# Episode 96: A Familiar Uncertainty

**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. Once again, the US appears to be in a period of uncertainty in this pandemic, a feeling that by now has become quite familiar. Clearly the country is in a far better position than it was just two months ago when we were averaging more than 740,000 COVID-19 cases a day. But with cases rising in Europe and the BA.2 sub-variant now accounting for more than a third of new US cases, it appears an uptick in infections is likely. What is uncertain is what the uptick will look like. Will it be a small increase or a new surge? And are we prepared to handle a new surge when so many people and policymakers are done with the pandemic and mitigation efforts are unlikely to return? That will be our focus today on this March 24th episode of the podcast as we assess the state of the COVID-19 pandemic here in the US and around the world. We'll also get an update on the discussions around the potential fourth dose of COVID-19 vaccines, talk about the latest news on COVID-19 vaccines for young children, answer a COVID query about the Johnson and Johnson vaccine, 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:** [00:01:54] Thank you, Chris. And welcome to all of you to another episode of the update. As I say, weekly and meant very sincerely, for those of you who are coming to visit us for the first time, we welcome you. We hope that we can provide you with the kind of information that you find helpful. For those who are part of the podcast family, buckle up your seat belts. This is going to be another one of those episodes where unfortunately, the more I know, the less I know. And today I'm going to share that context with you. We are in a period right now, I think, of real uncertainty. What will happen over the course of the next few weeks? I know what we want to have happen, particularly here in the United States, but I'm not sure what that necessarily is going to look like yet. It's in that regard with our 102nd episode that we should be finding ourselves with more clarity, but in many instances it's just the opposite. And as for that reason, today I dedicate this podcast to all of us, not you, all of us who remain confused about what the immediate or even intermediate future looks like with regard to COVID. We want to find a reason why we can stop listening to this podcast or for us recording it because you have other, more important things in life to do that aren't really dependent on knowing about COVID. So, again, dedicated to all of us that understand how confused we feel. Now, the good news, of course, is that we are still at that point in the year where the sunlight is becoming a more and more wonderful commodity every day. Today, here in Minneapolis-Saint Paul, on March 24th, we will have 12 hours, 22 minutes and 14 seconds of sunlight. Compared to just one week ago, Saint Patrick's Day, we've gained 22 minutes and 5 seconds of sunlight just in the past week. And this is obviously a wonderful gift. We've gained 3 hours and 26 minutes of sunlight since the winter solstice on December 21st. And it'll only get better from here. For those in the southern hemisphere, we're sending our light to you. So in short, buckle your seat belt. We will begin trying to decipher all this confusing information and what it means.

**Chris Dall:** [00:04:09] Mike, let's start our international section once again with the Western Pacific region, where several countries that have been hit hard by Omicron appear to be starting to see cases decline. Is Omicron peaking or has it peaked in this part of the world?

