

AMERICAN PUBLIC HEALTH ASSOCIATION
and
THE NATIONAL ACADEMY OF MEDICINE

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RESPONDING TO COVID-19: A SCIENCE-BASED APPROACH

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WEBINAR #9: THE ROAD TO IMMUNITY DURING
COVID-19: DEVELOPING & DISTRIBUTING A VACCINE

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WEDNESDAY
JUNE 10, 2020

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The webinar convened at 5:00 p.m.
Eastern Daylight Time, Paul A. Offit, MD,
Moderator, presiding.

PRESENT

PAUL A. OFFIT, MD, Director, Vaccine Education
Center and Attending Physician, Children's
Hospital of Philadelphia; Moderator

SETH BERKLEY, MD, Chief Executive Officer, Gavi,
The Vaccine Alliance

RICHARD J. HATCHETT, MD, Chief Executive
Officer, Coalition for Epidemic
Preparedness Innovations

JOHN R. MASCOLA, MD, Director, Dale and Betty
Bumpers Vaccine Research Center, National
Institute of Allergy and Infectious
Diseases

KATHLEEN M. NEUZIL, MD, MPH, FIDSA, Myron M.
Levine, MD Professor in Vaccinology and
Director, Center for Vaccine Development
and Global Health, University of Maryland
School of Medicine

ALSO PRESENT

VICTOR J. DZAU, MD, President, National Academy
of Medicine

SUSAN POLAN, PhD, Associate Executive Director,
Public Affairs, APHA

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P-R-O-C-E-E-D-I-N-G-S

5:00 p.m.

DR. POLAN: On behalf of the American Public Health Association and the National Academy of Medicine, I'm Susan Polan with APHA.

Today's webinar has been approved for 1.5 continuing education credits or CE, CHES, CME and CPH.

None of the speakers have any relevant financial relations to disclose.

Please note that if you to continue education credits you should have registered with first and last name. Anyone who wants credit must have their own registration and watch today's event in its entirety.

All of the participants today will receive an email within a few days from cpd@confex.com with information on claiming credits. And all online evaluations must be submitted by June 26th to receive their continuing education credit.

If you have questions or topics you'd

like us to address today for future webinars, please enter them in the Q&A box or email us at apha@apha.org.

If you experience technical difficulties during the webinar, please enter your questions also in the Q&A. Please pay attention to chat for announcements about how to troubleshoot.

This webinar will be recorded and available on covid19conversations.org within the next day or two. More information on this series can also be found on that website, as well as recordings of past webinars and the slides on the previous webinars.

Now I would like to introduce Dr. Victor Dzau, President of the National Academy of Medicine to provide some opening remarks.

DR. DZAU: Thank you, Susan, and good evening. I'm Dr. Dzau, the President of the National Academy of Medicine and welcome to the 9th webinar in the COVID-19 Conversation Series brought to you by the National Academy of Medicine

and the American Public Health Association.

The purpose of this series is to explore the state of science on COVID-19. To inform policy makers, public health and health care professionals, scientists, business leaders and the public.

I'd like to thank my co-sponsor and my good friend, APHA Executive Director Georges Benjamin. I'd also like to thank the co-chairs of webinar series advisory group, Carlos Del Rio of Emory University and Nicki Lurie, former Assistant Secretary for Preparedness and Response.

Now, today's webinar you're in for a treat. It will be a dynamic and up to date discussion on vaccines.

As you all know, the coronavirus is still very much with us. And is likely to remain with us for some time.

Through social distancing efforts we were able to slow down the spread. However, given the recent reopening and the many public events, including protests, we likely will see an increase

in cases again.

Furthermore, there has been increased cases in the South. In Brazil and Mexico. Given the global nature of the virus, I'm sure we'll continue to face threats on COVID-19 U.S. regardless of whether the virus has seasonality or not.

We all know the way to stop this virus is to achieve herd immunity. Therefore a vaccine is the ultimate solution.

Recently we've been hearing a lot of news about different promising vaccine candidates reaching different stages of development. The U.S. has developed a public private partnership called ACTIV, which you will hear about shortly. And U.S. is moving warp speed to secure vaccines with agreements with many companies in place.

Globally, you will hear also many countries are trying to do the same and you will hear about the global initiative called ACT Accelerator, which countries are coming together to address this problem collectively.

So, we want to be sure there is global equitable access to COVID-19 vaccine. But while we talk about global equity, we need to remember equity starts at home.

In the United States we are seeing stark racial disparities in terms of who gets sick, who is hospitalized and who dies from COVID-19 with Black and African-Americans, in particular, experiencing disproportionate bad outcomes.

We know there are already significant barriers to testing and treatment for people of color. We don't want to see those barriers perpetuated when there is a vaccine.

So I look forward to a discussion what we can do to ensure equitable access to a vaccine within our own borders and globally.

So today's panel we have an all-star cast, I can tell you that. They are just the world's experts in the area of vaccines.

They will cover a number of important areas including likelihood, that we will have a vaccine for COVID-19 by next year, early or later.

And they'll talk about this.

And of course, many other issues. So without further ado I'd like to introduce our moderator for today's webinar, Dr. Paul Offit.

Paul is a member of National Academy of Medicine and an internationally recognized expert in virology and immunology. He's advised the CDC on immunization practices. He is a founding Advisory Board Member of Autism Science Foundation and the Foundation for Vaccine Research.

Currently he's Director of Vaccine Education Center at Children's Hospital of Philadelphia and a professor of the University of Pennsylvania.

Paul, over to you. Thank you very much for taking this on.

DR. OFFIT: Thank you, Dr. Dzau. The purpose of today's webinar is for science and policy around vaccine development as it relates to the COVID-19 pandemic.

We will learn about what goes into developing a COVID-19 vaccine and hear about the

status of U.S. government vaccine initiatives and the state of global clinical trials. Along with distribution, to ensure equitable global access through conventional vaccine. An absolutely crucial consideration.

Next slide. So can we advance it? There we go, thank you.

So what I'm going to do, I just have two slides. I want to give kind of an overview of where things stand. Some of which may be repeated as we move on in this discussion.

The good news is every possible strategy that has ever been used to make a vaccine is being used to make this one. Because it is unclear which strategy will work the best.

In addition, there are several strategies that have never been used to make a vaccine before that will be used to make this one.

So for example, there are some groups are using a whole killed viral vaccine, like the inactivate polio vaccine, hepatitis A vaccine, rabies vaccine.

Others a live attenuated viral vaccine, like measles, mumps, rubella, varicella, one of the rotavirus vaccines.

Others still a purified viral protein. And that's one of the sort of bright spots here. We know the protein we're interested in, that spike protein that emanates from the surface of the virus that's associated with attaching the virus to the cells.

If we can prevent viral cell attachment we're going to be able to prevent a cell virus entry and disease, similar to the strategies we use to make the human papillomavirus vaccine or the hepatitis B vaccine.

In addition to vector vaccine where you essentially have a weakened virus into which you then genetically engineer the gene that codes for that surface protein. That spike protein.

Which is the way that the dengue vaccines and the Ebola vaccines are made there. In the dengue vaccine it was the yellow fever 17d strain that serves as the vaccine, the virus

template. And the for Ebola the vesicular stomatitis virus.

And then there were three other sort of novel strategies. One is to use a replication-defective adenovirus by replication defective.

What I mean is, the virus can't reproduce itself. It can't form new viral particles, but it can make proteins. And the protein that's been genetically engineered into these viruses like adenovirus 5, adenovirus 29, replication-defective simian adenoviruses, is that gene that codes for the spike protein.

