Northeastern

Virtual Journal Club

First Friday every month, 12-1 pm ET

7/02/2020

Healthcare Systems Engineering Institute
Northeastern University, Boston MA
www.HSyE.org

HSyE

Agenda

- 12:05 – 12:20 pm — Paper 1 overview
- 12:20 – 12:30 pm — Discussion
- 12:30 – 12:45 pm — Paper 2 overview
- 12:45 – 12:55 pm — Discussion
- 12:55 pm — Adjourn

Slides and discussion summary posted on journal club webpage (hsye.org/journal-club)

Announcements / Upcoming events

1. Journal Club Calendar (August 7)

- *Inferring change points in the spread of COVID-19 reveal the effectiveness of interventions*
- *After COVID-19: How To Rejuvenate Primary Care For The Future*
- Archive on website - hsye.org/journal-club

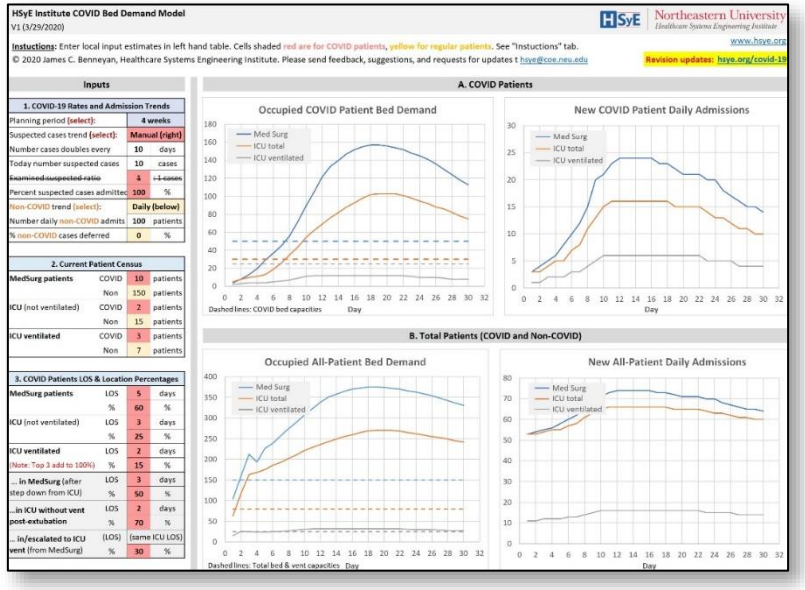
2. Collaborative Research Center

- Center for Healthcare Engineering Research
- Get involved – fall projects!
- hsye.org/cher

3. IE Senior Projects, fall semester projects?

4. COVID Tools Webpage

- Surge capacity model
- Epidemic prediction models
- Statistical detection
- Testing
- School and workplace opening

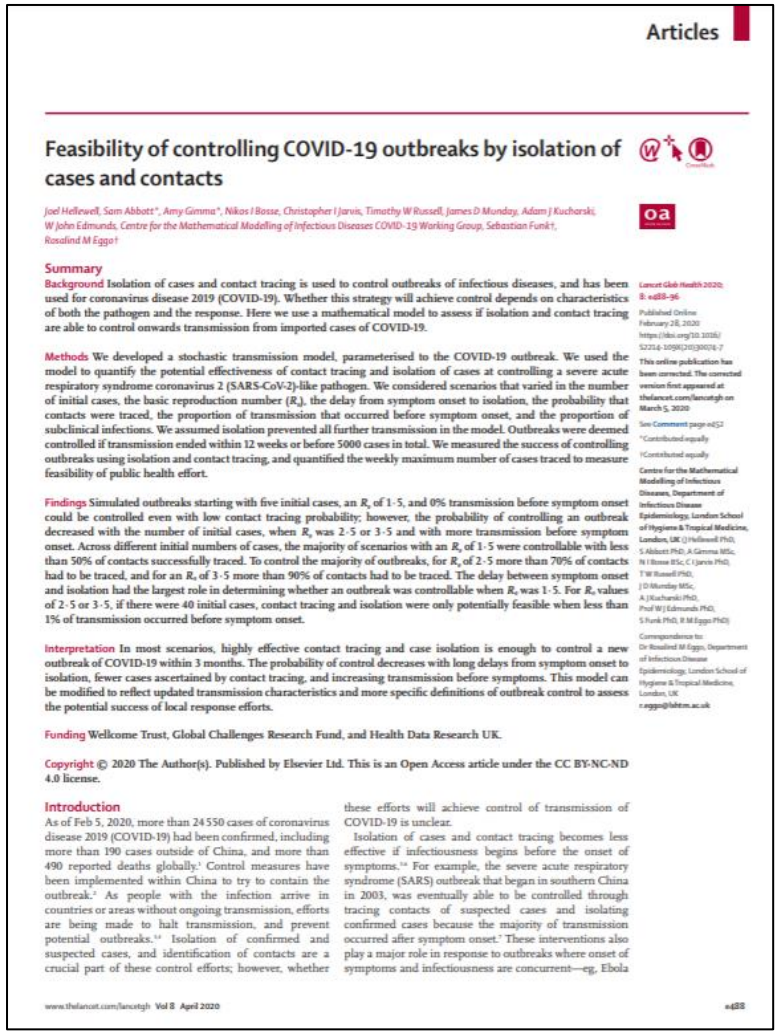


Paper 1

Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts, *The Lancet Global Health*, 2020

Joel Hellewell, Sam Abbott, Amy Gimma, Nikos I Bosse, Christopher I Jarvis, Timothy W Russell, James D Munday, Adam J Kucharski, W John Edmunds, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Sebastian Funk, Rosalind M Eggo

Centre for the Mathematical Modelling of Infectious Diseases, Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK



Articles

Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts

Joel Hellewell, Sam Abbott*, Amy Gimma*, Nikos I Bosse, Christopher I Jarvis, Timothy W Russell, James D Munday, Adam J Kucharski, W John Edmunds, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Sebastian Funk†, Rosalind M Eggo†

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Summary

Background Isolation of cases and contact tracing is used to control outbreaks of infectious diseases, and has been used for coronavirus disease 2019 (COVID-19). Whether this strategy will achieve control depends on characteristics of both the pathogen and the response. Here we use a mathematical model to assess if isolation and contact tracing are able to control onwards transmission from imported cases of COVID-19.

Methods We developed a stochastic transmission model, parameterised to the COVID-19 outbreak. We used the model to quantify the potential effectiveness of contact tracing and isolation of cases at controlling a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-like pathogen. We considered scenarios that varied in the number of initial cases, the basic reproduction number (R_0), the delay from symptom onset to isolation, the probability that contacts were traced, the proportion of transmission that occurred before symptom onset, and the proportion of subclinical infections. We assumed isolation prevented all further transmission in the model. Outbreaks were deemed controlled if transmission ended within 12 weeks or before 5000 cases in total. We measured the success of controlling outbreaks using isolation and contact tracing, and quantified the weekly maximum number of cases traced to measure feasibility of public health effort.

