The Exponential Power of Today (and Yesterday?)

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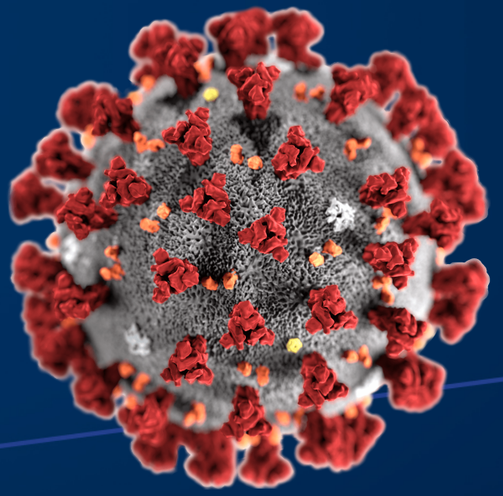

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Global Novel Coronavirus Cases and Deaths (as of 21 Apr 2020)

Cases: ~3.5M

Deaths: ~249K

Attack Rate: ???

Attack rate for 1918-19 influenza: about 33% (20-50M deaths worldwide; 675K in USA)
Attack rate for H1N1: about 10-20% (284K deaths worldwide; 12K in USA)

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Myths about COVID-19

- China travel ban in late January saved many lives it didn't (it bought us a little time at best)
- The US acted quickly we didn't
- We are testing adequately we aren't
- It's time to open up we need to thread a needle
- Per capita rates are not comparatively useful early on

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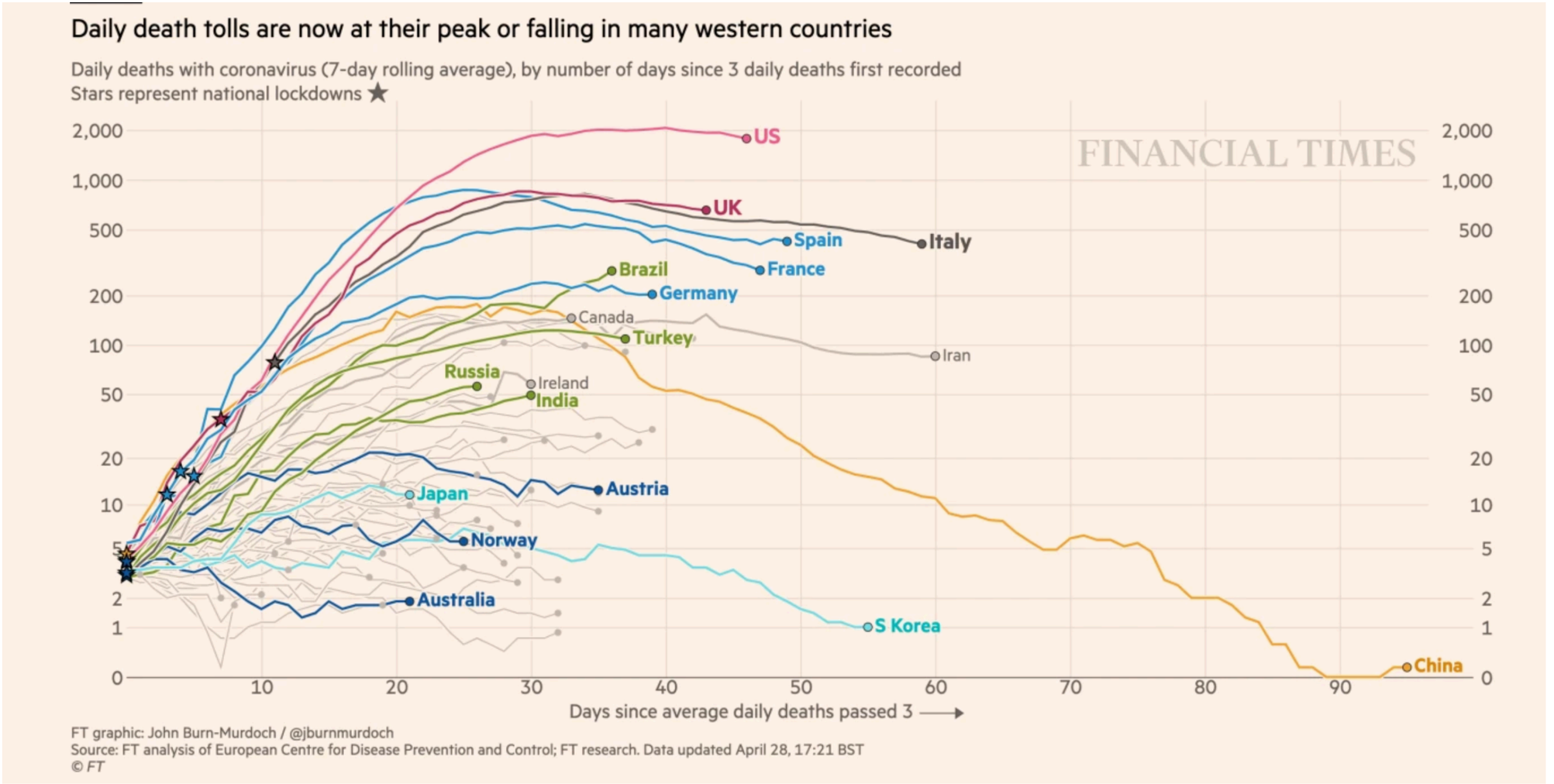

