AVALON HEALTH ECONOMICS

BROADSTREET

ISPOR 2021 Presentation

W5: Lost in Transmission- Analytic Applications of Public Health Data to Inform Evaluations of the Efficacy, Effectiveness, and Value of Interventions for COVID-19

18/05/2021

Welcome and introductions

Session leaders

- John Schneider, CEO, Avalon Health Economics, New Jersey USA
- Karissa Johnston, Adjunct Professor, Memorial University, Newfoundland CANADA
- Scott Emerson, Research Analyst, Broadstreet HEOR, Vancouver CANADA
- Shelagh Szabo, Scientific Director, Broadstreet HEOR, Vancouver CANADA

Workshop objectives

- To define and discuss COVID-19 disease burden and transmission parameters
- To visualize and interactively explore how public health data can illustrate trends in the incidence and severity of COVID-19 across jurisdictions
- To understand how these epidemiologic parameters can inform economic models to predict the value of upcoming interventions for COVID19

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Outline

Welcome	• Objectives, background	*5 min*
Available COVID data		*10 min*
Calculating R0/Rt	• Interactive session: Explore the app	*15 min*
Modeling COVID	• Identify issues • Interactive session: Q&A, Ask a modeler	*25 min*
Wrap up		*5 min*

COVID-19 data: Sources and (mis)-interpretation

COVID-19 epidemiologic data

We are all familiar with the common metrics now: COVID-19 cases, hospitalizations and deaths.

But what do these really mean, and how is that related to what is being counted?

While similar metrics are reported across jurisdictions, their definitions can vary hugely!

In this section, we will explore a number of these metrics, discuss their strengths and limitations, and have a look at some actual data that can help illustrate these issues.

Understanding what these data mean, and challenges with their interpretation, will be important for accurately modeling COVID-19 interventions

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Available COVID-19 data

> In the absence of national COVID-19 data standards, states and territories defined and presented their COVID-19 data in 56 different ways. Harvesting data from 56 dashboards, in turn, **created 56 opportunities a day for late or missed updates, for anomalous spikes and drops, and for new or disappearing metrics.**
>
> *Atlantic COVID tracking project*

Anomalies

[NJ] - On March 6, 2021, New Jersey's Ever hospitalized decreased by 916 without explanation.

[MT] - On March 6, 2021, Montana's Confirmed cases decreased by 173 without explanation.

[TX] - On March 6, 2021, Texas announced that due to a technical issue, fewer lab results will be reported on March 6, 2021. Additionally, their Total antibody tests (specimens) decreased by 162 without explanation. We urge caution when interpreting their testing data for this day.

[SC] - On March 6, 2021, South Carolina's data on individuals with symptom onset data decreased by roughly 31,000 without explanation. As a result, their Recovered, which is calculated as individuals with symptom onset data multiplied by the percentage of these cases which are recovered, decreased by about 12,000.

[IN] - On March 6, 2021, Indiana announced that a new testing facility had been added to their electronic reporting system, resulting in 1241 Total PCR tests (people), 3769 Total PCR tests (specimens), and 445 Cases (confirmed in probable) reported on March 6, 2021. Additionally, their Ever in ICU decreased by 2 without explanation.

[IA] - On March 6, 2021, Iowa's Negative antibody tests (people) decreased by 35 without explanation.

And this is just for one country!

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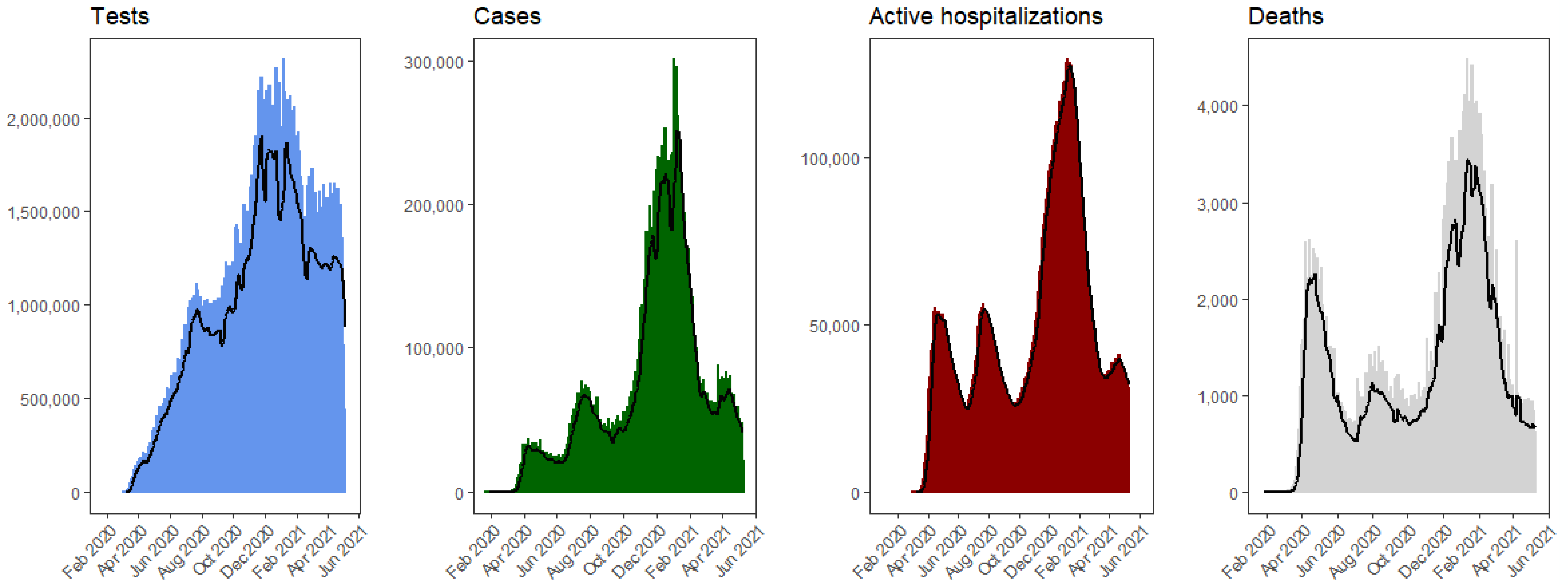
Commonly-reported metrics, USA



Source: New York Times; U Minnesota COVID-19 Hospitalization Tracking Project

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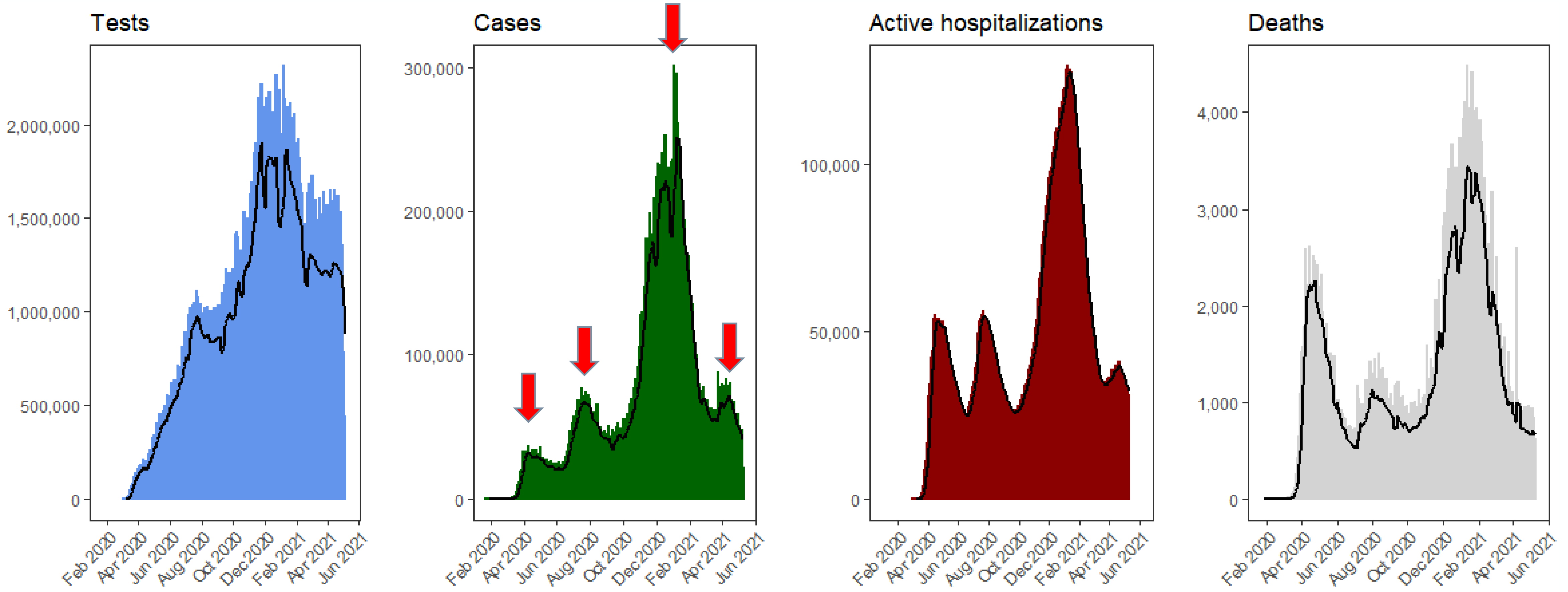
Commonly-reported metrics, USA



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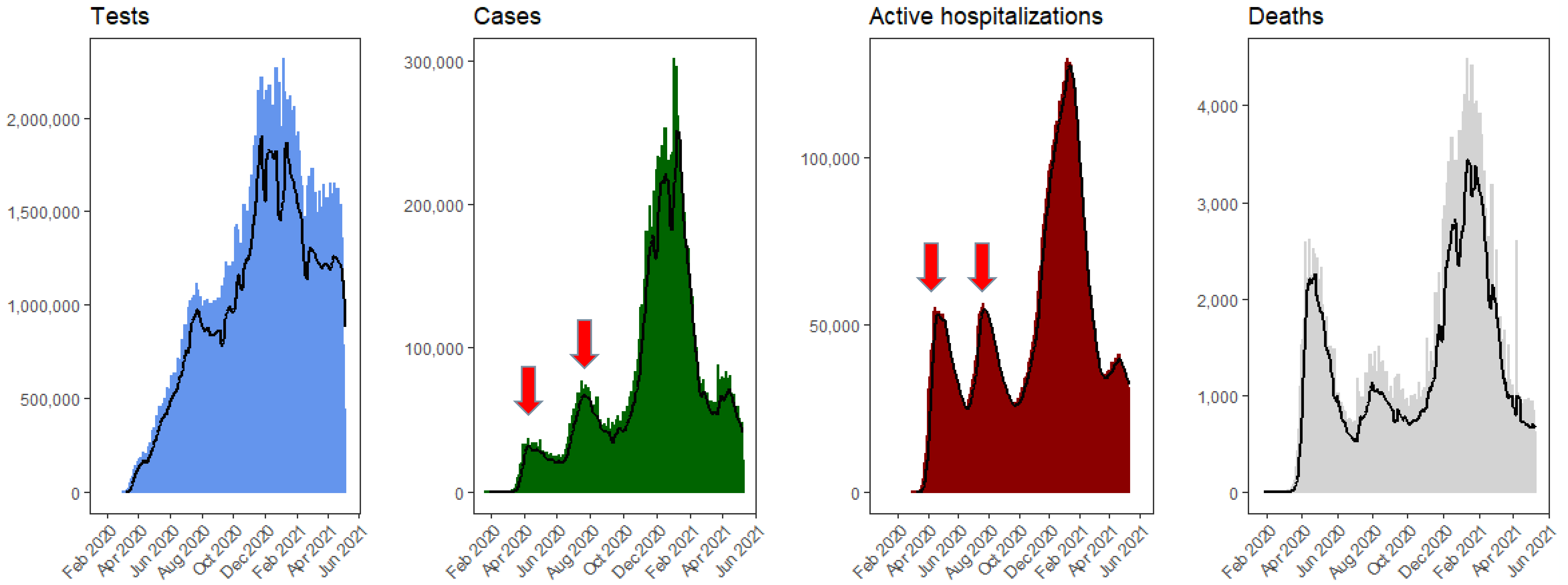

