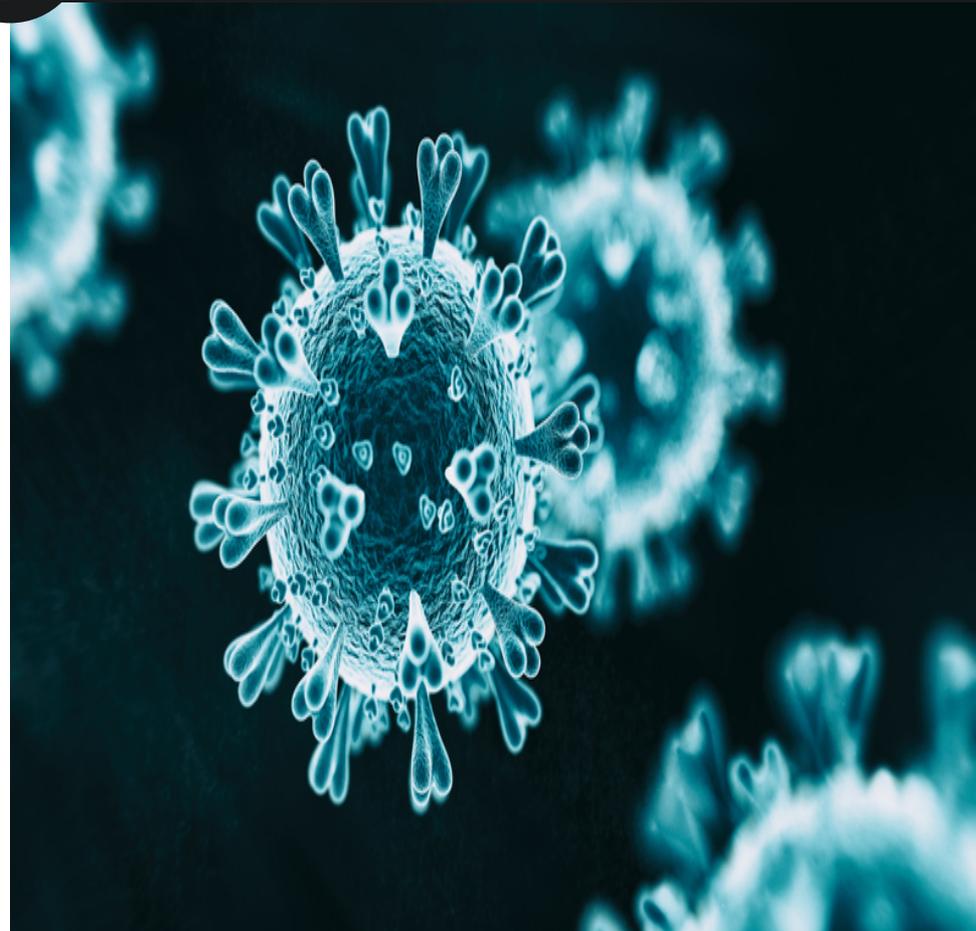




COVID-19: APRIL 30 UPDATE

April 30, 2020



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OUTLINE

- Overall Observations
- C19 Case and Death Count Update, by Country
- Latest IHME (Washington University) Projections for United States
- New Data on True Deaths v. Reported Deaths from the FT and NYT.
- Antibodies Explained: Serum Testing and Treatment
- Early-Life Cross-Reactivity and the Spanish Flu (Preview)

OVERALL OBSERVATIONS

- Mixed news on U.S. case & death trends:
 - U.S. daily new cases declining—amid rising test counts and falling positive %.
 - U.S. daily deaths erratic but still high; Wash U. projected total is rising.
- In confusion, states start opening up. IMO, boost to economy will disappoint and accelerating infections will be evident by end of May. Reckoning for markets: June.
- What exactly is the difference between a C19 plan and a C19 strategy?
 - A plan is just a single policy or tactic. E.g., “mitigation.”
 - A strategy tries to bring about an ultimate goal or outcome. E.g., “containment.”
- Antivirals: Mixed results thus far for remdesivir and hydrochloroquine as “wonder drugs.”
- Did millions of Americans get C19 last year? Post by Victor Davis Hanson reflects widespread impression. C19’s genetic phylogeny, however, makes this highly improbable.

CONTAINMENT & HERD IMMUNITY

CONTAINMENT is a strategy.

- Its component tactics are, in this order: (a) mitigation serious/long enough to get new cases to very low levels; (b) comprehensive testing and tracing; (c) identification and isolation of all cases plus border controls (“containment”).
- Its purpose is to ease mitigation (“suppress and lift”) & get back to normal.

HERD IMMUNITY is a strategy.

- Its component tactics are, in this order: (a) isolation of the most vulnerable; (b) mitigation light enough to maximize infections without overwhelming health system.
- Its purpose is to ease mitigation (after reaching threshold immunity) & get back to normal.

Where **CONTAINMENT** is official national strategy:

- Taiwan
- Hong Kong
- Singapore
- South Korea
- New Zealand
- Australia
- Germany (?)
- China (?)

Where **HERD IMMUNITY** is official national strategy:

- Sweden (?)
- Netherlands (?)
- UK* (originally announced but now abandoned)

CONTAINMENT & HERD IMMUNITY

When **CONTAINMENT** makes more sense...

- When case fatality rate is higher
- When R_0 (infectiousness) is lower
- When immune % of population is lower
- When economic cost of strategy is lower
- When demands on healthcare are higher
- When near-term prospect of “cure” (vaccine or treatment) is higher
- When civic trust/compliance is higher

When **HERD IMMUNITY** makes more sense...

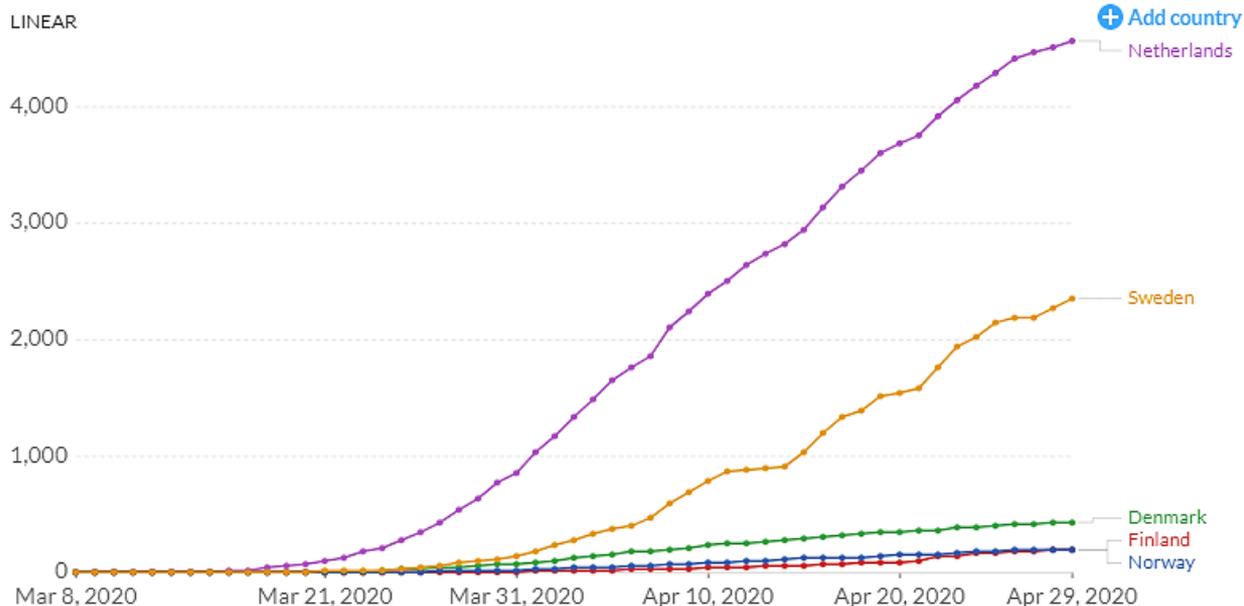
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- When civic trust/compliance is lower

NORDIC “HERD IMMUNITY” OUTLIERS

Total confirmed COVID-19 deaths

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.

