

# COVID-19 update

June 2021

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“Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning”

– Winston Churchill



# COVID-19 update

## Treatments and therapies for COVID-19

In most cases, there is no treatment. Bed rest is sufficient.

However, for the most severe cases oxygen and dexamethasone tend to be the main treatments. Mechanical ventilation is for the very worst cases.

- The worst cases develop a condition called Acute Respiratory Distress Syndrome (ARDS). As this appears to be caused by an overactive immune response, treatments that modulate this response have been the most successful to date. Dexamethasone (a corticosteroid) falls into this category. It appears to reduce deaths by around a third in patients on a ventilator or receiving oxygen.

Anti-viral compounds are much harder to develop. Remdesivir was hoped to be a cure given it targets a key enzyme used for viral replication. However, it was not as effective as hoped.

- Trials suggest it can reduce the duration of illness (from 15 to 11 days) but not the mortality rate.

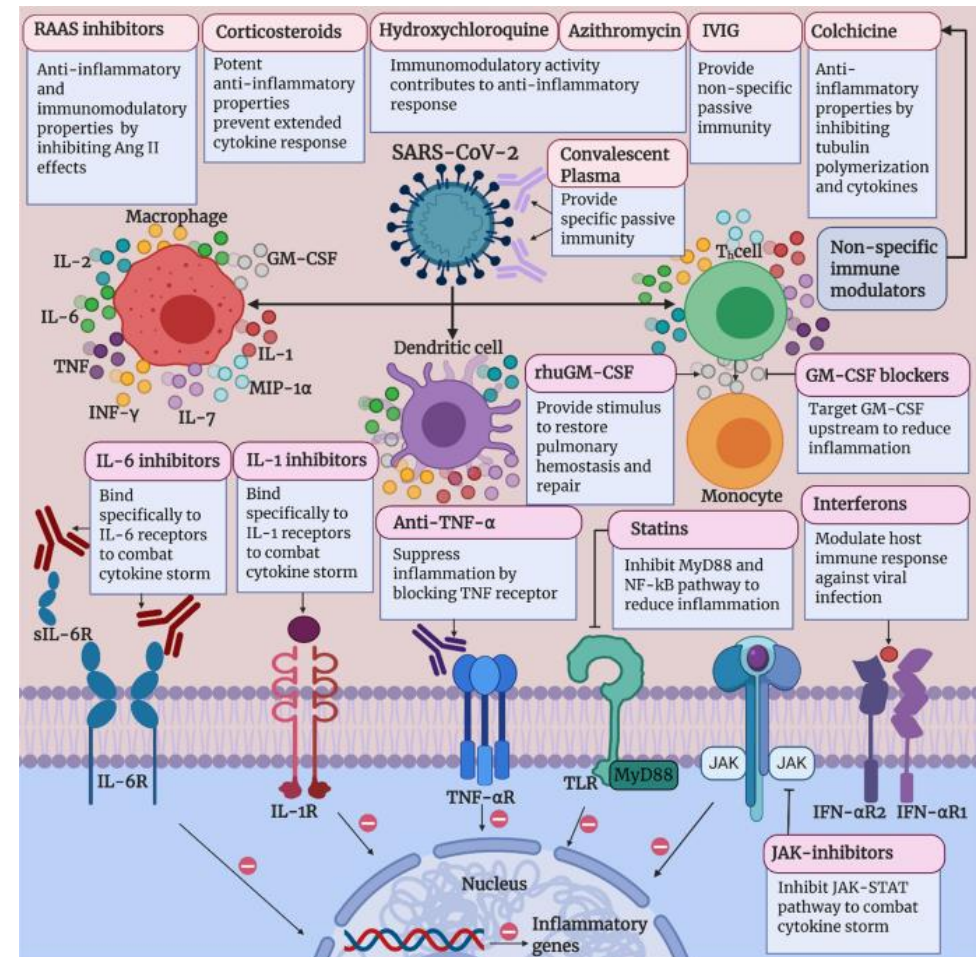
Vaccines were a clear early focus for development.

- These depend on prevention of infection or reducing the severity of infection. They also have the benefit of reducing person to person transmission. But they are mostly ineffective once someone has already caught the virus.
- Vaccines are relatively simple therapies, so can be developed rapidly (clinical trials and approval process tend to slow the development process).
  - This proved to be the case with numerous highly effective vaccines appearing less than a year after the emergence of SARS-CoV-2.

There are a range of other approaches, but many of these will take time.

- Ultimately vaccination programs will remain the cornerstone to controlling SARS-CoV-2.

