

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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THE THIRD YEAR OF COVID-19:
IS THIS THE NEW NORMAL?

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WEDNESDAY
JANUARY 26, 2022

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The webinar convened at 5:00 p.m. EST,
Megan Ranney, Moderator, presiding.

PRESENT

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JENNIFER NUZZO, Johns Hopkins Center for Health
Security
LARRY COREY, Fred Hutchinson Cancer Research
Center
ROY GULICK, Weill Cornell Medicine
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5:01 p.m.

DR. BENJAMIN: Well, good evening. Or good afternoon, or good morning for anyone who is tuning in globally. I'm Dr. Georges Benjamin, the Executive Director of the American Public Health Association.

Welcome to the 22nd webinar in the COVID-19 Conversation Series, entitle The Third Year of COVID-19: Is this the New Normal? It's brought to you by APHA and the National Academy of Medicine.

Now, today's webinar has been approved for one and a half continuing education credits for CHES, CME, CNE, and CPH.

And please note the speakers have a disclosure -- have disclosed conflict of interest.

If you want continued education credit, you should have registered with your first and last name.

Now, everyone 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 cpb@confex.com with information on claiming credit.

All online evaluations must be submitted by October 4 to receive continuing education credits.

Now, the COVID19 Conversation Series has been on break for a few months. But, with the rise in Omicron and the conversation about what we can expect in coming months, we thought now would be a good time to come back and have that conversation.

If you have any questions or topics you'd like us to address today, or on future webinars, please enter them in the Q&A Box, or email us at APHA@apha.org. That's for questions, APHA@apha.org.

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

So, questions in the Q&A, and pay attention to the chat for announcements about how to troubleshoot.

Now, this webinar was being recorded. And the recording and transcript will be available on the COVID19Conversation.org site in a couple of days.

More information on this series and records of past webinars, are also available at this link.

Now, as you know, we are all really kind of all zoned out on COVID. And we are all trying to figure out where we go next.

So, with that, I want to introduce our moderator today, Dr. Megan Ranney. Dr. Ranney is a practicing emergency physician, researcher, and national advocate for innovative approaches to public health.

She holds The Warren Alpert Endowed Professor of Emergency Medicine at the Alpert Medical School of Brown University, and is the Academic Dean of the School of Public Health at Brown University, as well as the Founding Director of the Brown Lifespan Center for Digital Health.

She has obviously served multiple national leadership roles, including cofounder of

the getusppe.org, which is a start up nonprofit that delivered donated personal protective equipment for those who needed it most.

She is a Fellow of the fifth class of the Aspen Institute of Health Innovators Fellowship Program, and a member of the Aspen Global Leadership Network.

Lots of awards for technology innovation, public health and research, including Rhode Island Women of the Year, and American College of Emergency Physicians Policy Pioneer Award.

She's also a frequent media commentator on outlets ranging from the BBC, to CNN, to the New York Times.

She got her Bachelor's Degree in History and Science, graduating Summa Cum Laude from Harvard University, her Medical Doctorate graduating Alpha Omega Alpha from Columbia University, and a Master's in Public Health from Brown University.

She completed her residence in emergency medicine and a fellowship in the Injury Prevention Center at Brown University. And she was previously a Peace Corps volunteer.

Megan, it's all yours.

DR. RANNEY: Thank you, Dr. Benjamin.

It is an honor and a privilege to be moderating this webinar today with you as always, with so many colleagues who I've known and admired for many years.

Now, I think it's safe to say that we are all tired of COVID-19. And a year ago, even four months ago, we would have had trouble imagining that we would be where we are today. It's yet another international surge, yet another variant.

So, in this webinar, we're going to hear from much admired experts from across the country, about the current state of the pandemic, with a focus on preparing for new variants that may yet be coming, the role of vaccines and therapeutics moving forward, and how to shape our public health guidance as we move into this next phase.

We will address not only those issues, but also talk about where we're going next, and how all of you can help integrate the ever-changing guidance and science into your own work and your own communities.

I will remind you all to please use the

Q&A feature to ask questions as they arise. I will be keeping track of them, and will ask them towards the end of the presentation.

I thank you in advance for your engagement and your questions. And with that, I'm going to introduce our panelists.

And then I'll turn it over to each of them in turn to give a brief presentation, again, followed by a Q&A.

So, I'm going to start with Dr. Nuzzo.

Dr. Jennifer Nuzzo is a Senior Scholar at the Johns Hopkins Center for Health Security, an Associate Professor in the Department of Environmental Health and Engineering, and the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health, and a Senior Fellow for Global Health at the Council on Foreign Relations.

An Epidemiologist by training, her work focuses on global health security, with a focus on pandemic preparedness, outbreak detection and response, health systems as they relate to global health security, biosurveillance, and infectious disease diagnostics.

She directs the Outbreak Observatory, which conducts, in partnership with front line public health practitioners like many of you, operational research to improve outbreak preparedness and response.

She's also the lead Epidemiologist for the Johns Hopkins COVID-19 Testing Insights Initiative, housed within the Johns Hopkins Coronavirus Resource Center.

And she will also be moving up here to Brown in just a couple of months, to run our Center for Pandemic Preparedness and Response.

So, I'm excited not just to welcome her to speak on variants, but also as a future colleague.

She's going to be talking about what we've learned from Omicron, what's happening now, what's coming next, and how do we prepare.

The next speaker will be Dr. Larry Corey, an internationally renowned expert in virology, immunology, and vaccine development, and the former President and Director of Fred Hutch.

His research focuses on herpesviruses, HIV, the novel coronavirus, and other viral

infections, including those associated with cancer.

Dr. Corey is the PI, or Principal Investigator of the Fred Hutch based Operations Center of the COVID-19 Prevention Network, or CoVPN, and CoVPN Network Testing Pipeline.

And no one better than him to speak to us about vaccines, the state of what we know about vaccine efficacy, and how the strategy will change going forward.

And I'll stop with my intros actually, and let Dr. Nuzzo speak. Then have Dr. Corey speak.

And then I'll introduce our last two speakers after that.

So, Dr. Nuzzo, take it away.

DR. NUZZO: Thank you so much. Sorry, I couldn't get off mute for a second.

I appreciate the warm introduction. And also appreciate the opportunity to speak at this session.

I, like many others, didn't expect us to be having to talk about COVID in the way that we are right now at this point.

But, nonetheless, here we are. And what

I'm going to do today is just talk about where we are in the general sense.

And talk about variants in the general sense, to focus really on what the impact has been, rather than the variants themselves.

So, if you could advance to the next slide, I'm going to start first by taking about the situation in the United States.

And as Megan mentioned, I'm on the team that is behind the Johns Hopkins Coronavirus Resource Center.

And what I'm showing you here are data from today, showing the case situation in the United States.

So, we have to date reported over 72 million cases. And continue to be one of the countries that has been hardest hit by this virus in terms of the number of cases being reported.

But, I want to call your attention to the upper right-hand side of the graphic that I'm showing you, where you see these sort of red bars.

And that is basically the seven-day average of cases that are reported. And as you

can see, you know, we basically are in a skyscraper.

The cases, you know, around the holidays began shooting straight up. And everybody knows this.

You've heard the news stories. You've felt it. You've seen it. You know, you probably know lots of people who have gotten the virus. And that is absolutely reflected in the numbers that we're seeing.

So, this is a situation that truthfully, you know, I did expect that we would have an uptick in cases around the holidays, based on the fact that we had an uptick at the end of summer.

