SCICAFE: COVID-19 Pandemic Today
March 3, 2021

JAY VARMA (Senior Advisor for Public Health, Office of the Mayor of New York City): Thank you to everybody for taking time out tonight to- This pandemic, I know it's been exhausting really for all of us. I think so many of us have suffered either because of illness that we or our loved ones have had, or just simply because of the mental and physical exhaustion from all of this and the inability to do the things that we really love. And so, we're really hopeful about what the future holds, but at the same time also quite concerned about the present. And we have to sort of, really, as we have so many times during this difficult experience, keep both feelings in our heads at the same time—how to persist and do very difficult things, but also maintain some measure of hope about what the future holds.

So, I'm gonna try- because I know this is a topic that that really lends itself primarily to question and answers. I'm gonna keep my comments fairly short tonight. I'll talk for maybe about 10, 15 minutes to set the stage on some kind of important issues and then open it up, because I think, really, the best way to really get people engaged and understand and get the information you need is to have that interactive question and answers.

So, since most of you are in New York City, I'm going to focus first on the situation in New York. And as everybody here knows, last spring was- it was a truly awful time for the city. As Rob alluded to, I was here from 2011 to early 2017 overseeing infectious diseases at the City Health Department, but then actually moved to Ethiopia where I was based at the African Union, and I was helping to create a new public health agency in Africa called the Africa CDC. And I came back here, actually, quite abruptly almost exactly a year ago on April 4th.

i had gotten a request actually from the Mayor and the team at City Hall to come back and help guide strategy for the covid response and for personal and patriotic reasons, it seemed like the right thing to do and my family at that time had actually already evacuated from Africa and come back to the U.S.

So, you know, I'm quite aware of the incredible challenge that so many people have faced during that that time. And during the summer months of last year we really had a tremendous ability to drive case numbers down. Some of that was related to the large number of people infected before that. Some of that was attributable to our expansion of a testing and tracing program. And a small part of that was probably also due to some seasonal factors, as well.

But we did experience another surge and that was fairly predictable. I think what was good about what happened here in New York City is because of our extensive testing and tracing programs we were able to delay and diminish the size of the peak that we had this winter. If you look the curves and the number of cases, you'll see that New York's peak didn't come until much later compared to the rest of the United States and much of Europe, and also peaked at, you know, quite a bit lower. But nevertheless, we had a surge like everywhere else.

If you look at our case numbers after Thanksgiving and you look at what happened after Christmas, we saw sort of a 20 to 40% increase in- bump in each time. So, since that time we have now- case numbers have come down fairly markedly, but unfortunately in the past two weeks or so we've seen, you know, quite a plateau. And we're at a fairly high level of case numbers, still—somewhere around 3,500 to 4,000 cases a day. And just for reference's sake, you know, during the lowest points that we were in August, we were down to 200 or fewer cases a day.

The other thing we like to look at and that's important for people to track is not just the absolute case numbers, but to also look at something we call the test positivity. So, this is of all of the people that come to get tested, what percentage of them actually end up having covid. And this is a number that's quite useful to follow in New York City because we have, really, probably the most expansive testing program anywhere in the United States. On average right now, you have about 70,000-80,000 people who get tested for covid. About 20% or fewer of those tests are the kind of rapid point-of-care tests and about 80% of those are the sort of standard what we call PCR tests.

And so, tracking the positivity rate—at least as it relates to those PCR tests—also gives us another window into this. And so, what we've seen is that our positivity peaked at around nine and a half or so percent. That means about nine and a half percent of all people that got tested for covid actually had the infection, but it's come down to around six percent. But again, just like our case numbers in the past few days, has tended to plateau a little bit. So, both those signs are worrisome for us.

So now, the question becomes so why is that? Why are we in that situation? And I think it's important to think about, you know, five major factors that drive case numbers either up or drive them down. There are actually quite a number of factors, but these are the five that are really probably the single most important to what we have right now.

The first are the individual measures that we can all take. And I assume you all know these very well, but I always repeat them because they're so important. They're wearing face masks, they're keeping physical distance, they're washing our hands regularly, they're isolating ourselves when we have symptoms, and we don't feel well. So, those individual measures are really powerful at driving cases down, but of course, when we relax them, they can also drive cases up.

So, what we have been concerned about is something very real and it's something that back in April, when I first flew here and talked to the Mayor about what the future of this held, I said that among the biggest concerns I had was epidemic fatigue—that this was going to go on for quite some time. And it is very hard for all of us to maintain those things. So, individual measures—number one most important factor to think about.

The second are what we call community measures, so not the individual behaviors that we do, but the restrictions that we place on society. Because, as we know, it's very difficult to modify

individual human behavior. So, in this epidemic we've had to adopt regulations on what happens in the community and what happens in businesses. And those limits that we place on gatherings and high-risk activities, particularly indoor activities, are critically important. So, that again has the power to drive cases down when you limit those gatherings, in particular, in indoor settings, but has the ability to drive cases up when you relax things and open them. So, that's the second factor—community measures.