Our World
in Data



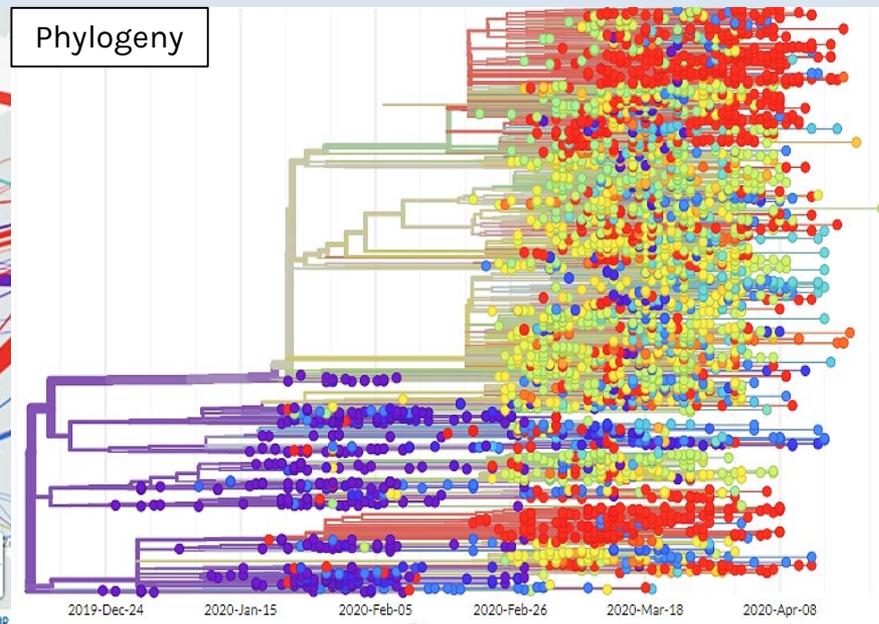
Source: European CDC – Situation Update Worldwide – Last updated 29th April, 11:30 (London time)

CC BY

▶ Dec 31, 2019 Apr 29, 2020

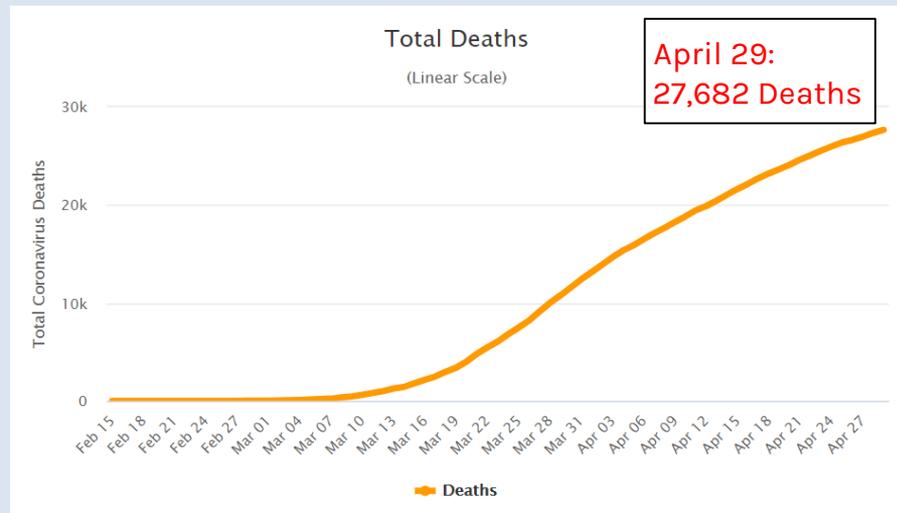
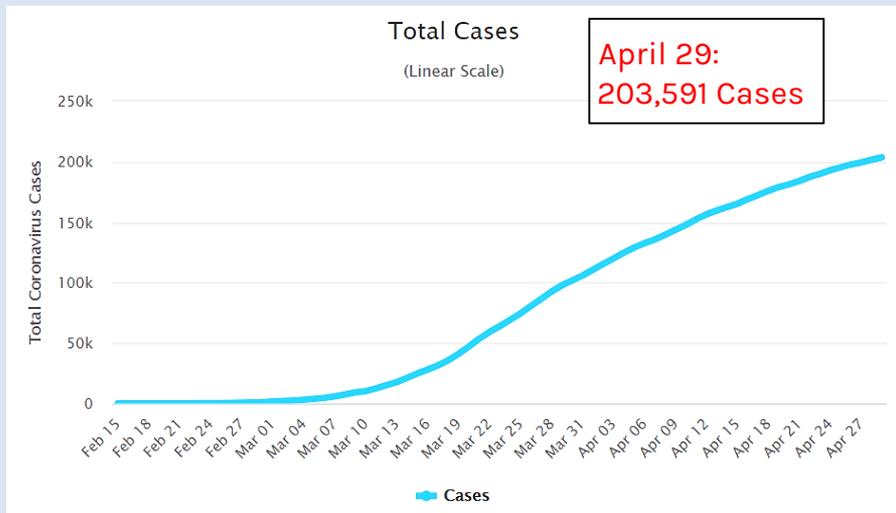
WHEN DID NOVEL VIRUS FIRST APPEAR?

Genomic Epidemiology of Novel Coronavirus - Global subsampling, Genomes Sampled Between December 2019 and April 2020



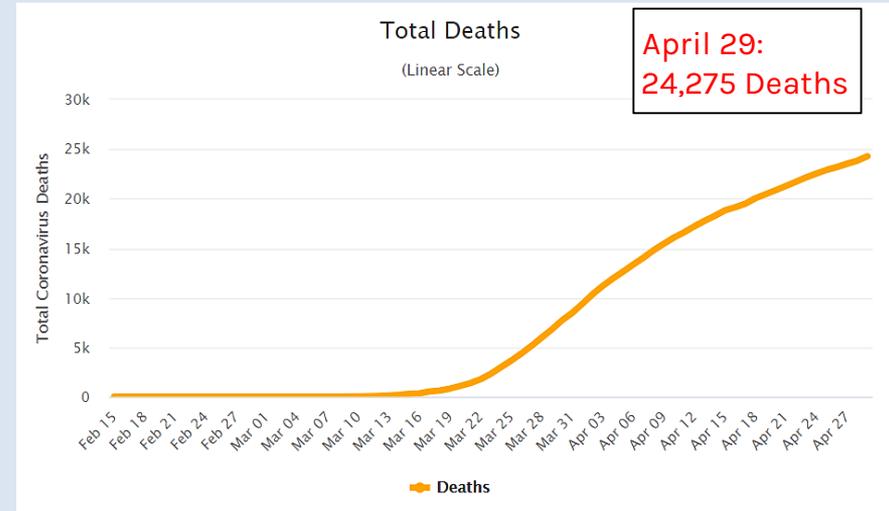
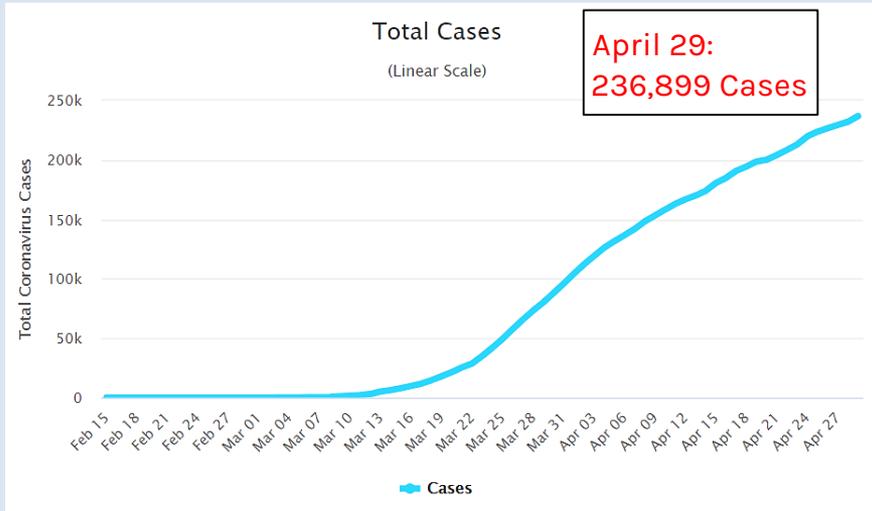
THE SITUATION IN... ITALY

