

The effects of lockdown timing on COVID-19 cases across Europe: A counterfactual modelling study

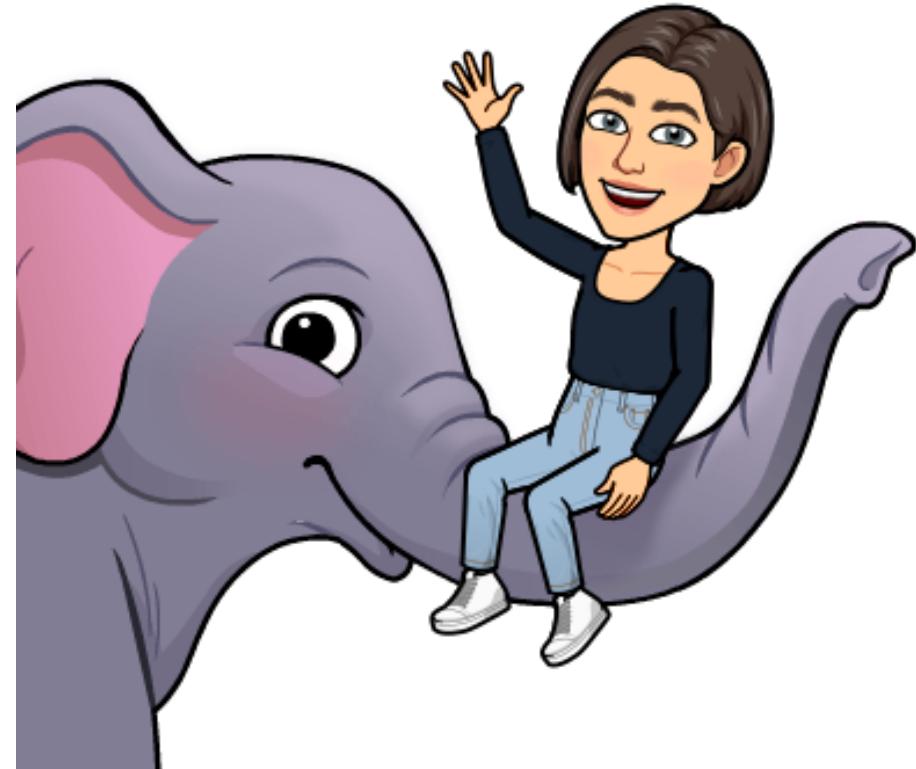
Kellyn F Arnold

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A bit about me

- Postdoctoral research fellow at the University of Leeds
- Research focusses on the integration of formal causal inference methods with simulation-based methods in longitudinal settings



Causal inference

- The formal processes by which we infer cause-and-effect relationships from data
- Sometimes referred to as “*counterfactual prediction*”
- “If I changed X , how would Y change?”

COVID-19

- Contagious respiratory disease caused by SARS-CoV-2
- First reported in Wuhan, China in December 2019
- Global pandemic declared by WHO on 11 March 2020
- Many features unknown, but clear that virus had high potential for transmission and induced substantial morbidity/mortality

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Coronavirus

• This article is more than 1 year old

New 1,000-bed Wuhan hospital takes its first coronavirus patients

Facility was built in less than two weeks in city at the centre of the viral outbreak



▲ Medical workers in protective suits help transfer the first group of coronavirus patients into the newly completed Huoshenshan temporary field hospital in Wuhan, China. Photograph: Xiao Yijiu/AP

Agence France-Presse

Tue 4 Feb 2020 06.30 GMT

Non-pharmaceutical interventions (NPIs)

- Public health measures that aim to prevent and/or control community transmission of SARS-CoV-2
- Common examples include:
 - Limits on mass gatherings
 - Closing of schools and non-essential shops
 - Restrictions on internal/external movements
 - Orders to stay at home or shelter in place (i.e. 'lockdown')

Lockdowns

- Lockdowns generally carry substantial social and economic costs
- Single-country studies (first wave) have generally found that delaying lockdown measures can be even more costly
 - 57% of deaths in the USA could have been avoided by implementing a national lockdown 1 week earlier (Knock et al. 2020)
 - 74% of severe cases in England could have been avoided – and the required length of lockdown halved – had social distancing and lockdown measures been implemented 1 week earlier (Arnold et al. 2022)
- Multi-country studies are much more equivocal

How effective are lockdowns?

Worldwide

- Full lockdown reduced R_0 by 64-85% (Oraby et al. 2021)
- National lockdowns reduced R_t by 0.8-14% (Haug et al. 2020)
- Stay-at-home orders reduced R_t by 13% (Brauner et al. 2021)

Within Europe

- Lockdowns reduced R_t by 81% (Flaxman et al. 2020)
- Stay-at-home orders reduced number of new infections by 4% (Banholzer et al. 2021)

Common methods of analysis

Descriptive or correlational

- Pachetti et al. (2020)
- Plumper and Neumayer (2020)

Regression

- Li et al. (2020)
- Papadopoulos et al. (2020)
- Liu et al. (2021)
- Fuller et al. (2021)

SEIR

- Davies et al. (2020)
- Hyafil and Morina (2020)
- Pei et al. (2020)
- Oraby (2021)

