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INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE
Focussing on immunity and vaccine development

Produced by Dr Doug Quarry
18 December 2020

A. Vaccine Development & Approval

1. Pregnant women should be offered COVID-19 vaccine

Medscape reports (limited access site) that: “COVID-19 vaccines should not be withheld from people who are pregnant or lactating and want to be vaccinated, despite a lack of safety data in these populations, according to guidance from the Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal-Fetal Medicine.

“Pregnant women who opt not to receive the vaccine should be supported in that decision as well, a practice advisory from ACOG recommends.

"’Pregnant women who experience fever following vaccination should be counseled to take acetaminophen (aka paracetamol),’ the ACOG advisory notes.

“In addition, women do not need to avoid pregnancy after receiving the Pfizer-BioNTech COVID-19 vaccine, according to the CDC's interim clinical considerations for its use.”

2. FDA Advisory Panel recommends approval of the Moderna vaccine

The independent Advisory Panel of the US Food and Drug Administration (FDA) has recommended that the FDA approve distribution of the Moderna COVID-19 vaccine.

It is likely that the FDA will grant Emergency Use Authorization (EUA) on Friday, 18 December, EST.

3. Europe set to approve COVID-19 vaccine in Christmas week

Reuters reports that the European Medicines Agency (EMA) expert panel will convene on 21 December to evaluate the vaccine Pfizer/BioNTech vaccine.

“EU Commission President, Ursula von der Leyen said on Twitter: ‘(It is) Likely that the first Europeans will be vaccinated before end 2020.’"

EMA said in early December that it planned to issue its view on the Moderna candidate vaccine by 12 January.

4. Four vaccines in human clinical trials in Cuba

In a letter to the British Medical Journal, a doctor from the Ministry of Public Health has stated that there are four vaccines undergoing human clinical trials in Cuba. These include Soberana 01 and Soberana 02, both developed by the Finlay Vaccine Institute, whose trials began in August and November respectively.

More recently, two additional vaccines developed by the Center for Genetic Engineering and Biotechnology (CGEB) have been authorised to start human safety and efficacy trials. The first, called Mambisa (CGEB 669), will be given nasally and the second, called Abdala (CIGB 66), will be given intramuscularly.

Clinical trials analysis should be finished in January 2021, with predictions of vaccinations starting in Cuba as early as February.

5. WTO delays decision on waiver on COVID-19 drug and vaccine rights

Reuters reports that the World Trade Organization delayed a decision on a proposal to waive intellectual property rules for COVID-19 drugs and vaccines.

“Big Pharma” has rejected an idea proposed by India and South Africa that would grant compulsory licensing of the vaccines and drugs allowing generic or other manufactures to make the new products.

The proposal is opposed by Western countries, including Britain, Switzerland and the United States, which have strong domestic pharmaceutical industries.

6. With and without Pfizer and Moderna vaccination is like “Night and Day”

Vincent Rajkumar, Editor in Chief, Blood Cancer Journal, has on Twitter combined data from the Pfizer Phase 3 trials and the FDA briefing documents for the Moderna trials to produce this impressive table showing the number of COVID cases when data from the two vaccine trials is combined.

“Night and Day”, he calls it!

Vaccine	Vaccine Arm	Placebo Arm
Pfizer/BioNTech (n=36523)	8	162
Moderna (n=27817)	11	185
Combined (n=64340)	19	347

7. Singapore approves Pfizer/BioNTec vaccine

Singapore has become the seventh nation to approve Pfizer's COVID-19 vaccine and expects to receive the first shipment by the end of December.

The vaccine will be given to all citizens and long-term residents for free, and Singapore predicts that there will be enough vaccine supply for everyone by late 2021.

8. Sputnik V vaccine efficacy is 91.4%, lower than original report of 96.2%

The Moscow Times reports that Russia's Sputnik V coronavirus vaccine has an efficacy of 91.4%

The Gamaleya National Center of Epidemiology and Microbiology in Moscow that developed Sputnik V said the data was obtained 21 days after volunteers received the first dose of the two-shot vaccine.

The latest 91.4% figure is lower than its previously reported efficacy 96.2%.