And then we have two other novel strategies. One is messenger RNA which is, again, is the gene that codes for that surface protein that's then taken up by dendritic cells or macrophages. So your body makes then the protein, the spike protein of interest.

And then finally a DNA platform where, again, you're inoculated with DNA, the gene that codes for that surface protein that's then

transcribed to messenger RNA that's then translated to a protein of interest.

Next slide. So, typically when you make a vaccine, I'd say the average length of time is about 15 to 20 years.

And I was fortunate enough to be part of a team at Children's Hospital Philadelphia. They've created the rotavirus vaccine. That was a 26 year effort. That's a little longer than usual.

But there are -- so here I think it's very likely that we'll have a vaccine by the middle of next year, which would mean a time from having the virus in hand to actually having a commercial product of about one and a half years.

So, I'm going to go through sort of the typical vaccine development and how's that sort of contrasts with the current vaccine development strategies.

Typically people spend sometimes years doing animal model studies where you inoculate an animal, in this case SARS-CoV-2. Right now it

looks like the Syrian hamster is the best of the animal models.

And then that model mimics disease. So now you can look at your concept, whether it's an activated virus RNA vaccine or a DNA vaccine and then challenge your animal with that particular virus in interest to see whether or not it's protected. And more importantly, to look at the immune response because you can carefully dissect the immune response in an experimental animal in ways that you can't do it in people.

That's being very much truncated here. The numbers of animals are much smaller than typical, some groups aren't even doing animal model studies so that's one way in which things are truncated.

Now you do sort of dose ranging studies, often with hundreds of people, sometimes more, to make sure you have the right dose that you're interested in. Not too much, which therefore would make it a safety issue, not too little, which would be then an efficacy problem.

So again, often hundreds, and sometimes thousands of people have done it, Phase I, II trials. That's generally much smaller here.

The key thing is the Phase III study. All of the things that I've talked about before can be truncated or even arguably skipped for the animal model studies.

The Phase III trials have to be done. When people say the proof is in the pudding, the pudding is the Phase III study.

So, for RotaTeg, for example, and for RotaRix, rotavirus vaccines, those Phase III studies for prospected placebo controlled, three to four year, 11 country or more studies that probably cost somewhere in the \$350 million range to do those studies.

Now, those are big studies. Bigger than typical. The reason is, is that a previous rotavirus vaccine, RotaShield, was found to be a rare cause of the intestinal blockage called intussusception. So you were put in a position where you had to really rule out a relative adverse

event pre-licensure.

More typically, the studies that are done are something that you see, for example, with the human papillomavirus vaccine or the pneumococcal conjugate vaccine, the original seven-valence strain, where it's 30 to 35,000 people.

And that's really what's being recommended here. The National Institutes of Health ACTIV Group, which is a group that was put together to facilitate or accelerate the development of these vaccines by Dr. Francis Collins, the National Institute of Health, has basically recommended a baseline trial of 20,000 vaccines, 10,000 placebo recipients.

So at least you can rule out with that kind of 20,000 person vaccine study. At least a relatively uncommon side effect, and by having 10,000 placebo recipients, assuming you can have an adequate number of people who are sickened by the virus during these trials, you can then make a pretty clear comment about efficacy. Even

though you're not going to know duration of protection, at least you know sort of the degree of protection.

So, I'd like now to introduce our expert presenters. John Mascola is Director of the Vaccine Research Center at the National Institute of Allergy and Infectious Disease, U.S. National Institutes of Health.

His background is in infectious diseases, viral immunology, and vaccine research. He provides leadership to the scientific and clinical research activities of VRC and develops vaccine research programs for diseases of public health importance, including human immunodeficiency virus, influenza, Ebola/Marburg, malaria, Zika and SARS-CoV-2.

Dr. Kathleen Neuzil directs the University of Maryland School of Medicine, Center for Vaccine Development and Global Health. She has extensive experience in vaccine policy and is a member of WHO SAGE. The SAGE Group stands for Strategic Advisory Group of Experts on

Immunization.

Dr. Richard Hatchett is CEO of the Coalition for Epidemic Preparedness and Innovations, otherwise known as CEPI. A public private partnership that finances and coordinates the developments of vaccine against emerging infectious diseases.

Previously he served as the Chief Medical Officer and Deputy Director of the U.S. Biomedical Advance Research and Development Authority, otherwise known as BARDA, which has been instrumental in moving us forward on deciding which vaccines will go into the Warp Speed Program, which is basically a program whereby vaccines are made at-risk.

Meaning, not knowing whether they're proven safe, not knowing whether they're proven effective. But assuming if one or more are, that you can then roll that vaccine off the assembly line into people's arms fairly quickly.

Seth Berkley is CEO of Gavi, the Vaccine Alliance and Global Health Organization, dedicated

to improving access to vaccines in developing countries.

At Gavi he is leading efforts to vaccinate 300 million children in the next five years. Previously he served as founder and CEO of the International AIDS Vaccine Initiative.

So, Dr. Mascola, I turn it over to you lead the, kick things off here.

DR. MASCOLA: Thank you very much, Paul. And thank you, Victor, and the American Public Health Association and National Academy of Medicine for putting on this discussion.

So I'm going to start us off here. I'm going to show a few slides and give you all some background on vaccine development.

So, we can go to the next slide please. So, to start off, a little bit of background on the surface protein of SARS-CoV-2 that Paul mentioned.

So you can see on the left the transmission of electron micrograph that I think is unattributed but is widely available. And it very nicely shows where actually the main

coronavirus comes from when investigators first saw that crown or light sort of view of the virus and the surface protein.

We now know that surface protein to be the spike protein and scientists know that spike protein in atomic level of detail, as shown on the slide there. So we know exactly what the immune system sees when the immune system is trying to target the virus, in particular that spike protein.

So, just to recap what a vaccine does. It teaches the immune system to make antibodies that block the virus from infected the cells, but also a vaccine activates other immune responses that fight viral infection.

So, next slide please. I want to give just a couple examples. So these are examples not all-encompassing of the way we can approach vaccine development.

One is to take that surface protein as a subunit protein itself. So not the whole virus. Not a whole killed virus, but just a part of the virus, and make that the vaccine and inject that

into muscle.

The body sees that foreign protein, makes an immune response, and as you see on the right, antibodies and other types of responses. And hopefully those immune responses are protected.

That's a pretty classic approach. As was mentioned, we do that for hepatitis B and other viruses. Influenza.

But there are some newer approaches where there is some enthusiasm for but for which we don't have as much experience. These includes DNA and RNA.

And so I give an example of how that would work. We can put the gene for the spike protein into DNA or RNA. And then when that genetic material is used as a vaccine, it's injected into the muscle, the muscle takes up that genetic material and then the muscle cell makes the protein rather than injecting the protein directly itself.

But the end result is the same. The

immune system sees a foreign protein and makes an antibody in a cellular response against that.

Next slide. So here are some examples. This is not an all-inclusive set of examples but it gives one a sense of the types of approaches that are being considered.

And so we see, first on the left, a protein subunit vaccine schematic and the companies. Again, some of the major companies that are pursuing this approach include Novavax and Sanofi.

We see genetic vaccine approaches. That includes DNA and RNA. And some of the companies that are pursuing that, including Inovio and Moderna and Pfizer.

And then viral vector approaches. Like the Ebola vaccine that Paul mentioned, but also adenoviral vaccines in companies such as AstraZeneca, Janssen, and Merck pursuing those.

So there is a broad approach and there are more than these shown on the slide that really cover the various types of vaccine platforms that

you can envision for COVID vaccines.

Next slide. So this is a slide that shows the public private partnership that was mentioned, that's called ACTIV, Accelerating Therapeutic Interventions and Vaccines.