Findings Simulated outbreaks starting with five initial cases, an R_0 of 1·5, and 0% transmission before symptom onset could be controlled even with low contact tracing probability; however, the probability of controlling an outbreak decreased with the number of initial cases, when R_0 was 2·5 or 3·5 and with more transmission before symptom onset. Across different initial numbers of cases, the majority of scenarios with an R_0 of 1·5 were controllable with less than 50% of contacts successfully traced. To control the majority of outbreaks, for R_0 of 2·5 more than 70% of contacts had to be traced, and for an R_0 of 3·5 more than 90% of contacts had to be traced. The delay between symptom onset and isolation had the largest role in determining whether an outbreak was controllable when R_0 was 1·5. For R_0 values of 2·5 or 3·5, if there were 40 initial cases, contact tracing and isolation were only potentially feasible when less than 1% of transmission occurred before symptom onset.

Interpretation In most scenarios, highly effective contact tracing and case isolation is enough to control a new outbreak of COVID-19 within 3 months. The probability of control decreases with long delays from symptom onset to isolation, fewer cases ascertained by contact tracing, and increasing transmission before symptoms. This model can be modified to reflect updated transmission characteristics and more specific definitions of outbreak control to assess the potential success of local response efforts.

Funding Wellcome Trust, Global Challenges Research Fund, and Health Data Research UK.

Introduction

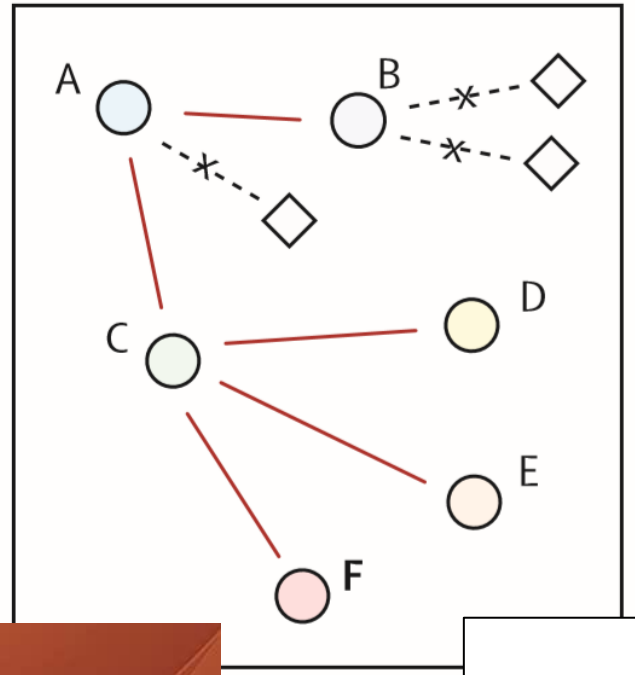
As of Feb 5, 2020, more than 24 550 cases of coronavirus disease 2019 (COVID-19) had been confirmed, including more than 190 cases outside of China, and more than 490 reported deaths globally.[1] Control measures have been implemented within China to try to contain the outbreak.[2] As people with the infection arrive in countries or areas without ongoing transmission, efforts are being made to halt transmission, and prevent potential outbreaks.[3,4] Isolation of confirmed and suspected cases, and identification of contacts are a crucial part of these control efforts; however, whether these efforts will achieve control of transmission of COVID-19 is unclear.

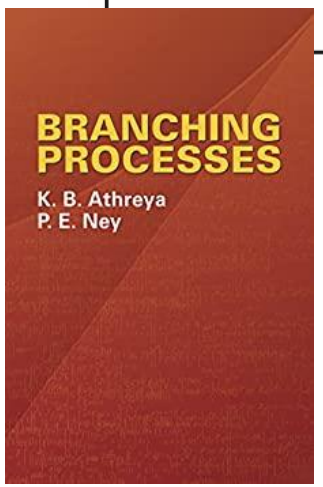
Isolation of cases and contact tracing becomes less effective if infectiousness begins before the onset of symptoms.[5,6] For example, the severe acute respiratory syndrome (SARS) outbreak that began in southern China in 2003, was eventually able to be controlled through tracing contacts of suspected cases and isolating confirmed cases because the majority of transmission occurred after symptom onset.[7] These interventions also play a major role in response to outbreaks where onset of symptoms and infectiousness are concurrent—eg, Ebola

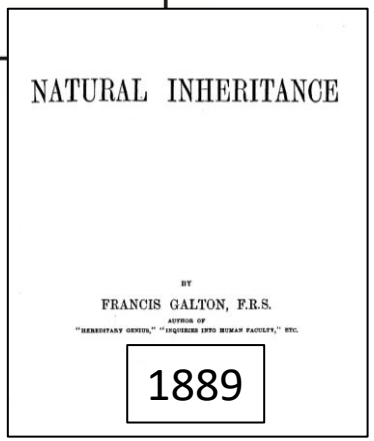
www.thelancet.com/lancetgh Vol 8 April 2020 e488

Overview

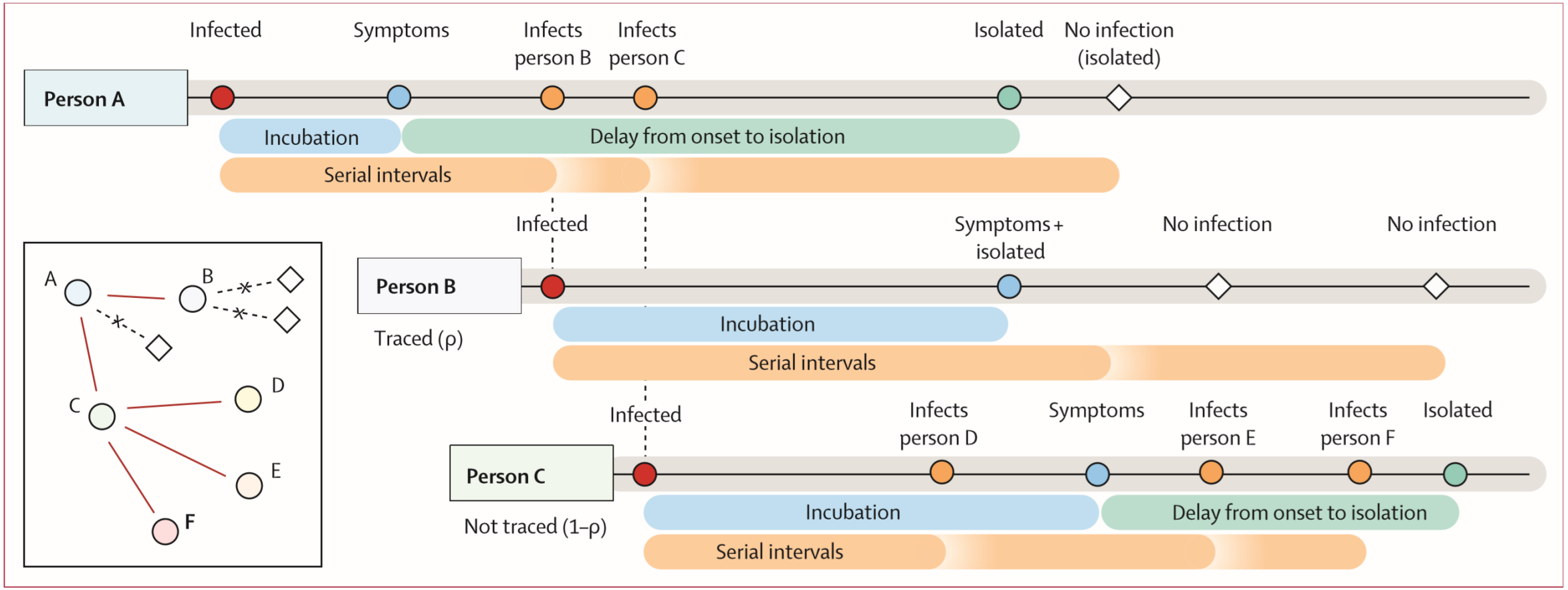
- SARS-Cov-2 pandemic continuing problem
- Contact tracing effective solution?
- Branching process stochastic (simulation) model
- Used model to analyze range of scenarios
- Identified conditions under which contact tracing will be effective and ineffective
- Nice example of art of modeling (Box)