9. AstraZeneca to trial use of one of the Sputnik V adenovirus vectors

According to the Sputnik V website, AstraZeneca has accepted a proposal from the Russian Direct Investment Fund (RDIF) to begin clinical trials of its vaccine in combination with Sputnik V's human adenoviral vector type Ad26. This research will allow AstraZeneca's scientists to study the possibility of boosting their vaccine's efficacy by using different vectors for each dose, as Sputnik V does. This research will begin in December 2020.

10. China's COVID-19 vaccine development and availability

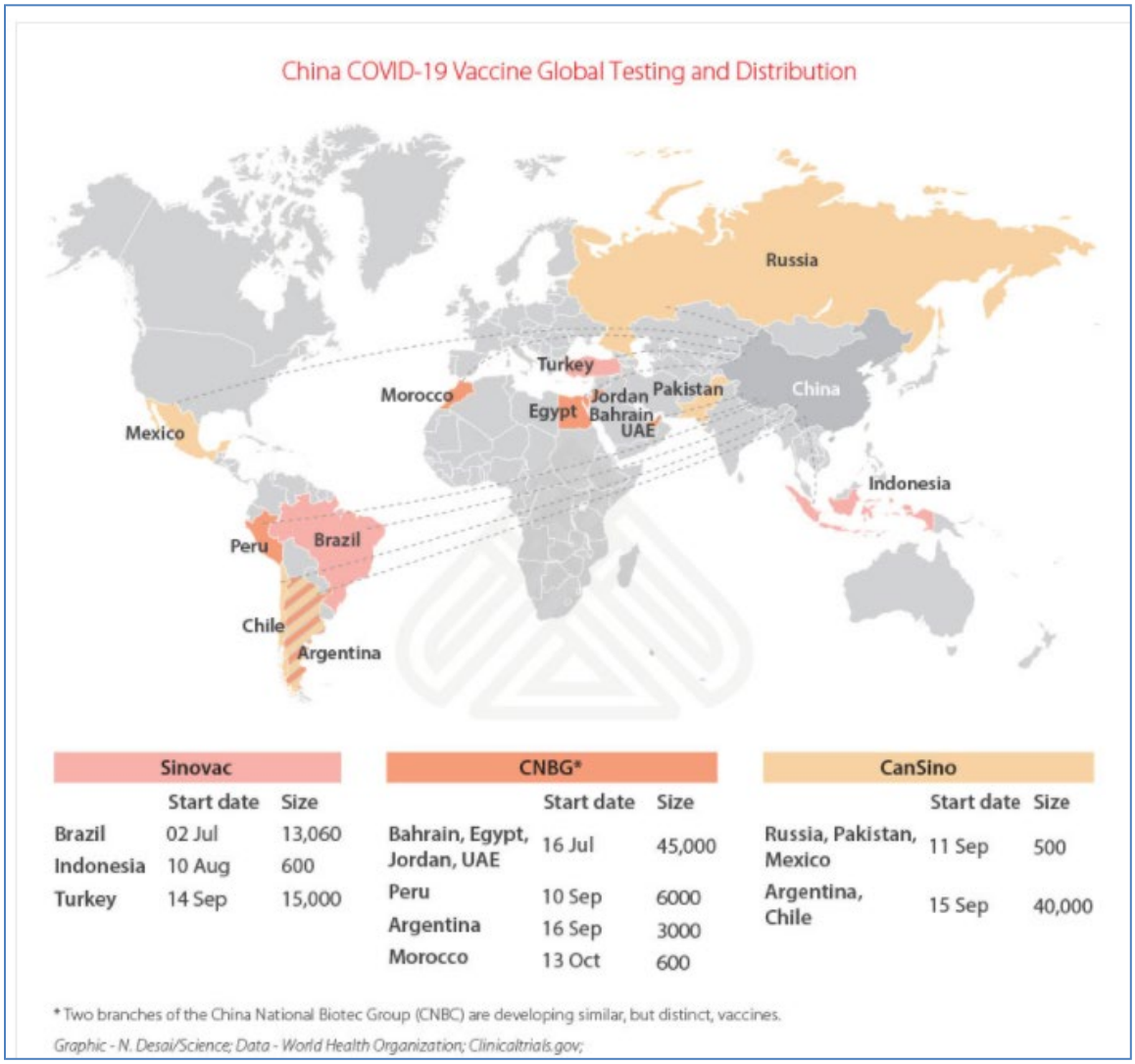
China Briefing reports on China's vaccine development and availability.

