# Episode 42: Calling an Audible

**Chris Dall:** [00:00:05] Hello and welcome to the Osterholm Update: covid-19, a weekly podcast on the covid-19 pandemic with Dr. Michael Osterholm. Dr. Osterholm is an internationally recognized medical detective and director of the Center for Infectious Disease Research and Policy, or CIDRAP, at the University of Minnesota. In this podcast, Dr. Osterholm will draw on more than 45 years of experience investigating infectious disease outbreaks to provide straight talk on the covid-19 pandemic. I'm Chris Dall, reporter for CIDRAP News, and I'm your host for these conversations.

**Chris Dall:** [00:00:41] It's February 4th, and while the days are getting longer, the coronavirus vaccine rollout is picking up speed and the United States continues to see a welcomed decline in new covid-19 cases and hospitalizations, there are dark clouds on the horizon. The widespread global transmission of the virus has promoted the emergence of mutations that have enabled several sars-cov-2 variants to flourish and spread, and those variants now threaten to bring a resurgence of infections and return us to the dark days of the fall. But are there ways to get ahead of the variants and the threat that they pose? On this episode of the Osterholm Update, we're going to explore whether switching up the nation's vaccination strategy could be one way to blunt the impact of the variants. We'll also take a look at some of the latest vaccine news, the current state of the pandemic here and in other parts of the world, answer some listener emails on the effectiveness of double masking and hear about an act of kindness from one of our listeners. But first, we'll begin with Dr. Osterholm's welcome and dedication.

**Michael Osterholm:** [00:01:38] Oh, thank you, Chris. Welcome, everyone, to another weekly podcast of the Osterholm Update. We welcome you. I also appreciate all you do to contribute to the acts of kindness in the world. We keep hearing about more and more of them. And I can't tell you how much we appreciate hearing from you in any number of ways questions, comments, advice, sometimes criticism and often well-founded, as well as just sharing with us your acts of kindness. So thank you very, very much for being with us this week. I have good news to report to you that again, our journey for an increased light length is marching along just fine. Thank you. And here today, on February 4th, the sunlight length in Minneapolis/St. Paul is nine hours and fifty nine minutes. We've gained 18 minutes since last Thursday, one week ago, and now we have gained seventy one minutes since the winter solstice on December twenty first. One hour and 11 more minutes of light. Boy, isn't that wonderful. It's getting there. Hang in there. We're going to get to those longer days yet. In terms of the dedication for this podcast this week, I've thought long and hard about why I'm able to do what I do every day at work, working on all aspects of the covid-19 pandemic, but in addition, so many other areas that our Center is involved with. And I kept coming back to one central theme. It's my family. I have the most incredible family. They are a rock and they are there for me day in and day out. They tolerate me when I'm tired. They encourage me when I'm discouraged and they celebrate with me when we have a success. So today I would like to dedicate this podcast to Fern, my partner, who is beyond anything I can put into words in terms of soulmate/partner. To the kids, Erin and Ryan, Monica and Chad. To Jack, Will and Trip. To the grandkids, Connor. Thomas, Henry, Ethan, Greta and James. And to Peg and Craig, members of the inside family here. Thank you for what you do for me every day. Thank you for helping me get through this pandemic, just like so many other families out there are helping you get through this pandemic. I owe you so much. In fact, you might say everything, in terms of what I do. So with that dedication, and some might argue long overdue, I thank all of you for being part of the podcast family. So in that regard, I'll make that extension of family wide and far. One more thought, the title for this week's podcast. I've decided to call it, Calling an Audible. It's notable that this is Super Bowl week, so our title is quite fitting. Some of you may have seen me this past Sunday on NBC's Meet the Press with Chuck Todd. Chuck, who is one of the best and informed television interviewers in the business, asked, "Do you believe we are now at a point where we may have to call an audible on how we distribute the vaccine?" My answer to him was, "No doubt about it, the surge that is likely to occur with this new variant from England is going to happen in the next six to 14 weeks." So what exactly is an audible? Well, it's what the person in charge, the quarterback on an American football team, decides to do, spur of the moment. For each play, there's a great deal of planning that goes into that play. There's months of preparation for the season, weeks of anticipation of this game, game time decisions of which players to use. Who is the opponent? Then finally, the decision in the huddle. We're going to go with, for example, sixty five toss power trap. The plan is that every one of those 11 football players knows their assignment. But then as the quarterback walks up to the line of scrimmage, he notices something is different. Something unexpected is coming from the defense. So he makes a last minute change by shouting out a different play. That is an audible. And that's what I'm saying is the potential need right now for what we must do as we see our distribution of covid-19 vaccines. We'll talk more about that. Why I think we are now at a point of calling an audible. A lot of you responded favorably with the analogy I provided on the approaching hurricane when I was on Meet the Press. I said, "Imagine where we we're at Chuck, you and I sitting on this beach where it's 70 degrees, perfect blue skies, gentle breeze. But I see that hurricane, category five or even higher, is 450 miles offshore and it's heading our way. Telling people to evacuate in that beautiful blue sky day is going to be hard, if not almost impossible." As I leave us here in this opening, keep in mind, that's, I think, where we're at. And what we have to do today is understand why that hurricane might be occurring, what we can do about it, and how do we help all those around us begin to understand why we have to deal with this potential hurricane.

