# Episode 103: Words Matter

**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 I like to do every so often in preparing for another episode of the podcast, I recently went back and looked at my script from last year at this time, specifically the May 13th, 2021 episode. At that time, India was a house on fire with the Delta variant of the coronavirus, while US cases were rapidly declining amid the nationwide vaccine rollout. It seemed here in the US at least that the end of the pandemic was near, but what was happening in India would turn out to be a portent of the coming Delta wave in the US. In retrospect, though, Delta was not the first variant, it was the first indication that vaccines, as effective as they have been at preventing severe disease and death, were not going to end the pandemic. And here we are a year later on our third and fourth doses of the vaccine with yet another coronavirus variant causing a rise in infections. The threat is different now as the rising cases we are currently seeing in the U.S. does not appear to be causing the level of severe disease we've seen with previous waves. But it's a reminder that the virus is not yet done with us, no matter how much we want it to be. That will be the focus of our discussion here on this May 12th 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 discuss the mixed messaging we're getting from government officials on the pandemic, review some recent news about the Johnson and Johnson vaccine, answer a COVID query about Paxlovid and share our latest beautiful place submission. But before we get started, as always, we'll begin with Dr. Osterholm's opening comments and dedication.

**Michael Osterholm:** [00:02:14] Thank you, Chris. And welcome back, everyone, to the update. This week, as I always say, when I start these, welcome back to those who have been long term listeners this week, the group we call the podcast family. And we welcome any new listeners this week and hope that we can provide you with the kind of information that you find useful and would want to come back. Each week, as we prepare for these podcasts, I keep thinking to myself, How can things get more complicated? How can things get more challenging than they have been over the course of the past two years? And somehow each week I seem to find a way to understand. Yep, it's more challenging and today is not going to be an exception to that. We will find ourselves trying to interpret information that at the very best is going to leave us. Well, I don't know. As we start this podcast, let me take a step back and focus on something that surely has been collateral damage with this pandemic and something that as a nation and even as a world we are struggling with, to both understand and to respond to. And that is our mental health. Many of you may know that May is Mental Health Awareness Month. The pandemic has made it challenging for many patients with mental health conditions to get the treatment they need, especially those with unreliable internet access that struggle with telehealth therapy. Those that are unable to get the kind of psychiatric care that they needed or even make any kind of mental health care appointments. Many patients may have avoided necessary inpatient treatment due to fears of contracting COVID. Additionally, there are many pandemic related factors that have contributed to poor mental health in the last few years, such as fear of being hospitalized or dying from COVID, a fear of developing long COVID, loneliness due to limited in-person interactions, hopelessness among those with preexisting conditions, and of course, sadness from grieving the loss of friends and family members that have died from COVID. This is a challenge. All of these factors have led to worsening mental health during the pandemic. A study published in the Journal of American Medical Association in 2020 found that depression rates in adults had tripled in all demographic groups in the US. A survey done by the Kaiser Family Foundation found that in 2021, four in ten adults reported symptoms of anxiety or depression, up from one in ten adults pre-pandemic. A study published a few months ago in JAMA Psychiatry found that surges in mental health related emergency department visits increased following each of the surges in COVID hospitalizations. This is true for adults as well as for adolescents. As you may recall, last week I addressed the issue of the challenges with mental health in our adolescents. According to the report published in CDC's Morbidity Mortality Weekly Report in February, mental health conditions accounted for a greater proportion of pediatric emergency department visits in 2020, 2021 and January 2022 compared to 2019. We also must acknowledge that those suffering from mental health conditions, especially those with severe mental illness, are at an increased risk of being hospitalized and actually dying from COVID-19. It is unclear how long many of these mental health impacts will be. It is possible that some of the depression and anxiety that we are seeing will subside with some when the pandemic ends. But it's also very likely this could persist long after the pandemic is over. The one thing that we do know is that the pandemic has been incredibly hard on mental health. And though we may not acknowledge this in our every episode, it is certainly something that we think about and something that we can never forget. I personally can attest to the challenges of mental health during the pandemic. So let me just say at the beginning today, this podcast is dedicated to all of us, all of us who are having mental health challenges. And I want to acknowledge the many mental health professionals who have themselves to take care of themselves while at the same time taking care of a very rapidly growing public that needs them so badly. So this is to all of us who have those mental health challenges. We dedicate this podcast to you today. Also, I want to do something a little bit unusual, but it's for a very, very good cause. I want to give a shout out to someone, and this person is someone whose mother has been a very important person in responding to this pandemic here in the Minneapolis-Saint Paul area. And the shout out is to Marion, who will have her 13th birthday, her golden birthday, this Friday, May 13th. Marion, we are so, so happy to have you as part of this podcast family, and thank you for allowing your mother to spend so much time working on this pandemic. The combination of her efforts and your kindness have surely had a big impact. Happy birthday, Marion. We're really all very happy for you. Now, let me just move on and get to that good news segment. This is one segment, at least for the next few weeks, no one can deny it's good news. Now, some of you may, in fact, think it's crazy. Again, it's light. I am very, very happy to report that today in Minneapolis-Saint Paul, March 12, 2022, we'll have 14 hours, 44 minutes and 31 seconds of sunlight. That's 17 minutes more than we had just last week at the time of this podcast. And we're a long ways from that December 21st winter solstice of 8 hours and 46 minutes. But we're still climbing. We have until June 21st when we'll be at 15 hours and 36 minutes and 50 seconds. So enjoy the sunlight for those of you in the northern hemisphere. For those in the southern hemisphere, your turn's coming. It's just around the corner. And in the meantime, we continue to share with you the love of our light.

**Chris Dall:** [00:08:27] Mike, let's start our international update once again this week in South Africa, where COVID-19 cases continue to rise amid a wave of BA.4 and BA.5 infections. The increase we're seeing in South Africa is smaller than the initial Omicron wave we saw in that country. What does that tell us, if anything?