COVID-19 Cases and Deaths in Italy Updated April 30, 2020



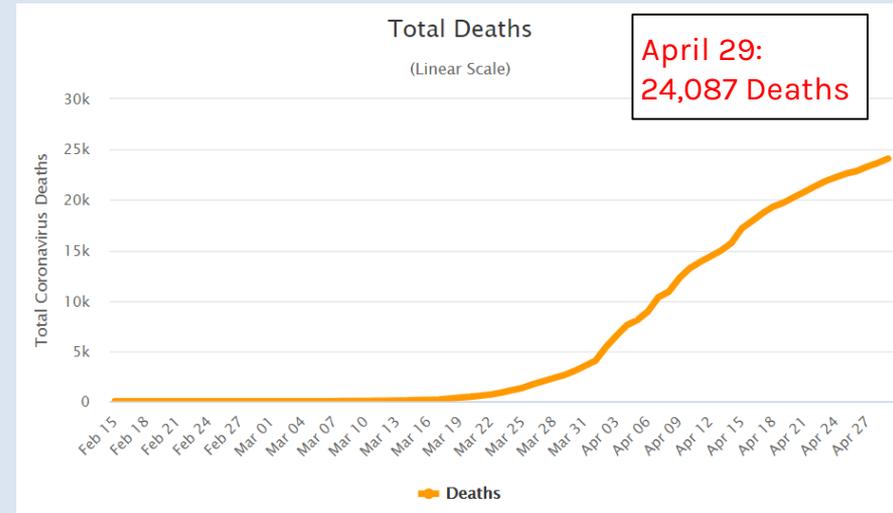
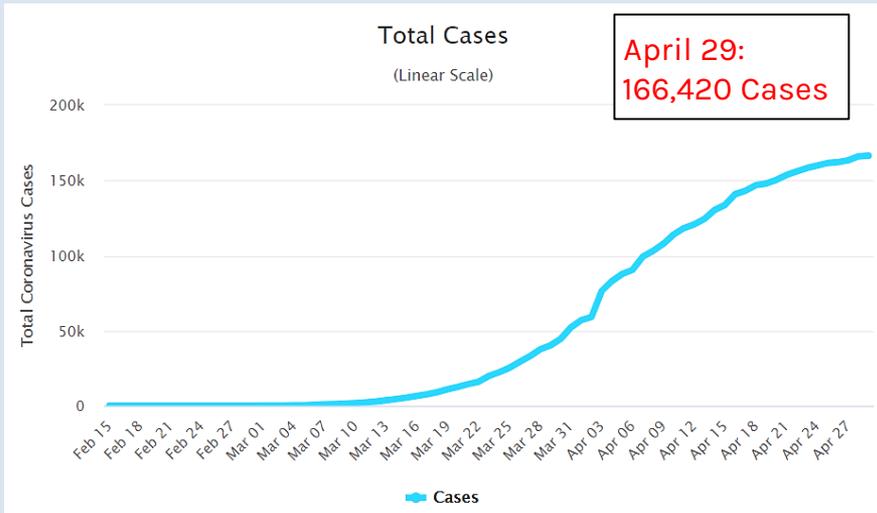
THE SITUATION IN... SPAIN

COVID-19 Cases and Deaths in Spain Updated April 30, 2020



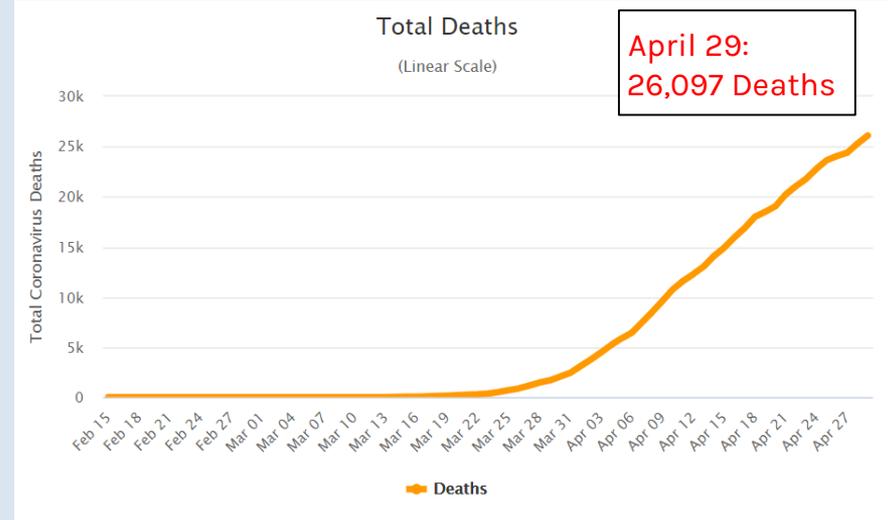
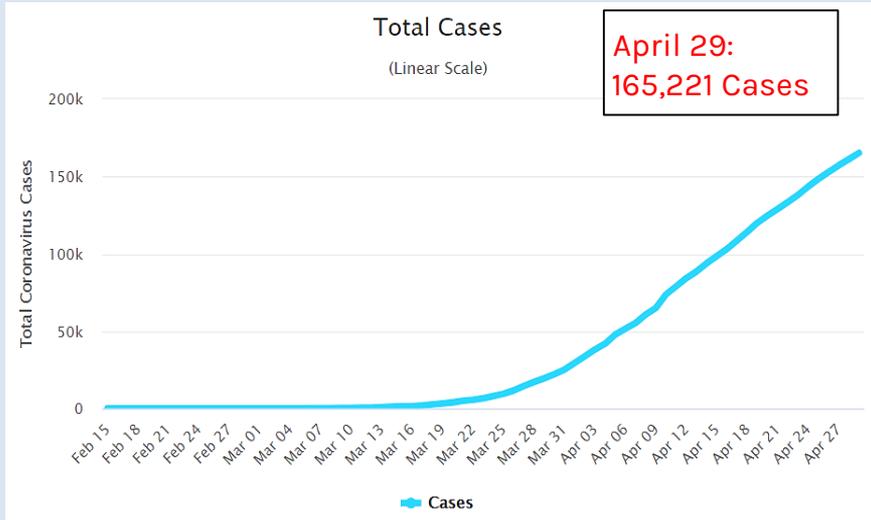
THE SITUATION IN... FRANCE

COVID-19 Cases and Deaths in France Updated April 30, 2020



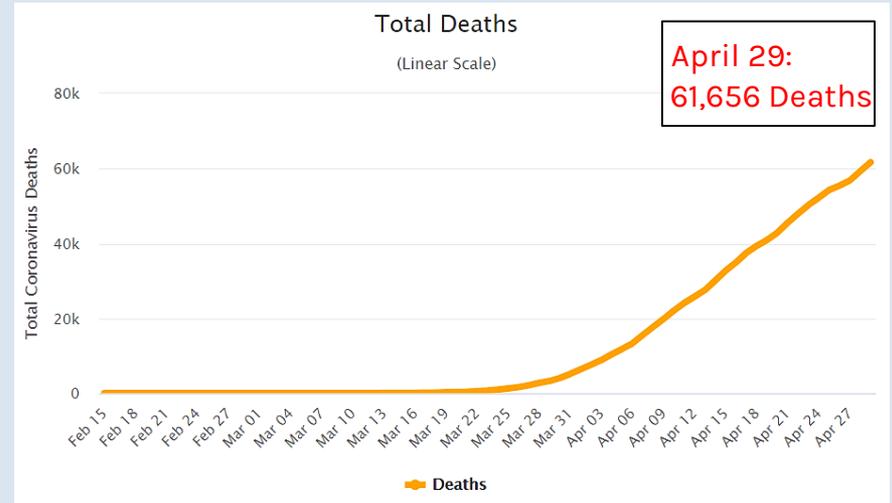
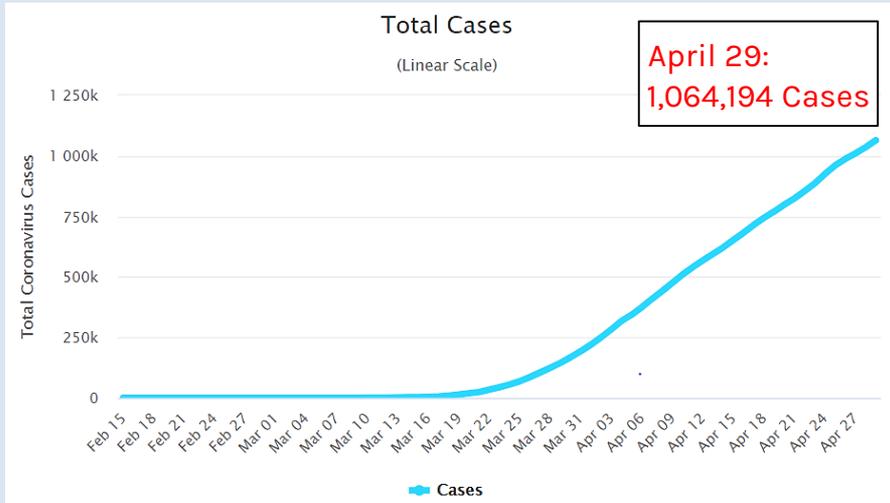
THE SITUATION IN... UK