The third is what I've alluded to before, which is our testing and tracing program. So, one of the things we want to do is when you think about an infectious disease, we think about a continuum. You start off with people who are what we call susceptible. They're at risk of getting infected and they move into a population if they're exposed what we call the exposed population and some people who are exposed end up developing an infection and some people who get infected then end up either getting very severely ill and in a very few cases dying or they eventually recover.

So, that is the continuum that we follow. And by testing we can actually remove people from that chain so that they don't progress from one step to another. So, people who are exposed we find them by interviewing cases and saying, “During the period when you had symptoms and/or right before you diagnosed positive, who did you possibly expose?” And we try to remove those people so that they are what we call quarantined, so that if they develop the infection, they don't spread it to other people. And for the people who have the infection, we do what we're saying—isolate them. We try to separate them from other people until they are no longer infectious. So, this important aspect of testing and tracing has the power to drive cases down when it is large and extensive enough. So, that's the third factor.

So, individual measures, community measures, testing and tracing. Now we get into the last two factors that are really the, I think, probably the most difficult for many people to grasp, including myself even though I'm an expert in this field. And they are immunity, which is how our body reacts to viruses and the next is what we're now calling variants or new strains, which is how the virus adapts to us.

Okay, so we're going to spend some time talking about immunity and about what we call the variants. So, immunity—how my body adapts to the virus, variants—how the virus adapts to us. Now, the most important aspect of immunity that we have right now is we have vaccines. The problem with relying on immunity that comes from what we call a natural infection—that is somebody coughing on me—is that it's not very predictable. That's one thing. We don't know how much virus I was exposed to. We don't know how reliable my immune response is going to be and of course, most worrisome, will I get sick from that exposure.

So, that's why relying on natural infection is just a very bad idea. And we can talk about that some more because there have been some prominent proponents of that method, but we think in a public health perspective it's just not good. It's not going to provide you- give you reliable immunity, and it's also going to result in a lot of people who are sick and suffering.

So, the best way that we can achieve immunity is through vaccines and this has been really the most important source of hope that we have. As of today, we now have three vaccines that are authorized for use here in the United States and I want to emphasize a few critical points. And then I think when we get to the question and answer we can talk about them more. Are they safe? And the answer quite simply is yes, absolutely. All three vaccines have now been studied in highly controlled clinical trials and now—at least for the two mRNA vaccines—have been used in tens of millions of people here in the United States. So, we have extensive data to know that these are very safe.

The second is do they prevent severe illness and death? I know there's a lot of concern about, okay, what is the percentage effectiveness of this or that. I really want people to understand this and be a messenger to other people: the single most important reason this virus is so worrisome to us and the reason we had to shut society down for it is because it leads to two things. It leads to overrunning our health care system because people get sick and very severely ill and, second, it leads to people dying. So, what is most important about these vaccines is that they prevent both of those outcomes.

The data from Pfizer, Moderna, and Johnson & Johnson is absolutely stunning, and it basically shows that they prevent hospitalizations, and they prevent death. And those are the two reasons that we had to go to all of these restrictive measures. So, we now have vaccines that prevent, really, the most important thing that we were worried about, which is hospitalizations and death.

The next question people ask is, “Well, do they prevent any infection with covid? Is it still possible even though I've been vaccinated I could get infected a little bit?” And the answer is they are good at preventing infection. The question that a lot of us are asking is we just don't know how much. We know they prevent a lot more than zero percent of people who are vaccinated are prevented. We just don't know if it's a 100% of people who are vaccinated also can never be infected. But, again, I want to pivot back to this important point—they may not 100% protect everybody from getting an infection, but they do protect people from getting the severe illness and dying.

The next question that's often asked is, “Which vaccine should I get?” And the answer I say unequivocally is really get the first vaccine that you are offered. This is really such a critical, important time that there really, when it comes to these important outcomes, is no real functional benefit for society to pick one versus another or for yourself. You really should get the first one you're offered.

And then the other point to keep in mind is that when are you protected—and this is really important to understand, and we can talk about it during the question-and-answer session—your body's immune system needs time to adapt. It's like training for an event and so, you know, you don't really get full protection from the Pfizer and Moderna vaccines until at least two weeks after you've received your second dose. And we also see a similar lag with the Johnson & Johnson vaccine.

The point at which it became really effective in people was about four weeks after you got the shot and that's because your body needs time to adapt. Okay, so that's vaccines. So, that is how immunity, how my body reacts to the virus.

Now let's talk briefly about the thing that people are scared about. Okay, the virus, however, is in competition with us. It's like a like a football game—you know, we've studied all the plays that the virus has and we've now used science to figure out what they are, but the virus doesn't have its own intelligence, but it has evolution and it has numbers on its side. And so, it can go through evolution in a matter of weeks, whereas for us it takes thousands or tens of thousands or even millions of years to evolve.

