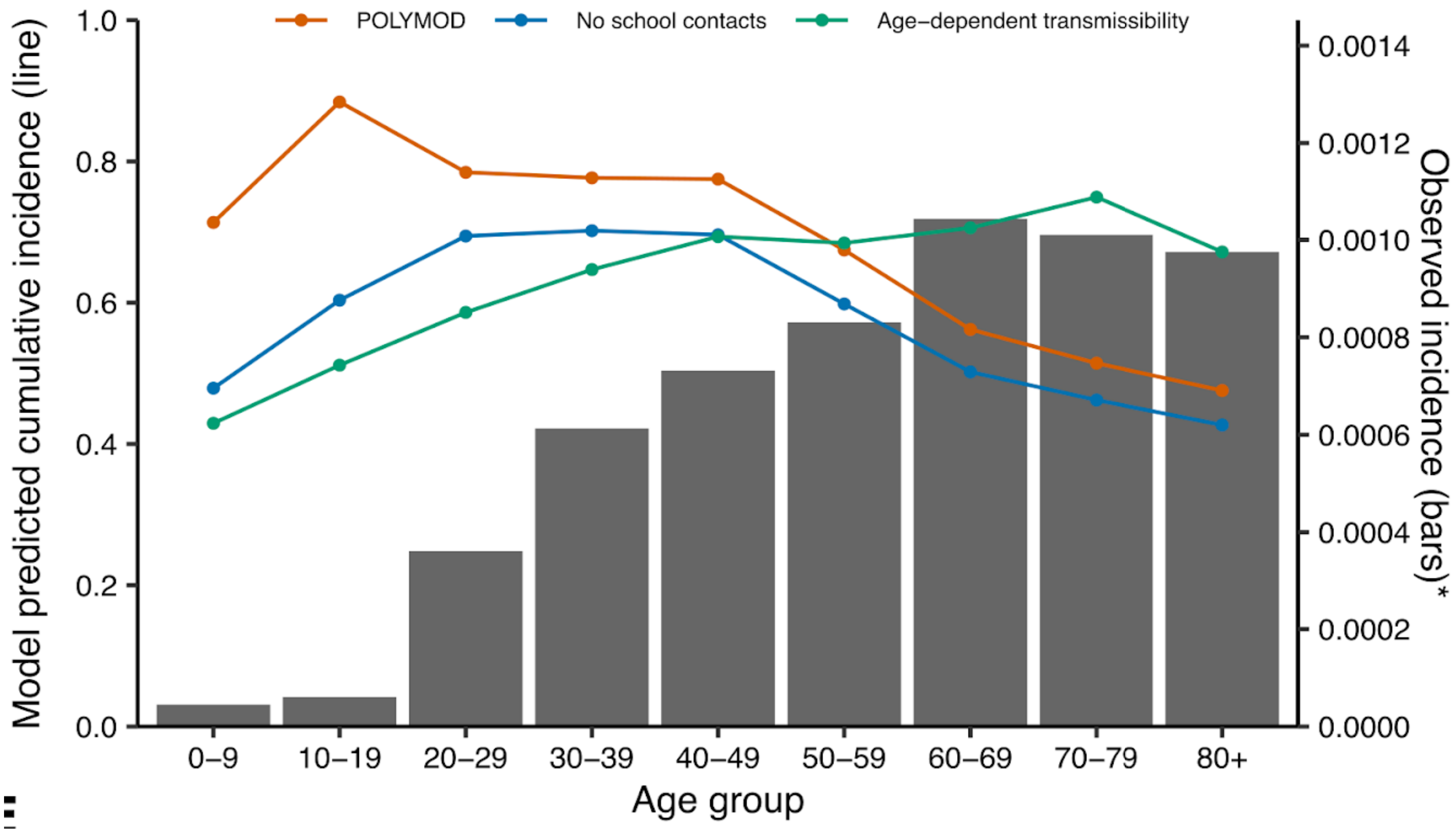
Variable	Value	Contact-based surveillance (N=87)	Symptom-based surveillance (N=292)	Unknown/other (N=12)	Total (N=391)	P-value
sex	female	63 (72.4%)	131 (44.9%)	10 (83.3%)	204 (52.2%)	<0.001
	male	24 (27.6%)	161 (55.1%)	2 (16.7%)	187 (47.8%)	
age	0-9	13 (14.9%)	6 (2.1%)	1 (8.3%)	20 (5.1%)	<0.001
	10-19	5 (5.7%)	6 (2.1%)	1 (8.3%)	12 (3.1%)	
	20-29	11 (12.6%)	23 (7.9%)	0 (0.0%)	34 (8.7%)	
	30-39	15 (17.2%)	71 (24.3%)	1 (8.3%)	87 (22.3%)	
	40-49	9 (10.3%)	49 (16.8%)	2 (16.7%)	60 (15.3%)	
	50-59	10 (11.5%)	63 (21.6%)	1 (8.3%)	74 (18.9%)	
	60-69	20 (23.0%)	60 (20.5%)	6 (50.0%)	86 (22.0%)	
	70+	4 (4.6%)	14 (4.8%)	0 (0.0%)	18 (4.6%)	
severity	mild	18 (20.7%)	82 (28.1%)	2 (16.7%)	102 (26.1%)	0.03
	moderate	66 (75.9%)	180 (61.6%)	8 (66.7%)	254 (65.0%)	
	severe	3 (3.4%)	30 (10.3%)	2 (16.7%)	35 (9.0%)	
symptomatic	no	17 (19.5%)	8 (2.7%)	0 (0.0%)	25 (6.4%)	<0.001
	yes	70 (80.5%)	284 (97.3%)	12 (100.0%)	366 (93.6%)	
fever	no	25 (28.7%)	34 (11.6%)	2 (16.7%)	61 (15.6%)	<0.001
	yes	62 (71.3%)	258 (88.4%)	10 (83.3%)	330 (84.4%)	

A model of covid-19 in Wuhan

- Construct a model with POLYMOD mixing of age groups
- Run an SIR model with the age-distribution of China, the population of Wuhan and an incubation period of 5 days.
- R0 = 2 overall
- If kids do not transmit, how transmissible must it be in adults?