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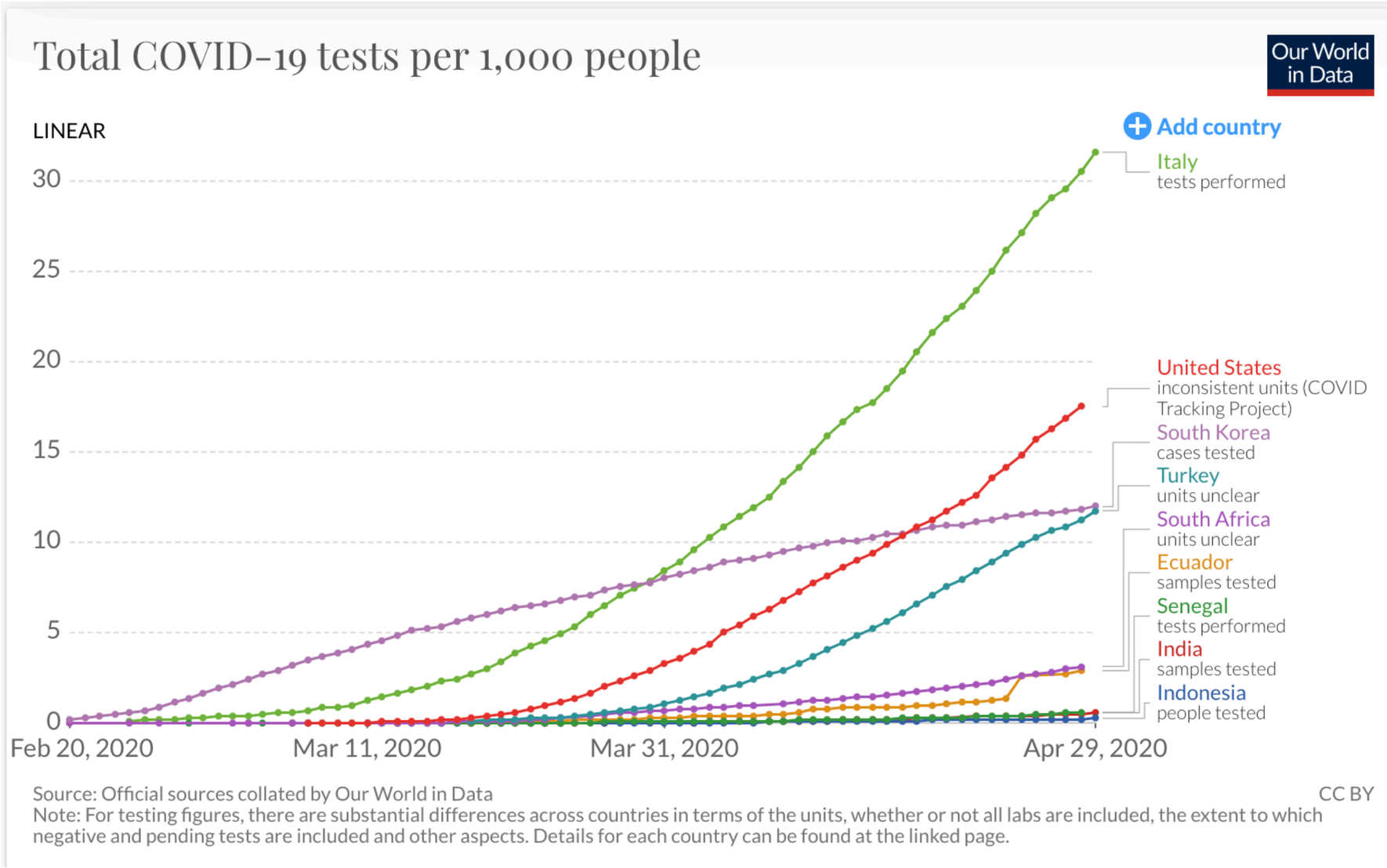
Testing