COVID-19 Cases and Deaths in UK Updated April 30, 2020



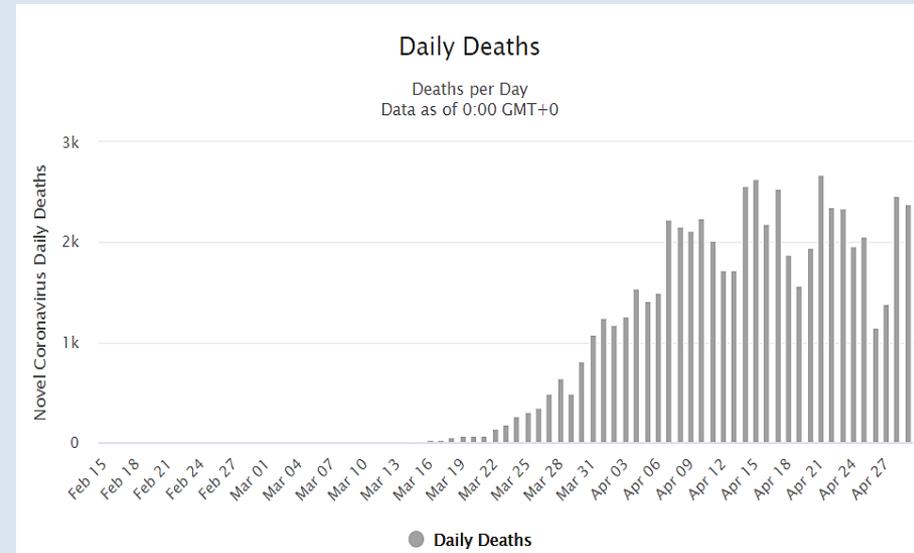
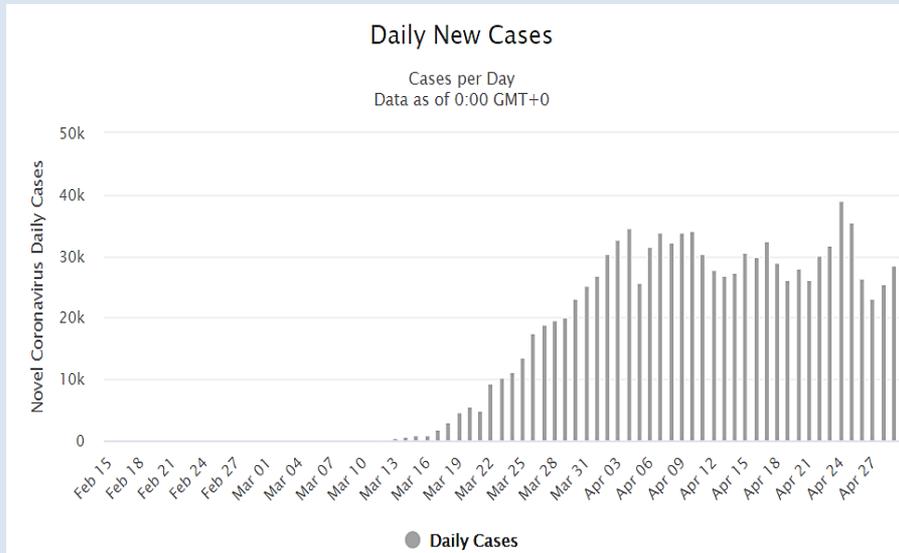
THE SITUATION IN... USA

COVID-19 Cases and Deaths in USA Updated April 30, 2020



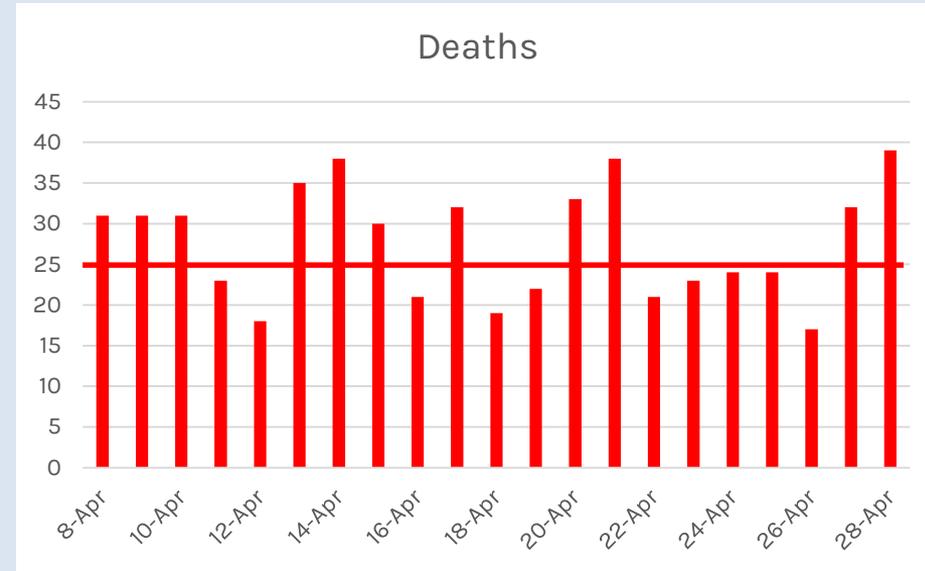
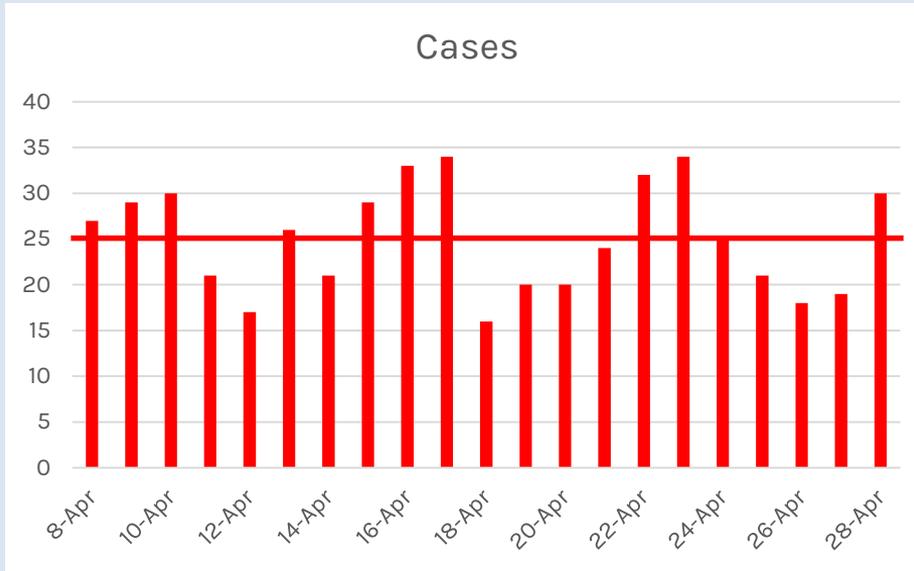
THE SITUATION IN... USA