**Michael Osterholm:** [00:04:25] Well, that's a great question, Chris, and I'll do my best to provide some sense of the situation in the Western Pacific. But before I do that, let me start out by adding some additional perspective. At face value, a question like this might seem fairly straightforward and actually simple. However, as I alluded to in the opening of the podcast, there remains a fair amount of confusion. When you really start to dissect the question, you can see that there are a couple of different layers that exist. And while these different layers don't make the question endlessly complex or unsolvable, I think they can occasionally add some important context. And this is context that we will refer to when we talk about the incidence of disease around the world and specifically here in the US. So with a question like, has Omicron peaked in the Western Pacific region? There are a couple of things I want to point out. The first isn't anything new or earthshaking. In fact, it's been reality since the pandemic began, and that involves the concept of generalizing trends across different scales. And as everybody knows, discussing COVID trends can be very different depending on when and where you're looking. Just look at India and the US. From December 2020 to January 2021, India was seeing some of the lowest activity since the start of the pandemic. If I heard it once, I heard it 100 times, we should be doing what India is doing. Meanwhile, the US was facing its deadliest surge to date. By May of 2021, things were completely different. India's delta surge was resulting in the highest number of deaths reported out of a single country each and every day. And the US was coasting into that summer valley. So there's always that nearsightedness that we can fall victim to based on what's happening in our own backyard. In addition, when you see activity take off in countries with larger populations, you're obviously more prone to see that impact represented in regional or even global trends simply due to the sheer number of people. So when we talk about the Western Pacific region as a whole, it's important to remember that we're really lumping together 37 different countries. Some might have minimal activity, some might have record high activity. And depending on the population sizes, you can see where a handful of countries or even a single country can drive the overall regional trends. Of course, looking at those larger trends still has a lot of value and is necessary since there's not enough time in the day, and particularly in this podcast, to really focus on what's happening in detail everywhere. But it's important to remember that there are always exceptions to the larger trends with this pandemic, meaning that even during global valleys there can be those places that are experiencing their darkest days. On top of that, you mentioned the Omicron variant in your question. Well, we're seeing more and more discussions about the possible role and impact that the different Omicron sub lineages BA.1 and BA.2 could be playing. Again, whether it's Europe or the US there are a lot of questions about what BA.2 which is estimated to be around 30 up to 80% more transmissible than BA.1 is capable of doing. So why bring this up? Well, I don't want to overcomplicate things or confuse anyone, but I think it's important to recognize that, number one, depending on your own situation or scale you're using to look at activity such as local, state, regional or even global, our perception of the pandemic can sometimes be a bit skewed, and it's all in many instances, based on a single point in time. Number two, the variants and even the sub lineages of variants clearly continue to play an important role. And while that role isn't always immediately obvious or written in stone, it's a reminder that we're still playing cat and mouse with this virus and oftentimes we're losing. That being said, let's take a look at the latest update from the Western Pacific. Based on data from the WHO dashboard, it's clear that the Western Pacific region as a whole is still in the throes of what's been its most challenging surge since the start of the pandemic. Last week's case totals there surpassed 6 million, up from 5 million documented the week prior. Overall, this was the region's 12th straight week of growing cases, which has been at record high level since the start of the new year. In addition, deaths there grew for the sixth consecutive week and have officially reached record high levels of their own. Last week, the death toll was 7,000. The previous record was 6,900 deaths, which was reached last September when countries like Japan, Indonesia and Vietnam were dealing with the delta waves. Of course, if you zoom in a little further, you'll find that the bulk of the region's most recent activity has been driven by surges in a number of locations, including Hong Kong, Japan, Malaysia, South Korea and Vietnam. And you can see how the timing of these various surges in different places and their overlap have also played an important role. For example, when the region first started to reporting upticks in late December and throughout January, it was primarily due to the Omicron surges in Australia and Japan. But by mid-January, cases peaked in Australia and a few weeks later Japan reached their peak. And although both would start seeing declines, they hit record highs for cases and deaths. At the same time, things were really just starting to heat up for Hong Kong, Singapore, South Korea, Malaysia and Vietnam. And we've seen what's happened in these places since then, particularly in Hong Kong, which has reported per capita deaths at a level far beyond anything the US, the UK and many other places have experienced during even their most deadly surges, many of which occurred at a time when vaccines weren't even available. Again, it's a tragic reminder of what can happen when a variant as transmissible as Omicron hits a population with wide gaps in protection among its most vulnerable. As I've mentioned the last few episodes, basically just one third of Hong Kong residents 80 years of age or older were fully vaccinated when the surge took off. However, even in South Korea, where higher vaccination rates, particularly among the elderly, have clearly helped blunt the impact of Omicron, you can see the challenge that this variant poses with cases, hospitalizations and deaths in the country all reaching record high levels. In fact, in a story published by ABC News this past Tuesday described the situation in Seoul, where hospitals, funeral homes and crematoriums are struggling to keep up with the death toll, which is leading to a backlog of bodies. Remember, this is happening in a country where the per capita deaths are nearly six times lower than they are in Hong Kong. And I want to put this into context, because, as I noted earlier about India, oftentimes we have heard over the course of the last two years, if the United States had just handled COVID the way Hong Kong did, we would be in a much better place. And let me just summarize the deaths per million population for Hong Kong, which reached its peak on March 14 at almost 38 deaths per million