Evidence current as of 20/4/2020

COVID-19 Rapid Review

Tuesday, 21 April 2020
Review 5

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The purpose of this regular review, is to present COVID-19 related questions in Emergency Medicine

We accept that available literature on the topics covered in these reviews may be scarce, but shared discussion of novel front line strategies may be a tool to augment our clinical practice and develop future policy

Topics:

Flattening the Curve

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Flattening the curve

Covid-19

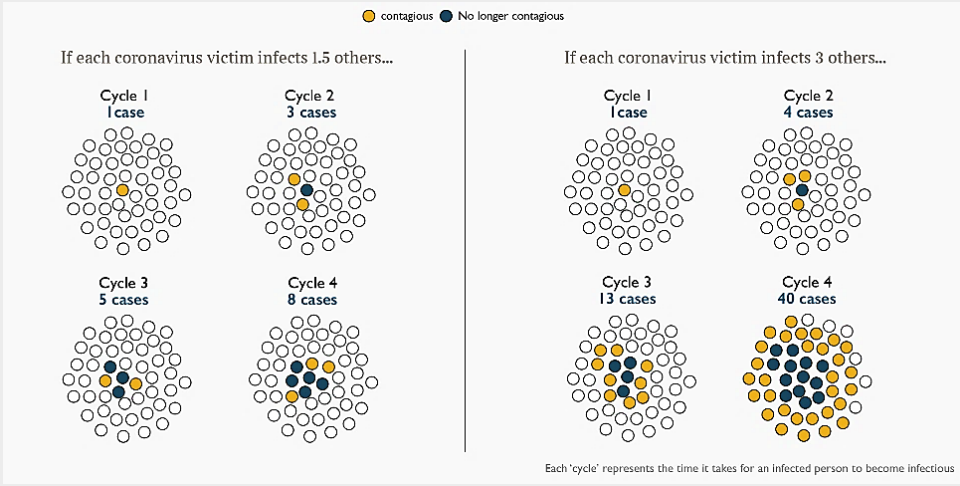
Advice

Flattening the curve involves trying to get the reproduction number, R_t <1 down below one for as long as possible. This is termed
SUSTAINED EPIDEMIC SUPPRESSION

By reducing the R_t the spread of SARS-CoV-2 is slowed, likely saving many lives.

With fewer people infected at any one time healthcare systems may have a chance of coping with the number of patients with severe disease, whilst still trying to have capacity for their normal case load.

The $R_0 > 1$



The basic reproduction number, R_0, is the typical number of infections transmitted by an individual in the absence of widespread immunity. From Italian data estimates of R_0 were 2.43-3.1(1), meaning that every infected person transmitted the infection to up to 3 new people. This represents exponential growth.

If a R_0 is >1 then the number of those infected will continue to increase until such time as a vaccine is available. At this point it is unclear whether there is lasting immunity to the virus, but herd immunity (estimated to begin following infection of 60-70% of the population(2)) would also see the R_0 decrease to below 1.

There is evidence that transmission of the virus not only occurs from symptomatic individuals but also those who are pre-symptomatic and asymptomatic (3). Asymptomatic individuals may account for up to 50% of those infected(4) and as such containing viral spread without significant intervention is unlikely.

"Even modest outbreaks will see fatality rates climb as hospital capacity is overwhelmed, and the indirect effects caused by compromised health care services have yet to be quantified(3)."

The R_0 can be decreased through mitigation strategies to give the R_t or the effective reproduction number at a given time

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Are we flattening the curve?

It is very difficult to compare countries to each other so early in the Pandemic, particularly when their reporting of disease, response, internal characteristics and disease patterns are dissimilar. *(The following examples show general patterns and are not a suggestion of causation in their own right)*

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New Zealand was one of the first to institute an **INTERNATIONAL TRAVEL BAN** and have almost flattened their curve by decreasing imported cases and limiting community spread.

Singapore and South Korea instituted extensive **TESTING AND CONTACT TRACING**. This has worked for South Korea but Singapore has recently seen a change in its trajectory.