COVID-19 Daily Cases and Deaths in USA Updated April 30, 2020



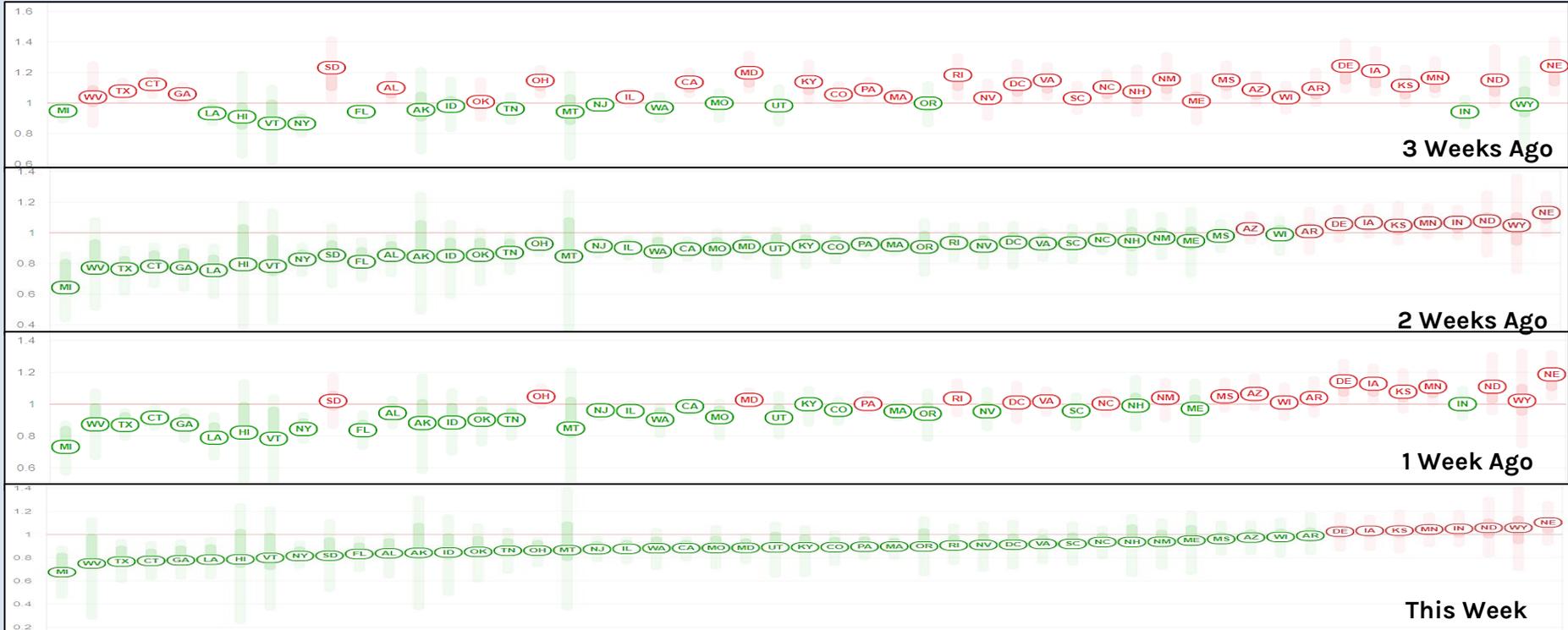
STATE DIFFUSION INDEX IN CASES & DEATHS

Number of US States Whose Case and Death Count Was Larger or Equal Than Previous Day.



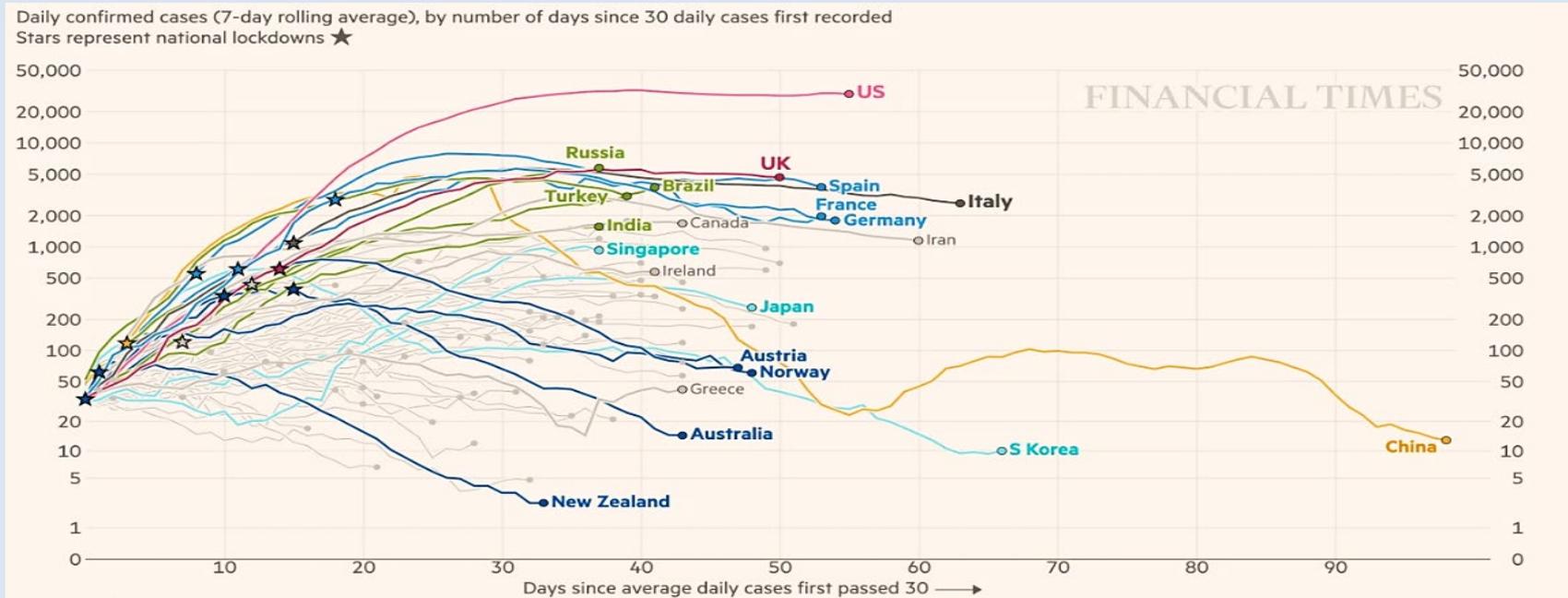
DROPPING R_0 IN MOST STATES

States' Estimated R_0 , March 29-April 29
Green States Below 1, Red States Above 1