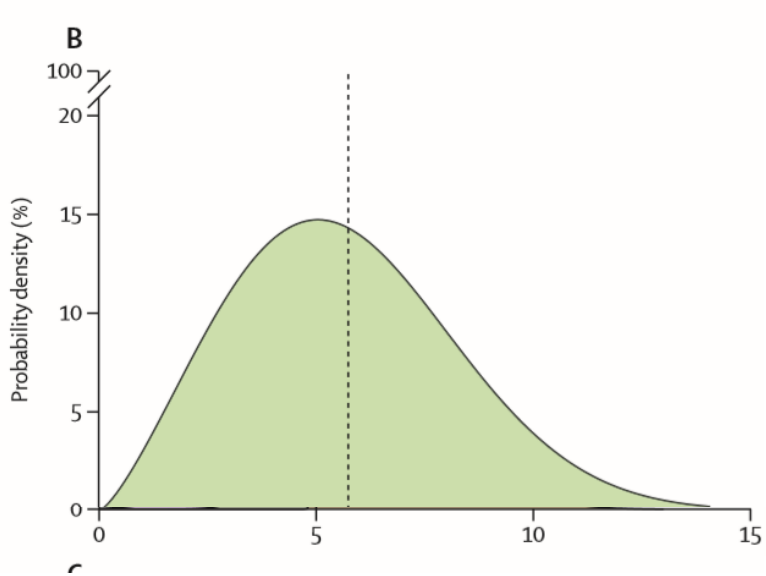
Model details (1/3)



Secondary cases ~ negative binomial, Incubation period ~ Weibull, Time of new infections ~ serial distribution skewed normal up to time of isolation, nonclinical probability, new nonclinical cases only detected by self-report or testing

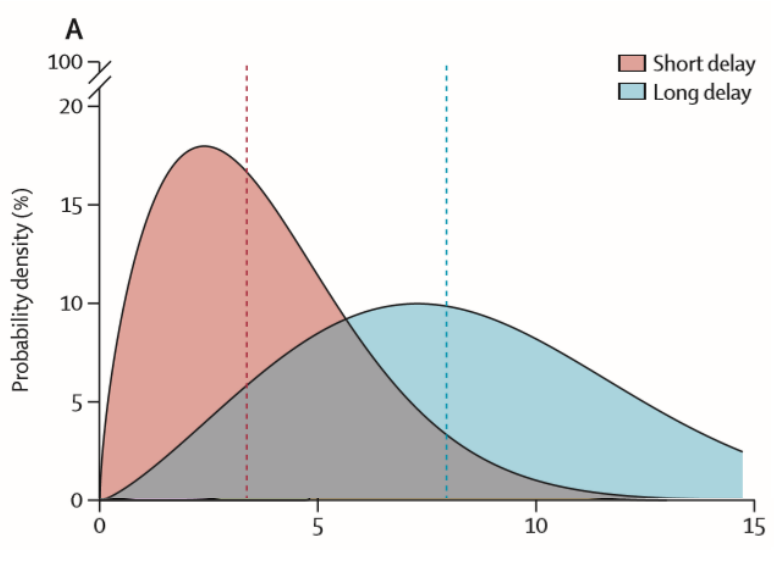
Model details (2/3)

Infected to symptomatic incubation period



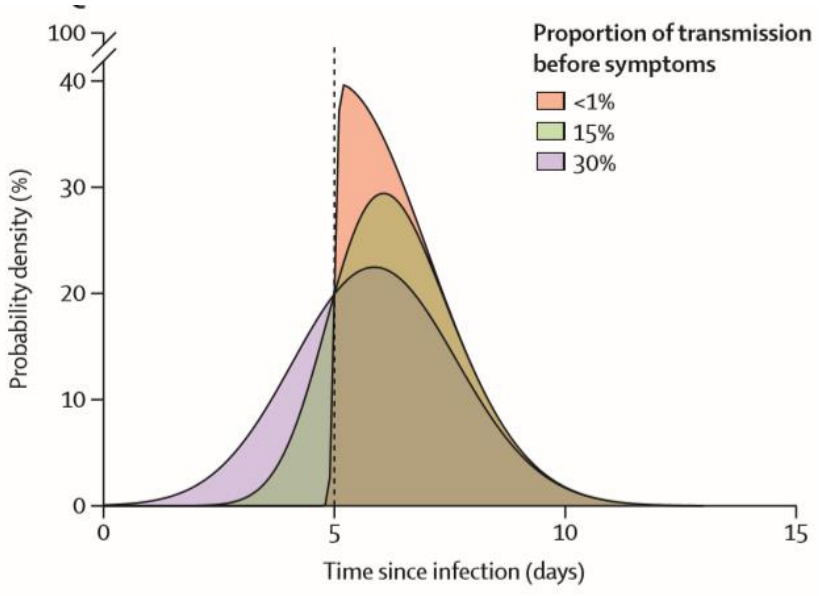
Blue interval (prior figure)

Symptom onset to isolation



Teal interval (prior figure)

"Infected to infectee" serial interval: posterior distribution of time until infect other people



Orange interval (prior figure)

Model details (3/3)

Varied input/assumption scenarios

Assumptions (naïve?):

- 90-100% cases symptomatic & tested
- 100% test accuracy
- Unlimited tracing resources
- Immediate isolation of traced+ cases (i.e. no “just one last errand”)
- No isolation transmission (family, room mates, bubble), 100% isolation compliance

Outcomes:

- *Effort*: Weekly cases to trace
- *Effectiveness*: Probability (%) outbreak is controlled (defined as: case transmission ends < 12 weeks, < 5000 infected)