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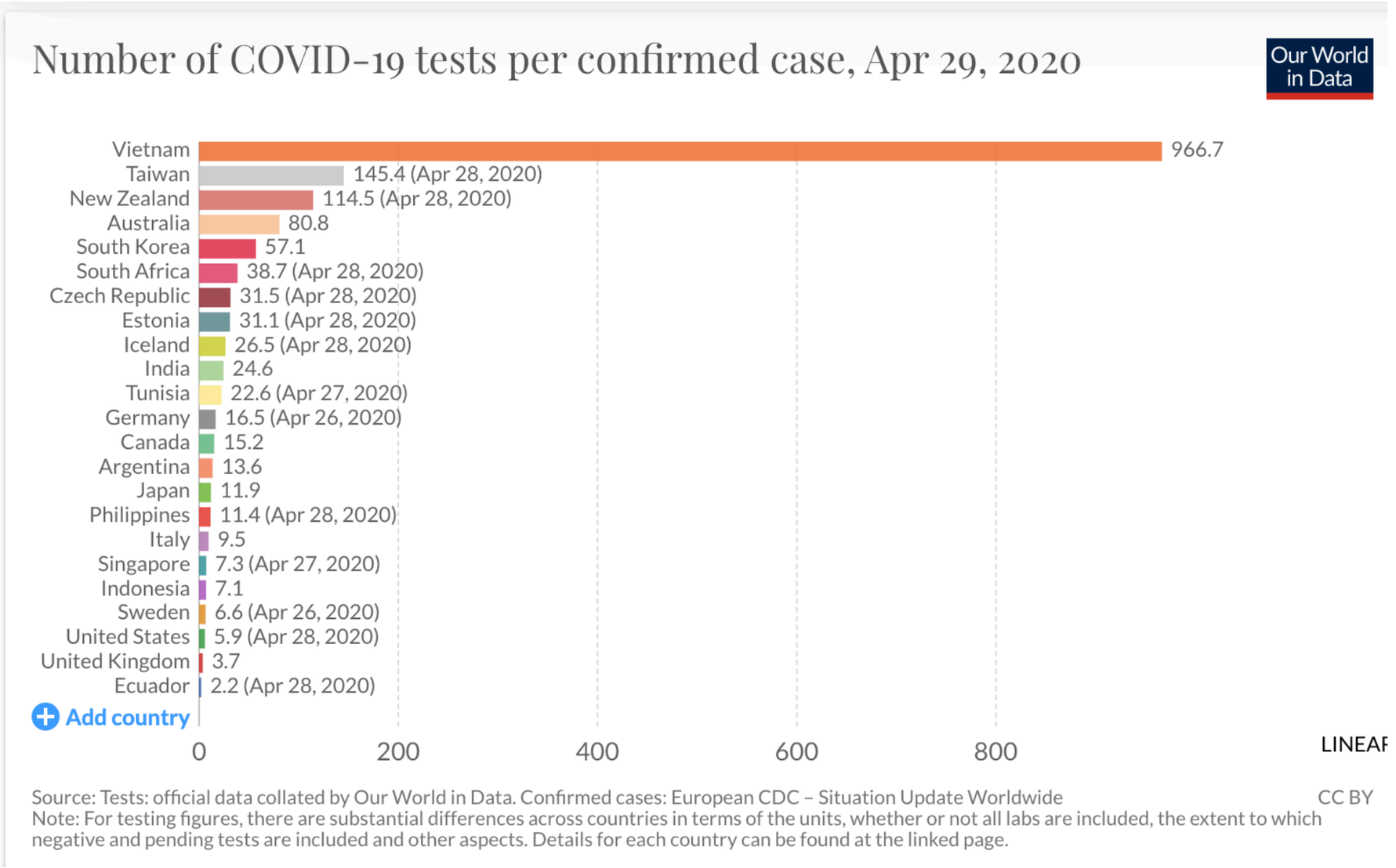
Testing

Test positive rate is the inverse of what is shown here



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SEIR Mathematical Models

- “The tendency of some modelers to present them as scientific predictions of the future rather than models does not help. Models are widely used in government, and some models have arguably too much influence. They are generally most useful when they identify impacts of policy decisions which are not predictable by commonsense; the key is usually not that they are ‘right’, but that they provide an unexpected insight.” (Chris Whitty, CMO England, 2015)

Models:

- Provide projections of the likely future (hard to predict peak)
- Provide descriptions of the natural history of infections at a population/individual level
- Provide insight into the impact of possible interventions

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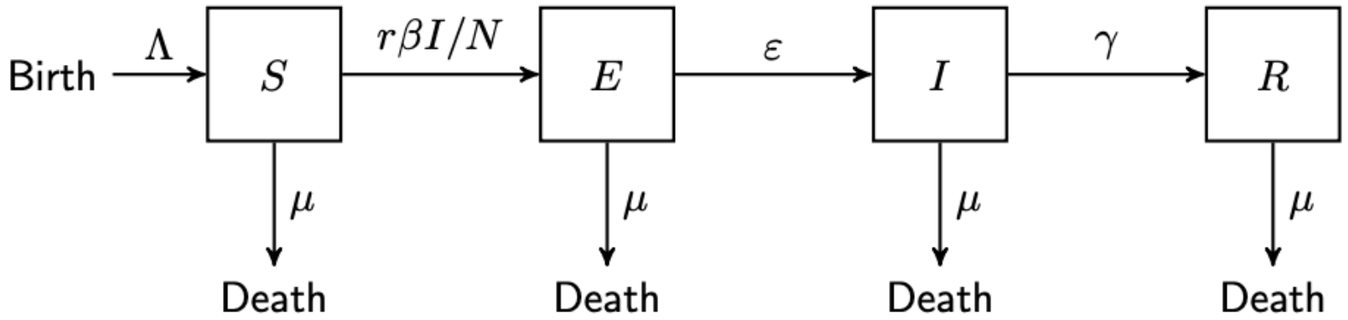
SEIR Mathematical Models

Susceptible-Exposed-Infectious-Recovered Model: applicable to measles, mumps, rubella.



