# Episode 101: Class in Complicated Times

**Chris Dall:** [00:00:06] Hello and welcome to the Osterholm Update COVID-19, a 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. Welcome back, everyone, to another episode of the Osterholm Update podcast. As we near the end of April, U.S. COVID-19 cases are climbing once again. But in many respects, the pandemic trends are positive. The increase in cases appears to be a fraction of what we saw with the initial Omicron wave, hospitalizations remain at their lowest level since the early days of the pandemic, and COVID-19 deaths continue to decline. While there's no guarantee those trends will continue, there is hope in some quarters that the country is entering an era in which COVID is much more manageable. That will be one of the topics of discussion here on this April 28th episode of the podcast as we assess the state of the COVID-19 pandemic in the U.S. and around the world. We'll also provide an update on the Johnson and Johnson vaccine, talk about the Biden administration's effort to make COVID-19 treatments more available, answer a COVID query about the fourth dose of COVID-19 vaccines, and share the latest beautiful place submission from one of our listeners. But before we get started, as always, we'll begin with Dr. Osterholm's opening comments and dedication.

**Michael Osterholm:** [00:01:43] Thanks, Chris. And welcome back to all of you to the podcast update, our 101st podcast, of which many of you realize that last week was the 100th podcast. And to my complete surprise, the staff organized very kind comments to be made and included at the end of the podcast by a number of dear, dear friends and colleagues. I can't begin to tell you how much that meant to me. It was one of those tear jerking moments, and that absolutely was solidified when the very final comments came from my grandkids and family. That was truly a very moving experience. So I want to say thank you to all of you and just remind all of you that this particular podcast is a combination of efforts by a number of people. And if it were just up to me, we wouldn't have a podcast. I couldn't do this. So I want to thank them as much as anything that could be said about me and the podcast. So thank you. In terms of of this week, I think you're going to find that we're going to be continuing in a world of complicated interpretation. There's just so many things we don't understand what's happening with this pandemic at a time when we want it behind us. We're ready to be done with it, but we don't know what will be the next day's events with this virus. And that that challenge is so difficult. It's psychologically challenging. Clearly, financially, economically it's challenging. And because of the ongoing number of cases and the deaths we're seeing, it still is a substantial physical challenge. So let me just say at this point that hold on, we'll try to provide you some useful perspective this week. In terms of the dedication this week, we're addressing it to a very special group in our society, one that has surely suffered immensely from this pandemic, both from the physical impact, but also psychologically. And it was really highlighted in a recent survey released by the CDC on the Adolescent Behaviors and Experience survey, which highlights the magnitude of the challenges our nation's youths have faced during the COVID pandemic. This particular survey is the first one that's been done to measure the impact that this pandemic has had on our youth. As the CDC summarized, many populations that experienced more inequity before the pandemic also had greater risk during the COVID-19 pandemic related to mental health, suicide, substance abuse and racism. And when specifically looking at adolescents experiencing a mental health crisis, more than one in three high school students experienced poorer mental health during the pandemic, and nearly half of the students felt persistently sad or hopeless. If you look, more than half the students experienced emotional abuse in the home and more than 10% reported physical abuse in the home. Lesbian, gay and bisexual students were far more likely to report physical abuse, with 20% reporting that they had been physically abused by a parent or other adult in their home, compared to 10% of heterosexual students. Black students were most likely to report hunger, with nearly a third reported that there was not enough food in the home during the pandemic. Now, one could suggest that maybe this is the background that occurs all the time. We don't have the before and after pandemic data to address that, but everything that we do know tells us, no, the pandemic was in fact, a major reason for the increases that we see in this area. So our podcast dedication this week goes out to the adolescents, not just in our country, but worldwide and what they went through in this pandemic. So we are thinking about you and we hope for the best for you in the days ahead. Now in terms of moving on, this is the highlight period for me and the podcast, what some would call the silly moment that Mike has to have, and that is it is getting really light out there. Today we will have 14 hours and 8 minutes and 7 seconds of sunlight in Minneapolis, Saint Paul. That's 20 minutes more than it was just one week ago with 13 hours, 48 minutes and 7 seconds. Boy, I love these long days. Now, don't forget also that we've gained 5 hours and 19 minutes of sunlight since the winter solstice in December. And we're marching forward to that June 21st date. And I can't wait. And for all of those who live in in the southern hemisphere, as I say weekly, we are sending this down to you as best as we possibly can.

**Chris Dall:** [00:06:31] Mike. Let's take a quick look at the international situation. And let's start once again with China, where it appears Chinese officials are trying to avoid a Shanghai style lockdown in Beijing. Is this a sign that the government there is realizing that zero-COVID is not sustainable?