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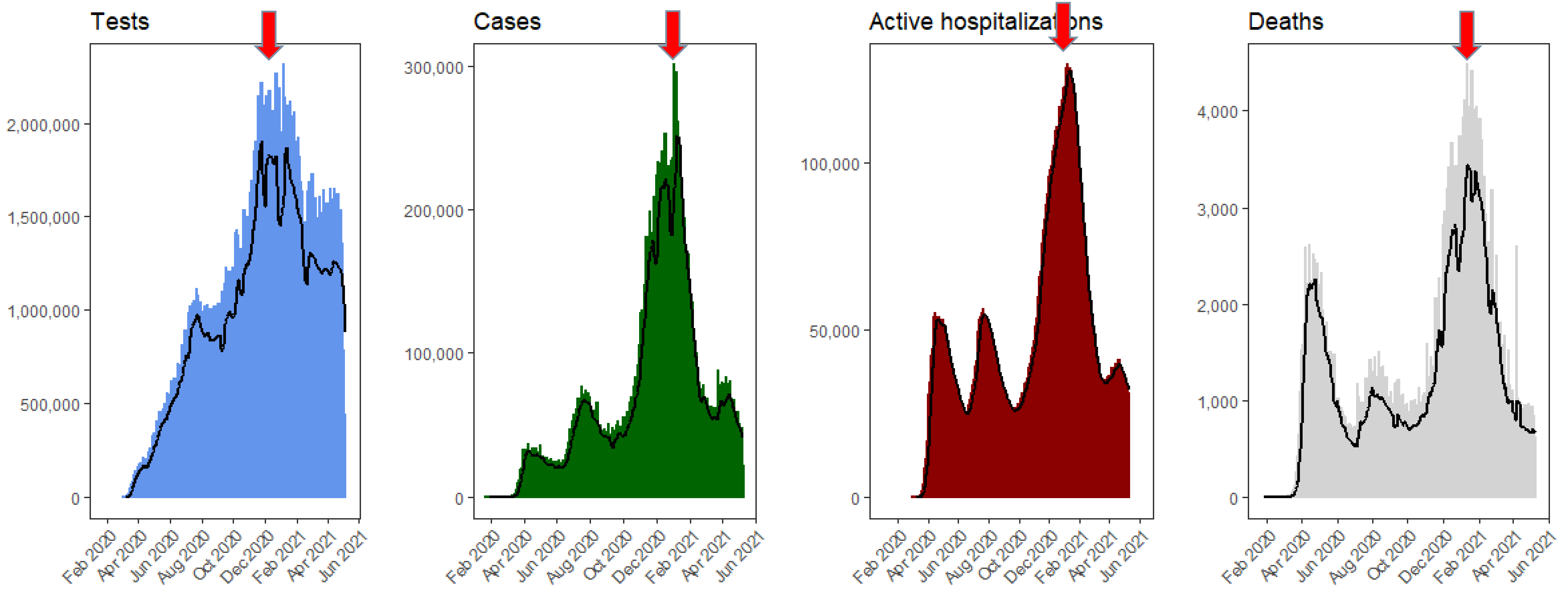
Commonly-reported metrics, USA



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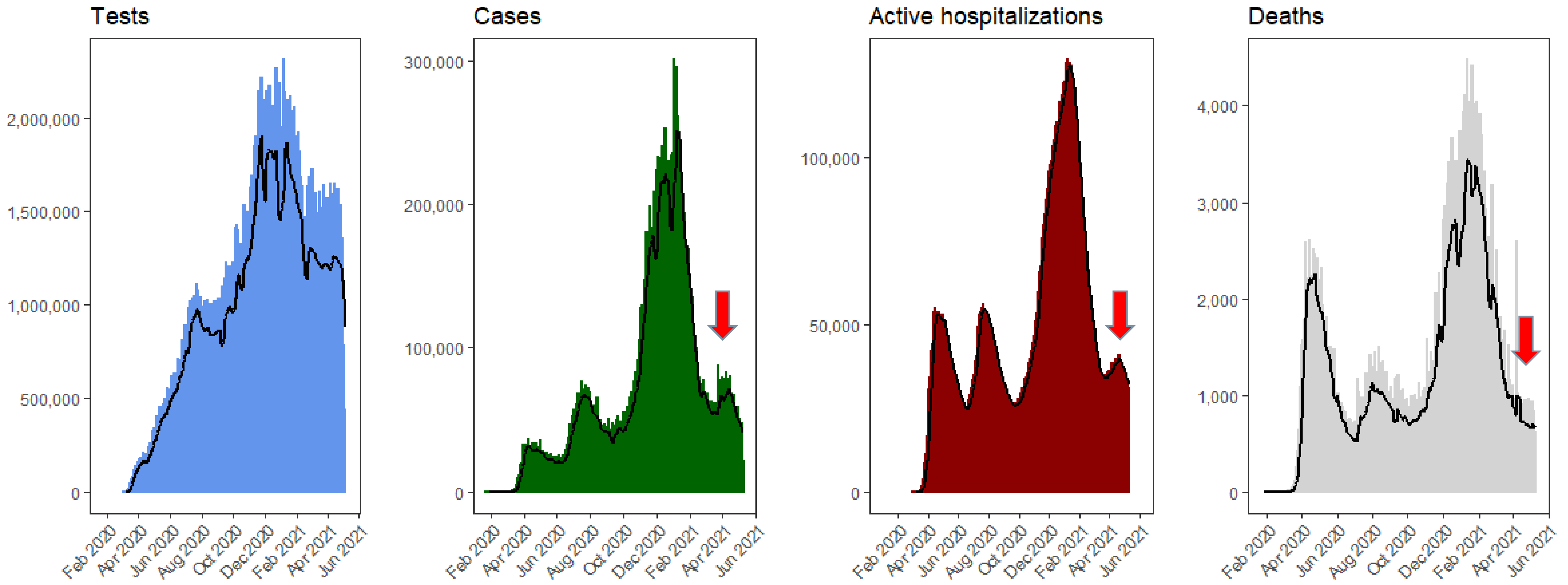
Commonly-reported metrics, USA



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Considerations about the common metrics

Cases

- The availability of testing and testing rules
  - What % of cases likely captured?
- What are the implications for comparing cases over time in the face of changing disease severity and increasing vaccination rates?
- Implications for comparing **percent positivity**; and for percent positivity, whether they are counting tests or counting people tested?
- What about asymptomatic cases?

Mortality

- How comprehensive are the data? Are long-term care deaths counted? Deaths outside of hospitalization?
- Assigned to date occurred (ie. Daily counts inaccurate until all deaths finally counted) or to date recorded (i.e. daily counts inaccurate because they count deaths occurring over a varying period)
- Adjusted for differences in the distribution of key factors (e.g age) in the underlying population?

Hospitalizations

- Who gets hospitalized
- Impact of limited capacity

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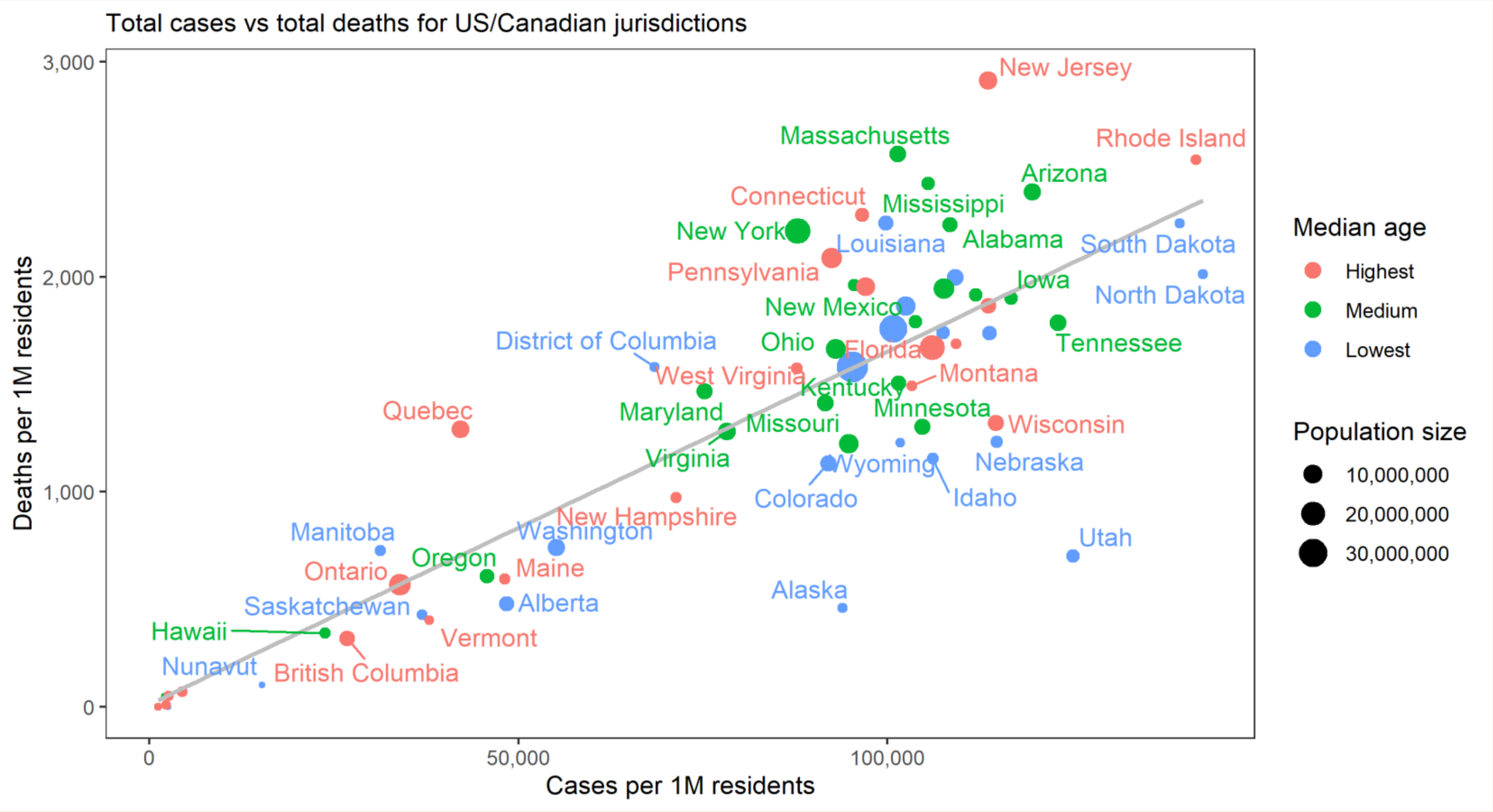
Exploring cases vs. mortality