This was something that Dr. Collins at NIH established in April. And the idea of this partnership is to bring numerous groups that are interested in responding to COVID together, in a forum where they could interest, share information and plan responses.

That includes academic groups, U.S. government groups, philanthropic groups, biopharmaceutical groups, all talking together to share ideas on therapeutics. But in particular, here on vaccines and approaches to vaccines.

Next slide please. You may also have heard of operation Warp Speed. And this in particular is a U.S. government effort, if you read it, I'll just read a couple of the bullets there, a national program to accelerate development, manufacturing and distribution of COVID vaccines,

therapeutics and diagnostics.

And in particular for vaccines, this is a U.S. government group that will include the various organizations within U.S. government, CDC, FDA, NIH, and BARDA and DoD agencies, working together with the biopharmaceutical companies that have vaccine programs towards a goal of testing and producing vaccines in response to the COVID epidemic.

And you can see there that Dr. Moncef Slaoui has been asked to be the chief scientific advisory, and General Gustave Perna as the chief operating officer.

Next slide. Importantly, when we think about vaccine development, there are some principles that have elucidated in a discussion by Larry Corey and myself, and Tony Fauci and Francis Collins. And I'll just read that. I think the text there is important.

So the full development pathway for an effective vaccine for SARS-CoV2 will require that industry, government and academia collaborate in

unprecedented ways, each adding their individual strengths

So we discuss the collaborative platform for conducting harmonized, randomized controlled vaccine efficacy trials. This mechanism aims to generate essential safety and efficacy data for several candidates in parallel, so as to accelerate the licensure and distribution of multiple vaccine platforms and vaccines, to protect against COVID-19.

Next slide please. And I'll show you just schematically what we mean by harmonized Phase III trials.

So there is an intent and perhaps a necessity to test more than one vaccine. And certainly we'd like to have several successful efficacious vaccines.

And to do that, certain principles are espoused in this piece and in our U.S. government approach harmonizing the clinical trials so that the design of the clinical trials are similar using a collaborating set of clinical trials networks

using a data safety monitoring board and having overarching statistical support for the trials that are done.

So this allows us and the public and the National Institute of Health broadly to understand how various vaccines look with regard to their safety and efficacy, and take all of that data in in one large package to make that public health recommendation.

Next slide. This is a network that has been formed by the National Institute of Health, called the COVID Prevention Network, that is a group of existing networks that already had been doing work in other areas.

And then this combined network structure will help to conduct some of the clinical trials that needs to be done. Particularly the large Phase III trial, as Dr. Offit had mentioned, that are required to know if the vaccine works.

Next slide. So, just to end here with a little bit of a summary. So, Phase III trials are several types of vaccines will progress to test

is the vaccine can actually be effective in preventing COVID disease.

And in parallel to the vaccine testing, there will be scale up and manufacturing of vaccine. And this will be funded in part also by U.S. government funding.

So there is no gap between the information above. That is, the efficacy of vaccines and the availability of a vaccine.

In the U.S., the FDA would review the clinical data that's generated and decide if a vaccine should be licensed. And the CDC would make recommendations for who should get the vaccine.

And again, timelines are hard to predict but these Phase III trials will be initiated in the upcoming months. And if those vaccine trials enroll and end points can be achieved, then there will be a potential to get answers on vaccine efficacy by the end of the year.

Next slide. I think that was my last. Thank you.

DR. OFFIT: Thank you very much, Dr.

Mascola. So we'll turn it over now to Dr. Kathleen Neuzil. Kathy, you're up.

DR. NEUZIL: Okay. Thanks, Paul. And Dr. Offit and Mascola really set the stage nicely for the next segment here. And I'm going to talk about COVID vaccine development from discovery to impact.

Next slide. So if we look at this schematic we see a lot of what's been explained where we start on the left side with the discovery and an exploratory stage.

And for example, Dr. Mascola told us about the S protein and identifying important epitope on that S protein that will help us understand the best immunogen for vaccine development.

Similarly, Dr. Offit talked about animal testing. We moved through phases of clinical development. And I'll talk a little bit more about that.

We have the regulatory, the policy, the financing and the launch. What's really important

though, is that these vaccines have to be delivered. They have to get into the arms of humans. And that's the only way they're going to have an impact.

And really going across this continuum are these two other key ideas that are illustrated on this slide. And one is that a vaccine has to have a public health need. And this is usually described in burden improvements or economic consequences and a market move.

For example, if you intend to bring the tenth influenza vaccine to market, then that influenza vaccine should have something special or different, or nobody is going to buy or use your product. So these are all considered in vaccine development.

And at the bottom there needs to be political will. There needs to be the type of public-private partnerships and collaborations that have been described. People working together to say, this is important, and again, we're going to ensure that if these vaccines are made, they get

into the arms of people.

And finally at the bottom, this concept that Dr. Dzaou really introduced about COVID disproportionately affecting people of certain races, African-Americans, disproportionately affecting Hispanics, certain occupations, low socioeconomic groups.

And really this call that vaccines have to be a tool for health equity. You know, it can be very difficult, and there can be a lot of barriers as was described to testing and treatment.

But theoretically, a prevention should be able to remove those barriers and help achieve that equity.

Next slide. So, again, I don't feel that I need to spend time making the case for a coronavirus vaccine.

These were the statistics as of this morning by the World Health Organization. This is clearly a global disease. More than 7 million cases, more than 400,000 deaths and counting.

And of course, the economic

consequences have been absolutely disruptive and paralyzing to countries throughout the world.

Next slide. So in terms of a clinical vaccine development for COVID or any other disease, it's important to say what is the goal. And that helps us define where we begin and where we want to get to.

And so with vaccines we start with something called an indication. So, am I trying to keep people from dying from this disease? Am I trying to keep them from getting infected? Am I trying to keep the population healthy and at work and functional? Or maybe I'm trying to decrease the spread of the disease.

I think for COVID we might like to achieve all of these things. But depending on the vaccine and depending on the population that's vaccinated, we will have different ultimate outcomes in how that vaccine is used and the impact that it has.

In terms of safety and reactogenicity, we certainly put a lot of effort into vaccine

safety. And we don't want anyone to have the impression that Warp Speed means we're compromising in any way on safety.

Early on in Phase I scientists give the vaccine to a small number of healthy people at a gradual pace, in very controlled and closely monitored circumstances.

And again, safety is monitored throughout this process. And if you even look to the right of the line that I have there, it's even monitored in post-licensure situations for very, very rare outcomes.

Dr. Offit talked about clinical trials of 30,000 to 70,000 people. You know, post-licensure we continue to work with partners at the CDC and the FDA to make sure if we have side effects of one in a million, that we're able to detect those and understand those.

Now again, most side effects are minor, they're tolerable, they're short-lived. It may be some pain at the injection site, it may be a little bit of a fever. But we have to take seriously the

potential for allergic reactions or these other rare side effects.

Next slide. Now, the other important piece that we test in clinical trials is the immune response. And what's challenging in this situation with COVID is that we don't know a lot about natural immunity in humans. We've only recognized this virus for about six months. People are being infected and we're beginning to understand natural infection.

We do know if people are infected they do have an immune response to that spike protein. And that's a reason that it's a target for vaccine development.

And they have what's called neutralizing responses. Meaning, antibodies that can stop the growth and the spread of the virus.

So we feel these are likely key. And in these early clinical stages we will be looking for neutralizing antibodies.

What we really don't know at this point is what level of antibody is needed to prevent

infection or prevent reinfection. We don't know yet the duration of protection from natural immunity.

If I get sick or if I get a vaccine, will it protect me for six months, a year, a year and a half?

