

Imperial College London

MRC Centre for Global Infectious Disease Analysis

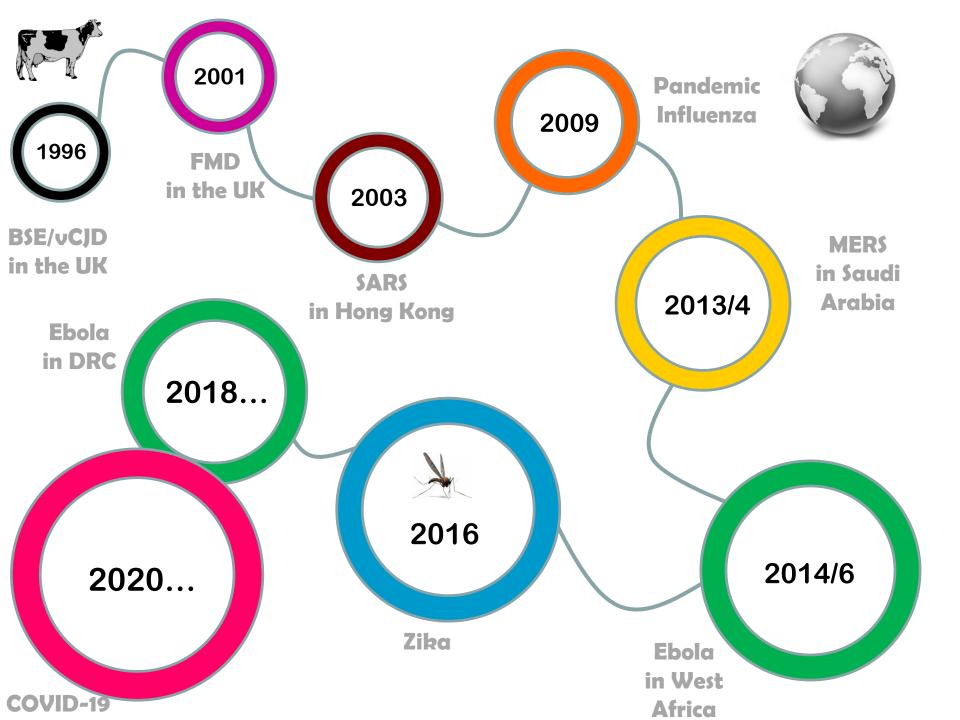
# Real-time analysis of COVID-19 – epidemiology, statistics and modelling in action

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## What do you most want to know?

- What are the symptoms?
- How many cases are there?
- How many cases might there be?
- How serious is the disease?
- If someone is exposed to infection, how long till they know if they are free of infection?
- How might we control the disease?

Characterise cases

Estimate cases in source from exportations

Estimate epidemic growth

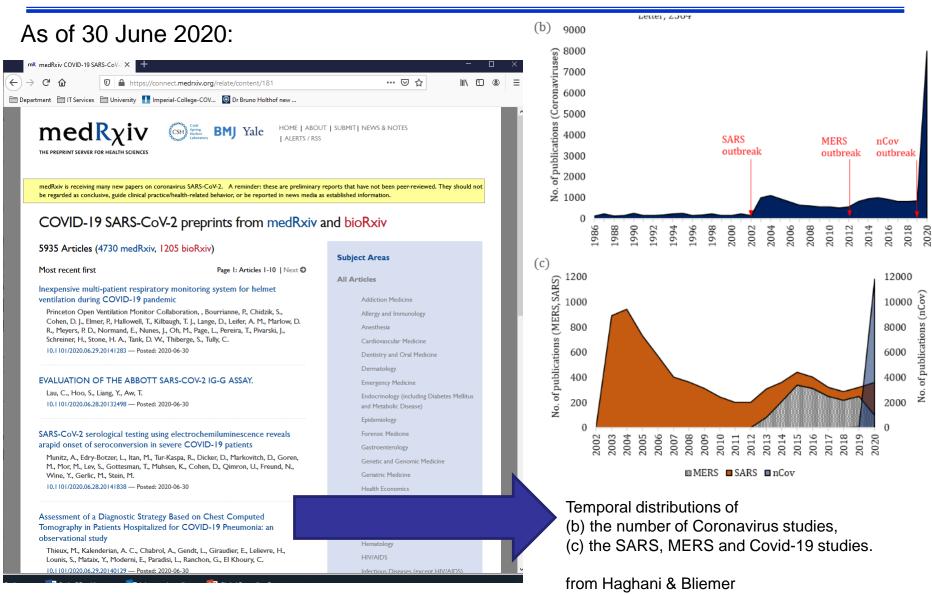
Estimate the CFR

Estimate the incubation period distribution

Consider options, including isolation, quarantine, vaccination, as data allow.