**Chris Dall:** [00:07:36] Mike, although covid-19 deaths remain very high, the seven day average in new covid-19 cases continues to fall, as do the numbers of covid-19 patients in US hospitals. And we're seeing similar trends in other parts of the world. This is encouraging news, especially for our hospitals. But is it just a brief respite?

**Michael Osterholm:** [00:07:54] Well, if you've heard me discuss in the last four or five podcasts, we have to understand this concept of shifting baselines and what we're thinking about in terms of what we must do to respond to this pandemic. We know during the duration of the last six weeks we've seen the best of times and the worst of times. The best of times being right now, the worst of times being in that first week in January. But let me just remind you one more time. I know for some of you this is getting boring, you hear it over and over again, but it bears repeating. Last April when we were in such dire straits with case numbers climbing greatly every day in New York City, when we saw the number of cases in Atlanta, Chicago, Detroit, Seattle, Southern California increasing, we were at thirty two thousand cases reported per day. And we thought, "Oh, boy, this can't get any worse." And we did all that work to bend the curve, flatten the curve, all those terms, and we got case numbers down to about twenty thousand reported new cases a day by right around Memorial Day. At that point, we saw the ever growing issue of pandemic fatigue, pandemic anger, and people begin to dismiss that this was really a problem anymore. Twenty thousand cases seemed to be a baseline we would all accept. Well, by mid-July, as you know, case numbers climbed precipitously in this country, particularly in the southern Sunbelt states from southern California all the way across the south to South Carolina. And those case numbers jumped over 70 thousand new cases reported per day. More than twice the number when it was at its peak in April and we said, "oh my, this can't get any worse. This is a challenge, what can we do to bring these cases down?" And again, particularly in the southern states where hospitals were basically overrun, intensive care units were full, we saw people taking more efforts to distance themselves, mask wearing, etc.. And what we saw was, again, case numbers coming down. By September, we were back to twenty six thousand cases per day being reported. Not that different from twenty thousand, but still higher. And then pandemic fatigue set in again, particularly in the upper Midwest. We also saw this increase for which we really can't explain geographically why we see this southern versus northern states flip flop. But on November 20th, we hit two hundred thousand cases reported in one day. Boy seventy thousand cases, thirty two thousand cases seemed so much easier to deal with. Again, the northern states went through all of its "lockdown activities", a change in everyday life as we know it. And by December 1st, the cases came down to one hundred sixty thousand a day, forty thousand drop. Imagine if that same drop had occurred in April, we would have been in the minus ten thousand cases. Well, what happened? The southern states lit up again. California to South Carolina, and by the twenty ninth of December we were two hundred thousand cases a day. By January 8th, we were at three hundred thousand cases a day. Three hundred thousand cases a day. Think about that again in context of baseline. Peaks at thirty two thousand, seventy thousand, two hundred thousand, and now three hundred thousand. But here we are, now early February, and we're watching the case numbers get down to one hundred and thirty, one hundred and forty thousand cases a day, which would have been twice the peak in July when the house was on fire. And we're thinking, "Wow, we can open up again. Things are getting pretty good." How we've lost perspective, not to say that we should or shouldn't open up, but again, it's a different mindset. We're looking at hospitalizations now at ninety three thousand this week. That would have been considered an unbelievable number back just several months ago. So I worry that we've come to almost be numb to what's happening. And therefore, what we're going to do about these case numbers is very different than we would have considered doing as a society, as individuals, just five months, six, seven months ago. Today, forty seven states have cases dropping, that's great news. Three states are about the same. And people are now seeing vaccine and they're saying, "Wow, this is great, we are in good shape". This is where that hurricane analogy comes in, because I don't believe we're in good shape. Now, some are going to be very upset with me. Some people are going to, you know, I'll get the emails about why do I scare everybody so much? And I'm not telling you on this podcast to scare anyone. This is about let's get ready. It's like that blizzard. Let's get ready. And what we have to know is with these variants, and particularly the B117 variant, I think the case numbers could increase substantially in the course of the next six to 12 weeks. And if they do, they're starting from a base right now of one hundred and thirty five to one hundred and forty thousand cases at that high level already. We're already starting from a base of two thousand to two thousand five hundred deaths a day already. So the challenge is there. Now, we're going to talk about vaccine in a moment. And vaccines are going to have an impact here. But let's make no mistake about it. We are not in a race with the vaccine with the variants, for example. As I said last week, if that's the place you think we are, we've already lost because even under the best of conditions for us to get out one hundred million doses of vaccine by the end of March, sixty five days after the inauguration, not one hundred days, that will still only protect about 12 percent of the US population with the two dose need as we have it now. So we have to understand these next six to 12 weeks could be by far the most difficult of the pandemic. And we have to get through them. And I hope I am wrong. But if I'm not, then I think we're going to have to ask ourselves, what have we done to get ready psychologically? From a control standpoint, prevention standpoint? And what have we done with our opportunities to reduce severe disease, hospitalizations with our vaccine programs? At this point, Chris, I have to say, I just want people to understand this should not be a reason to give up. This should not be a reason to say surrender. Remember last week? Nuts to the virus. Nuts to the virus. But we have to be in place, what I call, situational awareness. We have to know what we're up against.