The USA where there was initial **LIMITED TESTING CAPACITY** likely had early infections that were not identified and the UK, where the **TESTING POLICY** has been to test only hospitalised patients, may have a higher CFR not reflecting the true burden of disease.

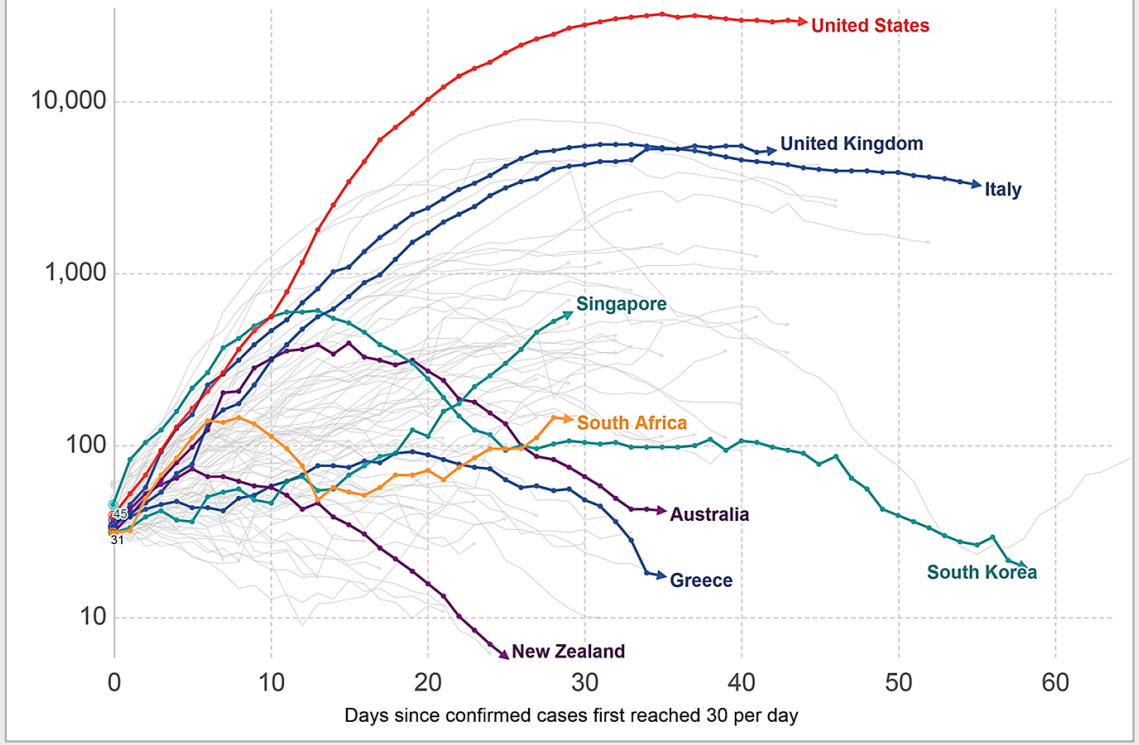
Countries where the population has **CHANGED THEIR BEHAVIOUR** in line with physical distancing or lockdown procedures have also fared better.

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See further graphs on page 6

Daily confirmed COVID-19 cases:

Because not everyone is tested the total number of cases is not known. Shown is the 7-day rolling average of confirmed cases.



South Korea and South Africa thus far have an **AVERAGE AGE OF CONFIRMED CASES** closer to 40, and so fewer deaths at this point would be expected. The same would be expected going forward in countries whose population have a younger average age.

Countries are **REPORTING ON DEATHS DIFFERENTLY** with some only including deaths of hospitalised patients, or those who have tested positive, thus excluding those that die at home or in care facilities.

Italy and Algeria have a greater proportion of elderly people than their respective regions and it follows that they would have a greater number of deaths as people **OVER THE AGE OF 65** are disproportionately affected by SARS-CoV-2.

Greece has a had well **CO-ORDINATED RESPONSE** and have fared better than some of their local peers where regional politics may have interfered.