E: Exposed (latent) humans

ε: Per-capita rate of progression to infectious state

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - r\beta S\frac{I}{N} - \mu S$$
$$\frac{\mathrm{d}E}{\mathrm{d}t} = r\beta S\frac{I}{N} - \varepsilon E$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = \varepsilon E - \gamma I - \mu I$$
$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma I - \mu R$$

Also *Agent-Based Modeling*

with

$$N = S + E + I + R.$$

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SEIR Mathematical Models

$$R_0 = \left(\begin{array}{c}\text{Number of}\\ \text{contacts}\\ \text{per unit time}\end{array}\right)\left(\begin{array}{c}\text{Probability of}\\ \text{transmission}\\ \text{per contact}\end{array}\right)\left(\begin{array}{c}\text{Duration of}\\ \text{infection}\end{array}\right) \times \left(\begin{array}{c}\text{Probabililty of}\\ \text{surviving}\\ \text{exposed stage}\end{array}\right)$$

$$R_0 = r \times \beta \times \frac{1}{\gamma + \mu} \times \frac{\varepsilon}{\varepsilon + \mu} = \frac{r\beta\varepsilon}{(\gamma + \mu)(\varepsilon + \mu)}$$

- If $R_0 < 1$, the disease-free equilibrium point is globally asymptotically stable and there is no endemic equilibrium point (the disease dies out).
- If $R_0 > 1$, the disease-free equilibrium point is unstable and a globally asymptotically stable endemic equilibrium point exists.

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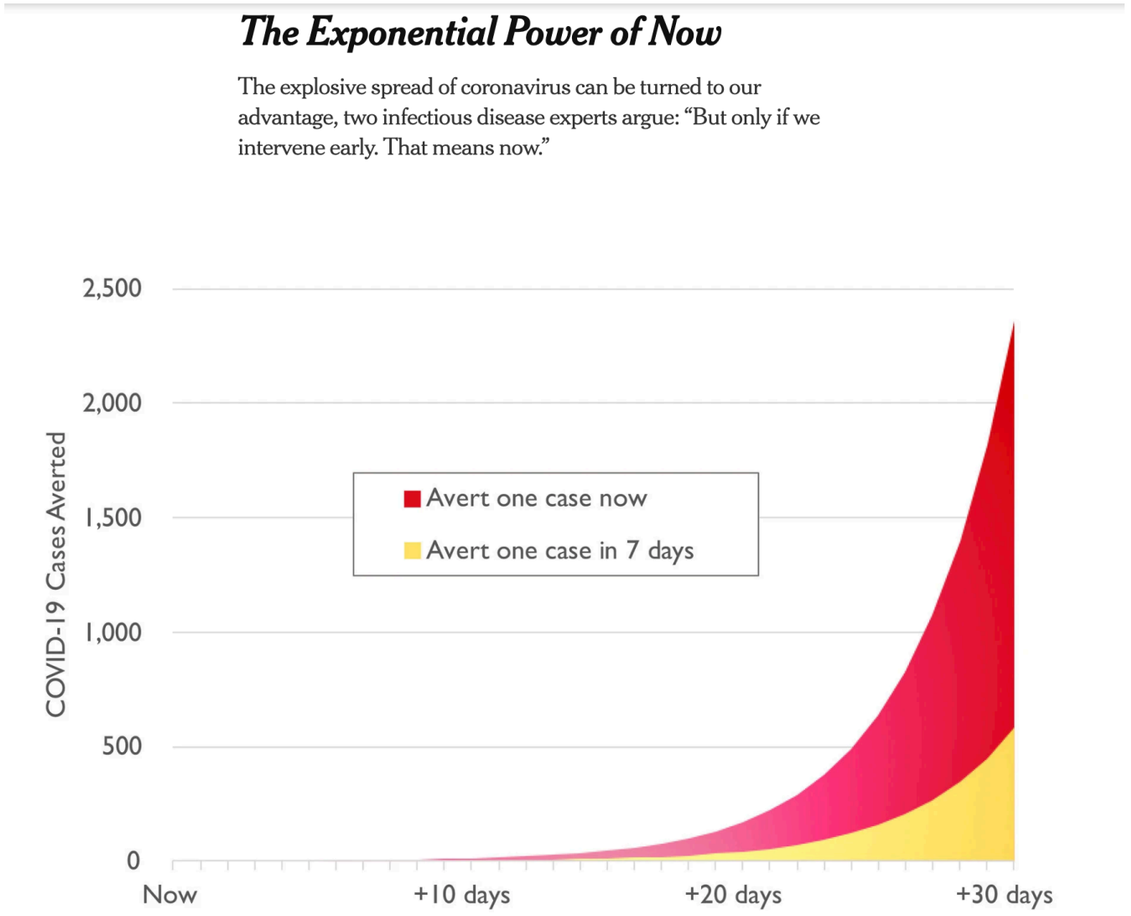
Timing of Mitigation Measures