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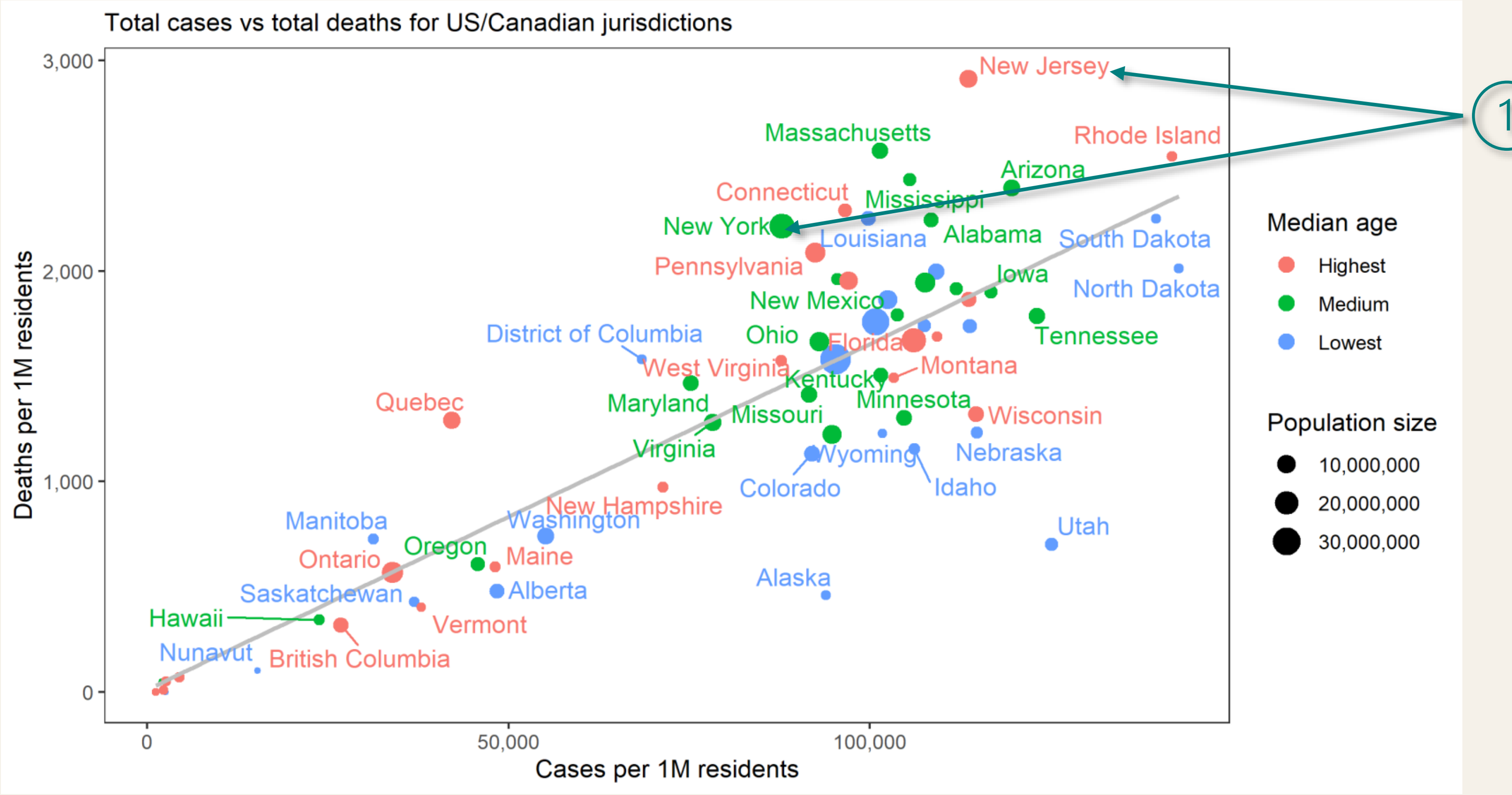
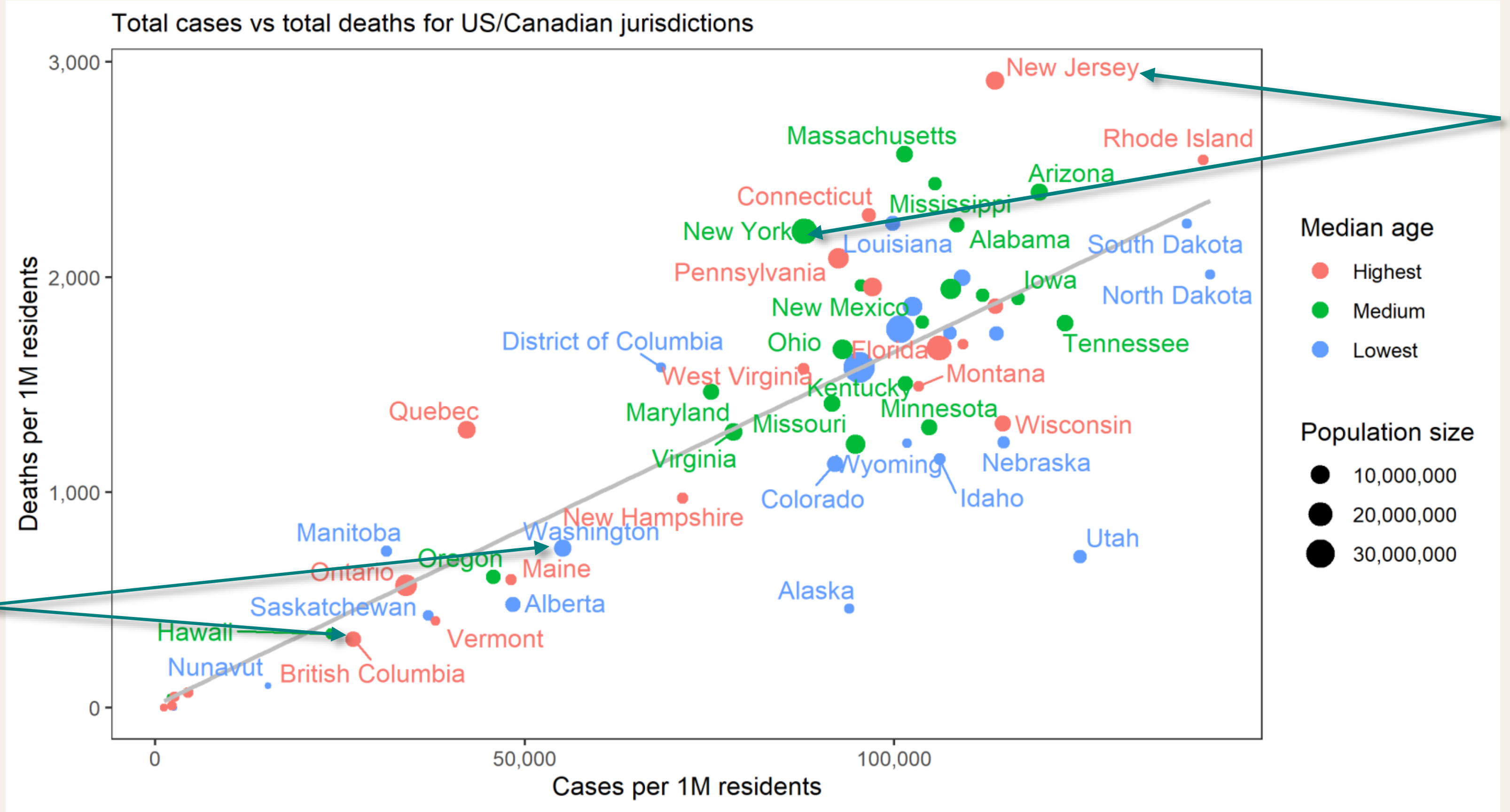
Exploring cases vs. mortality



Some of the first states to be hit

Exploring cases vs. mortality



Some of the first states to be hit

But BC and WA were also hit early

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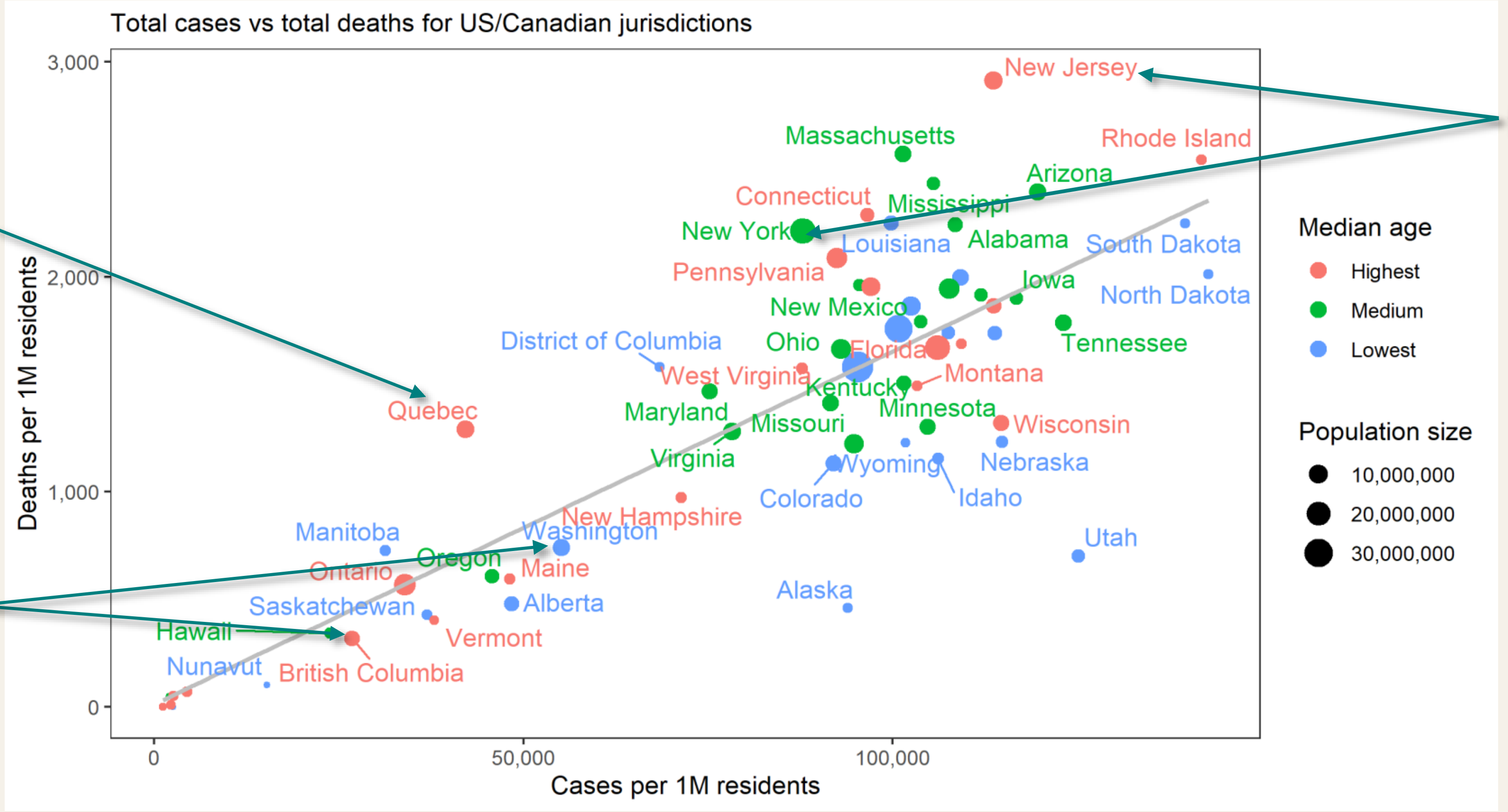
Exploring cases vs. mortality

Long term care homes hit early, and hard

But BC and WA were also hit early



Some of the first states to be hit

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Exploring cases vs. mortality