- Having largely controlled coronavirus, there has been less urgency for China to vaccinate its population. Herd immunity is expected to develop over the longer term
- In an outbreak, ring-fence vaccination methodology could be employed
- China's COVID-19 vaccines are expected to be manufactured in bulk and exported in 2021

The three main vaccine producers are Sinovac, CNBG and CanSino.

- **Sinovac and CNBG:** Killed virus
- **CanSino:** Human adenoviral vector (Ad5)

China's global vaccine testing and distribution



B.

11. **India is critical to the global supply of COVID vaccine**

India manufactures more than 60% of the world's vaccines. Its $40 billion pharmaceutical industry is currently freeing up capacity, to be able to ramp up COVID vaccine manufacture, reports Reuters.

While its $40 billion pharmaceutical sector is not yet involved in the production of the expensive Pfizer and Moderna vaccines, Indian companies are preparing to produce eight, more affordable COVID vaccines, including AstraZeneca's Covishield, called the "vaccine for the world" by its developers.

The Serum Institute of India (SII), the world's biggest vaccine maker, has already stockpiled more than 50 million doses of the AstraZeneca vaccine, as it awaits emergency-use approvals from both British and Indian authorities.

SII plans to make a total of 400 million doses of Covishield by July and is setting up new production lines to roll out one billion shots a year.

12. Possible AstraZeneca US EUA application in late January

Reuters reports that Professor Adrian Hill, who oversees the Oxford/AstraZeneca COVID-19 vaccine research and development, said that their vaccine may not be available in the US until mid-2021 if regulators wait for the end of their vaccine trial. Dr Hill said he hoped that the US Food and Drug Administration (FDA) would review their trial data at the end of January 2021.

Moncef Slaoui, Chief Adviser for the U.S. Operation Warp Speed vaccine program, said last week that a request for US Emergency Use Authorization by AstraZeneca could come in late January.

B. Vaccine Distribution

1. Africa CDC head calls on rich nations to share excess COVID-19 shots

John Nkengasong, the Head of Africa Centres for Disease Control and Prevention (CDC) has said that countries that have ordered more COVID-19 vaccines than they need should consider distributing excess doses to Africa.

"'Some countries have got like three times to four, five times more than what they need,' Nkengasong told a news briefing."

2. Canada to donate excess COVID vaccines to lower-income countries

Justin Trudeau, Prime Ministers of Canada, has announced that Canada will provide COVID vaccine free-of-charge to every Canadian. Canada has also ordered more vaccines per capita than any other nation however the country is planning to donate excess supply to impoverished countries.