Other

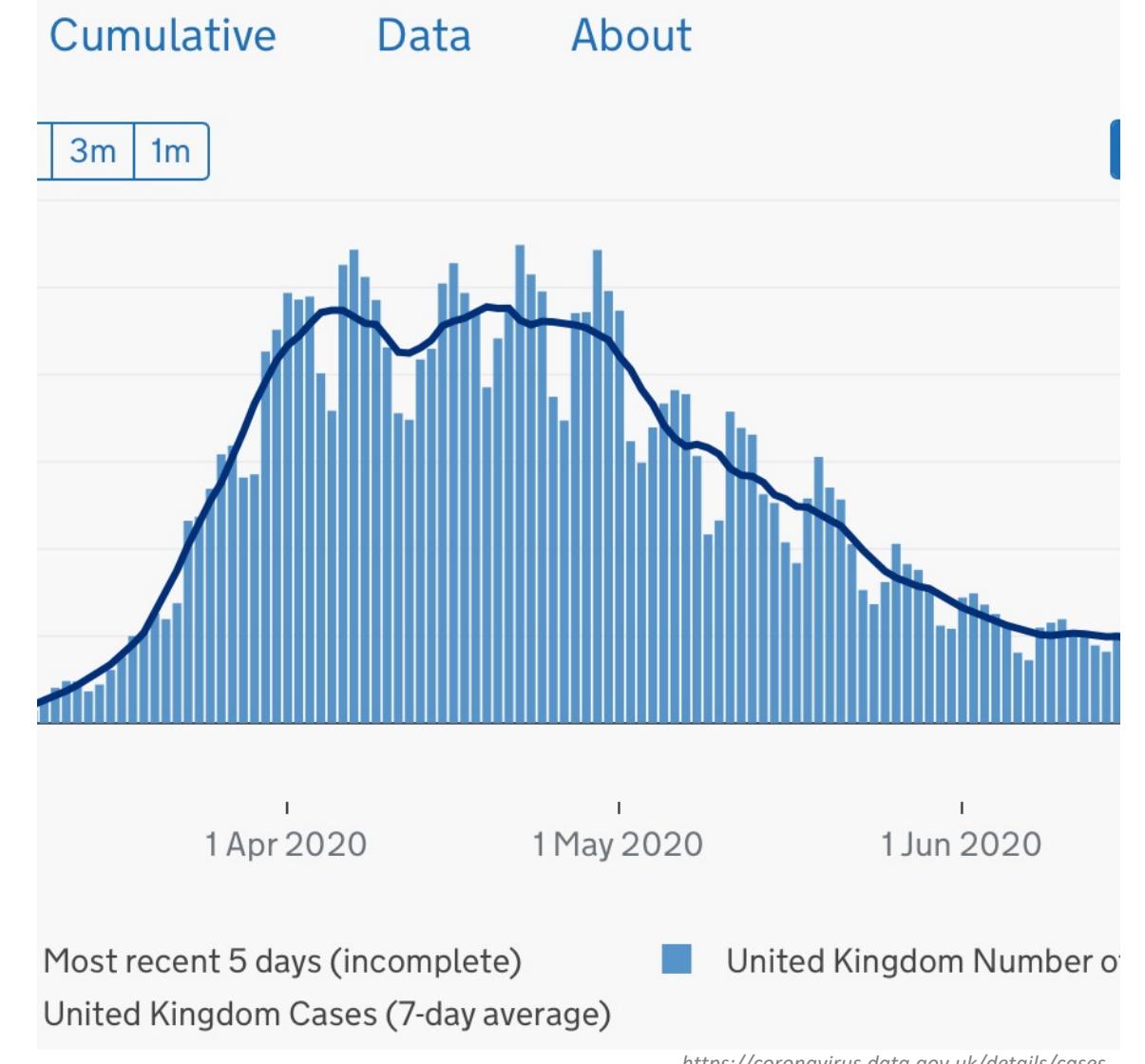
- Baunholzer et al. (2020)
- Flaxman et al. (2020)
- Haug et al. (2020)
- Islam et al. (2020)
- Kontis et al. (2020)
- Brauner et al. (2021)

Methodological challenges

- Between-country heterogeneity makes standard correlational and regression studies impractical to implement and difficult to interpret
 - Demographics
 - Cultural norms
 - Incentivisation systems
 - Testing criteria, procedures, and capacities
- Many methods rely on (and are sensitive to) assumptions about unknown features of the infection and disease processes
 - Transmission rates
 - Basic (R_0) and effective (R_t) reproduction numbers

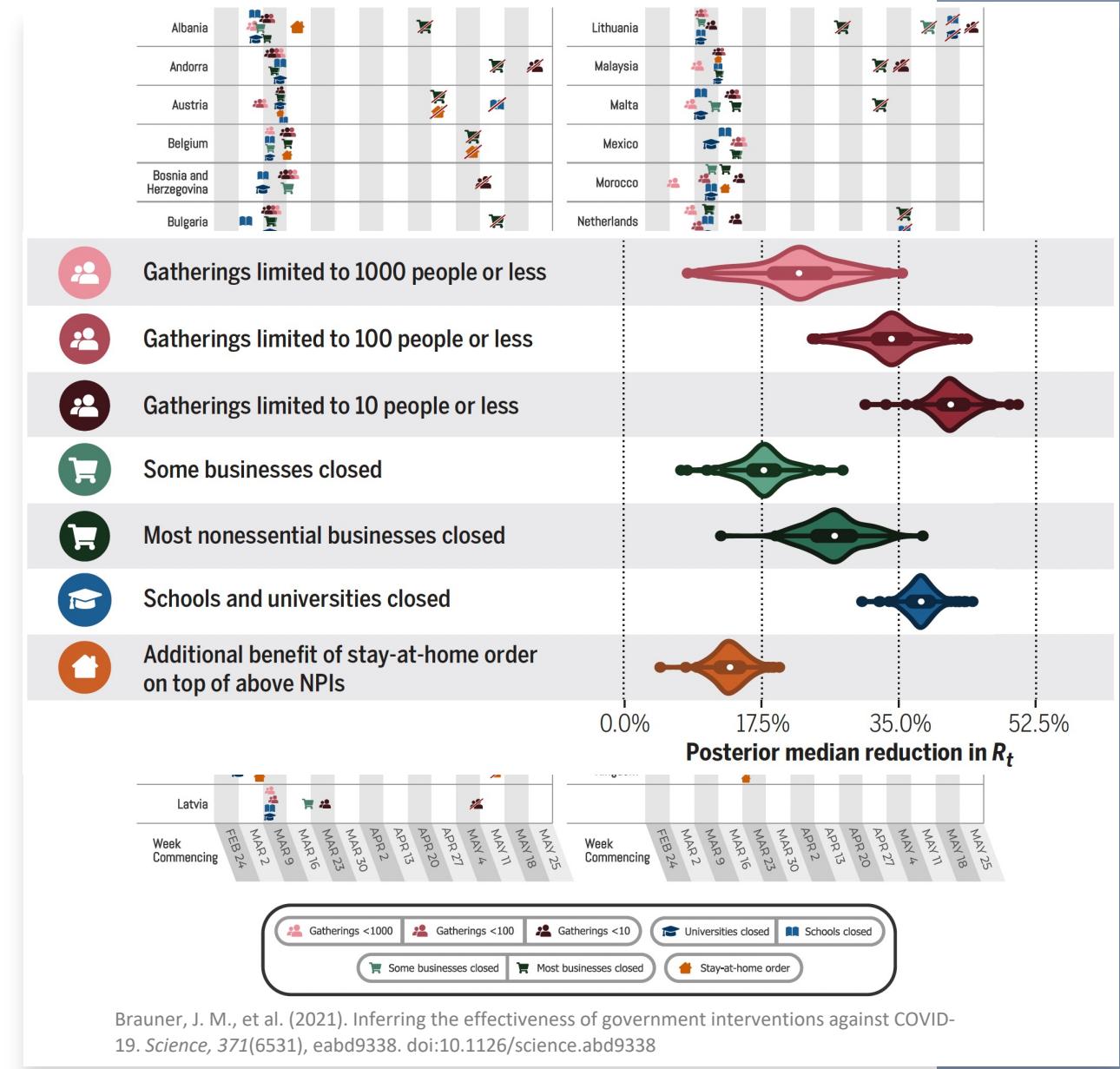
Methodological challenges (cont.)