**Chris Dall:** [00:15:09] So, Mike, the concern about the coming months is being driven by the emergence and spread of the sars-cov-2 variants. Can you give us an update on where we are with these variants.

**Michael Osterholm:** [00:15:19] Well, I'm very concerned about the variants. They are a curve ball that we probably should have at least anticipated, but I don't think we could have ever expected to the extent to which they are challenging us the way they are. Not only just in terms of transmission, but also the potential impact on the vaccine itself. Again, let me remind everybody, kind of a primer here, for those who have been with this podcast before, you'll know this. For those that aren't aware of what these variants are remember these viruses have mutations that allow them, and in some cases enhance their ability to be transmitted in the human population. Many mutational changes on these viruses don't help the virus in the human population, and they tend to be the ones that die out. They don't survive. Remember, the characteristics that we're most concerned about with variants is, number one, do they cause more transmission of the virus? Two, do they cause more serious disease? Or three, do they in some way impact the protective immunity that we get from either vaccines or from natural infection? They also can, of course, impact on immunotherapy, the treatment we use where we're using antibodies. When we look at the variant that I think is front and center, it's the B117. This is one that is also known as the UK variant. It has been associated with increased transmissibility as high as 50 to 70 percent. At this point, we have emerging data that shows that it is involved with more severe illness, but no evidence to date that it actually has any impact on the immunity that we get from either vaccines or natural infection. I'm going to come back to that because that may be changing. The other variant that we look at is the B1351 or the South African variant. This virus has been associated with increased transmission in its local area, but it hasn't demonstrated yet its ability to really move around the world and spread widely in other locations outside of the South African area. At this point, we have really no clear evidence of greater severity, although there's some suggestion of that. And there is a concern about a very specific mutation on this virus called an E484K mutation. And this is the one that actually may reduce vaccine and antibody therapy efficacy. It may also evade, and it may evade the antibody that we acquire from natural infection. The other variant of primary concern is what we call a P1 linage. This is the Brazil variant. It has been associated with increased transmission, at least Manaus, Brazil and those locations there. We haven't seen it widely spread through the other countries of the world. It, too, has that similar mutation that increases its likelihood of evading immune protection from both vaccine and from natural infection. This variant may very well cause more transmission and a higher risk of severe disease. We're surely seeing that in Manaus, Brazil at this time. It's unclear, however, if that transmission is unique to that area of Brazil because we just haven't seen widespread transmission elsewhere in the world. This virus has two mutations the N501Y and the E484K. This mutation has been associated with a reduced protection of antibody from both vaccine and from natural infection. And it's of a real concern in terms of looking at the impact that we're now seeing on our vaccine trials and the various vaccines that are conducting trials in South Africa and in Brazil. On Tuesday of this past week, the CDC updated the number of variants reported in the United States. And for the B117 or the UK variant, there are now five hundred and forty one cases reported identified in thirty three different states. Clearly, this is a very wide spread variant at this point. The B1351, or the variant from South Africa, there have been three cases identified located in two states. And finally the P1, there have been two cases identified in one state and that state happens to be Minnesota here. When one looks at the number of cases here, we still have to understand that we are really flying largely blind based on a lack of comprehensive testing of the viruses for their sequences. So it is, however, I think, instructive that the B117 is so much more widespread than either the South African or Brazilian strains. And I think that's why this is the variant of highest concern right now in the United States. If we're going to see a big surge, it's going to be around this increased number of cases. And this is where we're going to be talking about the issue of vaccine. And now with this newly acquired mutation that the B117's now have been documented to have per this week in England, it's now clear that it has acquired the E484K mutation, the one that impacts on the protection of vaccine and natural infection induced immunity. We have not seen that here yet in the United States. We have lots of B117s, as I just noted, but not that particular one. However, again, we're flying pretty much blind because of our reduced sequence surveillance here in the US. And it'll be important for us to learn over time what we have here. So I just keep coming back to the issue of the variants over and over again. More transmission, more serious disease, ability to impact on the vaccines. This is a challenge. But the one thing that we can say over and over again is get vaccinated when you can, because stopping the virus from causing infection is also what will stop the virus from mutating and so that we don't have new variants emerge. And this is what we need right now.

**Chris Dall:** [00:21:50] So, Mike, as you stated in your opening remarks, it may be time to call an audible on our vaccination strategy to try and blunt the impact of B117 and the other variants. So what exactly would that mean?