Relevant paper: Cori A., Donnelly CA, Dorigatti I, *et al.* Key data for outbreak evaluation: building on the Ebola experience. *Phil. Trans. R. Soc.* B372, 20160371, 2017. <u>http://dx.doi.org/10.1098/rstb.2016.0371</u>

## **Real-time analyses**



https://www.biorxiv.org/content/10.1101/2020.05.31.126813v1.full

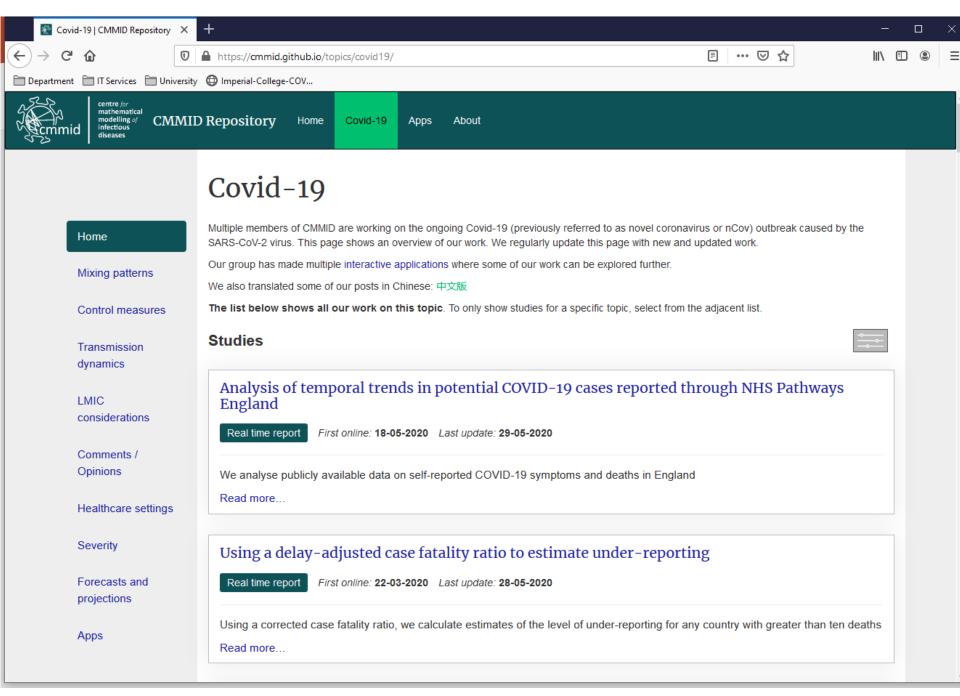
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For any enquiries related to	Excess non-COVID-19 deaths in	Adapting hospital capacity to	Reduction in mobi	lity and
the MRC Centre please	England and Wales between	meet changing demands during	COVID-19 transmiss	
contact:	29th February and 5th June 2020	the COVID-19 pandemic		
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Sabine L. van Elsland	Report 25: 29 May 2020	Report 24: 29 May 2020	Report 23: 21 N	iay 2020
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Response to COVID-19 in South

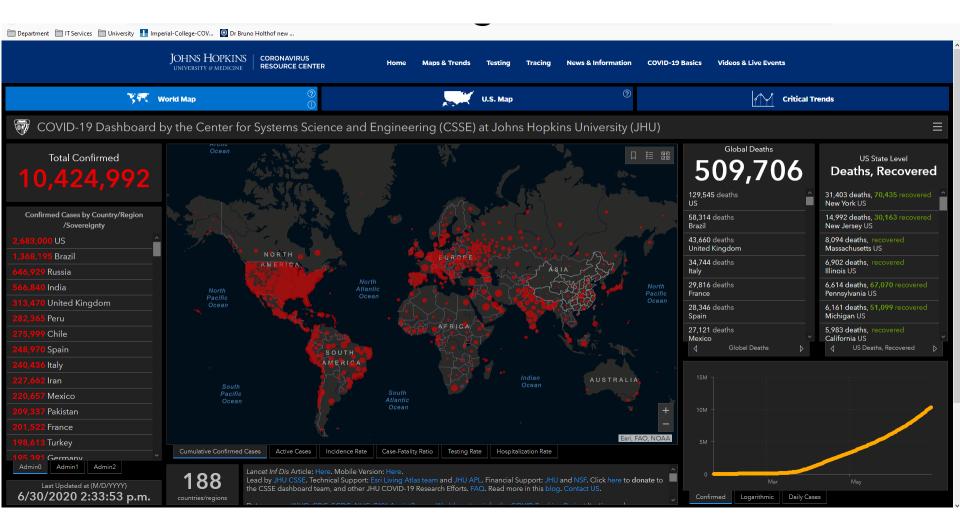
Anonymised and aggregated

State-level tracking of COVID-19

>



https://cmmid.github.io/topics/covid19/



https://coronavirus.jhu.edu/map.html

## Magnitude of the epidemic

 $Total number of cases = \frac{number of cases detected outside China}{probability any one case will be detected outside China}$ 

where the probability any one case will be detected overseas (p) is given

 $p=daily\ probability\ of\ international\ travel\ imes\ mean\ time\ to\ detection\ of\ a\ case$ 

The daily probability of travel is calculated by:

daily probability of international travel daily outbound international travellers from Wuhan

catchment population of Wuhan airport

Finally, the mean time to detection can be approximated by:

mean time to detection

= incubation period + mean time from onset of symptoms to detection

### 17 January 2020 Report 1

	Baseline	Smaller catchment	Shorter detection window
Exported number of confirmed cases	3	3	3
Daily international passengers travelling out of Wuhan International Airport	3,301	3,301	3,301
Effective catchment population of Wuhan International Airport	19 million	11 million	19 million
Detection window (days)	10 days	10 days	8 days
Estimated total number of cases (95% CI)	1,723 (427 – 4,471)	996 (246 – 2,586)	2,155 (535 – 5,590)