We don't know the importance of T cell immunity. We have learned from prior trials of related viruses, SARS and MERS, that we do have vaccines that can induced broadly neutralizing antibodies. And again, we will take all these lessons learned to inform the current trials as we go forward.

Next slide. Now, vaccines are intended to spur the body to develop immune responses so that when you're later exposed to the virus, you will be protected from disease.

Now rarely, there are instances where the vaccines may make the disease worse when you're later exposed to the pathogen. Again, this is very rare and it's a concept called vaccine enhanced illness.

And that may happen by two main immunologic mechanisms. I won't go into the details here, but just to say that one of these mechanisms has to do with increased viral growth because of immune complexes and easier entry of antibody into cells.

And an example of this would be dengue. After receiving the dengue vaccine.

And the other example is something called antibody dependent enhancement. And this may occur, again, when you don't get a lot of that neutralizing antibody that I described that can stop the growth and spread of virus. And this may lead to a dysregulated immune system.

And we saw an example of this in the 1960s with a respiratory syncytial virus vaccine that was given to young children.

So again, these trials are designed, and animal studies are being designed, to look for hints of this type of immune dysregulation so that we can protect from this phenomenon happening with COVID vaccines.

Next slide. Now, the other question that's come up, it's come up in the lay literature. There are websites about this and there are certainly publications in the scientific literature, about controlled human infection models or challenge studies.

And what a challenge study is, is when we deliberately infect a healthy individual with a microorganism, with a virus, with a bacteria, to understand the pathogenesis of the disease, to understand the immune response.

And we can also use these challenge models then to test the vaccine. So I give half of the people in my challenge study a vaccine, I give the other half a placebo, and then maybe a month from now I deliberately challenge them with the pathogen.

So, controlled human infection models have helped with development of other vaccines. The challenge here with using them for SARS-CoV-2 is that we first have to manufacture a challenged strain.

We would like to understand more about the disease and how the disease effects and how to best enroll healthy people who won't get sick from this disease. And it's also optimal if you have a drug to treat these diseases.

So we use challenge models for cholera, typhoid, influenza. All of those diseases have treatments. So if the people in these studies get sick from those diseases they can be treated.

We're not quite there yet with easy treatments for SARS-CoV-2 or understanding the disease well enough. However, thinking about these models now, perhaps starting to develop these models, may help us in a year or a little bit more when we have vaccines.

Maybe we want to understand if, how long the immunity lasts to those vaccines. So it's unlikely to accelerate vaccine development. And it's really not our preference over those gold standard clinical trials that Dr. Offit described.

Next slide. So, overall I want to come back to this slide again and remind people that even

after we go through these stages of development we have to ensure that people receive the vaccine.

And one thing that will help that, as Dr. Mascola alluded to, is if we have multiple vaccines that come to market. You know, we have over 300 million people in the U.S., nearly 8 billion people in the world, and a very large segment of those populations will need a vaccine.

This is not going to be accomplished by one manufacturer, we're going to need multiple wins to accomplish this goal.

Next slide. And I believe that Dr. Berkley will touch on this, but again, this is not only accelerated development but it's really equitable global access to safe quality effective and affordable vaccines. And you can see the many organizations that have signed on to this goal.

Next slide. I just want to remind you, this is some work that we've done here at the University of Maryland that while infant immunization programs exist around the world, actually adult immunization programs, if you see

in those blue bars, are really fairly rare in low-income and lower middle-income countries.

So when we talk about parallel development of vaccines, we also have to think about preparedness for delivery of these vaccines so that these low and lower middle-income countries can benefit.

Next slide. So in conclusion, again, safe and effective vaccines, plural, are needed for COVID-19. Vaccine development is a staged, deliberate, and very careful process.

There are many challenges with COVID. This is a new disease. Have poorly understood immunity and we have an uncertain trajectory of the outbreak. We don't know where the next outbreak is going to occur, we don't know how many people are going to get sick.

Vaccine safety will be meticulously assessed in all of these trials. And if enhanced illness does occur, it will be carefully assessed and immune mechanisms will be carefully investigated. Thank you.

DR. OFFIT: Thank you very much, Dr. Neuzil. Now I'm going to turn it over to Dr. Richard Hatchett. Richard.

DR. HATCHETT: Sorry, I was having trouble unmuting myself.

Next slide please. So, very quickly, just going to introduce the coalition for epidemic preparedness innovations, or CEPI. Is an organization that many of you may not have heard of before the COVID-19 pandemic or may not have heard of it at all.

It's a new organization. We were established in 2017 after the Ebola epidemic in West Africa with a mission to essentially accelerate the development of vaccines against emerging infectious diseases into enable equitable access to those vaccines for affected populations during outbreaks.

With most emerging infectious diseases that means we have a very deliberate focus on ensuring equitable access in lower and middle-income countries, since that is where most

diseases have emerged, at least in recent decades.

With COVID-19, obviously we are concerned about global access. Next slide.

I think Kathy's numbers were even more up to date than mine. These were from yesterday.

Obviously I don't need to belabor the point that the COVID-19 pandemic is really unprecedented, certainly in our lifetimes as a global public health catastrophe with -- that is just reverberating in terms of its human, its humanitarian, and its economic implications.

Next slide. I'm going to talk, both John and Kathleen gave excellent introductions to vaccine development, I'm going to talk about our efforts to actually develop vaccines against COVID-19 and do that in a context of the global effort.

One of the most outstanding features of the global scientific response to COVID-19 is the solidarity that has been demonstrated with scientists coming together to both understand the virus and to begin working on countermeasures,

including diagnostic therapeutics and of course, vaccines.

This is just a visual representation of where vaccine development efforts that we know about are taking place. As you can see, it's truly a global effort, albeit concentrated in North America, Europe, and South East Asia.

Next slide please. CEPI has been tracking the global vaccine landscape very carefully. We are aware of 256 vaccine efforts that are underway. We've been able to confirm 228 of those.

John spoke about the different approaches to developing vaccines. And you can see the great diversity of approaches that have been undertaken against COVID-19.

You can also see how these vaccines are beginning to move through the vaccine pipeline with, at this point, 11 now in human clinical trials. Next slide.

Oh, sorry. I -- this got converted. This was a presentation of the CEPI portfolio. It

was not meant to be redacted. But, apparently the slide conversion redacted it.

So, what I can say is that we have nine programs. Our criteria for selecting these programs was -- are speed, scale, and access. Those are the goals that we're trying to achieve.

So, we have deliberately put together a diverse portfolio of candidates using a variety of different approaches to vaccine development that is also geographically diverse. We have three of our partners based in North America, three based in Europe, and three based in Asia, in the Asia/Pacific region.

We have tried to select candidates that have the ability to scale. And that also have the ability to be easily transferred to other regions so that the production can be globalized.

Right now four of the candidates that we have selected are in human clinical trials. That represents four of the five non-Chinese vaccines that are in human clinical trials right now. Go to the next slide, please.

This is just a listing of the 11 vaccines that have made it into clinical trials. As I just alluded to, six of these are Chinese-based vaccines.

Many of those are inactivated vaccines. Five of them are -- have been developed by companies that are based outside of China, several in the U.S., in Europe, and -- I believe U.S. and Europe essentially.

The vaccine trials began in early March. If you go to the next slide. Oh, dear. Sorry about the slides.

What this slide was meaning to show is the clinical development is moving very fast, as John and Kathleen have said. The first vaccine to enter clinical trials was the Moderna vaccine.

We actually partnered with John's organization, the Vaccine Research Center in Moderna to help that vaccine get off the ground. It entered clinical trials on March 16, just nine weeks after the release of the vaccine sequences.

