

INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE

Focussing on immunity and vaccine development

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9 MARCH 2021

1. VACCINES & VARIANTS

1.1 Number of possible SARS-CoV-2 mutations may be limited

Jason McLellan, a structural biologist at the University of Texas, Austin, has discussed [in the New Yorker](#) magazine the concept that SARS-CoV-2 has only a limited number of variations available that will increase its “fitness”**.

“There’s just not a lot of space for the spike protein to continue to change in ways that allow it to evade antibodies but still to bind to its receptor,’ he said. ‘Substitutions that allow the virus to resist antibodies will probably also decrease its affinity for ACE-2’ – the receptor that the virus uses to enter cells.”

[Eric Topol comments](#): “Yes, let’s hope we have seen peak fitness. It’s certainly possible and it would accelerate our re-entry towards pre-covid life.”

**[Viral “fitness”](#) is defined as: “...the ability of a virus to replicate and dominate or replace the other strains/mutants...”

1.2 Pfizer vaccine (two doses) neutralized all three major variants

A new article in the [New England Journal of Medicine](#) (NEJM) reports that the three major variants (B.1.1.7, B.1.351, P.1) were neutralized by serum from people vaccinated with two doses of Pfizer vaccine at titres of greater than 1:40.

[Eric Topol](#) describes this as: “Quite reassuring.”

1.3 Powerful antibodies in patients recovered from the B.1.351 (South Africa) variant

A [non-peer-reviewed preprint from multiple authors in South Africa](#) has demonstrated high levels of antibody with cross-reactivity for the original variant (from the first wave of COVID-19) and the P.1 (Brazil) variant now circulating globally.

“Collectively these data suggest that the antibody response in patients infected with B.1.351 has a broad specificity and that vaccines designed with the B.1.351 sequence may elicit more cross-reactive responses.”

The authors hypothesize that a vaccine based on the B.1.351 (South Africa) variant may elicit antibodies that can protect against multiple circulating SARS-CoV-2 lineages.

1.4 AstraZeneca CEO speaks about its COVID-19 vaccine

In an interview with The Australian newspaper, the company's CEO, Pascal Soriot (based in Sydney) has reiterated that the AstraZeneca vaccine is 100% effective against severe disease.

Mr Soriot went on to compare the AstraZeneca and Pfizer vaccines and then **discussed data that is “yet to be released”.**

“Clinical data in recent weeks had put the AstraZeneca vaccine at about 76% to 83% efficacy compared with Pfizer’s 93%, but Mr Soriot said results from the clinical trials were measured differently.

“He said after one month AstraZeneca’s clinical trials showed 100% protection against severe disease. Importantly, there **was real-world evidence from the vaccine rollout in Britain that if anything put AstraZeneca ahead of Pfizer.**

“In Scotland with 1 million people vaccinated, there is a 94% reduction of hospitalisations for vaccinations,’ he said. ‘The Pfizer vaccine in those studies is 85%, but it varies.

“One difference between the two vaccines was that the second dose of the AstraZeneca vaccine needed to be given three months after the first. If you do that you get north of 80% efficacy long term.

“I would say there is more and more data coming out to say the vaccines are very similar,’ Mr Soriot said.”