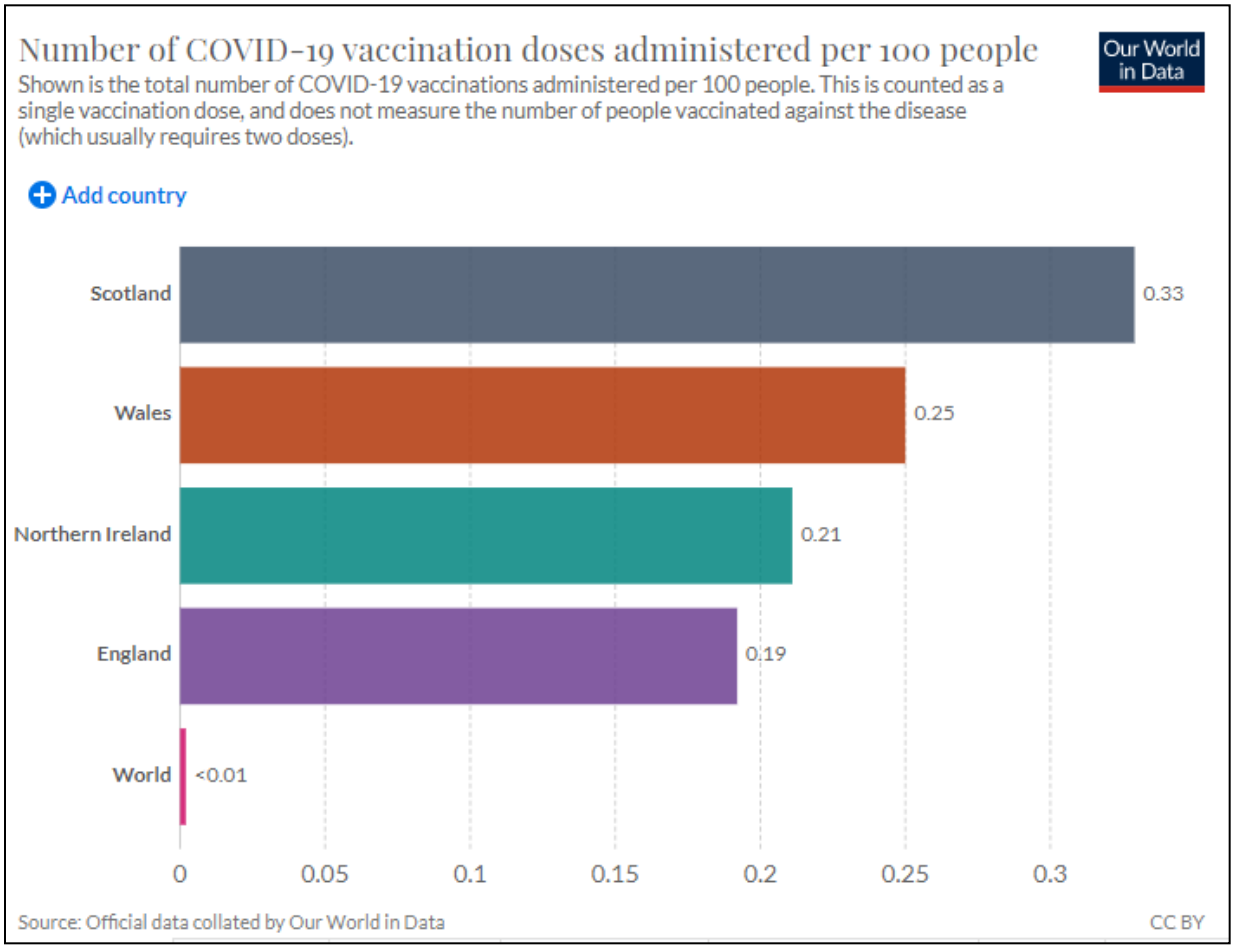
In addition, Mr Trudeau said that Canada will develop a compensation program for Canadians who suffer an adverse reaction to (any) vaccine – including COVID-19 vaccines.

3. FDA says pharmacists may use the extra doses in Pfizer coronavirus vaccine vials

The Washington Post reports that the US Food and Drug Administration (FDA) announced on 16 December that pharmacists can draw additional doses from vials of the Pfizer coronavirus vaccine.

This comes after pharmacists noticed vials contain more than the expected five doses.

4. Scotland leads the way on vaccinations



5. How the US should best use the first 40 million COVID vaccine doses

By the end of 2020, the US Government hopes to have close to 40 million doses of COVID-19 vaccine. It plans to distribute half of those in December and hold back the other half to give the same people their second dose of the two-shot regimen.

However, Dr. Scott Gottlieb, a Pfizer board member, and US Food and Drug Administration Commissioner from 2017-2019 disagrees. Gottlieb told USA Today that he would vaccinate 35 million people now and presume the second doses will be available when people need them. He says that in that way, a lot more people can be protected

"'We should get as many shots in our arms as possible right away. The idea that we need to cut [the number of people being vaccinated] in half and give half of it now and hold on to the other half [of the vaccines] so we have supply in January to get the second dose … I just fundamentally disagree with that.'"

C. Outbreaks and Epidemiology

1. WHO comments on new strain of COVID which has emerged in UK

The World Health Organisation (WHO) says its “virus evolution working group” is studying a new variant [N501Y] of SARS-CoV-2 that has emerged in the United Kingdom. However it says there is no evidence the strain behaves differently to existing types of the virus.

"We are aware of this genetic variant reported in 1,000 individuals in England," said Mike Ryan, Executive Director of the World Health Organization's Health Emergencies Programme, at the WHO Press Conference on 14 December 2020. [Dr Ryan speaks to this issue at about 41 minutes]

"Authorities are looking at its significance. We have seen many variants, this virus evolves and changes over time," he said.

Dr. Maria Van Kerkhove, WHO Technical Lead COVID-19, then explained that all variants of SARS-CoV-2 are subject to rigorous international evaluation. [Dr. Van Kerkhove follows Dr Ryan]

D. COVID Testing

1. FDA issues EUA for BinaxNOW home antigen test

Second home test for coronavirus approved in two days

On 16 December the FDA issued an Emergency Use Authorization (EUA) for the BinaxNOW COVID-19 antigen test for at-home use **with a prescription**. BinaxNOW is a lateral flow antigen test that detects fragments of proteins from SARS-CoV-2 from a nasal swab sample.