**Michael Osterholm:** [00:22:04] Well, let me start out by saying you have heard me say on this podcast a number of times that I believe we have to stick with the two dose approach that has been approved by the FDA for both the Moderna and the Pfizer vaccines. I'm not deviating from that. I still believe that to be true. But the audible we're calling right now is is that we do have, I believe, enough data to support that one dose of those two vaccines may very well protect us sufficiently that we can, by expanding on the number of people who get vaccinated with one dose now and who then get their second dose three to four months later after this potential surge occurs, we could save many, many lives by getting one dose into people. Now, there's a lot of hesitation. They say, "Well, we got to follow the science," which is absolutely not a factual statement because the science would be what are these vaccines telling us about how well do they protect after one dose? We should be pursuing that. And I'm open and willing to do that. As you know, on Meet the Press on Sunday, I called for that and it surely has caused a backlash. People are upset about that because somehow it appears that we're trying to change what has already been a difficult vaccine rollout. Others will say we don't have enough data to support this. Yet, when you ask them what data they're talking about or what do we know about this, I think there is more data than we realize that could help us address this issue. Now is the time for us to bring together the highest levels of our government in terms of science and public health, public policy, along with the outside experts to determine is now the time to consider trying to vaccinate, for example, as many sixty five year old individuals and older, the people who are really most likely to be impacted by this next surge in terms of hospitalization, serious illness and death? And I have no hope here that we're trying to lower our case numbers down to some low number. I'm trying to keep us from basically from having our hospitals be so overrun that they just can't function. That's a crisis statement right now, and this is a tough time. It takes a lot of humility to admit I don't know, but we've got to look at this. It takes a lot of courage to say, "Wait a minute, what if this is wrong? What if this surge doesn't occur?" And in public health, I learned a long time ago I'd much rather be sorry for something I did than something I didn't do. And I hold by that today. It takes courage at this point from government leaders to come forward and say, "We've got to take a look at this," even though we know how complicated this has been. So let me just share with you this information I just mentioned. Two of the giants in the world of vaccines over the course of the past 40 years or more published an article in last week's Clinical Infectious Disease journal, the journal that is published by the Infectious Society of America, an organization that I belong to. The authors Stanley Plotkin and Neal Halsey are familiar names to anyone who is in public health and vaccines. They have done more over the course of their time to further vaccine research and development, vaccine availability, than in almost any two people I know combined. And in this particular statement, they went so far as to say that they believed at this point that it was critical that we move forward with a reconsideration of a dose delaying strategy. And in fact, Neal, in a interview with our CIDRAP news reporter for a story about this, actually said he believed it was time for an emergency meeting of the CDC's Advisory Committee on Immunization Practices to review in depth the strategy to give one dose as rapidly as possible based on data that are available, that are not necessarily in the public purview, on how well does one vaccine dose work? Remember that when the trials were set up for both the Moderna and Pfizer vaccine, there was never any intent to find the maximum immunological response model, meaning when to give doses. Remember, we have vaccines today like shingles, where we can give it from, on average, four to six months after the first dose. We learned we can give hepatitis booster doses a year apart. Many of our vaccines have months between the time that the first dose is given and a booster. What we were trying to do, which was very appropriate, was kind of take a risk and say, "If we measure this for the shortest time we can between one dose and two doses and then a follow up of two months, can we in fact show that these vaccines work?" And if not, it's not because maybe they didn't work its that we didn't have time for the immune system to adequately respond. Remember, in many cases when we have a vaccine in our body, it takes weeks to months before that full immune response is matured and ready for, in a sense, that prime. And I'll come back to that in a minute in terms of more information. But so in this case, what Neal and Stanley said was very important. They shared, for example, in their paper, they said, and I quote, "For both vaccines, the curves of cases in the vaccine and placebo groups diverged at about 12 days after the first dose and few cases occurred in vaccinees thereafter. For the Moderna vaccine, thirty five cases occurred in the placebo recipients from 14 days after the first dose until the second dose, compared to two in the vaccine recipients for an efficacy of greater than 90 percent. The Pfizer study reported an efficacy of fifty two percent from the time of the first dose until the second dose. But the efficacy from 12 days after the first dose can be estimated to be similar to the Moderna vaccine from the curves," referring to the antibody. "Both vaccines induced neutralizing antibodies after the first dose, which was boosted by a second dose, and the longer term efficacy was approximately ninety five percent." And they did say, "Although much more work is necessary to find correlates of protection," those measures of what means your protected, "Induction of neutralizing antibodies appear to be protective. Other vaccines produced by other methods may soon achieve emergency authorization in the United States, but their efficacy after one or two doses and adequacy of supply are