UGANDA MEDICAL ASSOCIATION WEBINAR

COVID-19 VACCINE DEVELOPMENT

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Scope of the presentation

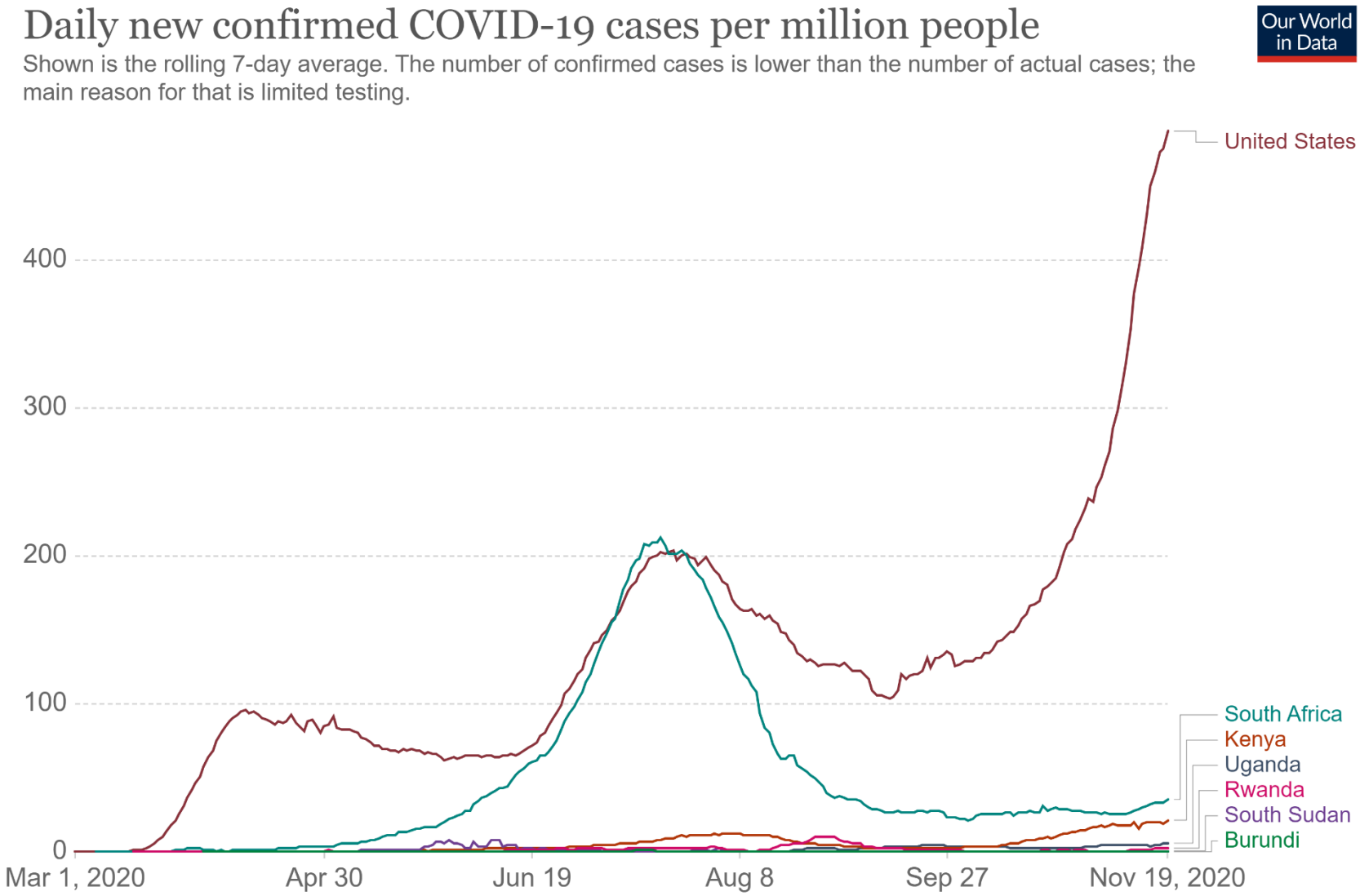
- Review current burden of COVID-19
- Review of the journey of vaccine development for COVID-19
- Reflect on the bottlenecks to current vaccine development efforts