population. Right now it's down to about 35 deaths per million population, but again, 38 deaths per million. And South Korea, with their Omicron peak, which is still growing, is only at 6.3 deaths per million. And finally, the United States, as bad as we have all described the situation has been over the past several years, with our Omicron Peak on February 10th, we were at 7.8 deaths per million. Remember, Hong Kong was at almost 38. Our all time high is still as horrible as it was, was 10.2 deaths per million. And now today it's at 3.2 deaths per million. So just think how we have actually outperformed a place like Hong Kong in deaths when in fact just a few months ago it was seeming as if somehow they were the great success and we were the failure. So this situation surely has not been smooth sailing in the Western Pacific region. However, if there's any good news in all of this is that the surge appears to have peaked in many of these locations. In fact, Hong Kong has now been reporting case declines since early March, and deaths are also now starting to descend just a bit. Similar situations are playing out in Malaysia, Singapore and Vietnam. And finally, even South Korea is seeing signals of a dip in cases over the past week, which will hopefully continue. Now, that being said, I honestly think it's far too early to conclude that the Western Pacific region as a whole will only see improvements from here. Why do I say that? Well, there are a couple of reasons. First, there's the potential that a few of these places seeing recent improvements could follow paths similar to those being reported in a number of European countries, which I'll cover in just a little bit, at least part of which is being attributed to growth of the BA.2 sub lineage. Of course, there are still quite a few unknowns when it comes to BA.2. So ultimately time will tell. And it's worth mentioning the BA.2 appears to have been dominant in places like Hong Kong, Malaysia and Vietnam for a month or more. But in other places like South Korea, BA.2 isn't dominant. However, it's growing. According to the latest sequencing data, at least 30% of the cases in South Korea are now BA.2, up from 10% in early February. And then there's Australia. Now I mentioned earlier that Australia was hit by their initial Omicron surge in December before reaching a peak in mid-January. From that point, cases there would drop going from over 100,000 cases a day to less than 25,000 cases a day by the end of February. However, cases there have been back on the rise again throughout the past month, with Australia's daily average now approaching 46,000 as of this past Tuesday. So it's come back up from 25,000 up to 46,000 cases a day. For context, Australia's latest daily rate of 1,928 cases per million population based on a seven day average has more than doubled over the past month. It is now more than 20 times higher than the rate of the US current 93.5 cases per million. If you look at the sequencing data from the country, you can see that BA.2 appears to have taken over as the dominant lineage right around the same time that this uptick began. So that's something to keep an eye on. However, I also want to point out that despite the rises in cases over the past several weeks, Australia hasn't experienced a similar increase in ICU admissions or deaths. Both have remained relatively flat over the past week or two. In fact, on a per capita basis, the number of Australians currently admitted to an ICU with COVID at about 3.7 per million is less than half of the US rate of 8.9 per million and their death rate 0.8 deaths per million is more than three and one half times lower than what we're reporting here in the US of 2.9 deaths per million. Even relative to the levels reached during the peak of Australia's initial Omicron surge in January, severe disease and death there remains several times lower as of right now. So that's important. But the increases in cases still raises concerns. And finally, there's China. I know I've said it time and time again, but it bears repeating. The situation that China is finding itself in is precarious, to say the least. And with a population of 1.4 billion, which accounts for nearly three out of every four individuals across the entire Western Pacific region, I think it is clear that any significant outbreak in China will dictate overall trends for the entire region. And with cases continuing to rise there for more than a month now, including more than 4,600 locally transmitted cases reported on Monday, I think they're finding themselves in deeper and deeper water. Now, these numbers you might interpret as being very, very low given the size of the population, and they are. But when you have a zero-COVID policy, even ten cases can create a crisis. On Saturday, the country did report two deaths, which is clearly a small number relative to what we've seen here in the US. However, they represent China's first COVID deaths in more than a year and matched the country's total for all of 2021. One of the cities continuing to see cases is Shanghai, which reported its fifth consecutive day with record high locally transmitted infections on Tuesday. Despite being China's most populous city with more than 26 million residents, officials there have recently conducted more than 30 million tests and are soon moving forward with block by block testing. Meanwhile, a province in the northeastern part of the country, which is where most of the cases from this surge are being identified, is still dealing with an outbreak. On Monday, symptomatic cases in the province capital city hit a record high after five straight days of increases, prompting city officials to suspend all indoor shopping, even at grocery stores for at least several days. Of course, this rule only added to an existing catalog of restrictions that residents have had to follow. In fact, all 24 million residents across the entire province have essentially been locked down as mass testing is underway. So there's no doubt China is throwing the proverbial zero COVID kitchen sink at this. However, at the same time, there are some signals of the country struggling to maintain that status quo. In the past couple of weeks, the Chinese National Health Commission has authorized use of at home tests to help ease the strain on PCR capacity, started pivoting away from a policy that required all cases to be admitted to health care facilities regardless of their symptoms, and announced the mobilization of vaccination units to try and improve uptake in elderly residents, particularly in rural areas of the country. So we'll have to wait and see what's in store for the Western Pacific region as a whole. For those places with recent peaks where BA.2 is already dominant, like Hong Kong and Malaysia, the coming weeks will hopefully bring about substantial relief. Otherwise, I think the Western Pacific overall is encountering a lot of the same questions and possibilities that many other parts of the world are dealing with. Now, I think everyone can agree this virus has been an equalizer across all geographies. The entire world can understand the impact of COVID in ways they hadn't even just six months ago.