Work with James Hay, David Haw, Jess Metcalf and Michael Mina - submitted



R0= 2

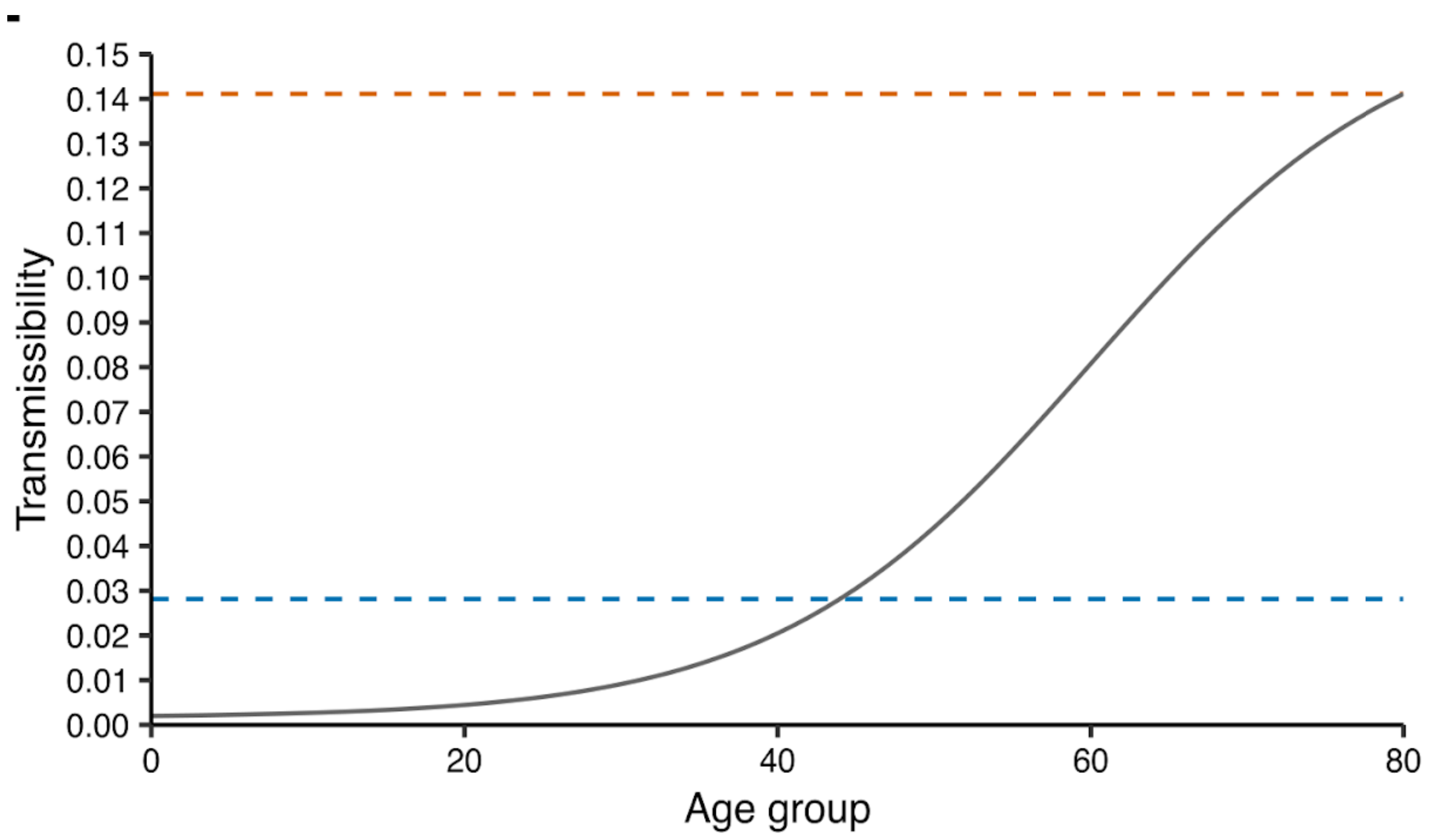
Orange line POLYMOD mixing

Blue line is expectation if contacts made in school are removed

Green line is age dependent transmissibility

Work with James Hay, David Haw, Jess Metcalf and Michael Mina - submitted

Inferred variation in transmission with age

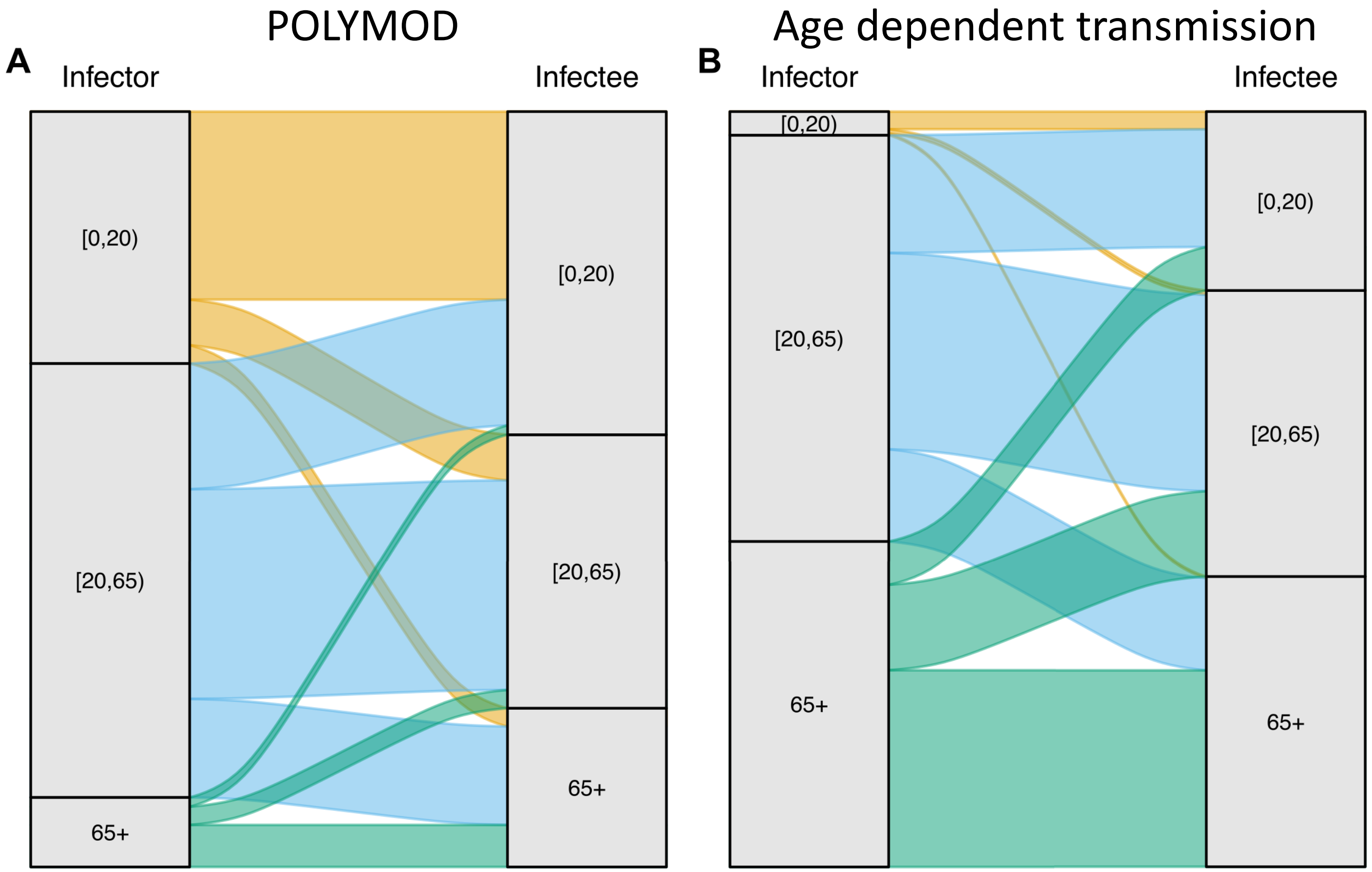


From the green line on the previous slide

In order to explain observations from Wuhan, it is necessary to have a profoundly strange profile of transmissibility with age