So, what we have are these variants, which is that viruses mutate naturally when they're inside a human or animal. They have errors when they copy themselves and those errors can get selected by the virus in your body and so the more people that are infected, the more opportunities there are for the virus to mutate. And each mutation produces what we would call a variant. But we really have to differentiate them because not all changes in the virus' sequence cause any type of public health impact. We need to worry about whether it actually is more contagious, does the mutation make it more lethal, does it kill more people, does it make it more likely to evade our immune system and infect people who've been vaccinated.

So, it's very important people understand that we can't actually stop this process. Viruses will mutate. That is what they do. But we can delay these variants from emerging and that's really what we want to do. We want to slow down the process of evolution and the single best way we can do that is through all of those things I talked about at the beginning—individual measures, community measures, getting tested frequently, and, you know, picking up the phone and contact tracer's call, and then when your turn comes in line to get vaccinated, making sure you get vaccinated.

So, that's how we delay the virus from adapting to us quickly. So, I want to sort of close my opening comments by trying to give you some window about what the future holds, because I did say despite my kind of, you know, discussion here about very complicated and worrisome things that I do feel actually quite hopeful about what the future holds. You know, again, to keep things in perspective, it's close to zero probability that the virus is going to go away from this Earth. And that's because there are so many people around the world that will not have access to this vaccine in the near future and likely won't have a vaccine for a long time.

We know from the experience of trying to. First, the only preventable disease we've ever eliminated from the Earth in humans is smallpox, and we know from decades of trying to get rid of polio and measles that it's very, very hard to do so. So, too few people will immunize and the other thing we know is that these strains will evolve and emerge. And we also know that this virus can infect animals and when there's an animal cycle to this, opportunities for evolution become great.

But- So, that's the bad news. But the really good news is that we have these tools to drop the rate of severe illness and death dramatically through immunization. And it's likely in the future that we will also develop treatments, as well, so that if you do get sick we can help address them. So, it may very well be that we have to get updates of vaccines and get regular boosters in the future, but we know that that's okay because when you're a child and you get vaccinated you get multiple boosters of the polio vaccine of the pneumococcal vaccine or varicella, or other vaccines. So, boosters shouldn't be a surprise to us.

But what I do feel very strongly about is once we get to a point where these vaccines are widely available, we will be at a point where people will be protected from the most severe outcomes. And even more hopeful, I really do feel like this has been a really critical- even though it's been absolutely devastating, it's been a very critical moment for awareness in the United States and Europe. I spent eight years in Asia working on emerging infectious diseases. I was based in Thailand for five years and then based in China for three years, because in China in particular, I was invited there to help the Chinese government with the response after the first big coronavirus epidemic, SARS. And this is going to be like that moment was in China and East Asia or a 9/11-like moment for the U.S. and Europe.

We're going to have to accept the fact that we live in a world where there is a risk at any given time of new infectious diseases, but we also have the ability to invest in public health and research to ensure that we have a much swifter and more effective response in the future.

So, I'm gonna stop there because I want to open it up for people to ask questions and then have some dialogue.

ALONSO TERUEL (Moderator, American Museum of Natural History): Thank you, Dr. Varma. I really appreciate it. We've got a lot of questions from the chat. We'll try to get to as many as possible. If you have a question, please put it in the chat and we'll call upon you. Our first question today comes from Jolina's iPad. Now you're there.

QUESTIONER: Yes, I'm here. Hi, Dr Varma. Good evening. Greetings from the Bronx. Actually, very much affiliated with Montefiore hospital and I'm still on the waitlist for the vaccine. My concern is I have two children, 14 and 5, both with autism and asthma. So, the concern is, hypothetically, I would get my daughter vaccinated, if available, but what about my son. I wouldn't want one or two people in the household to get vaccinated without everyone getting vaccinated. So, what is the update in regards to vaccine in children?

VARMA: Yeah, no, that's an excellent question. Let's talk first about your decision-making, but then we'll talk about the issues related to your children. So, first of all, I would absolutely recommend that however soon any of you or your family members are eligible, and of course that you get a spot, that you get vaccinated. Because it's like the saying that they use on an airplane, you know, if there's an oxygen mask put it on yourself first. And that's particularly true with adults because, as we'll talk about in a moment, with kids, in general—as long as they don't have severe underlying medical conditions and other problems—tend to do quite well

with this infection. So, absolutely if and when you get an appointment and your time is up, please make sure you and any other adults in the household get vaccinated.

So, the issue with children is that the original clinical trials that were done, the Pfizer trial only enrolled people 16 and up, and the Moderna and Johnson & Johnson vaccines only studied people 18 and up. And really that was a decision that had to be made during- well, one, because it was a rush, you know. They were trying to figure out what to do first and we really did want to prioritize adults because we saw that age was really the single biggest predictor of bad outcomes.

That was number one, and then number two, that's oftentimes the way we develop vaccines because we have a much higher safety threshold when we give vaccines to children. So, what they do now is that they- the process that's generally followed for vaccines is progressively doing trials in younger populations. So, right now there are trials enrolling for the mRNA vaccines for teenagers—basically, 12 to 16 or 12 to 18. And then eventually, hopefully very soon, you know, later this year, they will start developing trials for a group under that. Likely between the ages of five or six and 12.