**Chris Dall:** [00:19:45] Let's turn now to Europe, which a lot of people have had their eye on, because what happens there tends to hit the U.S. a few weeks later. Mike, what are you seeing in Europe and are there any other parts of the world that we should be keeping an eye on?

**Michael Osterholm:** [00:19:59] Chris, cases are continuing to increase in many countries throughout Western Europe. In the last 14 days Italy, the UK, France, Ireland, Belgium, Austria, Switzerland and Germany all saw an increase in cases, with Italy seeing the greatest increase at 85% and Germany seeing the lowest at 14%. In Germany and Austria, cases are now higher than they were at the initial peak of their Omicron surges. It is not entirely clear what is causing the surge in Europe. As we discussed last week, bhere are likely multiple factors at hand, particularly the BA.2 sub variant, waning immunity, and easing of COVID restrictions. Let's first look at the data we have on BA.2, and the role it may or may not be playing in these surges. In many of the countries that I mentioned, there are increasing cases begin within two weeks of BA.2 becoming the dominant variant, including the UK and Belgium, where BA.2 now accounts for 85% of cases, Switzerland, where it accounts for 72% of cases, and Germany where it accounts for 54% of cases. However, there are also some examples where BA.2 has not caused these type of surges. BA.2 accounts for 90% of cases in Norway and 87% of cases in Sweden, but both countries have continued to see ongoing declines in cases, with cases in Norway down by 65% and Sweden by 39% in the last 14 days. This is similar to what we saw in South Africa, where BA.2 became dominant after Omicron cases had peaked, but no additional surge occurred and cases remained low. It's unclear the role that BA.2 has played in countries like Denmark, where it became dominant very early on. Denmark's peak in daily cases was much higher than what most countries in Western Europe experienced at 797 daily cases per 100,000 population. But it's worth pointing out that the only country in Western Europe with a peak close to this was the Netherlands at 730 daily cases per 100,000 population, but they did not see BA.2 become dominant until most other Western European countries did and after their peak in cases. BA.2 now accounts for 70% of cases in the Netherlands, but their cases are declining, with a 20% decrease in daily cases over the past 14 days. As I said earlier, it's also possible that waning immunity from both vaccine and previous infection is contributing to these surges. With Omicron arriving in most of these countries in late November and becoming dominant by mid-December, there's a rapidly increasing number of people who are now at 90 days out from their Omicron infection. This is the point at which we begin to see more women and immunity from infection. In addition, although these are some of the most vaccinated countries in the world, all the countries in Western Europe that I mentioned that are seeing an increase in cases have less than 65% of their populations having received all three doses of vaccine, which still leaves at least 35% either unvaccinated or under vaccinated, at an increased risk of being infected. Additionally, all of these countries have lifted many of their COVID restrictions, and this could also be contributing to surges in cases. Although some of the restrictions like mandating masks but allowing the use of face cloth coverings were likely not all that effective. Some of the restrictions in place probably did reduce transmission. For example, the UK ended its isolation requirement in mid-February, meaning that those infected with COVID-19 were no longer required to stay home. Shortly after this rule went into effect, the country began to experience an increase in daily cases. Austria lifted its mask mandate, which required the use of FFP2 masks, the European equivalent of an N95 on March 5th. They then saw an increase in cases shortly after. In response to the rise in cases, Austria's health minister made the decision last week to reintroduce these requirements, still allowing only FFP2 respirators rather than the less effective cloth or surgical masks. In addition to the lifting of these more effective strategies, it's also possible that the removal of any restrictions at all may have caused a cognitive shift for many individuals that resulted in them taking fewer COVID precautions and increasing their own risk of exposure. The combination of these factors BA.2, waning immunity, and the removal of COVID restrictions has appeared to send many of these countries back into a viral blizzard, while other countries, like Sweden and South Africa have seen cases return to levels more similar to viral flurries. As more data becomes available, we hope to see a more clear reason as to why this is. But in the meantime, all we can do is respond the best we can to whatever the virus does, however unpredictable it may be. Now you understand more my sense of confusion. The other important thing to consider about the surge in Europe is whether or not it's leading to an increased number of hospitalizations and deaths, or if high vaccination rates and immunity from previous infection still offer a high level of protection in these countries. Let's look at the data on new weekly hospitalizations, number of patients currently in the ICU, and daily deaths in four of the countries that I mentioned earlier the UK, Germany, Italy and France. The UK has seen an increase in weekly hospitalizations at 19 per 100,000 population, approaching the rate of 24 per 100,000 population that they saw with their initial Omicron Peak, but still much lower than the 44 per 100,000 during their 2020-2021 winter surge. Hospitals in Germany are actually down from what they saw earlier in their Omicron surge at just seven per 100,000, down from 12 per 100,000 last month and 16 per 100,000 during their 2021 winter surge. Hospitalizations in Italy are starting to increase again, but are still only at seven per 100,000, down from 19 per 100,000 during their Omicron peak, and much lower than the rate of 31 per 100,000 that they saw in March of 2020. We're seeing a similar trend in France, where hospitalizations are increasing, but still at a rate far lower than we saw earlier in their Omicron surge, now at 11 per 100,000 compared to 30 per 100,000, which occurred during the original Omicron surge. And these rates are even lower than what they saw in their peak during March of 2020 of 37 per 100,000. If we look at the number of COVID patients currently in the ICU, which may be a better reflection of disease, severity and strain in the health care system, these numbers are also somewhat promising. The UK currently has just 0.4 patients per 100,000 population currently in ICU, down from 1.3 in January. Germany has seen an increase in their number of ICU patients at 2.8 per 100,000, which is close to what they saw back in February at 3 per 100,000, but still much lower than the 6.8 ICU patients per 100,000 that they saw during their 2021 winter surge. Italy and France both have less than half of the number of ICU patients per 100,000 that they did during their peak at 2.4 and 0.8 ICU patients per 100,000 populations, respectively. Finally, let's take a look at deaths. New daily deaths in the UK are increasing slightly at 0.17 per 100,000, but still far lower than the 0.4 per 100,000 during their Omicron Peak and 1.8 per 100,000 during their 2020 winter surge. Deaths in Germany are decreasing currently at 0.18 per 100,000, down from 0.27 per 100,000 back in February and 1.1 per 100,000 during their 2021 winter surge. Deaths in Italy and France are also decreasing in a very similar manner. So overall, new hospitalizations, ICU patients, and deaths in these countries remain lower than they were during the country's initial Omicron Peaks and drastically lower than they were during their previous peaks in the winter of 2021. And in addition, in some countries in the spring of 2020. High vaccination rates and high rates of protection from previous infection are both likely contributing to this relatively low burden of severe disease compared to previous surges. This gives us reason for optimism that even though the case numbers may be increasing with some of these variants or the relaxation of certain restrictions, the overall increase in serious illnesses still is substantially reduced compared to our previous experiences. Finally, let me address one last issue. If you look at Eastern Europe, particularly at the countries that are housing the majority of Ukrainian refugees, Poland, Romania, Hungary and Slovakia, they have all seen a decline in cases in the past 14 days, though the rates of declines are slowing. This is very promising, though there is still some concern that the influx of refugees could create conditions that may result in increased transmission. Additionally, BA.2 is becoming more prevalent in the region, just as we saw in Western Europe, and it is unclear whether this will result in a surge in these countries too. As for other parts of the world, Israel has also started seeing a rise in cases again, with a 31% increase in the last 14 days despite some of their population, 60 years of age and older and health care workers receiving a fourth dose of vaccine. This increase is similar in timing to many in the Western Europe in that it began at around the time that BA.2 became dominant in the country. Just as with many parts of Europe, it is unclear if BA.2 is the only or even a factor responsible for the increase, or if there was other factors that were also at play as well. In Latin America, cases are continuing to decline. BA.2 has appeared to mostly avoid that region so far, though there is little sequencing data available for many countries in Latin America, so it's difficult to know this for certain.