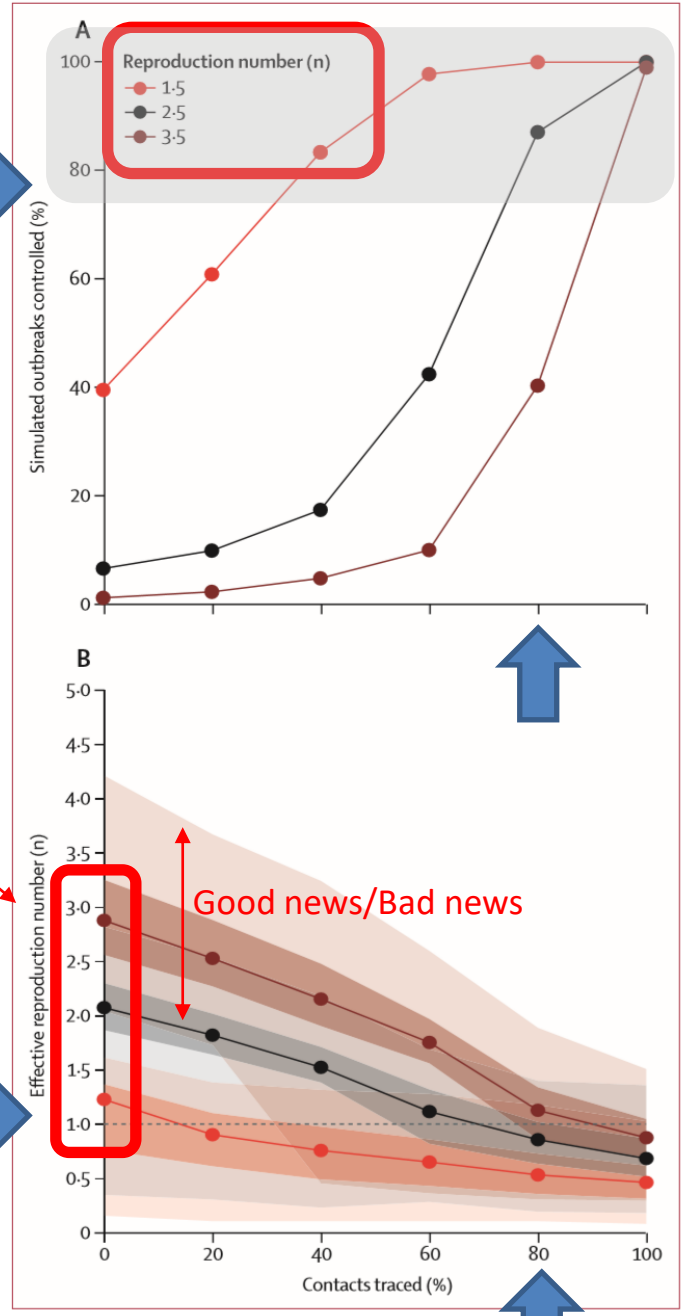
	Value	Reference
Sampled		
Delay from onset to isolation (short)	3·43 days (2·02–5·23)	Donnelly et al[20]
Delay from onset to isolation (long)	8·09 days (5·52–10·93)	Li et al[21]
Incubation period	5·8 days (2·6)	Backer et al[22]
Serial interval	Incubation period (2)	Assumed
Fixed		
Initial cases	5, 20, and 40	Public Health England[11] and Klinkenberg and colleagues[14]
Percentage of contacts traced	0%, 20%, 40%, 60%, 80%, 100%	Tested
Reproduction number (R_0; low, central, high estimate)	1·5, 2·5, 3·5	Kucharski et al[17] and Imai et al[18]
Overdispersion in R_0 (SARS-like)	0·16	Lloyd-Smith et al[19]
R_0 after isolation	0	Assumed
Cases isolated once identified	100%	Assumed
Isolation effectiveness	100%	Assumed
Subclinical infection percentage	0%, 10%	Tested

Data are median (IQR) or mean (SD), n, or %. Sampled values are probabilistically sampled during the simulation, and fixed values remain constant during the simulation. The mean of the short and long delays are 3·83 and 9·1, respectively. SARS=severe acute respiratory syndrome.

Table: **Parameter values for the model**

Results (1/2)

- Effective -- if low initial cases (5), low R_0 (1.5), low pre-onset transmission (0)
- Ineffective -- if R_0 at epidemic levels (2.5-3.5), pre-onset transmission >1%, initial cases > 40
- As R_0 increases (2.5, 3.5), tracing needs to be more complete (70-90%)
- Very sensitive to number initial cases (< 20) and pre-symptomatic transmission (< 1%)
- '80-80 rule': In general, tracing + isolation > 80% → 80% chance end outbreak < 12 weeks



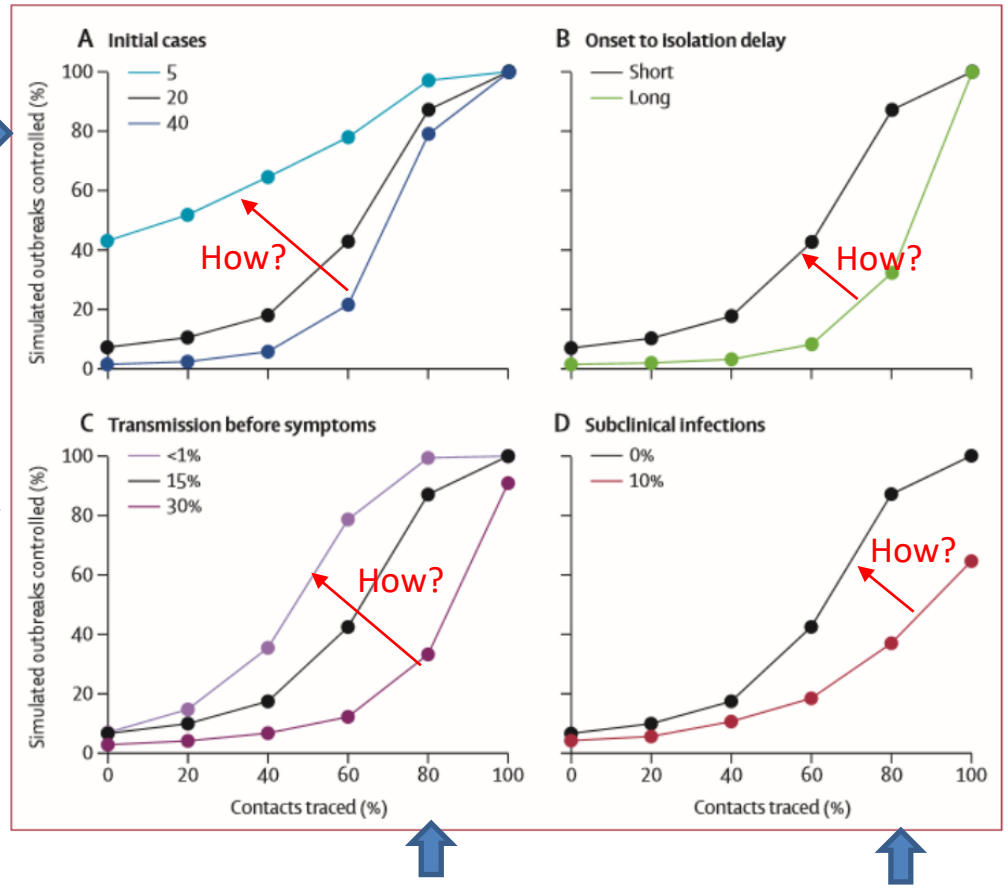
Desired results region

Pop quiz

Results (2/2)