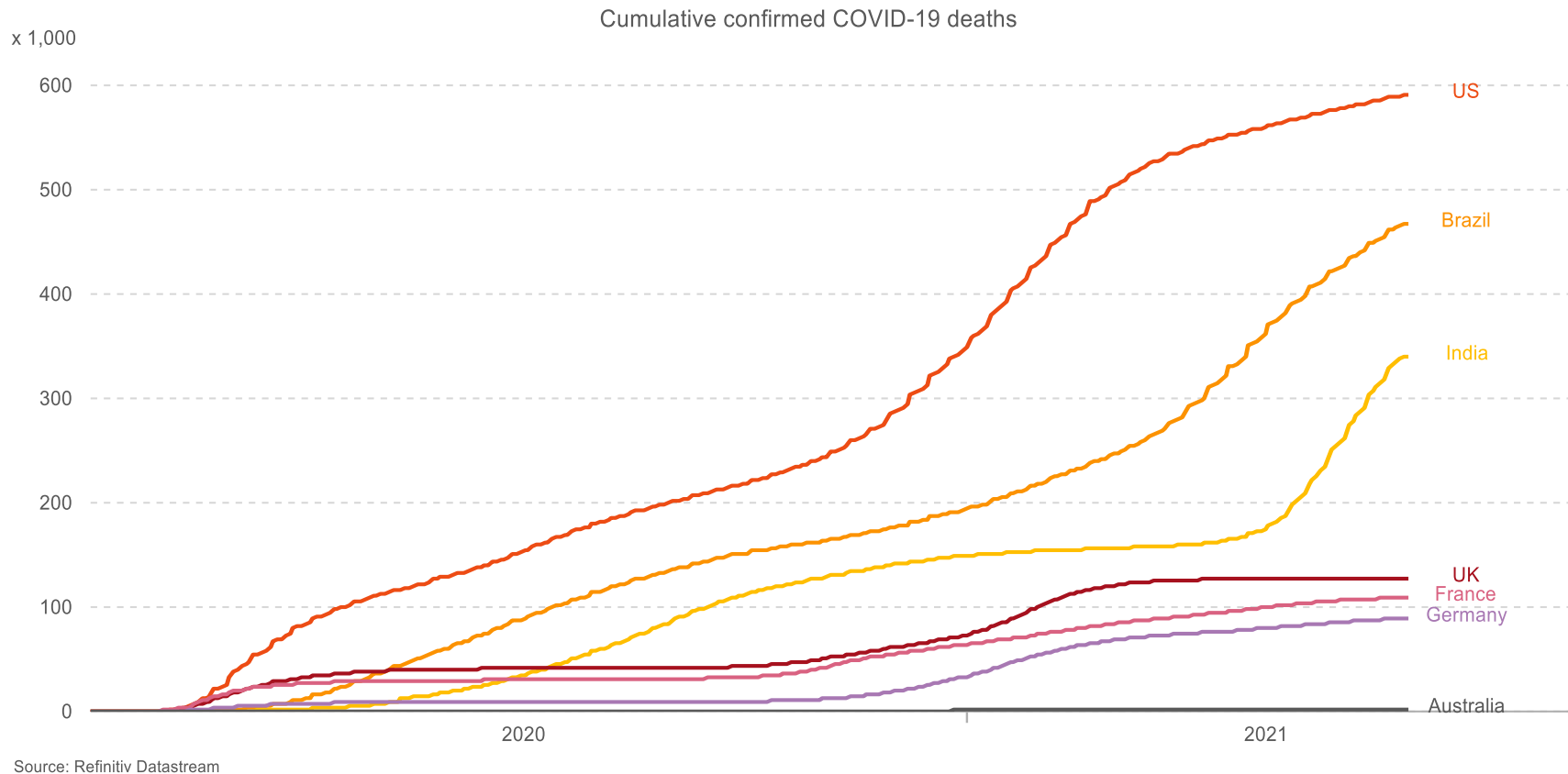
Pharmaco-immunomodulatory therapy in COVID-19



Source: Rizk, J.G., Kalantar-Zadeh, K., Mehra, M.R. et al. Pharmaco-Immunomodulatory Therapy in COVID-19. *Drugs* 80, 1267–1292 (2020). <https://doi.org/10.1007/s40265-020-01367-z>

# COVID-19 update

## The COVID-19 fight by country



The US leads in terms of numbers of confirmed deaths from COVID-19. Brazil and India are still rising quickly.

- Many, many deaths are likely unconfirmed however, meaning the true numbers will potentially differ quite a lot from this.
- The US has experienced 1,791 deaths per million people (i.e. about 0.2% of its population). This is marginally less than the proportion of the population in the US that died during World War II, but this is only around 1.5 years into the pandemic and it is still going.