**Michael Osterholm:** [00:08:45] Well, Chris, at this point, it's very clear that South Africa is experiencing its fifth wave. Early on, there was some initial speculation or at least hope that the rise in cases there, which began in mid-April, was potentially an artifact of reporting disruptions brought about by the holiday weekend of Easter, Passover and Ramadan. But with cases there climbing for almost a month now, going from 1,200 cases a day to 6,000 cases as of this past Tuesday, it's another example of this virus doing what it does. Now, that being said, it's also becoming increasingly clear that the BA.4 and BA.5 sub-lineages of Omicron are playing the key role in this. Throughout March and into early April, it became apparent that they were growing in frequency and outcompeting BA.2, which was dominant at that time, but we didn't really know what this meant. Again, there are plenty of examples where a variant has become dominant without cases rising, at least right away. In fact, as you might recall, that's exactly what appeared to play out in South Africa when BA.2 overtook BA.1. However, in the case of BA.4 and BA.5 their dominance coincided with the rise in infections. So it passed that eye test. Of course, the eye test is far from official and can be deceiving. But having seen the data that's emerged over the past several weeks, I think it's clear that these sub-lineages are driving South Africa's latest wave. A look at their sequencing data shows that BA.4 and BA.5 now account for virtually all the infections in the country. And as we're seeing, a pretty significant reason for this success appears to stem from their ability to sidestep the defense against infection that's provided by recovery from BA.1. Again, according to the recent lab based serologic study, which we touched on briefly in last week's episode, unvaccinated individuals who recovered from an infection with the BA.1, the original Omicron variant saw limited neutralization levels against BA.4 and BA.5. In other words, despite the relatively recent recovery from an initial Omicron infection, unvaccinated individuals relying solely on that protection might very well be reinfected by BA.4 and BA.5. Meanwhile, the vaccinated individuals who experienced a BA.1 breakthrough infection also saw a noticeable reduction in the neutralization of BA.4 and BA.5. However, the overall neutralization levels for individuals with this hybrid immunity people who had protection from both vaccination and from recovery from infection was five fold higher than unvaccinated levels. So ultimately, BA.4 and BA.5 seem to have a knack for dodging some of the neutralizing antibody that can help prevent infection. But whether that actually translates into a wave of cases might depend on the overall vaccination rates in a given population. Well, for a country like South Africa, where less than one third of the population are fully vaccinated and just 5% of the residents have received an additional dose, BA.4 and BA.5 might have the conditions they need to drive up cases. So even though the country experienced record breaking case numbers from their initial Omicron surge, which was driven by BA.1, and it's believed that the vast majority of residents there have been infected at least once up to this point, most South Africans still lack the protection provided by vaccines. As a result, BA.4 and BA.5 might have plenty of opportunity to find suitable hosts in South Africa. At the same time, if BA.4 and BA.5 showed up in a different country take, for example, South Korea, things might not play out the same way. South Korea, like most other countries, experienced their own record breaking Omicron surge from BA.1. However, they've also managed to fully vaccinate 86% of their population up to this point, with 70% of South Koreans having received an additional dose as well. So the conditions there might be far less suitable for BA.4 and/or BA.5 to have this noticeable impact. Ultimately, we'll have to see how these sub-lineages fare in other countries to know for sure. As of this past Monday, there were only 21 countries outside of South Africa that had reported a combined total of just 574 cases of BA.4 and BA.5. So it's just too early to tell. However, while it remains to be seen if other countries might experience waves driven by BA.4 and BA.5, I think it's also really important to note that despite South Africa's rise in cases, the number of hospitalizations and deaths in the country have remained low relative to previous waves. So although there's been an increase in the number of patients hospitalized with COVID, they're climbing from 1,900 to 2,800 over the past two weeks, more than 90% of the country's beds designed for COVID patients are currently empty. In fact, for context, the 2,800 total admissions as of Tuesday compares to a peak of more than 17,000 hospitalizations during the country's Delta surge last July and 10,000 hospitalizations at the height of their initial Omicron surge in December. Otherwise, the number of COVID patients in an ICU, which was below 300 countrywide as of Tuesday and average deaths, which stood at just over 20, also remains far below previous highs. Again, by no means do I want to minimize these numbers or outcomes. But when you consider the ICU admissions during the country's Delta surge surpassed 1,400 and the average daily deaths climbed above 400, it can help put this current wave into some perspective. So there's clearly some built up protection against severe outcomes that's playing a role. And barring the emergence of a variant that could better evade the protection against severe disease that's offered by cellular immunity, I think most places will see a noticeably lower level of severe outcomes than might have been seen during previous waves. However, some of these places, like South Africa, have paid a much higher price to obtain this protection. In fact, a recent analysis in the country determined that there may have been more than 300,000 excess deaths in South Africa since the start of the pandemic, which is four times higher than their official number of deaths from COVID. If you assume that most of these excess deaths are actually due to the virus, it would mean that COVID killed one out of every 200 South Africans. A tragic and painful situation. So overall, Chris, I think what's happened in South Africa could provide a glimpse of what case surges might look like in places with high population level immunity. However, at the same time, there's a lot more that can and should be done. Again, the vaccines can make a huge difference when it comes to minimizing severe outcomes, and treatments will also help. So I hope we don't pass up opportunities to further improve these. And finally, as always, I'd be remiss not to provide that frustrating yet real reminder that this outlook could easily change depending on things like waning immunity or more importantly, I think, even new variants.

**Chris Dall:** [00:16:14] So let's take a look at some other parts of the world, and let's start with the United Kingdom, a country that we've often looked to for a glimpse of what we may see here in the U.S.. COVID-19 cases in the U.K. are continuing to drop from their BA.2 peak and are as low as they've been in a year. So, Mike, what's going on in the United Kingdom and beyond that, what's new out of China and Taiwan?