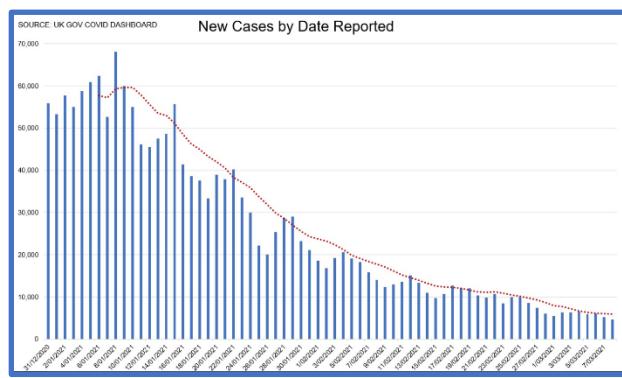
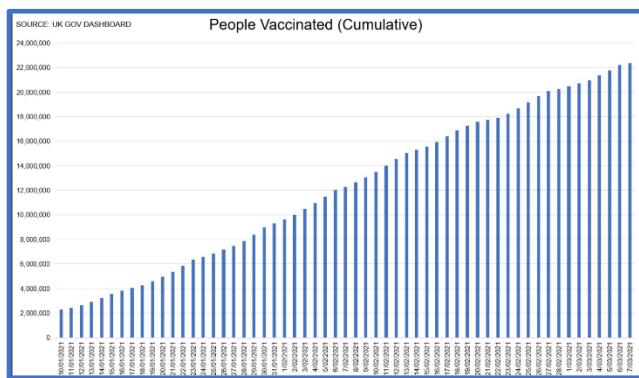
1.5 Germany approves AstraZeneca vaccine for over-65s

[The BBC reports](#) that “Germany's vaccine commission has approved the use of the Oxford-AstraZeneca jab in people aged over 65. The country previously approved it for under-65s only, citing insufficient data on its effects on older people.

“That led to public scepticism about its effectiveness, with some Germans spurning it and leaving many doses unused. But German Chancellor Angela Merkel said recent studies had now provided enough data to approve it for all ages.”

2. EPIDEMIOLOGY UK & US

2.1 Focus on the UK's success

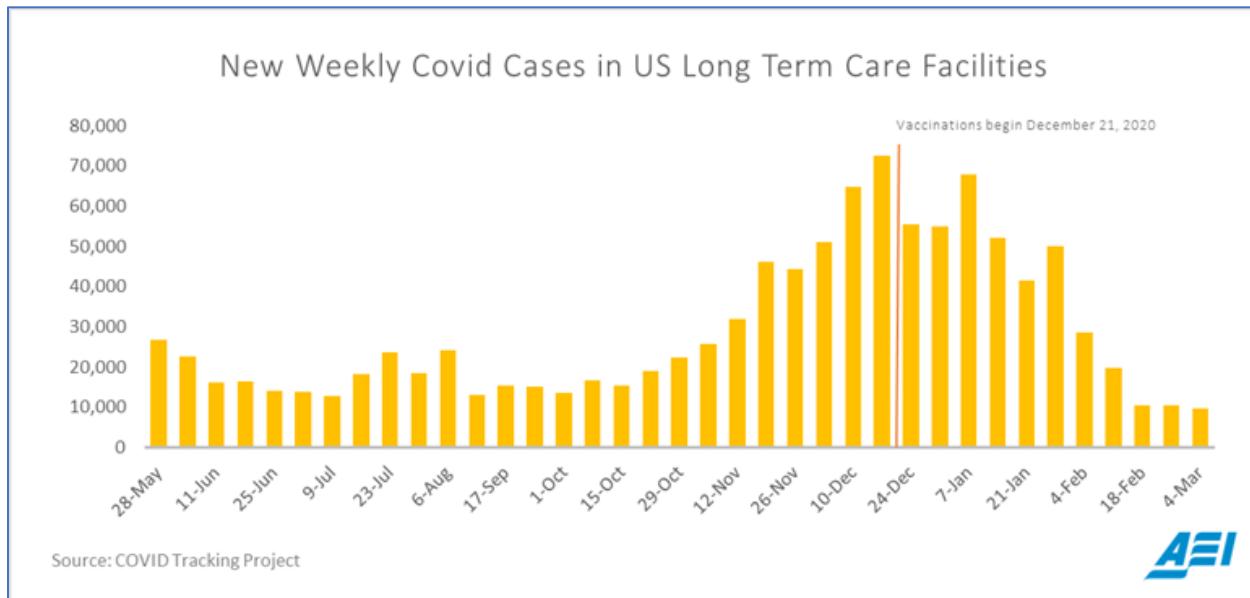


2.2 Assess the vulnerable population when measuring vaccination programs

Scott Gottlieb has tweeted about the importance of assessing risk reduction when assessing vaccination programs, not only the pure percentage of the population vaccinated.