- Observed data are subject to a high degree of autocorrelation and weekday effects
- Intervention effects are observed with an unspecified delay
 - Lag periods vary widely by geography (Liu et al. 2021)
 - Lag periods are generally much longer than incubation period for SARS-CoV-2 (e.g. 2-3 weeks in Canada, Stockdale et al. 2020)



Methodological challenges (cont.)

- High degree of intervention clustering
- Ordering of interventions affects apparent effectiveness
 - Lockdowns are often introduced after a series of less-stringent measures
 - NPIs introduced earliest tend to have greatest effects (Li et al. 2021)



Solutions

- Model a standardised sequence of interventions:
 1. Initial uncontrolled growth
 2. Growth under initial restrictions
 3. Growth under national lockdown
- Allow for varying lag periods between and within countries
- Accommodate autocorrelation and weekly effects
- Use countries as own comparators
- Bypass need for assumptions about transmission rates
 - Directly model exponential growth

Exponential growth

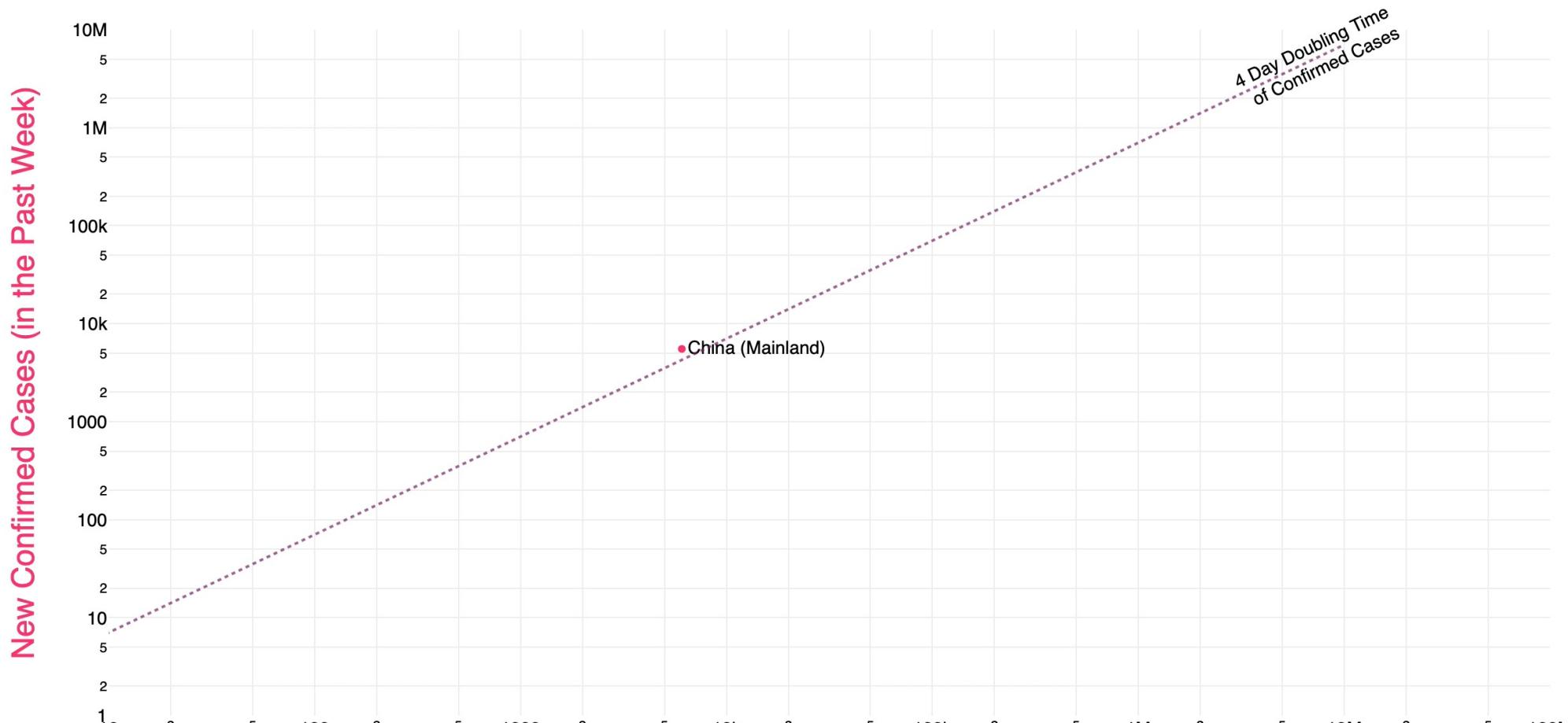
A causal process whereby the total number of cases on a given day (t) is a multiple (r) of the total number of existing cases:

$$\text{Cumulative cases}_t = \text{Cumulative cases}_{t-1} \cdot r$$

$$\text{Incident cases}_t = \text{Cumulative cases}_{t-1} \cdot (r - 1)$$

This equation implies a linear relationship between cumulative and incident cases over time... *the slope of which should change due to social distancing and lockdown measures*

Trajectory of World COVID-19 Confirmed Cases (2020-01-29)



2020-01-29



Logarithmic Scale



Research question

To what extent does delaying implementation of initial (often voluntary) measures and more severe lockdown measures increase total case numbers and ultimately prolong the length of lockdown required?