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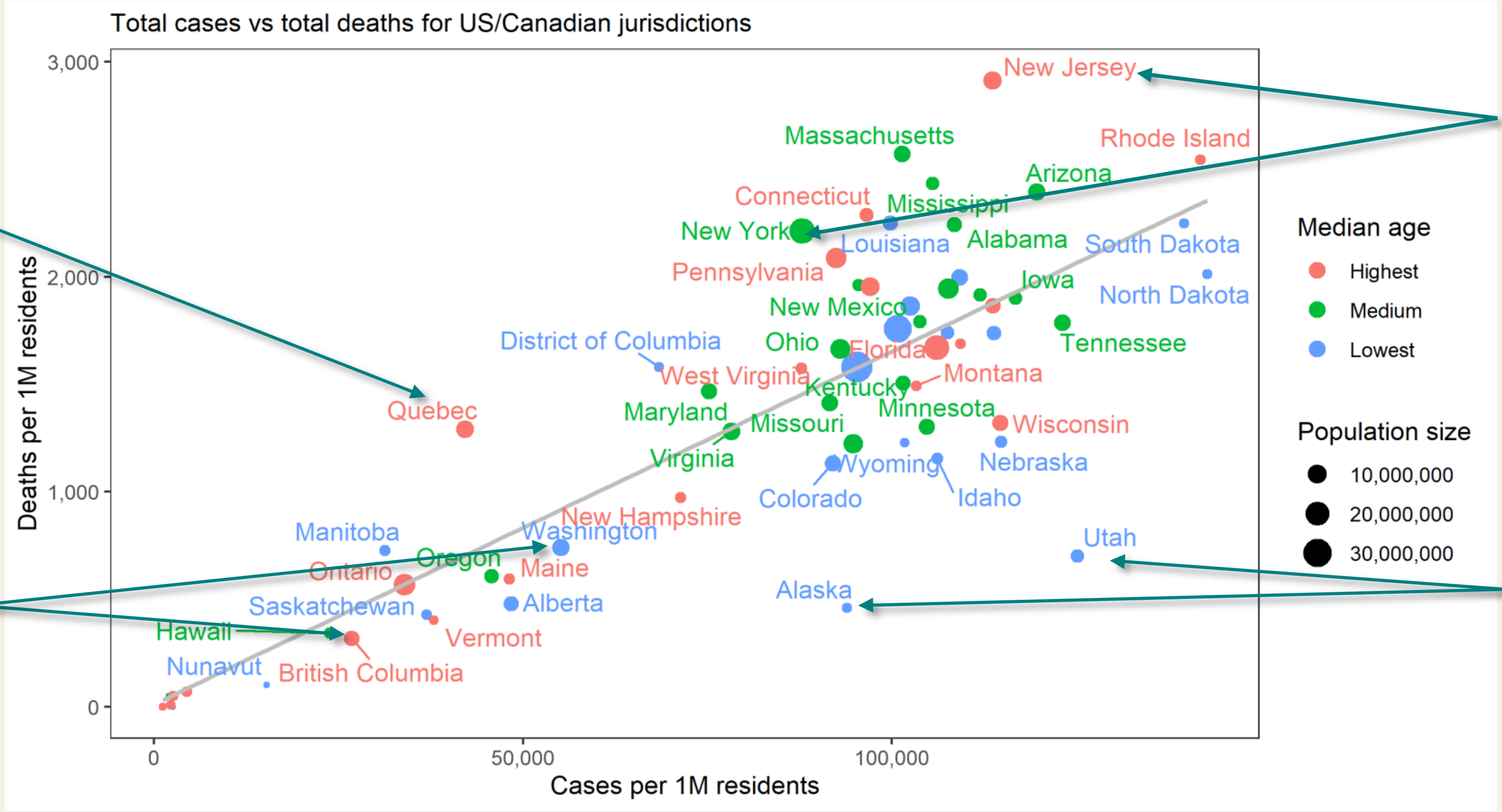
But BC and WA were also hit early



Some of the first states to be hit

Impact of younger populations, and low density?

Fair comparisons must consider/understand the underlying population characteristics

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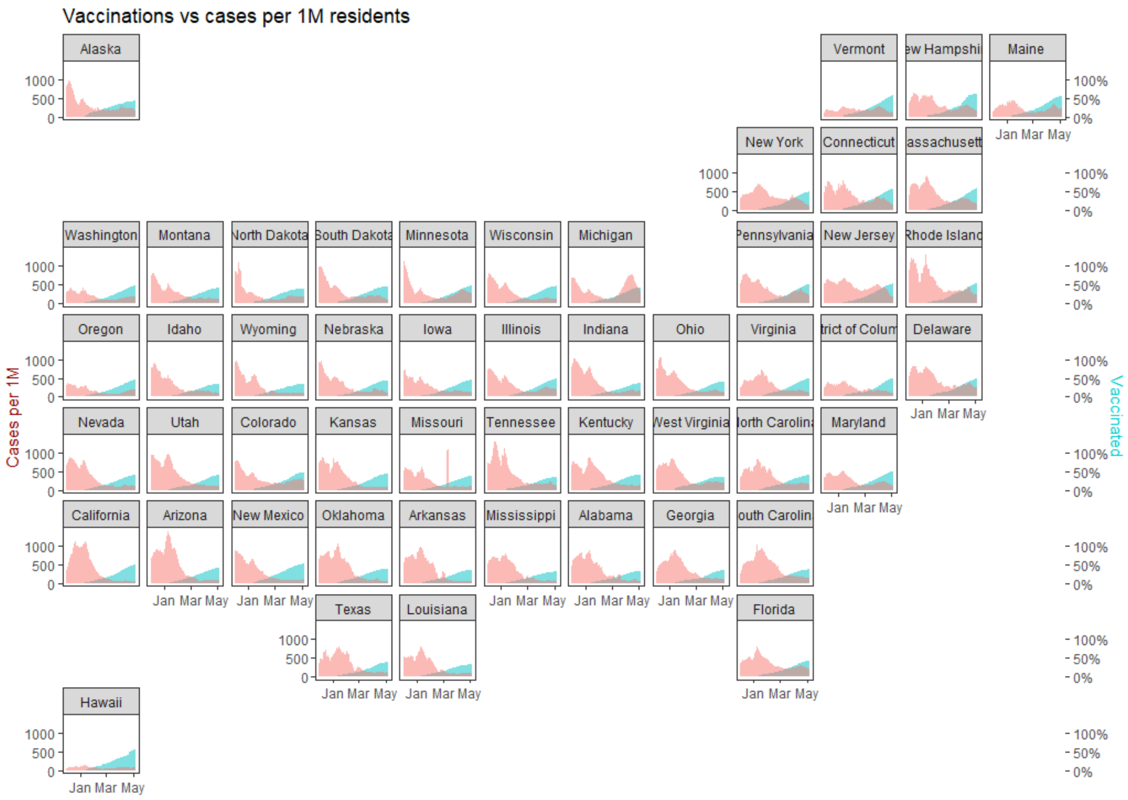
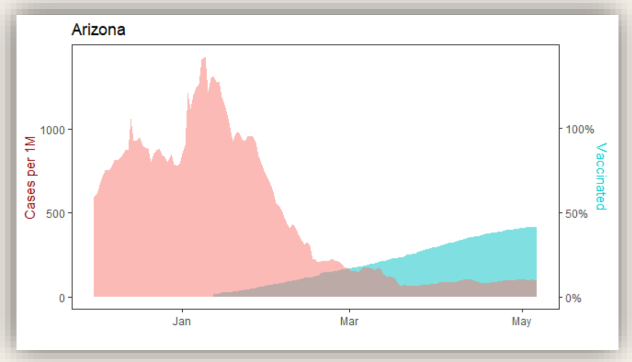
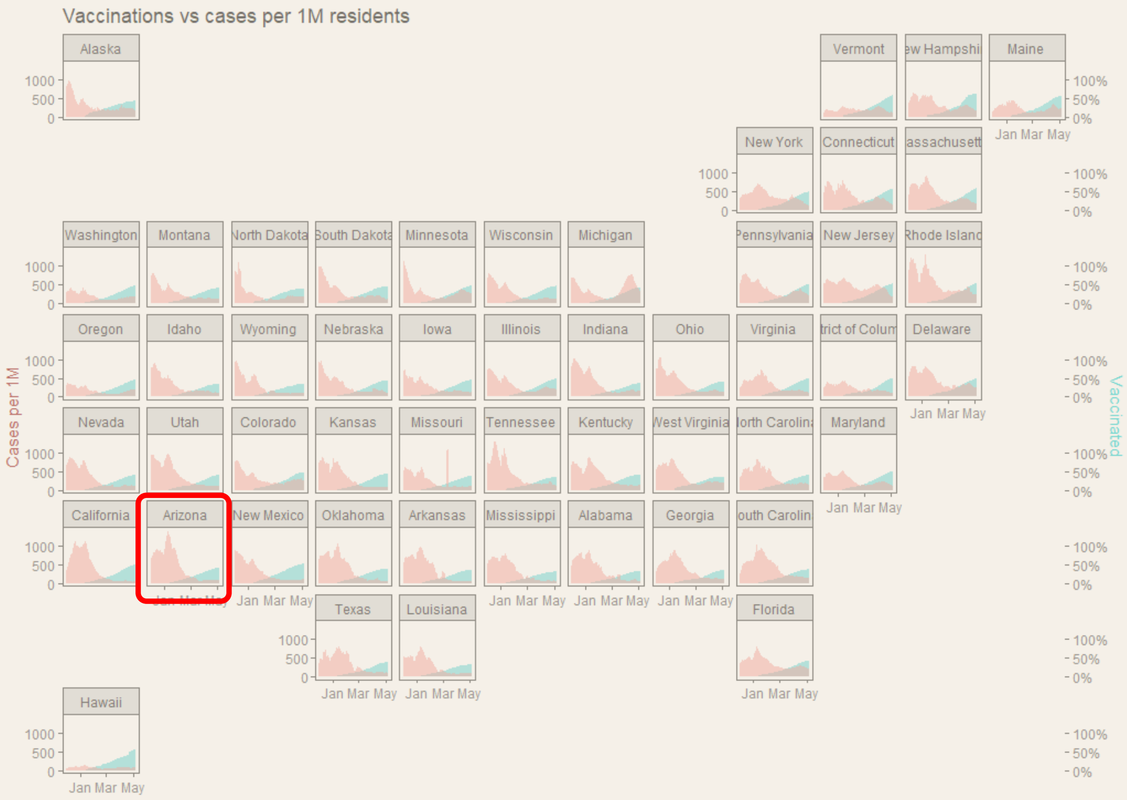
Effectiveness of vaccination