**Michael Osterholm:** [00:06:48] Well, Chris, let me just start out by saying that the recent news of cases in Beijing are ultimately just the latest example of where China stands in this game of cat and mouse on steroids. Clearly, a lot of the attention has been on Shanghai, which makes sense with what's been happening there. And we're seeing the situation in Beijing generate more and more headlines. But the country's battle with this virus aren't limited to those two places alone. In fact, if you look at the numbers reported out of China on Tuesday, there were locally transmitted cases identified across a total of three municipalities, two being in the Shanghai area and Beijing, of course. But in addition, 15 provinces. As expected, most of the country's activity is still being reported out of Shanghai, where more than 500,000 cases and 190 deaths have been documented since early March. I will repeat, as I do every week, I do not have much faith in these numbers coming out of China and for lack of a better way to say it, I think they're cooking the books. However, seeing these daily updates in new cases popping up in so many different parts of the country just highlights what they're up against. In the past, I've likened it to a high stakes game of Whack-A-Mole, and while that's still the case with Omicron, it almost feels like the playing surfaces quadruple in size and someone just really sped up the game. But to get back to your question, Chris, I have to say that China's response to the outbreak in Beijing, at least as of right now, doesn't offer up any signal that the country wants to acknowledge its position relative to this virus, at least not publicly. Instead, I think their response really just lends support to the notion that they're quite faithfully committed to their pursuit of zero-COVID. However, although this commitment is evident and has been emphasized by the lengths they're willing to go to prevent cases, even if it means accepting the humanitarian issues and economic hits that emerge, it's only a matter of time before the virus wins out. At this point, we know it's not going to go away in China. So once again, that raises the question, what's the endgame for China? Do they keep at it until the costs become too much to bear for the leaders there? Clearly, the costs are already building up. With hundreds of millions of residents in some form of lockdown, one can imagine that there are plenty of instances where people are suffering mentally, emotionally and physically. And as we've seen in Shanghai, people don't like being left to wonder when the next time they'll be able to leave their home is, when their next meal will be, or how their loved ones, even they themselves, will get appropriate care for their serious chronic medical issues. Well, with Beijing's outbreak, the approach from officials is essentially the same. In fact, in an attempt to try and avoid what's been happening in Shanghai, they seem to be wasting no time in showing their commitment to stamping out cases. With Beijing reporting a growing number of cases over the past week, the city has already announced mandatory testing for most of its nearly three and one half million residents living in just one city district, where most of the cases have been documented to date, have been told to stay home. Seeing that all of this has been rolled out in response to a total of just 70 cases over the course of several days time, or at least 70 reported cases. Some might wonder why they've turned to such widespread measures instead of starting with a more targeted approach. Well, if you take a look at the early days of the Shanghai outbreak, that targeted approach is exactly what was attempted there. Then by the time officials there realized it wasn't stopping transmission, they turned to more widespread and disruptive measures, many of which are still in place today and have been for months. So with Beijing, it looks like they're hoping earlier use of a more wide scale approach will contain the fire while still smoldering rather than waiting for it to reach the brush. And if your goal is zero COVID, that makes sense. They want to jump on to it quickly and ideally, if they can contain it, relaxing some of the measures that have been taken to date. Well, although the approach might give them a better shot at controlling this outbreak, there is no guarantee that will happen. According to a Chinese health official, Omicron has been in the city for a week before it was picked up, and it sounds like cases have been found in several settings, including among families, schools and even tour groups. In fact, the same official described the situation there as grim. So Beijing is casting a wide net to try and wrangle in whatever transmission might have occurred. And who knows, maybe they will. But if that's the case, it's really just a temporary fix. And although it could be a matter of days, weeks or even months, the virus is going to pay another visit. So as long as their reaction is the same, they're merely buying more time before more mass testing and lockdowns. Well, as I shared last week, if they recognize the reality that this is a short term solution, it becomes a matter of what are they doing with the time that they have bought? Are they tenaciously vaccinating their population? There are few reports of incentives being offered to vaccinated residents of Beijing. However, one was $150 shopping voucher for residents 80 and older, which might encourage some to get vaccinated. But how big of an impact will it have? Who knows? On top of that, what are they doing to administer additional doses which we know are important, particularly for the vaccines they're relying on? Could they improve the situation by using vaccines made outside of China like the mRNA vaccines? Are they constructing or refining plans to make more effective treatments available? What are they doing to help better prepare their health care system should a surge occur? There's a laundry list of questions and obviously many aren't easy to answer and couldn't have changed the situation overnight. In fact, with the status of their health care system, which has very limited capacity compared to many other countries, there's only so much you can do to make improvements with this bought time. But my point is that the time being bought is essentially only as good as the things you do with it. And to date, there haven't been any clear messages from officials about strategies being looked into or undertaken. Instead, it's largely been doubling, tripling or even basically quadrupling down on zero COVID. And if their belief is that zero-COVID constitutes a plan, that message hasn't exactly been resonating with people. For residents of the country, there's a constant threat of being stuck somewhere at a moment's notice. As you may have seen, the announcement of cases in Beijing had residents rushing to store and stocking up on supplies in case they've been confined without warning. In a different Chinese city, there were reports of more than 30 people locked inside an Internet cafe for nine days after a case was identified in an adjoining building. And of course, there are the businesses. How are you expected to run a business when your operations could be paused at the blink of an eye? And even if it's not your business, what if it's your supplier? Well, that's the current reality. At the end of the day, this has global implications. I've said that time and time again and for months and months. Results from a survey by the American Chamber of Commerce in China that was conducted in late March found that more than 80% of respondents reported disruptions to their supply chains. In addition, a growing backlog of cargo ships is building up at Chinese ports, including Shanghai's. And administrative officials in the US recently stated that they're seeing significant impacts to air cargo shipments. So overall, the costs that come with this approach are clearly mounting. Again, I understand why China doesn't want transmission to take off there, since the consequences would surely be significant. However, until they make a clear and concerted effort to address the vulnerabilities that they're citing as reasons for this approach, they can expect to not only pay a high price now, but they will pay it later also.