Work with James Hay, David Haw, Jess Metcalf and Michael Mina - submitted

Radically different frequencies of transmission pairs among age groups



Work with James Hay, David Haw, Jess Metcalf and Michael Mina - submitted

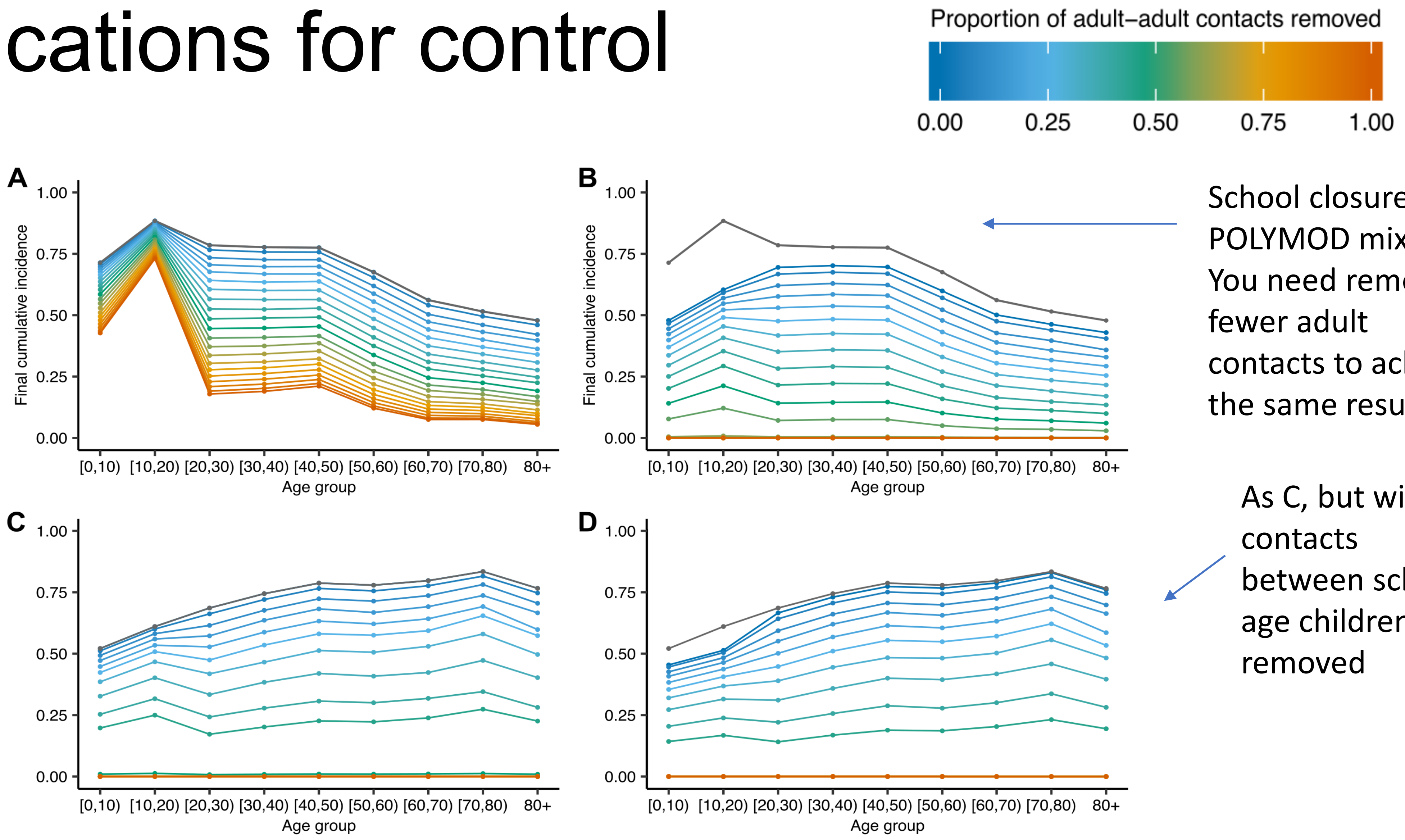
Implications for control

No school closure, POLYMOD mixing

School closure, POLYMOD mixing. You need remove fewer adult contacts to achieve the same result

As A, but with age dependent transmission

As C, but with contacts between school age children removed



Work with James Hay, David Haw, Jess Metcalf and Michael Mina - submitted

Summary

- In the presence of uncertainty around the role of different age groups in transmission, interventions need to target all age groups
- Determining the role of children in transmission is essential
- Some household studies suggest it is limited but note bias – because primary cases are more likely to be detected in older age groups
- Also note that transmission in schools may be different in character from in households
- We will be getting data soon – schools are planned to reopen in some places

Health care, the pandemic and the non-covid cohort

- A feature of the pandemic has been outbreaks in healthcare
- A large number of early cases of infection in both Wuhan and Italy were healthcare workers
- Protection of the non-covid cohort is essential

ORIGINAL ARTICLE

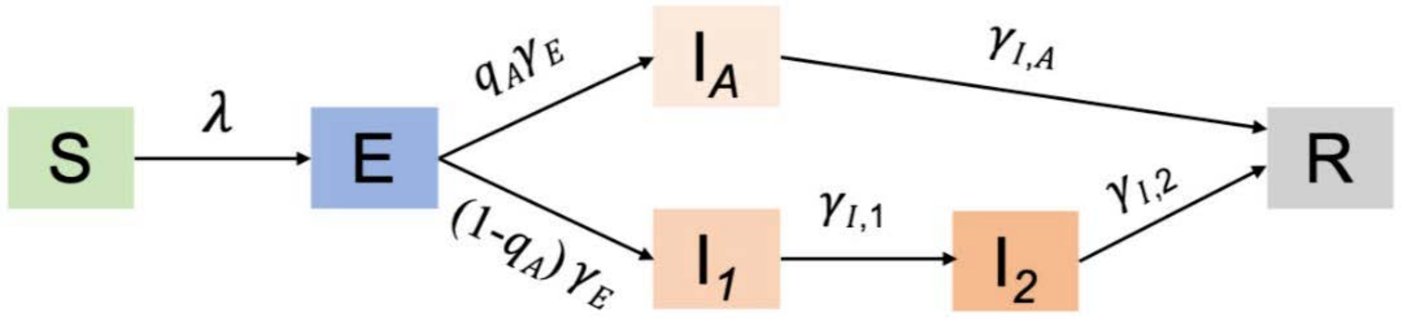
Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility

Melissa M. Arons, R.N., Kelly M. Hatfield, M.S.P.H., Sujan C. Reddy, M.D., Anne Kimball, M.D., Allison James, Ph.D., Jesica R. Jacobs, Ph.D., Joanne Taylor, Ph.D., Kevin Spicer, M.D., Ana C. Bardossy, M.D., Lisa P. Oakley, Ph.D., Sukarma Tanwar, M.Med., Jonathan W. Dyal, M.D., et al., for the Public Health–Seattle and King County and CDC COVID-19 Investigation Team*

Modeling transmission in the non-covid cohort

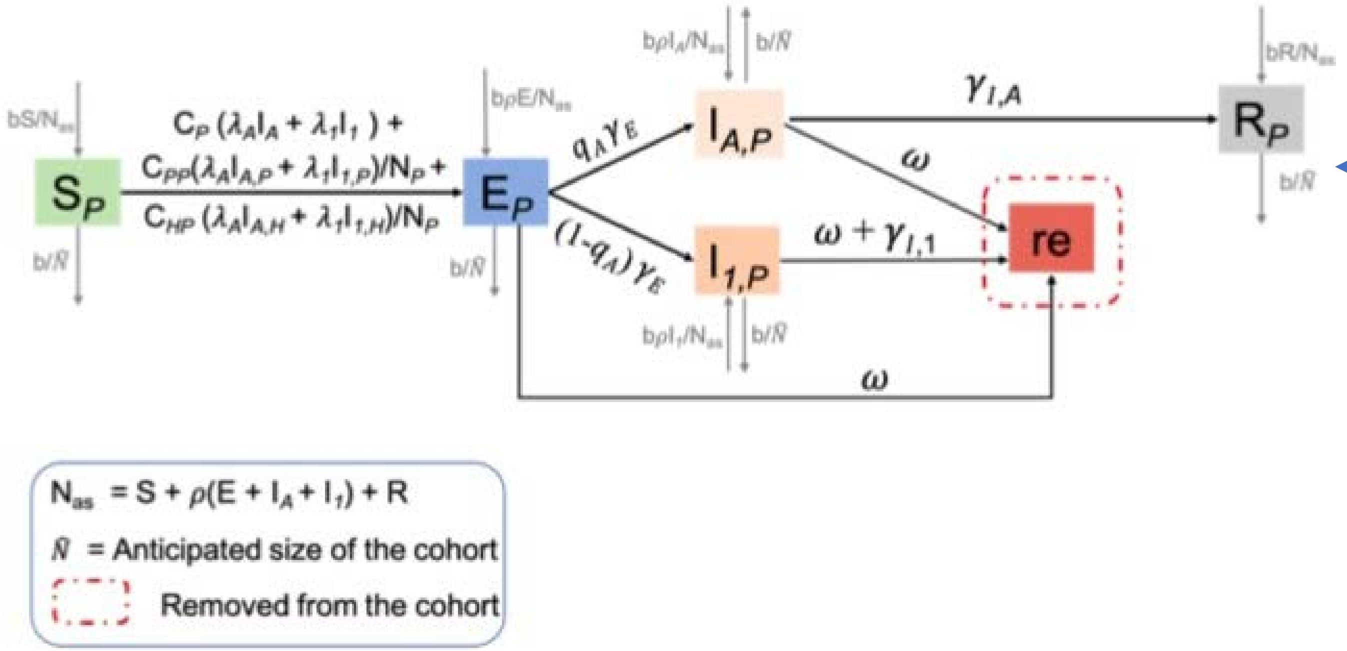
Work by Joel Miller and Xueting Qiu

- We developed a deterministic SEIR model for the general population as shown, including a subset of presymptomatic and asymptomatic infections