But, I don't think anybody ever expected the case numbers quite this, you know, staggeringly high. Would you go to the next slide.

There has clearly been a reason for that.

And that is this new variant, Omicron that we've been hearing so much about for the last month.

It is now the dominant virus circulating in the United States. And it is the dominant virus circulating in many countries.

And it has come with it, a number of

really important features. The key being, probably the most important feature being, its incredibly high transmissibility.

Where we are seeing people spreading the virus and spreading the virus more quickly. And spreading the virus to more people than we had seen.

So, the case growth has been really quite explosive over a relatively short period of time.

Now, you've also heard in the headlines, some evidence that on a per-case basis, it maybe less severe. Meaning most, you know, fewer people who get it are going to the hospital.

And for those who are going to the hospital, perhaps they aren't requiring the level of intervention that they may have with earlier forms of the virus.

But, I have to stress that those attributes, while welcomed to some extent, don't completely make up for the fact that this virus is so incredibly transmissible.

And what we're basically looking at here, has been a flash flood. And so when the flood waters

come very quickly over a short period of time, that comes with it, you know, brings with it, its own challenges. And it's very, very hard to absorb.

So, that is what we have been living through for the last month or so. But, if you go to the next slide, you know, the situation is -- is beginning to turn a bit.

Where we are now, fortunately, starting to see, finally, a decrease in the cases being reported in many states.

So, what I'm showing here, is a graphic, and this again, is pulling fairly recent data, showing the growth in cases recently. And you know, the weekly change in cases.

So, I generally like this graphic to have a lot of green. And the darker the green, the better.

Reds are not great to see. And a couple of weeks ago, there were a lot more reds on this graphic.

So, it's good news that we have less red. But, as you can see, we still have red. So, we're seeing still a growth of cases in several

states.

So, not all states are seeing the declines that you may have been hearing about in those, on the east coast for instance.

So, we, you know, in fact 19 cases -- states this week are reporting case increases.

But, the rate of change in most of these states is slowing. So, that is certainly welcomed news. And we'd like to see this trend continue.

Now, you may have heard that Omicron has, in other countries, sort of come and gone. You know, perhaps in a period of, you know, a couple of months.

Or not gone, it's not gone. But, the case of numbers will start to decrease relative -- you know, once they start to decrease, they decrease rapidly.

I think it's going to play out differently in the United States. In part because we're such a geographically diverse country.

And in part, because we've seen over and over again, this virus spreads in social clusters.

And not all social clusters mix with each other.

So, I think we're going to continue to see spread and possibly not as rapid declines as other countries have reported.

So, this next slide is showing the hospitalization. And the hospitalization is a lagging indicator in the sense that we see the trends turn a bit delayed from the trends that we see in the case numbers.

So fortunately, we are now starting to see the hospitalization numbers, which are staggeringly high as you can see.

I like showing the kind of time theories here, because it shows the hospitalizations that have, you know, occurred due to this flash flood, have eclipsed what we have seen prior, you know, in earlier stages of the pandemic.

So, that is in part due to the very, very transmissive nature of this variant that we're dealing with.

Fortunately as a nation the hospitalizations are starting to come down. But again, we're a very big nation.

And that is not true in all places.

And so, there are places where their hospitalizations are, you know, still very much climbing.

And certainly in the western part of the country, you know, there are still deep worries there that the trends are not yet in the direction that they need to be.

Similarly, we are seeing some, those concerns with the death data. They lag hospitalization.

So, while the case numbers of hospitalizations nationally maybe coming down, the death numbers are still climbing, because we are seeing the results of the cases that occurred weeks and weeks ago. Next slide, please.

So, one of the big concerns that I have about the situation that we're in, is very much the case that testing is highly constrained. And perhaps the most constrained it's been at any point in this pandemic.

And one of the metrics that I have spent a lot of time looking at is test positivity, because it's, I think, probably one of the better metrics we have to gauge the operational situation that

we're in.

And when I see a test positivity number that's high, and in this case over 25 percent for the nation, what that tells me is that the answer to the question, are we testing enough, is you know, a resounding no.

And unfortunately, the answer to that question, are we testing enough, has been no for most of the pandemic.

But, certainly you know, we like to see test positivity much lower, you know, than 5 percent.

And 25 percent is just far too high.

And so what that means is that we are missing more and more infections that are occurring.

They're not turning up in our surveillance numbers, because people aren't getting tested.

Maybe they're testing themselves at home, but that's not being captured by our surveillance.

And we're possibly, you know, turning our telescope to a different part of the sky, and seeing cases in a different population than we were

when we had more widespread, or more available testing.

So, that is a real worry. And I think it really starts to occlude our vision in terms of, you know, where we're going in this pandemic.

And it, you know, certainly deprives us of opportunities to interrupt transmission, to connect people to potentially lifesaving care, and to otherwise just improve outcomes.

So, this is something I think is going to be the dominant issue in the coming months. Is trying to figure out how we expand testing in a way that's accessible to everybody who needs it.

Next slide.

And because we started talking about variants, I have to absolutely stress the fact that, you know, what we know about variants and where they are occurring in the world, and where they're coming from, and how frequently they occur, is a completely capacity dependent exercise.

It's all about how much sequencing is being done, and being done by whom. Unfortunately, as you can see from this graphic, there is a real

range in terms of how, what percentage of cases are being sequenced by countries out there.

And it's really interesting, because this graphic's lasted as a function of the countries income.

And as you can see, it's not purely an income dependent exercise. There are many low income countries that are doing more than their fair share of sequencing.

The blue dot, if you can see it, the dark blue dot is the United States. And about half a year ago, the blue dot was much more lower on the curve.

But, in recent months we've really started to catch up in terms of the amount of sequencing we're doing.

But, we're still not the leader in terms of sequencing. So, keep that in mind when you hear about a new variant.

One of the questions you have to ask is, is this all we know? And usually the answer is, probably not.

There's probably a lot more going on

out there with respect to variants that we just don't know, because we are so far behind in our surveillance in terms of looking for them. Next slide.

So, I just want to sort of end on the global picture. Because, you know, you can't talk about what's happening in the United States without rooting it in a larger context, which is, and particularly when we're talking about variants.

And so, we have to also look at what's happening. And the Omicron trends that I describe today are very much playing out in other countries.

If you look again, look at the upper right-hand corner, you will see those seven day averages.

And again, we are in another skyscraper. We, you know, this is the glo -- these are the global case numbers.

I mean, they're just hideously large. And when you see that scrap -- you know, skyscraper, you understand why that is.

And when people ask me about the variant, I have to pivot to the global picture, because this

is -- this is, you know, the context that we find ourselves in.

If want to stop fretting about, you know, every other Greek letter that there is to come in the alphabet, the way that we do that is that we have to bring these case numbers down.

And the way that we bring these case numbers down and limit opportunities for variants to arise and spread, is by allowing more countries greater access to vaccines.

So, if you go to the next slide. You can see that we're still in a situation where there is intense spread in much of the world.

Many countries are seeing intense spread. And there is a high degree of variability in terms of how much access countries have had to the vaccine.

Yesterday a reporter asked me, basically, you know, a simple question. How is the case that vaccination reduces the likelihood of variants emerging?

And to understand that, I use a basic -- it's basic sort of math. Which is that, the

more copies of the virus that there are in the planet, the more the virus has to copy itself.

The more opportunities there are for mistakes to be made in the copying process, and that is what contributes to the rise in variants.

Genetic mutations that occur in that copying process.

And so, if we are able to vaccinate more people to reduce transmission, to reduce the amount of virus, you know, we know that vaccines may not prevent infection, but they certainly may reduce the amount of time that people carry it.