**Chris Dall:** [00:15:07] Last week we talked about the emergence of the BA.4 and BA.5 Omicron sub-variants in South Africa. Do we know yet whether those sub-variants are driving an increase in cases in the country?

**Michael Osterholm:** [00:15:19] Well, let me just start out with my weekly acknowledgment of humility. Anyone right now who is closely studying the variants have to acknowledge, I don't know what's going on for sure. And I think this is absolutely true also with BA.4 and BA.5 in South Africa. Let's take a look at some of the numbers being reported out of South Africa over the past couple of weeks. It's clear that something is going on there right now. Of course, this is the same country that really provided the world with the earliest look at what Omicron was capable of last year when cases were spiked from less than 300 a day in mid-November to more than 23,000 a day in mid-December. Well, as we know now, it didn't take long for that initial dramatic spike in South Africa, which was driven by Omicron sub-lineage BA.1 to play out elsewhere. In fact, as cases started taking off in virtually every country that detected the variant, many of us kept tabs in South Africa to try and get some sense of just how long the surge might last and what the recovery phase might look like. Well, when cases peaked there in mid-December, roughly four weeks after they first took off, there was a pretty dramatic descent. As it turns out, we'd see the descent there continue pretty consistently for a span of several months, bringing us to April. Although cases in South Africa remained above levels being documented pre-Omicron, you can see that the country, which was reporting an average of around 1,200 cases a day two weeks ago, has found itself in a much better position than it was in last December. Well, since April, 13 cases in the country have now been back on the rise. And as of this Tuesday, the daily average has climbed to 3,250 cases a day, more than doubling in a week's time. Of course, the latest total still places South Africa in a position where things remain well below levels reported in previous peaks. But the fairly sudden reversal, coupled with rising test positivity that went from less than 8% early last week to more than 19% as of this Monday has garnered some real attention. In particular, if you look at sequencing data from the country, you can see that this reversal has occurred around the same time that BA.4 and BA.5 sub-lineages of Omicron became dominant there. According to some analyzes that have been done, both these sub-lineages have a growth rate advantage over BA.2, which was previously documented there, and that was similar to the advantage BA.2 had over BA.1. In other words, we're seeing some signs that the members of this expanding Omicron family just continue to outcompete their predecessors with more and more transmission. However, it's still a little too early to know exactly what is giving BA.4 and BA.5 this advantage in South Africa. As I mentioned last week, the sub-lineages do contain some mutations that have been previously associated with additional immune evasion, and that's surely could be playing a role, especially when you consider the number of individuals in South Africa who are very likely previously infected but have yet to receive a vaccine. Again, this is a country where just 31% of the population are fully vaccinated and less than 5% have received an additional dose. So any improvements made to the virus's immune evasion properties could be heightening the risk of infections. But we're still waiting to see more data on these sub lineages to get a better sense of what's happening. Until that data is available, it's difficult to determine what role BA.4 and BA.5 are playing in South Africa's latest uptick in cases. And of course, we have to see what happens with hospitalizations and deaths there. So overall, we'll be monitoring South Africa in the days ahead and we'll keep you posted if any updates or new information emerges. Obviously, it's just another reminder that this virus hasn't gone away. And as soon as you think it has, it will come back to find you.

**Chris Dall:** [00:19:26] Now to the U.S.. I put a fairly positive spin on the U.S. situation in my introduction, but it is clear that we are seeing cases rise across the country, which in turn could lead to more hospitalizations and deaths in coming weeks. In an opinion piece for CNN, White House COVID-19 response coordinator Dr. Ashish Jha called it a complicated moment. Do you agree?