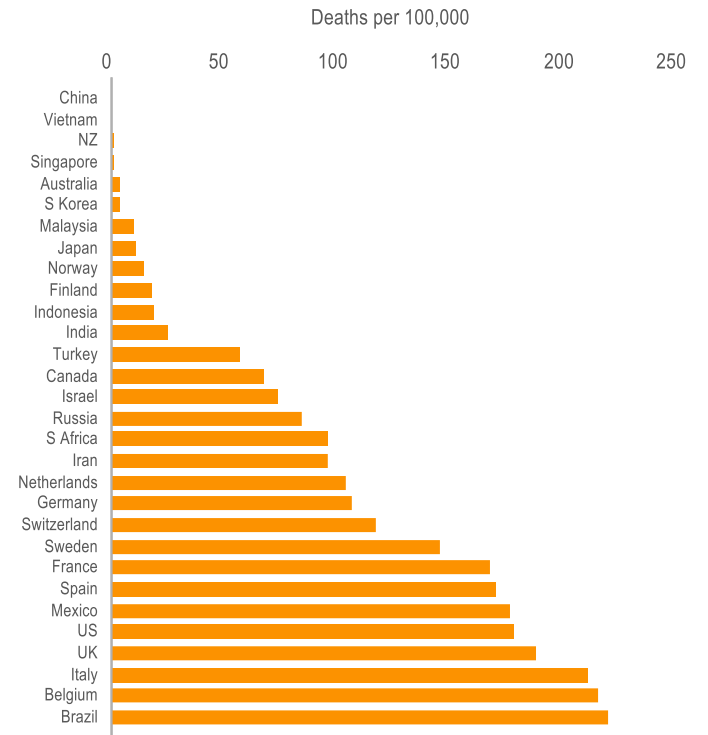
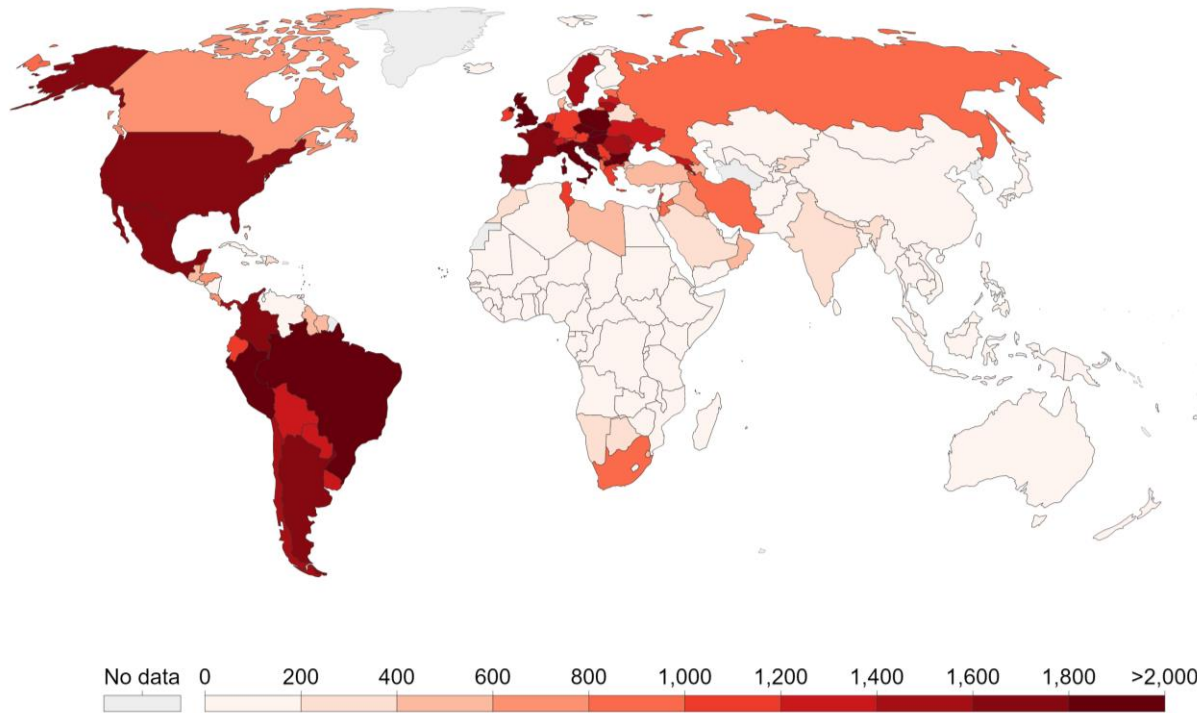
**The pandemic still has a while to go.**



# COVID-19 update

## The COVID-19 fight by country

Cumulative confirmed COVID-19 deaths per capita (June 2021)