Study sample & data sources

Study sample

- First wave of COVID-19
- 44 European countries eligible for inclusion

Data sources

- COVID-19 Data Repository by the Center for Systems Science and Engineering at Johns Hopkins University
- Oxford COVID-19 Government Response Tracker
- World Bank

Analysis overview

01

Identify
important
dates

02

Estimate
growth
parameters

03

Simulate
counterfactual
scenarios

01

Identification of important dates

Date of first restriction:

- First date where any of the specified containment and closure policies were recommended or required

Lockdown:

- First date for which either a stay-at-home order or 3+ other containment and closure policies were required nationally

Date of lockdown easing (*i.e. end of full lockdown*):

- First date subsequently for which the total number of measures required nationally decreased

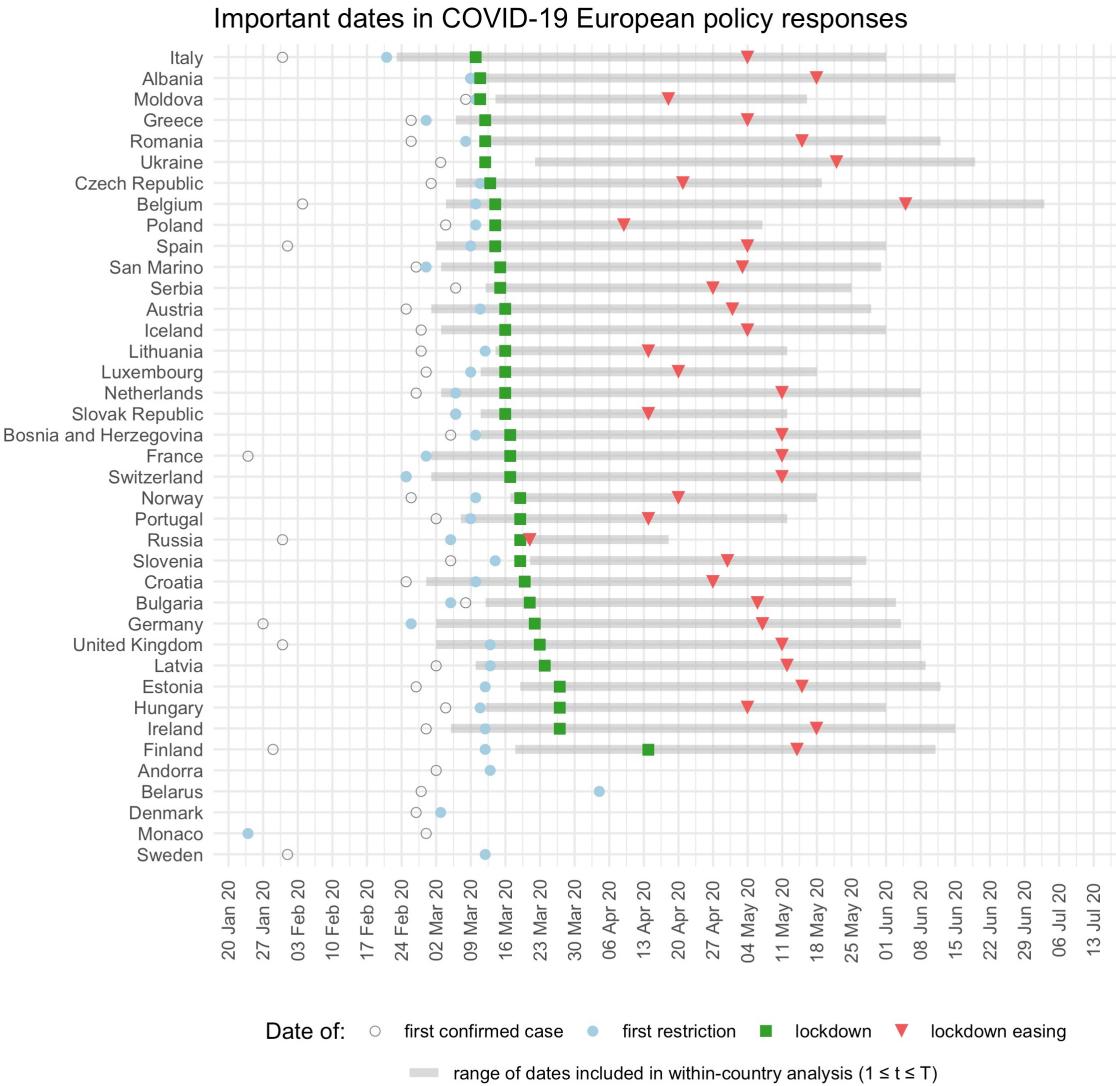
End of first wave:

- 28 days after the date of lockdown easing

39 European countries
had both cases and
policy data available



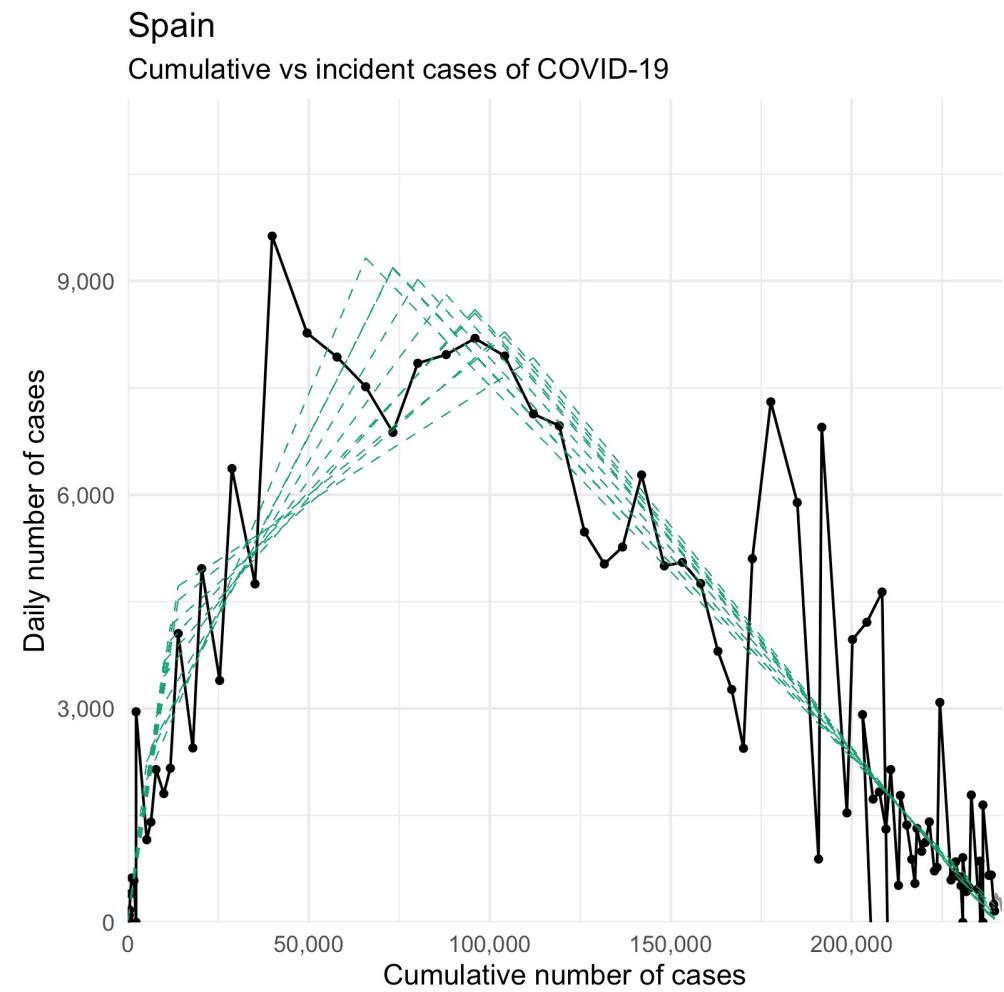
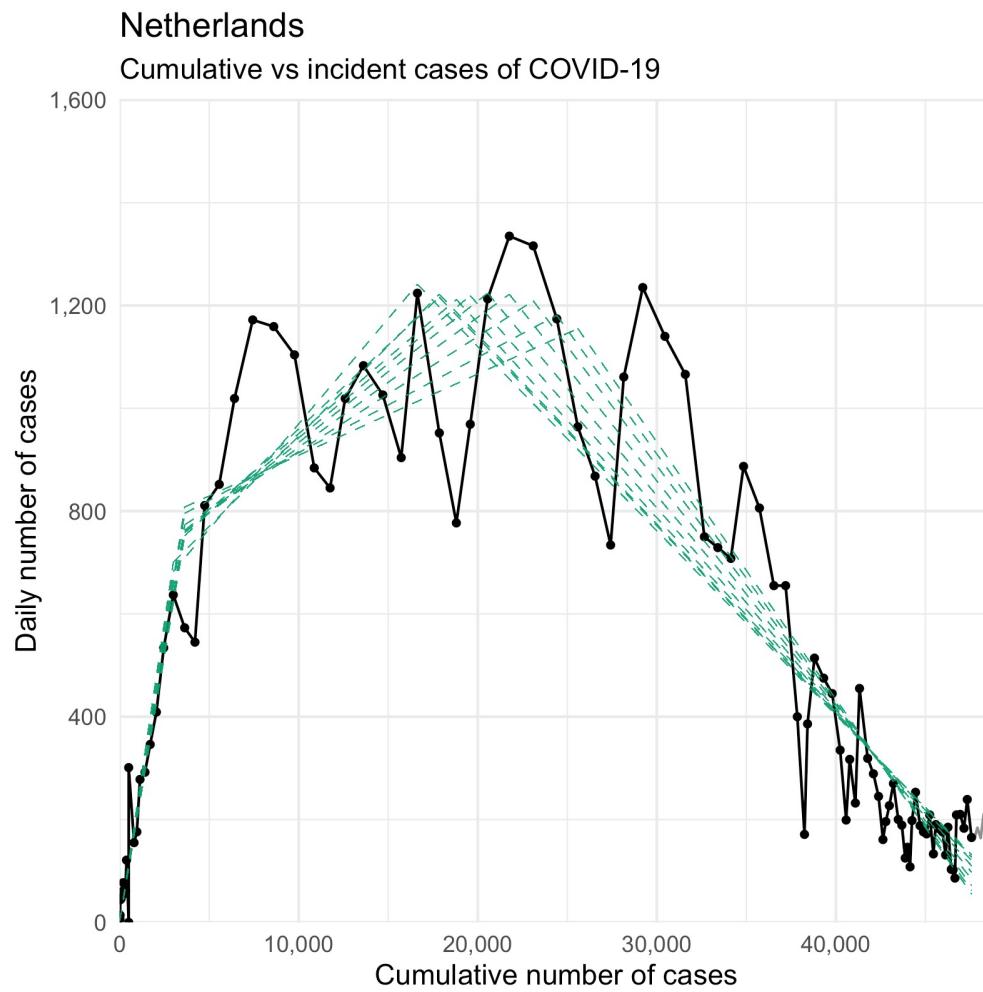
33 entered lockdown &
had estimable growth
parameters



02

Parameter estimation

- We considered 3 potential periods of growth:
 1. Initial uncontrolled growth
 2. Growth under initial restrictions
 3. Growth under national lockdown
- Using Arima spline models, we estimated for each country:
 - The 10 most likely dates for which each period of growth began (i.e. the knot dates)
 - Relative likelihood of each pair
 - The growth factor r (and standard deviation SD_r) governing each period of growth



Key findings from parameter estimation

- Weighted median lag periods across all countries:
 - 14.0 (Q1-Q3: 10.7-18.0) days from the first restriction to the first knot date
 - 20.2 (Q1-Q3: 16.0-24.0) days from lockdown to the second knot date
- Weighted median growth factors across all countries:
 - 1.222 (Q1-Q3: 1.156-1.296) during initial uncontrolled growth
 - 1.048 (Q1-Q3: 1.015-1.060) during growth under initial restrictions
 - 0.957 (Q1-Q3: 0.944-0.971) during growth under lockdown

03 Counterfactual simulations

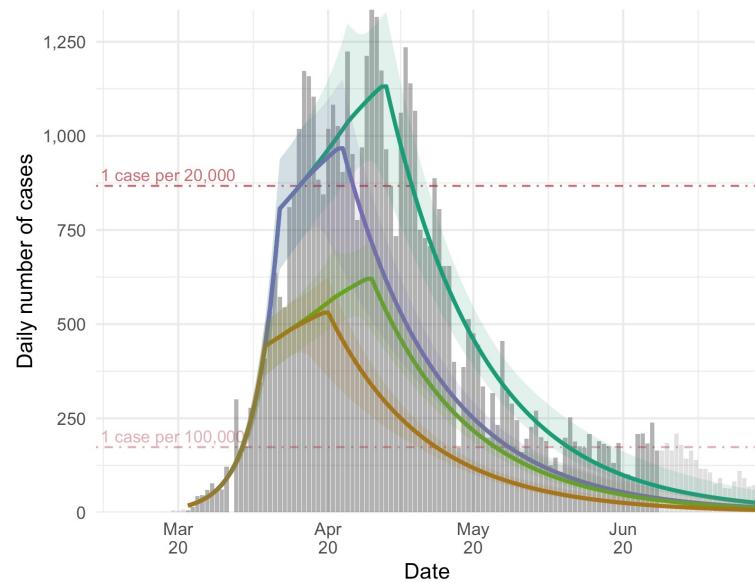
- We used stochastic simulations to estimate the growth of COVID-19 cases within each country during the first wave under 4 scenarios:
 1. Natural growth
 2. Earliest possible lockdown
 3. Earlier intervention sequence (3 days)
 4. Earlier first restriction (3 days) and earliest possible lockdown
- Under each scenario, we estimated:
 - The total number of first wave cases
 - The required length of full lockdown (*i.e. the number of days to reach the same daily case threshold that was observed when lockdown was actually eased*)