**Michael Osterholm:** [00:19:48] I completely agree. It is very complicated. Overall, the US has seen a 53% increase in cases now averaging just under 49,500 cases per day as of Tuesday, with 68% of these cases being BA.2 and 29% being BA.2.12.1. It seems we may be headed into a wave of cases fueled by BA.2.12.1, though it's unclear how big this wave will be. 42 states and Washington, D.C. have seen an increase in COVID-19 cases in the past two weeks. Last week, only 21 states and Washington D.C. were seeing increases from two weeks prior. As of Tuesday, 22 states had over a 50% increase in cases in the last 14 days. 20 states and the District of Columbia are seeing at least 15 cases per 100,000, up from 14 states last week. Vermont is seeing the highest daily case average of 46 cases per 100,000, followed by Rhode Island and New York at 34 and 33 cases per 100,000 respectively. Now, we have to remember, however, if we look at what's happening in terms of cases, one, this is difficult to interpret because of the inability today to test many individuals by PCR. And when people test at home with lateral flow tests, we surely are not finding out about these results. So if anything, these numbers really represent an underestimate of what's happening with clinical cases. That's why, as you know, I have continued to look much more closely at hospitalization data, realizing it's a delayed indicator, but it gives us the best understanding, I think, of what has happened in our community. As of Tuesday, just over 15,600 people were hospitalized with COVID-19 in the US, up 4% over the past 14 days. 24 states are also seeing an increase in hospitalizations. But as I've mentioned over the past several weeks, these numbers are still relatively low. Overall, the US hospitalization rate is about five per 100,000. Now to give you some sense of what I'm talking about, during the peak of Omicron in the United States, we were talking about 159,000 people being hospitalized at any one time. On April 17th, we're talking about 13,000. And now this past Tuesday, 15,600. So I think you can see that the numbers, even with some increase, are still very, very low compared to just what we saw a few months ago. And we mustn't forget that when we talk about some numbers doubling or tripling, even though cases and hospitalizations are up, deaths are still continuing to decrease, down 32% compared to two weeks ago, with an average of 363 daily deaths. 15 states have seen increases in the last seven days rolling average of daily deaths per 100,000 residents. But these numbers are also very, very low. Let me just remind you that during Omicron, we actually hit about 2,700 deaths a day. But I do want to put into context this 363 daily deaths. That sure is a lot less than 2,700. But if you added those up, if they were to occur day after day for an entire year, that would still be 132,500 deaths. So even at this lower, 363 deaths per day number, we can't take consolation in that if we think about the cumulative impact that that has. Despite the fact that deaths are currently decreasing, a few important reports released in the past week have highlighted the death toll that COVID has taken in the US and how many cases could have been avoided. The first is a report that was released by CDC on Friday that declared COVID-19 is the third leading cause of death again in the US in 2021, only behind heart disease and cancer. It was the underlying cause of death in 415,000 deaths or 13% of all deaths. In 2020, it was the third leading cause of death, making up 10%. These numbers do not include deaths in which COVID-19 was a contributing factor. Only those for which COVID was the primary underlying factor. Another CDC report released Friday explained that the racial and ethnic disparities and age adjusted death rates narrowed from 2020 to 2021. They credited this narrowing to vaccination and other preventive measures and interventions. The last important report that was put out by a group was from Peterson Kaiser Family Foundation. As we see daily deaths decline, we are still moving towards a devastating milestone in the pandemic. Since the beginning of the pandemic, we have lost almost 1 million lives to COVID in the US. The Peterson KFF group have analyzed how many deaths could have been prevented by vaccines. Their analysis concluded that approximately 234,000 deaths from June 2021 through March 2022 could have been prevented with vaccination. Let me repeat this. This deserves repeating. The Peterson KFF group analyzed how many deaths could have been prevented by vaccines. Their analysis concluded that approximately 234,000 deaths from June 2021 through March 2022 could have been prevented with vaccination. This is 60% of the deaths since vaccines became widely available and a quarter of all deaths since the start of the pandemic. Their analysis only considered deaths that occurred after vaccines were available to all adults in the US and they also excluded children from their analyzes. This limited their analysis to 389,000 total deaths, which they then narrowed to include only deaths among unvaccinated adults using CDC data on deaths by vaccination status. It is important to note that they acknowledge that not all deaths could have been prevented with vaccines. These vaccines are not perfect. They are not 100% effective. No vaccine is. Their analysis also took into account the decline in vaccine efficacy over time from 91% to 79% effective over several months. Well, there may be some limitations in this analysis, 234,000 lives lost that could have possibly been saved with vaccination is an incredibly large amount that just simply cannot be ignored.

**Chris Dall:** [00:26:33] Mike, the Biden administration announced this week that it's going to make COVID-19 antiviral treatments more widely accessible to the US public. To date, the rollout of drugs like Paxlovid has turned out to be more complicated and less efficient than many had expected. Will getting this drug into more pharmacies help?

**Michael Osterholm:** [00:26:52] Chris, my short answer to the question is getting the drugs into more pharmacies is absolutely essential. But I think it is very important to understand that we also have to turn these pills into prescriptions and people have to take them at the right time relative to the status of their infection. And that makes this a complex situation. I want to acknowledge that we've discussed some of the opportunities and challenges of rolling out oral antiviral therapies on the podcast back in February on Episode 91. As a recap, some of the largest barriers to uptake that I've noted were the ability to find treatment in a nearby location, access to primary care, availability of highly sensitive tests, and provider and patient knowledge on eligibility. We've seen some improvements in these factors since February. Bloomberg reports that the use of oral antivirals in the US jumped from 103% between March 27th and April 10th. The announcement from the White House this week also gives us some promising direction. The most notable theme here seems to be that at this moment in time we have the supply of these therapeutics. We just need to be strategic about getting them to the patients who need them. This latest announcement from the Biden administration first addresses the issue raised around availability of treatment at a nearby pharmacy. The announcement states that they will be doubling the number of locations that have oral antivirals available. There are currently around 20,000 sites with these medications, including pharmacies, community health centers, hospitals and VA clinics. Starting this week, the administration is now allowing all pharmacy partners in the federal antiviral pharmacy program to order antivirals directly from the federal government. This should increase the number of sites to more than 30,000 locations. Health and Human Services plans to increase these partnerships to 40,000 locations in the coming weeks. The second barrier I mentioned contributing to low uptake of antivirals was access to primary care. This is relevant for a number of reasons, particularly since access to these medications requires a prescription from a medical professional such as a physician, an advanced practice RN, or a physician assistant. The White House launched a test to treat program this past March in pharmacies and clinical settings, currently with about 2,200 locations. These sites offer testing and consult with a medical provider who can prescribe antivirals in a combined location. The announcement from this week notes a commitment to expand the number of these sites available. The test-to-treat program also gets at our third barrier access to highly sensitive testing. The final barriers surrounding provider and patient education are also touched on in this announcement. The administration plans to increase guidance and tools to medical providers on utilizing antivirals effectively. They also committed to increasing communication to the public about the safety and efficacy of these treatments. On Monday, CDC issued a health alert network what we call a "HAN," health advisory that gives providers, public health departments and the public updated information on availability and the use of outpatient COVID-19 treatments. Overall, these are some very positive developments. However, we still have considerable work to do, especially considering the significant health disparities in this country and across the globe. The Test to Treat program does offer free testing and medication. However, clinics administering the program can charge for a medical consult, sometimes upwards of $100. This is without mentioning the barriers to booking an appointment online, transportation to the appointment, and other factors that disadvantage those in rural areas with disabilities or those whose primary language is not English. W.H.O. expressed concerns this past week that similar to the vaccine rollout, low and middle income countries will be pushed to the end of the queue when it comes to accessing these treatments. Like all public health issues with COVID therapeutics, we need to have health equity at the front of our mind, not as an afterthought.