### https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/covid-19-reports/



Health

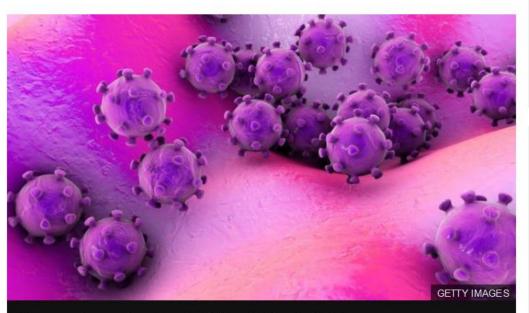
# New virus in China 'will have infected hundreds'

By James Gallagher Health and science correspondent

① 18 January 2020



Coronavirus pandemic



There were six coronaviruses known to infect people before the latest discovery

The number of people already infected by the mystery virus emerging in China is far greater than official figures suggest, scientists have told the BBC.

There have been **more than 60** confirmed cases of the new coronavirus, but UK experts estimate a figure nearer **1,700**.

Two people are known to have died from the respiratory illness, which appeared in Wuhan city in December.

"I am substantially more concerned than I was a week ago," disease outbreak scientist Prof Neil Ferguson, said.

The work was conducted by the MRC Centre for Global Infectious Disease Analysis at Imperial College London, which advises bodies including the UK government and the World Health Organization (WHO).

#### https://www.bbc.co.uk/news/health-51148303

	17 January 2020 Report 1			22 January 2020 Report 2			
	Baseline	Smaller catchment	Shorter detection window	Baseline	Smaller catchment	Shorter detection window	
Exported number of confirmed cases	3	3	3	7	7	7	
Daily international passengers travelling out of Wuhan International Airport	3,301	3,301	3,301	3,301	3,301	3,301	
Effective catchment population of Wuhan International Airport	19 million	11 million	19 million	19 million	11 million	19 million	
Detection window (days)	10 days	10 days	8 days	10 days	10 days	8 days	
Estimated total number of cases (95% CI)	1,723 (427 – 4,471)	996 (246 – 2,586)	2,155 (535 – 5,590)	4,000 (1,700 – 7,800)	2,300 (1,000 – 4,500)	5,000 (2,200 – 9,700)	

### https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/covid-19-reports/

## How have case numbers grown?

Table 1: Best-case, central and worst-case estimates of 2019-nCoV human-to-human  $R_0$  compatible with either 4000 (top half of table) or 1000 (bottom half of table) total cases by 18/01/2020. Values of  $R_0$  >1 represent self-sustaining human-to-human and are highlighted in red. Baseline estimates highlighted in bold.

					20000 -	
Number of cases		Best-case R <sub>0</sub>	Central	Worst-case		
caused by	number of cases		(median) R <sub>0</sub>	$R_0$		
zoonotic	by 18/01/2020				පී 15000-	
exposure	-					
40	4000	2.1	2.6	3.5	inciden	
80	4000	1.8	2.2	2.7	.⊑ ⊛ 10000 -	
120	4000	1.7	2.0	2.4		
160	4000	1.6	1.8	2.2	Cumulativ	
200	4000	1.5	1.7	2.0	5000	
40	1000	1.4	1.9	2.7	0 0000	
80	1000	1.2	1.5	2.0		
120	1000	1.1	1.3	1.7	0	
160	1000	1.0	1.2	1.5		ec 16-Dec 30-Dec 13-Jan 27-Jan
200	1000	0.9	1.1	1.3	02-DE	ec ro-Dec 30-Dec 13-Jan 27-Jan

Assuming an 8.4 day average generation time

Natsuko Imai, Anne Cori, Ilaria Dorigatti, Marc Baguelin, Christl A. Donnelly, Steven Riley, Neil M. Ferguson WHO Collaborating Centre for Infectious Disease Modelling, MRC Centre for Global Infectious Disease Analysis, J-IDEA, Imperial College London

Report 3, 25 January 2020 https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/covid-19-reports/

## **Case fatality ratio**

- Proportion of cases who eventually die from the disease;
- Often estimated by using aggregated numbers of cases and deaths at a single time point:
  - E.g.: case fatality ratios compiled daily by WHO during the SARS outbreak:

estimate of the case fatality ratio:

number of deaths / total number of cases.

• Simple estimates of these reports can be misleading if, at the time of the analysis, the outcome (death or recovery) is unknown for an important proportion of patients.

### **Proportion of observations censored in the SARS outbreak**

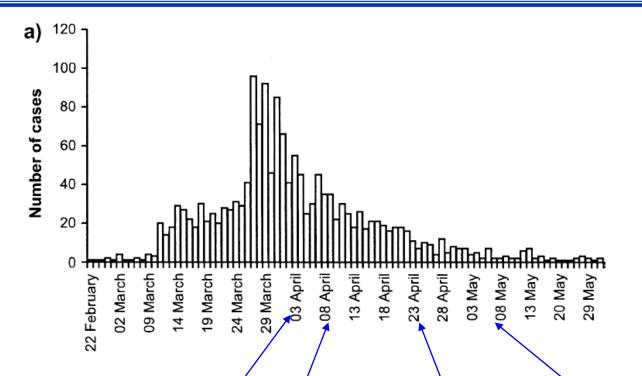


TABLE 1. Summary of the number of cases and the degree of censoring at different time points for the epidemic of severe acute respiratory syndrome in Hong Kong, 2003

				Date			
	April 2	April 9	April 16	April 23	April 30	May 7	May 14
No. of cases	925	1,201	1,367	1,489	1,547	1,582	1,607
% of observations censored	85.9	81.2	71.5	51.6	35.1	25.2	17.3

We do not know the outcome (death or recovery) yet.