A number of other vaccines have entered

clinical trials. The estimated dates of completion of trials and potential availability of vaccines extends from late this year, it remains to be seen how late this year.

But, some vaccine possibly becoming available within calendar year 2020. Likely under emergency use provisions.

So, possibly not fully licensed. With increasing availability going into 2021 and increasing across the course of the year.

The dots in the lower right corner were just some comparator vaccines. This is the period of clinical development for these vaccines will be about 15 to 18 months for the COVID-19 vaccines.

And we -- I was just going to compare that to Ebola, where the clinical development was about five years from first clinical trials to licensure.

Pandemic influenza where it was about seven years. And Hepatitis B where it was about 15 years. So, this is truly accelerated. Next slide.

We are, as I said, we are tracking the global vaccine portfolio. We are aware of possibly up to 60 vaccines that will enter phase one clinical trials by the end of 2020.

This for a virus that we only learned about at the very end of 2019. That is an extraordinary demonstration of the commitment of our private sector, academic, and nonprofit partners to develop vaccines at just an incredible speed. Next slide.

This focus on speed really has required a paradigm shift. Kathleen talked about some of the very significant potential safety concerns that we could face with immune enhanced disease, antibody-dependent enhancement.

But, we must make sure that in speeding the vaccine development that we do not cut corners in demonstrating safety and efficacy. John spoke about the need to perform the phase three clinical trials. Or actually, I think it was Paul, the large clinical trials.

To develop vaccines at speed, faster

than the normal five to ten or more years the vaccine development takes for traditional commercial vaccine development, we're going to have to overlap a number of the phases.

And particularly, we are going to have to conduct manufacturing, which is an extremely expensive part of vaccine development. To scale up that manufacturing and to begin to manufacture at risk, while we are waiting for the clinical trials to reach fruition and to demonstrate conclusively that the vaccines are safe and effective.

That means that we will speed things up by -- essentially by taking significant financial risks.

We do not want to take risks with the safety and efficacy of the vaccine obviously, given that the vaccines will be distributed to tens or hundreds of millions, or even billions of people when they become available. Next slide.

I probably don't need to dwell on this slide. I had put it in just to talk about some of

the different platforms.

John gave a very nice summary, high level outline of the different technology approaches that could be used to develop vaccine. As my earlier slides demonstrated, you know, a wide variety of approaches have been adopted.

And so we do think that we are very likely to have successful candidates. And hopefully we will have many successful candidates, because we are trying to develop vaccine at scale for billions of people as rapidly as we can.

And we know that no single vaccine can be scaled to the numbers of doses that we need within a reasonable time frame. Next slide.

So, these were my concluding thoughts. I was also asked to talk about some of the outstanding questions that we may still have when our vaccine development is completed.

The first thought that I wanted to share was that there really is no scenario in which we will have an oversupply of vaccine in 2021.

Even the best scenarios, we're talking

about potentially multiple billions of doses. But we also anticipate that many of the vaccines may require two doses to effectively immunize.

And so that means, and I hope this will lead into Seth's discussion, we need to be very careful stewards of vaccine as a scarce resource.

The goals ultimately should not be for individual countries to have as many doses of vaccine as possible, but for vaccine to be used as a global but scarce resource to achieve the end for which we have developed the vaccine.

Which is to end the pandemic by protecting our healthcare workers and protecting our healthcare systems by protecting the most vulnerable populations, the elderly, those with preexisting conditions.

And essentially to bring the pandemic under control until we can globally distribute vaccine to everyone who wants it. And that's going to take several years.

And so we need to be very careful stewards of the vaccine that we have as it begins

to become available. It will be in short supply.

And it will need to be prioritized. There will be many remaining questions about the vaccine.

We won't know initially how long the immunity will endure. We won't know if we need to boost people with vaccine every year or every couple of years.

We won't know if the evolution of the virus as it circulates in the human population will require us to develop new vaccines either annually as we do with seasonal flu, or you know, at some periodicity. These are all critically, critically important questions.

The final thought, you know, I have talked about our efforts at CEPI to develop a, you know, a broad-based portfolio where we hedge risk by pooling our investments into a number of vaccines.

We don't know in advance which vaccine is going to succeed. So we want to have multiple vaccines under development so that we can be

assured of at least some success.

I think there are also advantages for countries given the scarcity of vaccines that I've mentioned, the criticality of treating vaccines as a scarce resource.

There will be advantages for countries to work together collectively to collaborate in the procurement of those vaccines and in the distribution of those vaccines so that we can achieve equity in how those vaccines are distributed and used to the greatest extent possible.

And I've been working very closely with Seth under the ACT Accelerator that Kathleen talked about. And I believe he will talk a little bit more about that in his remarks and efforts to achieve global equity around vaccines.

Thank you.

DR. OFFIT: Thank you very much Dr. Hatchett. We'll now turn it over to our final speaker, Dr. Seth Berkley. Seth?

DR. BERKLEY: Thanks Paul. And thanks

for all the other speakers for setting up this discussion.

I'm going to have a slightly different task, because I want to talk a little bit more about the policy side of things. And I want to start because like with CEPI, people may not be familiar with Gavi, and it's important.

And Gavi is an organization, a public/private partnership. Just celebrated its 20th year anniversary.

And it was set up because there were new and powerful vaccines that weren't getting used in the countries that you could argue most needed them, the developing world.

And it's been very successful. We've launched 496 new vaccines in the 73 poorest countries of the world, where 60 percent of the world's children live.

We're now -- we've grown from five -- vaccines against five diseases to those of 18 diseases. A total number immunized, more than 760 million.

Now, why is that important? Vaccines are the most widely distributed health intervention. More than 90 percent of people on the planet received at least one dose of a routine vaccine.

So, this in a sense already is one of the most equitable tools we have in health. And it's important to say that up front, because this is a problem that can be solved.

But what is the problem that we're trying to solve here? Well, first of all, and others have said this, this COVID problem is a global problem.

And it really does require a global solution. Because we are not going to be safe anywhere unless we're all safe.

And I think this disease shows us that it started, you know, in a point outbreak. And it was in 180 countries within the course of about three months.

So, even if a few countries go ahead and have vaccine, if there are raging outbreaks in

other places, large reservoirs of virus, that is going to continue to threaten the world and the return to normality.

As Richard has said, there's no scenario if it says we're going to have an aggregate supply that is large enough in the next 18 months, to exceed demand.

And I think the other thing we have to put on the table is that there is now intense pressure on leaders, demands from their populations to secure vaccines. And that is leading now at a national competition where countries are trying to cut deals.

And what that will do, is create a misallocation of some of the scarce vaccine resources that Richard talked about. And that will lead to a continuation of the pandemic, unnecessary deaths, and deepening of the economic crisis that exists.

Now, you know, what are we doing about that? Well, you've heard Kathy introduce this. But the EC and WHO together launched this W -- this

ACT Accelerator.

The ACT Accelerator is access for COVID Tools Accelerator. And it's for diagnostics for drugs and for vaccines. And Richard and I are leading the vaccine pillar.

And the idea of that is to have a coordinated program that brings both the pushes, as Richard just described, along with the pull of purchased mechanisms that have vaccines available.

Now, what is the selling point here for this? Well, the selling point is, if we can have a system set up that can have guaranteed access of products, it will change these dynamics.

It will optimize the capital allocation, which will prevent countries from scrambling to try to invest. Because if you're investing in one or two vaccines, of course the a priori probability of those vaccines working, is quite low.

And so yes, you may hit the jackpot and have a vaccine that works. But, you also may end up with no vaccine, and be left behind.