yet unknown." Stanley and Neal shared an example, they said, "To give an answer to the first question," meaning how many people could be protected, "Suppose that one million people are to be vaccinated, but only one million doses are available. If two doses are given to each vaccinee and the efficacy is ninety five percent, four hundred and seventy five thousand people will be protected. If single doses are given and the efficacy is 80 percent," meaning it's lower, "Eight hundred thousand people will be protected." Almost twice as many. So what we have to look at right now is, in fact, can we establish that in the real world that that protection for the first dose of vaccine goes well beyond the period of three to four weeks, needing a booster dose at that point? CDC has long recognized that there are delays for some doses of vaccines and had a policy of not restarting immunization schedules because of delays, sometimes for at least 20 years. For the available messenger RNA vaccines, the CDC says the following, "There is no maximum interval between the first and second doses for either vaccine. Therefore, if the second dose is administered greater than three weeks after the first Pfizer vaccine dose, or greater than one month after the first Moderna vaccine dose, there is no need to restart the series." The CDC is saying that. So shouldn't we consider the possibility that in fact this might work and that we may actually be giving more doses, one to twice as many people in that age over sixty five right now, that should that next surge occur in the way that we think it might, what we might do to save lives? Now, I've had a lot of opposition and pushback, but I've also had comments and discussions with some of the best and brightest in the business. I've heard from so many colleagues, who I have great respect for, who believe that this is something we must look at and that we may decide maybe it wouldn't be what we hoped it could be in terms of one dose providing greater protection. I actually had one very senior vaccine immunologist say to me, "I think the bigger question is arguing why do we need two doses with these two vaccines?", which is kind of a flipping the whole question on its head. One very senior immunologist who has studied this area substantially said to me, "You know, the regret I have is I don't want my booster dose until four months after I get my first one to maximize." So I think there is a legitimate argument here to be made that we have to look at this and we can't wait, because if we do vaccinate these individuals with one dose, one, we have to really understand how we're going to communicate this to the public. How do we make sure people don't think they're being cheated? They still will get their second dose, but they don't need it yet. The one dose will protect them literally at a level very similar to two doses and at least, and most importantly, reduce serious disease and hospitalization, if nothing else. How do we then also get people into our programs to get vaccinated with one dose? I don't think you can today take people who are scheduled for their second doses and cancel them. I think you got to finish those. But you know what? Starting next week, we could say, "OK, we're going to do as many first doses as we can for those sixty five years of age and older. And we're going to protect as many as we can to keep them out of hospitals, from serious illness and dying during the next surge." And it's of note that this week the AstraZeneca study from England was published in Lancet. This is the study where they actually did do the initial dose and then didn't give a second dose immediately. They were waiting on this. This was done because they believed they have the data to support that. And also, again, it was a crisis in England. They used the chimp adeno vaccine, which is different than the mRNA vaccine. But it's also one that I think teaches us some real lessons. And in their summary published this week, looking at vaccine efficacy, they showed and I quote, "Vaccine efficacy after a single standard dose of vaccine from day 22 to day 90 post vaccination was seventy six percent. Confidence interval of fifty nine to eighty six percent. And modeled analysis indicated the protection did not wane during this initial three month period. Similarly, antibody levels were maintained during this period with minimal waning by 90 day." Now, that right there gives you some understanding and some hope that, in fact, if that could happen, could it happen with the mRNA vaccines? So I bring this back to a common point. This is going to be a tough one. It's going to take some courage if we're going to decide to do this. But it's courage, I believe, that if it's based on the science, and I have to come back to that, it has to be. It has to be based on the premise that everyone will get their second dose. But if we could double the number of people starting next week who get one dose of vaccine over sixty five years of age, I am convinced we will save thousands and thousands of lives. And if I'm wrong, so what? People got protected and they can come back and get their second dose. Same thing is true, if the surge doesn't occur, you just still protected more people. This is a very important issue and I hope we don't find ourselves arguing about positions that we had established. I've already said I'm a two dose guy. But I'm willing, under these conditions, to call an audible and say I'm more concerned about how are we going to keep our hospitals from overflowing during this possible surge? How many more lives can we save just because of an administrative decision we make? How do we best communicate this to the public? I believe they will accept this if we explain it in the ways that we should. No one's being cheated. No one will be denied the kind of protection that will keep them from the hospital or keep them from dying, but it will allow potentially many more people to avoid that same outcome. Now is our time. It's got to be done quickly. We'll see in the next week or two if our government and this administration takes that topic up. I know it's not easy, but when you think about all the lives that are at risk here, I don't know how you can't make this a high priority.