The US is soon to cross 60% of those over age 65 vaccinated and 70% of those over 75 vaccinated. The overall vulnerability of the population to COVID-19 is obviously declining.

The table below shows the reducing number of cases in a high-risk population in the US – residents in long-term care facilities.



Source: COVID Tracking project

2.3 Prior COVID-19: no increase in antibodies or memory B-cells from second dose

Eric Topol has commented on a new non-peer reviewed longitudinal analysis of antibody and memory B cell responses in SARS-CoV2 in naive and recovered individuals following mRNA vaccination, published on medRix.

The finding of no increase in circulating antibodies or antigen-specific memory B-cells from a second dose provides more support for one-dose for those who have previously had confirmed COVID-19, according to Topol.

- [SPAIN](#): has imposed a six-month vaccine delay on those who have had COVID-19
- [FRANCE](#): has recommended a single vaccine dose for people who have had COVID-19

2.4 Remember: there were NO COVID-19 deaths in anyone vaccinated in a clinical trial

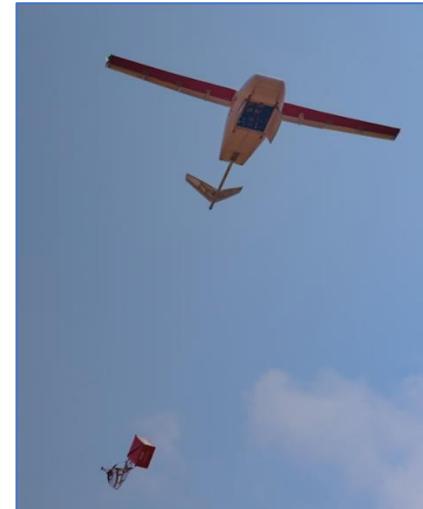
[Monica Gandhi's](#) table reminds us that there were no COVID-19 deaths in anyone vaccinated in a clinical trial.

Company	Platform	Doses	Non-clinical results	# who got vaccine	Protection from hospitalization from COVID-19	Protection from COVID severe dz (some at home)	Efficacy against milder COVID
moderna	mRNA-1273 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+, CD8+; protection from challenge (macaques)	~15,000	97% (1 in vaccine arm <u>after 2nd dose hospitalized</u>)	97% (30 cases in placebo arm; 0 in vaccine reported but 1 severe per FDA)	94.1%
Pfizer	BNT162b2 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+, CD8+; protection from challenge (macaques)	~18,600	100%	100% (9 cases in placebo arm; 0 in vaccine- <u>1 initially severe but not</u>)	95%
Johnson & Johnson	JNJ-78436725 Non-replicating human adenovirus/DNA	1	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; challenge protection (macaque)	~22,000 US, Latin America, S. Africa	100%	85.4% across 3 sites (7 deaths, 16 hospitalizations, all in placebo arm)	72% US; 68% Latin America; 64% S. Africa (96% B1.351)
AstraZeneca	AZD 1222 Non-replicating Chimp Adenovirus-DNA	2	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; protection from challenge (macaques)	~8588	100%	100% (15 in placebo – all hospitalized; 0 in vaccine)	70% overall; 76% 1 dose; S. Africa trial halted for mild
NOVAVAX	NVX-CoV2373 Spike protein/RBD + Matrix M adjuvant	2	Neutralizing Abs; Strong Th1 CD4 > Th2; challenge protection (macaques)	~9700 (Phase 3, UK; 2b SA)	100%	100% (but only 1 severe in placebo; 0 in vaccine)	96%; 89% B117 UK; 60% SA (94% B.1.351)
Sputnik V	Ad26 and Ad5 adenovirus/DNA	2	NAbs; IFN- γ secretion PMBCs, cellular response	~14964	100%	100% (20 in placebo; 0 vaccine)	91.6%
sinovac	Inactivated virus	2	Antibodies (T cells next)	~12500	100%	83% (tx needed)	50.7% across

3. OTHER NEWS

3.1 First delivery of COVID-19 vaccine by drone

[Gavi](#) has made the first deliveries of COVAX-19 vaccine by autonomous drone. The delivery of approximately 2.5 million doses began this week in Ghana.