But I would plan on the assumption that during this calendar year it's very likely- this would be my best guess: it's very likely that we will have a vaccine that is authorized for people 12 and up, but I think it is very unlikely that during this calendar year- it's likely going to be 2022 that we start to get a vaccine that's available for younger children.

My science belief is that these are going to be incredibly safe, but again, as parents- You know, I have three children myself. You know, as parents, you'll take risks yourself that you wouldn't ever take for your children. And so, it's gonna probably take some time into a way of childhood vaccines.

TERUEL: Thank you Dr. Varma. Our next question comes from Leah. Leah, are you there?

QUESTIONER: Hi, yes. I have a few questions, actually. First thing I wanted to ask is I was concerned with the variants. Like, I read an article that's supposed to be from a legit source that says that, unfortunately, because of these new variants that it's possible that for the two-dose vaccines—the Moderna and the Pfizer—that we might have to get a shot, as well. I don't know how true that is with that.

And also, I read somewhere—I don't know how true it is—that if you're fully vaccinated when you go to another state or another area, that you don't have to quarantine. I don't know how true that is. My younger daughter is supposed to- She and I will both be fully vaccinated before she goes back to NYU in the fall and she's gonna, if she can- if there's enough people, because I don't know how many people are social distancing, that she should be able to go fully on campus. And not have to do hybrid or remote. So, I don't know how it works, because I don't know if my husband's gonna be vaccinated. So, I don't know if, like, there'll still be a quarantine

thing or should she be able to go on campus if one person in the household isn't vaccinated, but we are.

And then I also wanted to know if you're out with people who are already fully vaccinated and everything, can you not have to wear a mask and social distance around them? Or is it true that you can't because you might be a carrier?

And then the last question I have is I'm concerned about future- I know I sound paranoid, but this pandemic has really put a strain on me and other family members. It caused my daughter to have anxiety, put me in my depression worse, and I'm concerned about other pandemics in the future. Like, what can we do to prevent- what can we do so this won't go like this or become a global pandemic? Because it's really upsetting and depressing. I know there's a lot of questions, I'm sorry.

VARMA: Let me try to do my best. I mean, first, I just want to say I- you know, I'm very sorry to hear about the mental health toll that it's taken on you and your daughter, as well. And I think that the most I can just say is that we all- I mean, this is a time we all need to be able to support each other. It's bizarre that we have to support each other in this virtual way, you know. We're humans. We're social creatures. You go to the Museum of Natural History, you learn the evolution of animals and humans and this is what we are. And so, I am sorry to hear that. And I can just tell you that, you know, from a personal perspective, we've had the same issues in our family, in our house. And I know many of our friends'.

And so, I do want to try to reassure you as best as I can, but also give you the accurate information. And there's always a balance between those. So, let me try to get through those, you know, reasonably quickly. So, yes, it is true that the virus, as we said, is adapting. But what we know so far is that the vaccines that we have available to us still appear to be very effective. Again, they may lose a little bit of effectiveness or maybe a few more people that are potentially going to be at risk, but against that most important outcome which is severe illness, like hospitalization and death, they appear to be very effective. And I have a fair amount of confidence that they're going to continue to show that effectiveness, because the virus can only mutate so much.

Because, you know, it's not very long and the more it mutates it also has the risk of reducing its ability to infect other people. So, I do think it's very likely- It's important for people to get vaccinated because even though the virus is evolving, this type of immunity that you get from vaccines is still going to protect most people. That's number one.

Number two is, yes, it is possible that we may have to update the vaccines in the future, but that shouldn't be too surprising to people. You know, the reason we get a flu vaccine is because the flu mutates much more rapidly. The reason the flu can mutate so rapidly is because it has this cycle in birds and pigs, migratory birds in particular. It has the opportunity to evolve very much. So, that's why we need a new flu shot over here is because the virus evolves.

So, if I had to make a prediction, it's going to be that we are probably going to need either annual, or every couple years or something, boosters, but I don't think that's- And the other thing to think about is what happens when you go to the emergency department. They ask you, "Do you need a tetanus shot?" you know. So, we should be used to the concept of getting booster shots and that shouldn't worry or scare us. I hope we don't need it, but my expectation is that we might.

The next question you asked was about what can two people do who are vaccinated together. And I do have to say we've been sort of behind the ball in talking about this publicly. Mostly, it's because so few people publicly have been vaccinated that we're a little wary of messaging that, but to be very honest- And I'll just give you a perfect example. My wife is a doctor. She's fully vaccinated. Her parents live in a retirement community. They're fully vaccinated. They're in California. She hasn't seen them in 15, 16 months, you know, and she's going to go see them now in a few weeks. And that's because we feel confident that two people who are fully vaccinated can spend time together with a very, very low likelihood that anything bad will happen.

So, basically, I would try to just emphasize to people we should think about this in private settings. Let's not go out in public and say, "Oh we're all out at a-" you know, you're hanging out together and not obeying mask rules in indoor dining or other places. We have to be aware, one, of social norms. You know, we need to model good behavior for other people. And number two, we have to know that other people don't know. You know, we're not wearing a big sign on us that says we're vaccinated, and they can prove that. So, in public settings we still want people to act as if nobody is vaccinated. But I do feel comfortable that in private settings people who are fully vaccinated can spend time together and do things that they want to do.