**Chris Dall:** [00:31:13] Our next few questions here are going to be about vaccines. And we're going to start with the Johnson and Johnson vaccine. Many people who received the J&J vaccine, including those in our audience, have been frustrated with the scarcity of information about efficacy and lack of guidance on booster shots. So Mike, what do we know at this point about the levels of protection offered by the J&J vaccine, how long that protection lasts, and what the booster guidance is for people who received it?

**Michael Osterholm:** [00:31:40] Well, first of all, let me offer an apology to our listeners. Two weeks ago, I noted that we'd be covering the J&J vaccine last week, and then, in fact, we were still looking for additional data that we wanted to share with you to complete the picture and that was not available at the time of our recording last week. But we should have told you that we weren't going to cover it when we said we would. So I apologize. It's here today. We've tried to get you the latest and the best information. When the COVID vaccines first became available, there was a real difference in vaccine efficacy in terms of prevention against symptomatic infection, as reported in the clinical trials. We saw that the mRNA vaccines had over 90% efficacy while the J&J vaccine was about 65% effective at preventing symptomatic infection, but over time was originally perceived to be underwhelming performance by the J&J vaccine has shown to be more equivalent or even offer some advantage over mRNA vaccines in terms of long term protection or durability. During the Delta surge in August and September of 2021, breakthrough infections were higher among those who got the J&J vaccine compared to those who receive the mRNA vaccines. But we saw that over time, these differences became less pronounced as the effectiveness of the J&J vaccine remained stable and the mRNA vaccines waned. During the Omicron surge in January, breakthrough infections were higher among those who got either of the mRNA vaccines compared to those who received the J&J vaccine. Why are we seeing that the J&J vaccine may be just as if not more effective at preventing infection and severe disease in the longer term? First, the vaccines work differently. They're different platforms and work differently to elicit an immune response. The mRNA vaccines basically deliver instructions to create the spike protein to train the immune system. The J&J vaccine is an adenovirus vector vaccine, meaning it uses an adenovirus as a shell to disguise, known as a Trojan horse. Then once in the body, it then releases genes that encode the coronavirus spike protein. There are two important buckets of the immune system that work together to protect you from infection and severe disease, antibodies made by B cells and T cells. It appears that the mRNA technology elicits a quick and very good antibody response, but it wanes relatively quickly, which is why we see good protection in the months after vaccination, followed by waning over time. CD8 T cells are important to prevent severe illness. So while infection may occur, these T cells protect against severe disease and death. For a variant like Omicron that seems to have evaded much of the antibody protection, the T cells still provide a protection against severe disease and death. The good news of the people who received J&J vaccine look to have good protection for a longer period of time with robust CD8 T cells. Interestingly, there was a preprint recently released that compares the all cause mortality comparing adenovirus vector vaccines to mRNA vaccines using data from the vaccine randomized controlled trials. The study found that both mRNA and ad-vector based vaccines protect against COVID-19 mortality, and they found that the adenovirus vector vaccines were also associated with lower overall mortality and lower non accident non COVID-19 mortality. As they mentioned in the paper, the phenomenon has been observed with BCG, vaccination against tuberculosis, and other live attenuated vaccines in low income countries. The prevailing hypothesis being an induction of innate immunity and a reduction in systemic inflammation. But no mechanism has been proven yet. Definitely an area where future research is needed and could actually provide us with an additional benefit of the J&J vaccine, not once considered. So what is the recommendation for people who have received J&J vaccine in terms of boosters? The CDC currently recommends that anyone who received the J&J vaccine as their first dose should get a booster. People are eligible for a second booster if they get two doses of J&J Janssen vaccine with the last dose at least four months ago, they recommend that people received one dose of J&J COVID-19 vaccine who want a booster encouraged to get an mRNA COVID-19 vaccine, either the Pfizer or Moderna. We'll keep a close eye on these recommendations to let you know if there are any changes as more information is learned about the long term effectiveness of these vaccines and the impact of boosters on vaccine durability. I do believe this may very well end up being the story of the tortoise and the hare, where in fact, in the end, the J&J vaccine over time may actually provide superior protection, at least as good a protection as the mRNA vaccines. And frankly, I look at this now and I think to myself personally, I wish I had started out with the J&J vaccine with multiple boosters, including either both J&J or mRNA. And I think I might have had actually a better T-cell response that in the long term could be very, very important.