3.2 Russian disinformation campaign against Pfizer and other vaccines

[The Wall Street Journal reports](#) that Russian intelligence agencies are trying to undermine confidence in Pfizer's and other Western vaccines, using online publications that have questioned the vaccines' development and safety.

The article reports that there are Russian websites linked to Russian intelligence services publishing false information questioning vaccine safety and efficacy.

3.3 Cyprus to accept vaccinated Britons

[The New York Times](#) reports that: "Cyprus has announced a plan to allow vaccinated residents of Britain to visit the island beginning in May, a further signal that countries, particularly those dependent on tourism, could resort to inoculation certificates to reopen their borders."

3.4 FDA warns against using ivermectin to treat or prevent COVID-19

The US Food and Drug Administration (FDA) has [issued guidance warning consumers](#) against using the antiparasitic drug ivermectin to treat or prevent COVID-19.

The agency says it issued the guidance in light of growing interest in the drug as a COVID-19 treatment and multiple reports of patients hospitalized or needing medical support "after self-medicating with ivermectin intended for horses".

Ivermectin, which is not an antiviral, has not been approved by the FDA for treating or preventing COVID-19, the guidance emphasized.

"Using any treatment for COVID-19 that's not approved or authorized by the FDA, unless part of a clinical trial, can cause serious harm," the FDA says.

12 MARCH 2021

1. FOCUS ON THE ASTRAZENECA VACCINE

1.1 France uses only quarter of AstraZeneca vaccine doses

On [3 March](#), [Reuters reported](#) that: "France has used only a quarter of its AstraZeneca COVID-19 vaccine doses, a health ministry official indicated on Tuesday, saying its utilisation rate stood at 24% as of Feb 28, well below a target set at 80%-85%.

"This compares with 82% for vaccines made by Pfizer/BioNTech and 37% for those made by Moderna."

1.2 What happened to the confidence in the AstraZeneca vaccine?

The [European Medicines Agency approved the AstraZeneca vaccine](#) for all adults in late January.

However, several European countries, including France and Germany, restricted its use in over-65s due to a lack of data about its effectiveness in older people. French President, Emmanuel Macron, said that the vaccine was "[quasi-ineffective](#)" in older age groups. Quoting an anonymous source in Germany's health ministry, the German newspaper Handelsblatt reported that the jab was [more or less ineffective in the elderly](#).

However, the [French](#) and [German](#) regulators have both now reversed their advice not to give the vaccine to over-65s. Data released by Public Health England, currently in a non-peer-reviewed pre-print version, found that in the over-80s, a single shot of either the AstraZeneca or Pfizer vaccine appears to be over 80% effective at preventing hospitalization.

There is no evidence that the French and German regulators' prevarications – as well as loose talk from politicians and bureaucrats – have undermined confidence in the AstraZeneca vaccine. German Chancellor, Angela Merkel, has said that there's now an "[acceptance problem](#)" with the vaccine.

The millions of unused AstraZeneca doses in France and Germany highlight that it is crucial to understand how fragile vaccine confidence is in some European countries and to make sure ill-advised comments do not undermine demand.

(Précise from an article in [The Conversation](#))

1.3 CEO, Pascal Soriot, continues to talk up the AstraZeneca vaccine

[The Guardian has published an article by Mr Soriot](#): "As discussed in our update on 9 March, the CEO of AstraZeneca is attempting to counter the (probably unwarranted) somewhat negative perception of the AstraZeneca COVID-19 vaccine. We have provided most of the statistical data presented by Mr Soriot in our previous article, so it will be summarised here.

"We at AstraZeneca, working with our partners in the multilateral COVAX initiative, are doing all we can to make sure people around the world have access to safe, effective COVID-19 vaccines, wherever they live and regardless of income level. AstraZeneca was the first global pharmaceutical company to lend its support to the initiative and our vaccine will be the single biggest contributor in the first half of this year.