U.S. STAYS ABOVE THE REST

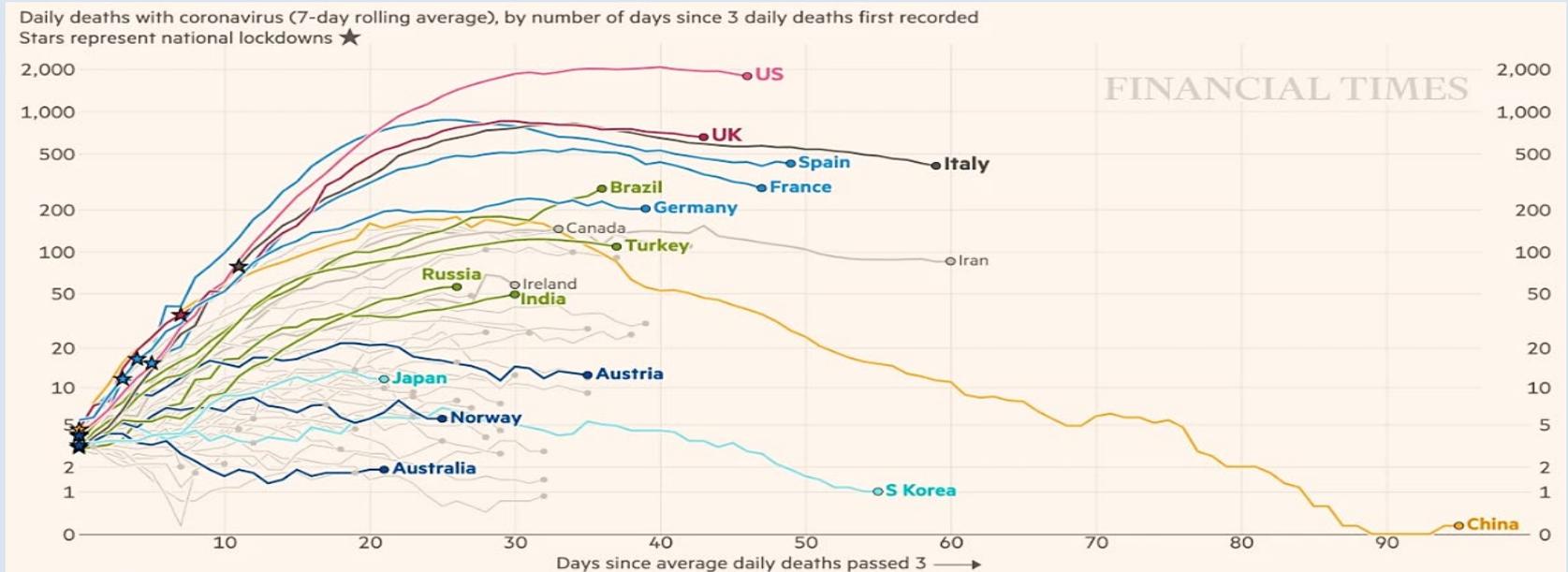
Daily COVID-19 Cases, Seven Day Rolling Average. Updated April 30, 2020.



FINANCIAL TIMES

U.S. STAYS ABOVE THE REST

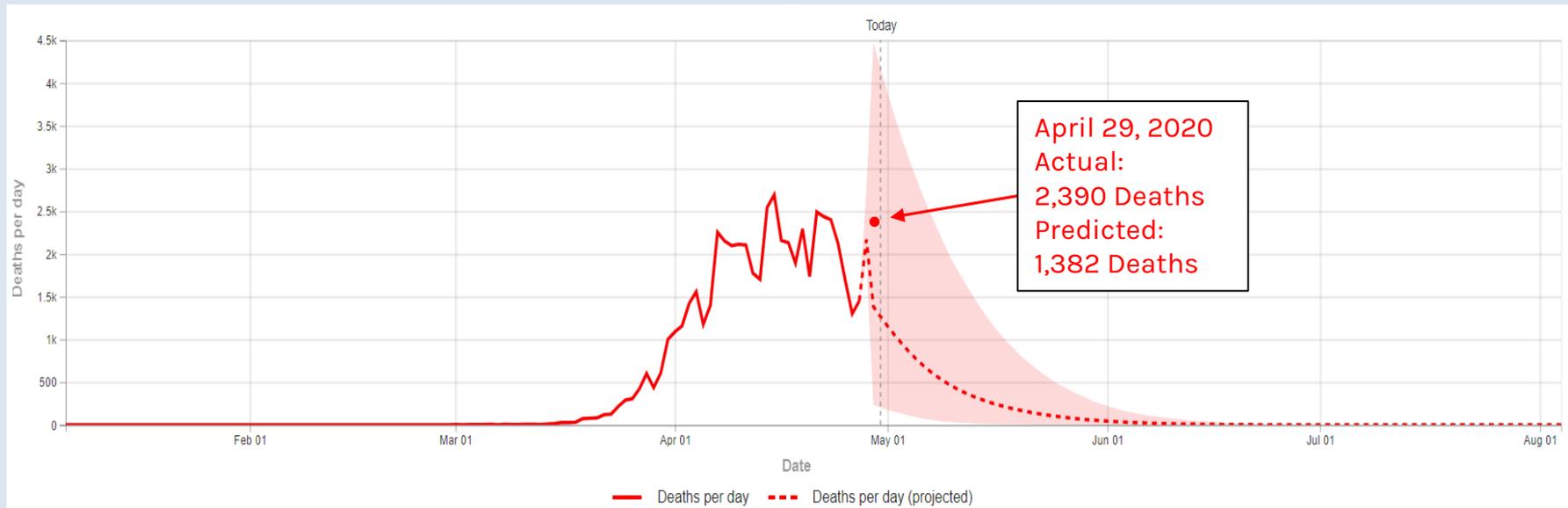
Daily COVID-19 Deaths, Seven Day Rolling Average. Updated April 30, 2020.



FINANCIAL TIMES

THE PEAK IS OVER?

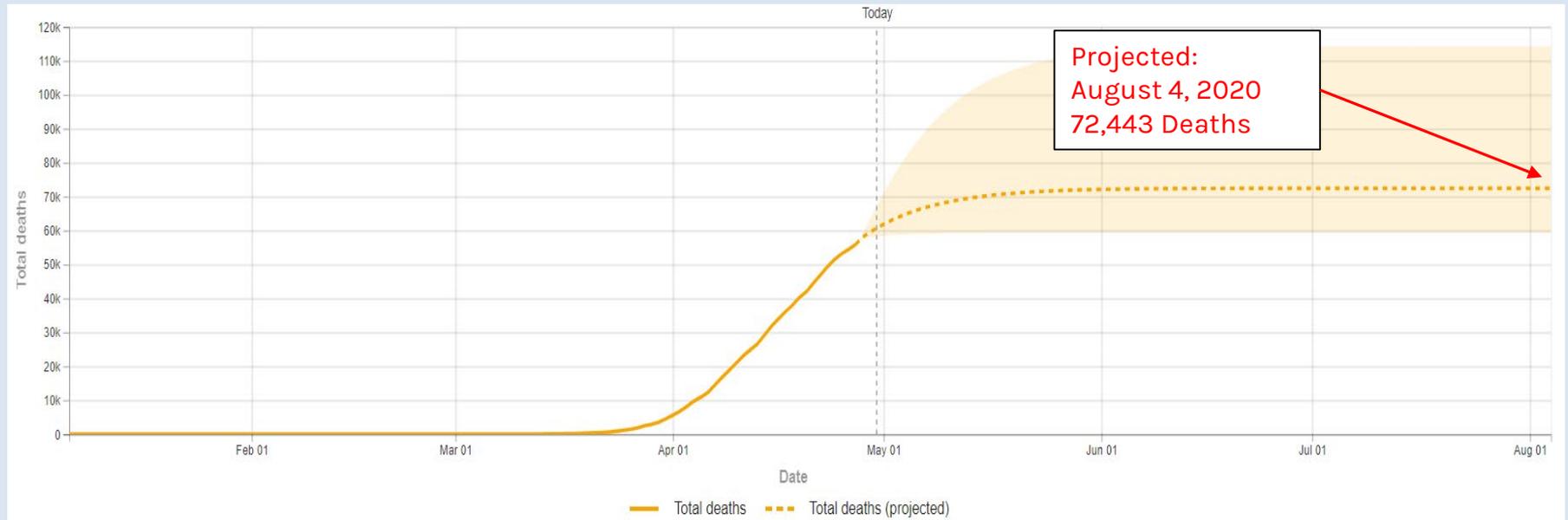
Projection of Daily COVID-19 Deaths, Last Updated April 30, 2020.



“Current social distancing assumed until infections minimized and containment implemented.”

THE PEAK IS OVER?