4 times as many infections averted in a month if we start today rather than a week from today



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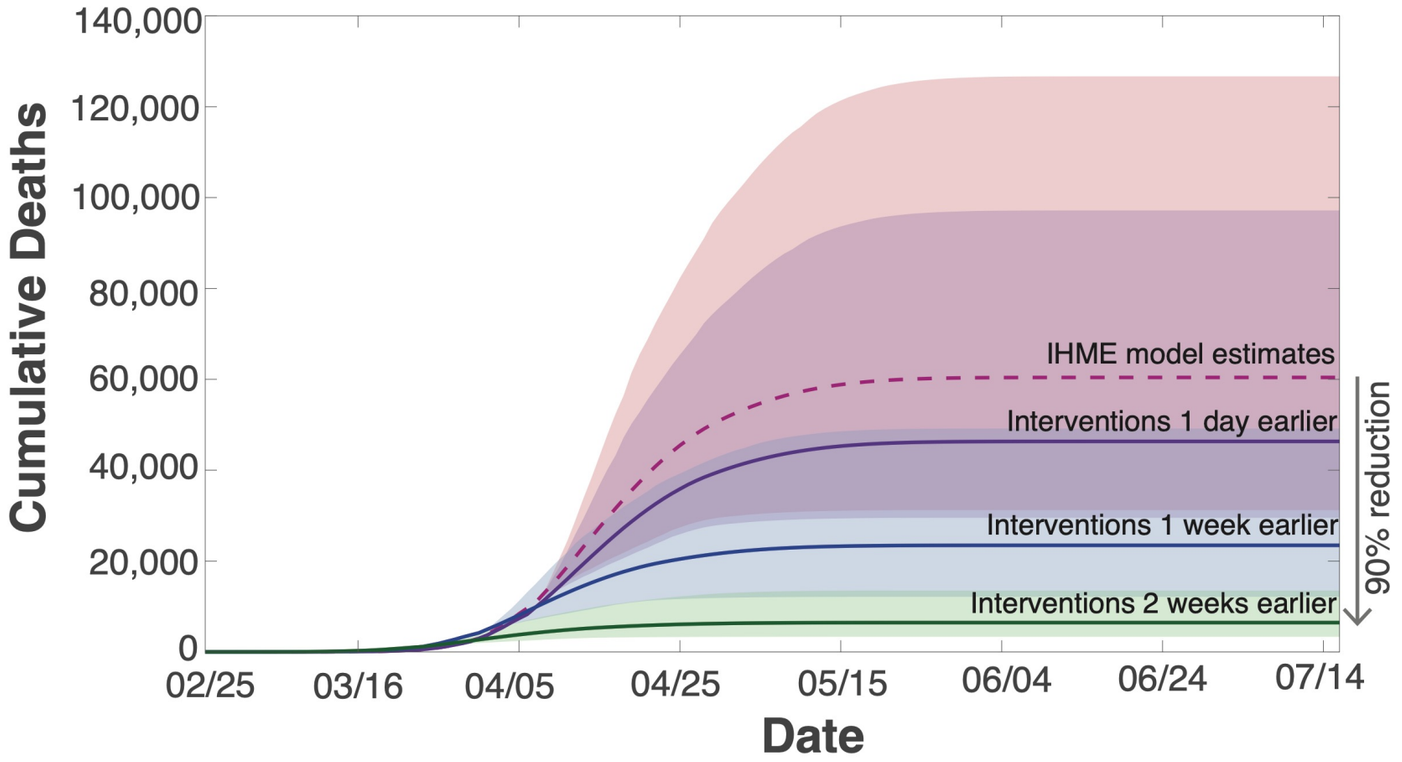
Timing of Mitigation Measures Looking Back

90% of US deaths averted in first wave if we had started full mitigation on March 2 instead of March 16

Note averted may only be postponed depending on second wave etc and how that is mitigated



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Timing of Mitigation Measures Looking Forward (Exponential Power of Yesterday)

- Metric for assessing cost of ‘too early’ release can’t be ‘deaths averted’ since this will depend on subsequent mitigation strategies
- Metric should be length of time between (i) easing of mitigation policies, and (ii) resurgence of infections

The IHME "Model"

Annals of Internal Medicine®

LATEST ISSUES CHANNELS CME/MOC IN THE CLINIC JOURNAL CLUB WEB EXCLUSIVES AUTHOR INFO

IDEAS AND OPINIONS | 14 APRIL 2020

Caution Warranted: Using the Institute for Health Metrics and Evaluation Model for Predicting the Course of the COVID-19 Pandemic FREE

Nicholas P. Jewell, PhD; Joseph A. Lewnard, PhD; Britta L. Jewell, PhD

Article, Author, and Disclosure Information

FULL ARTICLE

References

Comments

MORE

A recent modeling analysis by the Institute for Health Metrics and Evaluation (IHME) (1) projecting deaths due to coronavirus disease 2019 (COVID-19) has attracted considerable attention, including from the U.S. government (2). The model used COVID-19 mortality projections to estimate hospital bed requirements and deaths. We agree with qualitative conclusions that demand for hospital beds may exceed capacity and efforts to enhance mitigation policies and surge planning are essential. Data endorse shelter-in-place orders and suggest that these measures must remain while awaiting advances in surveillance, treatment, and vaccines.