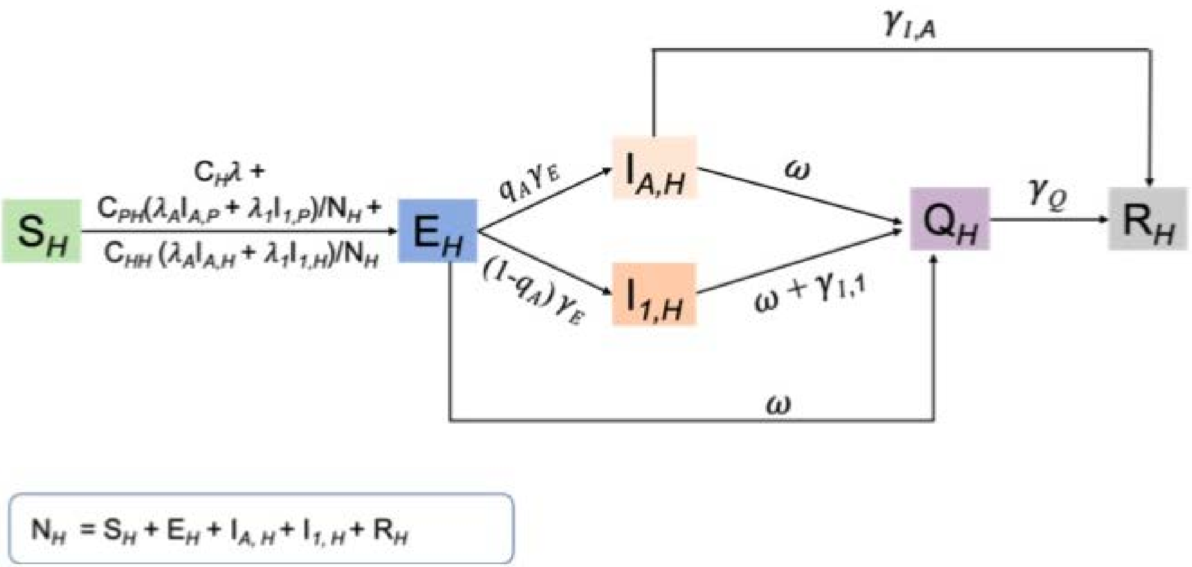
Force of Infection $\lambda = \lambda_1 I_1 + \lambda_2 I_2 + \lambda_A I_A$

Extending to health care



These are the (presumed) uninfected patients

These are the health care workers (HCWs)



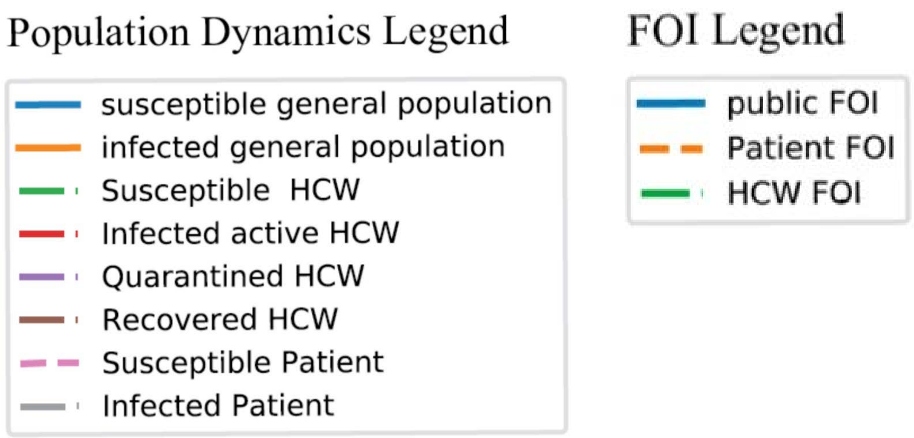
Model is a stochastic simulation

The risk of SARS-CoV-2 transmission in the healthcare setting and potential impact of cohorting strategies

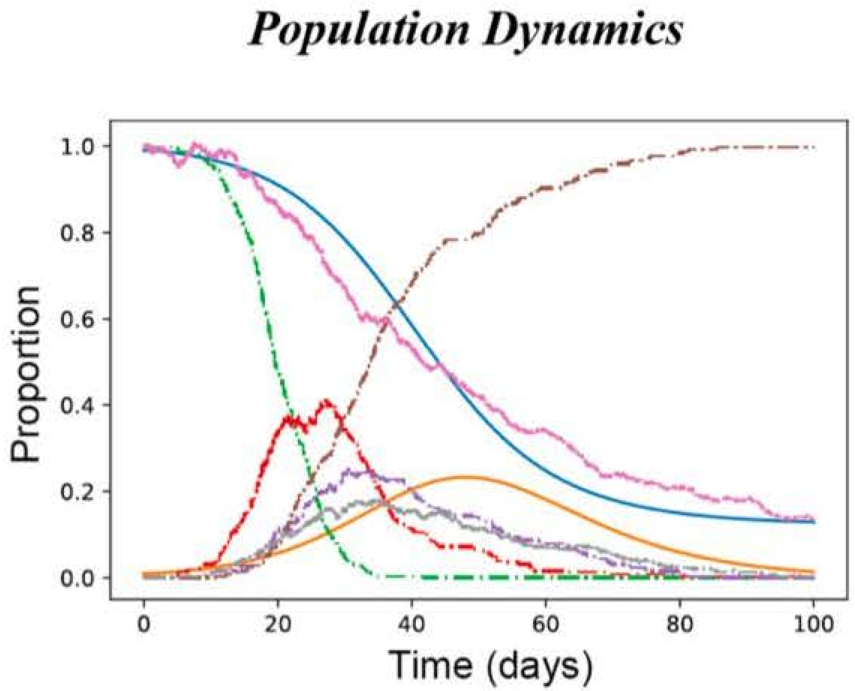
Joel C. Miller[1*], Xueting Qiu[2], William P. Hanage[2]