**Chris Dall:** [00:30:38] That brings us once again to the United States. As I laid out in the introduction, we are in a far better position than we were just two months ago. And nationally, cases, hospitalizations and deaths are continuing to decline. So, Mike, has the past week brought you any clarity on what might happen next here in the US and are we prepared for what might happen next?

**Michael Osterholm:** [00:30:58] Chris, it has brought me clarity in that right now we're looking pretty good. But I can't give you any sense of what the future might look like in 1, 2, 4 or 5 weeks with any clarity. Let's just take a look at where we're at right now. As of this past Tuesday, the US as a whole continue to see declines in cases. Overall, the US is seeing a daily seven day average of about 23,011 cases a day, or about nine cases per 100,000, which is 30% lower than the daily average we saw just two weeks ago. And this is despite BA.2 now making up 35% of all US cases. In some areas of the US, particularly the Northeast over 70% of the cases. This is the lowest daily average we have seen since July 16th, 2021, prior to the Delta surge. On Tuesday, hospitalizations were nearly at 19,305, which is down 30% from the previous two weeks. Remember that last week we covered the increasing wastewater trends in the US and discussed how we could expect to see an increase in cases in locations where COVID is showing up in increasing levels of wastewater. As of Monday, five states were seeing increasing cases. Over the past two weeks, Nevada has seen a 29% increase, New York has seen a 21% increase, Arkansas 18%, Colorado 10%, and Rhode Island 4%. Note as they are geographically dispersed throughout much of the country. There is growing concern that a rise in cases similar to what Europe is seeing right now may be coming to the US. And it's something we need to be prepared for, even though we can't predict when, where or how big the surge might be. A dear, respected colleague, Eric Topol, had an op ed in The Guardian this past week in which he explained that Europe's previous surges have been warning signs to the US and yet the US continues to ignore and deny what is likely coming our way. He also explained the uncertainty surrounding the use of Europe's increasing numbers, but waning immunity could be one of them. This is particularly concerning because the US vaccination rates are very low compared to other countries ranking 65th for vaccination rates with two doses and 70th for three doses. This is much lower than European and Asian countries and coupled with decreasing funding for preparedness and response, is setting the US up for a potentially dangerous situation. Despite these warnings, many states are slowly closing their testing sites that were once home to long lines of people hoping to get a test. Similarly, several states have pulled back from their daily COVID reporting and move to reporting their cases, hospitalizations and death numbers only once or twice a week. As you all know from our previous podcast and continuing to this week, funding for COVID response is now stalled in Congress. And because of this, the White House has announced this week they will not have money to order fourth doses for all Americans should that become a recommendation. Ultimately, what is happening in any given country could be here tomorrow and the US continues to be ill prepared to protect against or respond to another surge or another new variant. Unfortunately, given these circumstances, we will find ourselves again largely at the mercy of the virus, and only with time will we understand what our likely outcome is to be.

**Chris Dall:** [00:34:35] Last week, we answered a COVID query about whether a fourth dose of the COVID-19 mRNA vaccines might be authorized soon. Mike, do we have any updates on that issue?

**Michael Osterholm:** [00:34:46] Well, Chris, as we discussed, last week Pfizer requested authorization for a fourth dose or a second booster for those 65 years of age and older. Two days later, Moderna requested authorization for a fourth dose for all adults. Currently, the only adults in the US eligible for a fourth dose are those who are immunocompromised, which leaves millions of Americans over six months out from their third dose and unable to get a fourth dose. Currently, the federal government has enough funds to cover fourth doses for those 65 years of age and older, as well as the initial vaccination series for children under five. But the Biden administration has stated that they currently lack the funds that would be needed to cover fourth doses for all Americans. There is no question that we are seeing waning immunity after the third dose of vaccine and the early data out of Israel who began giving fourth doses to those over 60 back in December, has shown that this additional dose increases protection against severe disease and death in this age group, at least in the short term. Many other countries, including Chile, Sweden and the U.K., are now administering fourth doses to their older populations. That said, I think it is still unclear when and for what population we will see a fourth mRNA dose approved in the US and whether or not the federal government will have the money to pay for it. In the meantime, for those that want fourth doses, you will be challenged to get those doses, particularly as the vaccine supplies begin to run short.

**Chris Dall:** [00:36:21] We also have some news this week on COVID-19 vaccines for young children, as Moderna announced that they are seeking emergency use authorization for a two-dose primary series of their vaccine for children ages six months to six years. Mike, the parents of young children have been waiting for news on vaccines for a long time. Is this closer to becoming a reality?