Disclosure

Relationships with commercial interests:

- **NONE**
- **No conflict of interest**

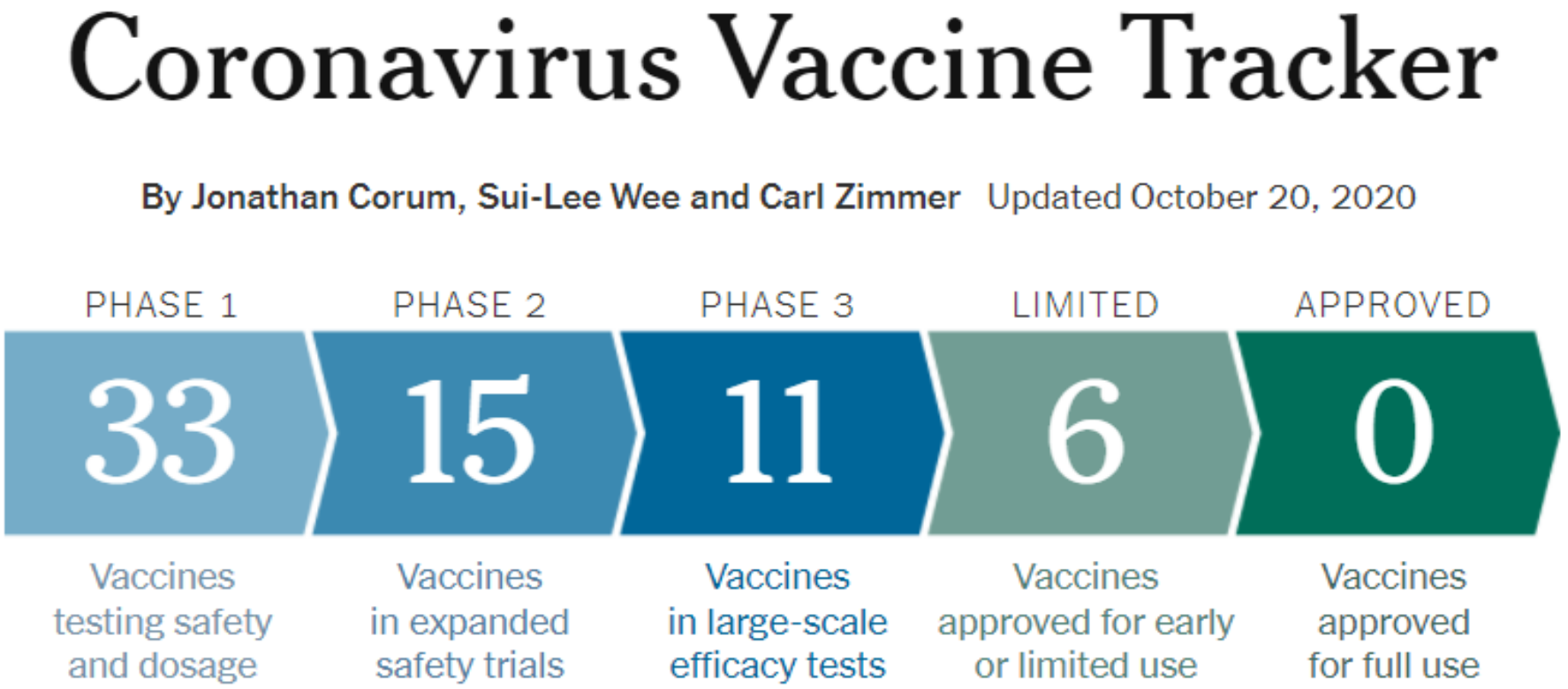
Current COVID-19 Burden - Cases



Background – Vaccine development

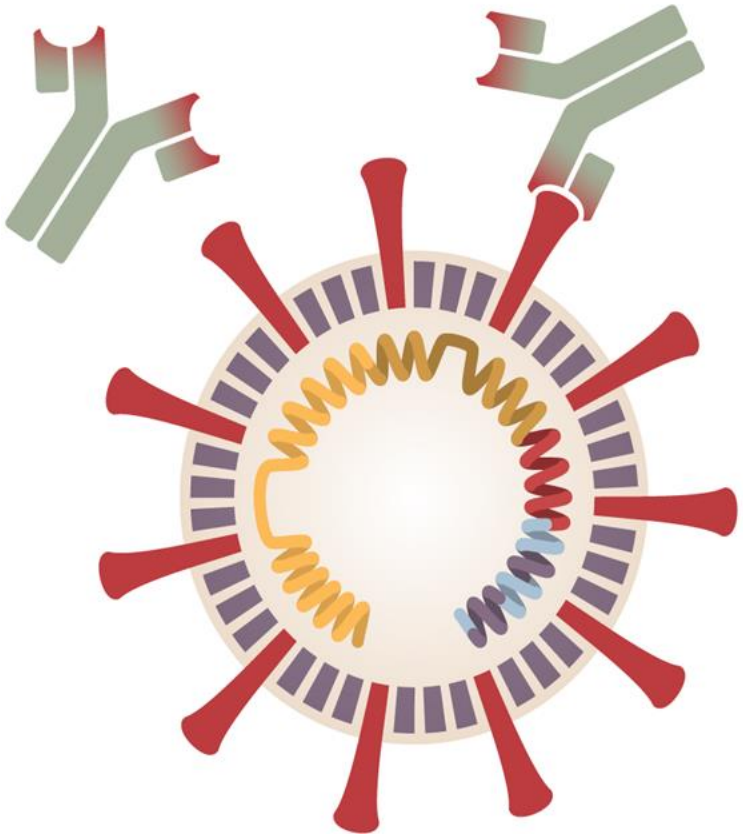
- The race to find vaccine is on.
- Immunization currently prevents 2-3 million deaths every year - There are now vaccines to prevent > 20 diseases.
- There are currently > 100 COVID-19 vaccine candidates under development.
- When a safe and effective vaccine is found, COVAX (led by WHO, GAVI and CEPI) will facilitate the equitable access & distribution of these vaccines in all countries. People most at risk will be prioritized.

48 vaccines currently in clinical trials on humans, & at least 89 preclinical vaccines are under active investigation in animals



Vaccine development work

- Work began in Jan 2020 with the deciphering of the SARS-CoV-2 genome.
- The first vaccine safety trials in humans started in March, & now 10 have reached the final stages of testing.
- Some of these trials will fail, and others may end without a clear result.



The Process

PRECLINICAL PHASE:

- Test a new vaccine on cells and then give it to animals such as mice or monkeys to see if it produces an immune response. We have confirmed 89 COVID preclinical vaccines in active development.

PHASE 1 SAFETY TRIALS:

- Give the vaccine to a small number of people to test safety and dosage as well as to confirm it stimulates the immune system.

PHASE 2 EXPANDED TRIALS:

- Give the vaccine to hundreds of people split into groups, such as children and the elderly, to see if the vaccine acts differently in them. These trials further test the vaccine's safety and ability to stimulate the immune system.

The Process

PHASE 3 EFFICACY TRIALS:

- Scientists give the vaccine to **thousands of people** and wait to see how many become infected, compared with volunteers who received a placebo.
- In June, the F.D.A. asked for evidence that vaccines can ***protect at least 50 percent of those who receive it.***
- In addition, Phase 3 trials are large enough to reveal evidence of relatively rare side effects that might be missed in earlier studies.

EARLY OR LIMITED APPROVAL:

- China and Russia have approved vaccines without waiting for the results of Phase 3 trials. *The rushed process has* ***serious risks.***

The Process

APPROVAL:

- Regulators in each country review the trial results and decide whether to approve the vaccine or not. During a pandemic, a vaccine may receive emergency use authorization before getting formal approval. Once a vaccine is licensed, researchers continue to monitor people who receive it to make sure it's safe and effective.

COMBINED PHASES:

- One way to ***accelerate*** vaccine development is to combine phases.
- Some coronavirus vaccines are now in Phase 1/2 trials, for example, in which they are tested for the first time on hundreds of people.