Source: Johns Hopkins University CSSE COVID-19 Data

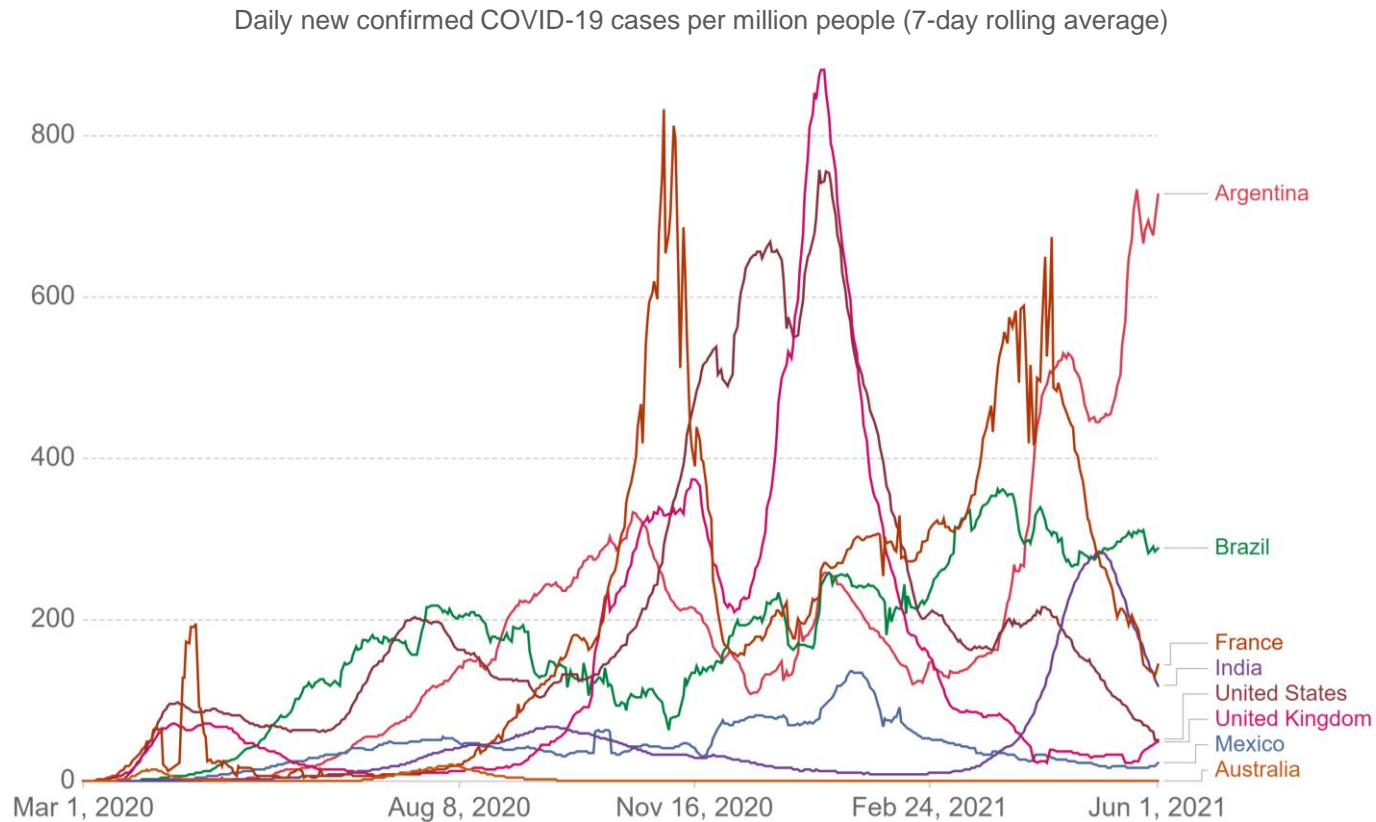
Source: Refinitiv Datastream

The Americas and Europe have been heavily impacted by the pandemic, but lack of data means the true picture is not known for many countries.

But, it is clear Australia has performed very well relative to the rest of the world.

# COVID-19 update

## The COVID-19 fight by country



Source: Johns Hopkins University CSSE COVID-19 Data

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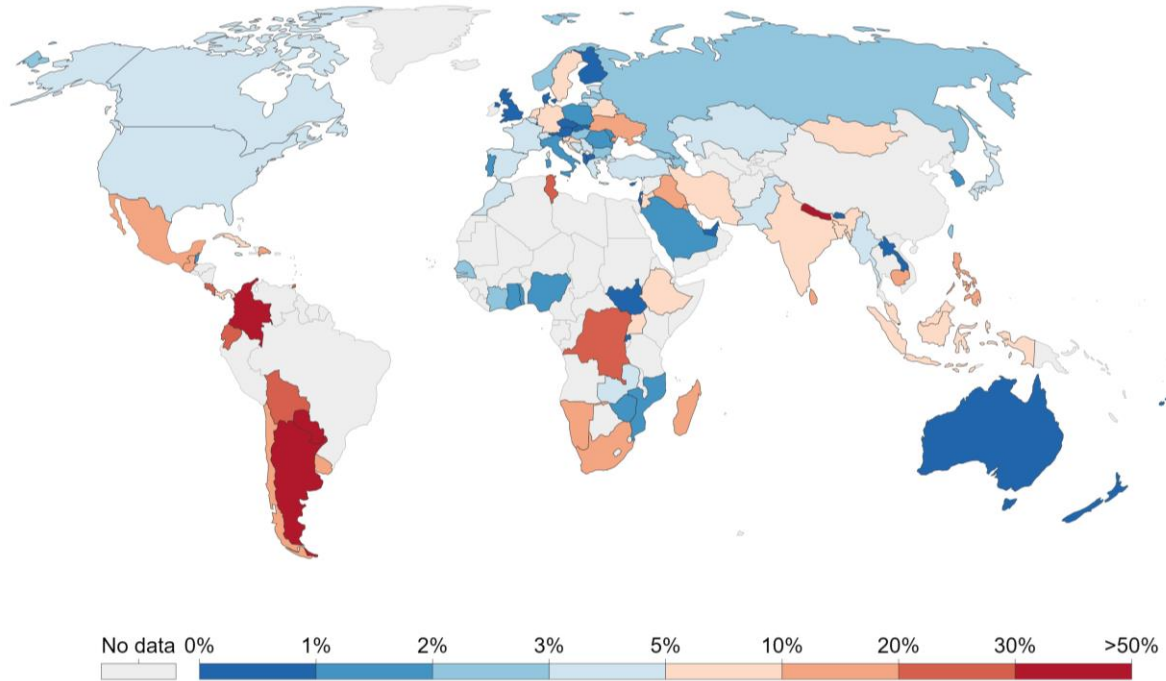
While most Western countries appear to be getting the disease under some sort of control through a combination of vaccinations and public health measures, there are still places where second or third waves are occurring.