**Michael Osterholm:** [00:36:43] Well, let me share with you what information we have as it's been publicly made available by Moderna in their request on Wednesday for additional approvals. Moderna reported interim data for their Phase 2/3 study of their mRNA vaccines, which included approximately 4,200 children, ages two to under six years and approximately 2,500 children ages six months to under two years. Children in these trials were given a 25 microgram two dose primary series. This dosing is one quarter of that given to adults. Overall, the vaccine was safe in these age groups, with no safety concerns identified. The majority of adverse events were mild or moderate and more likely to be reported after the second dose. Rates of fever were similar to other recommended pediatric vaccines. The primary endpoint or outcome in this study was a measure of the level of SARS-CoV-2 neutralizing antibody, a measure of the immune response. The study found that the immune response in children was similar to the response in young adults, inferring that protection provided is similar in children as we would expect to see in adults. In terms of efficacy against symptomatic disease, the vaccines were 43.7%. Let me repeat that 43.7% effective in preventing symptomatic disease in the youngest children, those six months to two years and 37.5% effective in children 2 to 5 years of age. Fortunately, there was no severe disease, hospitalizations or deaths reported among any of the children in the study, vaccinated or otherwise. So these endpoints cannot really be assessed. The evolving variants during the time period of a clinical trial is one of the many challenges of conducting vaccine trials for COVID-19. This study was done when the Omicron variant was predominant in the US and we saw among adults the protection provided by these vaccines decreased with the Omicron variant. So we would reasonably expect the same to happen among younger children. Moderna plans to evaluate the effectiveness of a third dose of vaccine, a booster, and will continue to monitor safety of participants for 12 months after their second shot to assess long term protection and safety. So in summary, similar what we've been saying for vaccines among adults and older children, these vaccines are not perfect at preventing infection. But all the information we have here supports they're safe and they surely likely provide some benefit, which is better than having no protection. I'm sure there'll be those who will conclude from these data that the vaccines weren't all that effective. Others will take heart in the fact that once a child is vaccinated, they do have an immune response and thus it's less likely that they might experience serious illness. Either way, it'll be a very interesting process here for the FDA to consider this request given the number of parents in this country that want their children vaccinated and then those who say these data are not up to par for what we would expect to want to license a vaccine for. Stay tuned.

**Chris Dall:** [00:39:56] That brings us to this week's COVID query, which is about the Johnson and Johnson vaccine. Kevin wrote, "Should recipients of the Johnson and Johnson Vaccine who received a second shot usually of mRNA vaccine several months after the first, now receive a third shot? What do the data show? Should they seek out a third shot?" Mike, we've gotten several questions similar to this from listeners who initially received the J&J vaccine, many of whom I think are pretty frustrated because the J&J vaccine has really fallen out of favor. So what can you tell them?

**Michael Osterholm:** [00:40:28] Well, let me preface these comments with, I think, a reminder of the very important fable about the hare and the tortoise. And I think you're going to see that there are some similarities here. When COVID-19 vaccines were first authorized, mRNA vaccines with an efficacy over 90% appeared more effective at preventing infection compared to the J&J Adenoviral vector vaccine, which reported an efficacy of only around 65% for preventing symptomatic infection. But at the time, these vaccines were promoted because it was a single dose vaccine, and for those that might only have access to one dose or willing to get one dose, it was said, yes, get this one. This protection is better than not. But now we're beginning to get more insight into how long protection may last using these different vaccine platforms and how that, too is a very important point. As I've discussed before, the immune response is complex and complicated and involves a number of different responses, including B cells and T cells, resulting in both antibodies and T cells that can help fight off infection and disease when the body is exposed to a virus like SARS-CoV-2. A robust antibody response can be developed fairly quickly following vaccination with both the primary series and boosters. And this is what the mRNA vaccines excel at. But we're seeing that this protection decreases over time as antibodies wane. And this was evidenced by an increasing number of breakthrough infections, even among people who have received a third or booster dose of an mRNA vaccine. On the other hand, the T cell response called CD4+ and CD8+ cells appears to be a more stable response over time. And while it may not completely prevent infection in the same way that high levels of antibody can, it appears to be playing a very important role in protecting against severe illness. While the mRNA vaccines have decreased in effectiveness over time, the J&J vaccine appears to offer more durable, long lasting protection, likely because the Adenoviral vector platform induces a robust T-cell response. Since the end of December 2021, the J&J vaccine has had the lowest breakthrough rate of all the vaccines being used in the US. A study that was published in JAMA Network Open last week looked at US claims data through August 2021, which was a pre-Omicron period. The study showed that one dose of the J&J vaccine maintained about 75% protection against infection and 80% protection against hospitalization both before and during the Delta surge. This level of protection was stable for at least 180 days after vaccination, regardless of what point in the pandemic they received their initial dose. And finally, T-cell immunity may be less affected by new variants providing a greater breadth of protection. A study published in Nature by the team, led by Dr. Dan Barouch at Beth Israel Deaconess Medical Center, measured CD4 T cell and CD4 T cell responses to the original SARS-CoV-2 strain into the Delta and Omicron variants after one and eight months following vaccination. They found that the CD4 and CD8 T cell response were more than 80% preserved in the Delta and Omicron variants compared to the response to the original strain of the virus. So in short, I think we're going to find ultimately that the J&J vaccine, particularly this particular platform, may be a very important tool in providing long term durable protection rather than this almost roller coaster ride we may potentially be seeing with mRNA vaccines. So for all of you who felt like somehow you were left out or that you got an inferior dose of vaccine, today with at least one dose of J&J and hopefully two, you may have some of the best protection of all. And I know that for many of you, this is a message that you are looking for, hoping for and have not heard until now. I have a sense that these new results will give us even more reason to continue to look at the mix and match strategies of using different vaccines, one after another in terms of maximizing all the immune response. So stay tuned. This is another area where we're going to see a lot of information coming out in the days ahead. But at this point, I'm encouraged by the data from the J&J vaccine recipient follow up, suggesting that we can even do a better job at eliciting a long term level of protection with the J&J approach.