TERUEL: Thank you, Dr. Varma. Our next question comes from Ronan. Ronan, you are up.

QUESTIONER: Hi. Yeah, I had a question. Can you explain why immunity after infection has been considered to be only for three months? How long will vaccines protect, as opposed to an actual infection?

VARMA: Thank you very much for this question and it is it is one of these very difficult questions to answer because I'm going to give you an answer that isn't very satisfying, which is that we're still learning about all of this.

So, let's talk about natural infection. By natural infection I mean you get exposed to the virus in the wild. Different people have different duration of response and the reason that three months has been chosen here in the U.S. as the cut off—and, you know, there is a little bit of discussion about this. The UK, I think, talks about six months—is because it's not very predictable. So, it really depends on your estimation of what- of how you read the scientific information. And the scientific judgment is- based in the United States is that based on what we know, the vast majority of people retain immunity against reinfection for three months, but

that number does start to dwindle after that time. So that is the cut point that we have chosen here in the U.S.

It's not based on individual responses. Individual people may have stronger responses compared to others. Now I want to hit on a related point to this. So, people ask, “What if I get an antibody test? Doesn't that tell me for sure?” and this is where it gets quite complicated. The problem is that what we really need is a laboratory test that is what we call in science a “correlate of protection.” It basically means if you have this positive test it means that you are definitely protected. And, unfortunately, it turns out that the laboratory studies that we have, the commercial antibody tests are not a very reliable correlate for protection. There may be some that are. There's a lot of research going on right now in the vaccine studies and CDC and NIH have been in regular communication, but what we know right now is that we don't have a good laboratory test to say that you're absolutely protected or not.

So, that's natural infection. Now, let's talk about vaccine-induced immunity. So, the only thing that we can say for sure is that in the trials people were followed up for a minimum of 60 days and because of the way enrollment followed, several people were followed up for 90 days. So, we have quite a bit of confidence that, again, using that three-month interval that you are protected for at least three months.

The reality is, based on the laboratory studies that we have, we strongly anticipate that your immunity- assuming the virus doesn't change and evade us, but let's assume it's the regular virus, that you'll retain that protection for a longer period. The problem is we can't speed up time, you know. We don't have, like, a time machine to jump ahead six months.

If the body was a simple organism we could just say, “Okay, lab test and we know for sure it's six months.” We don't have that, so that's what we're kind of waiting for. But I do anticipate there's going to be more information coming out every month or so that's going to show us what happened to people who got vaccinated last summer, for example, as part of these trials. And we'll be able to use that to extend out the period that we're protected for.

TERUEL: Thank you, Dr. Varma. Our next question is from Preeti Gupta. Preeti?

QUESTIONER: Hi, Dr. Varma. Thank you for being with us. The question we have is, is it possible that a certain percent of the population has a T-cell immunity to covid-19? What's your opinion on doing T-cell tests?

VARMA: Yeah, excellent question. You know, this gets to the- one of the biggest problems that I tell people, not in our public forums, but often in quiet, which is that I wish we understood immunity better. If I had to guess, I think we probably, as scientists, understand maybe five or ten percent of all of immunity. We have a really good understanding of that five or ten percent, but there's so many mysteries to how the body reacts and responds to these things, which is why it is so important to do these clinical trials. The reason we need to do clinical trials is we

can't predict how the body is going to respond, so the best way to do it is take half of a group and do one thing and do another half and do another thing.

So, now, to get to your question—just so people understand, your body has many different ways of fighting off infections. We broadly define immunity into two kind of big categories. One is the category of what we call humeral or blood-based immunity, which is like the antibodies—which is little proteins that are released when you're exposed to something, that bind to that and then block it. The other is, as Preeti was asking about, is what's called T-cell immunity, or we call cell-mediated immunity. And there are many cells that you have in your body that are kind of like soldiers that just go out and kill things that look foreign. They don't need to have antibodies that float around and bind to something. They just see it and they grab it and they eat it up.

And the answer is yes, there are probably some people that have that type of cell-mediated immunity due to cross infection from other places. You know, we haven't seen, really- I, personally, haven't seen really good evidence that that applies to large swaths of people. A lot of people have been asking about, well, why weren't there more deaths in Africa or other parts of India. And they try to postulate it that it might be due to some form of cell-mediated immunity. I haven't seen really convincing evidence of that.

Everywhere that I've seen that studied it in developing countries that were supposedly protected actually found a lot of covid when they went and looked for it. That doesn't mean it doesn't happen. I mean, I think probably what cell-mediated immunity is probably doing is probably modulating why some people get very severe illness and why other people do not. But I honestly don't know the answer to that, and I do think it's something that we're gonna learn more about.