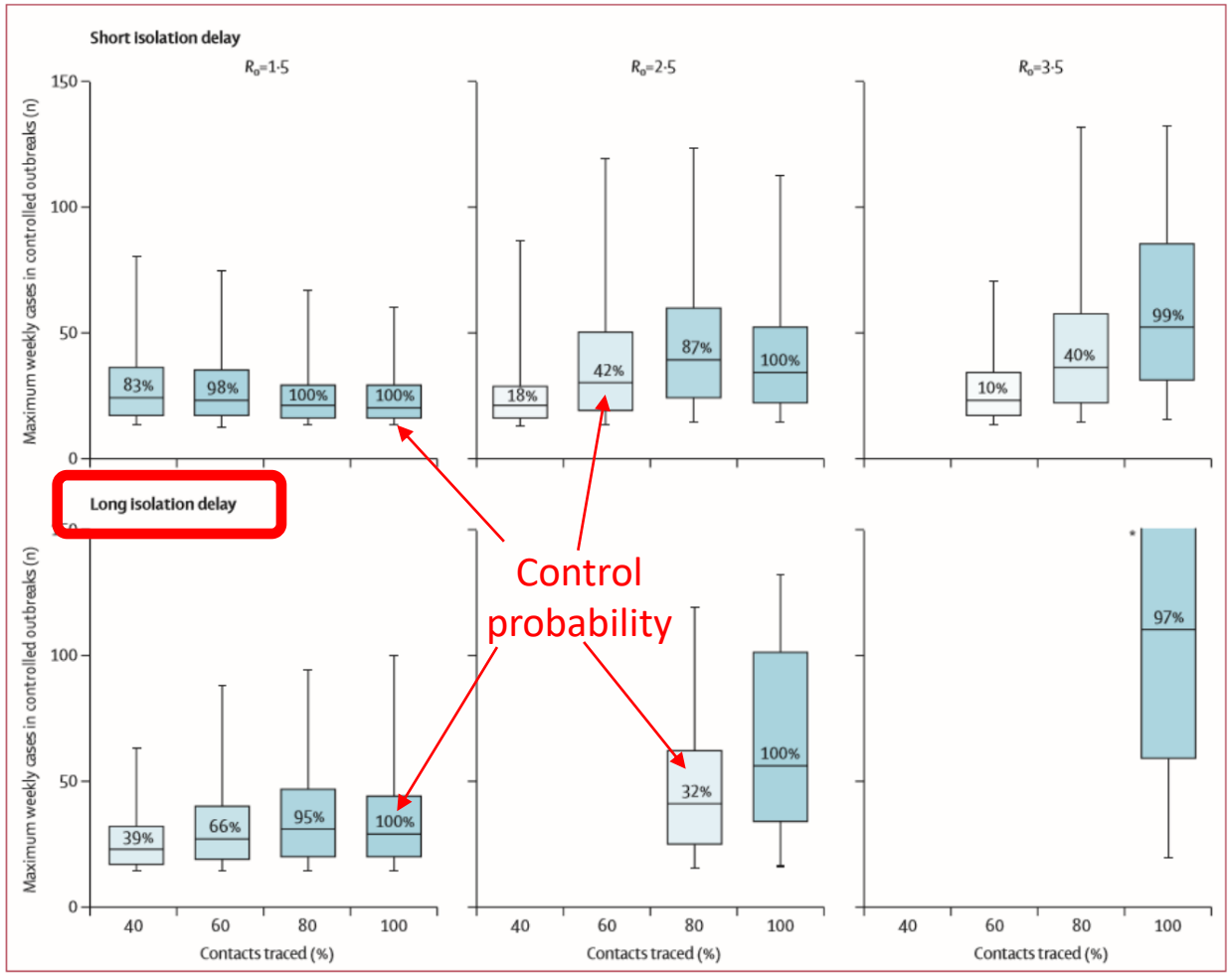
Sensitivity to assumptions – Initial cases, isolation delay, pre-symptomatic transmission, 'asymptomatic')

(Same '80-80' takeaway for reasonable control)



Weekly number of cases requiring tracing

esp for longer (COVID-19 realistic) isolation delays



Observations and implications

- Simple models can be useful (G.E.P. Box)
- Tracing as safety-net vs. upstream prevention
- Suppose school opens with >5-40 students infected on arrival (note: 1% x 10,000 = 100), tracing 25-75% possible at best, isolation 50-100% compliant, sensitivity 60-85%
- SARS 2003: Majority of transitions occurred after symptom onset. Tracing was effective
- COVID: 30-40% transmissions asymptomatic or pre-symptomatic. Effectiveness less clear
- Does control within 3 months matter to a 12-week semester? (better measures?: current and total # infected, isolated, dead)

Notable Quotables

Contact tracing and case isolation needs to be highly effective to control a Covid-19 outbreak within 3 months.

If Covid-19 can be controlled by isolation and tracing, then public health efforts should focus here; if not, then additional resources might be needed for additional interventions

In some plausible scenarios, case isolation alone would be unlikely to control transmission… [esp if pre-symptomatic transmissions, infectious-to-isolation delays]

Discussion topics

1. Paper strengths and weaknesses
2. Quality of text, presentation, exhibits
3. Implications to our/your work and issues
4. Potential extensions

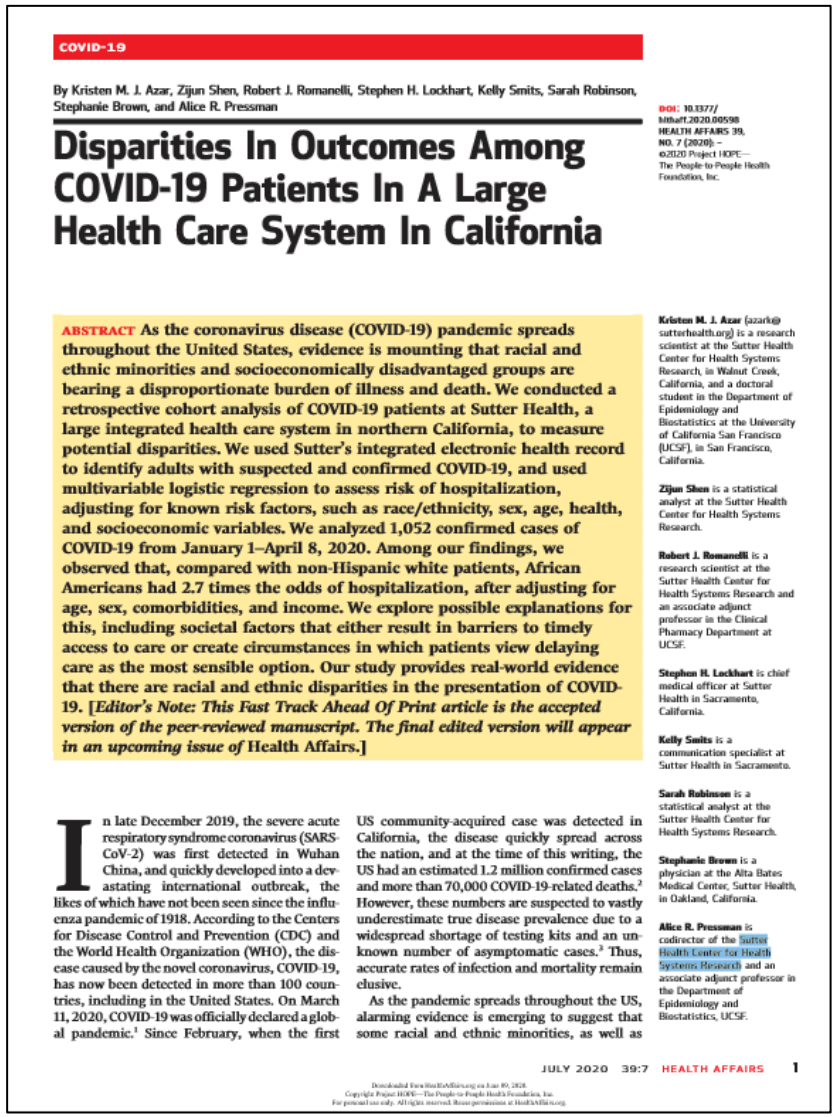
Paper 2:

Disparities In Outcomes Among COVID-19 Patients In A Large Health Care System In California

Health Affairs, 2020

Kristen M. J. Azar, Zijun Shen, Robert J. Romanelli, Stephen H. Lockhart, Kelly Smits, Sarah Robinson, Stephanie Brown, and Alice R. Pressman

Sutter Health Center for Health Systems Research, Sutter Health, University of California San Francisco



COVID-19

By Kristen M. J. Azar, Zijun Shen, Robert J. Romanelli, Stephen H. Lockhart, Kelly Smits, Sarah Robinson, Stephanie Brown, and Alice R. Pressman

DOI: 10.1377/hlthaff.2020.00598
HEALTH AFFAIRS 39, NO. 7 (2020): –

Disparities In Outcomes Among COVID-19 Patients In A Large Health Care System In California

ABSTRACT As the coronavirus disease (COVID-19) pandemic spreads throughout the United States, evidence is mounting that racial and ethnic minorities and socioeconomically disadvantaged groups are bearing a disproportionate burden of illness and death. We conducted a retrospective cohort analysis of COVID-19 patients at Sutter Health, a large integrated health care system in northern California, to measure potential disparities. We used Sutter's integrated electronic health record to identify adults with suspected and confirmed COVID-19, and used multivariable logistic regression to assess risk of hospitalization, adjusting for known risk factors, such as race/ethnicity, sex, age, health, and socioeconomic variables. We analyzed 1,052 confirmed cases of COVID-19 from January 1–April 8, 2020. Among our findings, we observed that, compared with non-Hispanic white patients, African Americans had 2.7 times the odds of hospitalization, after adjusting for age, sex, comorbidities, and income. We explore possible explanations for this, including societal factors that either result in barriers to timely access to care or create circumstances in which patients view delaying care as the most sensible option. Our study provides real-world evidence that there are racial and ethnic disparities in the presentation of COVID-19. [*Editor's Note: This Fast Track Ahead Of Print article is the accepted version of the peer-reviewed manuscript. The final edited version will appear in an upcoming issue of* Health Affairs.]

Kristen M. J. Azar (azark@sutterhealth.org) is a research scientist at the Sutter Health Center for Health Systems Research, in Walnut Creek, California, and a doctoral student in the Department of Epidemiology and Biostatistics at the University of California San Francisco (UCSF), in San Francisco, California.

Zijun Shen is a statistical analyst at the Sutter Health Center for Health Systems Research.

Robert J. Romanelli is a research scientist at the Sutter Health Center for Health Systems Research and an associate adjunct professor in the Clinical Pharmacy Department at UCSF.

Stephen H. Lockhart is chief medical officer at Sutter Health in Sacramento, California.

Kelly Smits is a communication specialist at Sutter Health in Sacramento.

Sarah Robinson is a statistical analyst at the Sutter Health Center for Health Systems Research.

Stephanie Brown is a physician at the Alta Bates Medical Center, Sutter Health, in Oakland, California.

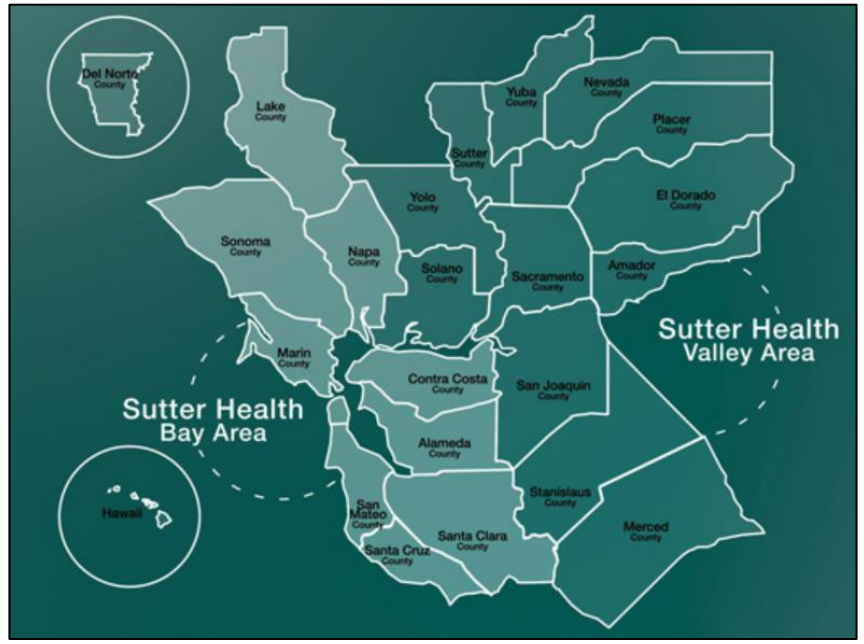
Alice R. Pressman is codirector of the Sutter Health Center for Health Systems Research and an associate adjunct professor in the Department of Epidemiology and Biostatistics, UCSF.

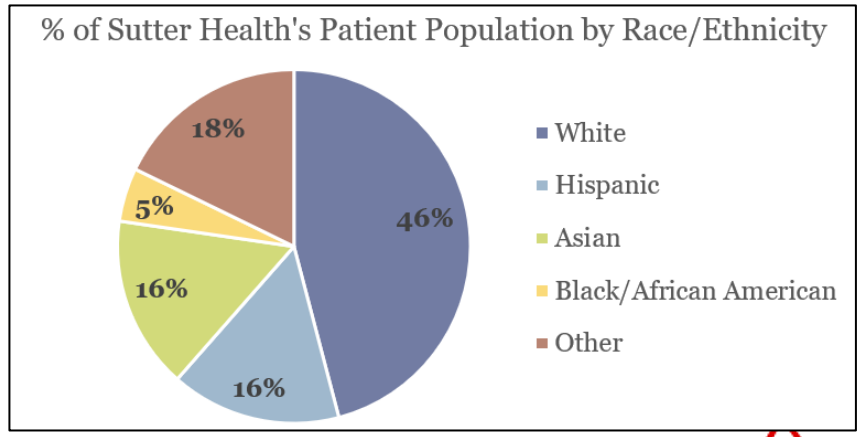
In late December 2019, the severe acute respiratory syndrome coronavirus (SARS-CoV-2) was first detected in Wuhan China, and quickly developed into a devastating international outbreak, the likes of which have not been seen since the influenza pandemic of 1918. According to the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO), the disease caused by the novel coronavirus, COVID-19, has now been detected in more than 100 countries, including in the United States. On March 11, 2020, COVID-19 was officially declared a global pandemic.[1] Since February, when the first US community-acquired case was detected in California, the disease quickly spread across the nation, and at the time of this writing, the US had an estimated 1.2 million confirmed cases and more than 70,000 COVID-19-related deaths.[2] However, these numbers are suspected to vastly underestimate true disease prevalence due to a widespread shortage of testing kits and an unknown number of asymptomatic cases.[3] Thus, accurate rates of infection and mortality remain elusive.