PAUSED:

- If investigators observe worrying symptoms in volunteers, they can put a trial on pause. ***After an investigation, the trial may resume or be abandoned.***

FDA strict guidelines to coronavirus vaccine makers seeking early approval

- Proof an experimental vaccine is at least 50% effective
- Vaccine makers to follow volunteers for a median of two months after the final dose- two shots spaced three to four weeks apart.
- Document at least five cases of severe COVID-19 observed in the participants who have received a placebo, - in order to determine the risk of respiratory disease induced by vaccination — a key safety worry for both developers and regulators.

Vaccine Types

What will a vaccine do:

- Produce antibodies against SARS-CoV 2?
- Prevent infection with SARS-CoV 2?
- Prevent severe infection with SARS-CoV 2?
- Make infection with SARS CoV 2 worse?

RNA vaccine

- While conventional vaccines work by presenting the body's immune system with the inactivated real virus or antigens derived from it, injecting mRNA into cells means that they produce the required viral proteins directly inside the human body.
    - "A big advantage of mRNA vaccines is that scientists can skip the laboratory production of proteins by directly injecting the molecular instructions to make the protein into the human body itself."
- In this case the RNA sequence is taken from the SARS-CoV-2 virus genome, stimulating an immune response that should later stop the COVID-19 disease.
    - One advantage to mRNA vaccines is a cheaper, faster production process, making them potentially the most scalable to tackle a global pandemic.

RNA vaccine

- Companies trying this approach:
  - Moderna , the Imperial College, London; the German-based company BioNTech, which is working in alliance with the drugs giant Pfizer; and CureVac, another German-based company. A Chinese consortium from Fudan University, Shanghai JiaoTong University and RNACure Biopharma is employing a second strategy of using mRNA to create “virus-like particles” in the body to activate an immune response.
- Moderna’s vaccine (mRNA-1273) was the first to be injected into human volunteers, in mid-March.
  - May 18 - announced that its vaccine candidate had stimulated an immune response with the production of neutralizing antibodies in eight human volunteers in its Phase I trial generated global media coverage and a stock market rally.
  - Moderna announced the start of its Phase 2 trial on mRNA-1273 in 600 human volunteers on May 29.
  - on 11 June it announced that a Phase 3 trial with 30,000 participants would begin in July.
  - Manufacturing capacity is being lined up for 500 million to one billion doses by 2021.
  - The company is confident enough to have announced a partnership – on 25 June – with a production agreement signed “to support production of an initial 100 million doses of the vaccine candidate intended to supply the U.S. market starting in the third quarter of 2020”, and hundreds of millions of additional doses thereafter.

RNA vaccine

- CureVac announced “positive pre-clinical results” for its lead COVID vaccine candidate on May 14 and received approval to start a Phase 1 clinical trial on June 17 in Germany and Belgium.
- BioNTech announced on May 5 that volunteers for its Phase 1/2 study have begun taking their first doses of its mRNA vaccine candidate, called BNT162, in the United States and Germany.

ANY DRAWBACKS?

- No mRNA vaccines have ever been used before, so failure is a big risk.
- Moderna’s mRNA vaccine did lead to some negative side-effects in some of the trial volunteers. Grade 3 reactions were observed – in one case including pain, nausea and high fever .
- Moderna has since announced it will be dropping the highest doses in the next phase of the trial as this was where the most adverse reactions were observed.

MODERNA RNA VACCINE

- Early data from their trial.
- There's more work to be done before they'll know if the vaccine really is safe and effective. And even if Moderna's vaccine gets the green light from the F.D.A., it will take months to reach widespread distribution.
- The scientists randomly assigned volunteers to get either the Moderna vaccine or a placebo. The trial was blinded, placebo controlled meaning that neither the volunteers nor the people running the trial knew who got what.

MODERNA RNA VACCINE

- Moderna recruited 30,000 volunteers across the United States to participate in its trial.
  - A quarter of the participants are 65 years or older.
  - White people make up 63 percent of the volunteers; 20 percent are Hispanic; 10 % are Black; and 4% Asian Americans.