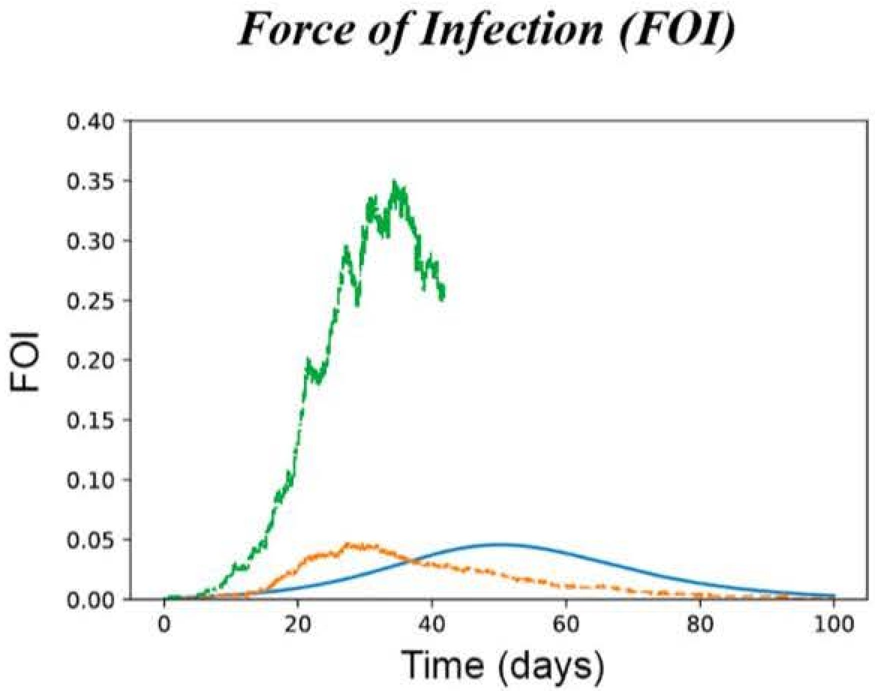
- https://www.medrxiv.org/content/10.1101/2020.04.20.20073080v1.full