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The IHME "Model"

- Quality of fatality reporting: underreporting and delayed reporting (most death counts refer only to deaths in hospital)
- Farr's Law (epidemic case counts follow a bell-shaped curve) and fallacy (eg HIV)
- Consistent of mortality curves across regions
- Assumption of same effects of social distancing everywhere
- Estimation of uncertainty
- Volatility of projections day-to-day

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Hospitalized Patient Characteristics

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Comment on this paper

Incidence, clinical outcomes, and transmission dynamics of hospitalized 2019 coronavirus disease among 9,596,321 individuals residing in California and Washington, United States: a prospective cohort study

Joseph A Lewnard, Vincent X Liu, Michael L Jackson, Mark A Schmidt, Britta L Jewell, Jean P Flores, Chris Jentz, Graham R Northrup, Ayesha Mahmud, Arthur L Reingold, Maya Petersen, Nicholas P Jewell, Scott Young, Jim Bellows

doi: https://doi.org/10.1101/2020.04.12.20062943

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Abstract | Info/History | Metrics | Preview PDF

Abstract

Background: The United States is now the country reporting the highest number of 2019 coronavirus disease (COVID-19) cases and deaths. However, little is known about the epidemiology and burden of severe COVID-19 to inform planning within healthcare systems and modeling of intervention impact. Methods: We assessed incidence, duration of hospitalization, and clinical outcomes of acute COVID-19 inpatient admissions in a prospectively-followed cohort of 9,596,321 individuals enrolled in

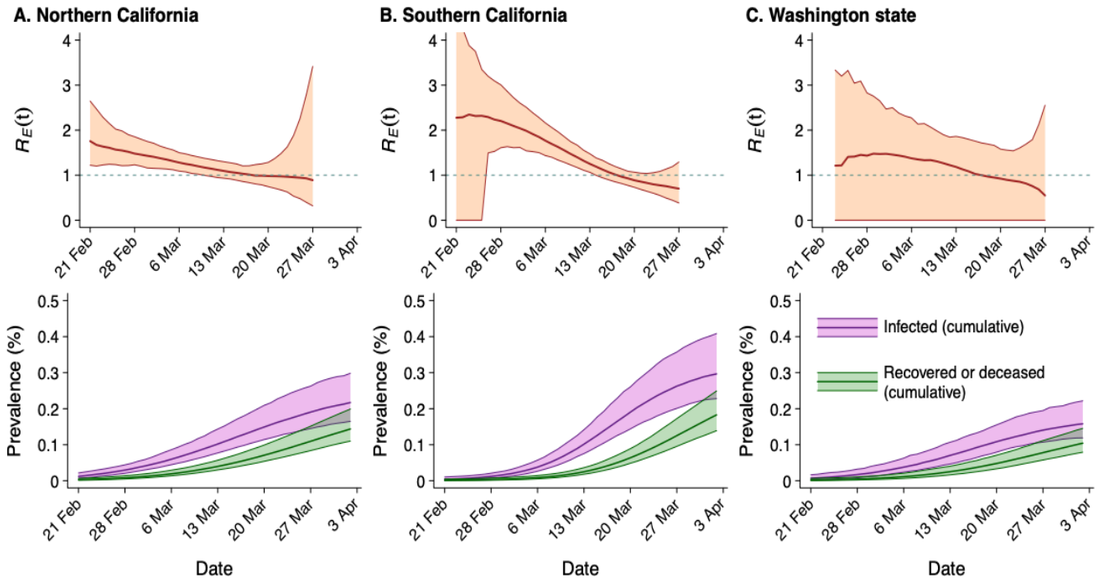

Figure 4: Dynamics of SARS-CoV-2 transmission in the cohort populations inferred from hospitalization data. We illustrate estimates of the effective reproductive number for infections acquired on day *t*, $R_E(t)$, describing the number of secondary infections each individual who acquired infection on day *t* would be expected to cause, for (**A**) Northern California, (**B**) Southern California, and (**C**) Washington state. Underneath, we plot estimates of the cumulative proportion of the population infected over time, and the proportion of the population that is deceased or recovered following previous infection. Shaded regions around point estimates (lines) indicate 95% confidence intervals.