India gets much of the media coverage, but many other countries are seeing a surge in cases (including Argentina, Nepal, Bahrain and Taiwan).

# COVID-19 update

## COVID-19 testing

The share of COVID-19 tests that are positive (31 May 2021)



Source: Official data collated by Our World in Data – Last updated 1 June, 11:10 (London time)

[OurWorldInData.org/coronavirus](https://OurWorldInData.org/coronavirus) • CC BY

Note: Comparisons of testing data across countries are affected by differences in the way the data are reported. Daily data is interpolated for countries not reporting testing data on a daily basis. Details can be found at our [Testing Dataset page](#)

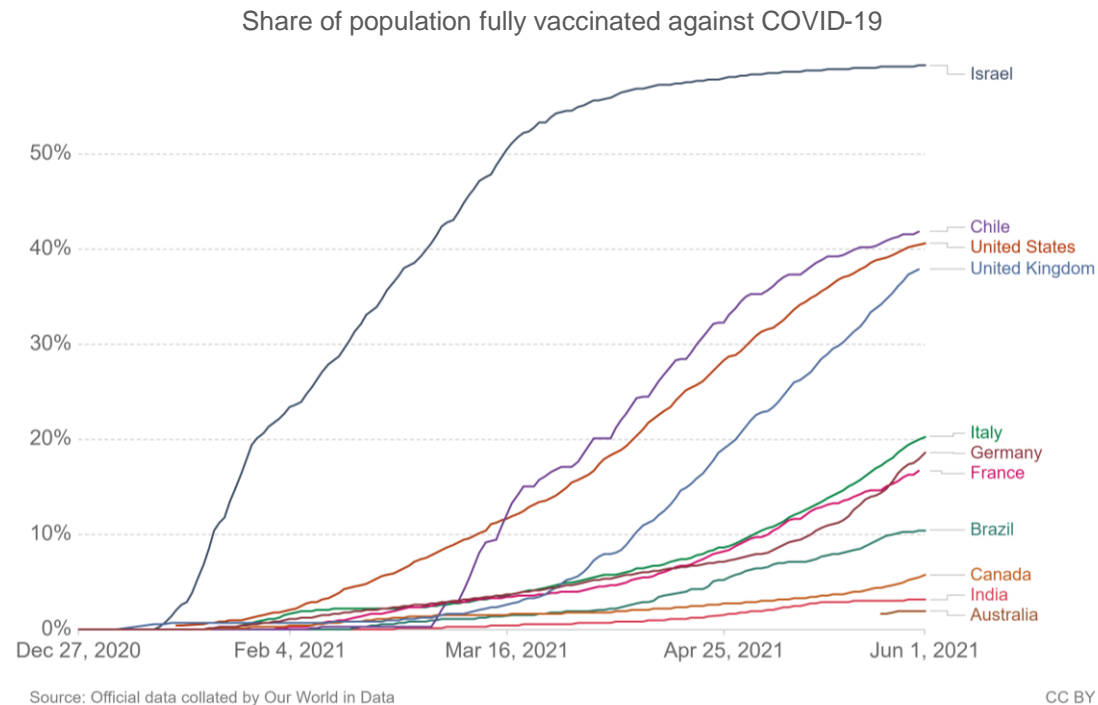
### Testing is of key importance to monitoring and managing the pandemic.

Test coverage is extremely variable across the world.

- As an indicator of testing sufficiency, the WHO recommends achieving a positivity rate of less than 10% and ideally less than 3%.
- Australia, New Zealand and the UK show good testing coverage, whereas even the US and Canada are not meeting the less than 3% hurdle.

# COVID-19 update

## Progress on vaccination programs



### Vaccination is the key weapon in the in long-term fight against COVID-19 but the coverage is extremely variable.

Herd immunity refers to the level of immunity in the community where a disease tends to die out due to lack of transmission.