- The 95 people who got sick with Covid-19 reflect the diversity:
  - Fifteen were 65 or older.
  - The group also included 12 Hispanic volunteers, four Black participants, three Asian Americans and one multiracial person.
  - The efficacy and safety appeared the same in all of the subgroups. But researchers will have to wait for the trial to advance further to confirm this finding.

Pfizer's Vaccine

- Pfizer developed the vaccine with its partner BioNTech NOW report that its coronavirus vaccine is **95** percent **though initially they reported 90%** effective and had no serious side effects
- The data showed that the vaccine prevented mild and severe forms of Covid-19
- And it was 94 percent effective in older adults, who are more vulnerable to developing severe Covid-19 and who do not respond strongly to some types of vaccines.
- The trial results — less than a year after researchers began working on the vaccine — shattered all speed records for vaccine development, a process that usually takes years.

How do Moderna's early results compare with Pfizer's?

Pfizer provided less detail in its announcement last week on Nov. 9 than Moderna did on Monday, Nov. 16.
Pfizer's outside board of experts analyzed 94 volunteers and estimated that the effectiveness of its vaccine was over 90 percent.
They did not specify how many people who got sick had received the vaccine or the placebo.

Nevertheless, the estimates for the two vaccines are clearly in the same ballpark. What's more, they both far exceed the F.D.A.'s requirement that coronavirus vaccines have an efficacy of more than 50 percent.

Pfizer did not report how many volunteers had severe Covid-19, or what fraction of those people got the vaccine. Findings like these are expected to come out in the next few weeks.

How do Moderna's early results compare with Pfizer's?

- The Pfizer and Moderna vaccines are similar not only because they use mRNA but also because they coax our cells to make the same viral protein, called spike.
  - Other vaccines that don't use mRNA also make the spike protein their target. The success of Moderna and Pfizer may bode well for them as well.

- Moderna vaccine is superie to Pizer vaccine in that
  - It can be kept at – 20 degrees temperature
  - Can be transported while frozen at - degrees c Pizers -7 degrees requirement
  - It is easier to distribute - favorable cold chain needs
  - Electiveness of 94.5 C – though now Pfizer has reported 95% -- higher than what they had earlier reported as 90%

How do Moderna's early results compare with Pfizer's?

- A number of teams have created vaccines based on another virus called an adenovirus, for example.
  - The adenovirus slips into cells, delivering the gene for the spike protein.
  - On Wednesday, a sponsor of a Russian vaccine announced that its adenovirus-based vaccine, called Sputnik V, was over 90 percent effective.
  - Outside experts wanted to see more data, however, because the announcement was based on just 20 sick volunteers — far fewer than in the Moderna and Pfizer trials.

- AstraZeneca and Johnson & Johnson are also conducting Phase 3 trials on adenoviruses that carry the spike protein gene.
  - And other companies, including Novavax and Medicago, are running advanced trials on vaccines that deliver the spike protein itself, or pieces of it, to the body.

What do the Pfizer and Moderna reports mean together?

- Pfizer and Moderna used the same basic design to build their vaccines.
- Both vaccines contain a genetic molecule called messenger RNA, which is wrapped in an oily bubble.
  - The bubble can fuse to a muscle cell and deliver the RNA. Encoded in that molecule are instructions for building a single coronavirus protein called spike.
  - When a vaccinated cell releases copies of the spike protein, the immune system learns to make antibodies against it.
- While scientists have investigated mRNA vaccines for years, no vaccine has yet been licensed as safe and effective to use in people.
- Neither trial has uncovered serious side effects from the vaccines, although studies on their safety are continuing.

What happens next?

- Both the Moderna and Pfizer trials are continuing to gather more data from large studies.
- The two companies expect to apply to the FDA in the next few weeks for an emergency use authorization to begin vaccinating the public.
- The F.D.A. will review the applications and consult with its own external committee of experts before making a decision.
- If it authorize the vaccines — as experts think it will — a committee at the Centers for Disease Control and Prevention will then make recommendations for who should be first to receive a vaccine.
- It’s possible that the distribution of one or both vaccines will begin by the end of the year.

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Thank you