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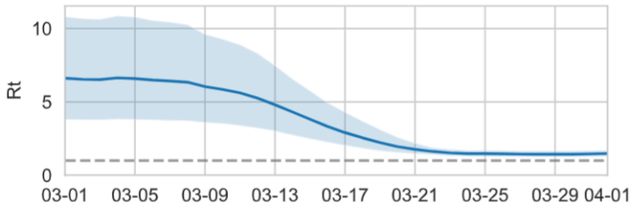
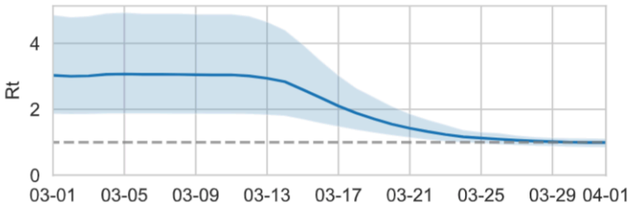
Mobility Data Analysis by State

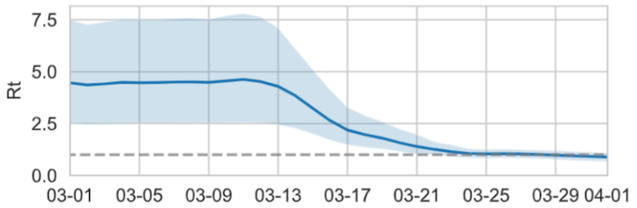
Apple mobility data: work of Emily Fox, Carlos Guestrin, Andy Miller, Nick Foti, Joseph Lewnard and Nick Jewell