Some simulation details

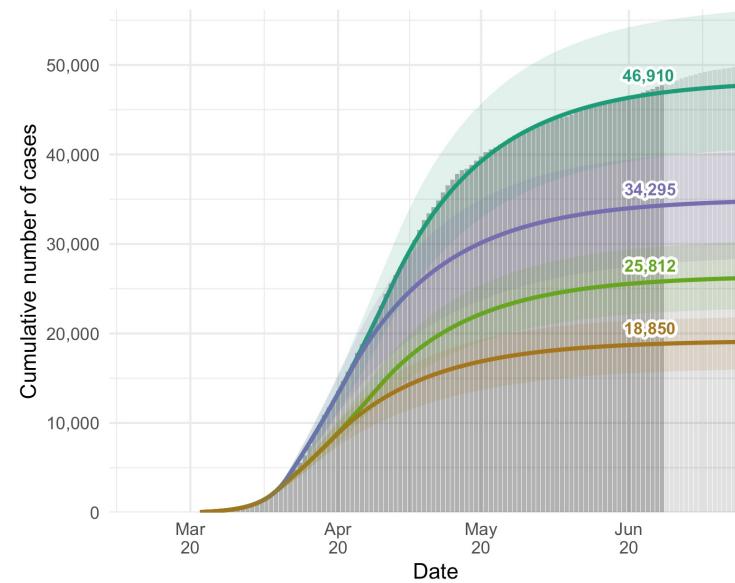
- All scenarios were simulated 100,000 times
 - Median and 95% simulation interval calculated
- A random growth factor was drawn from a lognormal distribution for each day in each simulation, according to the period of growth in which it fell
- All knot date pairs identified as most likely were used, with their frequency corresponding to their relative likelihood
- ***Note:*** *not all counterfactuals could be computed for all countries*
 - The first knot date could not occur (counterfactually) before the simulation period began

Netherlands

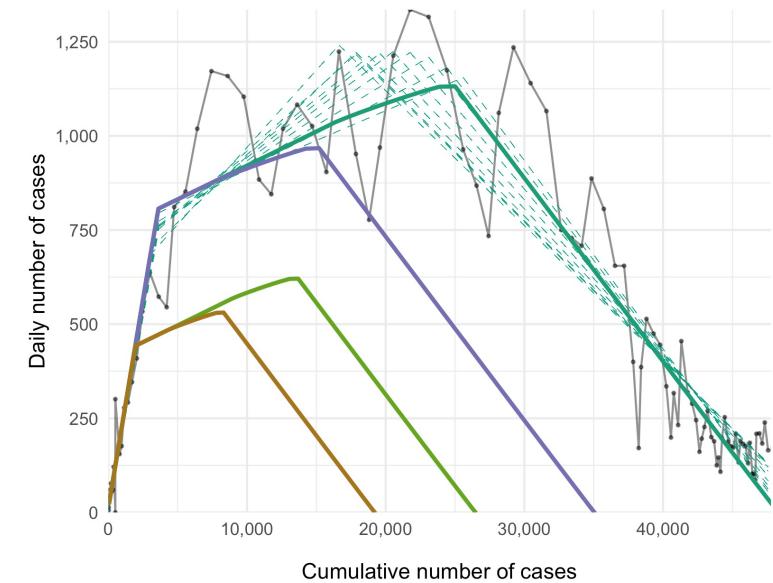
Incident cases of COVID-19



Cumulative cases of COVID-19



Cumulative vs incident cases of COVID-19

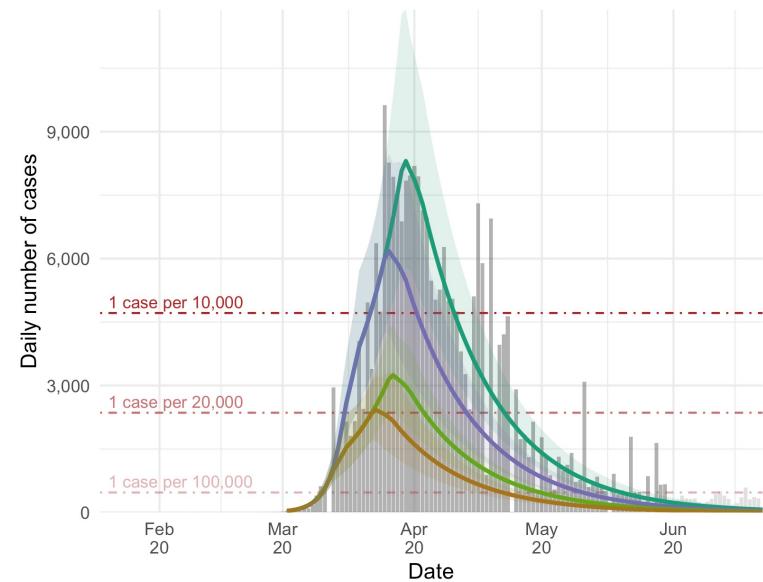


Simulation: █ Natural history █ Earliest possible lockdown █ Earlier intervention sequence █ Earlier first restriction & sequence