Doing nothing is a bad idea

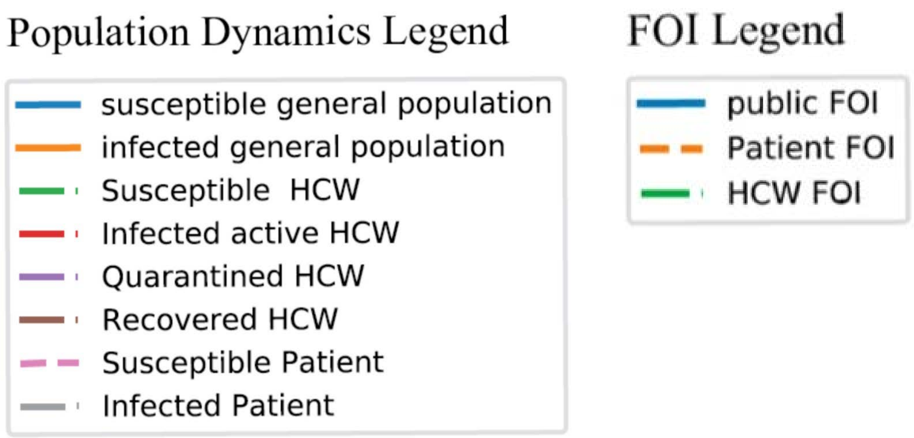


(a) No Testing; No PPE

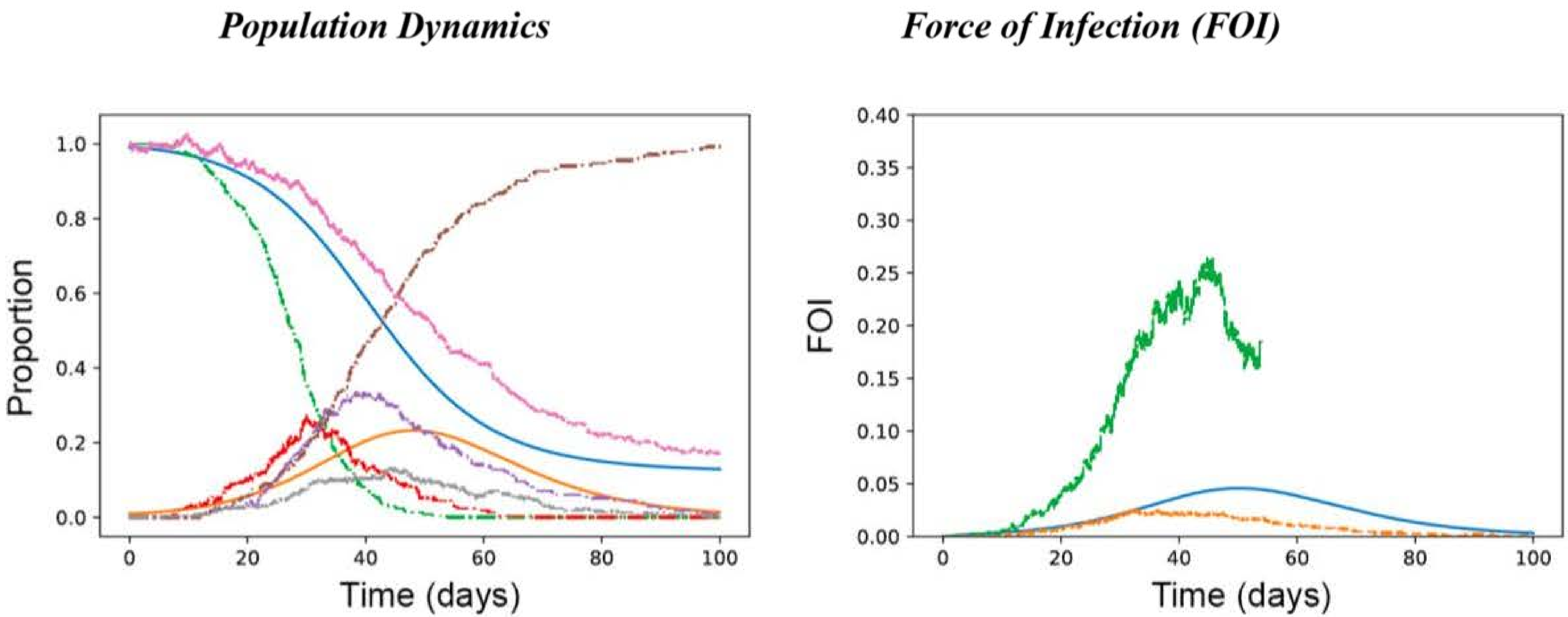




Testing alone helps – but doesn’t solve

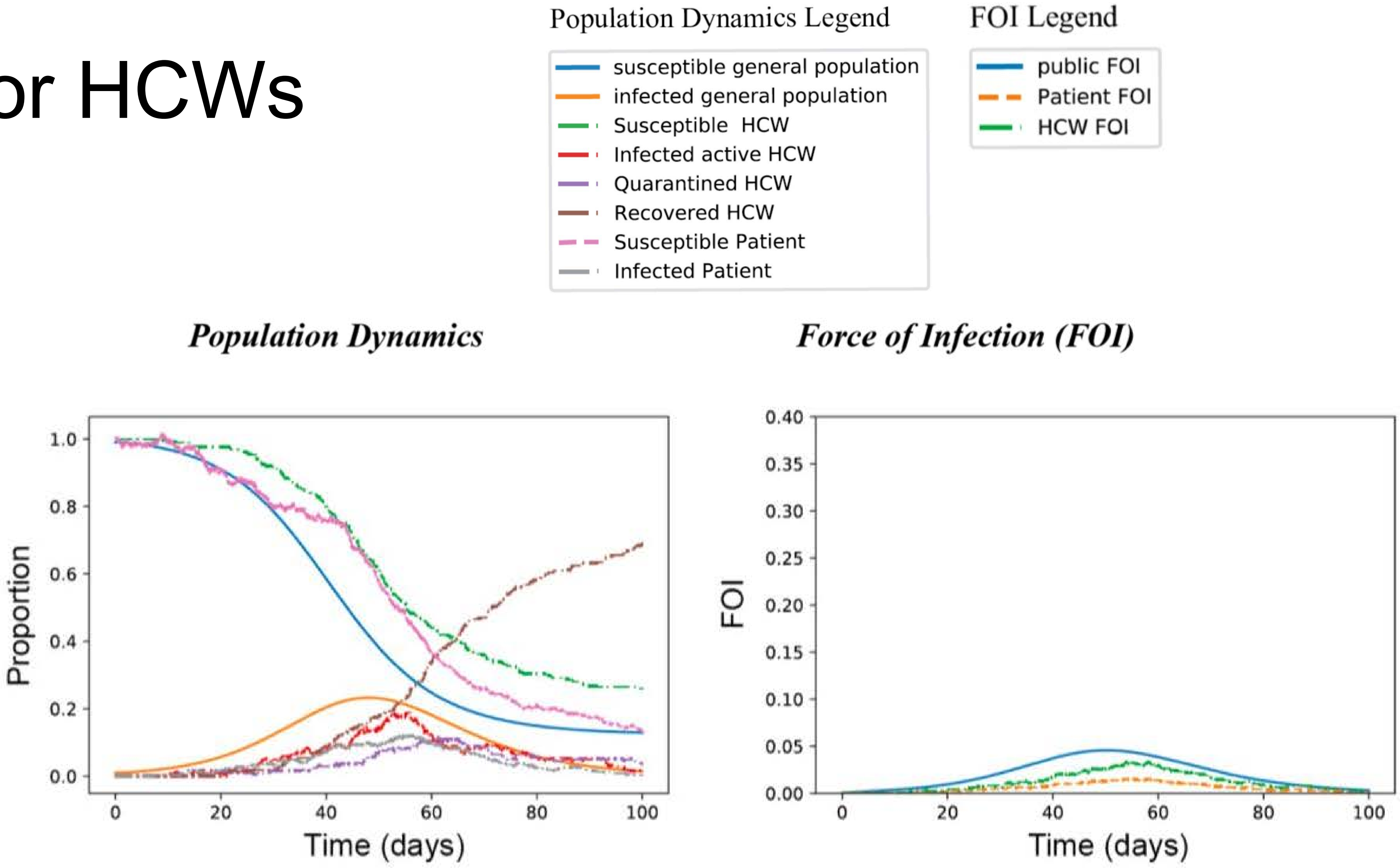


(b) 5% Testing; No PPE

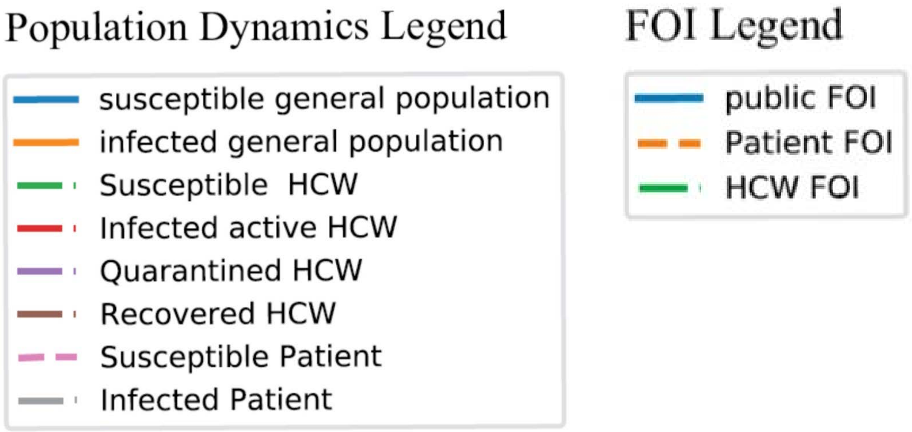


PPE for HCWs

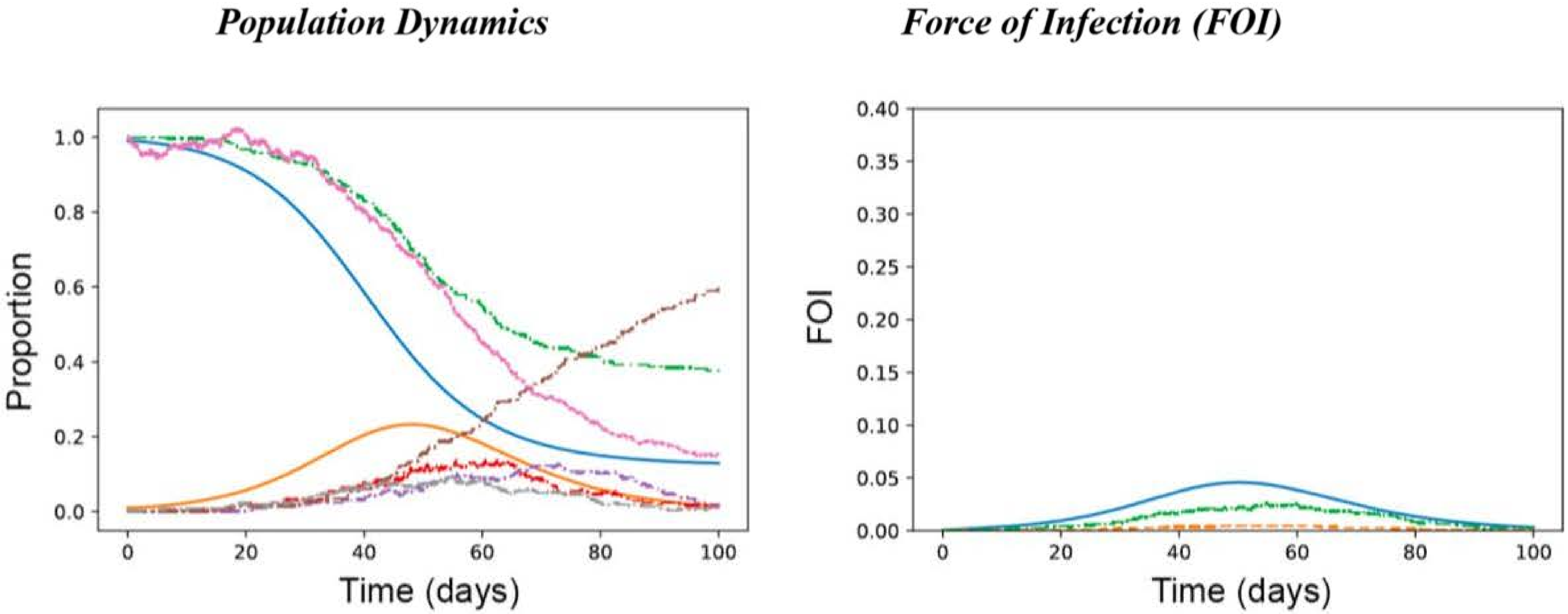
(c) No Testing; HCWs PPE only



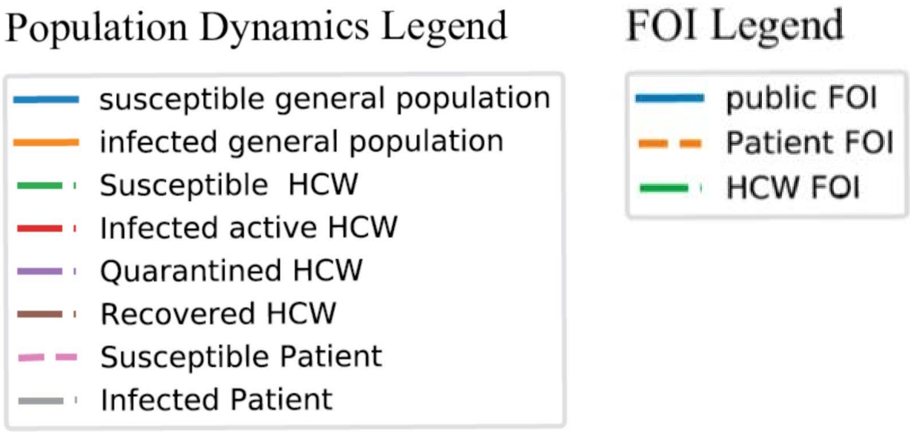
PPE for patients and HCWs



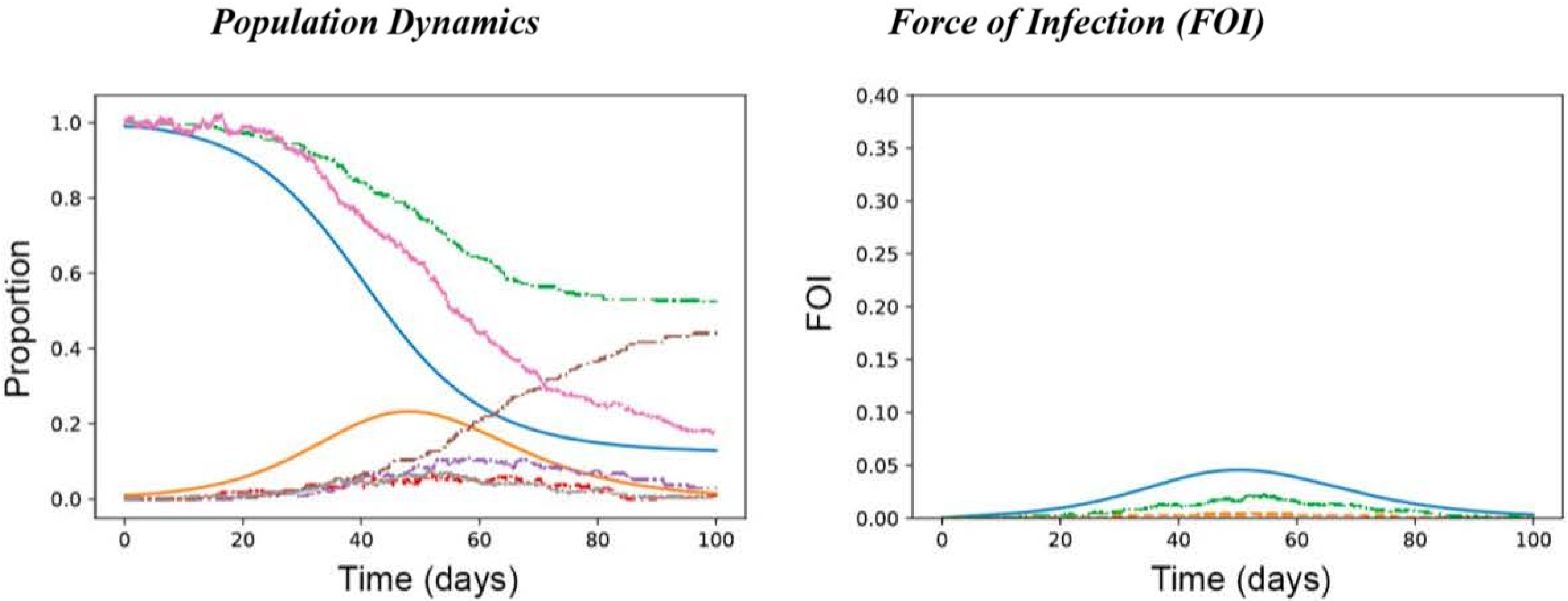