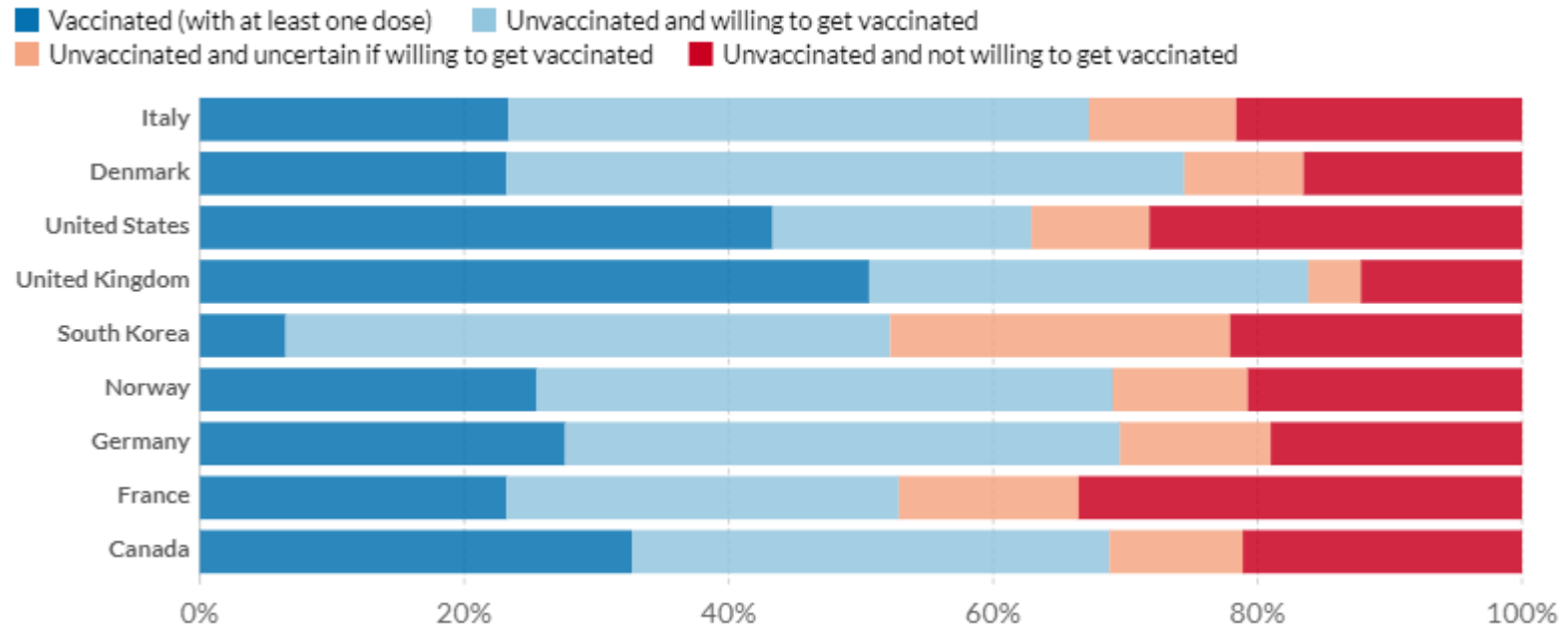
- This depends on both naturally induced immunity (from being infected) and immunity from vaccination.
- The theory is that the disease can be controlled and that those who cannot achieve sufficient immunity for whatever reason (e.g. immunocompromised) are passively protected.
- The required level of immunity depends on several factors, but transmissibility of the disease is key. As transmissibility appears to be increasing with new strains, the required level for herd immunity will also be rising. 60% was the rough estimate for herd immunity early in the pandemic but it could be 85% or higher now. No country has likely reached even the 60% level (given vaccines are not 100% effective).



# COVID-19 update

## Vaccine hesitancy

Willingness to get vaccinated against COVID, 30 April 2021



Source: Official data collated by Our World in Data – Last updated 11 May, 10:00 (London time)

OurWorldInData.org/coronavirus • CC BY

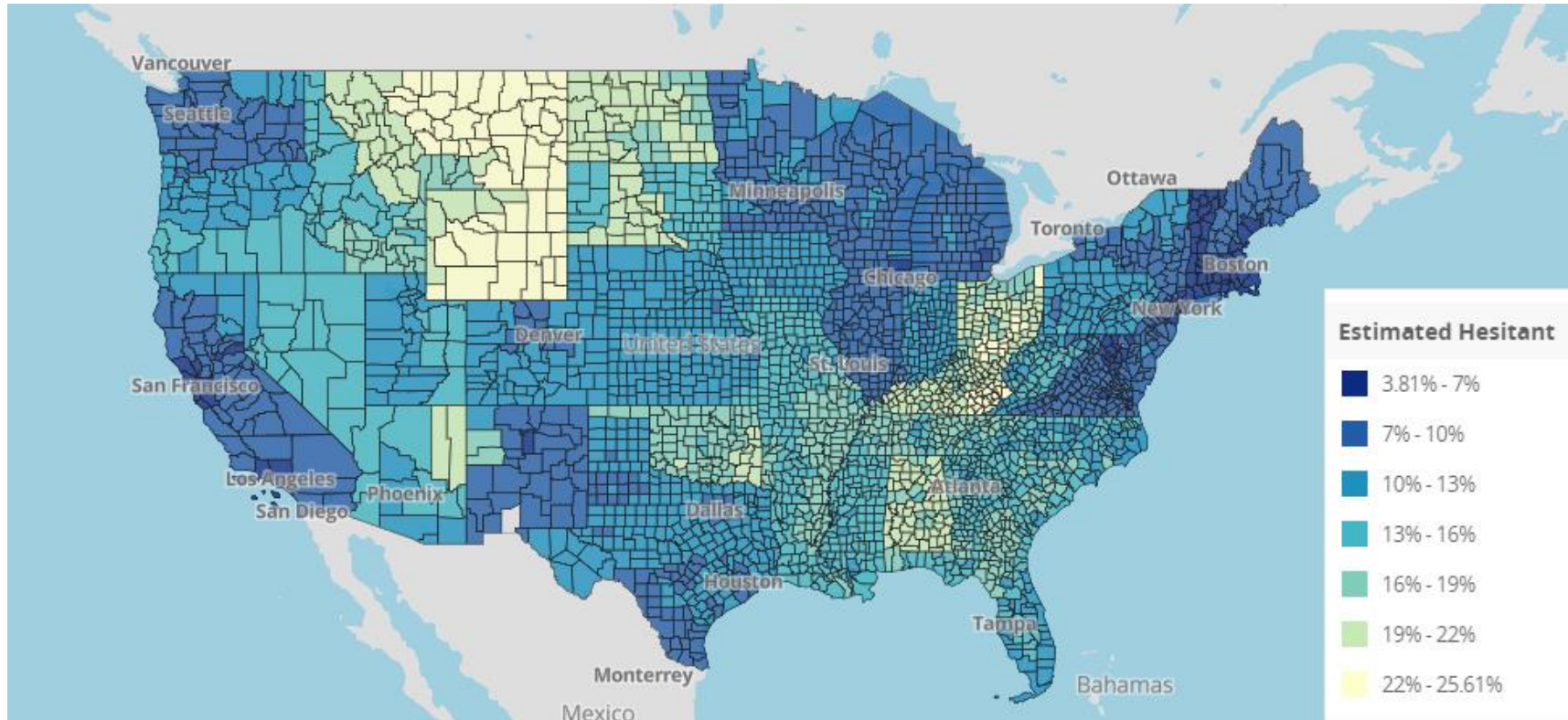
Vaccine hesitancy is a key impediment to achieving herd immunity.