BinaxNOW is authorized for use with self-collected samples for people 15 years or older and who are suspected of having COVID-19 by a health care provider within the first seven days of symptom onset.

The BinaxNOW test is being offered in partnership with eMed Labs, a telehealth service that will take users step-by-step through the sample collection process, explain how to perform the test, and provide assistance in reading and understanding the results.

This comes a day after the FDA issued an EUA for the Ellume COVID-19 Home Test, that **does not need a prescription**. Ellume is a rapid, lateral flow antigen test, a type of test that runs a liquid sample along a surface with reactive molecules.

In testing, the Ellume COVID-19 Home Test correctly identified 96% of positive samples and 100% of negative samples in individuals with symptoms.
In people without symptoms, the test correctly identified 91% of positive samples and 96% of negative samples, the FDA said.

The Chief Executive of Ellume, the Australian company that makes the test, said only 100,000 of them will be distributed at first. The company plans to ramp up production to about 1 million tests by mid-2021.

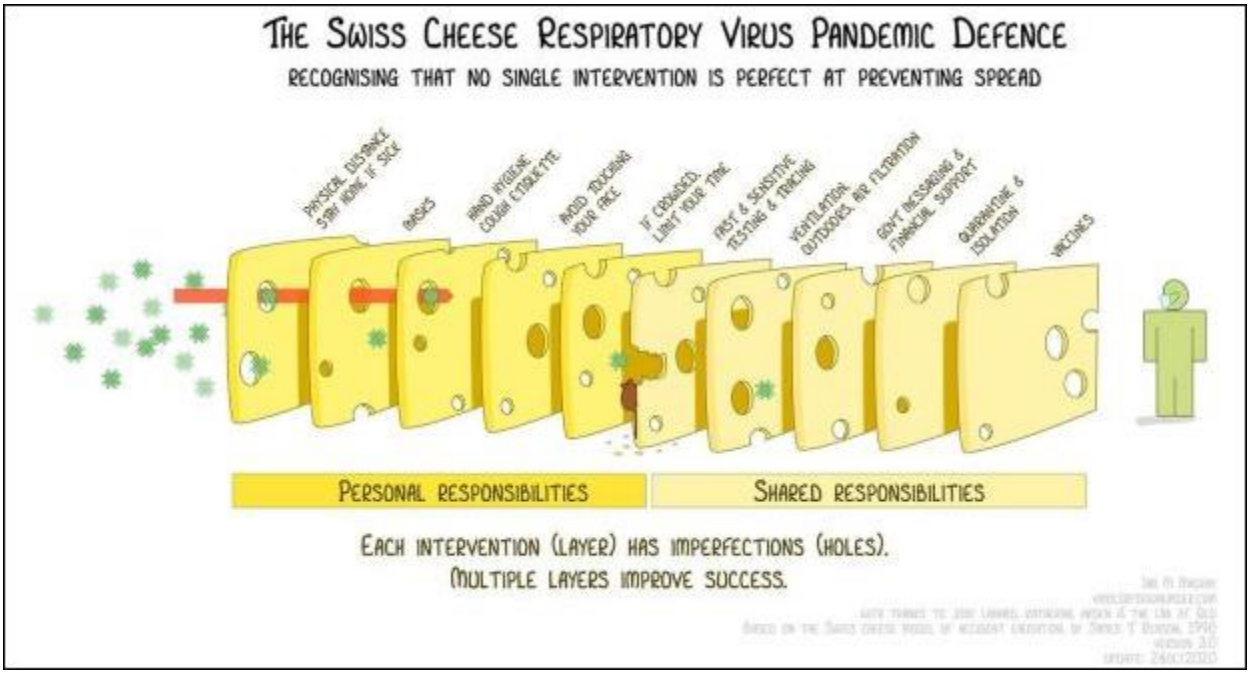
International SOS Comment: It is encouraging to see COVID-19 home antigen tests becoming available. Conceptually these antigen tests should help diagnose a person's "contagiousness".