(d) No Testing; Both HCWs and Patients PPE



Testing and PPE



(e) 5% Testing; Both HCWs and Patients PPE

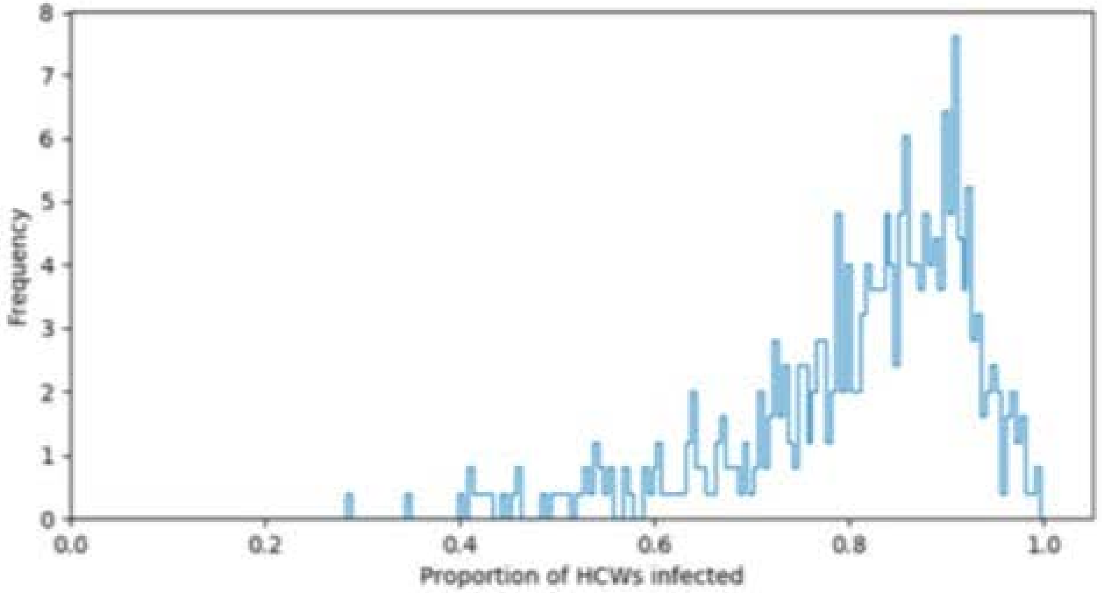


Smaller cohorts

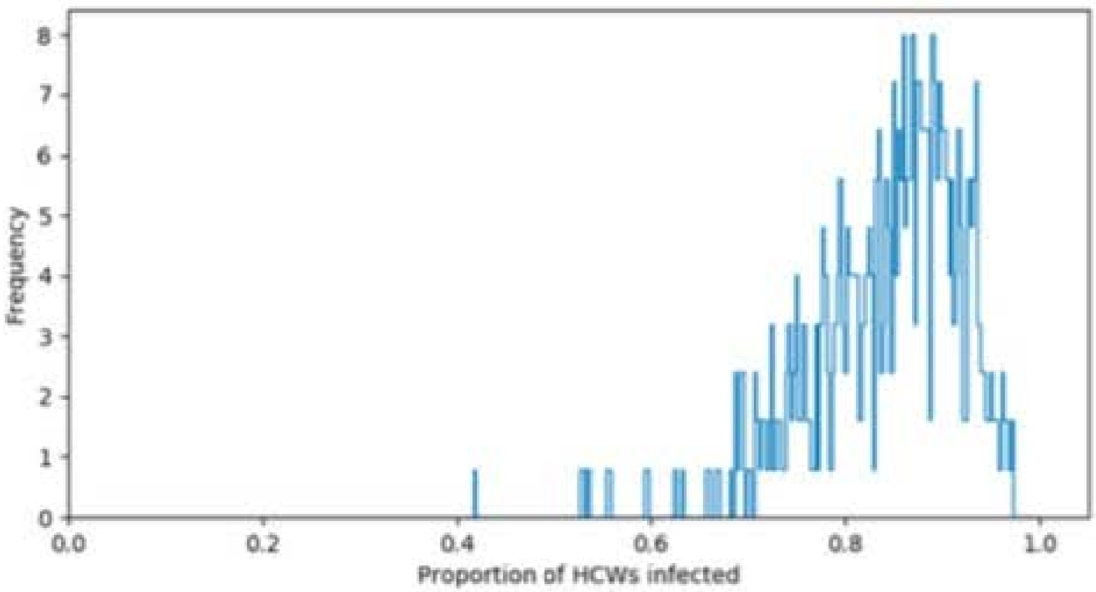
- By making your cohorts smaller, both for HCWs and patients you can limit the consequences of virus introduction
- Known for some time, see the Cruciform Building from UCL

Effects of sub-cohorting

- Run 500 simulations with same parameters
- Results are the distributions of the final size of the outbreak in the HCWs