[Ghani et al. AJE, 2005]

## **Simple methods**

• Method 1:

$$CFR = \frac{D}{C}$$

D = Number of deathsC = Total number of cases

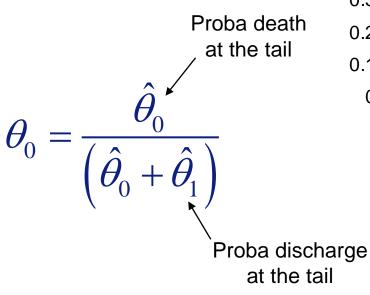
• Method 2:

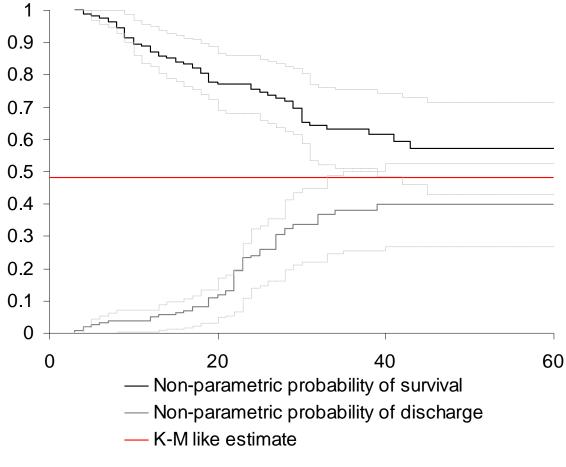
$$CFR = \frac{D}{(D+R)}$$

- D = Number of deaths
- R = Number recovered

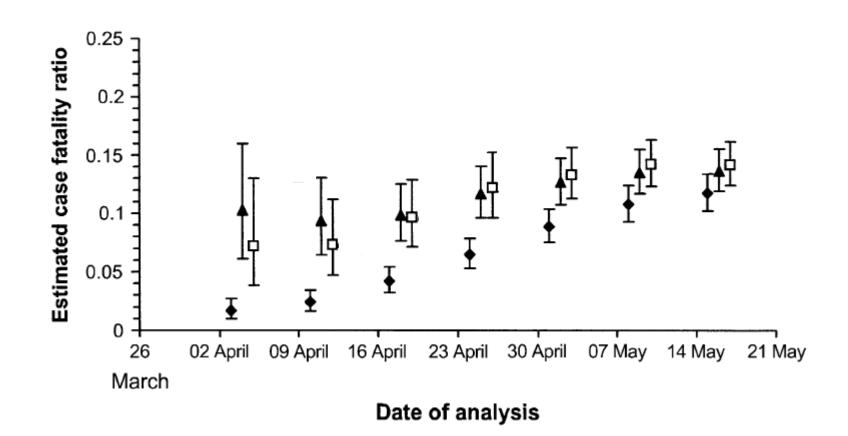
### **Adapted Kaplan-Meier method**

To extrapolate incomplete survivor functions, assume that death/discharge rate at the tail occurs at the same rate as previously:





### **Comparison of the estimates**



- Observed case fatality ratio
- ▲ Simple estimate 2
- deaths/(deaths+recoveries)

- Simple estimate 1 (deaths/cases)
- KM-like method

#### [Ghani et al. AJE, 2005]

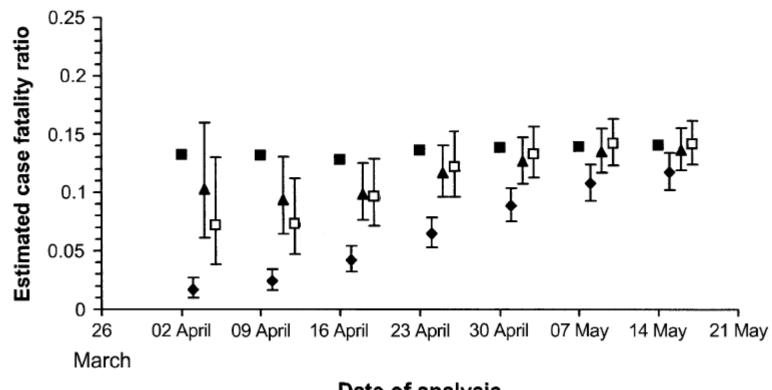
### **Misinterpretation of the trend**



The death rate from severe acute respiratory syndrome has more than doubled, to 5.6 percent, since the epidemic was first detected in mid-March, causing deep concern among health officials.

Although the overall death rate, according to World Health Organization statistics, has hovered around 4 percent in the last three weeks, it has varied widely among the 26 countries, plus Hong Kong, with cases of the disease, known as SARS.