**Michael Osterholm:** [00:16:35] Well, you're exactly right, Chris. Throughout the pandemic, we've kept a pretty close watch on what was happening in the UK with COVID activity. Of course, like you mentioned, the activity there and in several of the European countries has served as an early warning system for us here in the US on more than one occasion. So that's been extremely useful. I must admit I'm somewhat lost as to understand why Europe gets hit earlier than we do in North America. It seems to be a consistent pattern that I can't find any epidemiologic reason for to explain that. And I should add that I don't mean simply looking at the UK's case curve has been some kind of magic glimpse into our future here in the US. Instead, what's really established them as critical resources over the course of the pandemic has been the quantity and quality of analyzes, reports and data the scientists and health officials have been routinely publishing, offering early insight on everything from variants of interest and concern to vaccine effectiveness. They have been and continue to be a real consistent leader in that regard. Now, that being said, the UK, like many other countries, has started rolling back some of their initiatives. So while the work being done there is still very valuable, I'm still trying my best to understand what exactly these changes have meant. For example, at the beginning of April, so about a month and a half ago, the UK residents no longer had access to free universal testing for COVID. As a result, the country's daily PCR testing capacity went from 850,000 on March 31st to only 422,000 on April 1st, a decrease of more than 50% virtually overnight and daily PCR testing capacity has dropped even further since then, sitting at around 315,000 as of this week. Of course, maintaining initiatives like free universal COVID testing requires a lot of resources. So it's not at all that surprising to see this change being made. But now we're seeing the UK's daily PCR testing levels reach their lowest levels since May of 2020 or two years ago. In fact, the current daily average for PCR tests conducted in the UK around 85,000 is more than seven times lower than the number of tests conducted this past January at the height of the Omicron surge, about 650,000. So that's something to keep in mind when trying to interpret these data. Nevertheless, the test positivity rate there has also been falling, sitting at around 5% in England and average daily cases have dipped below 10,000 for the first time since last summer. On a similar note, the number of COVID patients in UK hospitals also fell below 10,000 as of this Tuesday, which is the lowest it's been since December. Still, the current levels remain higher than they were at this point last year. On May 9th of 2021, there were 1,120 cases that were hospitalized. And on May 9th, 2022, this past Tuesday, it was at 9,600, almost eight and a half times higher than it was a year ago. And finally, as far as UK COVID patients using mechanical ventilation beds goes, the number as of this Tuesday, which stands at 214, is also the lowest it's been since last summer. However, despite the relatively low number of patients in mechanical ventilation beds, deaths in the UK from COVID remain somewhat elevated. For example, at this time last year there were just under 200 patients on ventilators. Around that same time, the number of deaths within 28 days of a positive COVID test all across England were all in single digits. Meanwhile, the current daily average now is above 100, even if you look at the delayed but more thorough data using death certificates, which only includes deaths where COVID is listed as the cause, the latest total of 1,250 for the week of April 29 is more than five times higher than the 232 deaths reported throughout that same week last year. So I'm not exactly sure what's going on in the UK. Overall, the activity there is at levels much lower than we've seen in past waves, but at the same time I'm not really sure what their baseline looks like moving forward. So ultimately we'll have to see what the UK version of living with COVID really looks like. Overall, I think this dilemma of how to live with COVID is being confronted by most countries at this point, and they might expect to run into far more questions than answers over the course of the months ahead. In some ways, it almost feels like we've reached a point in the pandemic we're experiencing both the best of times and the worst of times. On the one hand, global deaths keep dropping lower and lower, with just over 12,000 reported throughout all of last week. Again, the lowest weekly total since the start of the pandemic. In fact, for context, there have been multiple points in this pandemic where the average number of daily deaths surpassed 12,000. So compared to where we've been, we can at least acknowledge that although this isn't optimal, is still really major progress. At the same time, the general sentiment is that this is done and that is so shortsighted. On Tuesday, WHO's Director General Tedros noted that more than 50 countries are seeing an increase in COVID cases, with some of the rises linked to different Omicron sub-variants. As a result, countries with low vaccination rates remain highly vulnerable. Yet in some of these countries, little progress is being made. For example, in South Africa, a country I just got done talking about, vaccination campaigns are being cut back due to an overall lack of demand. Remember, this is a country where less than a third of residents have been fully vaccinated, including just half of the adults. But they're at the point where doses of vaccine might have to be destroyed due to approaching expiration dates and a general lack of arms. So ultimately, I'm concerned that more often than not, the concept of living with COVID is being used as an appeal to inaction. And while I completely understand that most people would prefer to never hear the word COVID mentioned again for the rest of their lives, nor would they ever like to hear my name mentioned, I'm sure that pretending it no longer exists is not the best option. That being said, living with COVID isn't exactly a universally accepted approach. In fact, for China, which is officially the world's final zero-COVID stronghold, living with COVID has really become synonymous with surrender. Over the past week, officials there have retightened restrictions in Shanghai, which have been under lockdown for six weeks, and they have expanded mitigation measures in Beijing, where several dozen cases are being detected each day. According to reports, the lockdown in Shanghai is now anticipated to last until at least late May. And the outbreak in Beijing was described as a stalemate by one city official on Tuesday, with cases there remaining steady despite the city closing schools and gyms, restricting in-person dining and sealing off selected neighborhoods. Again, what's driving this unabated commitment to Zero-COVID? Well, as I've mentioned before, one of the primary reasons is the low vaccination rate among China's elderly population. In fact, the country's head epidemiologist stated explicitly that vaccine coverage among both children and the elderly in China wasn't high enough to shift away from Zero-COVID without overwhelming medical resources. Well, according to a modeling study published in Nature this past Tuesday, which attempted to account for things like vaccine effectiveness coverage across different age groups and death rates from open infections, if China were to suddenly abandon a zero-COVID approach and let transmission occur unabated, they could see millions of hospitalizations and more than a million deaths by the end of the summer. However, I believe strongly that there's a lot of middle ground between their current zero-COVID approach and opening the floodgates, which is what the worst case estimates in that study were based off of. So I don't view the study as justification for China to stick with their current approach. Rather, I see it more evidence that the commitment to zero-COVID alone isn't enough. Again, what good does buying time do if that time isn't used to address the vulnerabilities? Interestingly enough, a recent survey by the U.S Chamber of Commerce in China showed that a vast majority of the nearly 400 businesses that responded believe that the country should focus more attention on improving vaccination coverage among the elderly. Likewise, a study in Nature emphasized the expanded access to vaccines and antivirals among China's most vulnerable. In fact, in an interview, one of the study authors said China would be even better off embracing Western made vaccinations as opposed to sticking with their own inactivated forms. Regardless, there doesn't seem to be any sign of China changing course in the near future. However, as we've seen in Taiwan, which had also embraced zero-COVID up until Omicron's arrival recently pivoted and into what's now being referred to as the new Taiwan model. In other words, they're shifting from elimination to mitigation. Of course, if you look at what has happened in Taiwan, where cases have spiked from a few hundred a day to tens of thousands a day in just a few weeks, you could argue that they're only pivoting because they're too overwhelmed for any successful attempt to elimination. I like to think the fact that this is just a lesson that we all have had to learn, that no country, no approach was magical. No one had exactly the right answers and how to deal with this. And it's just taken variance with more infectiousness to really accentuate that very point. Looking again at Taiwan. News of testing delays and public confusion surely support the notion that the country is overwhelmed. But they've also embraced Western made vaccines, with most administered there being either AstraZeneca or one of the two mRNA vaccines. And they have higher coverage across their elderly population than China. For example, if you look at China through mid-March, the vaccination coverage in those 80 and older, only 50% fully vaccinated, only 20% with a booster. Whereas you look at Taiwan with vaccine coverage among those 75 years of age and older, up to 60% are fully boosted besides being fully vaccinated. However, it's worth noting that still 20% of Taiwan's elderly population remains completely unvaccinated. So pretty sizable gaps remain there as well and could play a significant role in determining how severe this surge ends up being. But overall, Taiwan recognized that Omicron was a different ball game and they reasonably adapted their strategy. With China, I'm just not sure when and how the same will exactly happen. It's clear that China's total commitment to zero-COVID approach has tremendous implications for its residents and global supply chains, something we are now only really beginning to understand.