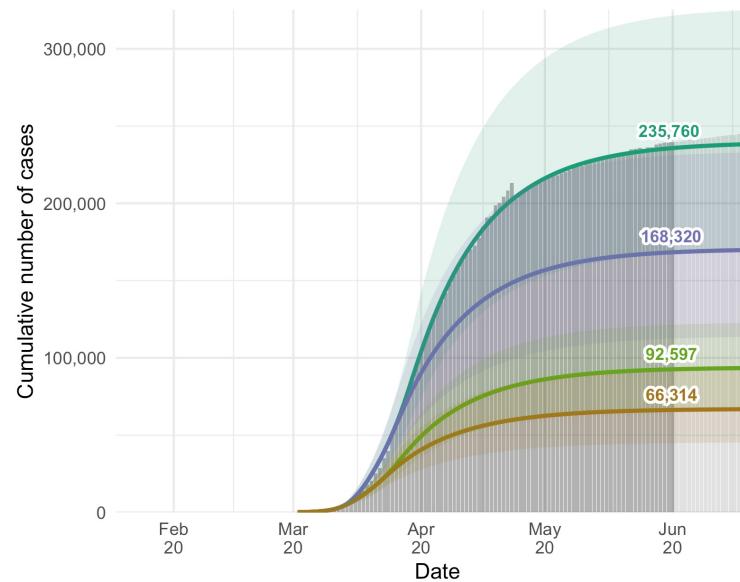
Data from <https://github.com/CSSEGISandData/COVID-19>

Spain

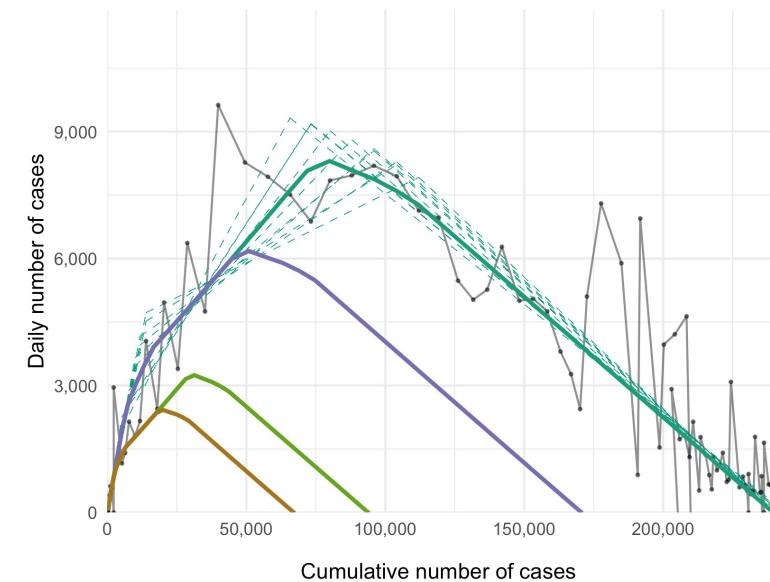
Incident cases of COVID-19



Cumulative cases of COVID-19

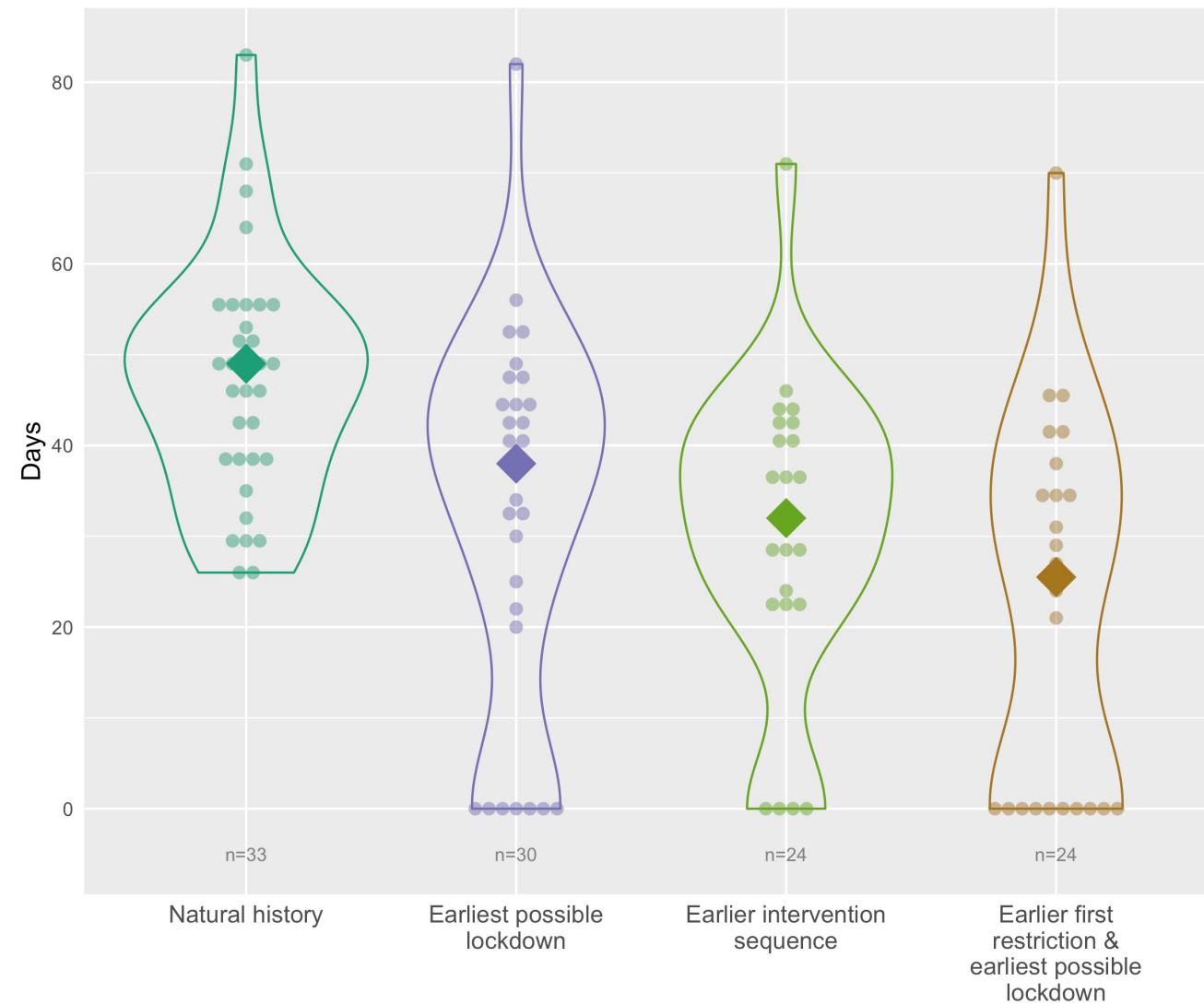


Cumulative vs incident cases of COVID-19



Data from <https://github.com/CSSEGISandData/COVID-19>

Length of full lockdown required in all simulations



Simulation	<u>Total cases in first wave</u>		<u>Length of full lockdown</u>	
	<i>Median percentage change* (Q1, Q3)</i>	<i>N</i>	<i>Median percentage change* (Q1, Q3)</i>	<i>N</i>
Earliest possible lockdown	-28.61 (-51.18, -7.22)	33	-18.63 (-57.73, 0.00)	30
Earlier intervention sequence	-44.98 (-54.41, -34.08)	25	-28.84 (-43.04, -19.48)	24
Earlier first restriction and earliest possible lockdown	-60.15 (-71.87, -49.10)	25	-36.92 (-100.00, -19.35)	24