And of course the last part is, it's critical as we've heard from many of the speakers, to manufacture at risk, to try to scale up and make sufficient volumes.

And of course in an active portfolio, it allows you also as vaccines begin to show non-promise, you can shift resources, shift manufacturing. Although that does take some time. It's not easy to turn on and off. But at least for similar vaccine platforms to use those facilities.

Now, we have worked, how are we thinking about doing this? We've had a system of advanced market commitments.

We've put together, for example, for the pneumococcal vaccine. That was a way to put aside a fund.

To work with industry. To plan how to scale up volumes to put financial incentives in place to work on having equitable prices.

And with that program, we were able to immunize 225 million people in 60 countries rather quickly. Introduced the vaccine at the same time

in the north and south.

And we also worked to create an advanced purchase commitment for Ebola. Again, to work with industry to accelerate.

So, there is some experience with these types of instruments. And as part of this, what we've done is talked about two ways to think about this.

One is contingent advanced market agreements. And those are really to look at products that, for example, CEPI is producing now.

And to work with the manufacturers to say, we would like to go ahead and have scaled up vaccine production. And then purchase of those for the global portfolio obviously when vaccine is licensed.

We also have a traditional advanced market commitment that would allow any manufacturers, even if not engaging with CEPI. So, this is open to anybody to enter the effort.

The way we're thinking about this being financed, is that high income country will be

self-financed. That's high income countries and upper middle income countries.

And then lower middle income countries and low income countries will be financed by ODA donor aid in the traditional way that Gavi helps countries with its vaccines.

The advantage of this is you end up with a sizable portfolio to liken your chances of success. You end up balancing that national and global.

You reduce these competitive dynamics that I've talked about. The portfolio is actively managed. And you ultimately have fair access.

Now, Kathy talked about ultimately the only way this works is with delivery. And so, what's critical here is working with countries ahead of time to prepare them for the delivery, for the reasons Kathy talked about.

Of course, we tend to vaccinate children. But, we also vaccinate whole populations for epidemic diseases.

And so, it's a matter of doing the

planning for that. Making sure if a cold chain is required, that's adequate. Making sure that the teaching materials are available. Making sure transport, et cetera.

So, that's critical in terms of thinking about it. And also making sure pharmacovigilance is in place, because of course, different populations, different potential disease patterns, you know, different people's you know, genetics, et cetera. We want to make sure that's important.

Now, a couple of other points that are going to be important here. And I can't emphasize this enough, is the issue of public trust.

We normally have to deal with rumors. We have to deal with vaccine hesitancy. I think this, everybody understands, this is a problem we've seen primarily, initially, in high income countries. Partially, because diseases -- the vaccines are so successful, these diseases have disappeared.

And certainly I don't need to tell Paul

about this, because he spent a lot of his life dealing with this. But, we would have thought that the silver lining behind COVID is an appreciation of why we need vaccines, and that everybody would want them.

But, we have had incredible rumors. We have had, you know, unlikely partners coming together with negative information, conspiracy theorists, you know, joining with the anti-vaccine community. And this has now spread globally.

So, and many surveys have said 50 percent of populations will not want to have vaccines. And so this is something that we are going to have to deal with ahead of time.

And it's a challenge, because we have a challenge right now in trust in government, to trust in public institutions. And so we've got to bring this, you know, to the front of what we're thinking about.

And the last thing I'd say is, that political will as you heard on Kathy's slide is critical. But we just had a global vaccine summit

a week ago today.

This was connected to our normal replenishment for Gavi. And it was held by the U.K. government.

And I have to say, it was an extraordinary event. We had 42 heads of state come and talk about the importance of equitable access, the importance of trying to work across the many countries.

And we also raised about 600 million dollars to jump start this advanced purchase commitment.

But the reason I think the political will is important is, if I take me back to where I started in my talk, this idea of vaccine nationalism, of trying to just protect your own population, there is a real danger we'll end up with, a few countries will end up with all of the vaccine.

And they will vaccinate their whole population while epidemics spread elsewhere. And that is not the way we're either going to have, you

know, fair access, or we're able to end the pandemic as soon as possible.

So Paul, let me turn it back over to you.

DR. OFFIT: All right. Thanks, Seth. We have about 20 minutes or so. Maybe a little more to go through the questions that you guys have sent. And I'll turn it over to the other panel.

All right. So the first one, and I'm going to -- Kathy, I'm going to start with you. And then ask each of the other three speakers to weigh in as well. So Kathy, here's the question.

Well, a tough question, but would any of the panelists be willing to share their own assessment of how soon a vaccine or vaccines might become available?

DR. NEUZIL: Okay. So, Vegas has reopened. So, maybe that's good timing here, because this is going to be quite speculative.

You know, vaccine development is inherently a risky process. And you've already heard us talk about how financially we are accelerating it.

I thought that was a good way that Richard put that. But that again, we don't want to compromise on safety.

And so we already have several vaccines in development. We have a vaccine in the U.S. that will be, should be in a phase three clinical trial in July.

If we are able to catch the outbreak, then, you know, we could perhaps have results by the end of the year.

So Paul, if you are going to make me commit, then I will say the soonest that I think realistically we could have a vaccine, and again, everything would have to fall into place, would likely be early 2021.

DR. OFFIT: All right. Richard, you're next.

DR. HATCHETT: I think Kathleen made a very reasonable case. I think that one other challenge to bear in mind with the clinical trial efforts is obviously when you're conducting a clinical trial, you have to have enough disease

occurring among persons participating in your trial that you can discriminate between an effective vaccine that prevents disease, and those who receive the placebo and obviously have some incidence of disease.

And that's very difficult to predict. And the trials that are starting now, what incidence is declining, may have challenges or take longer to accumulate cases.

And so, I would -- I maybe, if things went very well, I think we could possibly see a vaccine, again, not licensed, but possibly for emergency use, maybe a little bit earlier than Kathleen said.

But, I think the first half of 2021 is a very safe bet.

DR. OFFIT: John?

DR. MASCOLA: I agree with both of our speakers that first of all, it's hard to predict, but early next year sounds reasonable.

I would emphasize that it's very important to do the placebo controlled study we've

all been talking about. Because what we really don't want for the global public health sort of perspective, is ambiguity about whether a vaccine works.

And the only way to get there is to do the trials.

DR. OFFIT: Okay. Thank you. And Seth?

DR. BERKLEY: So, I want to build on a little bit of what everybody else said. I think the timing they've talked about is reasonable.

But, I want to talk a little bit about, when people ask me when it's going to occur, I always say, what do you mean by when?

Is when meaning I go to my doctor's refrigerator and I open it up and there's a, you know, a product in there that's licensed and in everybody else's doctors' refrigerators?

It's going to be a lot longer than that time period. I do think, and you heard the term of emergency use, and what does that mean?

You know, these would be early products

that were produced at risk. You would have the incredibly important point that John just made, you'd have to have a placebo control efficacy trial.

But, then you might use it under that license until you've finished, you know, all of the work and end up with a licensed product.

And just to say that this can be a really helpful initiative. We did this around Ebola, where we had a product that, you know, showed very high efficacy, close to 100 percent in a, you know, a reasonable sized clinical trial.

But, from the time until that happens until they finished all the work to get regulatory approval, figure out all the manufacturing, the stability, all those issues, we were able to use that vaccine in an emergency use setting under a clinical trial protocol, and vaccinate another 300 thousand people.

And the reason that was important, it both had a public health use, and that would be the case here. But, we also ended up with 300 thousand

more people for safety, understanding the vaccine better, and being able to use it.

The last thing I'd say, and people implied this, but generally, and most of us have been working in vaccine development for, you know, a large part of our lives, is not linear.