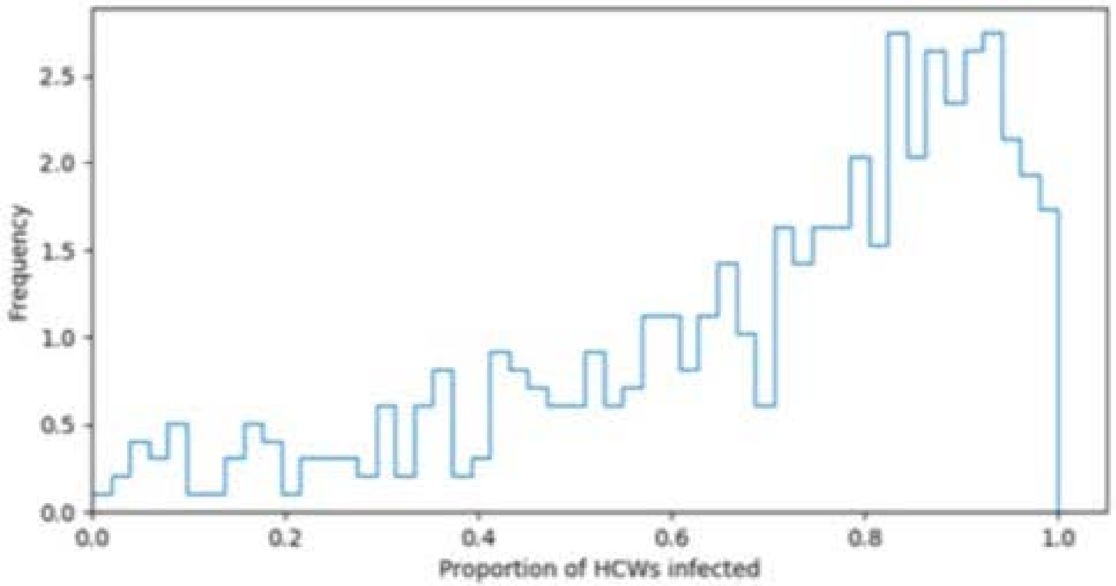
(e) $N_{Patient} = 800; N_{HCW} = 200$



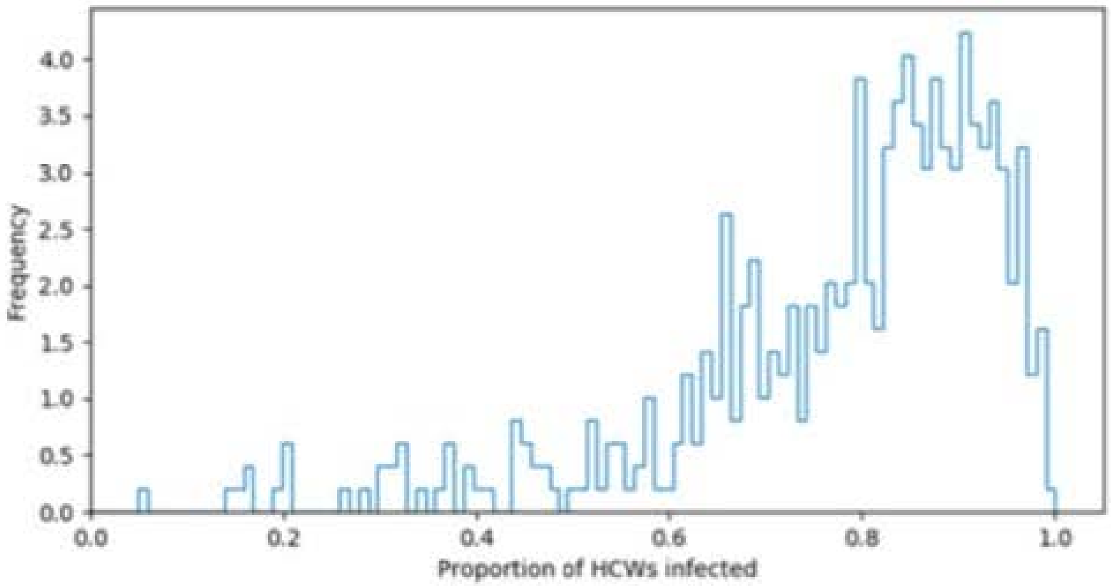
(f) $N_{Patient} = 1600; N_{HCW} = 400$

Effects of sub-cohorting

- Smaller cohorts reduce the probability of a large outbreak in HCWs
- This is in the absence of other control measures, and does not include any action taken to prevent transmission



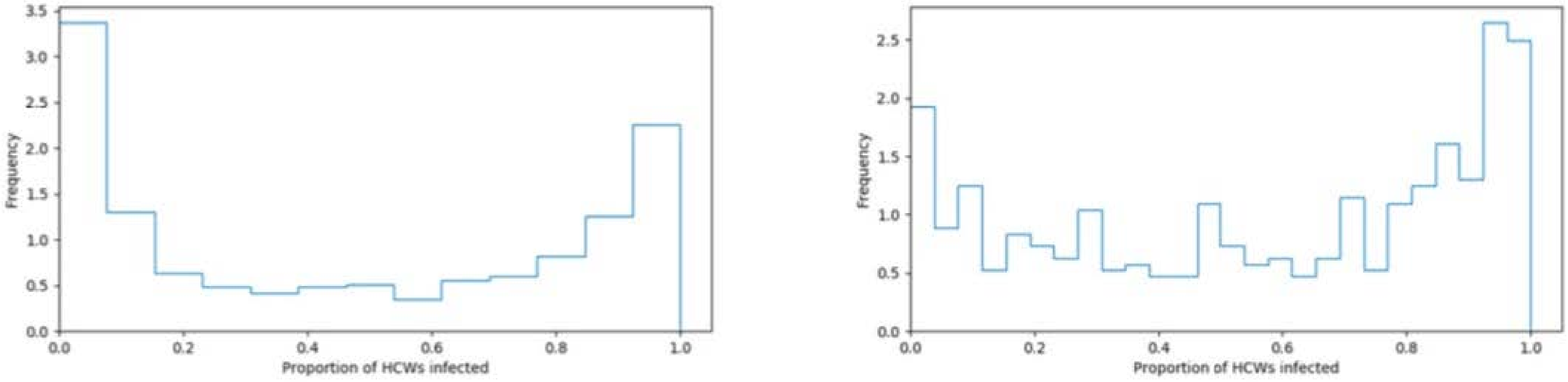
(c) $N_{Patient} = 200; N_{HCW} = 50$



(d) $N_{Patient} = 400; N_{HCW} = 100$

Effects of sub-cohorting

- In very small cohorts, you approach a bimodal distribution
- This suggests benefit of small cohorts especially when the force of infection from the community is low (infrequent introductions)



(a) $N_{Patient} = 50; N_{HCW} = 12$ (b) $N_{Patient} = 100; N_{HCW} = 25$

Issues

- We do not model what happens to the patients removed from the model after diagnosis of covid
- We do not model any mitigation strategies in the community
- Like all models, dependent on assumptions

Acknowledgments

- Staph aureus: Rose Chang and Marc Lipsitch
- Transmission in children: James Hay, David Haw, Jess Metcalf and Michael Mina
- Transmission in Healthcare: Joel Miller and Xueting Qiu

https://ccdd.hsph.harvard.edu/covid-19/

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH Quicklinks

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Work on COVID-19 (Coronavirus)

The Center for Communicable Disease Dynamics is closely monitoring the progress of COVID-19 (coronavirus). Explore what CCDD has discovered and published about the Virus below.

Publications

Research published by the CCDD.

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Op-eds and Other #scicomm

National coverage written by and featuring CCDD faculty.

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Twitter Feeds

The latest updates from CCDD faculty.

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CCDD COVID-19 team

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- Yonatan Grad
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- Rene Niehus
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NIH National Institute of General Medical Sciences