### **Comparison of the estimates**

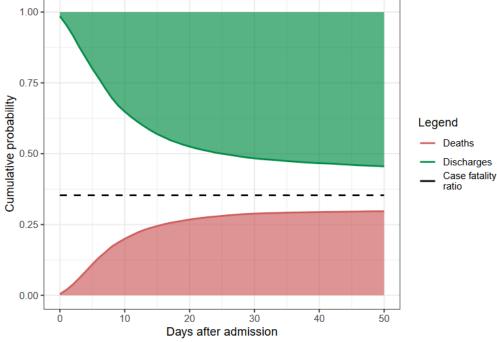


### Date of analysis

- Observed case fatality ratio
- ▲ Simple estimate 2
- deaths/(deaths+recoveries)
- Simple estimate 1 (deaths/cases)
- KM-like method

#### [Ghani et al. AJE, 2005]



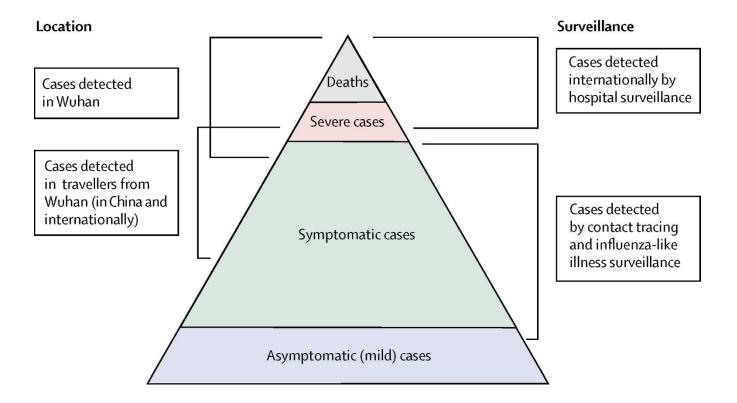


Probabilities of death (red curve) and recovery (green curve).

The black line indicates the case fatality ratio (CFR).

The point estimate of the CFR is 35% (95% CI: 34-36%).

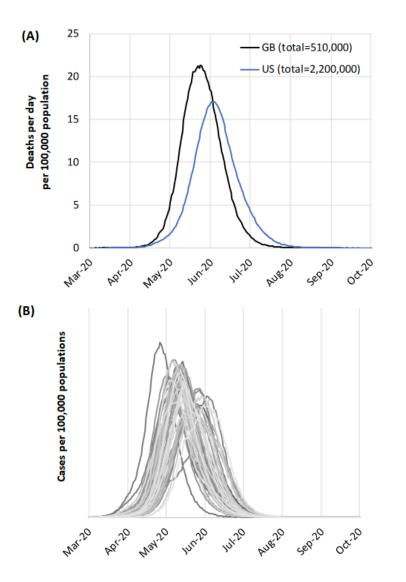
### **CFR vs IFR**



Verity et al. The Lancet Infectious Diseases 2020 20669-677DOI: (10.1016/S1473-3099(20)30243-7) Copyright © 2020 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license <u>Terms and Conditions</u>

## **IFR estimates**

Authors	Estimate	When available	Where
Verity <i>et al</i> . Imperial College London	1% (0.5-4)	Posted 10 Feb	https://www.imperial.ac.uk/media/i mperial-college/medicine/mrc- gida/2020-02-10-COVID19-Report- 4.pdf
	0.66% (0.39-1.33)	Posted 13 Mar	https://www.medrxiv.org/content/10 .1101/2020.03.09.20033357v1
		Pub. 30 Mar	https://www.thelancet.com/pdfs/jou rnals/laninf/PIIS1473- 3099(20)30243-7.pdf
Chow <i>et al</i> . National Institutes of Health	0.17% (0.05-0.9) first week 0.8% (0.2-4) as of 15 April	Posted 5 May	https://www.medrxiv.org/content/10 .1101/2020.04.29.20083485v1
Grewelle & De Leo Stanford	1.04% (0.77-1.38)	Posted 18 May	https://www.medrxiv.org/content/10 .1101/2020.05.11.20098780v1
Rosenfeld <i>et al.</i> Institute for Disease Modelling	0.9%	"Results as of May 25"	https://covid.idmod.org/data/Modeli ng_countermeasures_for_balance d_reopening_King_County_Washi ngton.pdf
Wood <i>et al.</i> University of Bath	0·43% (0·23–0·65) China 0·55% (0·30–0·82) UK 0·20% (0·11–0·30) India	Pub. 28 May	https://www.thelancet.com/journals /laninf/article/PIIS1473- 3099(20)30437-0/fulltext



Individual-based simulations of transmission was used to explore scenarios of unmitigated epidemics, mitigated epidemics and suppressed epidemics in the UK and elsewhere.