Certain **CO-MORBID DISEASES** are a significant risk factor for severe illness and death and so countries with a higher prevalence of the implicated diseases would be likely to have a greater disease burden.

The above don't include many other factors, such as the **healthcare capacity and PPE** that each country is able to provide or other characteristics that are still to be defined such as: any **seasonal variation**, and the effect of **malnutrition** and **other co-morbid diseases** more prevalent in LMIC and low income countries. These and other factors that we are still unaware of are likely to have an effect on outcomes that is specific to certain regions.

Can we continue flattening the curve out of a lockdown?

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Mathematical models of SARS-CoV-2 infectiousness and transmission

THE LANCET Infectious Diseases — Early dynamics of transmission and control of COVID-19: a mathematical modelling study

THE LANCET Global Health — Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts

Science — Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing

Implications for isolation, contact tracing and quarantine

AJ Kucharski et al. estimated that there was a decline in reproduction number (R_t) from of 2.35 (95% CI 1.15–4.77) 1 week prior to travel restrictions (lockdown scenario) in Wuhan to 1.05 (0.41–2.39) one week after the restrictions.

Their estimates of the R_t suggest that once there are at least four independently introduced cases to an area, that there is a more than 50% chance the infection will establish within that population.

This has proved to be true as the virus has spread and established rapidly throughout the world.

Hellewell, J *et al.* simulated outbreaks starting with five initial cases, an R_0 of 1.5, and 0% transmission before symptom onset. They found that outbreaks with the above values could be controlled even with low contact tracing probability, but that with more initial cases, an R_0 greater than this, delays in isolation or with transmission prior to symptom onset, that the probability of controlling an outbreak decreases.

The model produced by **L. Ferretti et al**. predicts that the spread of SARS-CoV-2 is, ***"to fast to be contained by manual contact tracing."*** The researchers have suggested that a contact-tracing App may be able to achieve epidemic control if used by enough people and that this might reduce the need for lockdowns that are harmful to society.

It is highly unlikely that the spread of SARS-CoV-2 can be contained outside of a tight lockdown scenario.

Ongoing mitigation will still reduce the R_t but infections can still be expected to escalate.

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What next?

Context specific choices based on evidence

It is clear that a strict and lengthy **lockdown** works in slowing the spread of SARS-CoV-2 by reducing the R_t to below 1. Some countries have shown a greater or lesser tolerance to the measures imposed during lockdown and at present over 2.6 billion people are currently in some form of lockdown.

There are mathematical models that have been built in an attempt to predict future outcomes in multiple scenarios and thus guide response planning. Some of these models have been more accurate than others but the idea behind them is to guide attempts at **sustained epidemic suppression through various mitigation strategies.**

Lockdown in any format comes with a significant cost that is clearly apparent in all societies, but is less easily quantified than the lives saved by it.

Each country will have a different ability to be able to absorb the ongoing shocks to its society as a result of SARS-CoV-2. Each country will have to decide how best to try and contain its spread whilst mitigating the other costs to society, thereby avoiding systemic collapse of healthcare, their economies and even potential societal disintegration.

A lockdown is the most effective means of reducing the R_t - flattening the curve.

Post lockdown there will be sustained efforts to keep the R_t below what it would be in an unmitigated position and in so doing reduce the direct and indirect number of deaths.