As the pandemic spreads throughout the US, alarming evidence is emerging to suggest that some racial and ethnic minorities, as well as

Overview

- CDC Report of Disparities in COVID Hospitalizations
  - African Americans represented 18% of cases and 33% of those hospitalized
- California
  - Expanded no-cost COVID-19 testing to all state residents
  - African Americans = 6.0% of the population, 6.1% of COVID cases, 10.3% of COVID-related deaths
- Sutter Health
  - Large mixed-payer, integrated health care delivery system serving highly populated and racially diverse regions
  - African Americans had 2.7 times the odds of hospitalization, after adjusting for age, sex, comorbidities, and income





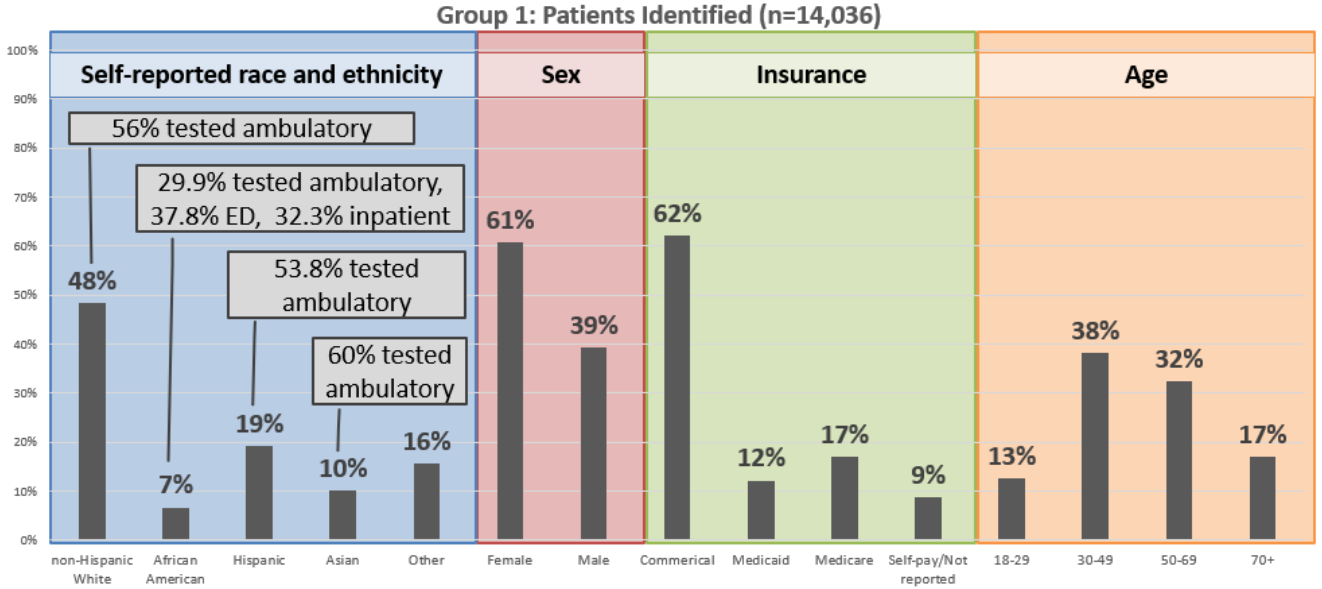
Study Design

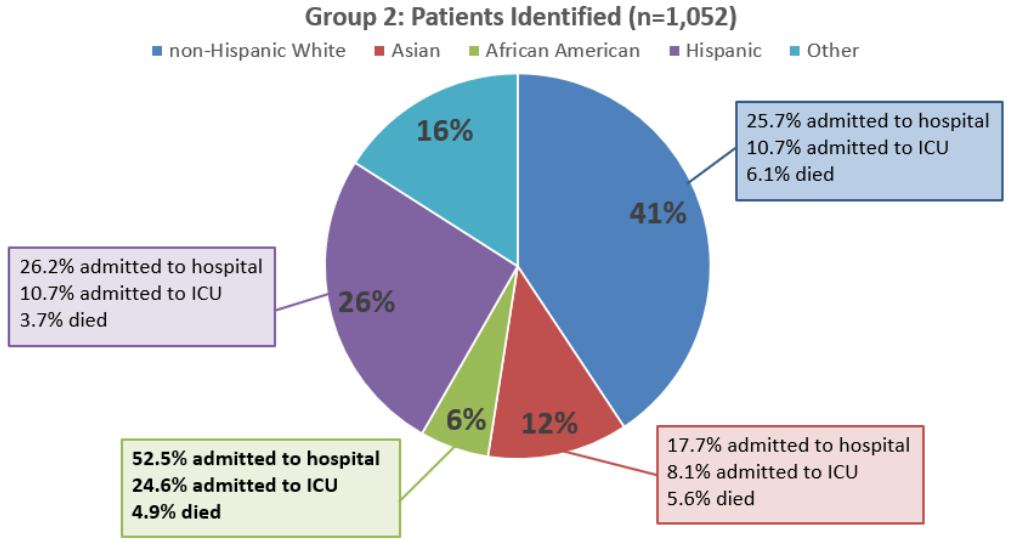
- Study Period: January 1 – April 8, 2020
- Extracted E.H.R. data
  - Date of birth, age, sex, self-reported race and ethnicity
  - Primary insurance
  - Co-morbidities
  - Hospital admission data
  - Mortality data
- Geocoded median income level by zip code
- Analyses
  - Descriptive statistics
  - Group 2: Logistic regression to associate clinical and demographic factors and hospital admission
    - 4 types of models
    - Calculated odds ratios (95% CI) and p-values

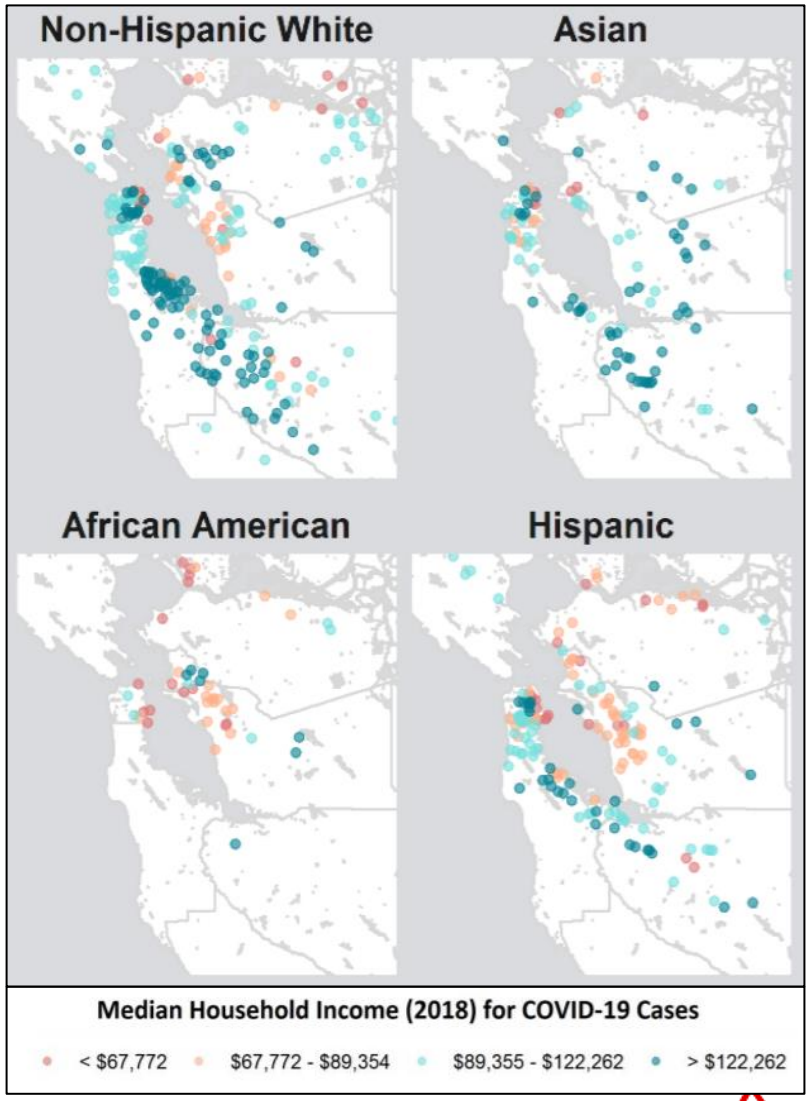
Patient Criteria	
Group 1	**Suspected cases with evidence of testing** (includes patients with record of COVID-19 test in E.H.R. regardless of test result)
Group 2	**Confirmed cases** (includes patients with evidence of positive test result in E.H.R. or patients who had documented ICD-10 diagnosis of confirmed COVID in E.H.R. without positive test result)