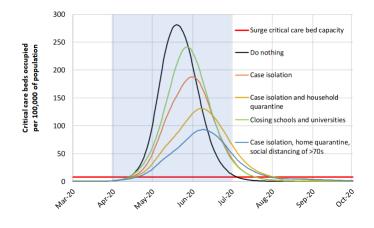
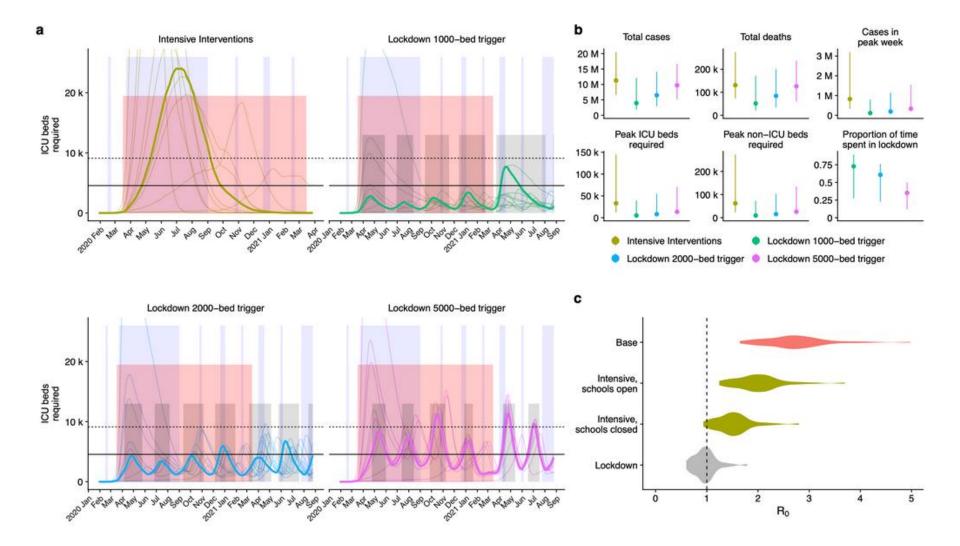


Figure 1: Unmitigated epidemic scenarios for GB and the US. (A) Projected deaths per day per 100,000 population in GB and US. (B) Case epidemic trajectories across the US by state.

https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-03-16-COVID19-Report-9.pdf Published 16 Mar 2020



*Figure:* Projected impact of intensive control measures with reactive lockdowns. (a) Dynamics of the epidemic under different triggers for introduction and lifting of lockdowns (median timing of lockdowns shown as grey shaded areas). Bolded lines show ICU bed occupancy in the median run under each scenario. Horizontal guides show the estimated number of ICU beds in the UK as of January 2020 (solid line) and with a hypothetical doubling of capacity (dashed line). Blue shaded regions show school closures, while the pink shaded region shows a background period of intensive interventions. (b) Summary of epidemic runs. (c) Estimated distribution of R0 under three different interventions: intensive social distancing with schools open and closed, and lockdown.

#### https://cmmid.github.io/topics/covid19/uk-scenario-modelling.html Published 1 Apr 2020

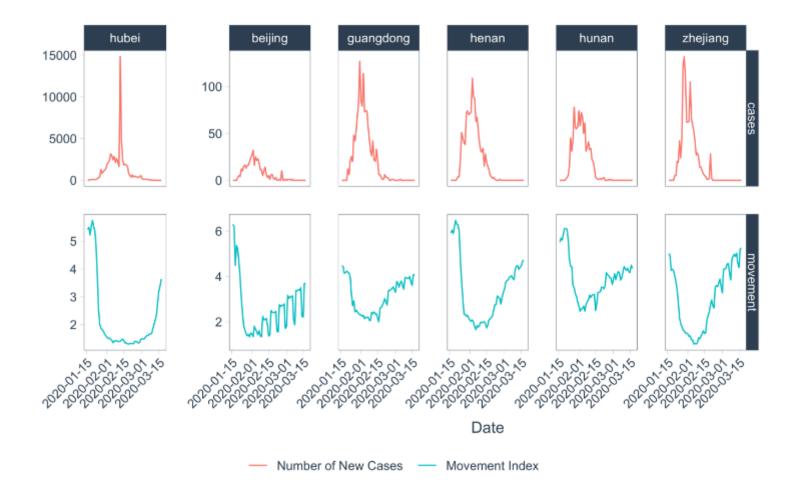
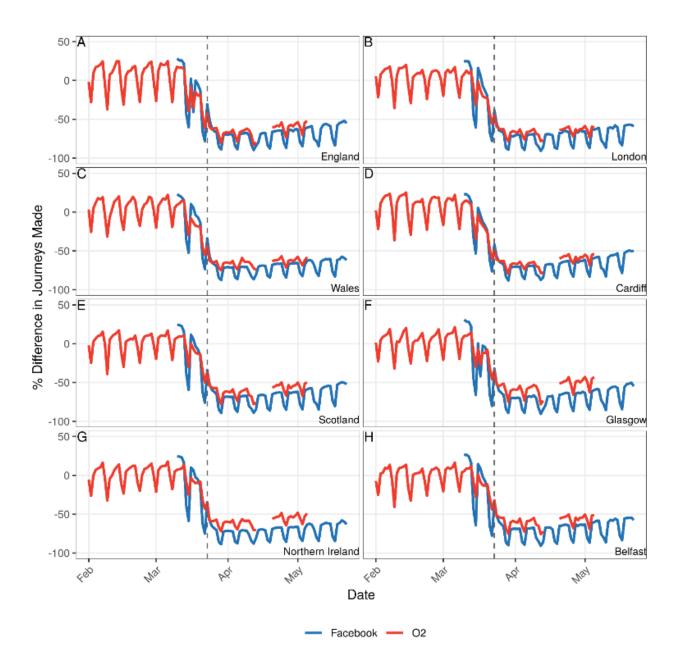


Figure 1. Plots of daily new confirmed cases (red line, top row) and daily movement index (Exante Data Inc, NY, blue line, bottom row) for Hubei, Beijing, Guangdong, Henan, Hunan, and Zhejiang. The cyclic movement patterns seen in Beijing and toward the end of February in Zhejiang are the result of decreased travel on weekends.



https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-05-29-COVID19-Report-24.pdf Published 29 May We would like to thank O2 and Facebook Data for Good for making their data available to us.