- Ultimately as much of a population as possible needs to be vaccinated to account for the unknown herd immunity level, vaccines not being 100% effective, virus mutations and naturally declining immunity over time.
- Wide coverage of very rare side effects has not helped the situation.
  - Thrombosis with thrombocytopenia syndrome (TTS) with the AstraZeneca vaccine has an incidence (not deaths) of around 8.5 per million vaccinations in over 50-year-olds, compared to a death rate of around 530 deaths per million in a scenario similar to Victoria's second wave.

# COVID-19 update

## Vaccine hesitancy

Vaccine hesitancy across the US



Source: data.CDC.gov

This highlights just how variable vaccine hesitancy can be, even within a country that has been extremely heavily impacted by COVID-19.

# COVID-19 update

## Strains

### **New strains of the virus continue to arise.**

Periodically new strains have arisen and have taken over the viral population, at least in defined geographic areas. This occurs through mutations within the virus' genome.

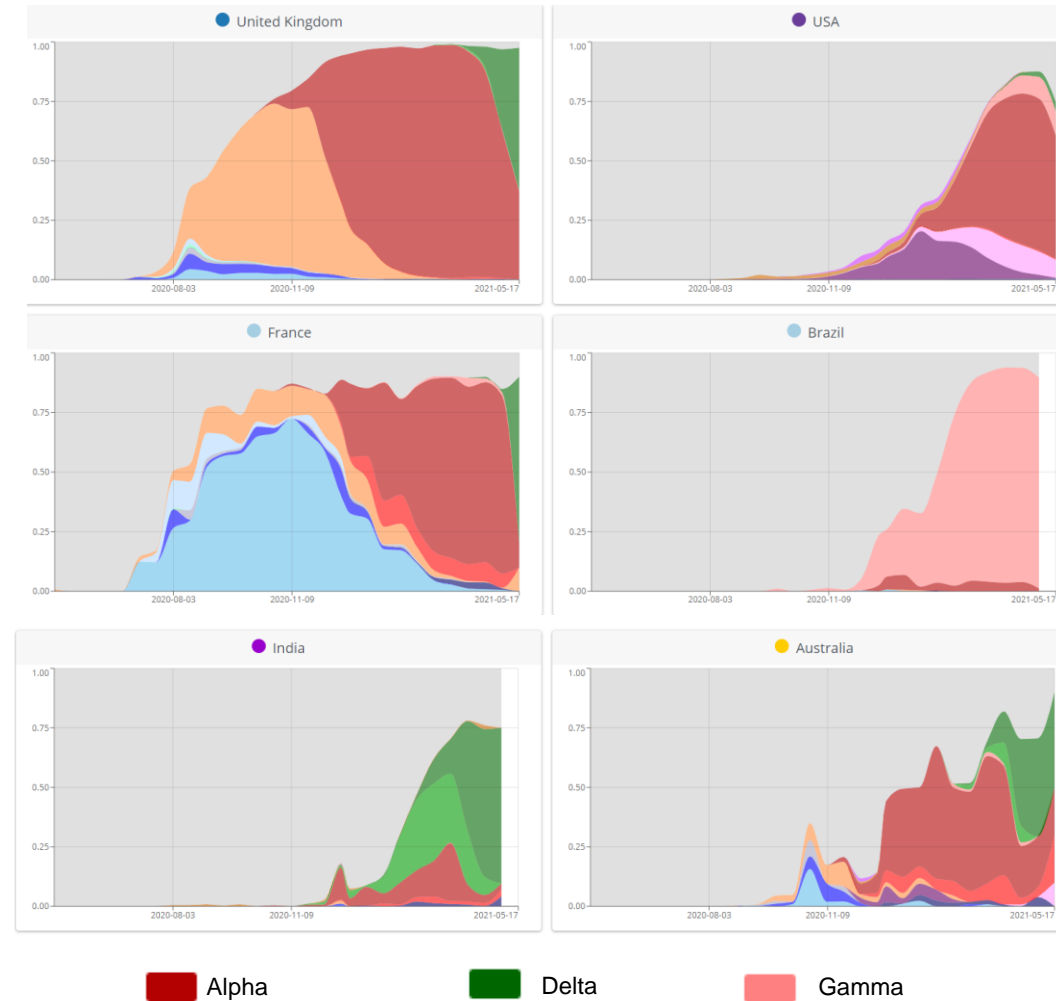
- One of the first mutations that arose was the D614G mutation in the virus' S-protein, which is now in all widely spread strains. It's believed to confer additional transmissibility and is also associated with the loss of smell and taste symptoms of COVID-19.
- The takeover of the viral population by a new strain is suggestive of increased 'fitness' in the human population.
- This happened in the UK with the Alpha strain (B.1.1.7) in late 2020 and has also occurred in India with the Delta strain (B.1.617.2).
  - These are tracked by sequencing (reading) the viral RNA, which means the exact mutations that have occurred have been identified.
- The key questions are how the mutations affect the rate of spread of the variant, the potential to evade immunity and if it results in more severe disease.
  - The breakout variants appear more transmissible (some estimates have Delta at four times more transmissible than the original Wuhan strain and 50% more transmissible than Alpha), while some appear to partially evade immunity (vaccine induced and natural) and potentially cause a worse disease.