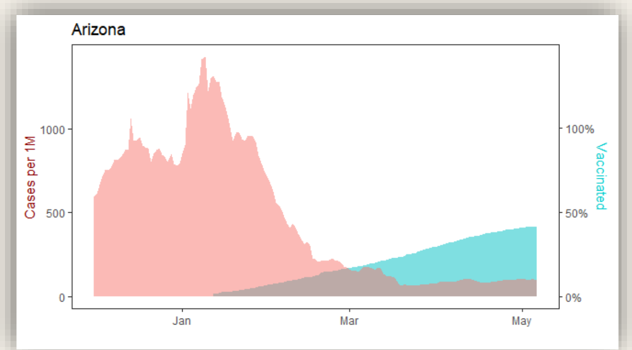


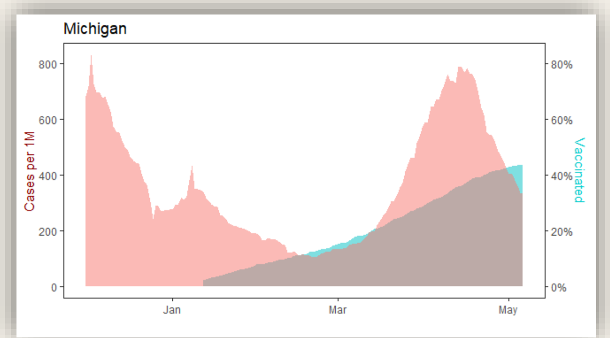
Effectiveness of vaccination



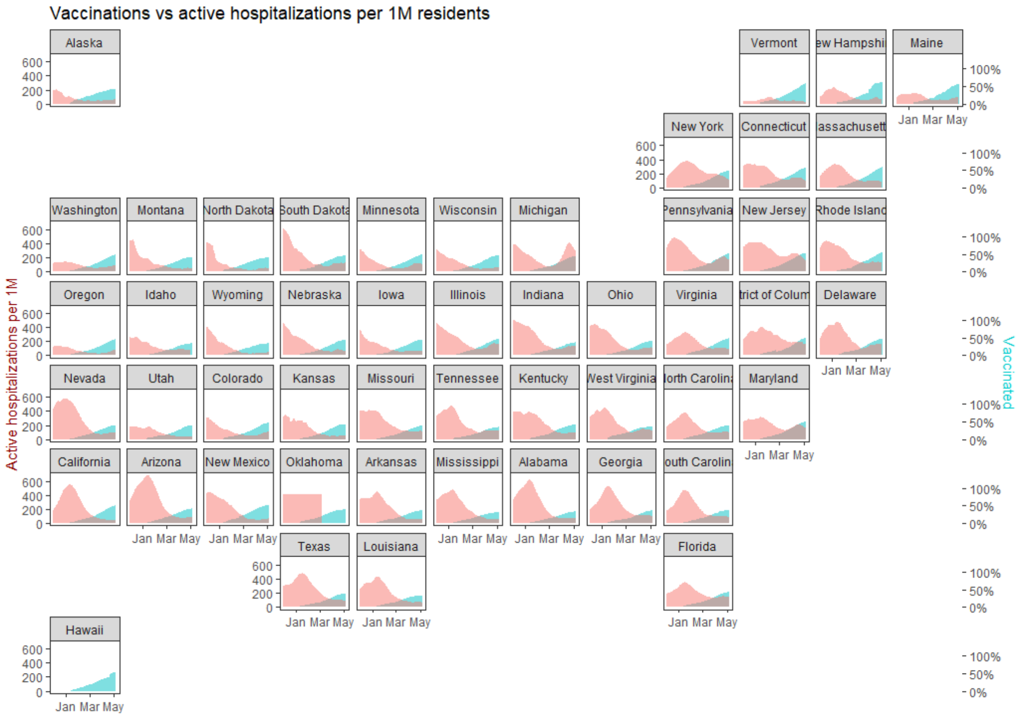


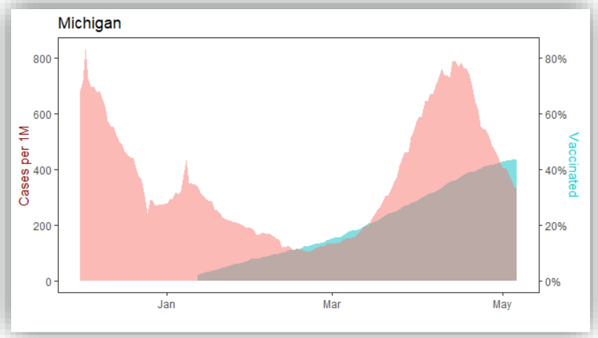
Effectiveness of vaccination





Cases, vaccinations and hospital capacity

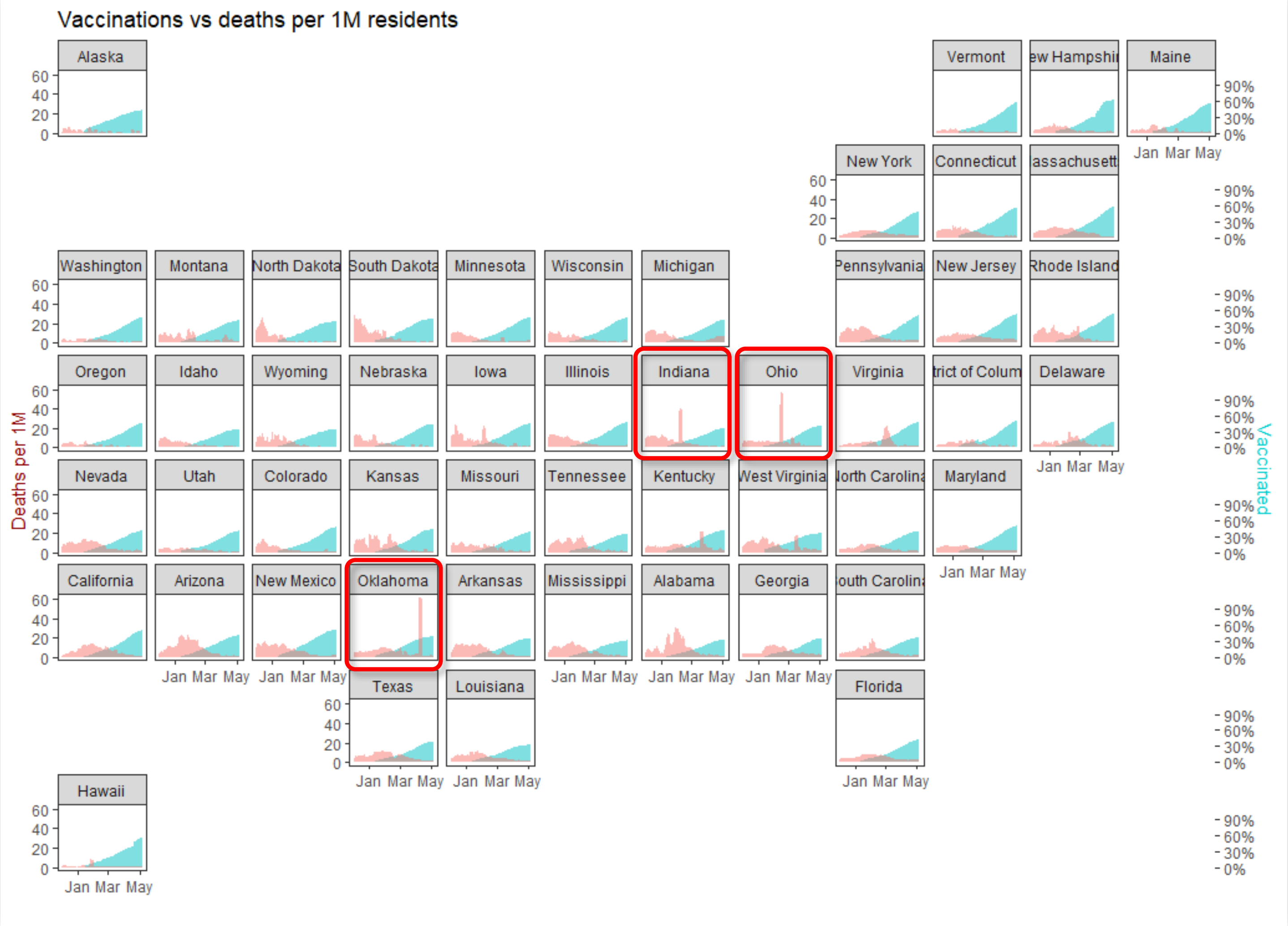


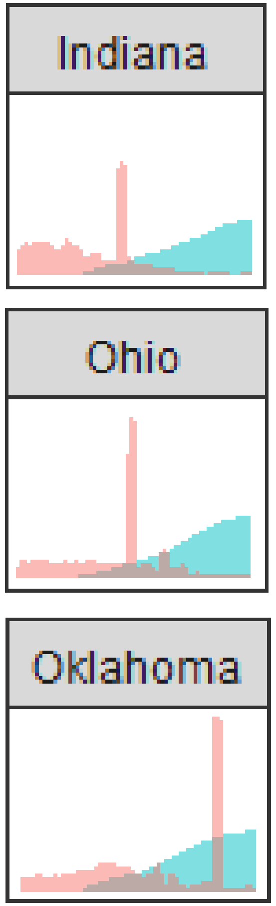


Despite good vaccination rates, hospital burden still high this spring – evidently driven by severe infections in younger unvaccinated adults

Vaccinations vs. mortality

A mostly reassuring plot





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Recoveries

Understanding who recovers, and when, is important for modeling; but recoveries are often counted differently, dumped in periodically, or remain uncounted

The Atlantic

Sign In

HEALTH

We Don't Know How Many People Have Recovered From COVID-19

Recovery has no standard definition, and some states, including California and Florida, do not report such data at all.

AMANDA FRENCH AND QUANG P. NGUYEN JANUARY 14, 2021

- Definitions of 'recovered' vary
  - Negative test after a positive test? Free of long COVID? No symptoms after XX months? Lack of death?
  - CDC recommends a 'symptom-based strategy': Can release from isolation those with mild symptoms 10 days after onset if improvement in symptoms noted
- Several states report no recoveries data officially
- For jurisdictions that do report recoveries, what is the source of their data?
  - Simply assumptions?
  - What % come back to get a negative test?
  - If based on death, distinguishing deaths due to COVID from deaths due to other causes
- If you never get tested, you can never get counted as a case, never mind being recovered!

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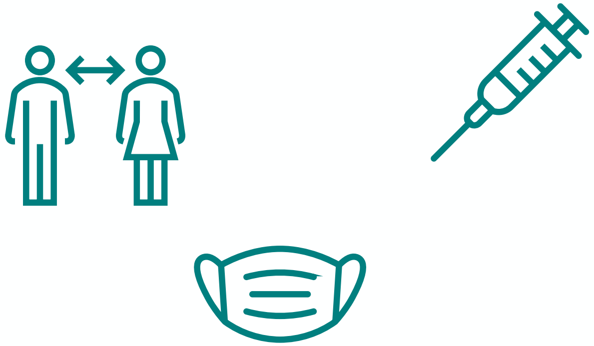
The pandemic narrative

- We have seen the effect of data measurement issues that are pervasive, and affect our interpretation of estimates of COVID-19 indicators and metrics
- But also, that there is a narrative to the trajectory of the pandemic in each jurisdiction, and numerous factors feed into that narrative that aren’t readily captured in administrative or surveillance data.
- Not just estimates of epidemiology but numerous other sociodemographic, economic, environmental, and political factors like:
  - Pharmacologic and non-pharmacologic interventions
  - Socioeconomic status, % living in multigenerational dwellings
  - Baseline health status and comorbidity burden of the underlying population
  - Timing of vaccination of frontline workers and other high risk populations



- A whole host of factors that are difficult to characterize, but are also essential for understanding why the pandemic has unfolded in an area in the way that it has.

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Challenges in interpreting COVID data: The take-homes

- **Ultimately most COVID-19 surveillance data are at the ecological level and should be treated as such**
  - Not able to establish causal links; suggest trends but many explanations possible
  - Compare jurisdictions with caution! Definitions are not standardized
  - When looking at the data, if you hear hooves, think horses not zebras
    - Change in reporting vs. a sudden dramatic shift in the patterns of the epidemic

- **There are many more factors that contribute to COVID burden in addition to cases, hospitalizations and deaths**
  - Many of these are frequently underreported, hard to investigate, or difficult to link directly to surveillance data
  - Need to understand the narrative, in addition to measuring the data points

- **Now that we have considered the ins and outs of commonly reported burden metrics, we are going to discuss how these can feed in to epidemiologic and economic COVID-19 models.**

- **So first, on to R0 and Rt.**

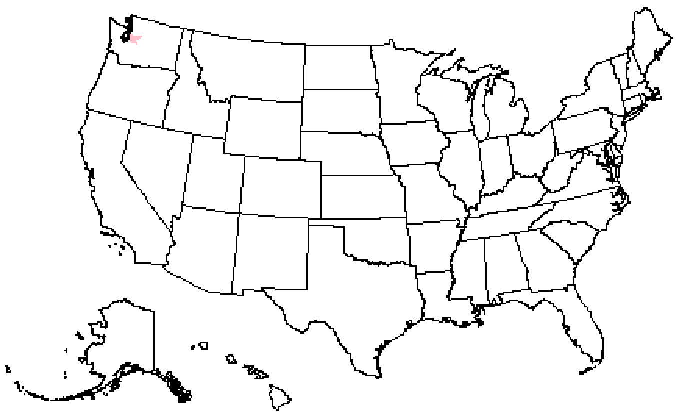
What is R0

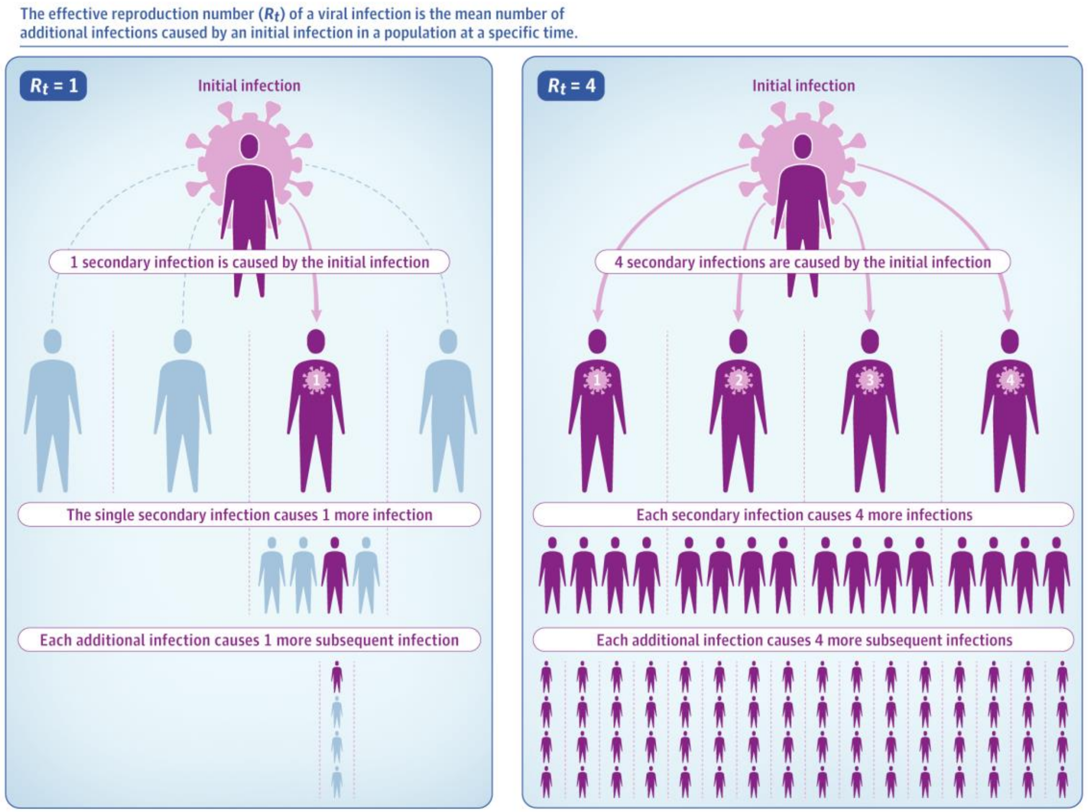
- The basic reproduction number (R0) indicates the number of cases resulting from one infectious person in a susceptible population