Usually there are problems in different phases of it. That's often why it takes so long.

So, I think we have to keep in mind that, you know, in linear predictions, they can be relatively quick. But, usually there's some step that one has to go back and solve and work on, or do more of, et cetera.

DR. OFFIT: Thank you. Okay. Here's another provocative question. And I'm going to come back to Seth for this again. And then if anybody else wants to chime in, please do.

Is there any concern that proprietary commercial financial interests may work to prevent equitable access to vaccines?

How can we prevent profiteering?

DR. BERKLEY: Well, those are two sets

of issues. So, first of all, you know, what's interesting about industry right now is that industry in a sense is on our side.

Because all of them understand, first of all, we're in a pandemic. It's not, you know, business as normal.

And second, they worry that if they're in a situation where they only provide vaccine to a small couple of countries, and the rest of the world is out there that are being sick, then, you know, that doesn't look very good for their business.

And they will, you know, be dragged over the coals. And of course, it later on has an effect on their, you know, their image and the perception of them. So, they really want to work to see about a global access.

Now, the other part of the question though was this question of profiteering. And what price point will be done.

And I think the challenge here is that most of the manufacturers are part of these

public/private partnerships. And therefore are accepting public finances as part of their, you know, the programs that they're developing.

And therefore, our expectation is, they're not going to be ultimately turned into not-for-profit institutions. Although some have said that they will price it in a not-for-profit fashion.

But, they should not have excessive profits during a pandemic period, because that would not be appropriate. That is at least the conversations we're having over.

DR. OFFIT: Thanks Seth. Okay. John, this next one's for you.

What might a distribution strategy look like in the United States and globally? Who gets it first, high risk groups, older adults, healthcare providers? And who makes that decision?

DR. MASCOLA: Sure, thanks Paul. So, the distribution strategy, I think, will depend first of all on how well the vaccine works and

exactly what the study showed.

But, to take the last part of your question first, in the United States that will be a decision that will be taken by the Centers for Disease Control. And they're already beginning to think about this.

And certainly if the vaccine is in short supply, or as Seth just mentioned, we do a study, there's an initial result, and all of the full licensure is not done yet, but there's a decision to do an emergency use authorization, that is, to begin to use the vaccine in certain population, then rather than broad distribution, there would be selective populations.

And those have yet to be determined. The FDA and the CDC would work together on those. But you could envision people at highest risk certainly healthcare workers and first line workers, people in essential jobs where there's a high density type of employment, where they are at risk.

So, those are the types of discussions

that are happening.

DR. OFFIT: Thank you.

DR. HATCHETT: And Paul, like I said, I would just add, from an international perspective, I'm not aware of any instance in which the transactions that are being proposed are other than between vaccine companies and national governments.

Or possibly with a group of governments purchasing together. But, that means that those who will be dispensing the vaccine will ultimately be the national authorities.

And presumably through ministries of health, and presumably they would certainly look to international organizations like WHO that might offer normative guidance about how vaccine ought to be prioritized.

But, most countries will reserve ultimately the right to make their own determinations, and to allocate vaccine according to whatever prioritization scheme they develop.

But likely, if the vaccine is shown to

be generally efficacious, and not to have particular safety risks, you would anticipate healthcare workers would be very highly prioritized, likely. Followed by those at greatest risk.

DR. OFFIT: Thank you.

DR. BERKLEY: And can I, if I could just add one other point, Paul. Which is, I think of it in kind of two axes.

One is the one we just talked about. So, healthcare workers, those at risk, maybe the elderly.

But, there is also a public health axis. So, I think we do need to think about, when vaccines come out, wherever we are in that time line that people have been guessing about, where is the epidemic?

And are there places where the epidemic is raging out of control? Are there other places that have fairly good control?

And we'll need to think about both of those. Because again, our goal here is to stop the

pandemic and return to some normalcy.

So, we're going to have to think about that also. Over.

DR. OFFIT: Thank you. All right, Kathy, you're next. In current trials, is consideration being given to safety and effectiveness in children and pregnant women?

DR. NEUZIL: Yeah. So, that's an excellent question. As I explained at the beginning, we generally start testing vaccines in healthy adults again, in very controlled conditions.

And then we move to special populations. And so Paul, you know, pregnant women, children, are special populations.

Essentially, we don't have a vaccine. Everybody's talked about prioritizing healthcare workers. We don't have a vaccine for healthcare workers unless we have a vaccine for pregnant women.

We cannot not test these vaccines in pregnant women. They must be included. But of

course we would like the toxicity studies to be first done in animals and to first have done them in non-pregnant women of childbearing age.

You know, similarly with children, we want to do it in a controlled, deliberate fashion. We want to look at the appropriate dose for children. We want to make sure that that's, the safety profile is there.

So, yes, we need to get there. We need to get there fast. But, we need to get there in this careful way.

DR. OFFIT: Thank you. Okay, John, this is for you. Could Dr. Mascola expand on the relationship between ACTIV and Warp Speed?

DR. MASCOLA: Sure. Well, that's a very rational question, because it's an area of some confusion.

So, the way I would look at it is, ACTIV is a much broader public/private partnership. It includes representation from really all groups of scientific and interested parties with regard to COVID vaccines.

So, whether that's biopharma that's interested in making a vaccine, philanthropic organizations that are contributing, academic scientists that are participating, government scientists and the way they're funding it, all of those groups to come together for discussions.

When we get to Operation Warp Speed, it's really a subset of that group of people. Specifically for vaccines, the groups and the biopharma groups that are specifically working to develop a vaccine, and are ready to move that vaccine to the clinical pipeline, including phase three.

And at that point, Operation Warp Speed is working closely with those groups to work in a very tangible way to operationally test the vaccine candidates. Over.

DR. OFFIT: Thank you. Okay, Richard, I'll give you this one. How is it possible for manufacturers to begin scaling up before a vaccine is approved?

DR. HATCHETT: Well, the scaling up of

the manufacturing, I mean, that's essentially a financial decision. When they begin clinical trials, they work out a small scale process for production to allow to have enough vaccine for the phase one trials, typically the phase two trials.

Ordinarily, during what you would think of as commercial vaccine production, you would wait to learn something about our vaccine.

And you would wait before making the very significant investments required in scaling up the manufacturing until you had evidence that the vaccine was safe, that it was immunogenic, that you thought it was going to have the benefit that you were seeking, before you would make those large scale investments.

And in order to speed the vaccine development, we want to make those investments immediately, while we are beginning to conduct the phase one and phase two trials, while we're waiting for the data to unfold, and certainly before the phase three trials are initiated.

The idea being that, you know, if the

phrase three trials demonstrate that the vaccine is safe and efficacious, you want to have, you know, already built up an inventory of potentially tens or even hundreds of millions of doses that you can then begin deploying very, very quickly.

That raises concerns of its own. I mean, I think observing the safety of the vaccine once it rolls out into very large scale populations, there's something called pharmacovigilance, is going to be critical.

But, we do want to move vaccine out as quickly as we possibly can. And to do that, we have to take these financial risks.

DR. OFFIT: Thank you. Okay. Seth, I'm going to come back to you. And this would be, you had a little of this in your talk. But this will give you a chance to expand.

What challenges might we face in terms of educating the public about a new vaccine, particularly among vaccine hesitant or resisting groups?

In other words, how can we manage

expectations prior to release of this vaccine for trying. It means lessen the impact of the, not just skepticism, but cynicism that often surrounds vaccines.

DR. BERKLEY: Well, I mean, I think in a sense, you know, Paul if this is, if this is pure anti-vaccine, I'm not sure we have an easy solution.