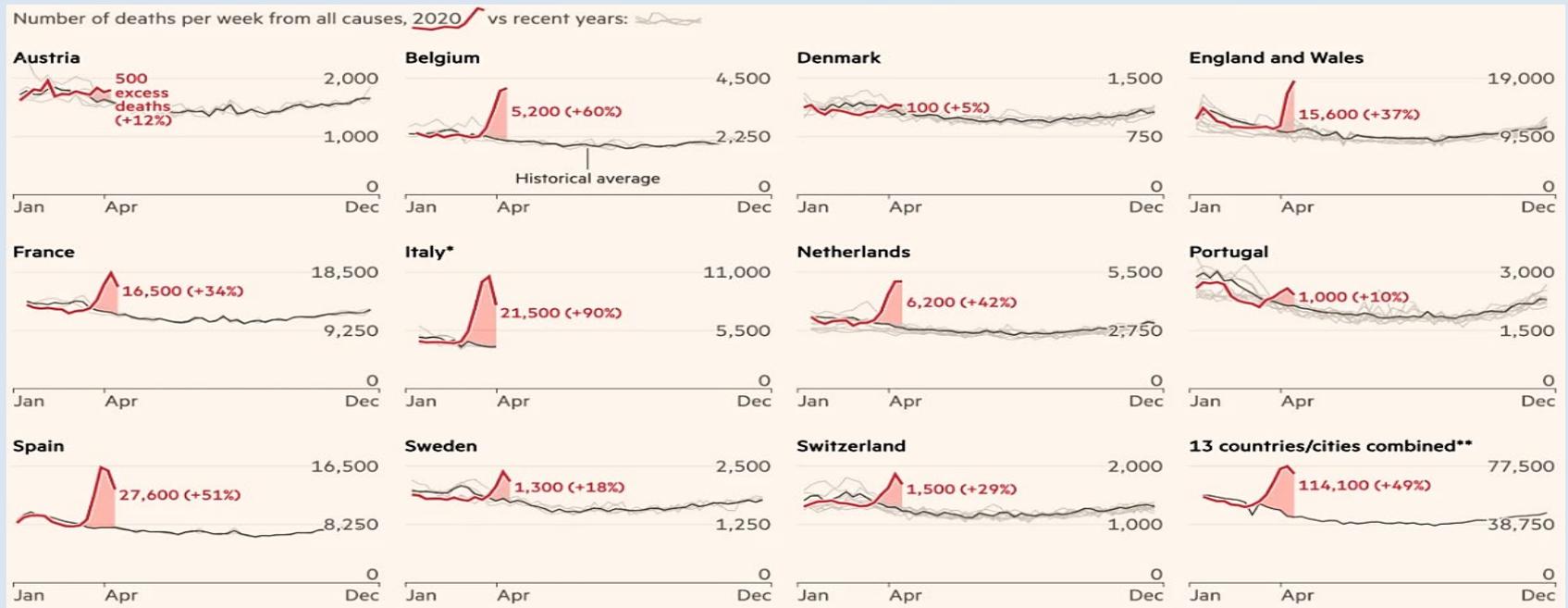
Projection of Total COVID-19 Deaths, Last Update April 30, 2020.



“Current social distancing assumed until infections minimized and containment implemented.”

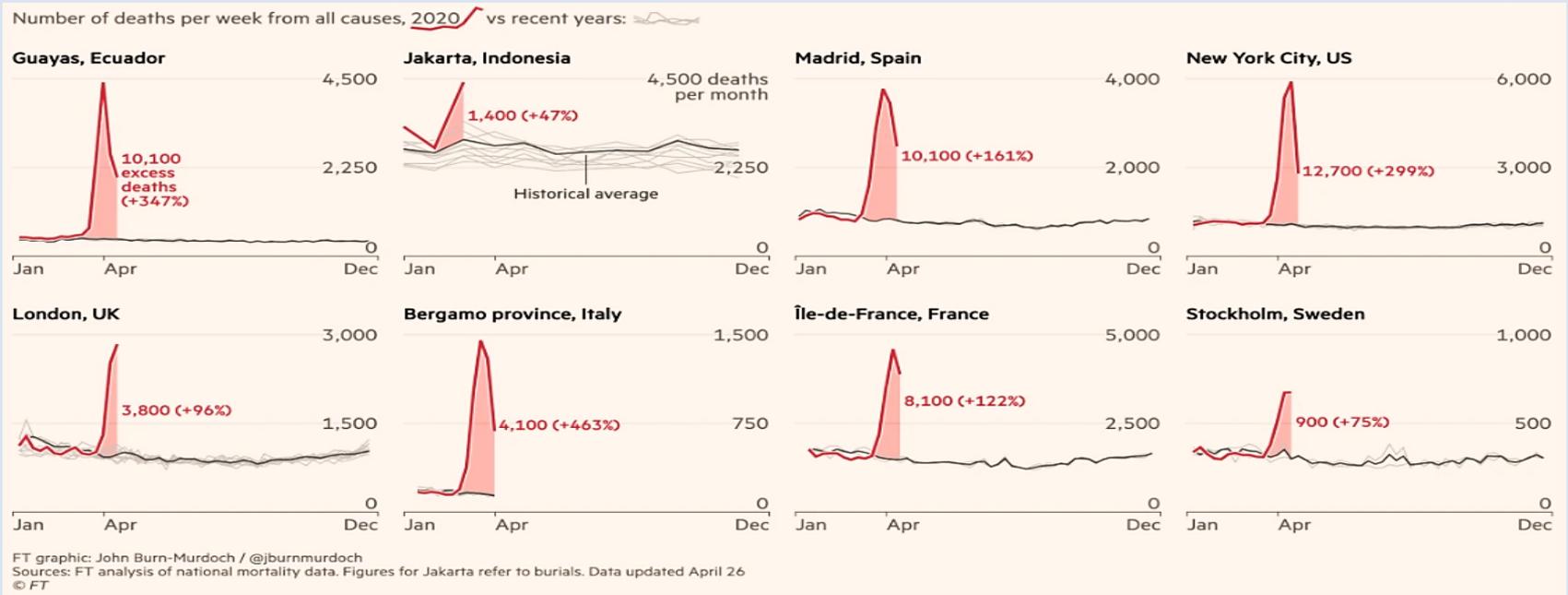
2020 DEATHS SOAR

Number of Deaths Per Week From All Causes by Country, 2020 vs Recent Years, Updated April 26, 2020.



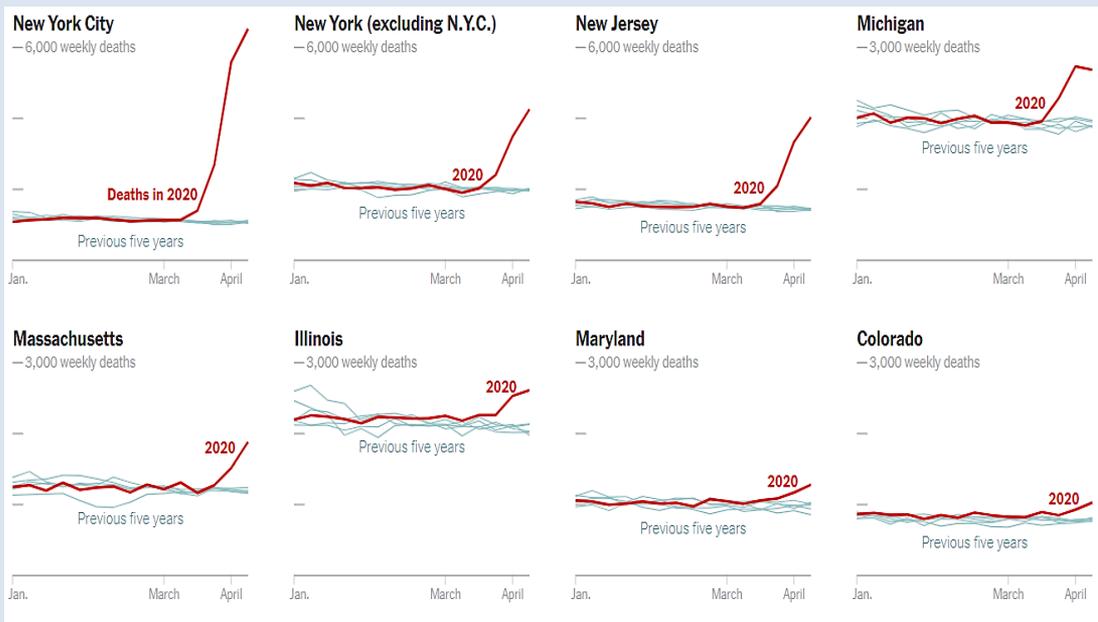
2020 DEATHS SOAR

Number of Deaths Per Week From All Causes by City, 2020 vs Recent Years, Updated April 26, 2020.



2020 DEATHS SOAR

Number of Deaths Per Week From All Causes by State/City, 2020 vs Recent Years, Updated April 28, 2020.



How reported coronavirus deaths compare with deaths above normal

Numbers are from March 8 to April 11, 2020.