**Chris Dall:** [00:45:24] Mike, what can you tell us about our latest beautiful place submission?

**Michael Osterholm:** [00:45:30] As I have shared on many occasions with beautiful places in my mind, there are two kinds of beautiful places. There are those which geographically are obviously breathtaking. And then there are those places that people go, not talking about a space but in some cases, it's where they take their hearts. It's where they share their love, it's where they share life in general. That, too, can be a beautiful place. We are so fortunate this week to have a beautiful place from Martha, which actually combines both of these, both a place geographically and a place in one's heart. Martha wrote to us and said, "Dear Dr. Osterholm, Chris Dall, and all the CIDRAP team. Like many people around the world, I've listened to your weekly COVID podcast for nearly two years now. The combination of data based information, candid guidance, honesty, even when it involves acknowledging uncertainty and empathy, have been the true North Star for me as I navigate the pandemic." Thank you, Martha, for that. She went on to write, "I wanted to share my beautiful place with you, or more precisely, my beautiful places. My father passed away from complications of Parkinson's disease two years ago this week, just as COVID was beginning to spread beyond its initial footholds in the US. After nearly 62 years of marriage, my mother was suddenly alone and due to the COVID regulations at the continuing care facility where she lived, no one could visit her inside her apartment. However, she was allowed to come visit me. And since I am something of a crazy cat and dog lady hermit on a rural property, the risk of exposure was low. Mom, 85 and still withdrawn in her new widowhood, reluctantly agreed to come with me on day trips within an hour or two drive of my home. To avoid the virus, I searched for outdoor destinations that were not hazardous for an octogenarian, ideally with a nice spot for a picnic lunch. I found the fantastic Virginia State Park System. There are more than 40 state parks in Virginia, and we discovered that the original six parks constructed by the Civilian Conservation Corps workers were established the same year that my mother was born. The first sorrowful months after Dad's death were softened by walking along welcoming trails and letting the vibrant Old Dominion springtime unfold around us. We saw trees leaf out at the Blue Ridge Mountains and lady slippers bloom in the woods. My father loved the outdoors and gradually the comment, wouldn't dad have loved this spot, became less painful and more peaceful. In Virginia, history is everywhere. A couple of hours to the south, we crossed the Appomattox River at Highbridge Trail State Park, where Lee's retreating troops tried in vain to stop Grant's advancing army by burning the bridge just days before the end of the Civil War. And 2 hours to the east, we took in sweeping views of the York River from one of the newest parks, Machicomocco, where an interpretive pavilion evokes the shape of the Paul Wheaton Chieftain's longhouse and traces back human habitation along what is now the Chesapeake Bay for thousands of years. Our first sad spring together turned into a healing summer and as a gorgeous autumn, followed by a not too severe winter. And then Mom and I got to do it all over again. Along the way, there have been vaccines, safer times for extended family visits, relaxed restrictions at her continuing care facility, new variants and tightened restrictions again. The roller coaster of pandemic life. But while the Blue Ridge, Virginia Piedmont, and Chesapeake Bay estuaries changed with the seasons, their comforts remain the same. Mom now about to turn 87, and I am sure grateful for the generous foresight that set aside open, undeveloped lands for public enjoyment. No matter what the future holds, we can always go back to our beautiful places. Thank you for all you do. Speaking of nature, I've never been to Minnesota, but I want to see some of that native tallgrass prairie Dr. Osterholm has mentioned whenever I do get to go there. Martha." Martha added a P.S.. She said, "My dad was an internist and radiologist and taught at Harvard Medical School for 50 years. A few years ago, I asked what was the greatest achievement in medicine during his practice career, given his specialty in nuclear medicine, I expected him to say something about imaging or targeted therapy for cancer, so I was surprised when he replied instantly without looking up from the newspaper, eradication of diseases through childhood vaccinations." Martha, thank you so very, very much for sharing this beautiful place with us both sharing the hearts of your mother and yourself along with the beautiful state of Virginia. I hope everyone visits the website photos that you've shared with us that you can see your mother and these many wonderful, beautiful locations and just thank you. Thank you. Thank you for sharing that beauty with all of us.