And like a lot of crises- you know, look at the HIV epidemic, which has been the single biggest devastating epidemic globally. Even more, I would argue, than covid—it just was stretched out over decades. We learned so much of science. We didn't really understand T-cell immunity at all. We had nothing to understand until we had HIV because HIV specifically infects T-cells. So, I do think we're going to learn a lot more and that's going to help us with other diseases as well

TERUEL: Thank you, Dr. Varma. Next question is from Miriam Danar. Miriam, are you there?

QUESTIONER: Hi. Can you hear me now?

VARMA: Yes, I can hear you.

QUESTIONER: Okay, thanks. I have a question. Do you see a future with perhaps the mRNA vaccines not only for addressing covid, but possibly other viral diseases that have been difficult to treat like herpes or maybe even something like cancer? These ones that are hard to address.

VARMA: Yeah, the answer is yes. And I will tell you that I have spent my career working on infectious diseases, mostly in the developing world and I'm generally a pessimist when it comes to technology. I tend to think that we need to invest in a lot of human things—getting people tested, getting them vaccinated. Certain things, you know, the things that we know how to do.

I was surprised when the U.S. did this huge investment to mRNA vaccines. If it had been me, I would have said we should invest in technologies we already know, like the inactivated viruses vaccines, things like that. And I would have been completely wrong and I was completely wrong. mRNA vaccines have been absolutely extraordinary and stunning in their effectiveness and I think everything that we have learned and I personally have learned from now understanding the evolution and development of these technologies better is that they will absolutely be able to do the things that you just mentioned.

Let's talk about infectious diseases. You know, really, when you think about it, it's really quite an amazing thing that the body has developed. The body has developed this kind of secret library of information that it keeps inside you, the nucleus of your cells. And to protect anything from actually accessing that it says, "Anytime I want to make a protein, anytime I want to make this secret recipe, I'm not going to open up that that secret book and send it out into the rest of the cell to make the recipe, I'm going to just make a copy of it and send that message out to the rest of the cell to manufacture the response. And that's what we have—this sort of secret book is our DNA that's bound up in chromosomes, and it sits inside of our nucleus and the mRNA is just a messenger that goes out into the outer part of the cell and it's called the cytoplasm and then prints and produces the things that we need.

And the fact that these vaccines, that they've figured out how to modify the mRNA in such a way that it gets directly into the cell, doesn't modify anything, destroys itself, doesn't cause any other dangerous immune reaction—which was the problem with mRNA in the '90s and 2000s—has been absolutely extraordinary. And I think it's going to change the way we have vaccines for infectious diseases.

And, as you just mentioned, there is an enormous field of what we call immuno-oncology. You know, one of the challenges with cancers is the fact that your body thinks that what's growing inside itself is actually part of your regular body and there's some failure of the immune system to recognize those cancer cells as bad, as abnormal, as foreign. And I do think that mRNA technology is going to be very important for, maybe not all cancers, but certain cancers and helping to address it, as well.

TERUEL: Thank you, Dr. Varma. We have time for a few more questions, so please bear with us. Our next question is from Reina Goodman. Reina, hi how are you?

QUESTIONER: Hi, can you hear me okay? Hello. Hi, thank you Dr. Varma. It's a wonderful, wonderful lecture. I have a question about transmissibility. If I get vaccinated, which I will hopefully in the near future, my son and daughter-in-law are vaccinated already fully and then I have my seven-year-old granddaughter, so when I go to visit them- In other words, can a

person who's vaccinated transmit the disease to an unvaccinated person? Can they carry that that virus in their nose and mouth from maybe somebody coughing or whatever the heck it was and then just pass it on to somebody else? Whether I wouldn't get, you know, where I wouldn't get the disease myself- I wouldn't get the- Yeah that was my-

VARMA: This is an excellent question, and we have an unsatisfying answer. The unsatisfying answer is that, you know, we, as sort of scientists and from all the literature I've read and reviewed and what I know about infectious disease, can say that if you get vaccinated, the chances of you having the infection sort of land in your nose, you not getting sick, but you spreading the virus to somebody else, are not going to be very high, but they're not zero. At least that's what we know right now. And the problem is I don't know between, you know, zero percent likelihood of it happening—that means you're totally protected, you can go out and cough on anybody, you're never going to give them covid—or 100% which means you're not really protected at all. I don't know what the right answer is right now. We're still learning what that is.

If I had to guess, it's going to be something on the order of 50, 60, 70%—that it's, like, the chances of you getting that infection and spreading to other people is low, but it's not exactly zero. So, that's kind of this weird situation that we're in right now. That's why I feel very strongly that two vaccinated people can spend time together, whereas a vaccinated person and an unvaccinated person, I'm very cautious right now about recommending people spend that much time together.

You know, what people individually take as their own risk is fine. It's just as a public official, I have to be a little bit more cautious, but I think the only reassuring thing there, of course, is at an individual level, again, kids tend to have very good outcomes from this. But again, it's all about your risk threshold. Some people don't want anything ever exposed to their children, which is their right and they need to have a higher threshold. And other people are a little bit riskier, so that's where the balance comes in.