**Chris Dall:** [00:37:05] Speaking of booster doses, that brings us to this week's COVID query, which is from Adam, who's looking for some clarification on your thoughts about a fourth dose of mRNA vaccines. He wrote, "I'm confused about whether to get my fourth shot. I was scheduled for it, but canceled after listening to the April 14th episode, when you stated that data from Israel shows infection rates are lower if you get a fourth dose but there was no protection after eight weeks. The study was limited and looked at only those over 60. I'm 55. You suggested that we needed to wait and see as more data is needed. You also mentioned that boosters are not a sustainable approach, but on the April 21st episode you stated that you're confident that you should get the second booster if you're 50 and older. Can you please clarify this for me?"

**Michael Osterholm:** [00:37:49] Well, Adam, thank you very much for your very thoughtful question and for piecing together the different statements that I've made that may appear to be contradictory and hopefully I can straighten out this discussion because in fact they are all consistent. When I was talking about the situation with the fourth dose in Israel, what I was really referring to is clinical illness and the fact that after 6 to 8 weeks, the vaccine appeared not to provide protection against clinical illness, but there was still an important protection that was afforded against severe disease, hospitalizations and deaths, which in the end for most of these vaccine questions is going to become central to what does the vaccine do for us? So I don't want to confuse you about this. I would still tell you to get your fourth dose. But let me just try to summarize the entire complete picture, because this is a very important question. I want to make sure that my take home message is very clear. I fully encourage everyone who is currently eligible to receive a second booster to do so. There's plenty of evidence showing that these additional doses are safe, and though waning immunity is a challenge, it may be much more so in terms of clinical illness, not in terms of protection against hospitalizations and deaths. There, it appears that these boosters, as they're called, actually can play an important role. I have received my second booster dose and I'd encourage other people in my life that are eligible to do the same thing. I still believe that even though it's the best thing we have in the short term, it is not a sustainable approach to think of boosting our way out of this pandemic. We clearly cannot expect that we're going to see many people in the public taking additional doses of vaccine every 6 to 12 months. Look at the challenges we have with influenza vaccine and look at the challenges we've had just getting people to take booster doses for COVID. So what I believe we have to do here is ultimately develop better, longer lasting vaccines. And I'll elaborate on that in a moment. In the meantime, we need to use the tools we have to fight this pandemic the best we can. And for now, that means getting a second booster dose if you are eligible and are able to do so. Think of it like putting duct tape over a leaky pipe. The tape will need to be replaced after a while and you may still see water leaking out, but a lot less water than if the tape weren't there at all. The tape also won't do anything to actually fix the leak. It isn't a practical solution in the long run, but it will minimize the damage until the pipe can be replaced. No one would advocate for you to just continue to replace the duct tape every day and never fix the pipe. But most would suggest that you continue to use that strategy despite its imperfections, until you can find a permanent solution. That's what we're doing with these boosters. They won't end this pandemic, but they will help us minimize the damage in the meantime. The bottom line is that my concerns regarding waning immunity, vaccine performance against emerging variants, and the long term sustainability of the use of boosters should not be confused with the hesitancy regarding receiving a second booster at this time. They are safe vaccines, and at least in the short term, they are effective in reducing hospitalizations and deaths. They may not be perfect, but they are still remarkable tools. And I believe that we can both advocate for the use of these tools now and for the development of more sustainable ones in the future.

**Chris Dall:** [00:41:22] That need for better and more sustainable vaccines in the future brings this to some news made by CIDRAP this week. CIDRAP announced on Tuesday that it has received a $1 million grant from the Rockefeller Foundation and the Bill and Melinda Gates Foundation to create a Coronavirus Vaccines Research and Development Roadmap. Mike, what can you tell us about this effort?

**Michael Osterholm:** [00:41:45] Well, Chris, let me just say that we here at CIDRAP are particularly excited about this opportunity to work closely with the Rockefeller Foundation, the Bill and Melinda Gates Foundation, as well as the Wellcome Trust, and a number of key researchers around the world to address this issue. This effort is particularly important because, as I just talked about, there is a need for better vaccines to help us get out of this pandemic and potentially avoid a future one. This roadmap will help us figure out how to get there and anticipate what challenges we might face along the way. Over the past few years, our group at CIDRAP, and particularly under the leadership of Dr. Chris Moore, has developed similar vaccine roadmaps for Influenza, Zika, Nipah virus, and Ebola Marburg viruses and has developed expertise in doing this type of work. For this roadmap, we've put together an international expert steering group that will guide the project, inform roadmap development and facilitate collaboration and consensus among a wide range of stakeholders. We'll also have a task force that will be invited to participate in the development process to ensure that the key areas of expertise are included. Finally, there will be a public comment period to allow input from a diverse group of stakeholders. Our plan is for a near-final draft of the roadmap that will be available at the end of this year. We anticipate the specific goals and milestones in the roadmap will include first, identifying immunological considerations for developing broadly protective vaccines. Two, determining strategies for conducting clinical trials using different vaccine platforms. Third, identifying research needs towards developing broadly protective vaccines, such as having standardized reagents and immunoassays, identifying relevant animal models of infection, and ensuring availability of clinical samples from relevant geographies, including low and middle income countries. Fourth, clarifying the ongoing regulatory challenges for future broadly protected betacoronavirus vaccines. And finally, last, identifying issues to address the long term cost and financing of global coronavirus vaccine programs. The World Health Organization is taking the lead and providing global coordination for research and development related to broadly protective coronavirus vaccines. And our intent is that this roadmap can serve as an additional tool to define research priorities and to make it easier to track progress over time. We aim to clarify specific goals and milestones for R&D to move the process forward quickly and strategically. It's only a matter of time before another coronavirus spills over into the human population. A coronavirus vaccine roadmap will provide a framework for the development of broadly protective coronavirus vaccines to ensure that we are prepared to respond to SARS-CoV-2 variants and the emergence of future coronaviruses with pandemic potential in the future. This project is, in fact, at the very heart of what CIDRAP is all about merging science and policy, research and development, and economics into a way that we can realize these very, very important tools.