We reduce opportunities for the virus to mutate and spawn new Greek letters that we then have to worry about.

So, I'll end on that note. And looking forward to the question and answer session later.

Thanks so much.

DR. RANNEY: Thank you so much, Dr. Nuzzo.

Now, I will turn it over to Dr. Corey, who as I mentioned before, is the former President and Director of Fred Hutch, as well as the principal

investigator of the COVID-19 Prevention Network.

He's going to speak on vaccines, vaccine efficacy, and how our strategy is going to change going forward.

For those who are just joining us, there is a Q&A. Please put your questions in the chat. We'll be monitoring them.

And after all of our speakers have spoken, We'll have a time for question and answer with all of our speakers.

Dr. Corey, to you.

DR. COREY: Well, thank you Dr. Ranney.

As I think everybody has said, I just want that, you know, there is some, you know, issues with discontent at the moment.

We're at month 24. Just to remind that we really have developed highly effective biomedical interventions on COVID-19 with unprecedented scientific success.

We have highly effective vaccines. We have highly effective monoclonal antibodies, both for outpatient therapies and longer term prevention, and Trips' going to talk about that.

And increasingly effective outpatient antiviral therapy to prevent hospitalization with the protease inhibitors, IV, and remdesivir, and oral molnupiravir. Next slide.

As the Delta wave has become the Omicron tsunami of cases that we just heard, there's public fatigue. We go back a slide. Oh, I got it.

COVID-19 lifestyle restrictions are still operant for most of us. And it's clear the virus is firmly established in the human population.

New variants, as we've heard, are likely to emerge. And even the less lethal variants such as Omicron, does produce significant morbidity and significant mortality.

So, we have a delay here. Next slide.

So, the issue is, has science not led us out of this wilderness as well as we need, and our tools not good enough?

Or is it clear that the virus really is quite skilled at antigenic variation, altering itself and spreading quicker than any other human pathogen that we've encountered.

And that we must continue to build and

sustain an implementation science, a basic science, and a translational research infrastructure that matches these viral alterations.

And continue to improve our countermeasures, which are still subsequently quite okay. So, let me just review this.

I apologize for the -- what appears to be quite a delay between wanting the slides to shift and not. Susan, maybe you can take that control. Because I'm trying to.

So, my role is for, to give a quick review of the vaccine program. What has been the anticipated variant change?

How it has affected vaccine efficacy, and strategy? And a little bit about what's next. Next slide.

Just to remind us, from discovery to actually getting into people's arms for COVID-19 vaccine, was a remarkable 11 months.

The virus was first isolated on January 7. The sequence posted the 10th. They actually spiked protein sequences sent from Barney Graham's lab to Moderna as well as to Pfizer, was, you know,

within a week of that.

Within 66 days, RNA was bottled and put into a Phase One trial into humans. When Tony Fauci called me on March 3 to start getting us ready for designing a Phase Three program and mobilizing the academic and clinic research community to test these vaccines, we started working on that and really had that planned by April.

These Phase Three trials started in July, one a month, in July, August, September, October. But, the first ones with RNA in July.

And we actually had the interim efficacy data on November 9 for Pfizer, and November 16 for Moderna.

And the EUA for Pfizer and the EUA for Moderna in the mid-December. So, 11 months from beginning to end. Next slide.

Now, some of it is -- and the efficacy was remarkable. Ninety-four percent against symptomatic disease and essentially 100 percent against severe disease.

Against the ancestral strain, and the vaccine matched exactly the circulating strain for

the RNA.

For our first international trial, which was with the one-dose J&J vaccine, which was done in the United States, South Africa, and much of South America, efficacy was a little bit less, 72 percent overall.

But again, for hospitalization and death, it was in the high 80s. Next slide.

These vaccines were felt to be the breakthroughs of the year. We actually were sort of looking good, next slide, feeling really quite good about the whole thing.

And the issues of sort of just to review a little bit, because the question is, is how did you do this and were there any corners cut? Was sort of by the following.

We took an approach that was really pretty novel, which was to do large, next slide, single, individualized random, placebo-controlled randomized controlled trials for each vaccine.

Recognizing that the manufacturing time for each vaccine would be different. And that turned out to be the case.

RNA came out first. The viral vector second, and then the proteins are third. And they're hard to make.

There maybe other cheapest vaccine that could be utilized from a cost per unit, cost of goods. But, it does take longer to do this. And even one of the proteins currently is still in clinical trials.

We used a collaborative gradient. We took essentially the academic centers of our entire country participated in clinical trial sites.

Supplemented with the clinical research organizations from the pharmaceutical companies.

We averaged around 90 clinical trial sites per study.

The studies were harmonized. So they really all did have essentially the same end point.

We did that through discussion groups. Getting everybody to be bought on with that.

We used a common platform and a common laboratories to do the, both the COVID-19 detection, as well as the antibody assays.

We had consulting biostatisticians who

were with the HIV vaccine programs that really designed the studies and analyzed the studies, and are doing the correlates protection.

And there was a common DSMB to -- that monitored all the studies that the U.S. Government funded.

And made the decisions about when the trial was ready to mature commonly. So, it was an even playing field. Next slide.

We also were able to involve the citizens of the country in a very unique way. As I said, we were doing one 30 thousand person trial a month for a five-month period of time.

And we needed to enroll the citizens that we needed to enroll. The communities in which the force of infection was the greatest, which meant our black and Latinx population.

And to get them, to find that, we enrolled at the rate that we could tell that the vaccine would work in these communities.

And we were able to do that frankly, by a marketing campaign that was led by this lady, Sally Bock at the HIV Vaccine Trial Center here

in Seattle. Next slide.

We were able, if you could click at the bottom to get this going.

(Whereupon, the video was played)

DR. COREY: We were able to do a marketing campaign on television and social media.

We set up a natural registry for people seeing these kinds of ads to enroll by your risk factors, next slide, could be sent to the clinical trial sites. Let's go beyond that one.

And we were able to enroll these trials, each one, within a six to eight week period of time.

So, we were really conducting trials in which essentially two thousand people, between 15 hundred and two thousand people day were enrolled in these trials. And that's really the issues of the seamlessness of how this was achieved.

Now, the success was really not quick.

I mean, if you look at it, we were able to do this as a sort of scientific establishment, because we had put in 20 years of hard scientific effort in what I would say is four areas.

And it was like just in time, sort of

putting together with auto, an auto part, or a car.

Twenty years of working on mRNA. First, you know, 1992 was when it first showed. They translated it into a mouse.

The patent showing that you could get high transcription by -- through Weissman and Kariko, was in 2005. That's the patent that both Moderna and Pfizer have.

And much of that was done through funding through the HIV program. Which HIV has really been sort of the, I would basically say the NASA of vaccine development here.

Twenty years of structural biology that Barney Graham had been working on. First RSV, then the human Coronaviruses and then SARS.

And MERS with respect is showing that the prefusion portion of the viral, spike protein or the viral trimer for landing, was one that was the most immunogenic for neutralizing antibodies.

And then if you stabilized it in a particular way with some prolines, you could make a stable prefusion protein.

And this has been used in four out of

the five vaccines that we tested with very high neutralizing antibodies.

There was 20 years of pandemic preparedness in which the RNA platforms, the PAD 26 platforms, DNA platforms as well as some of the nanoparticle platforms had been worked on by the Vaccine Research Center, as well as within the HIV program.

And there's 20 years of building the research organizations that conducted this, the HIV vaccine network and the prevention network.