TERUEL: Thank you. Our next question is from Nick and Amanda [unintel]

QUESTIONER: Hello, hi. Thank you. So, I think this relates very much to what we were just seeing with Reina, which is basically how do public officials communicate with the public? So, my sense is that you know- in the absence of any real proof, but with other knowledge, people have defaulted to basically very cautious statements. As you said, you know as a public official you have to err on the side of caution. There's no proof that you couldn't get covid a second time. There's no proof that a vaccine doesn't prevent you from- or the vaccine prevents you from spreading it to others. And kind of, as the public, it's not so clear how to act on that. Yeah, so, I guess the question is what do you think is the right philosophy in terms of how to communicate uncertain science to the public when you do nevertheless have beliefs about what's likely to be true?

VARMA: No. I- you know, we could probably have this conversation, like, for a week. You're absolutely right and I will- I immediately confess that I have not cracked the code on how to do this well. And many of us have not. The way I talk to my friends is not exactly the way I talk to the public and I realize that somebody could logically accuse me of hypocrisy and say, "Well, why do you tell your friends one thing but you tell the public something else?" And it all has to do with this really challenging problem, which is we're trying to predict how people are going to behave based on what we do.

Because we know that behavior—not at an individual level, but at a massive level—it's not what you specifically do, it's what you and a hundred thousand other people do. And you know, we're learning a lot. We're learning a lot about how to communicate and not how to communicate. So, now let me try to answer a question a little bit more about the way I think people should think about it, because I don't really have the answer about how to communicate best.

I think the best way to communicate is to be as honest as we can about what we know and what we don't know. I also think it's very important not to shame and scold people. I've been very- I will say quite honestly- I don't say this publicly, but I've been very annoyed by a lot of sort of public health preaching that you see on Twitter and other places where people say, "I can't believe people are going there. I can't believe they're seeing their relatives." You know, we're humans. We need to behave a certain way and scolding people for their behavior hasn't worked with sexually transmitted diseases, it hasn't worked with anything. It's not going to benefit anybody.

So, what I like to do is try to communicate to people what the risks and benefits are based on what I know and what I don't know. And I do default to being cautious just because I think that human nature- and I know this just because it's myself. I know my family. You know, we're going to stretch the lines a little bit, so I always choose to be a little bit more cautious. But what I do like to say to people- I'm not sure if I'm exactly answering the question, but what I do like to say to people is to think of yourself as having kind of like a budget to spend. And take certain risks when they're absolutely necessary for yourself and your ability to make it through this epidemic. This is a marathon, you know, and if you need to go to, I don't know, the gym—which is a little bit riskier than something else—then do it. Just be safe, but also think about not taking so many other risks in other things that you do. Or you need to get on a plane because you need to see your relatives—well, think about reducing some of your risks in other places. This disease has a bit of randomness in how a transmission occurs, so I can't predict what's going to happen, but I just know that if most people most of the time take cautious behaviors, we can keep disease rates down.

So, that's really what we're striving to do, is get the most amount of- I really just need about 50-70% of the population to kind of 50-70% of the time do the right thing, and you'll see case numbers go down. But how you strike that balance is very challenging

TERUEL: Thank you, Dr. Varma. Our next question comes from Neerav. We have only time for a couple more questions, so make them count. Neerav, you're up.

QUESTIONER: All right, thank you. Some communities have done better or worse than others using metrics like case hospitalizations and deaths, despite having similar government restrictions, behavior, population density, and other factors. Do we have good explanations yet about what causes those differences?

VARMA: Yeah, I mean, just a quick question back to you. Are you referring only to the United States? Are you thinking globally or-

QUESTIONER: I'm thinking globally, but I would say at local levels, too.

VARMA: Yeah, let's talk about- I think it's very hard to analyze. I think we will- eventually, there's going to be an incredible amount of research that's going to come out over the next five to 10 years looking back. So, we'll know a lot more. I know a lot about globally because I spent a substantial amount of my time working overseas on building infectious disease surveillance and I can say quite strongly that the single most important things that that made a difference were where there are some things that people can control and some things you can't control.

The one thing that you can control, of course, is political commitment and making an early effort to either restrict travel or to devote energy to sort of contact tracing, other things like that. That did have an impact, not necessarily over the course of the entire epidemic, but very early on. Reactions that were taken early on, I think really did help slow the trajectory of it. And I say that as somebody who was very vigorously arguing when I was based in Africa not to shut down international travel because I've been- I spent two months in Sierra Leone leading the U.S. government response to Ebola and they saw the devastating impact when you cut off trade and travel and, you know, trade. You could basically let a place burn to the ground if you don't have travel. So, I was, you know, flights going on. So, I was very concerned about that, but I was wrong. It turns out that actually those travel restrictions earlier on really did help slow things. So, that's something you can control.

The second thing that you can't control is age structure. You know, what a lot of people don't realize is that vast- like, if you look at Africa, for example, the median age is 19. And we have seen that one of the reasons that, let's say, the advanced industrial economies or whatever the term is—broadly speaking, Europe and U.S. and North America—a lot of places have done badly because they actually have a lot of elderly population, which is very high susceptibility. And it turns out that medical care for this disease doesn't make a huge difference.