**Chris Dall:** [00:35:48] So it looks like there may be more vaccines on the horizon as Johnson and Johnson and Novavax released encouraging phase three data for their vaccine candidates last week. We also got official peer reviewed data on Russia's Sputnik vaccine this week. Mike, are you encouraged by the data on these vaccines?

**Michael Osterholm:** [00:36:04] You know, I am encouraged and at the same time, I think there is a subtle hint here that the variants are going to play a role in vaccine induced immunity and how well it works. Let's just look at the data we have for the three new vaccines, the Johnson and Johnson one dose vaccine, basically a harmless adenovirus-vectored vaccine, different than the messenger RNA. We have the Novavax vaccine, which was actually, again, a novel vaccine that actually is a purified protein encoded by the genetic sequence of the sars-cov-2 spike, and it's actually produced inside an insect cell. It's really a very novel type of approach. And then we have the other adeno vaccine that actually was published in Lancet this past week and it's the Russian data. And it's actually quite compelling. So let me start with the Johnson and Johnson vaccine. This is the one that when it first rolled out, a lot of people were disappointed in how well it worked and said, "You know, it's a real challenge in terms of how are we going to have a vaccine that appears to be inferior to two of the already on the market. How are we going to convince people to take it?" I think we have to do a little bit more looking here. First of all, the vaccine trials between the Moderna and the Pfizer and J&J were quite different. J&J looked at moderate to severe covid disease, as defined by the combination of a positive test and at least one symptoms such as shortness of breath, fourteen or twenty eight days after the last vaccination. Well, I got to tell you, I don't know if I call that severe disease. The Pfizer/Moderna data were different in that they had different endpoints. Pfizer evaluated their data seven days and later after the second dose, Moderna did it 14 days or later. It's hard to compare these in the sense of what just were the outcomes. But what was clearly a concern about J&J was that they only had a sixty six percent protection against moderate to severe disease. Now it varied. Was it in the US? Seventy two percent. South America? Sixty six percent. And in South Africa, fifty seven percent. After twenty eight days, however, following the one dose, there were no additional hospitalizations or deaths in the vaccinees. And what they really got hit by was, in fact, the occurrence of the variants in South Africa. And that brought their numbers down. And I believe that had the Moderne or Pfizer vaccines been evaluated in South Africa, that might have been the same thing. And so what we're still trying to understand, they did have this lower rate in the US of seventy two percent. But what it appears is that the vaccine was actually quite good at reducing severe illness and hospitalization. That, to me, is still a very important point in terms of what a vaccine can do. So I hope that we don't end up dismissing the J&J vaccine. And I think we're going to hear much more about it in the course of the next several weeks, some more data coming out, particularly as it's submitted to the FDA for approval as to just how well it can work, particularly as one dose. For those of us who have to administer vaccines that have been involved with vaccine programs, that means a lot because it's basically, in a sense, a shelf stable vaccine that you don't have to worry about the same critical refrigeration and freezer temperatures as you do with the mRNA vaccines. And this would make it much, much easier to deliver this vaccine in a number of locations. Now, in terms of the Novavax vaccine, they, too, had similar challenges with the protection there based on where the study was done. If you look at the vaccine efficacy as it was done in the United Kingdom, where, again, the variant there was the B117 with at that time, no evidence of the mutation that would reduce the immune protection. There the vaccine efficacy was 89.3 percent, virtually indistinguishable from what we saw with the Moderna and with the Pfizer vaccines. In the South African phase two clinical trial, they found 60 percent efficacy in the vaccine. The confidence intervals were wide, 19.9 to 80.1 percent. And this was for the prevention of mild, moderate or severe covid disease. It was ninety four percent in the study population that was HIV negative, not that dissimilar that you might expect to see in the United States. So we do see, however, this big impact where you have the variants and where you also, in this case, HIV positivity may have played some role. So it is worrisome about this situation in South Africa. We're going to learn more about what's happening with vaccines in Brazil in the near future. And I think this all poses challenge. All I would say is stay tuned. Again, a virus that doesn't occur, meaning is prevented from vaccination, is one that can't go through mutations. So, again, getting people vaccinated is so very, very important. I can't say enough how much that means. Now, in terms of the Russian vaccine, I think everyone was quite surprised to see the very detailed report in The Lancet this past week. And the good news with this vaccine, which again, as I mentioned, is an adeno vaccine, they actually found an overall efficacy of 91.6 percent. And it seems to be a very well done study. So hopefully this is going to add to the international vaccine availability. They've already been very clear that the Russian government is willing to provide vaccine to low and middle income countries. And so it's our hope that this will, in fact, get out, be used, and be part of the international program. So congratulations to the Russians on this one. They appear to have done quite a remarkable job.

**Chris Dall:** [00:42:34] Now to some listener emails. So we've received a number of emails from our listeners over the past week about the effectiveness of double masking, which is getting more attention in the media and in some cases is being recommended. The first one is from Susan who writes, "Over the past month or so, I have noticed more public figures wearing double masks. What do you think of double masking? Is it an effective way to increase our protection in light of the variants that we are all concerned about? If you think that double masking is a good idea, can you share any best practices?" And then here's one from Deborah who asks, "My husband has been doing the weekly early morning outings to the grocery store, and I was suggesting he might want to double mask or use one of our filters with his mask, but he does not think that will be much help and very uncomfortable. He added that if you learned from a credible science source that double masking was advised, he might consider that. Can you give any such recommendation?" So, Mike, your thoughts on double masking?