By that time, we had had 72 clinical trial sites already. We had a large computational and biostatistical group.

And we also had laboratories that had validated the neutralizing antibody assays and the binding antibody assays that we actually had just validated the submonoclonal antibody studies.

So, it was putting these together that led to this rapid success. Next slide.

Now, a lot of this has changed. And that the virus has fought back with rapid antigenic variation. The Delta wave and now the Omicron wave.

Next slide.

And this slide's actually already been shown by Jennifer. You know, Omicron is now essentially 99.9 percent of the isolates in the United States. And most of them globally. Next slide.

And what the virus has done, is change through selective pressure. And each of the variants has had a decrease in neutralization to neutralizing antibodies induced by the vaccination.

They're listed here. Alpha two fold, no really change in vaccination efficacy.

Beta, which was first discovered in sub-Saharan Africa, was eight and nine fold. Didn't really create much of an epidemic or outbreak in the United States.

Gamma, three and a half fold. Delta, four fold. And Omicron has upped the ante too essentially a 30-fold decrease in neutralization or resistance to neutralization by the variant. Next slide.

And this has affected our vaccine

efficacy. This just came out two days ago. It looks at the ER visits and the hospitalization visits in a large network of hospitals in the United States with the RNA vaccines.

Against Delta, when it came to ER visits, it's 86 percent. Within the first six months after vaccination, it drops to 76 percent.

It goes up to 94 percent with your third boost. And it works very effectively still for Omicron, 82 percent.

When it comes to hospitalization, the third boost is 94 percent against Delta. It goes up to 90 percent with Omicron.

These are large databases, the number of cases with Delta that are like 250 thousand. Omicron at the moment is around the 20 or 30 thousand.

The Omicron period is still short. We will obviously have probably some waning immunity.

But, as far as vaccination goes, we really do have quite good protection still with boosting, with both ER visits and hospitalization. Next slide.

So, we'll sweat through Omicron until

we make more monoclonal antibodies and the protease drugs in the field.

It is true that we've had drop out of both the Regeneron and Lilly monoclonal antibodies.

And Trip will say more about those things.

And MERS antibody as well as the Pfizer drug really come up in the, in the end of April.

And for breakthrough cases from vaccinated people, that should help.

I think better treatment options will alter our perception of risk. In the vaccine area we do have a durability issue.

And how to solve it is -- is where we're working on at the moment. With a variant come increase the immune response and give us better durability.

It's sort of remarkable that with the very -- huge variation we see in Omicron, that still ancestral strain gives us really good cross-reacting antibodies. Puts into memory a greater breadth than what we have seen.

And there are second generation vaccines in development. We're creating a research

infrastructure to evaluate which ones add major benefit over current platforms are needed.

And we may need to switch platforms to get greater durability. This is where the field is, and this is where active platform investigation is. Next slide.

So, the endemicity of SARS-CoV-2 does require us to sustain a proper research network.

The structure we worked on there had a terrific alignment between big pharma and public health.

We need a little bit more innovation.

We need to let the small guy in now. We need a sustained research program for the continued development of better vaccines and therapies.

Jennifer did talk about our global responsibility. That we need to vaccinate the world.

There -- a lot of these major mutational variants do come from immunocompromised people.

On the globe the highest number of immunocompromised people are in the HIV community.

And merging HIV and COVID-19 policies and treatment practices need to be done.

And we need to spend more time on our

policies and programs of getting low and middle income countries the ability not only to have their own vaccines, but to have vaccines be part of their culture and economy.

To overcome vaccine hesitancy that is occurring in their countries also. So, I'll end with that. And I think that's my last slide.

I want to thank the people that I worked with in the countermeasures activity group as well as Operation Warp Speed.

Kathy Neuzil, my co-chair with this, Mike Cohen, John Mascola, Barney and David Montefiori and the people illustrated here were -- worked tirelessly in this vaccine effort. Thank you.

DR. RANNEY: Thank you, Dr. Corey. What an extraordinary quick journey through the development and continued impressive efficacy of the vaccine.

And I'm going to use that phase, the winter of our discontent a fair amount going forward. Thank you for that.

It is my pleasure to now introduce Dr. Trip Gulick. Dr. Gulick is the Rochelle Belfer

Professor in Medicine, and Chief of the Division of Infectious Diseases at Weill Cornell Medicine, as well as an attending physician at New York Presbyterian Hospital in New York City.

Dr. Gulick's research interests include designing, conducting, and analyzing clinical trials to refine antiretroviral therapy strategies for HIV treatment and prevention, and assess antiretroviral agents with new mechanisms of action.

He serves as Co-Chair of the NIH COVID-19 Treatment Guidelines Panel. Is a member of the American Society of Clinical Investigation, the Association of American Physicians, the International AIDS Society, and the Infectious Disease Society of America.

He has presented at national and international meetings, and published widely.

Thrilled to have Dr. Gulick joining us today to speak about how new therapeutics are currently changing the game, and will continue to do so in our treatment of COVID. And to talk about the challenges of ensuring broad and equitable access.

Dr. Gulick, to you.

DR. GULICK: And I knew that. Thank you for that kind introduction. I have no disclosures. I'm pleased to be here with you today to really review where we are with COVID-19 treatment in 2022.

So, let's start by reviewing the clinical course of COVID-19 which is illustrated on the slide here. Over on the left, someone gets infected at the beginning of the illness and may not develop any symptoms at all, may be asymptomatic and may recover from the illness.

However, some will go on to progress to develop symptoms over two to seven days, and at that time, the amount of virus in the system, particularly the nose and throat, will increase to very high levels, reaching perhaps its highest levels a day or two prior to the development of symptoms.

Again, after the development of symptoms, which, as you know, can be very much like a common cold with cough, sore throat, congestion, many people will recover. However, some will go on to progress.

The virus that causes COVID-19, SARS-CoV-2, can be a potent stimulator of an inflammatory response, so stimulating inflammation.

Initially, this starts off in the lungs and can lead to severe COVID disease that requires a visit to a healthcare worker and perhaps admission to the hospital if oxygen is required.

Again, many people will recover, but some will continue to progress, develop increasing amounts of inflammation in the lungs and develop respiratory distress which may require high-flow nasal cannula oxygen or even needing to be on a respirator.

This may again progress over the course of weeks. Some will recover. Some will go on to die, and that is a consequence, as we know, of the most severe complications, not just of the lungs, but total body of COVID-19.

So, how can we impact the course of this illness? What treatment strategies have been employed? Well, two broad categories. One are antivirals. This, of course, is an illness, COVID-19, caused by a virus, SARS-CoV-2, and so

coming in with compounds that could interfere with the virus, antivirals, was a strategy thought about very early in the course of this epidemic.

Later on, as the inflammatory cascade gets induced, one could use a category of drugs called immunomodulators. These are drugs that dampen down inflammation and the immune response.

Now, remember when COVID-19 arrived at the end of 2019 and in the U.S. at the beginning of 2020, we had no effective therapies for COVID-19. We've now come quite a ways.

So, two arms of the COVID-19 treatment strategy, one, antivirals, one, immunomodulators. Antivirals take advantage of the fact that SARS-CoV-2, the virus that causes COVID-19, binds to a cell.

And in most cases, this would be a cell in the upper respiratory tract first, early in infection, and then goes through a series of processes where the virus essentially takes over the machinery of the infected cell and uses it to make copies of itself.

So, it makes copies of its genetic

material in the form of RNA and it makes viral proteins which are processed, and then these all assemble at the surface of the cell and then bud off into new viral particles.