"Recently, the WHO granted emergency use listing for the AstraZeneca vaccine, paving the way for its rapid rollout, including to low- and middle-income countries. In the past ten days, the first shipments of our vaccine have arrived in more than 30 countries and counting, including Ghana, Senegal, Rwanda, the Democratic Republic of the Congo, Cambodia, the Philippines and Moldova, with the aim of supplying 142 countries with hundreds of millions of doses of the vaccine over the coming months. This supply represents the first COVID-19 vaccine for many of these countries. For some, it will be their main source of vaccines.

"We have a growing and substantial body of data that demonstrates how effective this vaccine is. Recent [real-world data](#) from 1.1 million people in Scotland shows it is highly effective. It reduces the risk of being admitted to hospital because of COVID-19 by 94% after just one dose. These findings were backed by [data from Public Health England](#), which showed the very high effectiveness of our vaccine in vulnerable elderly members of society. Just in the last week in Europe, we have seen France, Germany and Sweden approving the AstraZeneca vaccine for people over 65.

"We made an early commitment to supply billions of doses around the world at no profit, irrespective of a nation's income level. If we stay the course, these highly effective vaccines will begin clearing the path towards something approximating normality throughout the course of this year. But we will only do this if we can make sure the vaccine is available to all. We continue to do everything in our power to make access to the vaccine broad, timely and equitable."

2. VACCINES, VARIANTS & COVID

2.1 Israel: 600 children given COVID-19 vaccination with no serious side-effects

[The Guardian reports](#) that hundreds of children in Israel between the ages of 12 and 16, who suffer from underlying conditions that make them vulnerable to coronavirus, have been given the Pfizer/BioNTech vaccination and have experienced no serious side-effects...

2.2 Sinovac's vaccine shows an 80-90% efficacy rate within two months after two shots

[The Global Times reports](#) on an interview with Yin Weidong (Yin), the CEO of Sinovac:

"Current figures show that the protection rate of Sinovac vaccines within two months after administering two shots is 80-90 percent, but the number of antibodies in recipients declines with time.

"We are now analyzing data on protection rates after six months as well as conducting experiments on administering the third injection to recipients to see if there is a higher protection level. Some results are expected to come out soon.

"Sinovac has expanded its annual production capacity to 2 billion doses and offered its inactivated vaccines to over 16 countries and regions."

2.3 US orders 100 million more doses of Johnson & Johnson COVID vaccine

[CBS News reports](#) that: "The Biden administration is purchasing an additional 100 million doses of Johnson & Johnson's coronavirus vaccine..."

"This order allows for the president to plan for the future and the latter part of the year,' Andy Slavitt, White House senior adviser for COVID-19 response, said during a briefing by the White House COVID-19 Response Team. 'This is war time, and as facts still emerge, it gives us maximum flexibility for our upcoming needs.'"

2.4 US now has enough excess doses ordered/optioned to help 1.5 billion people

[Sciencemag.org reports](#) on the over purchasing of COVID-19 vaccine by many high-income countries: "Like three dozen other countries, the United States contracted with multiple vaccine companies for several times the number of doses needed to cover its population. No one knew at the time which, if any, of the candidate vaccines would work or when they might prove safe and effective.

"But by now, most of the pre-purchased vaccines appear to offer solid protection—which means many countries will receive far more vaccine than they need.

"The excess doses the United States alone may have by July would vaccinate at least 200 million people.

Over the next year or two, US surplus doses and those from other countries could add up to enough to immunize everyone in the poorer nations that lack any secured COVID-19 vaccine."

Vaccines to spare—and share

These 11 countries alone have enough COVID-19 vaccine doses secured or optioned to immunize about 2.9 billion people beyond their own populations.