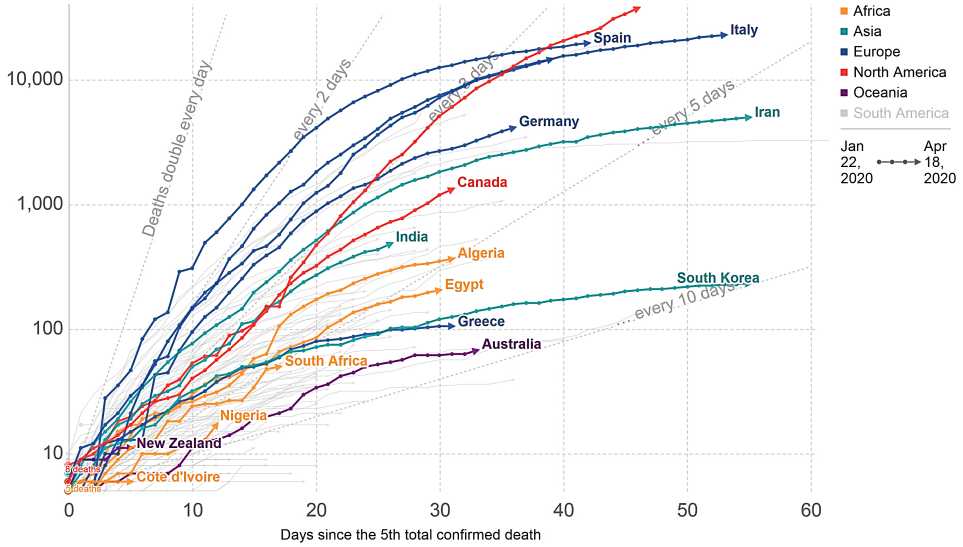
Attempts to restart economies without reversing the gains of a lockdown will be difficult and so there is the potential for further lockdowns if and when healthcare systems are unable to cope. This position is unlikely to change in the short to medium term, unless either a vaccine is developed or some form of herd immunity achieved, with likely significant loss of life and significant costs to society.

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Total confirmed COVID-19 deaths: how rapidly are they increasing?

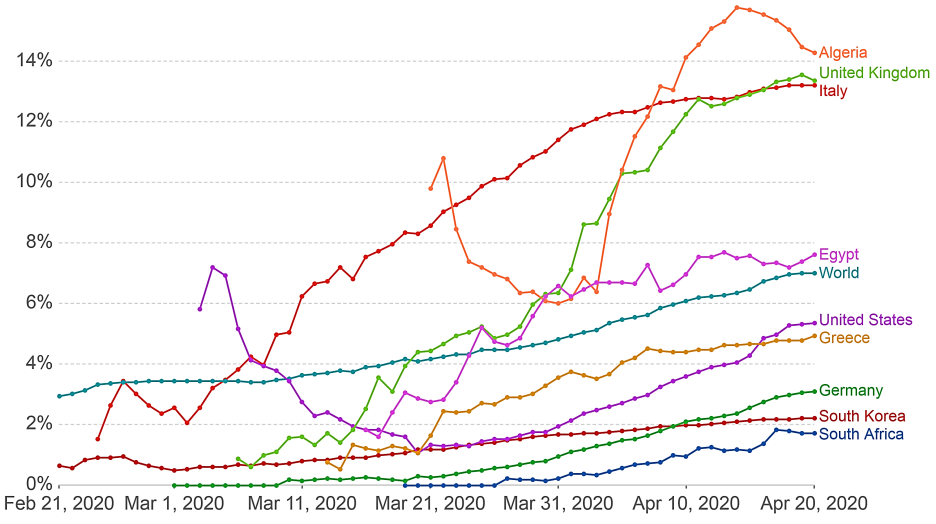
Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.



Source: European CDC – Situation Update Worldwide – Last updated 18th April, 11:15 (London time) OurWorldInData.org/coronavirus • CC BY