**Chris Dall:** [00:27:55] Here in the U.S., we continue to see a nationwide uptick in COVID-19 cases with the seven day average of more than 77,000 new cases a day. Hospitalizations are also rising, but at a slower rate, notably ICU hospitalizations. So, Mike, can we say at this point that this current wave appears to be causing less severe illness, or is it too soon to make that assessment?

**Michael Osterholm:** [00:28:18] Chris, before I give a national update with numbers, I want to state what I think is really been an unfortunate situation on the reporting of the current status of COVID in the United States. The media, I think, has missed a major piece of what's happening right now relative to reporting out these very rapidly increasing numbers of cases and even to the extent of reporting 50 and 100% increase in case numbers who are hospitalized, who are in ICUs, etc., when in fact, those are very, very small numbers that are being doubled as opposed to what we saw during earlier surges where it was very big numbers being doubled. So I'll come back to this, but I want to be very clear. I think that the public has not been well served by most of the media and how they've covered this issue. If you take a look at the 77,000 average daily cases or 23 cases per 100,000, it is clearly just a fraction what we're seeing from the time period in December, January and February. But also, we have to acknowledge I have no faith anymore in what these numbers mean. And I say that because with testing reduced substantially in terms of PCR based testing access and the fact that those people who are often being tested to know that they're positive are using at home lateral flow tests with results never being reported. I don't have a clue how many people actually have COVID now or have recently had it. In fact, I can tell you at no time in the pandemic have more of my family, friends and colleagues been infected than are happening right now, right this moment. And so to me, it's not just a fact of numbers. It's the fact that we're missing big numbers and we don't really understand what's going on. As you noted, hospitalization levels are incredibly low. I'll come back to this in a moment. And while they're a lagging indicator, I think right now they may be one of our best indicators for at least understanding what this virus is doing to us in our communities. As you pointed out, the US is averaging 1.9 new daily hospitalizations per 100,000. We have not seen hospitalization levels this low since July of 2021. Let me just give you a sense of what I think is being missed in the reporting. If one looks at hospitalizations per 100,000, as I just noted, it's roughly running about 1.9 per 100,000 population. If we look at what happened with the Omicron surge, that number was 8.3 hospitalizations per 100,000 population more than four times higher. If we look at the Delta surge, there were 5.3 persons hospitalized per 100,000 during that surge at this peak. Again, substantially higher than what we're seeing right now. It was only back in July of 2020 that we had a similar rate of 1.8 hospitalizations per 100,000 population. So hospitalizations are way down. But even more telling is what's happened in intensive care units. Now we have 2,096 individuals in intensive care as of this week. If you look back to the previous low, it was in July of 2020 when we were at 4,115, almost twice as high. If we look at what happened in Omicron, it was at 26,500. During Delta, we had 26,080 individuals hospitalized in ICU beds. And again, let me remind you we're at 2,096. I don't want to minimize these numbers that we're seeing right now, but we have not been reporting on how the impact of this surge has been much less dramatic with regard to serious illness, hospitalizations. And it really comes home when you look at deaths. Right now, we are averaging about 260 deaths a day in this country, 260 deaths a day. If you look back in June of 2021, just before vaccines began to roll out and that big peak that we saw back then, we were averaging 3,310 deaths a day. If you look at the Omicron surge at the height, we were at 2,600 deaths a day. And if we looked at Delta, we were slightly over 2,000 deaths a day. This is a different looking pandemic. It's really important to emphasize that point. So when I hear about case numbers doubling, but it's going from 2 to 4, that is so different than going from 200 to 400, and yet they both represent 100% increases. So I think this is a very, very important point that I wish we'd focus more on because it tells us a lot where we're at. If we look at cases in the US right now, as I pointed out, there have risen 52% over the last two weeks. But the numbers are still, to me, meaningless relative to what's happening with real case numbers because of all the things I just mentioned. It is clear that BA.2.12.1 is inching towards becoming the dominant strain, making up 43% of the US cases last week. Will that have an impact on what happens with the number of cases, the seriousness of those illnesses and the deaths? 46 states have seen an increase in reported COVID-19 cases in the past two weeks, and 35 of these 46 states have had more than a 50% increase. But again, smaller numbers. Only Alaska, Colorado, Pennsylvania and D.C. have seen their reported cases decrease over the past two weeks, and Montana's cases are the same as they were two weeks ago. Like last week, 24 states and the District of Columbia are seeing more than 15 cases per 100,000. Four states Rhode Island, Maine, Vermont and Massachusetts are seeing more than 50 cases per 100,000. Very important information, but I don't know what to make of it given the problems with testing and knowing what the case numbers are that are getting reported. The way I sum it up is a heck of a lot of cases out there right now. A lot. A lot. But the question is, what's happening to them? As I pointed out, if we just consider the percentage of hospitalized patients with COVID-19 or in the ICU as a measure of severity, we can make the statement that this COVID situation is much less severe now than it has been at any point during the pandemic. This is really good news. There could be a couple of reasons for this lower severity. One of the reasons could be the nature of the variants themselves. They are just less pathogenic or virulent. I don't think we have any data to support that, but that surely might be one issue. We don't know though, what any future Omicron sub-variant or for that matter, a brand new variant like Pi or Sigma might bring in terms of disease severity. Another possible reason for the decreased severity could be the immunity we've built for vaccination as well as previous infection. I think this is a very important point, but we have to acknowledge as immunity wanes and we need to remember that only 30% of Americans have received a booster dose of vaccine. So if immunity is driving the decreased severity and the immunity wanes, we are heading towards another very difficult situation. Couple this with a new variant or a sub-variant that causes more severe disease and we again could be in a world of hurt. I know no one wants to hear that. I want to also celebrate this moment of reduced, severe illness. But we have to be prepared for this. As I've been emphasizing for so long, we cannot tell the future. My crystal ball is not a telescope. It doesn't allow us to see some distant planet away or what might be coming. The virus has proven itself to be unpredictable time and time again. Anyone who says they know what will happen next or what will happen in six months simply does not. I don't care who you are. We need to be comfortable admitting I don't know and have humility as we continue through these uncertain times. I can hope so much that this disease becomes even less severe for the most of the population over time. But as you've heard me say time and time again, hope is not a strategy. So stay tuned. We'll give you the best balls and strikes assessment we can as time goes on.

**Chris Dall:** [00:36:35] So we've had some dueling narratives coming from the federal government in recent weeks about COVID-19. In late April, chief White House medical adviser Dr. Anthony Fauci said in an interview that the country is out of the pandemic phase. A comment which he subsequently clarified, saying that the country is out of the acute phase of the pandemic. Then late last week and over the weekend, White House officials warned that the country could see 100 million new infections in the fall and winter if Congress does not approve a funding package for more vaccines, tests and treatments. Mike, are you concerned about these mixed messages we're getting?