Models
Unadjusted Model: Univariate models for all covariates
Adjusted Model 1: Demographics
Adjusted Model 2: Demographics & clinical characteristics
Adjusted Model 3: Demographics, clinical characteristics, & sociodemographic characteristics

Results – Descriptive Statistics







Results – Multivariable analysis

Takeaways:

- Odds of hospital admission increased with age
- Male patients twice as likely as female to be admitted to hospital
- Individuals with Medicaid, self-pay, or no reported insurance had twice the odds of admission compared to commercial insurance
- COVID positive patients residing in zip codes within top two quartiles of income less likely to be admitted to hospital than those residing in bottom quartile
- Across all models, increased odds for hospital admission among African Americans vs non-Hispanic whites was statistically significant
  - Likelihood of hospital admission for African Americans more than double than of non-Hispanic whites

Appendix Table 3. Logistic Regression Output for Odds of Hospitalization

Odds Ratios shown with 95% confidence intervals in parentheses. Adjusted Model 1 = race/ethnicity, sex, and age; Adjusted Model 2 = Adjusted Mod clinical risk factors; Adjusted Model 3 (fully adjusted) = Adjusted Model 2 + social factors.

	Unadjusted Models	Adjusted Model 1	Adjusted Model 2	Adjusted Model 3
Race/Ethnicity				
NH White	Ref	Ref	Ref	Ref
NH African American	3.18 (1.84, 5.51)***	4.36 (2.34, 8.10)***	3.80 (1.97, 733)***	2.67 (1.30, 5.47)**
NH Asian/PI	0.62 (0.37, 1.04)	0.75 (0.43, 1.31)	0.78 (0.43, 1.43)	1.16 (0.61, 2.20)
Hispanic	1.03 (0.72, 1.45)	1.92 (1.28, 2.86)**	1.63 (1.06, 2.52)*	1.24 (0.78, 1.98)
Other/Unknown	0.42 (0.25, 0.43)**	0.55 (0.32, 0.96)*	0.55 (0.30, 1.01)	0.63 (0.34, 1.19)
Sex				
Female	Ref	Ref	Ref	Ref
Male	1.58 (1.19, 2.10)**	1.72 (1.24, 2.36)**	1.73 (1.22, 2.45)**	1.94 (1.33, 2.81)**
Age, Years				
18-39	Ref	Ref	Ref	Ref
40-49	2.11 (1.14, 3.90)*	2.40 (1.28, 4.50)**	1.91 (1.00, 3.65)	2.24 (1.13, 4.43)*
50-59	3.22 (1.84, 5.65)***	3.18 (1.78, 5.67)***	2.04 (1.10, 3.78)*	2.62 (1.37, 4.99)**
60-69	6.39 (3.72, 10.96)***	7.04 (4.02, 12.33)***	3.88 (2.10, 7.17)***	4.62 (2.39, 9.95)***
70-79	8.82 (4.94, 15.75)***	10.81 (5.88, 19.87)***	5.20 (2.61, 10.34)***	5.68 (2.60, 12.38)***
89+	22.18 (12.03, 40.91)***	30.93 (16.04, 59.67)***	12.94 (6.14, 27.26)***	19.08 (7.86, 46.32)***
Insurance				
Commercial	Ref	Ref	Ref	Ref
Medicaid/Government	2.95 (1.91, 4.56)***	--	--	2.13 (1.24, 3.68)**
Medicare	5.16 (3.61, 7.37)***	--	--	1.05 (0.59, 1.84)
Other	2.81 (0.25, 31.28)	--	--	4.43 (0.35, 56.48)
Self-Pay/Unknown	2.41 (1.43, 4.06)**	-	--	2.19 (1.03, 4.36)*
Income Percentile				
25th and below	Ref	Ref	Ref	Ref
26th to 50th	1.31 (0.90, 1.90)	--	--	1.20 (0.76, 1.90)
51st – 75th	0.26 (0.15, 0.44)***	--	--	0.24 (0.12, 0.46)***
75th and above	0.64 (0.43, 0.97)*	--	--	0.55 (0.33, 0.91)*

Concluding Remarks

- **COVID19 ≠ "great equalizer"** reports of disparities in testing, treatments, and outcomes are emerging
- CA death rate among African Americans is higher than representation in population (10% mortality vs 6% population)
- The California Health Care Foundation has identified the elevated risk among African Americans in the context of this pandemic as "a perfect storm of irrefutable evidence that **people of color are caught in a web of social inequality.**"
- African Americans are significantly more likely to be admitted to hospital
  - May indicate that African Americans have more advanced or severe illness at the time of presenting for COVID-19 testing and medical care
- Policies that support community-based outreach, testing, and access to culturally competent care within the African American community hold the promise of earlier testing, diagnosis, and the potential to have a positive impact on some of the disparities we have observed

Concluding Remarks

"The experience of Sutter Health highlights the fact that *race and ethnicity play a pivotal role in determining how and when care is accessed, and the outcome*. Our findings suggest that the greatest risk, in terms of hospitalization, is borne by the African American community. This pandemic offers the opportunity to identify and quantify these inequities, and to seek solutions. Health care systems have an **ethical obligation** to ensure that **all patients** receive the right care at the right time, especially in times of crisis."

Discussion

- What are people's overall thoughts, opinions?
- Did this paper miss out on other opportunities?
- What do results say about the importance of an integrated approach to healthcare (social work, education)?
- How do we tackle this from a multitude of levels (individual, communal, systemic)?
- Role(s) for systems engineering?

Next Journal Club Meeting	• August 7th, 12-1 pm ET • *Inferring change points in the spread of COVID-19 reveal the effectiveness of interventions*, Science • *After COVID-19: How To Rejuvenate Primary Care For The Future* • https://www.hsye.org/journal-club

Have a great weekend! (and stay safe)