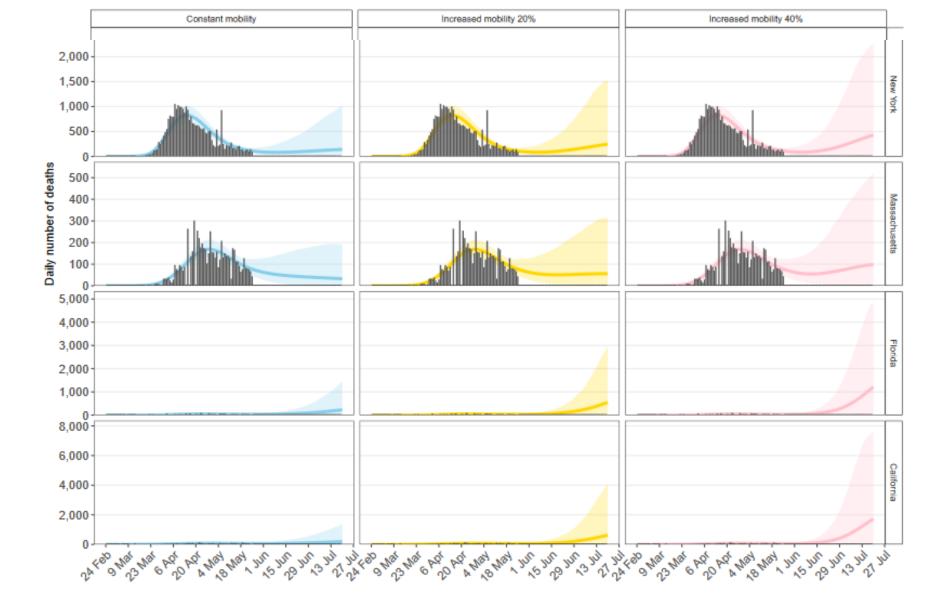


Figure 8: State-level scenario estimates of deaths for Washington, New York, Massachusetts, Florida and California. The

https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-05-28-COVID19-Report-23-version2.pdf Published 28 May 2020 Google's COVID-19 Community Mobility Report

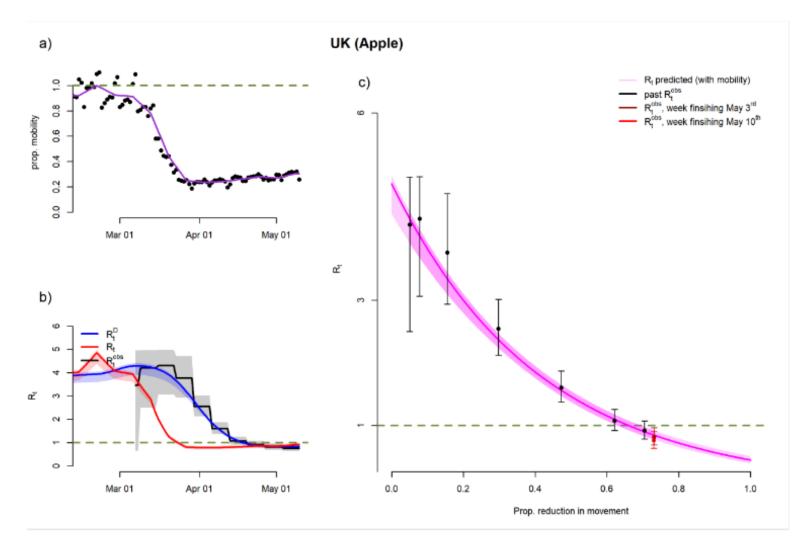
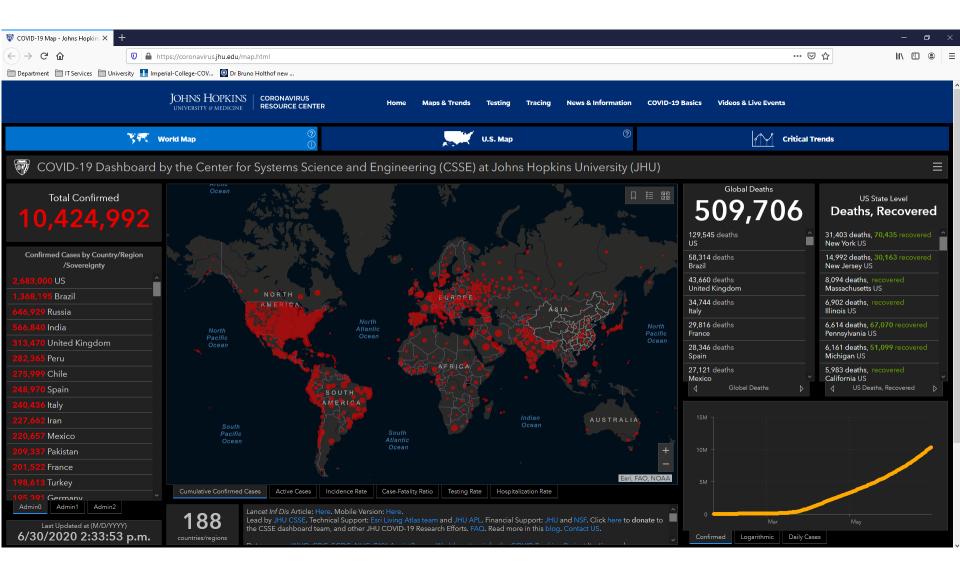