**Michael Osterholm:** [00:43:25] Well, first of all, thanks to Susan and Deborah for these really very good questions and ones that many people are asking in our community right now. But let me take a step back before I address the issue of double masking. Remember, respiratory protection is a gradient. From no protection at all, meaning you do nothing other than just breathe the ambient air around, that swapping air thing we've talked about. Or you have very high level personal protection equipment, such as an n95 respirator, other kinds of devices may even be more protective than that. And then you have everything in between. So staying with the gradient from the highest, we know that the n95 respirator works for two reasons. It's fit and filtration. Remember we've talked about that so many times, fit and filtration. That very tight face fitting device does not allow air to leak in and out. And that's why face fitting is important. The material is of a pore size that allows air to come in and out relatively easy compared to what other types of fabrics or barriers might be. But it works because it has an electrostatic charge that traps the virus coming through that pore size that otherwise would just allow it to come right through. So you get to breathe and you still get the protection of not having the virus. So again, fit and filtration applies as we move down to the next level of protection, i.e. medical masks or surgical masks. In that case, it is a combination of how much air is actually filtered through that surgical or medical mask, but also how much is actually leaking in and out of the sides, which is not tight face fitting. And then you get into the situation of the face cloth covering, which can be of any kind of material without any specific design necessarily for the purposes of tight face fit. And of course, then we get into gaiters. Now, if we look at how they each protect us, we have some data that actually one of our team members here extrapolated from studies done by the NIOSH, the National Institute for Occupational Safety and Health. They're part of CDC. Many of you know that. Dr. William Lindsley, a well-known researcher in this area, actually has done studies looking at the efficacy of face masks for source control of human's cough and exhaled breath aerosols. And what he found in his work and then extrapolated upon by our group here was that if you look at the outward leakage, meaning I've got this device on, I don't want to breathe my virus out into the ambient air, swapping air with others in that case. If I look at the different devices, the n95 respirator, I look at a procedure mask like a surgical mask, a three layer cloth face covering or a one layer neck gaiter, this is how much outward leakage you get. With an n95 respirator, one percent. With a procedure mask you get fifty two percent. With a three layer cloth face covering you get sixty one percent. And with a gaiter you get sixty one percent. Now that's, you know, better than one hundred percent leakage, but you get a sense of the relative issues. If I'm in an area with one of these other devices that I still leak. Now, that's better than zero. So that's why I keep coming back to saying continue to wear your mask. If you look at the inward leakage, now I'm worried about will I be breathing air in that grocery store or wherever. Using the same categories of devices, if you look at the n95 respirator, the leakage in is one percent. If I'm looking at a surgical mask or a medical mask, the leakage is 40 percent. If I'm looking at a face cloth covering with three layers, it's seventy seven percent. And I look at a gaiter, it's fifty nine percent. So what this also says again is, is that if I'm in an environment and the infectious dose means I have to breathe the air for 15 or 20 minutes before I have enough virus inhaled into my lungs to make me infected, one of these other devices other than an n95 surely can give me more time, but it doesn't buy me hours and hours. So we have to keep coming back to the issue, use your mask. And make sure first of all, it's always over your nose. That's a major challenge where we see sometimes up to twenty five percent of the public wearing something over their face, but it's below their nose. As I've said many times, that's like fixing three of the five screen doors in your submarine. But when you now get to double masking, you might assume, well, if one gives me this level, two may give me that level. And you know what? That might be possible. That's why I think people have been confused in saying it's a yes or no issue. It's not. It's an issue that says, if I wear a surgical mask or medical mask and I get this kind of protection that I just mentioned (fifty two percent outward leakage, 40 percent inward leakage), and I now wear some kind of a face covering that, basically a cloth of some kind that then holds the surgical mask tighter to my face, I actually get potentially improved protection from that. It doesn't open up more gaps along the side than it was before. The problem with that is, in many cases, the more layers you add, the more the pressure gradient is there to get air through it. So now I have to really suck harder to get the air through, which if you have resistance like that, guess what happens? Air then comes in and out of that leak that occurs at the side of the mask up against your face. Just like in swimming, your goggles, your mask, they don't leak at the glass, they leak at the fit. And so the concern has been, just you cannot automatically say if you wear a double mask, it's going to protect you more if, in fact, you actually make it so that you have more leakage, particularly around the side. It's not going to leak more across the gradient. You've actually improved that. So this is the challenge we have. There could be two layer masks that work better than one, if in fact, you don't greatly impede the air movement through and you don't open up those side leaks. But in many cases it is just the opposite. So this is where we have to answer the question is what I'm using better or not? And remember, it's always going to be about face fit and filtration. Now, I expect CDC to be coming out with guidelines potentially even any day on this very issue. And I hope they will address face fit and face filtration. The issue is use a mask of some kind, reduce your time. And remember, it is about time. If you're going to be in a public environment, you're going to be in a setting where someone's infected, the dose that you need to get infected will be a function of how much is in the air, how much you filter out or are exposed to because of that respiratory protection device and time. So I hope this helps explain to you here that, in fact, it could be a positive move and it could be a negative move. But to blanket say 'double mask for variants' is not a responsible answer relative to helping any one of us be better protected. I want everyone to remember that the n95 respirators should be saved for health care workers. We still have shortage of them relative to what we need to provide health care. So we are, as a country, still yet going to be using these other devices to help protect us. And I hope that over the course of the next days, one of the new major initiatives from this administration is to really take respiratory protection to a new level. We need to find ways to find better devices for the public for them to use, more like an n95 respirator that's comfortable. If it's not comfortable, people aren't going to use it. That's why also if you add more cloth on, you may actually end up not using it nearly as often because it's just too hard to breathe in. So I hope, Deborah and Susan, that answers your questions. It's really an issue right now of what's tight face fitting, which only you can know. And can you still breathe through the material in such a way that you're going to continue to use the device and you're not going to increase leakage along the sides?

**Chris Dall:** [00:52:28] Our Osterholm Update listeners continue to write to us with their thoughtful and inspiring pandemic acts of kindness. Mike, is there one you'd like to share with our listeners this week?