Case fatality rate of the ongoing COVID-19 pandemic

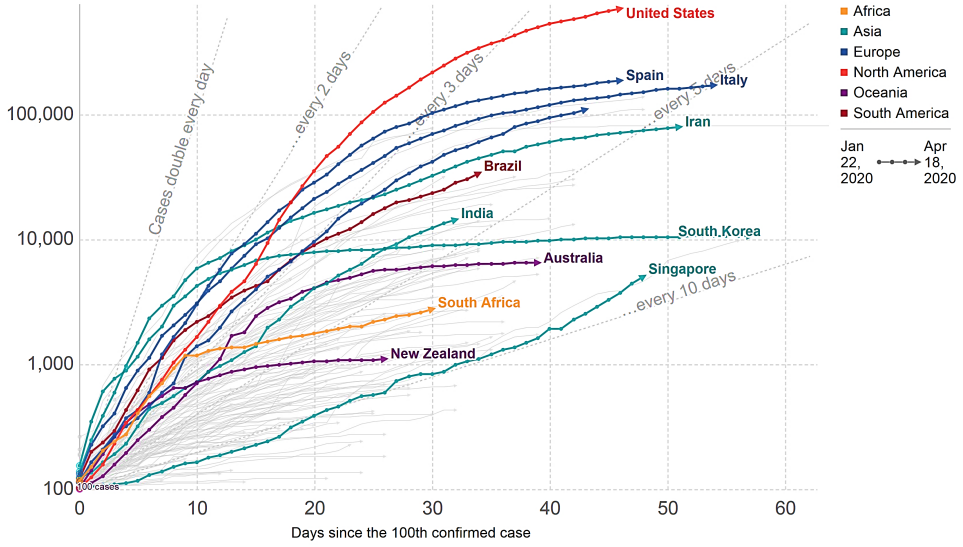
The Case Fatality Rate (CFR) is the ratio between confirmed deaths and confirmed cases.
During an outbreak of a pandemic the CFR is a poor measure of the mortality risk of the disease. We explain this in detail at OurWorldInData.org/Coronavirus



Source: European CDC – Situation Update Worldwide – Last updated 20th April, 11:30 (London time) OurWorldInData.org/coronavirus • CC BY
Note: Only countries with more than 100 confirmed cases are included.

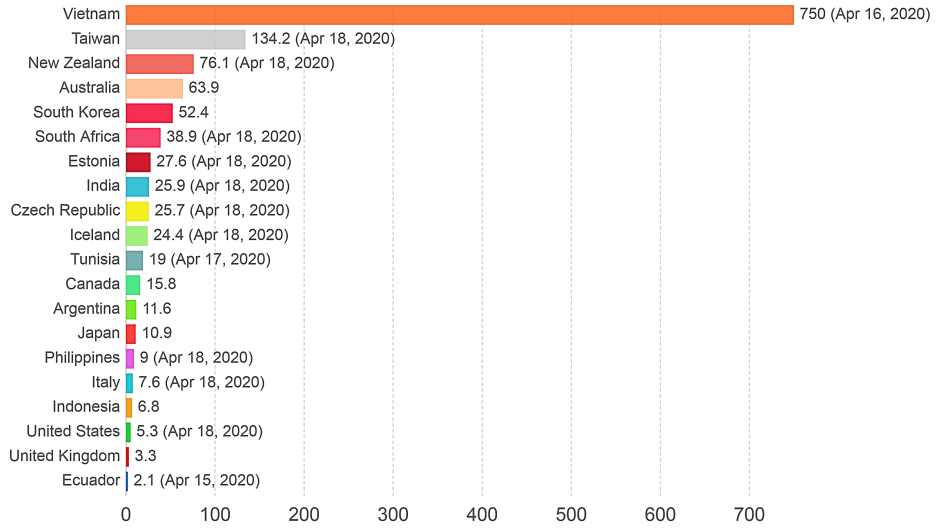
Total confirmed cases: how rapidly are they increasing?

The number of confirmed COVID-19 cases is lower than the number of total cases. The main reason for this is limited testing.



Source: European CDC – Situation Update Worldwide – Last updated 18th April, 11:15 (London time) OurWorldInData.org/coronavirus • CC BY

Number of COVID-19 tests per confirmed case, Apr 19, 2020



Source: Tests: official data collated by Our World in Data. Confirmed cases: European CDC – Situation Update Worldwide
Note: For testing figures, there are substantial differences across countries in terms of the units, whether or not all labs are included, the extent to which negative and pending tests are included and other aspects. Details for each country can be found at the linked page.
OurWorldInData.org/coronavirus • CC BY

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The above site, Our World in Data, allows you to choose individual countries and to plot their trajectory.

It is open source and they encourage use of the resources.

It is worth a visit.

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