**Chris Dall:** [00:50:40] Mike, what are your take home messages for today?

**Michael Osterholm:** [00:50:44] Chris. I feel like I'm becoming a broken record. And as a result of that, many of you will probably say, I don't even need to listen to this guy anymore. He just says the same thing over and over again. But I think it's a really important message to get across. One, is anyone in this business today that's purporting to be an expert, or at least someone who knows something about COVID, has to begin every statement with a pretext. Humility. We just are not certain what is next, what will happen, why will it happen, how will it happen. I just don't know where we're going with this virus right now. Will we see an increase in cases with BA.2 throughout the United States? Will it happen in some locations and not in others? We've been here before. Remember when Alpha was raging through Europe in November and December of 2020? We fully expected it to do the same in the United States and only Minnesota and Michigan got hit and they got hit hard with Alpha, but not the rest of the country. Delta. Delta has acted differently in different locations. Why did L.A. and New York not get hit with Delta throughout the entire Delta surge, whereas the Southern Sunbelt states, the western Rocky Mountain states, then finally eventually the Upper Midwest and to the Northeast did, but spared many areas. The bottom line is, we don't know what this virus is going to do. So our best hope is just trying to stay one step ahead of it. And that one step ahead of it is making sure that as many people as possible are vaccinated, fully vaccinated with three doses, and depending on what happens with fourth dose, that we in fact also use that. In terms of the second point, vaccines, we're learning a lot about vaccines and we're going to continue to learn. You heard me say today that vaccines can have a critical role in reducing the likelihood of serious illness, hospitalizations and deaths. So even if the vaccine isn't going to prevent infection, I would still opt any day for something that made it much less likely for me to be seriously ill. As I pointed out with regard to the discussion about J&J, we're going to learn more about how to make these vaccines better. We're going to learn more about the human immune response and what can we do to hopefully develop more durable protection. So stay tuned. There are going to continue to be some confusion. They're going to continue to be some questions about vaccines. But it's all part of the learning process that we're all coming together around to provide those tools that hopefully one day will really give us levels of protection we can all feel confident about. And finally, I've alluded to the issue that we are on the edge of running out of money in this country to support the basic purchase of vaccines and drugs. I can't believe we would be here after the trillions of dollars we've spent responding to this pandemic. Now, just deciding we're done with it, even though it may not be done with us, and it still will extract a real cost, not just in terms of dollars and cents, but in terms of human lives. We've got to get this issue in Congress dealt with. The money that was being requested is minimal compared to the cost of not providing it and having individuals unable to either get vaccinated or be tested. So we'll wait and see where we go with that. But today, the bottom line message is tighten your seatbelt. Hold on. We're still learning.

**Chris Dall:** [00:54:29] And Mike, I think your closing today is an oldie but goodie.

**Michael Osterholm:** [00:54:35] Thank you, Chris. We always love our oldies but goodies. You know, trying to find one today, given the world experience that we're all suffering through. Given the uncertainty over with COVID, we all want to go out and celebrate, enjoy life, come out into the springtime of our worlds and at the same time a little bit confused. And this is a time where we need to help each other. We need to share what we can, how we can in both not only enjoying life, but making sure that we do all we can to protect those who are most vulnerable. So I've picked a song that we've actually used twice before. The first time it was used was in episode 13 on June 24th of 2020. And the title of that episode is "What I Know and Don't Know About COVID." I have to go back and listen to that again, just to understand how much I really didn't know. We used it also in episode 48 on March 18th, literally almost one year ago, and the title of that podcast episode was "Amended Heart." This is a ballad that was written by Bobby Scott and Bob Russell, originally recorded by Kelly Gordon in 1969. The song became a worldwide hit for The Hollies later that year, and it was also a hit for Neil Diamond in 1970. It was recorded by many artists in subsequent years. The Hollies version was rereleased in 1988 and again was a major hit in the UK. Scott and Russell were introduced to each other by Johnny Mercer at a California nightclub. Although Russell was dying of lymphoma and the pair met only three times. they managed to collaborate on this song. The title of the song "He Ain't Heavy, He's My Brother," comes from at least one of several different stories about using that term. The first editor of Kiwanis magazine, Roe Fulkerson, published a column September of 1924 carrying the title "He Ain't Heavy, He's My Brother," the first use of the phrase exactly as is now rendered in the song title. In the 1940s, the words adopted "He ain't heavy, Father, he's my brother" were taken to be the slogan for Boys Town Children's Home by founder Father Edward Flanagan. According to the Boys Town website, the phrase as used by Boys Town was said to Father Flanagan in 1918 by one of the residents while carrying another up a set of stairs. The boy being carried is said to have had polio and worn leg braces. So here it is, a song that I think is one for the times. It's one that I hope we all can embrace today and actually make it a part of our lives today and for the days ahead. "He Ain't Heavy, He's my Brother." "The road is long, with many a winding turn. That leads us to who knows where? Who knows where? But I'm strong. Strong enough to carry him. He ain't heavy. He's my brother. So on we go. His welfare is my concern. No burden is he to bear. We'll get there for I know. He would not encumber me. He ain't heavy. He's my brother. If I'm laden at all, I'm laden with sadness that everyone's heart isn't filled with the gladness of love for one another. It's a long, long road from which there is no return. While we're on the way to there why not share? And the load doesn't weigh me down at all. He ain't heavy. He's my brother. He's my brother. He ain't heavy. He's my brother." Thank you so very much for being with us again this week. We're not done with this virus yet, or at least I should say the virus isn't done with us. Given the world is so filled today with painful sights of what's happening in Ukraine, we're reminded of other locations around the world where food supplies now because of the war may dwindle in size and leave even more people hungry night after night. It's a challenging time. So for us, I can only hope that we adopt this sense of "he ain't heavy, he's my brother." It's going to be tough moving forward for those who are being encouraged to come back to the workplace, people who are encouraged to be in social settings. But because you're immunocompromised status, you still worry. What does this mean for me? What can I do to protect myself? Are the vaccines going to do that? And I think about you every day. I think about you in particular. We will continue to do whatever we can to provide you with the information that will allow you to protect yourself. And again, just kindness. Now, if there was ever a time to be kind, to remember all the cases out there the mothers, the fathers, the grandfathers, the grandmothers, the brothers and sisters, the aunts and uncles, the colleagues, the friends. And as I said, even those that may not like you, you don't want them to have to suffer serious illness or even die from COVID. So be kind, be good, be safe. And I hope you can join us again next week. Thank you very much.

**Chris Dall:** [00:59:55] 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 Maya Peters, Cory Anderson, Angela Ulrich, Meredith Arpey, and Sydney Redepenning.