Many of these viral particles are fully capable of infecting the next cell that they come into contact with. So, we call these sequence of events the viral life cycle. It's how the virus reproduces in the body.

How do antivirals work? Well, they throw up roadblocks in this life cycle. The ones that act earliest are antibodies as Dr. Corey has mentioned. These actually bind to the virus and prevent it from binding to the cell.

Another group of agents are called polymerase inhibitors. These are drugs that interfere with the virus making copies of its own genetic material, RNA, inside the cell.

And a third group of drugs are called protease inhibitors. They interfere with the virus making its own proteins and then combining them into new viral particles. We now have examples of all three of these that are in clinical use.

Again, further along in the course of COVID-19, we see a tornado of inflammation and substances called chemokines recruit cells and inflammatory proteins, first into the lungs and then through many organs in the body. We call this the COVID-19 inflammation storm and it can lead to respiratory failure and severe complications and death.

We do have a whole host of compounds now that can modulate this response or dampen it down and we call these immunomodulators.

So, where are we in terms of treatment availability in 2022? For inpatients with COVID-19, we have an antiviral drug known as remdesivir.

It is the first and only FDA-approved drug for the treatment of COVID-19, and that harkens back to clinical trials that were completed in 2020 and showed benefit of remdesivir in decreasing clinical progression. And you can see FDA approved remdesivir for the treatment of COVID in October of 2020.

We also have three of these immunomodulator drugs that have been demonstrated

in clinical trials to decrease mortality, decrease death, and these are the corticosteroid dexamethasone and two other immunomodulators, one known as tocilizumab and one known as baricitinib.

And then finally, FDA uses a special program called Emergency Use Authorization when a compound shows promise in the treatment of a disease, and that's been employed widely in the treatment of COVID-19.

So, the Emergency Use Authorization is not full approval by the FDA, but conditional approval that allows access to promising compounds, and you can see two strategies that have received EUAs for inpatients.

What about for outpatients with COVID-19? Recently, three antivirals have been demonstrated to decrease disease progression in the highest-risk patients.

Who are the highest-risk patients? People who are elderly or have another disease called a comorbidity such as lung disease, heart disease, or diabetes, or many others, that increase their risk of developing moderate to severe progression

of COVID-19.

Three antivirals available, remdesivir, the same one we use for inpatients, was recently FDA approved just last week for the treatment of outpatients, and then the first two oral antivirals, one called molnupiravir and one called nirmatrelvir, and both of these are available through the FDA Emergency Use Authorization.

As mentioned, there are also three monoclonal antibodies, either in combination or singly, that have been demonstrated to decrease disease progression in those high-risk patients.

Two of the combinations of monoclonal antibodies have been found not to be active against Omicron, which, as you've heard, is by far the dominant species in the United States.

And just in the last week, the FDA Emergency Use Authorization programs have been put on pause, so these monoclonal antibodies no longer available. However, a third one called sotrovimab retains activity against the Omicron variant and is available by FDA Emergency Use Authorization.

Well, how do we know what to do? How

do we know what strategies work? And sometimes what we do is turn to guidelines. I'm really proud to be one of the three co-chairs of the NIH COVID-19 Treatment Guidelines Panel.

This panel was formed in April of 2020, soon after the first cases of COVID here in the United States, with the goal of assembling a group of about 50 people from the government and from academic institutions across the country, and our mission is to look at all available data, synthesize it, and then make practical treatment recommendations to practicing physicians and the general public in the United States. We know now that we also have a large audience of people internationally.

So, what do the guidelines say about COVID-19 treatment in 2022? Well, first, let's look at inpatients, and you can see the last time we updated the guidelines was just last month. In fact, we've updated the guidelines 40 times since we first began in April of 2020.

So, for inpatients admitted for COVID-19, and I underlined the word for because

there are patients who are admitted today with COVID-19, meaning that they're admitted for another reason, but are found on routine testing to actually be infected with the virus.

And so, for the group admitted for COVID-19, the least sick group are those who are hospitalized, but not requiring oxygen, and the guidelines say for those who are at high risk of disease progression, again, elderly or with co-diseases, the recommendation is the antiviral remdesivir. In this early stage of disease, no immunomodulators are recommended.

The more commonly admitted patient is hospitalized because they require oxygen, and the guidelines say if it's a minimal oxygen requirement, same strategy. Use the antiviral remdesivir.

However, more commonly for a significant oxygen requirement, use a combination of the antiviral remdesivir with the immunomodulator the corticosteroid, a powerful anti-inflammatory, dexamethasone.

And then for the sickest in this group, the people who need oxygen and have rapidly increasing

oxygen needs and have demonstrated significant inflammation, add a second immunomodulator, either baricitinib or tocilizumab, and we know that these three immunomodulators have been associated with mortality benefits.

And finally, the sickest group are those who are hospitalized and require high-flow oxygen or even being put on a respirator, and here the guidelines say really focus on the immunomodulator, dexamethasone, and within the first 24 hours of being admitted to an intensive care unit, add a second immunomodulator, in most cases, tocilizumab.

Well, have these made a difference? Have these interventions made a difference? Here is some data from a group called the Premier Health Database.

They looked at hospitalized patients in the United States in the second half of 2020 who had COVID-19, a large number of patients, over 190,000, cared for at over 800 U.S. hospitals.

Who were these patients? Older, the average age was 64, about half men, half women, good representations from Blacks, 19 percent,

two-thirds had either Medicare for seniors or Medicaid for economically disadvantaged people, and over 20 percent had other significant illnesses like chronic lung disease, obesity, or high blood pressure.

Well, what did we notice in this big cohort of U.S. patients hospitalized with COVID? Well, the treatment trends were notable. So, dexamethasone, that immunomodulator use as shown in the graph in blue, went from seven percent use all the way up to 77 percent use when clinical trials showed benefit and guidelines recommended its use.

Remdesivir, the antiviral, went from five percent shown in red up to 47 percent use, and in yellow, we see anticoagulants or blood thinners, which is an immersion therapy, at about 25 to 30 percent.

So, you can see the clinical trials really made a difference here. Demonstration of clinical benefits led to endorsement by the guidelines and very rapid uptake by the medical community.

Well, did it make a difference for patients? Well, the first thing to say is that

the length of stay was reduced over this time period.

Both hospital stays and intensive care unit, ICU, stays were reduced by a day. Well, that's impressive when you think of the tens of thousands of people involved, but even more significant was mortality.

So, over this time period, mortality, with the improved use of these proven interventions, was reduced by 35 percent, and that has continued to reduce across the country and across the world.

Well, let's turn to outpatients. And again, we just updated our guidelines on December 30 and here is what we say. For high-risk outpatients, again on the basis of their age or co-diseases, with mild to moderate COVID, we recommend four therapies and they're going to be listed here in order of preference.

Number one is the new antiviral protease inhibitor known as nirmatrelvir. This is an oral drug which is given for five days and clinical trials showed that it decreases clinical progression by 89 percent.

What are the issues with this drug? It needs to be given with a second drug called

ritonavir, which can cause drug-drug interactions with other important medications that people take.

An even bigger issue is that it is in limited supply in the United States right now.

The number two choice is the monoclonal antibody sotrovimab. That requires only a single intravenous infusion and in clinical studies showed decrease in clinical progression by 85 percent.

What are the issues? Well, it's an IV infusion, so the logistics of receiving it can be challenging, and once again, a limited supply.