E. NEWS

1. The Swiss cheese model of COVID-19 defence

Associate Professor Ian Mackay**, along with his Twitter community, has been improving the "Swiss Cheese Respiratory Virus Pandemic Defence" over several months.

In this latest version, it organises slices into personal & shared responsibilities. Professor Mackay advises to think that all the slices are important, rather than any single layer being most important.



** Ian Mackay is a virologist at the University of Queensland. He is also a Supervising Scientist in Queensland Health, supporting the detection and characterization of rare and emerging viral threats to public and environmental health.

2. "Stop Swapping Air" COVID campaign

Dr. Michael Osterholm, Director of the US Center for Infectious Disease Research and Policy (CIDRAP) highlighted in a briefing that the most important action to stop the spread of COVID-19 was to "stop swapping air".

"'It's clear that public health messaging is having, at best, limited impact on the transmission of the virus,' Osterholm said. 'What I kept hearing from people in the public is "what should we be doing?" People were confused about the mode of transmission.'"

CIDRAP has now launched an eight-week "Stop Swapping Air" public service messaging campaign in partnership with Clear Channel Communications, an outdoor billboard advertising company.

Photo: Clear Channel Communications

3. COVID lockdown of housing towers in Melbourne breached human rights

The Victorian Ombudsman has found the State Government breached human rights laws when it locked down nine public housing towers in inner Melbourne after a coronavirus outbreak in early July, reports the New Daily.

Health officials had agreed to the need for a lockdown on 4 July. They expected it would start the following day, which would give them time for planning food supplies and other logistics.
However, Victorian Premier, Daniel Andrews announced the lockdown of the towers in North Melbourne and Flemington would commence that day at 4pm.

"'In my opinion… the action appeared to be contrary to the law,' the Ombudsman said. 'The rushed lockdown was not compatible with the residents' human rights, including their right to humane treatment when deprived of liberty.'"

4. Twitter bans harmful false claims about COVID-19 vaccinations

"Twitter said on Wednesday that users will be required to remove new tweets that advance harmfully false or misleading claims about COVID-19 vaccinations, in an expansion of its rules on coronavirus misinformation", Reuters reports.
"The social media company said in a blog post that users could be required to remove tweets with false claims that suggest vaccines are 'used to intentionally cause harm to or control populations, including statements about vaccines that invoke a deliberate conspiracy.'"

5. WTO delays decision on waiver on COVID-19 drug and vaccine rights

Reuters reports that the World Trade Organization delayed a decision on a proposal to waive intellectual property rules for COVID-19 drugs and vaccines.

"Big Pharma" has rejected an idea proposed by India and South Africa that would grant compulsory licensing of the vaccines and drugs allowing generic or other manufactures to make the new products.

The proposal is opposed by Western countries, including Britain, Switzerland and the United States, which have strong domestic pharmaceutical industries.

6. COVID-19 vaccines: Preparing for patient questions

Medscape (locked article), a website providing access to medical information for clinicians, asked two experts, Krutika Kuppalli MD*** and Angela Rasmussen PhD****, what questions clinicians may expect about COVID vaccines and what evidence-based - as well as compassionate - answers might look like.

The questions and answers are provided here in full.

Q: Will this vaccine give me COVID-19?

"There is not an intact virus in there," Rasmussen says. The mRNA-based vaccines cannot cause COVID-19 because they don't use any part of the coronavirus itself. Instead, the Moderna and Pfizer vaccines contain manufactured mRNA molecules that carry the instructions for building the virus' spike protein. After vaccine administration, the recipient's own cells take up this mRNA, use it to build this bit of protein, and display it on their surfaces. The foreign protein flag triggers the immune system response.

The mRNA does not enter the cell nucleus or interact with the recipient's DNA. And because it's so fragile, it degrades quite quickly. To keep that from happening before cell entry, the mRNAs are cushioned in protective fats.

Q: Was this vaccine made too quickly?

"People have been working on this platform for 30 years, so it's not that this is brand-new," Kuppalli says.

Researchers began working on mRNA vaccines in the 1990s. Technological developments in the last decade have meant that their use has become feasible, and they have been tested in animals against many viral diseases. The mRNA vaccines are attractive because they're expected to be safe and easily manufactured from common materials. That's what we've seen in the COVID-19 pandemic, the US Centers for Disease Control and Prevention (CDC) says on its website. Design of the spike protein mRNA component began as soon as the viral genome became available in January.