**Michael Osterholm:** [00:37:11] Well, Chris, let me just say at the outset that one of the challenges we've had in public health has been just that of mixed messages or when we would lack the clarity to say we don't know, and this is the possible kinds of things that could happen, any one of them are a potential reality. The public becomes confused and frustrated when we don't provide that clarity of message. And let me be very clear. You can still have clarity of message in a time of uncertainty. Let me also just start out by saying someone who has been quoted in the public, as I have been oftentimes reading those quotes, to say, I wonder who said that? Only to have it conclude according to Osterholm. I'm sorry, what? And so I want to be certain that we don't take anyone out of context or that we somehow misrepresent what they said. As you noted, the first comment was made by Dr. Tony Fauci on April 26th in the PBS NewsHour interview. As many of you know, Tony is a dear friend and colleague and someone who I hold in very high regard. He did clarify the comments the following day, but there was still clear confusion with regard to his statement and what it caused. In his PBS interview, he was asked, how close are we to the end of the pandemic? He responded by saying the following and I quote, "We are certainly right now in this country out of the pandemic phase. Namely, we don't have 900,000 new infections a day and tens and tens and tens of thousands of hospitalizations and thousands of deaths. We are at a low level right now. So if you're saying are we out of the pandemic phase in this country, we are. What we do hope to do, I don't believe and I've spoken about this widely, we're not going to eradicate this virus. If we can keep the level very low and intermittently vaccinate people, I don't know how often that would have to be, Judy. That would be every year. That might be longer in order to keep the level low. But right now, we are not in the pandemic phase in this country. Pandemic means widespread throughout the world, infection that spreads readily among people. So if you look at this global situation, there's no doubt that this pandemic is still ongoing," unquote. Tony clarified his comments to The Washington Post the following day, explaining that the US was out of the full blown explosive pandemic phase, adding that we're really in a transitional stage from a deceleration of the numbers into hopefully a more controlled phase and endemicity. Let me just say that, you know, a pandemic is a worldwide epidemic for which we expect to see peaks up and down. And you're in that pandemic the whole time. I mean, how many times have we in this country been confronted with what appears to be a substantial, reduced number of cases, people all feeling like, hey, we're free of this thing, only to be shocked back into reality with new variants and how they emerged. So that is part of the statement of what a pandemic is. There isn't really a pre and post pandemic phase as such when you're in the pandemic. Sometimes you're seeing spikes in cases, other times you're not. So I understand what Tony was trying to say. We truly are, just as I said over the last 20 minutes in a new kind of pandemic stage where we are seeing increased number of cases, but we're seeing decreased number of severe illness, hospitalizations and deaths. So I think that is an important point, but that says nothing about the future. And my really big concern is what happened with the White House statement. You know, that I am a very, very strong supporter of the activities of this White House. I served on the Biden-Harris transition team for COVID. And, boy, for all the reasons for my family, friends, colleagues, for all of you, I want this administration to do really well. So it's hardly an issue of me at this point trying to be political or point fingers. But what we don't need is statements that just came out from the White House, particularly Dr. Jha. He had an off the record briefing with five news media sources at the end of last week. At that point, the information did get out about his statement that there would be 100 million cases this fall and winter, basically if a funding package from Congress was not approved. I'll talk about that more in a moment. From that, there were several print stories that came out, and then there were a whole number of stories that came off of the previous stories. On last Sunday's Sunday talk shows, Dr. Jha went so far as to say this very same thing publicly based on modeling. Well, let me just be really clear. Number one, is we do need the funding from Congress, but it will not have a major material impact on the next wave of this pandemic if, in fact, we can't get people vaccinated. Right now new vaccines coming down the pike. What good are they if very few people get vaccinated? We have a lot of vaccine right now. Well, you can say, well, but we want to get a variant specific vaccine. Well, if you're going to see big, big numbers in the fall or winter, it almost is a guarantee that it's going to be as a result of a new variant, not sub-variants we're seeing now. Well, if it's a new variant, there's already been tremendous debate about would a variant specific vaccine for Omicron be as effective against the emergence of a new variant, as is the current vaccines that we have? So, I mean, the logic of having to have this money to stop this next big surge just doesn't meet the smell test. It doesn't. So to actually, I think, put Congress in a place where they should fund this, they must fund this, but don't put out numbers like this that scare the hell out of people. And people will say to me, look at you're doctor Doom. But then I ask them to please go look at the predictions. I'm saying right now, I don't know what six months is going to look like. Let me remind you, it was six months ago right now that Omicron was just beginning to emerge. And if I had said to you six months ago, oh, my, look, what's going to happen? The darkest wave of the pandemic is about to wash over us. It's going to be horrible. You would have thought that I had been smoking something. And look what happened. So now to project six months forward, think about that. How are we really able to do that with any modeling you have? And you've heard me talk about these models. Anything beyond 30 day modeling is pixie dust, just frankly, pixie dust. We don't know what they mean. And those groups that continue to model far out into the future have been wrong time and time and time again, just as if they had modeled last November where we'd be today, they would have missed Omicron. So I come back to the fact White House to say you have model supporting this and then don't provide them to the media or to the scientific community, I can tell you that many people within the administration were caught flat footed on this number. They read about it in the media at the same time we did. That's not the way to do public messaging. So, number one, it could be possible we could have 100 million cases of infection in the fall/winter, particularly if a new variant emerges that is more highly infectious and can even do more evasion of immunity than we have now. But also, we could see a situation of where the continuation of what we have now of just more cases but milder illnesses, fewer hospitalizations, fewer deaths could also be the case. Just put those out there. Don't try to basically put forward a political message based on scientific data that we don't know what it means. And so I will leave this experience with the fact that words matter, words matter, and the public takes those words and they will not only listen to them, internalize them, but they'll use them later to say, look what you told us. You told us this and it didn't happen. And if I'm in Congress and I feel like I was pressured into certain kind of funding requests because of those kinds of numbers, I would be pretty angry six months from now if that doesn't happen. Rather, what we have to do is say they could happen and we absolutely have to be prepared, but they might not too. And I hope that the White House gets this message in a part. And please stop using six month models. We can show you that they've been wrong time and time and time again. So I hope this is a lesson for everybody on messaging. We are at a very critical point in this pandemic of trying to make transitions, of trying to understand where we're at. And when you have the lack of clarity like these two very different opposing positions, that by itself is a real challenge. And ironically, there's truth in both of them. There is truth in both of them. That's the challenge we have is how do we communicate that to the public?

**Chris Dall:** [00:46:19] Last week, the FDA announced that the Johnson and Johnson vaccine should be limited to adults who cannot or refuse to get the mRNA vaccines due to concerns about the risk of blood clots. And Mike, just a few weeks ago, we talked about some really positive efficacy data with the J&J vaccines. So what can you tell our listeners about this new information and what does it mean for the J&J vaccine?