  → “Cases per case”

- The interpretation of R0 is that an outbreak will propagate if R0 is >1 and dissipate if <1

January 22 2020 **Growth in COVID-19 infections**





Source: Inglesby. *JAMA.* 2020;323(21)

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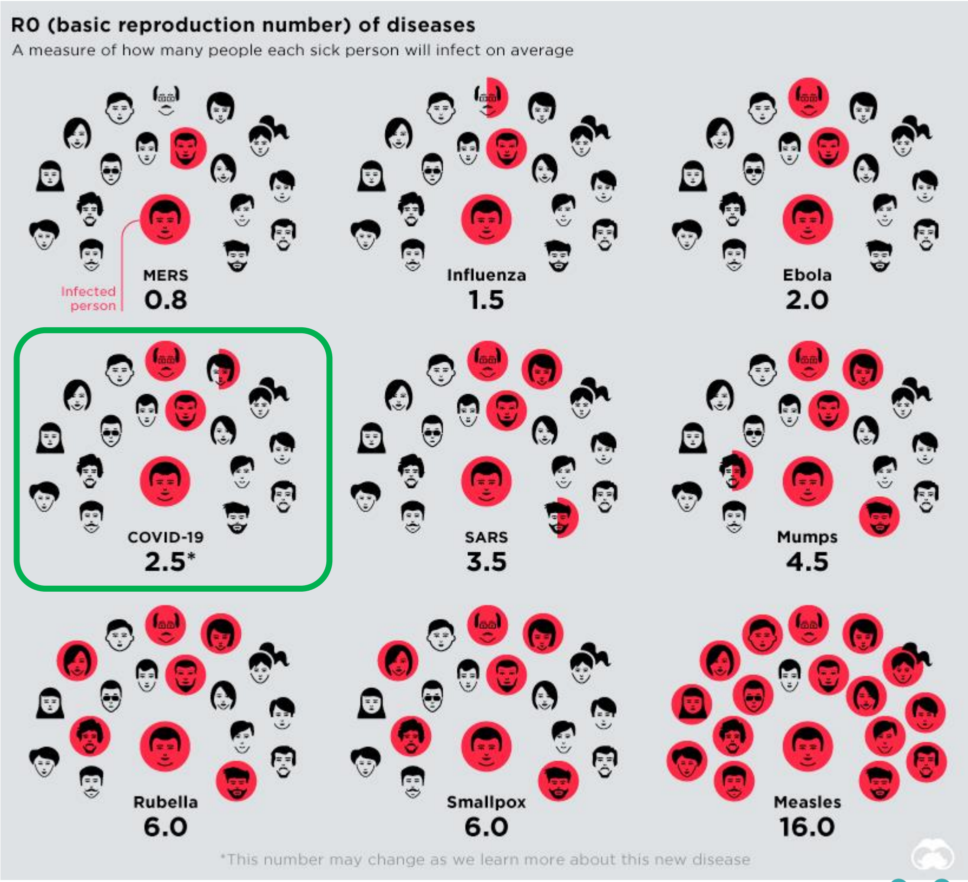
Estimating R0 of COVID-19

Estimating R0 is complex, requiring parameters unverifiable in real-world settings

> *The deeper understanding Faust sought*
> *Could not from the Devil be bought.*
> *But now we are told*
> *By theorists bold*
> *All we need know is R0.*

- Robert May, 1936–2020; in In Bauch. Lancet Inf Dis. 2020

- Estimates vary considerably, but several lie between 2 to 4
    - Some variants appear to have a higher R0



Source: Visual Capitalist. 2020

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What is Rt

Newly-developed methods for real-time approximations (Rt) offer promise for monitoring COVID-19 trends using real-world data.

Rt gives a sense of where the trajectory of the disease is heading

- Dynamic, real-time, relevant to specific epidemic situation at given time
- Different jurisdictions have focused on this to varying extents (e.g. UK)
- Easily calculated; relatively widely reported (the values, not the methods)

Useful in modeling

Source: David Parkins

Two approaches for calculating Rt

Cori et al. – uses number of daily positive increases and serial interval (assumed mean: 5.2, SD: 5.1 days) using Bayesian statistical inference based on a transmission model.

Contreras et al. – also based on a transmission model, uses cases as numerator; recoveries + deaths as denominator.

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The pandemic narrative in our target jurisdictions

BC (pop ~ 5million)
- Cases 26k per 1M
- Deaths 312 per 1M
- Never complete lockdown but some level of public health orders have existed

NJ (pop ~ 9 million)
- Cases 114k per 1M
- Deaths 2.9k per 1M
- Devastating outbreak early in pandemic

ON (pop ~ 15million)
- Cases 32.8k per 1M
- Deaths 558 per 1M
- Stringent restrictions; been in full lockdown several times

PA (pop ~ 13 million)
- Cases 91.5 per 1M
- Deaths 2k per 1M
- Also part of Tri-state area

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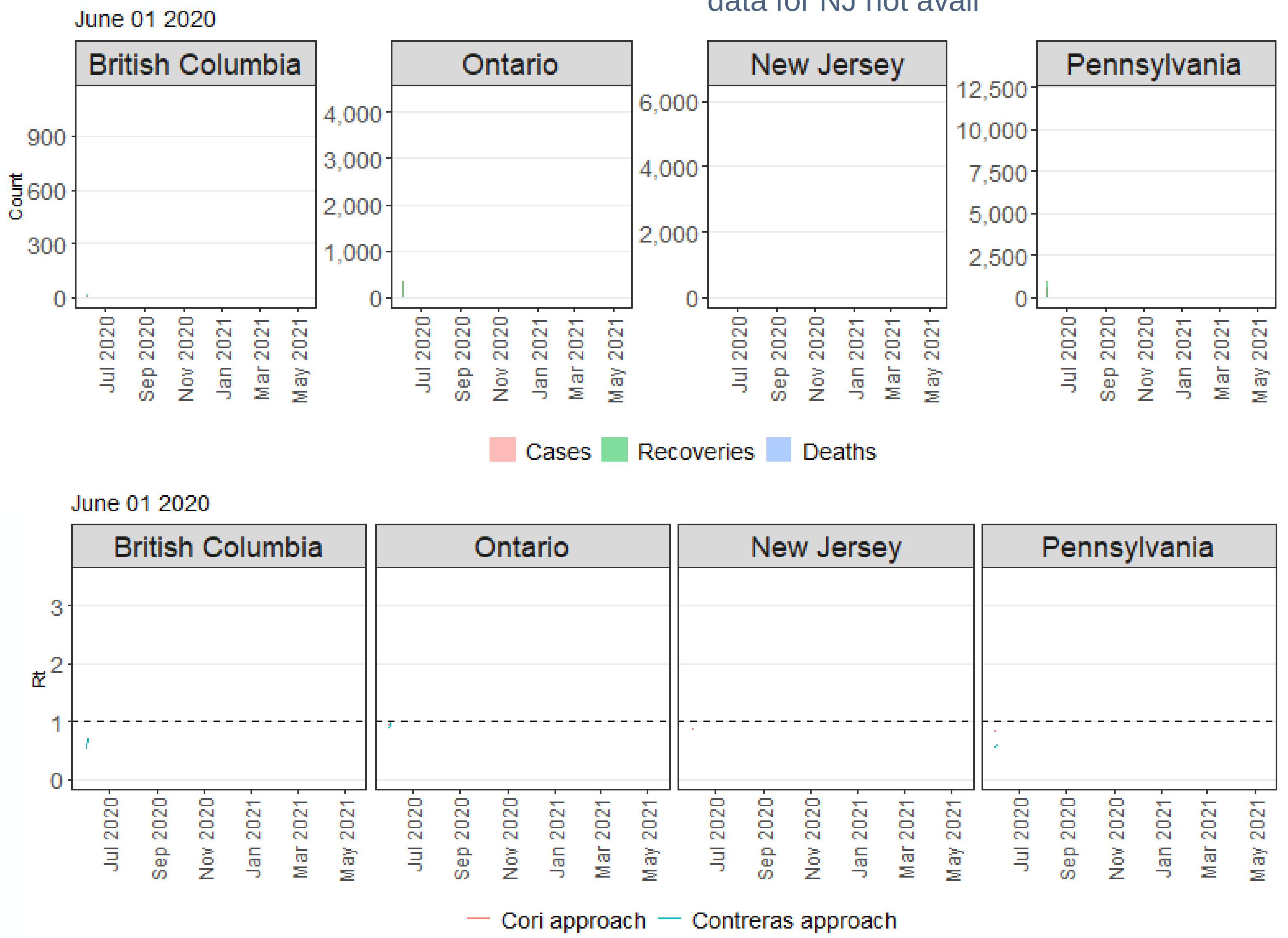
Examples of Rt estimates for the 4 jurisdictions

* Daily recoveries data for NJ not avail



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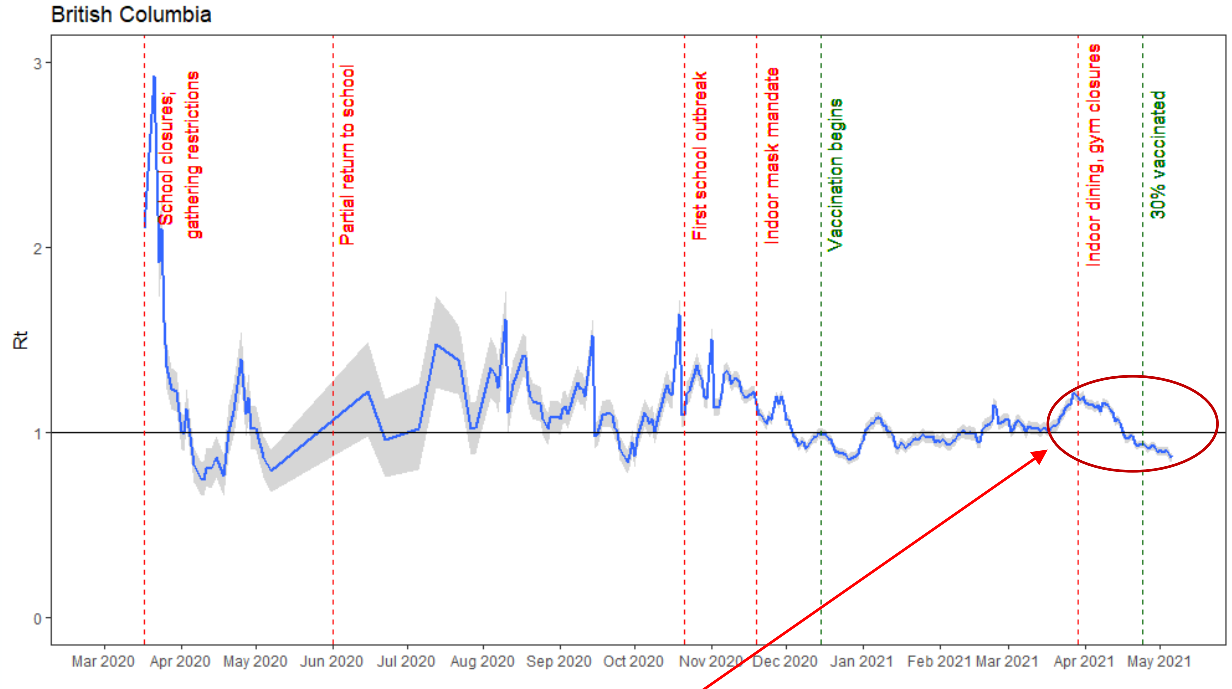
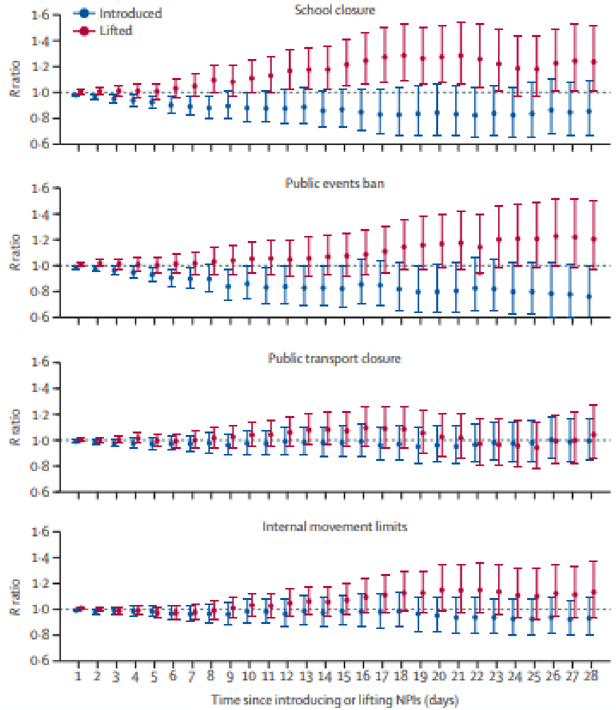
Overlaying public health interventions on estimates of Rt