Number three is remdesivir, the antiviral polymerase inhibitor, and we use for outpatients a shorter course of therapy, a daily IV infusion, but three days in a row, and that scheme led to a decrease in clinical progression of about 87 percent.

And as you can see, these three therapies are roughly the same in terms of reducing clinical progression, but you can imagine the daily IV therapy for three days also poses logistical issues.

Only when the three cannot be used is the fourth choice, and that's the antiviral

molnupiravir. This is a polymerase inhibitor that actually works against the virus by inducing mutations in the virus.

It's given orally for five days and is less effective than the three therapies above. It decreased clinical progression on clinical trials by 30 percent.

And you can imagine a drug or a compound that induces mutations, you would have issues giving it to pregnant or breastfeeding women or children.

I want to highlight two other issues with our current outpatient medications. The first is, as I've already suggested, some of these are in quite short supply, and what do we do when we have medications that can benefit high-risk patients, but we don't have enough of them? We're put in an uncomfortable position where we have to prioritize patients for the medications.

So, the guidelines have actually taken a step in this and considered which patients should be the highest priority to receive these medications which are in limited supply, and the basic thought here is the patients most in need should have the

highest priority.

So, tier one in our guidelines says that the group that should receive these first are immunocompromised individuals, people whose immune systems are not functioning completely well either because of another disease like cancer, or an organ transplant, or because they're on medications which decrease immune function, and that's regardless of their vaccination status. As you know, many immunocompromised individuals will not develop a suitable response to vaccines.

Then the second group are unvaccinated individuals who are either elderly over the age of 75 or are over the age of 65 if they have additional risk factors, and again, that would be a series of other diseases that they have that increase their risks. This is the group that's prioritized across the country in terms of who should receive the outpatient therapies.

You can see the other tiers here take into account vaccination status, age, and whether you have concomitant diseases.

And just to put it on the line, it's

uncomfortable for us as U.S. physicians to have to prioritize among our patients for therapies which we know work, so this is putting many providers in an uncomfortable situation.

And then my last point is just to point out that distribution of these drugs is not equal among all Americans. So, these are data on COVID patients, and they looked at over 800,000 of them across 41 healthcare systems in the United States, and looked and saw how many people got monoclonal antibody treatment, one of the treatments I've highlighted during this presentation.

The first answer is it's less than seven percent of all patients receive these therapies, but even more striking is when you look by race, you can see that white patients proportionally received monoclonal antibody treatment more than other groups, more than Blacks, more than Asians, and more than other races, so there is a racial disparity here.

Similarly, ethnicity, non-Hispanics received these therapies more frequently than Hispanics who had COVID disease. So, there is a

racial and ethnic disparity in who is receiving COVID-19 treatment here in this country right now and that is a problem we need to address.

Lastly, I'll just thank some colleagues for slides, and although I've focused on treatment, I want to echo Dr. Corey that vaccination is an important tool against this epidemic.

This is my Division of Infectious Diseases, and yes, that's me up here rolling up my sleeve. So, I'll stop there. Again, thank you for inviting me.

DR. RANNEY: Thank you, Dr. Gulick. That was so clear and helpful, and a huge thank you to IDSA for all the work that you guys have been doing in synthesizing this information so quickly for frontline physicians and other healthcare providers across the country.

So, last, but certainly not least, Dr. Georges Benjamin, who I think needs no introduction.

He's known as one of the nation's most influential physician leaders because he speaks passionately and eloquently about the health issues having the most impact on our nation today, including, of course,

COVID-19.

From his firsthand experience as a physician, and I will say he served for a while as Chief of Emergency Medicine, so I count him as an emergency medicine colleague, he knows what happens when preventative care is not available and when the healthy choice is not the easy choice.

He's been an Executive Director of APHA since 2002 and continues to lead the association in its amazing push to make American the healthiest nation in on generation.

Dr. Benjamin is, among many other accolades, a member of the National Academy of Medicine and the National Academies of Science, Engineering, and Medicine, and also serves on the board of numerous organizations.

He's been named one of the top 25 minority executives in healthcare by Modern Healthcare magazine three times, in addition to having been voted among the 100 most influential people in healthcare for a decade straight.

Dr. Benjamin, it is my pleasure to introduce you and to turn this presentation over

to you.

DR. BENJAMIN: Thank you, Dr. Ranney.

We can go to that next slide. Let me just say that, you know, when public health folks -- I'm going to pick up on the guidance discussion.

When public health folks make guidelines, like CDC, they make their guidance decisions based on science as we understand that science at that particular point in time, and that's important for people to understand.

We just heard a very eloquent presentation about our treatment guidance, which we know has gone from, quite frankly, just providing supportive care to now a range of therapeutic options for patients.

Public health has had to do exactly the same thing. We also have to communicate that science and the uncertainty around it, particularly when we have a challenge like this where we have an infectious disease that is with a high degree of variability and change, lots of variants, lots of understanding of what the virus actually does based on a lot of assumptions that turned out in some

cases not to be true, such as we thought this would be like SARS 1, but it turns out it's its own creature.

And we have to cover several audiences with different levels of understanding, and people with different desires to use the information for different purposes.

What I mean by that is policy makers have a reason for the information which is different from journalists, which is different from, you know, the average person on the street, which is different from the clinicians who have to implement that.

So, we're going to talk a little bit about some of the recent guidance that CDC did on masks, the one on isolation quarantine, testing in terms of return to work, and this issue around the definition of fully vaccinated.

DR. RANNEY: Oh, Dr. Benjamin, we just muted you by accident, apologies. I'm not sure how that happened.

DR. BENJAMIN: No problem.

DR. RANNEY: There you go.

DR. BENJAMIN: So, the masks issue, I want to make it clear. This has always been the

approach to masks. We recognize that the purpose of masks is as a risk reduction tool in addition to the other things.

Before we had vaccines, masks were extraordinarily important, but they are also still extraordinarily important, and we now know because of Omicron's significance in terms of its infectivity, masks still play a very important role.

So, obviously, not having a mask as a barrier in front of your face means you're not providing any protection at all. Cloth masks do provide protection, but they needed to be multi-layer. They're certainly better than no mask at all and they're probably a little less protective than surgical masks.

The benefit, of course, is that you can wash and clean your surgical masks, I mean your cloth masks, but your surgical masks essentially they're for all practical purposes really a one-time mask and you should throw it away.

But the gold standard of course here are the high filtration masks, N95, KN95. I want

to point out though that a high filtration mask that is not properly worn and tight is certainly not giving you the protection that you need, so you have to wear those masks, as well as the surgical masks and the cloth masks, properly to get the best seal that you possibly can for this disease. Next slide.

So, as we know very recently, CDC, using some new information, updated and shortened the recommended isolation quarantine period for the general population. They also made some recommendations for long-term care and clinicians in healthcare settings, acute healthcare settings as well.

But I think this quote, which actually Dr. Walensky said, really gives you a sense of what they were trying to achieve. They recognized that Omicron was spreading. They also recognized that they needed to give guidance that people could actually use in a functional way.

They pointed out that prevention is our best option, getting vaccinated, and still using at this point the term boosted, wearing a mask in

particularly indoor settings and areas of substantial and high community transmission, and, of course, take a test before you gather, particularly when you're around people you don't know.

This advice has been persistent and consistent, and I just want to encourage people to continue to follow this advice because I think it's really sound public health advice. Next slide.

Having said that, the way to think about the guidance is ten days. Everyone should focus on the number ten days. And they basically looked at some data which I'll show you in a minute which basically said that the greatest risk for you sharing your infection with others is the first five days, but that beyond that, there is still some risk, although it greatly diminishes after the five-day period.