# COVID-19 update

## Strains

The charts to the right show the percentage of the viral population in particular countries that are represented by different viral strains (each strain with its own colour).

- This data is a summary of monitoring where virus samples are “sequenced” (a process to read the whole virus genome).
  - This data then allows the comparison of different viral families, their relatedness and provides information on where changes are occurring.
  - This RNA sequence data can easily be translated to show how the viral proteins are changing.
- Coverage of such sequencing data is variable, but it clearly shows points where a new strain emerges and becomes the dominant strain in a region.
  - The Delta (B.1.617.2) strain that emerged in India is the most recent emergence of a “variant of concern” as defined by WHO.



Source: Nextstrain

# COVID-19 update

## India

**India is a major country that has recently experienced a major outbreak of COVID-19.**

- This appears to be driven in part by the emergence of the Delta strain, but a relatively weak health care system has exacerbated the problem.
- The health care system appears completely overwhelmed, which is the worst-case scenario since death rates can dramatically increase without appropriate supportive care.

One area of media coverage is the number of younger people becoming severely ill or dying from COVID-19 in India.

- COVID-19 primarily causes death in the elderly and those with other health conditions. This could indicate the nature of the illness is changing.
- However, there is no clear data to suggest this is happening – large numbers of young deaths are likely an outcome of the scale of the outbreak, a large and relatively young population, and the overwhelmed healthcare system.

As mentioned before, the emergence of the Delta strain is a concern given it appears to spread much more rapidly than early strains, making control a lot more difficult.



# COVID-19 update

## Summary

- When the first successful Phase 3 vaccine trials were announced around 6 months ago, it seemed like the end was in sight. However, there is still a long way to go with only Israel making it past 50% of the population being full vaccinated.
  - While herd immunity has likely not been reached in any country, vaccination rates do appear to be slowing the spread of COVID-19, which will ultimately reduce deaths.
- The road forward is likely to have bumps. The virus continues to mutate and become more transmissible, which makes it harder to control by public health measures alone. Some of the mutations also appear to confer some protection against pre-existing immunity, so “escape mutants” (virus not affected by the existing vaccines) could possibly arise, especially with an increasingly large population of vaccinated individuals in place.
  - The chances of this derailing the vaccination programs over the short to medium term is unknown, but new vaccines will need to be developed against the new strains regardless.
- Non-vaccine therapies have been slow to develop, but this is to be expected. The most effective non-vaccine pharmaceutical intervention appears to be dexamethasone, a drug first created in the 1950s.
  - Other therapies will arise but will be the second line of defence after vaccination.
- Given vaccines are not 100% effective, ongoing mutations in the virus, vaccine hesitancy, short lived immunity to coronaviruses, and the likelihood that a large percentage of the world’s population will never be vaccinated, it seems likely that SARS-CoV-2 will become an endemic virus like the flu and cold viruses.
  - This is not surprising given only one established human infectious disease has ever been eradicated (smallpox).
- At some point Australia will need to reopen its borders to the rest of the world at which point SARS-CoV-2 will enter the country.

## Author:

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Previously Martin has worked in technology commercialisation at the University of Melbourne and the Bio21 Institute, and virology research at Murdoch University. Immediately prior to joining Frontier, Martin worked at Starfish Ventures, an Australian venture capital fund manager focused on high growth life sciences, information technology, and clean technology companies.

Martin has a Master of Applied Finance through Macquarie University, a PhD in Molecular Cell Biology, and a Bachelor of Science with first class honours in Microbiology.





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