Implemented most stringent restrictions since early in the pandemic

Recent article by Li et al 2021 (Lancet Inf Dis):

- Estimated % change in Rt when introducing or lifting non-pharmaceutical interventions (NPIs) across 130+ countries
- School closure, public events ban, stay at home mandates, and internal movement limits had the largest impacts on Rt
  - The 'main effect' was the interaction

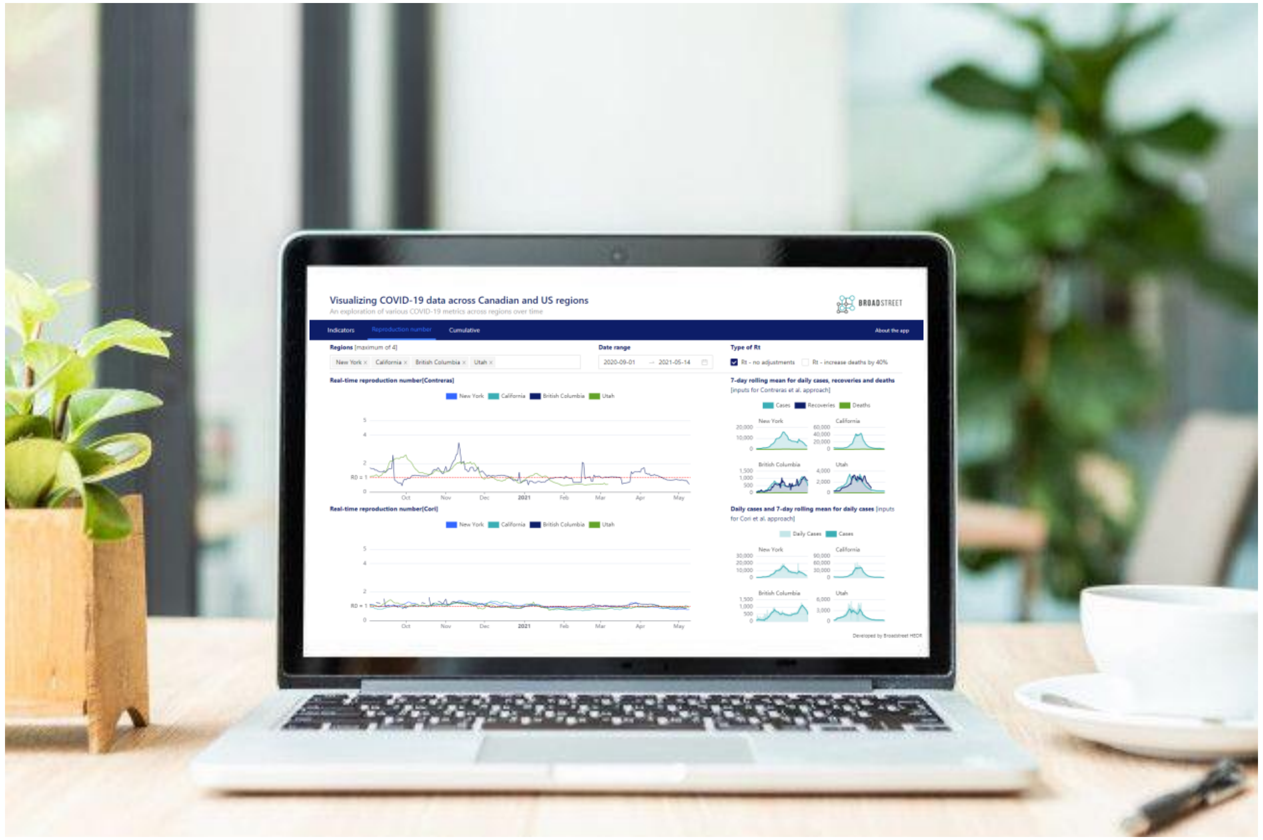


Overview of the app

covid19.broadstreetheor.com

We created an app to help visualize some metrics we've discussed today, including two Rt methods:

- For US States and Canadian provinces
- Over the course of the pandemic
- It also illustrates some data challenges such as missingness, or 'data dumps' when a certain metric (e.g., cases) are backlogged



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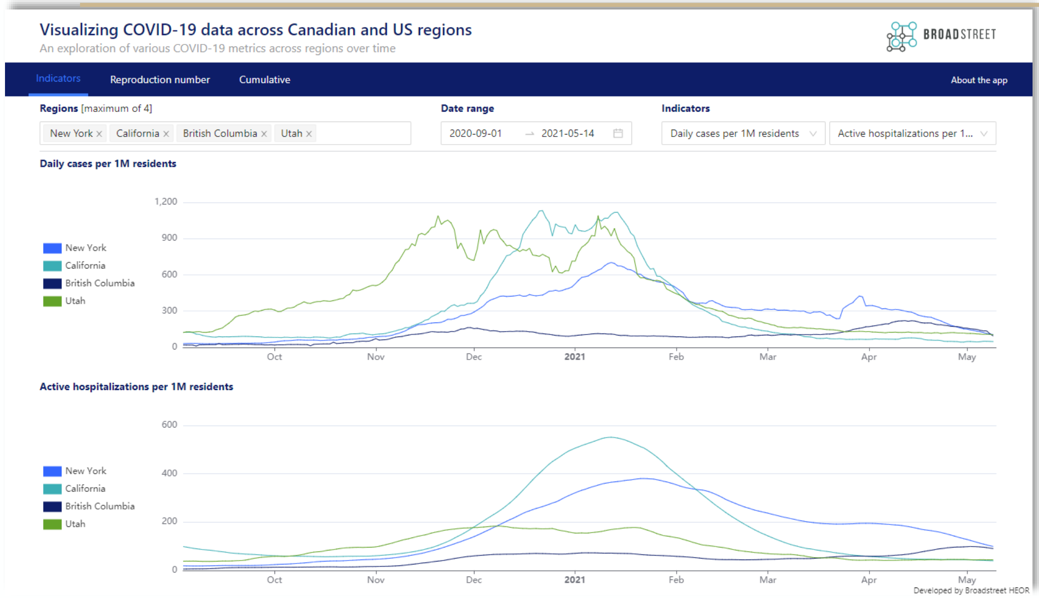

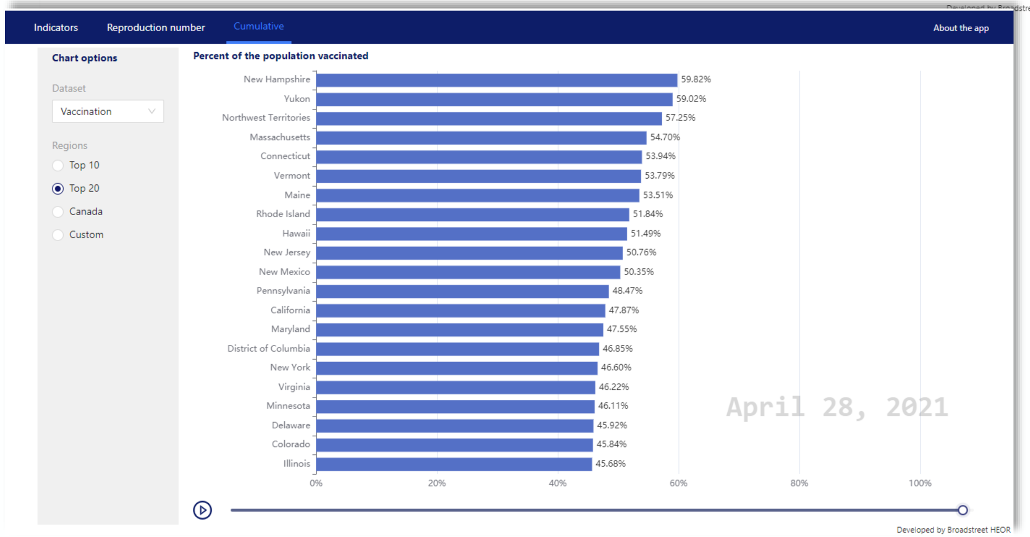

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Exercises

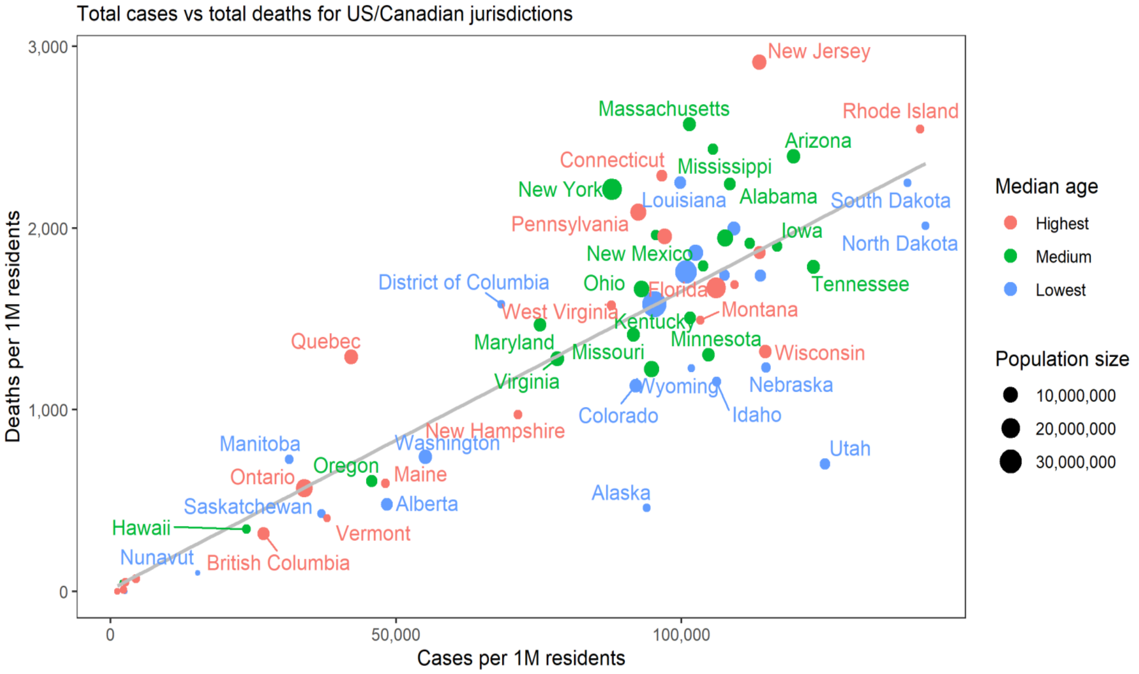
covid19.broadstreetheor.com

Choose a metric and try to identify a jurisdiction that is an "outlier" on that metric – and confirm how you would characterize "outlier"

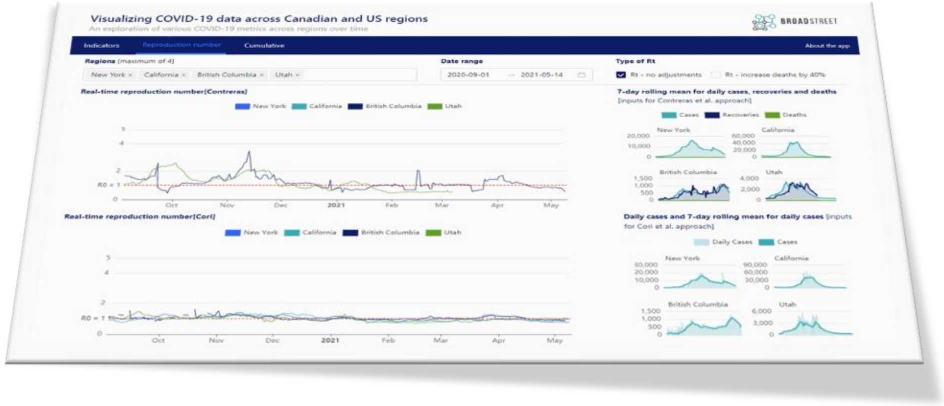
- **Then focus on that jurisdiction for other metrics – is it also an outlier for these?**
  - Can you think of a potential narrative? Do you think that data measurement issues may be contributing?