*compared to natural history

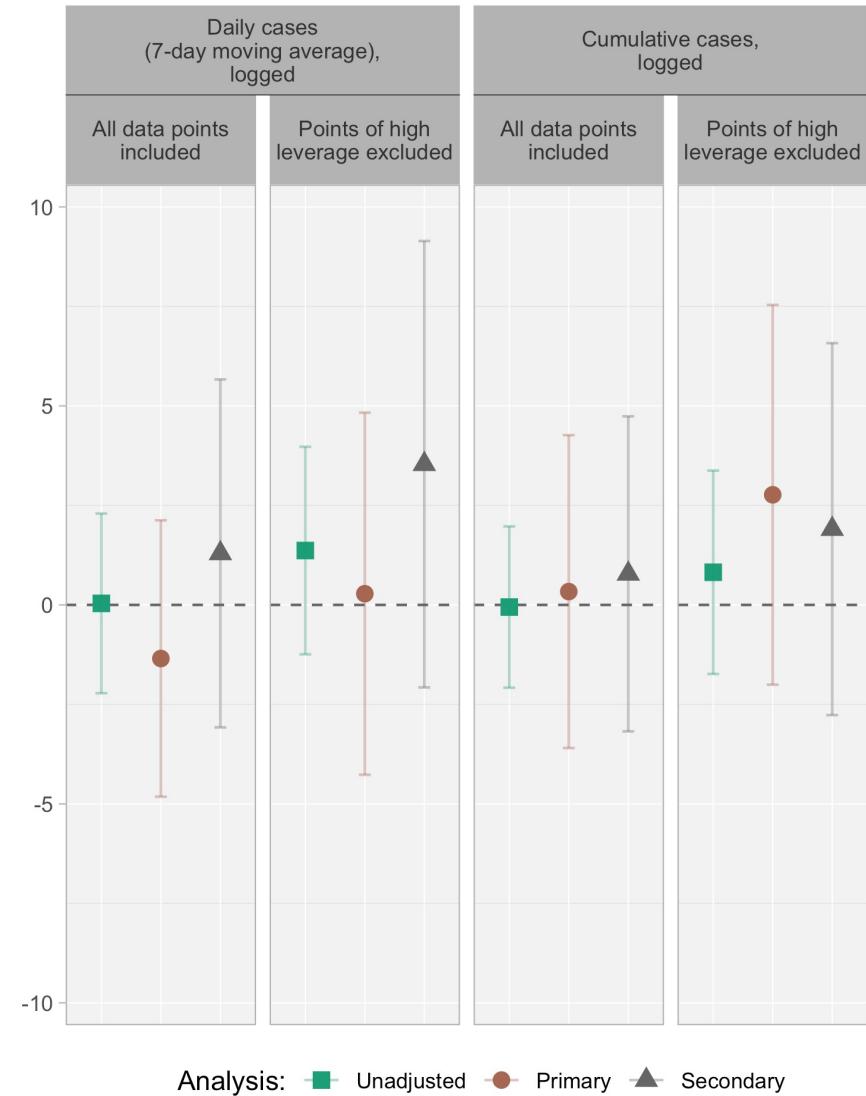
Other important findings

- Significant between-county heterogeneity wrt key parameters
 - Outbreak scales
 - Growth factors
 - Lag periods

Comparison with regression analysis

- Exposure: number of cases on the date of lockdown (logged)
 1. Daily (7-day moving average)
 2. Cumulative
- Outcome: length of full lockdown
- Covariates:
 - Area size, GDP, total population (primary analysis)
 - Area size, GDP, population (0-14, 15-64, 65+), urban population, total healthcare expenditure (secondary analysis)

- No clear or substantial relationship between lockdown timing and length of full lockdown
- Primary effect estimates ranged from -1.35 (95% CI: -4.82 to 2.13) to 0.33 (95% CI: -3.60 to 4.27)
 - *1 fewer day of lockdown for every 210% increase in daily cases to 1 more day of lockdown for every 2070% increase in total cases on the date of lockdown*



Strengths

- Simulations accounted for between-country heterogeneity by evaluating the counterfactuals within each country separately
- No assumptions about transmission rates or reproduction numbers were required
 - Parameters of interest could be directly estimated from observed data
- Accommodated variation and uncertainty wrt lag periods and growth factors
- Accommodated autocorrelation and weekly effects

Limitations

- Modelling provides only an incomplete summary of the first wave
 - Confirmed cases < true infections
- Analyses did not account for variation in lockdown stringency between countries or increasing stringency of restrictions within different periods of growth
- Other assumptions required:
 - Testing levels remained relatively constant across the first wave
 - Changes in the growth factor were the direct result of NPIs
 - Interventions produced a sharp change in the growth factor

Conclusions & implications

- It is important to act both strongly and swiftly to minimize the spread of COVID-19 when case numbers are increasing exponentially
- There exists substantial between-country heterogeneity that must be adequately taken into account when conducting multi-country studies
- A counterfactual framework is useful for conceptualizing and evaluating the effects of various non-pharmaceutical interventions

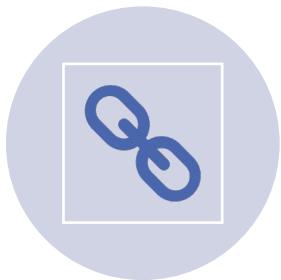
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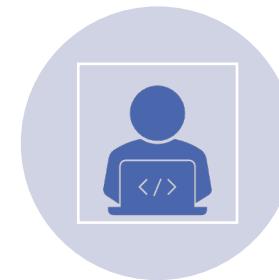
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Interactive dashboard



Link



Many thanks to Dr Camila Rangel-Smith and Dr James Robinson (both of The Alan Turing Institute) for creating the dashboard