**Michael Osterholm:** [00:46:40] This may be one of the most difficult questions I will have answered in all of the podcast history, because I am trying to thread the elephant through the eye of the needle. I want to be very clear that I very strongly support the vaccines we have. As I've said time and time again, they're not perfect. They're remarkable, but they're not perfect. So let me take a step back and try to add context to this issue, because, in fact, I think it has a really important implication for us moving forward and understanding how vaccines work, why they work, and how we use them. It was clearly a pretty significant action taken by the FDA, especially considering the bumps in the road that the J&J has faced over the last year. Last April, after nine reported cases of thrombosis with thrombocytopenia syndrome or TTS, the agency paused use of vaccine for ten days. Just this past December, the CDC Advisory Committee on Immunization Practices, or ACIP, made a preferential recommendation for mRNA vaccines over J&J due to this clotting risk. As you mentioned in their announcement last Thursday, the FDA stated that they were limiting the authorized use of the Janssen COVID-19 vaccine in adults 18 and older who cannot or choose not to take one or the other approved vaccines like Pfizer or Moderna. The FDA cited that their preference against the J&J vaccine is due to caution around the risk of TTS. The announcement did state that those who are already vaccinated with J&J shouldn't be fearful as TTS would occur in the week or two following a vaccination, not months or even years afterwards. This was a complex announcement and there are some concerns in a few merits that I see here and want to address them. I want to start with a few concerns. Over the course of this pandemic, we've been able to put more tools in our toolbox to address COVID prevention and treatment. This has included knowledge about best practices and treatment and clinical care, increase supply of 90 fives and of course, the major accomplishment of developing vaccines that are highly effective at preventing especially severe illness and death. The Johnson and Johnson vaccine has been one of those phenomenal tools, and as we discussed in previous episodes, we've seen a reduction in all cause mortality with its recipients and it is performing quite well in the age of variants. Logically, the fact that it requires fewer doses, has a lower cost to produce, and is thermal stable, meaning it doesn't need to be kept at low temperatures like the mRNA vaccines do are all major benefits, especially in resource limited settings. Taking J&J out of our public health toolbox would be a big loss. Now, I don't want to dismiss these cases of TTS. I also think we need to be realistic about tradeoffs with the mRNA vaccines like Pfizer and Moderna. I just don't think we're applying the same level of safety scrutiny to these mRNA vaccines as we are J&J. It's not to say that any of these three immunizations have major safety concerns. The clinical trials and subsequent studies have shown that each of them significantly reduce the likelihood of serious illness and death with only a very, very small chance of serious side effects. Where I am concerned about the comparison here and the actions taken between the mRNA vaccines and the adeno vector vaccines such as J&J, is that there have been a series of cases of myocarditis and pericarditis associated mRNA vaccines, yet we've seen almost no scrutiny of those by either the FDA or the CDC or a full and comprehensive review of how often they happen. Now, I would not at all suggest people not get an mRNA vaccine. I have had four doses personally. I've recommended my family get them. But it seems as if somehow we're focusing specifically on the safety of J&J and we're not providing an equal and comprehensive review of the mRNA vaccines. And let me just say that I think this is a huge issue, because I do believe that the technology that the J&J vaccine, specifically the Adeno vector vaccines bring, is really very, very important. And it has a lot to do with potential for long term durable immunity. So I worry that they've been dismissed off hand. And I really believe that if we were to take all the SARS-CoV-2 vaccines and put them together, their safety profile would not be necessarily a standout with regard to the other vaccines. I also think it's critical that we touch on the merits of publicly acknowledging adverse events with vaccines. In public health and health care settings, we have to be upfront about the full pictures of safety when discussing any medical intervention or lack thereof. We can't just sweep people's concerns about TTS or myocarditis under the rug because we're worried about eroding public confidence in vaccines. I will hear from a number of people listening to this podcast that I have now become part of the dark side because I'm suggesting that there may be some safety elements to these vaccines that we haven't fully acknowledged or understood. I think that's absolutely wrong. At the end of the day, we have to always tell the truth. It's that simple. And even with the truth, we can understand that there are clearly, clearly risk benefits decisions we have to make where we would still basically recommend strongly the vaccine. We have to tell the truth about the likelihood of these events to occur, balanced with the considerable risk of foregoing immunization. Public health professionals and clinicians should be a safe place for people to ask good faith questions. If we aren't a safe place to get answers to these questions, there are plenty of other sources out there that can provide, quote unquote, answers in the black hole of misinformation and probably have something to sell you to, including a bridge. I think there's also some benefit in the announcement demonstrating that agencies and committees like the FDA and the ACIP are taking seriously safety as an issue and continuing to monitor safety even after providing authorization for the vaccine's use. I want to end this question, Chris, by talking about risks. Humans are really bad at assessing risk. I'm a human. I'm bad at it. We want to think we see the whole picture and are accurately calculating probabilities, but we most rely on our instinct, impactful stories, and emotional responses to figure out if there is a danger. Intuitively, if you think there's a chance of injury, receiving the vaccine, forgoing this vaccine feels like avoiding the risk. However, in reality, avoiding the vaccine is just choosing a very different risk. For example, people generally accept that the risk associated taking aspirin because of the benefits aspirin offer. But in fact, we see about 104 deaths per million population per year for middle aged men who take aspirin. Let me repeat that 104 deaths per million. In the J&J situation. The FDA identified 60 confirmed cases of TTS, nine of which were fatal out of 18 million vaccine recipients, this is a rate of just over five TTS cases per million doses administered, and it is one death per 2 million doses of vaccine caused by TTS. I want to make it clear that based on the clinical studies and ongoing safety monitoring, all of the vaccines that currently have an EUA are relatively safe and effective. They provide us a much greater likelihood of avoiding a serious health outcome than not getting vaccinated. Rare occurrence of these events do not outweigh the major benefits of immune protection from COVID-19 and its significant lasting dangers. Risk of blood clots, myocarditis and deaths are all considerably higher for someone who contracts COVID-19 than for someone receiving J&J, Moderna or Pfizer vaccines. Having said that, I think that we have to also look carefully at what is happening with the safety issues of Moderna and Pfizer in a more open and transparent way than we're doing now, because I'm not sure that we would come to the same conclusion that the J&J vaccines are something that we should avoid and preferentially go to the mRNA vaccines. I think that's important from an overall safety standpoint, and I think it's also important because we do not want to lose that technology that these adenovirus vector vaccines have brought us. They are demonstrating something about durability, likely T-cell immunity, and by just dismissing them as a safety issue right now, I think we're going to miss the opportunity to save many, many, many, many lives in the future with improved and better vaccine technology.