**Chris Dall:** [00:45:05] Mike, I understand that we have another companion animal related beautiful place submission this week. What can you tell us about it?

**Michael Osterholm:** [00:45:13] Well, we have received a number of beautiful place submissions around companion animals. I think that we hit a particular sweet spot with this audience several weeks ago when I made the dedication to our companion animals. And so we're going to have a couple more because they really are wonderful and they do reflect such a positive aspect of this pandemic. So this one is from Amy, and she starts out by saying, "Dear Dr. Osterholm, thank you for dedicating this week's podcast to our companion animals. They truly are our sanity for many of us. That was true pre-COVID, but it's been especially true for me now. My beautiful places at my dogs side. Her name is Cricket and I would be all alone if I didn't have her. I'm high risk for a bad outcome with COVID, and my life has completely changed with the pandemic. I don't think I could do this without Cricket. I don't have family in Minnesota, and my health problems have always made it hard to socialize. I do have good friends and neighbors, but I don't get to see them often. Pre-pandemic, the only people I spent much time with in person were my coworkers. So my job was a source of income, but also companionship. Switching to telecommuting was so hard because of that. My coworkers and I are actually more productive when we telecommute as we have complex I.T. jobs that require lots of focus. Offices are often too noisy and distracting. I've expanded my skills in ways I simply could not do in the office, and my coworkers and I do collaborate and socialize over Teams, so we get to see each other on video. Still, I miss seeing them in person because being isolated and alone 99% of the time is hard. Human beings are social creatures and we're not meant to be alone. But alone I am. And now that COVID has come along, I'm even more alone. Cricket likes to sleep during the day while I work. She totally understands when I'm working, that it's not time to play. But before work, we snuggle on the couch for a few minutes and I divide my lunch break half for me and have to go outside and throw balls for her. She knows when it's time for work to end and comes trotting up to me a big smile on her face. She goes outside and if the weather is nice enough, I go with her. I throw balls for her and do a bit of gardening or just relax in the back patio. Then it's time for dinner. I learned a long time ago that Cricket is a homebody. She was a stray and starving the first year of her life, and perhaps that's why she prefers the security of this home we have together. She likes to walk in the neighborhood, but doesn't care about going other places. Last year I rented a house in Hinckley for a week to spend time hiking in Banning State Park. And she was so terrified the first night, she trembled and couldn't sleep until I let her in my bed with me. Normally, she sleeps in her own bed because my health problems make it painful to have a dog plastered against you while asleep. So I think if you were to ask Cricket, she'd tell you her beautiful place is by my side as well. Here are some pictures of Cricket. We played agility when she was young and she still loves going over jumps in the backyard. She also loves leaping for balls. As you can see, she's quite athletic. She also has quite a sense of humor and is a little bit of a goof ball. She likes to play wrestle with me, but is very gentle with her mouth so she doesn't hurt me. She's the smartest dog I've ever owned and she brings much joy to my life. So, yes, here's to all the companion animals who bring much to our lives and who ask only for food, a warm bed, and love in return. Amy." Wow. There are a lot of people listening to this that could absolutely relate to this. Amy, thank you for sharing this beautiful place with you and Cricket and us, and I wish you the very best for the years ahead with Cricket and enjoying life as you can. And please, if you have a chance, go look at the pictures of Cricket. When you see how high she can jump in those pictures, you'll be quite impressed.

**Chris Dall:** [00:49:12] Mike, what are your take home messages for today?

**Michael Osterholm:** [00:49:15] Well, Chris, when I come up with a summary, hopefully it should be something that's useful to people to kind of tie things together. I'm afraid I'm at the point often with summaries now that I just am really asking another new question, which doesn't give anybody any satisfaction. But let me come up with the three points I think today that really are at the heart of what's happening. Number one. It is really complicated. It is very complicated. I don't understand what these variants are doing, how they're doing it, why some variants are raising case numbers in some locations and not in others. Which variants are really the concern? What does waning immunity mean with these variants? How well are vaccines working over time? There's just so many questions. So it's complicated. Second of all is the fact that we have to anticipate the possibility, as we have really over the course of this pandemic, for new variants to arise. If you look about every six months, we've had a new major variant arise. Well, will that in fact be the case with what we've see now after Omicron has so dominated the global scene. I don't know. Don't be surprised, though, that if in one of these upcoming podcasts we're talking about a whole new variant of Pi or some other new name, it would not surprise me. And finally, we have to just acknowledge much of the world has moved on from COVID. Even though COVID is still real, it's still here, and the virus hasn't stopped looking for us. And any kind of public health recommendations we make, anything we do has to be kept in mind that, in fact, the public may not come along with us. They may not agree. And in fact, in many instances, I think they won't. And this creates an additional challenge. Not saying this is what we want to have. We'd like to have a coordinated public health response. But I'm not sure at this point how much the public will really listen to us. And therefore, what we do and how we do it has to factor that very, very important piece of information into our agenda.