And for that reason, you should certainly wear a mask, and these are for people who have obviously turned up positive and people who we have found are infected.

So, you know, it can get really complicated if you think about too many different

factors, but for the vast majority of people, we should think ten days, and that's for isolation.

And in quarantine, quite frankly, there is a variance on that, but at the end of the day, if you're going to quarantine, it's still five days, and then the next five days, you should wear a mask.

If you're boosted, if you're fully vaccinated and boosted, which the phrase we're now using is up to date, then you can not have to wear that mask after five days, but from a practical perspective, you should be wearing a mask anyway.

So, wear the mask, and if you're reinfected, obviously, for ten days, that's the period of time you ought to be thinking about it for most people as we think about the new guidance that they've put out. Next slide.

And to give you a sense of this, if you look at this graph, it just shows you that most people are not shedding virus after about five days, and this is from one pre-print study, but there have been many other studies that they looked at when they made that decision.

And again, the same point, regardless

of the duration of the incubation period, almost no transmission was predicted beyond the five days from the time you had symptoms. Next slide?

I think the other thing that's interesting, of course, is that viral clearance with vaccination is enhanced. And again, this is a strong, strong argument to get vaccinated, a strong argument that if you're vaccinated, you're less risk to others by viral shedding. Next slide?

And then the big debate about antigen tests for return-to-work, and, of course, as you know, we really have two tests that are out there that we're using with some regularity. One, of course, is the PCR test.

The challenge of using it for predictivity to go back to work is that it's quite often positive both before and after you are contagious, so it really isn't the best tool to use.

If you're negative, great, but far too many people are still positive, and not just a few days afterwards, sometimes weeks afterwards, and we still have people that are even positive months

afterwards.

But, if you use the antigen test, you're much more likely for that to be reliable as return-to-work, and if you combine that with the loss of symptoms, meaning that you're feeling better and you've lost all your symptoms, again, through a risk-based perspective, your risk of infecting others is greatly reduced.

This is an important thought process for people that are in the healthcare setting because while we'd prefer everybody to be totally, you know, asymptomatic and totally symptom free before they go back to work, the best tool to think about that in terms from a risk perspective is to make sure that you get a test, and if you're negative and you're symptom free, you're much more likely to be able to go back to work.

And again, that ten-day period is very, very important as part of that process for guidance for people who are having to make these kinds of decisions. Next slide.

So, obviously we don't want people to go to work if you're not feeling well. That just

makes a lot of sense. We don't want people at work because they're not going to be as productive at work.

We know that these symptoms from Omicron are often very mild, but very mild does not mean that it does not have significant morbidity and maybe significant mortality both for vaccinated people, which is very rare, but for some vaccinated people, but certainly for unvaccinated people. Again, and most transmission occurs early as we saw in those charts. Next slide?

So, finally, you know, CDC has been under some pressure to decide what fully vaccinated means, and I personally think that they've picked a reasonable term that does not create confusion as we go forward.

The concept of being up to date means that you've received all of the recommended vaccines, including, you know, recommended boosters when you're eligible.

And I think this is a more rational way for us to think about being vaccinated because this allows us to look forward in terms of whether or

not someone needs to be vaccinated in the future.

It also allows us to customize this from a clinical perspective for those people who are particularly immune-compromised and may need a fourth vaccination and maybe an additional one later as we get a better understanding of the durability of vaccinations in immunocompromised individuals.

Next slide?

So, you know, again, as people think about this in summary, we like to make this guidance based on the best biological science and evidence at the time, realizing that that will change over time, but we also have to utilize the best behavioral science to achieve compliance.

So, when a public health agency is saying well, this is the best science that we understand, but we want you to do X over Y because we think that's the best way to get people to do what we want them to do, that is taking both the biological science and the behavioral science and optimizing the guidance and the advice in order to actually achieve the public health goal that they're trying

to achieve, and that recognizes that you have to communicate this in a way that addresses the degree of uncertainty to ensure and maintain trust.

The challenge we've had is when we've come out and said things that sound like they're certain, like we did, quite frankly, when we said, you know, if you are vaccinated, you won't have to wear masks, and then had to reverse ourselves, that created some real challenges, and so we just have to be a little more thoughtful as we communicate what we know when we know it, and I think that's my last slide. Thank you very much.

DR. RANNEY: Thank you, Dr. Benjamin, well said. I mean, this is as much an issue as is true with so much of public health. It's as much a biological issue as it is a psychological, and behavioral, and instructional issue, so thank you for that.

I'm going to invite all of our speakers to turn their cameras on and turn their microphones on. I think we could probably go for another hour with the questions that have been put into the Q&A.

A huge thank you to all of you who are attending

who have put such thoughtful questions in.

Of course, they're not going to have time to get to all of them, so I'm going to try to direct a couple of quick questions at the various speakers and then I have a final question for the whole panel to weigh in on.

My first question for Dr. Nuzzo is during the current phase of the pandemic, is surveillance testing still a useful strategy? Can you talk about kind of how those case numbers are changing and about the concept of surveillance testing as we deal with Omicron and home tests?

DR. NUZZO: Yes, I mean, I think we will get to a point one day where we stop looking at cases in the way that we're looking at them now, but I think it is still helpful for us to understand how the virus is changing, whether there are new variants emerging, whether people are getting reinfected in ways that we don't expect.

So, I still very much look at cases and I think testing to try to understand this virus is still important, and also, you know, to try to get an idea of how much illness it's causing.

I mean, many of the questions that we wrestle with, you know, how severe is it, how transmissible is it, all of those things, you know, hinge on having good denominators, and surveillance testing is one of the ways that we get the good denominators that we can help sort of couch the, you know, concerning numerators against.

So, I still think it's important. Obviously, we have to interpret all of the data differently as we learn more, and when we're talking about testing in a highly vaccinated population, how we interpret those data is going to change than when we were talking about testing in a completely unvaccinated population.

But I think with all of those caveats and putting all of the data together, you know, hopefully we can continue to triangulate our way to the truth.

DR. RANNEY: Isn't that always the way, the triangulation to the truth? That's science.

Dr. Corey, for you, a lot of kind of really impressive thank yous for that extraordinary collaboration.

Folks had questions about the discussions that they've heard about a universal coronavirus and would love to hear your thoughts on that.

DR. COREY: Well, my thoughts are that would be great and there is work on it. There are -- you know, there's a monoclonal, sotrovimab, that is in a conserved area.

So, conceptually there are some nice ideas coming out. It's a little bit harder to both manufacture and work on it, but I do think that we will see some clinical trials of pan-sarbecovirus, which is sort of a pan across SARS-CoV-1 and SARS-CoV-2 kind of vaccines that will converge in the next six to nine months and we'll see where human testing brings them.

I mean, having said that, you know, ancestral strain is impressive. You know, we have put into clinical trials both Beta and Delta variants and used RNA for that. They really worked impressively different than ancestral strain. In other words, they were really quite not really quite as good.

So, you know, we will be looking at strain variation and platform variation to see if we can increase the durability, and frankly, increase the magnitude of the neutralizing antibodies response so these cross-neutralizations will still give us high titers.

DR. RANNEY: We should be so lucky, and of course we'll be watching in the months to come to see what happens with the durability. I know there were a bunch of questions in there about are we going to have more boosters coming? I think the answer is we're going to wait and see for now. Thank you.

Dr. Gulick, a question for you. There were a bunch of folks who wanted to learn a little more about Paxlovid, of course, which has been hailed as this miracle cure to COVID.