It's probably made a bigger difference now, but early on it didn't. So, that age structure is a huge determinant, I think, of why places in India and Africa and other places didn't see devastating runs on healthcare facilities and other things like that.

I would say the third factor is the data is really not great. I spent a lot of my time working on improving vital statistics around the world. I can even tell you from China, where I spent three years in China, China does not have universal registration of all deaths. China produces annual mortality statistics based on a sampling scheme. They sample from populations to extrapolate. The same is true in India. The same is true through large swaths of Africa. So, we're not going to really know until the end, when there's a little bit better effort at actually counting to understand what those differences are. But those would be my big, sort of, takeaway big messages.

TERUEL: Thank you, thank you. And we have the last question of the evening, which is going to come from Megan. Megan, how are you?

QUESTIONER: All right, thank you. Thanks for taking the questions for this evening. My question is actually in follow-up to your response to Reina's question about the vaccine. My understanding is that the vaccine is preventing severe disease, not disease. So, we're actually going to see a higher- likely a higher, even though we can't test for it, number of asymptomatic cases, versus severe disease. So, we're really vaccinating for severe disease, not against covid, period, like we're used to associating vaccines. So, isn't it that we need to even more so be masking when we are vaccinating because we are likely then carriers, while we have a large population that is still unvaccinated and unable to access the vaccine? So, once we get access to the vaccine—like, anyone that wants it can get it—that might be when socially, ethically the masks can go away, but can you confirm this understanding of the vaccine as well as the proper dissociation with the mask?

VARMA: No you're- First, I just want to thank you. You're absolutely- what you've been saying just now at the end is actually what I have been saying in policy advice to other people, is that when we look to the future, the real inflection point, the point at which this is going to change, is once we get to the point that everybody has access to the vaccine if they want it. So, I can just go to the corner drugstore and get it and it's free and it's available. Then you get into an issue of personal choice, right, and personal responsibility. And I do think the ethics of this are quite clear that there's no other infectious disease that we control people's behavior in society on a large scale if there's an option available for you to protect yourself.

So, I do agree that that's going to be kind of the inflection point, is once we get to the point that vaccines are so widely abundant, we have made them broadly available, we've done everything we can to educate and make people aware that it does become a point at which individual responsibility has to take over, and you don't have community requirements on masking or other things like that.

So, that's the second part of your question. The first part of your question is the really tricky one right now, so I will say this just to clarify one point—all the vaccines do prevent symptomatic illness, it's just that that's where you get into those numbers and as- I can't even keep them all in my head- 66% for J&J, when you look at it globally, 72%. When you look at just the U.S., you know, what is it against this variant for one vaccine, I can't even keep that

information in my head, and I do this for a living. And that's because that's what a lot of them are. All of them actually had slightly different definitions.

I've had a lot of conversations with my colleagues at CDC. They're trying to, like, map the definitions and go back and get the primary data and reanalyze them. So, I just want to clarify that all of the vaccines do have a fairly substantial impact on symptomatic infection, and even to a certain extent in the ones that did look at it. Like, in the J&J trial they looked at asymptomatic infection. They looked at it in the Moderna trial for between the first dose and the second dose. They do drop asymptomatic infection and symptomatic infection, it's just that the most important outcome, the single most common finding across all of them was that almost 100% protection against hospitalization and actually 100% protection against death. So, that's why I focus on those outcomes because those are things people can really focus on.

But it is important to understand that for the majority of people it does still have an impact on other forms of infection, as well.

TERUEL: Thank you, Dr. Varma. That is all the time we have for today. However, I was hoping that you might leave us with a parting thought if there's any key learning from today, what would you say it should be?

VARMA: I think this is the message that I try to give to every audience, which is really the need for persistence and also the possibility of the future. We are at a kind of a difficult time right here. We've been very concerned about this plateauing of our cases. It was among the things, the outcomes that I feared might happen. I think there's probably a lot of tension going on between variants and human behavior relaxing, which is driving cases up. And then we still have our efforts and our immunity and our vaccinations, our testing and tracing driving cases down, but it's really important for people to stay strong and persistent as much as they can for the next few months.

But I am incredibly hopeful, I have to just say, at a personal level. You know, I've talked to my wife and kids that I do feel like, you know, when the summer months come, I do think things are going to be- really going to feel- they're not going to be totally normal, but they're going to feel a lot more normal. And that's because we're going to have widespread availability of vaccines. I'm really quite confident about that. I think we're going to continue to see how effective these vaccines are and we'll see the accumulated effect of our testing and tracing and all those other things. So, I do think that things are going to get better. We're not out of this forever, but it's not gonna feel as gruesome as it has. And I'm personally quite hopeful about that.

TERUEL: Thank you very much and thank you everyone for watching today. Please let us know what you thought about today's program by clicking on the survey link that is in the chat. And now please join me in thanking Dr. Varma for his amazing talk tonight. Thank you very much and we'll see you next time.

VARMA: Hey, thank you very much. I appreciate it.