Figure 1: Relationship between mobility and transmission. a) Smoothed Apple mobility (purple line) and daily mobility (aggregated and scaled over the data streams). b) Estimated daily reproduction number for new

https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-06-08-COVID19-Report-26.pdf Published 8 June 2020 Report 26: Reduction in mobility and COVID-19 transmission

### Looking forward... more data



### Looking forward... more code

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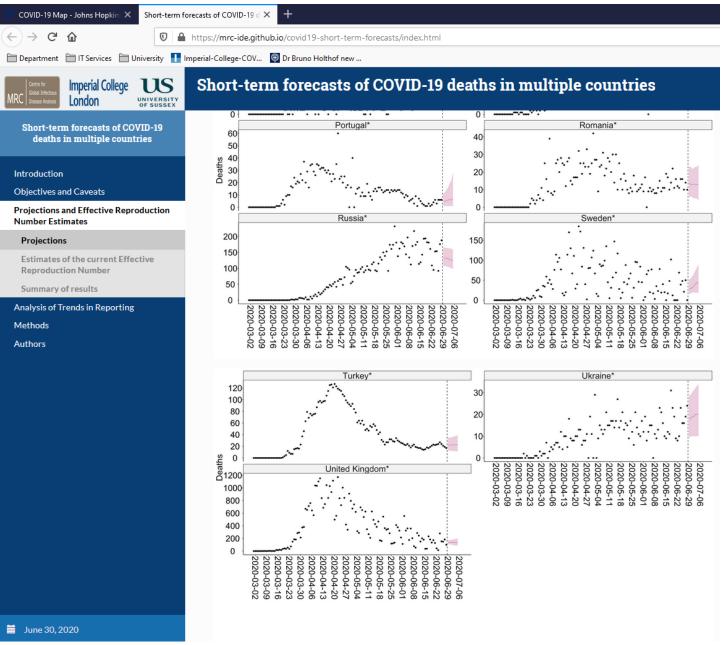
#### https://github.com/mrc-ide/COVID19\_CFR\_submission

### Looking forward... more open reviews

W Evidence of initial success for C X +		
← → C û https://wellcomeopenresearch.org/articles/5-81		
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Evidence of initial success for China exiting COVID-19		
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Abstract	_	All Comments (0) Add a comment
Background: The COVID-19 epidemic was declared a Global Pandemic by WHO on 11 March 2020. By over 440,000 cases and almost 20,000 deaths had been reported worldwide. In response to the fast-or which began in the Chinese city of Wuhan, Hubei, China imposed strict social distancing in Wuhan on followed closely by similar measures in other provinces. These interventions have impacted economis China, and the ability of the Chinese economy to resume without restarting the epidemic was not clear Methods: Using daily reported cases from mainland China and Hong Kong SAR, we estimated transme and compared it to daily within-city movement, as a proxy for economic activity. Begutts: Initially, within-city movement, and transmission were very strongly correlated in the five main the five main strongly constrained to the strong strongly correlated in the five main strongly correlated in the five main strongly correlated in the five main and compared it to daily within-city movement, as a proxy for economic activity.	prowing epidemic, 23 January 2020 ic productivity in ar. hissibility over time	Sign up for content alerts Email SIGN UP

Results: Initially, within-city movement and transmission were very strongly correlated in the five mainland provinces most affected by the epidemic and Beijing. However, that correlation decreased rapidly after the initial sharp fall in transmissibility. In general, towards the end of the study period, the correlation was no longer apparent, despite substantial increases in within-city movement. A similar analysis for Hong Kong shows that intermediate levels of local activity were maintained while avoiding a large outbreak. At the very end of the study period, when China began to experience the re-introduction of a small number of cases from Europe and the United States, there is an apparent up-tick in transmission.

## Looking forward... more updates



https://mrc-ide.github.io/covid19-short-term-forecasts/index.html

### Looking forward... more public engagement



### Abstract

The new coronavirus has already claimed the lives of hundreds of thousands of people. Different countries are taking different measures in the fight against this new threat. Many people are staying at home. But is it worth it? That's what we wanted to find out.

this new social distancing of the whole population, not just the elderly, would have the most beneficial effect. The combination of this measure with others would be even better.

We created a computer model that helps us assess the effect of different measures against COVID-19. We checked for the

### Introduction

Tired of staying at home and hearing about the new *coronavirus*? Perhaps you wonder: is it even worth it? What is the purpose behind it? In just a few months, the new virus has spread around most of the world and claimed the lives of hundreds of thousands of people. With so many lives

We set out to compare these two strategies. Which one will result in fewer deaths? Which one will relieve the healthcare systems?

impact on people's health and the state of the healthcare

systems in two countries: the UK and the US. We found that

#### https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-04-28-SJK-Report-9.pdf



Celebrating Florence Nightingale's 200th Anniversary STATISTICIAN • NURSE • REFORMER

*"When I am no longer even a memory, just a name, I hope my voice may perpetuate the great work of my life. God bless my dear old comrades of Balaclava and bring them safe to shore."* 

Florence Nightingale (1820~1910)

### A man for our time

### Sir Austin Bradford Hill (1897 – 1991)

*"All scientific work is incomplete—whether it be observational or experimental."* 

All scientific work is liable to be upset or modified by advancing knowledge.

That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time."