**Chris Dall:** [00:55:42] As the country nears 1 million deaths from COVID-19, STAT published a very interesting article this week that really broke the pandemic down into five separate pandemics. Mike, what was it that struck you about this article?

**Michael Osterholm:** [00:55:55] Well, as you know, Chris, I don't typically discuss other articles on this podcast unless they really have, I think, some real significance because right now our world is full of articles about COVID. I could spend 27 hours a day reviewing articles published that day. But this one really, I think, hit home in a way that I think it deserves for all of us to read it. I will note that this article is linked on our website. If you go back to the podcast website, you can find this article. The article titled "The Five Pandemics Driving 1 million US COVID Deaths" by J. Emory Parker was published on Tuesday in STAT. Let me at this point offer my sincere congratulations to Mr. Parker for what I think was simply an outstanding piece of work. Well done. Clear, compelling, and very helpful. This article outlines the different pandemics we've experienced in terms of deadliness based on five factors earlier versus later in the pandemic, older versus younger, unvaccinated versus vaccinated, rural versus urban, and poorer versus wealthier. The first factor earlier versus later was seen clearly in New York in the early days of the pandemic, when death rates climbed to 63 per 100,000 population. Even during the Omicron surge, their death rates were nowhere near this high. A better understanding of the virus, more available treatments, and immunity from vaccines and previous infection have led to much lower case fatality rates as the pandemic has progressed. We just got done talking about that very issue here. The second factor, older versus younger, has been seen clearly throughout the pandemic as the majority of Americans that have died due to COVID have been above the age of 65. Still, COVID has taken its toll on all age groups in the US. Now the fourth leading cause of death in the 15 to 24 year old age group, the second leading cause of death in the 25 to 34 year old and 35 to 44 year old age groups. And the first leading cause of death in all age groups above 45. Very sad. The third factor, unvaccinated versus vaccinated, is something that will sound very familiar to anyone who is listening to this podcast. As we have said time and time again, how important vaccines are in preventing hospitalizations and deaths. The death rate for unvaccinated Americans during the Omicron surge peaked at 26 per 100,000. But for vaccinated Americans it was just two per 100,000, and for vaccinated Americans who received a booster was only one per 100,000, 26 times lower than those who had not been vaccinated. The fourth factor, rural versus urban, is something we've touched on before in our discussions about access or lack of access to vaccines and COVID treatments. Though there have obviously been a substantial amount of transmission in urban areas, the cumulative number of deaths in non metropolitan areas surpassed that of metropolitan areas in December of 2020. The gap has only continued to widen since then, likely due to low vaccination rates and poor access to hospitals and other medical care, including COVID treatment. The fifth factor, poorer versus wealthier, is also something we've touched on before when discussing the many inequities we've seen in this pandemic. Cumulative COVID death rates have been higher in counties with higher percentages of their population living in poverty and in counties with high social vulnerability indexes. There are many intersecting factors, like a greater chance of being uninsured that have contributed to this. And unfortunately, there has been no consistent improvement in this disparity since the beginning of the pandemic. These five factors have created five pandemics that are causing the soon to be documented 1 million COVID deaths in our country. We all know that we've obviously had many more than a million deaths, but these are the ones that have actually been reported. Some of these factors, like earlier versus later, give us reason to be hopeful. Though the pandemic is not over and this virus surely isn't done with us, we are slowly learning how to live with it. Others, like the rural versus urban and poorer versus wealthier, which have seen little improvement as time has passed, are reminders that we still have a long way to go in getting over this pandemic, and that we cannot ignore the disparities that have caused many Americans to experience very different pandemics. These disparities are not new, and they will not disappear when the pandemic is over. So the really important trillion dollar question is what will the sub-variants and variants do to these five pandemics? Will, in fact, they impact some of them? All of them? We don't know. But over time, we can also assure you that these five pandemics are still alive and well and that we unfortunately need to understand, as we plan for the future what we're going to do in each of these five pandemic scenarios to improve upon whatever might happen with sub-variants and variants for the future.

**Chris Dall:** [01:00:56] That brings us to this week's COVID query, which is from Yvonne, who has a question about the antiviral Paxlovid and reports that some who've taken it are testing positive again a few weeks later. She wrote, "I have a friend who got COVID recently with mild symptoms and took Paxlovid. She got better quickly, but then about two weeks later had similar symptoms and tested positive for about a week using lateral flow tests. I've seen news that this is actually now being reported by many and the Paxlovid trial data are being reviewed. Can you provide your thoughts on this rebound COVID and any implications for use of Paxlovid?" And Mike, just to note, the reports we have right now are anecdotal, but what do we know about this?