- **If you're from the US or Canada, does your home jurisdiction look better or worse than you were expecting?**
  - And what do you know about the narrative of the pandemic in your jurisdiction that affects the interpretation of the data we see here?

- **Select two jurisdictions with relatively high cases and relatively low cases**
  - Do hospitalizations and deaths show a similar trend (high for high, low for low)
    - If yes, how do Rt estimates compare
    - If no, why do you think these differ? What effect is there on Rt estimates?



Take-homes from the app



There is value in visualizing COVID-19 data through considering:

- Multiple indicators
- Over-time and cross-jurisdiction comparisons

→ policies/interventions are often state/province specific

- Any metric must be interpreted within the context of the situation on the ground i.e. restrictions, testing rate, vaccines

→ ‘The truth is in the whole’

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Ask a modeler: COVID-related modelling issues

Summary

1. Surveillance & assessments of public health interventions
2. Economic models of infectious disease diagnostics
3. Economic models of treatments
4. Epidemiologic models based on disease transmission
5. Models using health-state utilities

1. Economic evaluation of public health Interventions

- Examples of interventions
  - Mandatory face masks
  - Social distancing / closure of certain businesses
- Challenges in economic evaluation of public health interventions
  - Accurate data on case incidence/prevalence of COVID, transmission rates, hospitalization rates, and attributable mortality are critical to the design of effective public health interventions
    - "Surveillance can directly measure what is going on in the population. Therefore, it useful both for measuring the need for interventions and for directly measuring the effects of interventions. The purpose of surveillance is to empower decision makers to lead and manage more effectively by providing timely, useful evidence." (Nsubuga et al.)
  - Choosing comparators and control groups ("natural" experiments vs. controlled experiments; difficulties with randomization)
  - Controlling for confounding factors (comorbidities; intervention design; adherence; enforcement)

2. Economic evaluation of infectious disease diagnostics

- Changes in clinical pathways for diagnosis and treatment
  - Many of the pre-COVID clinical pathways may have changed permanently
- Viral vs. bacterial differentiation
  - Models of infectious disease diagnostics may in some cases require a “front end” where patients undergo a viral vs. bacterial test prior to COVID testing
  - Avoids delaying treatment of patients with bacterial infections (e.g., lower respiratory tract infections) that symptomatically resemble COVID
- Economic models of COVID diagnostics
  - Sensitivity & specificity influenced by several factors (e.g., lack of gold-standard testing; asymptomatic disease presentation)
  - Value of diagnostics = avoided transmission, cost offsets associated with earlier treatment

3. Economic evaluation of COVID treatments

- Population
  - Transmission rates
  - Eligible populations
  - Cohort sizes
- Variation in characteristics of disease
  - Asymptomatic patients
  - Severity of disease among symptomatic patients
  - Disease progression
  - Effects of comorbidities (e.g., disentangling effects of comorbidities vs. type of treatment)
- Study design
  - Natural vs. controlled experiments
  - Controlling for comorbidities
  - Variations in treatment applications
  - Indirect costs: productivity; informal caregivers
  - Change in clinical pathways (e.g., withholding non-COVID care; telehealth; shift to app-based care)

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4. Cost-effectiveness analysis and R0 and Rt / Re

Cost-effectiveness models based on disease transmission models

- CEACOV models have been based on “effective reproduction number” ranging from 1.2-1.5
- Alternative economic models have used R0=2.7 (Sandmann et al. – UK population) and R0=2.4 (Thunstrom et al. – US population)
- All analyses found results sensitive to Re & R0 values

Reddy et al.

> “*__When Re was 1·5__, health-care testing alone resulted in the highest number of COVID-19 deaths during the 360-day period. Compared with health-care testing alone__, a combination of health-care testing, contact tracing, use of isolation centres, mass symptom screening, and use of quarantine centres__ reduced mortality by 94%, increased health-care costs by 33%, and __was cost-effective__ ...*
>
> *When __Re was 1·2, health-care testing, contact tracing, use of isolation centres, and use of quarantine centres was the least costly strategy, and no other strategies were cost-effective__.*
>
> *In sensitivity analyses, a combination of health-care testing, contact tracing, use of isolation centres, mass symptom screening, and use of quarantine centres was generally cost-effective, __with the exception of scenarios in which Re was 2·6 and when efficacies of isolation centres and quarantine centres for transmission reduction were reduced__.*”

CEACOV


medRχiv
THE PREPRINT SERVER FOR HEALTH SCIENCES
BMJ Yale
Comment on this paper
Cost-effectiveness of COVID-19 vaccination in low- and middle-income countries
Mark J. Siedner, Christopher Alba, Kieran P. Fitzmaurice, Rebecca F. Gilbert, Justine A. Scott, Fatma M. Shebl, Andrea Ciaranello, Krishna P. Reddy, Kenneth A. Freedberg
doi: https://doi.org/10.1101/2021.04.28.21256237
This article is a preprint and has not been peer-reviewed [what does this mean?]. It ... be used to
Preview PDF

Annals of Internal Medicine
ORIGINAL RESEARCH
College Campuses and COVID-19 Mitigation: Clinical and Economic Value
Elena Losina, PhD; Valia Leifer, AB; Lucia Millham, AB; Christopher Panella, BA; Emily P. Hyle, MD, MSc; Amir M. Mohareb, MD; Anne M. Neilan, MD, MPH; Andrea L. Ciaranello, MD, MPH; Pooyan Kazemian, PhD*; and Kenneth A. Freedberg, MD, MSc*
Background: Colleges in the United States are determining how to operate safely amid the coronavirus disease 2019 (COVID-19) pandemic.
mitigation to 493 with extensive social distancing and masks, and further to 151 when laboratory testing was added among asymptomatic persons every 3 days. Among faculty, these val- ...

THE LANCET Global Health
Articles
Cost-effectiveness of public health strategies for COVID-19 epidemic control in South Africa: a microsimulation modelling study
Krishna P Reddy, Fatma M Shebl, Julia H A Foote, Guy Harling, Justine A Scott, Christopher Panella, Kieran P Fitzmaurice, Clare Flanagan, Emily P Hyle, Anne M Neilan, Amir M Mohareb, Linda-Gail Bekker, Richard J Lessells, Andrea L Ciaranello, Robin Wood, Elena Losina, Kenneth A Freedberg, Pooyan Kazemian*, Mark J Siedner*
Summary
Background Health-care resource constraints in low-income and middle-income countries necessitate the identification of cost-effective public health interventions to address COVID-19. We aimed to develop a dynamic COVID-19 microsimulation model to assess clinical and economic outcomes and cost-effectiveness of epidemic control strategies in KwaZulu-Natal province, South Africa.

How to address uncertainty in policy decisions if narrow variation in R values leads to different decisions?

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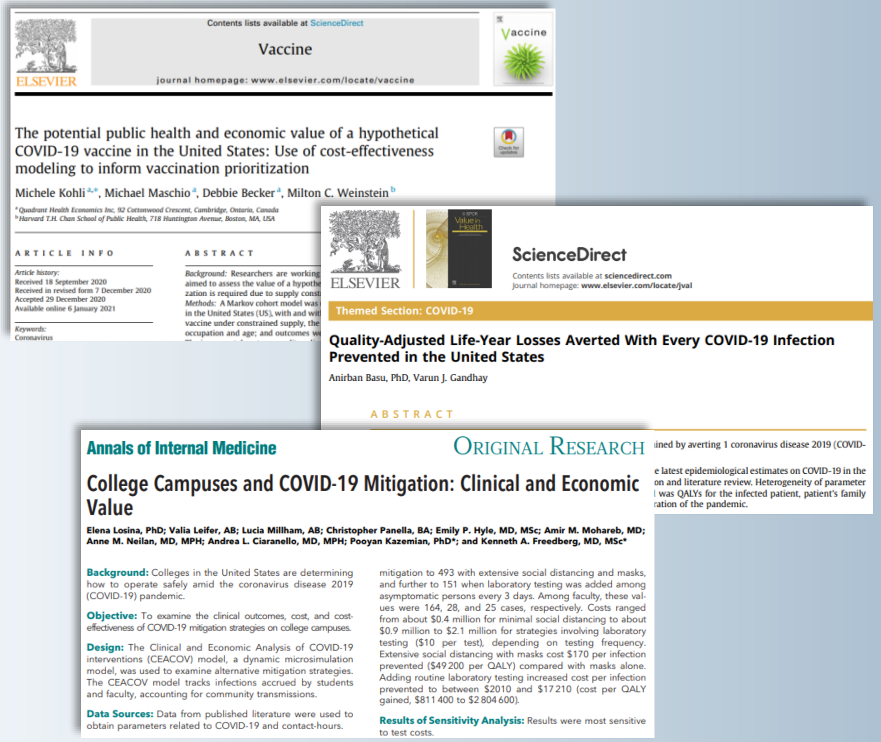
Alternatives to R0 and Rt

Novel approaches have been used in cost-utility and cost-effectiveness models

- Cost-utility of vaccines in the US (**Kohli et al.**): disease transmission assessed using a combination of mortality surveillance data (IHME) and assumptions regarding under-reporting, to adjust

Avoids need to estimate R0 but is reliant on quality of surveillance data if approach is taken in individual jurisdictions

- CEACOV model examining college campus transmission (**Losina et al.**) based on assumed contact-hours and transmission risk per contact
- "Reduced-form" model (**Basu et al.**) focusses on the experience and resulting transmissions from a single patient



These more "micro" or "bottom-up" approaches offer alternatives and may be based on more testable assumptions, but may be challenging to scale up to larger populations – need to account for variability

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5. And what about utilities?

To date, limited data are available around HRQoL & utilities for COVID patients

- ICER review of remdesivir based disutility values on published data for influenza and *C. difficile* patients, respectively
- These values have been subsequently utilized in other publications

Need for COVID-specific utilities – and better understanding of "long COVID" and its implications

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19

UPDATED REPORT

November 10, 2020

1. Model Inputs

	Value	Source	Notes
Model Wide Inputs, Moderate to Severe Population			
Disutility of COVID symptoms	-0.19	Assumption & Smith & Roberts, 2002	For duration of time to recovery
Disutility of COVID hospitalization with or without supplemental oxygen	-0.30	Assumption & Barbut et al., 2019	For duration of time to recovery; additive onto disutility of COVID symptoms
Disutility of COVID hospitalization requiring noninvasive ventilation or high-flow oxygen	-0.50	Barbut et al., 2019	For duration of time to recovery; additive onto disutility of COVID symptoms
Disutility of COVID hospitalization requiring mechanical ventilation or ECMO	-0.60	Barbut et al., 2019	For duration of time to recovery; additive onto disutility of COVID symptoms

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Ask a modeler: Q&A

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Wrap up