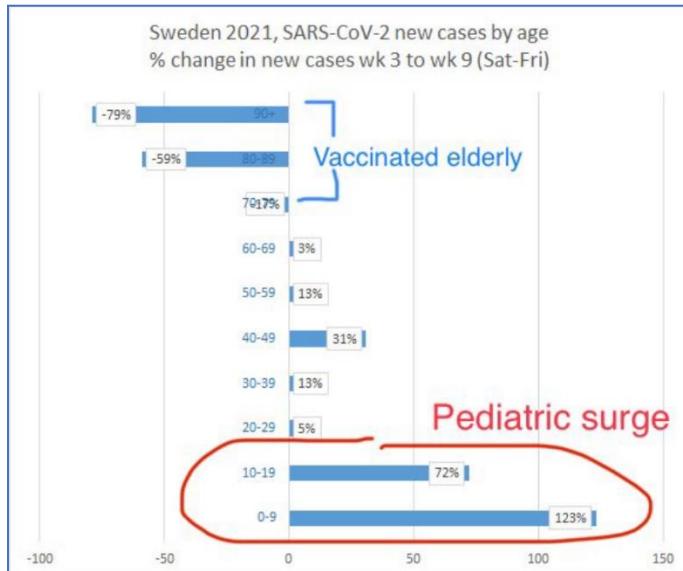
(*Based on secured and optioned vaccines, some still unauthorized for use, and whether they require one or two doses)

Country	Population (millions)	Population coverage (%)*	Extra people covered (millions)
Canada	37	609	188
United States	329	553	1490
Italy	60	422	193
United Kingdom	68	421	218
Germany	84	394	247
Poland	38	364	100
Spain	47	364	124
France	65	364	172
Australia	25	345	61
Mexico	128	158	74
Japan	127	124	31

UNICEF

2.5 New Swedish data shows surge in pediatric COVID-19 cases

[Eric Feigl-Ding reports on Twitter](#) that with the B.1.1.7 variant now causing about 50% of COVID-19 in Stockholm, there has been a significant increase in pediatric cases:



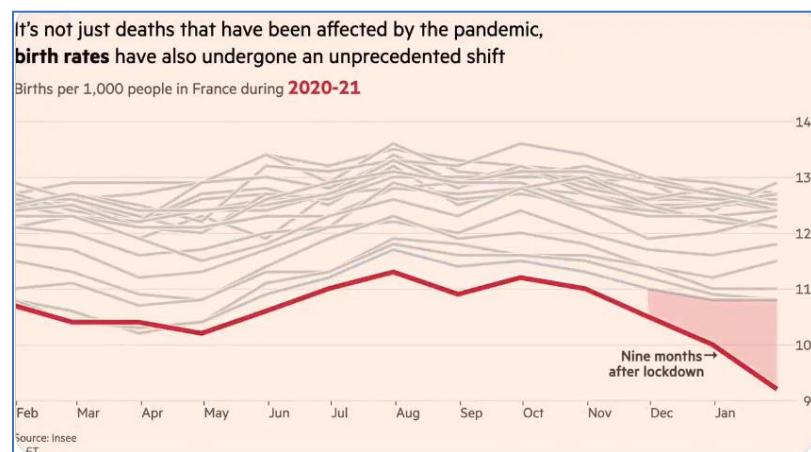
- Age 0-9: 123% increase
- Age 10-19: 72% increase

"This matches data in the UK... where B.1.1.7 is nearly completely dominant, and from Feb now have the highest positivity rate of all age groups - which was not previously the case."

"This also matches the data and warnings coming from Italy - health officials also concerned about the new sudden pediatric surge."

2.6 Pandemic blamed for falling birth rates across much of Europe

[The Financial Times](#) reports on the falling birth rates in Europe.



From FT: Birth rate in France nine months after the March 2020 lockdown

2.7 Of 1,400 people who developed “Long COVID”, 32% initially were asymptomatic

The [New York Times reports](#) that: “Many ‘Long COVID’ patients had no symptoms from their initial infection. An analysis of electronic medical records in California found that 32% started with asymptomatic infections but reported troubling after-effects weeks and months later.”