But we have some experience in working in those circumstances. And just for this group, I'll just throw out a fact that's kind of interesting.

The highest level of, you know, of concern about vaccine is actually in France, the home of Louis Pasteur. And the highest level of confidence is actually in Rwanda, which is quite interesting going back to that concern between develop and developing countries.

If it's just that, what we've learned is first of all, people tend to trust their healthcare provider. They tend to trust the front line health workers.

And that's an important tool. They also trust their peers. So, how you have information that can help to provide a way for people to reach out.

How you can take people who are asking questions, and have them not, you know, pointed to in social media, some nice sounding website that turns out to be full of misinformation. But instead take them to a site that has good information, because people have questions.

And sometimes turning those good information sites into making them more user friendly so people can do it.

So, there's a whole movement there. And we're working with all the social media companies to try to do that.

And that's an important priority that has really gotten some attention. But, we go beyond that now because of these conspiracy theories and other issues.

And some of this now is, you know, real malfeasance that's being done by groups to

destabilize governments. Where they're actually putting out information that is pro-vaccine, that's anti-vaccine, that's raising questions.

And of course in that circumstance, you know, it's much harder to use rationality to do that. And so, I think what we're going to have to do is, work hard at both of those fronts to try to make sure the information is there.

The last thing I'd say is that, you know, my hope would be that people are quite nervous now, fear because of the pandemic.

But, as vaccines start rolling out, as people start taking them, as they see there's no side effect, as people are protected and able to go back to, you know, a more normal existence, that that will also change the dynamic as well.

Because I think this is a vaccine that people really want. Over.

DR. OFFIT: Thank you. All right, Kathy, I'm going to give you this one. What are some strategies for policy makers and health care providers to overcome structural and systemic

barriers to vaccines for marginalized populations, including racial and ethnic minorities?

DR. NEUZIL: Yeah, so thanks Paul, for that simple question. No, it's a good question. And I think it follows nicely with Seth's answer. Because a lot of the issues we have to tackle require the same sorts of responses.

So again, it's trust of peers. It's trust of healthcare workers. It's making sure people get messages from those trusted sources.

It's making sure that people, you know, fully understand the vaccine. That we're listening to them, we're listening to the constituency that, you know, we have the backing of their leadership.

I also think it's helping people understand that sometimes it's not just an individual decision. So, let me give you an example.

This is true for influenza. It's certainly true for COVID. You know, in the United States nursing home residents have just been

devastated by this disease.

Well, your mother in the nursing home isn't going out into society and being exposed to COVID. COVID is being brought to her. Influenza is being brought to her.

So, really helping people understand too, that when they choose to receive a vaccine, it may be protecting them. And they may or may not get very sick from whatever disease we're trying to prevent.

But, it also may keep that from spreading disease to their loved ones from people that are too old or too young to perhaps have a good immune response.

So again, I think it can also be total education. But, to be fair here, you know, we also have to be sure, and it comes back to the access issues.

We've talked exactly about who has gotten this disease throughout the world. And there are a lot of disparities, racial disparities, socioeconomic and occupational.

And so we have to have a commitment to be sure that we provide for those people. And you know, we would like a very diverse population to be in our clinical trials.

And so we understand how this vaccine works in all types of populations. And again, I think then we owe those volunteers, and those populations, access to the vaccine as best that we can get it to them.

DR. OFFIT: Thank you. Okay. So, this is going to be the last question. And then I'll sort of have a summary.

But this is directed then to both Richard and John. It seems that a lot of the way that we learn about these vaccines through the companies is by press release.

I think to my knowledge only one group has actually published a paper in a scientific or medical journal. It was the Chinese group that published in Lancet about their experiences with the replication-defective adenovirus 5.

Could you comment on that? Do you

think that these companies should be held to a higher standard regarding giving information to the scientific community about how things are moving along with their vaccines?

Or are we just going to be subject to this sort of science by press release and have little to say about it?

We'll start with you, Richard. And then we'll go to John.

DR. HATCHETT: Well, I think we all support, I think every one of the speakers will say that they support data sharing. It's absolutely critical during a pandemic.

We have worked through new mechanisms for data sharing preprints. Journalists have been quite understanding of the need to share data before it can go through peer, full peer review.

And we do need, you know, full scientific presentation of data in order to be able to make the best choices that we can in a very complex environment.

DR. OFFIT: Thank you. John?

DR. MASCOLA: And I'll add to what Richard said. That, you know, we completely support and encourage the use of the public web, archive websites.

So, even while a paper is being reviewed in the traditional sense by journal referees, it is usually posted on a public website.

Now, with regard to press releases, we are in somewhat unprecedented times. And that has caused what the questioner has raised, which is press releases by companies before they are published data.

We prefer when that happens to, those of us who are involved, to make sure that the data follow rapidly. Whether there's a preclinical data or clinical data.

And I can say that in the instances that we're involved in, that that's the -- that's what we're strongly working with the groups to do. Is to get those data out into the public domain as quickly as possible.

DR. OFFIT: Thank you. Okay. So, I'm

just going to make a few concluding comments before I get to just some final housekeeping issues.

We have a novel coronavirus. A bat coronavirus that has just made its debut in the human population.

We've already found out a couple of things that surprise us. The nature of its transmission is not typical for what you see is what is usually a winter respiratory virus.

We've already found that there's a post-infectious phenomenon that occurs in children that's associated with multisystem vasculitis that can be fatal, associated with coronary artery vasculitis.

And then also there was a comment made by John Yewdell recently on something called TWIV, which is This Week in Virology, where he noted that the number of people who have, you know, pretty significant illness, don't develop neutralizing antibodies, even though they are being presented with an abundance of this spike protein, this surface protein on the virus and presumably the

receptor-binding domain that's part of that.

So, we're learning as we go with this virus. I think it's fair to say that as we move forward to a vaccine, we're going to continue to learn.

And we should be humble realizing that nature gives its secrets up slowly, grudgingly, and occasionally with a human price.

So, I think we need to make sure that as we move forward with these vaccines, that we keep that in mind. And that we manage expectations as Dr. Berkley alluded to earlier, so that we don't lose the confidence of the American public.

And even though there are certainly anti-vaccine activists that -- whose confidence we will never gain, the fact of the matter is, most people, certainly in the United States, do trust vaccines.

I mean, we ask parents in the United States to give 14 different vaccines to their children in the first years of life. That can mean as many as 27 inoculations during that time.

It can mean as many as five shots at one time, to prevent diseases that most people don't see, using biological fluids that most people don't understand.

We have the confidence of the American public. And in many areas where we have that confidence. We can't risk that confidence.

And make sure that as we move forward carefully with these vaccines. And that we mitigate any potential risks ahead by letting people know exactly what we know, and what we don't know moving forward.

Assuming that there's going to be some things we know as we -- the next year or two or three that we don't know now. And that maybe things that we wished we'd known earlier.

So, I'll just, I'll stop with that rather dour ending. And then I'll just make the following statements regarding housekeeping.

This concludes today's webinar. Our next webinar will take place Wednesday, June 24 at 5:00 p.m. Eastern time.

Everyone who registered for today's webinar will receive an invitation for the next webinar.

This webinar has been recorded. The recording, a transcript, and slide presentations will be available on covid19conversations, that's one word, dot org.

Thanks again for our panelists and for the American Public Health Association and the National Academy of Medicine for sponsoring this webinar series.

And thanks to our listeners for joining us today. Best wishes for all of you. Stay safe. Stay healthy. And we look forward to seeing you next time. That ends today's webinar.

(Whereupon, the above-entitled matter went off the record at 6:26 p.m.)