**Michael Osterholm:** [00:52:36] Well I, first of all, just want to thank everyone for submitting these. They are remarkable and it is absolute proof, scientific proof, that there truly are acts of kindness turning into a pandemic of their own. And this is one from Julie who sent this to us. And it is really quite remarkable that she shared a number of pictures with us, which obviously I'm not able to share with you and this microphone. But it starts out, "Julie's sewing crew is a group of women who are sewing and donating cloth hats to health care providers. To date, we have donated more than nine hundred hats to hospitals from Little Falls and Sauk Center, St. Cloud, most of the Twin Cities hospitals and even Green Bay, Wisconsin. Our group of women includes Anita, Mary Jo, Chris, Cathy, Jean, Cindy, Mary Jude, Vicki, Mary, Marilyn, Diane and Christine and of course, Julie. We have been helped in our mission by fabric donations from individuals and discounts from Gruber's Quilt Shop in St. Cloud and Dawn's Quilt Shop in Alexandria. The need is immense and will be ongoing for quite some time. So we'll keep washing and dry and fabric, cutting it up and sewing it into reusable hats for our most valuable resource in this country, our health care workers. We send love and light to every person receiving our hats. Stay safe and healthy, Julie." And again, I wish you could see these pictures and more importantly, the pictures with the health care workers wearing the hats. So thank you very much for that act of kindness. It is appreciated by all of us, not just those health care workers that are so fortunate to receive one of those hats.

**Chris Dall:** [00:54:20] And just a reminder to our listeners that if you want to share your pandemic acts of kindness with us, please email us at osterholmupdate@umn.edu. Your closing thoughts today, Mike?

**Michael Osterholm:** [00:54:31] I want to again just come back to a point that I tried to hit on last week. These are trying times. These are not easy. But again, we have to understand, like the discussion last week, nuts to the virus. These variants make it more complicated, surely, tough. But the vaccines are also advancing. And in the end, I'm going to take a bet on the vaccines. The viruses are surely going to still have a lot of tricks up their sleeve, but I think that we will find a way with these vaccines or even newer and and even more successful vaccines, a way to get around this virus. Now, I know in the meantime, we're all growing tired. I'm tired. Oh, I'm tired. I don't want to wake up any more days thinking about this virus as the first thing I think about or any more nights going to bed with this virus being the last thing I think about. And I know many of you feel the same way. I know many of you are also not only mentally tired, but in fact, financially, you're strapped. You're emotionally strapped for just trying to get through day by day. But we're going to do it. And that's why we're here. At this point, we're all going to start getting more and more crusty, a little more touchy as we get just so tired of this and we lose our patience. And what we have to remember, don't let the virus win that way as well as win physically. I find myself sometimes I'm just so frustrated, I'm so tired of this. And then I immediately catch myself rather than being nice or kind, I'm caught in that what that virus is doing to me? And I can't let that happen. And I hope all of you think the same way. You know, it's OK to feel tired and even angry sometimes, but let's make sure that we don't take it out on others and that we basically do everything we can to move forward knowing that there is light at the end of the tunnel. Remember, the days are getting longer. As I close, this is one of those experiences that somehow I don't know this person who wrote what I'm about to share with you. But oh, I know this person so well. I'm going to share a poem with you that was written by a young woman from the United Kingdom named Helen. She lost her father to covid-19 this past year. She wrote the poem that I'm about to share with you for a friend whose mother also died from covid-19 and then she read the poem on the morning news program, BBC Breakfast. It was through that that Claire heard the poem, actually shared it with us. And Claire, thank you for bringing this to our attention. It was very kind of you. So imagine a young woman who's lost her father writing a poem for a friend who lost their mother both to covid. Here is the poem. 'When your heart is feeling sad and the tears fall from your eyes, look outside your window and look up to the sky. Their presence is all around you. They're protecting you from above. They're watching over all of you and sending you their love. They'll visit you in your dreams to let you know that they're still around. They're the birdsong and the beauty and the feathers upon the ground. So though you'll miss them dearly, please know this to be true, that they will live in other ways and forever be with you.' Thank you, Helen. Thank you, Claire. Thank you very much for being part of this podcast, family. Thank you for sharing all you do with us. We do read your emails, every one of them. I try to respond to some, but they're really, really important to us. As I close here, I just want to go back to my introduction and dedication and again, I want to thank my family. You know, it is tough for all of us. We all need people right now to get through this situation. And I have been so fortunate to be blessed with the family that I have. In a sense, what I am able to share with you every week, what I'm able to do as part of the team at CIDRAP, in the first instance starts every day with my family and the support I've received. So again, I just want to resend that dedication to you. Thank you so very, very much for loving me and being there for me, even though sometimes I'm distant, I'm hours in an office and even sometimes frustrated and feeling short. Thank you so very much. So thank you very much. I appreciate you being with us and I look forward to being back with you next week. And I'm hoping and I'm looking for a good news somewhere. Let's try it. Be safe. Be kind. Good bye.

**Chris Dall:** [00:59:43] Thanks for listening to this week's episode of the Osterholm Update. If you're enjoying the podcast, please subscribe on your podcast platform of choice and write a review and be sure to keep up with the latest covid-19 news by visiting our website, CIDRAP.umn.edu. The Osterholm Update is produced by Maya Peters. Cory Anderson and Angela Ulrich are our researchers, and Randy and Eric Olson are Dr. Osterholm's story consultants.