We know that there are -- you know, you outlined some of the kind of ways that we're triaging who gets it first, but people were curious to know a little bit more about contraindications in terms of the age limits about Paxlovid prescriptions at this point.

DR. GULICK: Sure, the first thing to say is that miracle cure would be an overcall here.

What it did show was a decreased risk in clinical progression for people who were at high risk, but had mild to moderate COVID and were outpatients.

That was the group that it was studied.

Two important caveats about those data even though it was an 89 percent reduction, one was they were all unvaccinated. That was one of the requirements for the study, and the second is this was pre-Omicron, so that was likely in the era of Delta that we saw these effects.

Nevertheless, it's encouraging that we have an oral antiviral which could actually impact COVID-19 for outpatients.

The thorny part of this drug is that it requires that second drug called ritonavir which is a booster. It boosts the levels of nirmatrelvir, which is the protease inhibitor itself.

And the boosting is done by interacting with the liver and that can cause drug-drug interactions with many other drugs, so people need to be quite careful about that.

Why are the restrictions in place? Well, the supply was very limited at the beginning. It is scheduled to increase and the U.S. government has bought many more doses of this drug that are expected in the next couple of months, so we may see increasing supplies.

But as I've tried to emphasize, when you have limited supply, really you need to focus on the people that will benefit the most, that is the people who are at the greatest risk, and we know either being immunocompromised, not having an intact immune system, or being elderly are the two biggest risk factors for progression of disease, and that's where those prioritization schemes come from.

DR. RANNEY: Thank you, Dr. Gulick, and I will add for those who are prescribers in the audience that severe renal disease is also a contraindication.

And I will say personally as an ER doc, I have only prescribed Paxlovid for one person so far because everyone else I've wanted to prescribe it for had contraindications, medications they were

on that they couldn't come off of or had unfortunately renal disease, although my ID colleagues probably have had a lot more luck than I have in getting it prescribed.

There are also some great websites that provide access to both monoclonals and the new oral antivirals that HHS has created. If you Google HHS antivirals access, you can find there are real-time maps of access at pharmacies around you.

Dr. Benjamin, a question for you, and then I will have a final question if we have time for the panel, is to talk a little bit about the need for researching the improvement of public health education and how you would like to see the people attending this webinar today think about combating the distrust of the public health establishment, science, vaccines? If you could give people a couple of takeaways to bring back to their communities, what would they be?

DR. BENJAMIN: Yeah, I think the first thing is to recognize that we need to depoliticize this debate, and, you know, healthcare and the public health community are doing this based on the need

to try to protect people's health and well-being.

And so, we all need to take a deep breath and step back and recognize that people that are giving you the wrong information are doing it for a range of nefarious purposes, and I always used to tell my patients look, here is my best advice, but here is where you can go for a second opinion.

And so, I encourage people to go to authoritative sources like the National Academy of Medicine, like an academic health center, like the CDC, in most cases, the Infectious Disease Society of America, another authoritative place to go, but go to authoritative sources, and while Facebook and other social media tools may deliver authoritative information, always go to the source. Go to the original source.

DR. RANNEY: That is a great recommendation, I think, for all of us, and all of us that are teachers hopefully tell our students that as well, so thank you, Dr. Benjamin.

So, the final question, and I'm actually going to ask you each to just give me a sentence or two because I do know that we're coming right

up against the top of our 90 minutes.

You know, we've seen a lot of calls in the last couple of weeks to talk about this as now being in an endemic phase or that this is the new normal, that it's time for us to move past our COVID precautions.

And I would love to hear from each of you kind of what your response would be if you had a friend or family member ask you about whether or not we're currently in the endemic phase and how that changes what's next.

I'm going to go actually in reverse order of how you spoke, so I'll start with Dr. Benjamin, Dr. Gulick, Dr. Corey, and then Dr. Nuzzo.

DR. BENJAMIN: Look, all pandemics end, but this one is not there yet, and I think it's important for people to follow the current advice that we have, get vaccinated, wash your hands, wear a mask, keep your distance, and it will come.

The great pandemic in 1918 went three years too, so our species has seen this kind of problem before. It will end. Just be patient.

DR. RANNEY: Thank you. Dr. Gulick?

DR. GULICK: Well, I'll say that whenever we've tried to make predictions about COVID-19, we've often been wrong, and this virus continues to surprise us.

So, I'm an optimist. I think right now, enough people have either had Omicron infection and/or been vaccinated that there may be enough immunity to drive this infection to low levels. That's the hope, and could we actually continue there at low levels for a while.

The pessimist in the crowd would say yes, but what about the next variant that is already brewing somewhere and may come along? And only time will tell as to which scenario we're going to see.

DR. RANNEY: Thank you. May our crystal ball foresee the good side exclusively. Dr. Corey?

DR. COREY: Well, endemic is not over half a million cases a year, a day I mean, so I think we will get to endemicity.

And part of that will be perception and some of that will be when we not only have essentially baseline immunity that's in the 90s from either

prior infection and vaccination, but we also perceive that we will have drugs if you get a breakthrough infection that will not alter or make you sick and have the high incidence rate, and so I think we do have the tools to sort of change perception.

I would call endemicity eventually to happen. We will have variants, but we will have to learn with this pathogen, and I think our science, our remarkable science, will allow us to live back the way we did before.

At what level of case count, I don't know, and I hope that we're able to keep the mortality less than what we have for influenza.

DR. RANNEY: Thank you. Isn't that the debate right now? Saying that our goal is H1N1 levels is not, to me, a reassuring future. Dr. Nuzzo, your thoughts?

DR. NUZZO: Yeah, I agree with the statement that all pandemics end, but this virus isn't going away. It's not going to disappear.

And while we are going to at some point end mandatory measures, that doesn't mean that we can't and shouldn't continue to take measures to

protect ourselves individually and voluntarily elect to try to protect ourselves.

And the thing that I really stress to people, because I know lots of folks who are worried about the virus, but not yet vaccinated, is that, you know, all of us are probably going to meet this virus at some point, and really the vaccines, you know, offer us the armor, the best defense, you know, when we have that first contact with the virus.

And so, I think for people who are hoping they can just ride out this wave, just to let people know that, you know, COVID is in our future and we want to go into that fight with the best level of protection possible.

DR. RANNEY: Thank you. Well, a huge thank you to all four of you for this terrific hour and a half of presentations, a thank you to the APHA staff and to the National Academy of Medicine for organizing the webinar, but most of all, a thank you to all of you who've attended.

As both a physician and a public health professional, I know how tough the last few years have been. As a parent and a child of elderly parents,

I know how tough the past couple of years have been personally as well, and I want to thank all of you for continuing to show up day after day and continuing to do this work.

We wouldn't be in as good of a place as we are today if it weren't for all of you, and your taking the time to learn and to engage in webinars like this helps to move us more quickly towards a better future.

So, I just hope that you all, as attendees, can also give yourselves a thank you for everything that you are doing and have done.

With that, I will close up. I do want to remind folks that everyone who registered for today's webinar will receive an invitation to the next webinar.

Today's webinar has been recorded. I've seen lots of questions about that. The recording, a transcript, and the slide presentations will all be available on covid19conversations.org, and of course, if you have any ideas or suggestions for webinar topics, please email apha@apha.org.

Thank you again to our panelists, to

the National Academy of Medicine, and APHA for cosponsoring this webinar series, and please stay healthy and safe. Thank you all.

(Whereupon, the above-entitled matter went off the record at 6:30 p.m.)