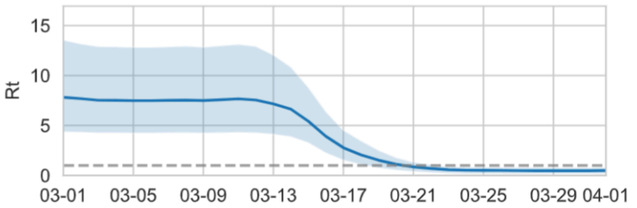
(a) California



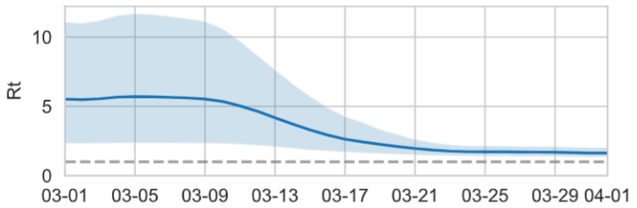
(b) Florida



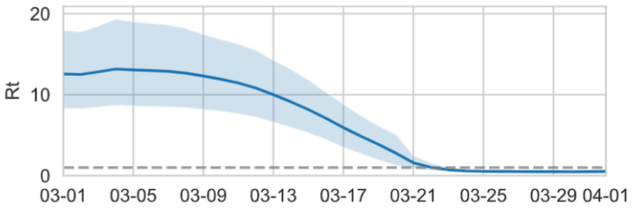
(c) Georgia



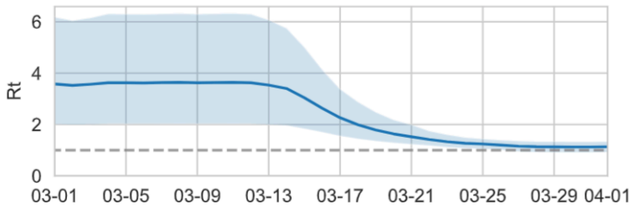
(d) Louisiana



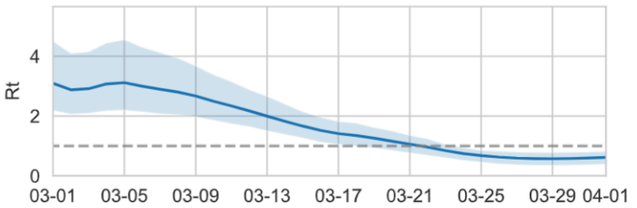
(e) Massachusetts



(f) New York



(g) Texas



(h) Washington

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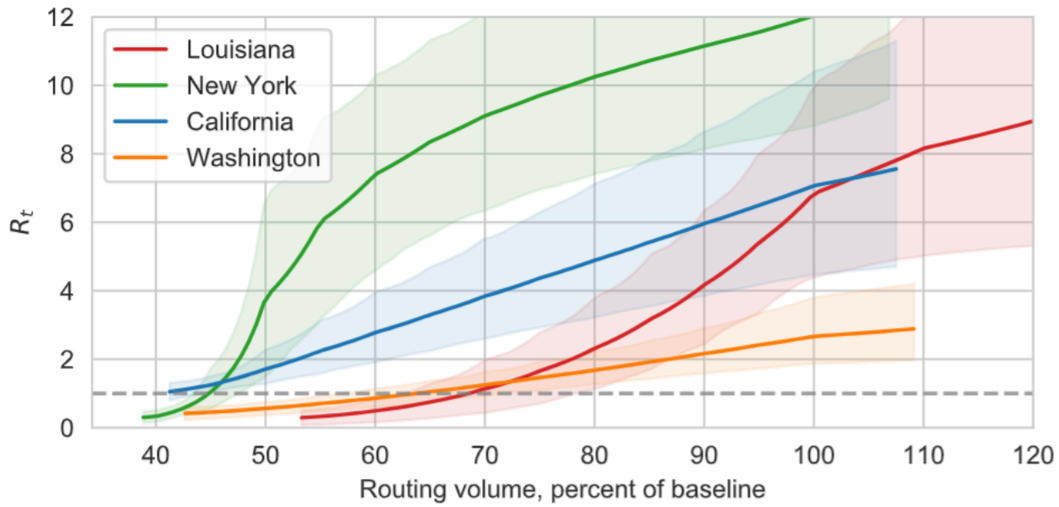
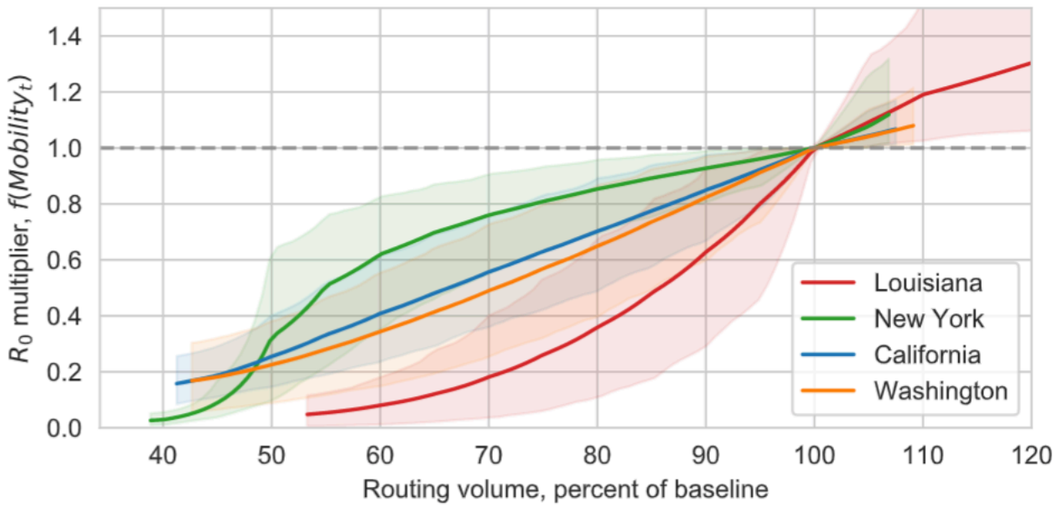
Mobility Data Analysis by State



(a) Effective R vs. mobility



(b) R_0 multiplier vs. mobility

Apple mobility data: work of Emily Fox, Carlos Guestrin, Andy Miller, Nick Foti, Joseph Lewnard and Nick Jewell

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Bay Area PCR/Serological Survey

The overall goals of this study are to:

1) better understand the short- and long-term prevalence and the spread of COVID-19 in Bay Area communities in order to inform virus-containment measures, assess epidemiologic characteristics of the virus including the probability of symptomatic or asymptomatic infection, and create predictive models of COVID-19 spread in the region

2) examine the participant characteristics (e.g., age, sex, underlying medical conditions), household, genetic, environmental, and viral factors that may affect the risk of infection and/or modify the manifestation of symptoms and other outcomes;

3) assess the sensitivity and specificity of fingerprick whole blood in commercially available rapid serological tests, and filter paper blood spots vs. serum from venous blood draw tested by ELISA;

4) assess immune protection against COVID-19 associated with responses to previous infection with SARS-CoV-2 and/or endemic seasonal coronaviruses.

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Bay Area PCR/Serological Survey

- Sample of 5,000 provide blood spots, saliva, oropharyngeal swab and whole blood (a subset of 500) samples for molecular and antibody testing, and b) complete an online questionnaire regarding personal and household characteristics.
    - Debacle of Santa Clara seroprevalence survey results from Stanford
    - Los Angeles County seroprevalence survey results from same team
    - New York results seem more persuasive

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More on Antibody Testing

- Antibody tests are not perfect: e.g. sensitivity of 93.8% & specificity of 95.6%
  - Not bad? . . . . At least at prevalence > 10%
  - But, with a prevalence of 1%, a positive antibody test result only has an 18% chance of truly being positive (i.e. PPV, and then no guarantee of current immunity)
  - Thus, no value of an ‘immunity passport’
  - But, wait . . . What if our test has sensitivity & specificity = 99%
  - Still only PPV of 50%

Current Statistical Issues

- Assessing test characteristics and the use of tests in different contexts and for varying purposes
  - PCR test (point of care tests)
  - Antibody (serological) tests
  - Antigen tests
  - What is the local strategy for testing when stay at home provisions are reduced? PCR/antibody?

Pooled testing strategies

- Assessment of measures of immunity
- Impact and assessment of relaxing mitigation policies
- Surveillance strategies (syndromic surveys, automated temperature checks, apps, mobility measures)?
- Vaccine and treatment development

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Summary

- Another newly emergent infectious disease
- A rapidly evolving epidemiologic situation and response
- Gaps remain in our global capacity to prepare for, predict, detect, and respond to newly emerging infections → invest in public health infrastructure!
- Mathematical models and statistical analysis of emerging data have crucial roles to play but caution is needed in interpretation

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