AREA	PCT. OF NORMAL	EXCESS DEATHS	-	REPORTED COVID-19 DEATHS	=	GAP
New York City	325%	11,900	-	10,261	=	1,700
New Jersey	172%	5,200	-	2,183	=	3,000
New York (excluding N.Y.C.)	142%	4,200	-	2,425	=	1,700
Michigan	121%	2,000	-	1,391	=	600
Massachusetts	120%	1,200	-	686	=	500
Colorado	116%	600	-	274	=	300
Maryland	115%	700	-	207	=	500
Illinois	113%	1,400	-	682	=	700

ANTIBODIES EXPLAINED

WHAT ARE ANTIBODIES?

Antibodies, the mainstay of our acquire immune system, are produced in our bodies by B lymphocytes. Their activation is triggered by specific antigen proteins—and that activation (through B memory cells) can last for months or years or a lifetime.

Antibodies (immunoglobulins) come in 5 types: IgA, IgD, IgE, IgG, and IgM. IgM is produced within first week after infection; IgG, produced 2-4 weeks after infection, is longer-lasting.

TYPES OF SERUM ANTIBODY TESTS

- Rapid Diagnostic Test (RDT): Qualitative (yes/no); 10-30 minutes on spot.
- Enzyme Linked Immunosorbent Assay (ELISA): Quantitative; 1-5 hours in lab.
- Neutralization Assay: Quantitative & Degree of Immunity: 3-5 days in lab.

ACCURACY OF TESTS

- Hugely variable; unregulated market; many are worthless; evaluation of tests underway.
- Problem is not sampling (as w/ PCR test), but analysis.
- Lab tests definitely better than RDT tests.
- Tests for IgG definitely better than for IgM... so testing recent patients is problematic.
- Accuracy less of a problem for population testing than for individual testing.

ANTIBODIES EXPLAINED

USEFULNESS OF ANTIBODY TESTS

- At personal level, tests can reassure high-risk workers. They may eventually enable issuance of “mobility credentials” to individuals deemed immune. Test accuracy is not ready for this yet.
- At population level, tests give us perspective. They seem to confirm avg infection rates in most seriously hit countries (e.g., US) at 2% to 5%—roughly 10X the official “confirmed” case rate.
 - Recent result of 21% for NYC and 14% for NY state conform perfectly to these avg’s—since NYC official rate is $\approx 6X$ larger than national avg and NY official rate is $\approx 3X$ larger.
 - It is consistent with IFR $\approx 0.5\%$
 - It is also consistent with ultimate deaths (at 50-70% of population infected) of 0.8 to 1.2M, which is 20X to 30X worse than typical U.S. flu season.

ANTIBODIES AS TREATMENT

- Antibody therapy (conferring “passive immunity”) is a third treatment modality—different from either antivirals or vaccines.
 - Old school “convalescent plasma therapy” has been used for over a century to treat viral and bacterial infections—and is now being used to treat C19.
 - New biotech firms hope to mass-produce therapeutic antibodies against C19 and make it much more widely available.
 - Former FDC head Scott Gottlieb calls this the “best bet” on effective near-term therapy.

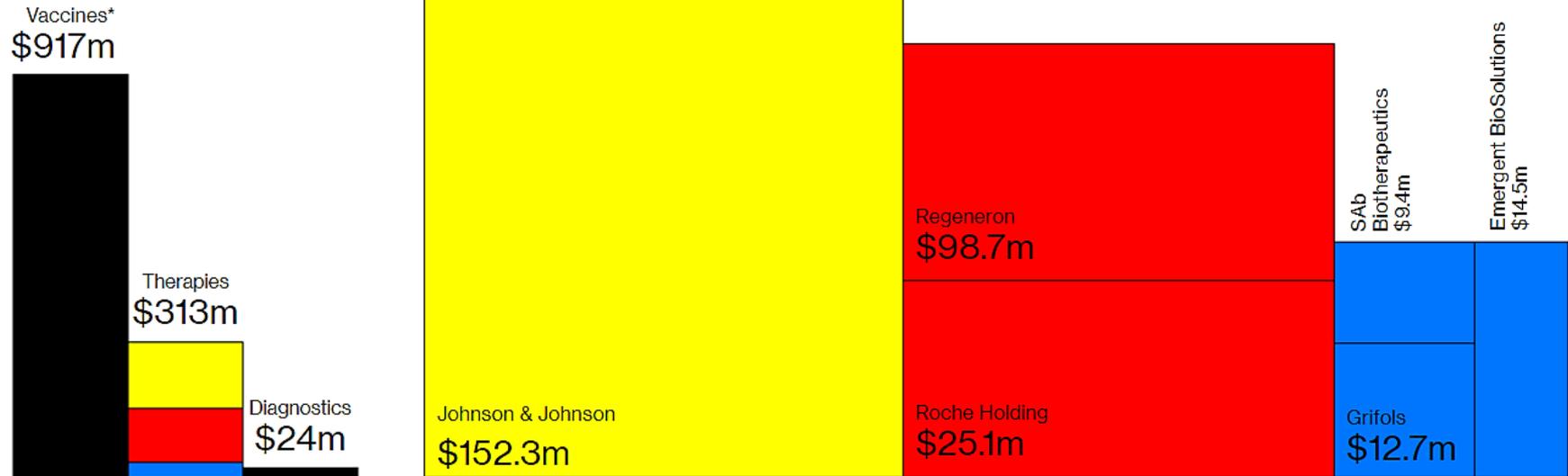
FED \$ BY TYPE OF THERAPY

U.S. Government Money Invested in Coronavirus Countermeasures

■ Antiviral ■ Monoclonal antibody ■ Other antibody

By type

By company working on therapies



As most recently reported by the Biomedical Advanced Research and Development Authority. May not include all funding awarded. *Funding for vaccines may be up to \$970 million, including options.
Data: U.S. Department of Health and Human Services, SAb Biotherapeutics

SPANISH FLU MYSTERY: DEATHS IN LATE-20S

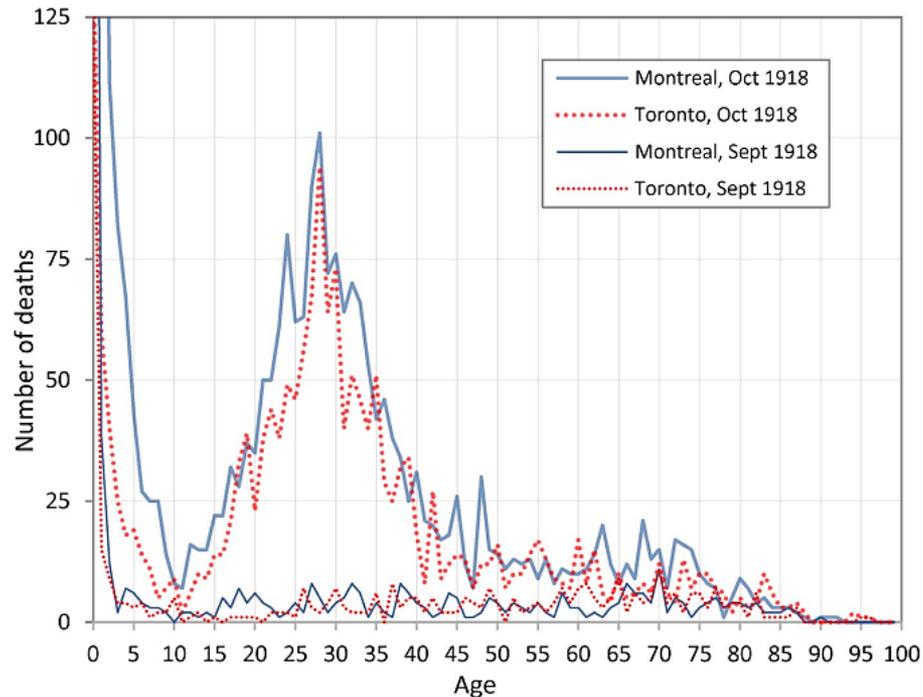


Figure 1. Recorded deaths (from all causes) by age in Montreal and Toronto, September and October, 1918.
doi:10.1371/journal.pone.0069586.g001