**Chris Dall:** [00:51:28] And do you have a closing song this week?

**Michael Osterholm:** [00:51:32] Actually, I don't. But I have something else. I've been thinking a lot about how we can share the essence of what this experience on this podcast is all about, what we are hoping to do in providing information to you that is useful that you can use in everyday life, but also a sense of purpose of what are we trying to do during this pandemic to improve our lives, to help others. And I want to tell a story today, a story that is very personal to me because it happened to me. And it is one that is all about what I call the concept of class. Class is a very, very important part of my life experience. So let me tell you this story. As some of you already know, because I have talked about Nana before in this podcast, one of the most special gifts, if not the most important of my childhood, was this relationship I had with the wife of the owner of the Iowa newspaper where my father was a photographer. She was in her mid forties when I was born. She had one daughter then me and I became her adopted son and she in turn really became the mother of my soul. Her spiritual DNA is still in every cell of my body, and it helped shape the very values I cherish today. Nana was her family name. She was the essence of a Renaissance woman having a degree in journalism from the University of Nebraska and fluent in French. Over the course of 20 plus years, she died when I was 27, we shared hundreds and hundreds of hours of soul searching conversations, and she wrote me hundreds of letters and notes that would appear in the mail, even though her house was just eight blocks away. Several years ago, when I was asked to give the commencement address at a midwest medical school, I had never discussed the special relationship in public before, but I decided I owed the graduates more than just another warmed over commencement address. So I shared some of the lessons I learned from Nana. One of the lessons which I would like to share with you today was all about the gift of class. I will share with you a story of Jack, a prestigious medical doctor in a major medical center and his sense of class. Now the words from my commencement address. Finally, let me say a few words about class. It's the ability to never forget who you are or what is most important in life. In particular, being a physician or a physician assistant means you're pretty important. The life and death status for our loved ones may be in your hands. But never forget class is a status you earn when your achievement allows you to go to the head of the line. And you don't think twice about standing in the back of the line because others were there first. Nana taught me the class comes in many different packages under many different circumstances. When I asked her once to better describe class to me, she replied, You'll know it when you see it. She was right and an experience several years ago, provided me such an example. I was given an endowed lecture at one of the largest teaching hospitals in the US. The chief of medicine at this prestigious institution is an internationally recognized expert in his area of medical specialty and was in charge of the day's activities. The only way I can describe it to say is a brilliant clinician and a wonderful gentleman. As we walked the halls, fellow physicians, nurses, security guards, nurses, aides and even station clerks addressed him by his name Jack or an affectionate doc. This lack of formality might be viewed by some as a lack of respect for someone of such stature. Nothing could be further from the truth. Jack seemed to know every one of them by their first name and address him as if he were talking to a dear friend or neighbor. The deep admiration and respect for the chief was obvious. After my lecture in the hospital's auditorium, Jack and I were taking the back roads to get to his office. It seemed like an endless maze of hallways. Suddenly, in a relatively out of the way hallway near the lab, we encountered an older gentleman who appeared lost and distraught. Jack asked him if he could help. The older gentleman seemed to almost surprise someone in a white doctor's coat would ask. He blurted out in a painful acknowledgment that his granddaughter had just been admitted to the pediatric intensive care unit and he was trying to get there. He was desperately lost. Jack looked at me and his eyes told me just to follow. He asked the grandfather if he'd mind taking some stairs to save time. He replied, Anything to get me to my granddaughter. After more hallways and two flights of stairs, we were in front of the intensive care unit. Jack put out his hand to the man and said, Please know the staff of this unit are remarkable. Your granddaughter is getting the best care possible. The grandfather got huge tears in his eyes, grabbed Jack's outreached hand with both of his eyes, and held it for a moment. I'll never forget that silent, but heartfelt gratitude. Obviously, the grandfather had no way of knowing that the physician whose hand he held was a prestigious and powerful individual in his field of medicine. But then that was not the Jack I saw standing there either. As we walked away, making another attempt to get to his office and continuing our previous discussion. I realized again that Nana was right. I would know class when I saw it and I was in the presence of real class. For all of you listening today, you have that ability to have class, to be class, to share class. And I think in a time when things are still so stressful and we are trying to recover not just from a pandemic, but from world events, from economic challenges, from so many other issues that are in our life. We are grieving for those we have lost. If there was ever a time that if we could find it in our hearts to have class, the world would be a better place and each of us would be better for that. And I know right now I feel very challenged with the events of what's happening with COVID. And to me, I can just hope that I can live my life with some sense of class as I know that for all of you too, what that would mean. So as I close today's podcast, I will always think of you as part of that class that happens in our communities day in and day out. When I say, you know, be kind. That's part of class. When I say think about how we can help others, that's part of class. So thank you for being with us again on this podcast. A lot of information. I know, a lot of information. But we'll try to do our best to distill it down and provide whatever support and help we can to you. In the meantime, till next week, be safe. Be kind. Live a life where class is part of that life. Thank you. Thank you. Thank you.

**Chris Dall:** [00:58:33] Thanks for listening to this week's episode of the Osterholm update. If you're enjoying the podcast, please subscribe, rate, and review, and be sure to keep up with the latest COVID-19 news by visiting our website CIDRAP.umn.edu. This podcast is supported in part by you, our listeners. If you would like to donate, please go to CIDRAP.umn.edu/donate-now. The Osterholm Update is produced by Sydney Redepenning, Cory Anderson, Angela Ulrich, and Meredith Arpey.