Usually, rolling out a vaccine takes years, so less than a year under a program called Operation Warp Speed can seem like moving too fast, Rasmussen acknowledges. "The name has given people the impression that by going at warp speed, we're cutting all the corners. [But] the reality is that Operation Warp Speed is mostly for manufacturing and distribution."

What underlies the speed is a restructuring of the normal vaccine development process, Kuppalli says. The same phases of development —animal testing, a small initial human phase, a second for safety testing, a third large phase for efficacy — were all conducted as for any vaccine. But in this case, some phases were completed in parallel, rather than sequentially. This approach has proved so successful that there is already talk about making it the model for developing future vaccines.

Two other factors contributed to the speed, say Kuppalli and Rasmussen. First, gearing up production can slow a rollout, but with these vaccines, companies ramped up production even before anyone knew if the vaccines would work — the "warp speed" part. The second factor has been the large number of cases, making exposures more likely and thus accelerating the results of the efficacy trials. "There is so much COVID being transmitted everywhere in the United States that it did not take long to hit the threshold of events to read out phase 3," Rasmussen says.

Q: This vaccine has never been used in humans. How do we know it's safe?

The Pfizer phase 3 trial included more than 43,000 people, and Moderna's had more than 30,000. The first humans received mRNA-based COVID-19 vaccines in March. The most common adverse events emerge right after a vaccination, Kuppalli says.

As with any vaccine that gains approval, monitoring will continue.

UK health officials have reported that two healthcare workers vaccinated in the initial rollout of the Pfizer vaccine had what seems to have been a severe allergic response. Both recipients had a history of anaphylactic allergic responses and carried Epi-Pens, and both recovered. During the trial, allergic reaction rates were 0.63% in the vaccine group and 0.51% in the placebo group.

As a result of the two reactions, UK regulators are now recommending that patients with a history of severe allergies not receive the vaccine at the current time.

Q: What are the likely side effects?

So far, the most common side effects are pain at the injection site and an achy, flu-like feeling, Kuppalli says. More severe reactions have been reported, but were not common in the trials.

Rasmussen notes that the common side effects are a good sign, and signal that the recipient is generating "a robust immune response."

"Everybody I've talked to who's had the response has said they would go through it again," Kuppalli says. "I definitely plan on lining up and being one of the first people to get the vaccine."

Q: I already had COVID-19 or had a positive antibody test. Do I still need to get the vaccine?

Rasmussen says that there are "too many unknowns" to say if a history of COVID-19 would make a difference. "We don't know how long neutralizing antibodies last" after infection, she says. "What we know is that the vaccine tends to produce antibody titers towards the higher end of the spectrum," suggesting better immunity with vaccination than after natural infection.

Q: Can patients of color feel safe getting the vaccine?

"People of color might be understandably reluctant to take a vaccine that was developed in a way that appears to be faster [than past development]," says Rasmussen. She says physicians should acknowledge and understand the history that has led them to feel that way, "everything from Tuskegee to Henrietta Lacks to today."

Empathy is key, and "providers should meet patients where they are and not condescend to them." Kuppalli agrees. "Clinicians really need to work on trying to strip away their biases."

Thus far there are no safety signals that differ by race or ethnicity, according to the companies. The Pfizer phase 3 trial enrolled just over 9% Black participants, 0.5% Native American/Alaska Native, 0.2% Native Hawaiian/Pacific Islander, 2.3% multiracial participants, and 28% Hispanic/Latinx. For its part, Moderna says that approximately 37% of participants in its phase 3 trial come from communities of color.

Q: What about children and pregnant women?

Although the trials included participants from many different age groups and backgrounds, children and pregnant or lactating women were not among them. Pfizer gained approval in October to include participants as young as age 12 years, and a Moderna spokesperson told Medscape that the company planned pediatric inclusion at the end of 2020, pending approval.

"Unfortunately, we don't have data on pregnant and lactating women," Kuppalli says. She hopes that public health organizations such as the CDC will address that in the coming weeks. Rasmussen calls the lack of data in pregnant women and children "a big oversight."

***Krutika Kuppalli, MD, Assistant Professor of Medicine in the Division of Infectious Diseases at the Medical University of South Carolina

****Angela Rasmussen, PhD, virologist and nonresident affiliate at Georgetown University's Center for Global Health Science and Security.