**Michael Osterholm:** [01:01:35] Well, first of all, I want to thank Yvonne for this very thoughtful question. As these rebound COVID cases are certainly concerning. Before I get into the significance of why these rebound cases might be happening and what this means for Paxlovid patients, I want to provide some background pn Paxlovid and COVID relapses, as it's been referred to. We covered Paxlovid in some of our previous episodes. As a reminder, Paxlovid is a five day oral antiviral treatment for Non-Hospitalized COVID patients with mild symptoms but at increased risk for developing severe COVID. In clinical trials, there was an 89% reduction in hospitalization and deaths in patients that took Paxlovid. Though these trials were done in unvaccinated adults. And it is possible that since the rates of hospitalization and death in vaccinated adults are so low to begin with, vaccinated adults may not see as large of a relative benefit. As more and more people have taken Paxlovid, we have seen reports of rebound effect in COVID patients, meaning that they see an improvement in their symptoms after taking Paxlovid. But a few days after their treatment course is over, they start to feel worse again. This is being described as a COVID relapse or rebound COVID. We do believe that this is somewhat rare. According to Pfizer, this is occurring in about one in 3,000 patients taking Paxlovid outside of clinical trials. I'm not sure exactly how they've gotten that data, would be interesting to see more of it. But in fact, those are the numbers we have. That being said, it is possible that this is occurring more frequently than one in 3000 and is going unreported. Patients may assume that they have developed a cold or some other respiratory illness after having COVID and may not even be tested for a COVID relapse at all. More studies will need to be done to figure out just how rare these events actually are, especially given these challenges around testing and reporting. Regardless of how common these relapses are, there's still a concern in terms of the health of the person infected and the potential transmission to others. When it comes to something like this, there are two major questions that we need to consider when evaluating how to proceed. Why is this happening and what does it mean? I will attempt to answer both of these questions, though much of my answer will stay consistent with a common theme that many listeners of this podcast are familiar with. I don't know. I will cover what I do know and what I think we need to learn more about, but unfortunately we still have a lot to learn about this issue. Let's first look at why this is happening. We still do not know for sure why we're seeing these rebound cases, but I will cover three important possible explanations as to what is going on potential drug interactions, reduce efficacy, and issues with dosing and duration of treatment. I'll start with drug interactions. There are a number of medications, like some anticancer and anticonvulsant drugs for which the use of Paxlovid is contraindicated due to interactions that result in a decreased virologic response and possible resistance. There are also a number of medications to which the use of Paxlovid is not necessarily contraindicated, but heavily cautioned due to interactions that could cause unpleasant side effects. Especially in the second case, physicians may still prescribe Paxlovid if they feel that the benefits outweigh the risk leading to these interactions. If a patient takes Paxlovid while taking a drug that may reduce its biologic response or effectiveness, it is logical that a rebound case may occur. We do not know whether that took place for any of the reported COVID relapses, but it surely is a possibility. It is also possible that the many medications in which an interaction may cause unpleasant side effects that a patient may elect to stop taking the drug before completing the full course of treatment due to intolerable side effects. This incomplete dose and duration could then result in inadequate treatment and lead to a COVID relapse. Again, we still need more data on these cases to understand if that is something that could be playing a role in the significant number of these relapses. The next possible explanation I'll address is reduced efficacy, particularly with the Omicron variant. The clinical trials that found that Paxlovid was almost 90% effective in preventing hospitalizations and deaths occurred pre-Omicron. This has led some to speculate that the variant could be the reason for these relapses or that the virus could be evolving to resist Paxlovid. But this is not likely the case. Studies done by Pfizer suggests that the drug should still be as effective against Omicron based on the mechanism of action against the virus. We cannot entirely rule out the possibility that the virus is evolving to develop some resistance against Paxlovid. But so far there is not a lot of evidence supporting that theory. Perhaps the most likely explanation for why these relapses are occurring is the third reason that I mentioned, issues with dosage, duration and timing. Currently, Paxlovid is prescribed as a five day treatment, but these relapse cases suggest that this may not be sufficient. This may be because a lower viral load is needed to cause rapid viral replication and clinical illness with Omicron compared to Delta and the other variants. Previously with Delta, a patient can take Paxlovid and have a small amount of virus still present in their body after day five of treatment, which their immune system could successfully attack. Now, with Omicron, if less virus is needed to cause rapid replication and clinical illness, the small amount of virus that remains after treatment may replicate before the immune system can sufficiently destroy it, resulting in these relapses in cases. We don't know for certain if this is the cause. However, given what we know about this drug and about these variants, it is a very probable explanation, particularly in cases where we can rule out drug interactions or patient non-compliance with their five day course of treatment as factors. It is possible that if we lengthen the course of Paxlovid treatment, more of the virus could be eliminated before the patient's immune system alone must fight the remaining virus and the relapses should not occur. Many are advocating for adjusting the Paxlovid dose to eight or even ten days to prevent these relapses. It is too early to know whether this will be 100% effective in preventing relapses in cases, since we do not yet know if this is the cause. Getting data on the incidence of these relapse cases with a longer duration of treatment will be an important next step in determining whether or not dose and duration is an issue here. Paxlovid is currently only approved under an EUA as a five day long treatment, so we will have to rely on the FDA to change their guidelines before this strategy can be widely implemented. Along with concerns regarding the duration of Paxlovid treatment, there is a similar concern about the timing of the treatment as well. Paxlovid is supposed to be given early in a COVID infection, but there is now some speculation that if treatment were delayed by one or two days, the immune system would have had more time to build up its own response, making it more equipped to fight any remaining virus at the end of the Paxlovid treatment. This would be especially important if the treatment were to remain only for a five day course. Again, we won't know if this is playing a role in COVID relapses and to what extent until more data are available on potential benefits and risks of delaying the start of Paxlovid treatment. In the meantime, we need to evaluate the impact of these relapse cases. I think there are two major questions we need to consider when thinking about what these relapses mean. How serious are they and do people become infected again during the COVID relapse? Let's talk first about the severity of illness associated with these relapses. Though it is certainly possible that a COVID relapse could lead to severe illness, hospitalization or death, it is not something we've seen so far or if it has occurred, it has not yet been reported. All the reported COVID relapses have caused mild symptoms, usually those similar to that of a common cold. Keep in mind, Paxlovid that is typically given to those who are at high risk of hospitalization and dying from COVID. So ultimately, even if a COVID relapse does occur, the most important thing is that these individuals are avoiding serious illness. This is not to say that these relapses are not an issue. They most certainly are. But we cannot ignore the fact that as of right now, it's still appears that Paxlovid is working to prevent hospitalization and death. The other important thing to consider regarding the impact of COVID relapses is whether or not an individual is considered infectious during their COVID relapse. There is still no clear data on this, but many individuals who relapse after taking Paxlovid do test positive on rapid antigen lateral flow tests. As we've discussed in multiple previous episodes, these tests are not highly sensitive, meaning that patients most likely have at least a moderate viral load if their testing positive. Unlike PCR, in which an individual can test positive with a very small viral load or none at all for months after an infection. A positive lateral flow test does not necessarily guarantee that an individual is infectious, just as a negative lateral flow test does not guarantee that they are not infectious. But it does give us reason to suspect these patients could be infectious and spreading the virus during their relapse, which makes these rebound COVID cases very concerning from a public health perspective. So what is the bottom line? Well, as I said earlier, there's still a lot that we don't know about these COVID relapses after Paxlovid treatment. It is likely that the duration and timing of the treatment could be playing a role, as well as drug interactions or maybe even some resistance to the medication. We will need more data before we can say which of these factors are contributing to the issue. The good news is that these rebound COVID cases do not appear to be severe, even though they're often occurring in patients at high risk for serious disease. But given the likely possibility that these patients could be infectious, there is still an issue that needs addressing. We need more data to determine the cause of these COVID relapses so we can make the necessary changes to prevent them in the future. In the meantime, patients prescribed Paxlovid should be assured by the fact that the drug is still effective in preventing hospitalizations and deaths. Physicians should not see these relapses as an indicator to stop prescribing Paxlovid altogether, but they should be mindful of potential contraindications that could contribute to the ineffectiveness and interactions that may result in their patients not completing the course of treatment. Keeping that in mind that there are other options available for these patients.

**Chris Dall:** [01:12:07] Mike, what can you tell us about our latest beautiful place submission?

**Michael Osterholm:** [01:12:11] Well, thank you, Chris. This is always one of the wonderful times of the podcast. I love this. I love all the people who have submitted beautiful places to us. This week, we've moved on a bit from the domestic companion animal picture that we've had for the past few weeks. We sure enjoyed those. This week's comes from Idy and she writes, "Our pandemic beautiful place adventure began with my seven year old grandson came to stay for a three week shutdown that our governor ordered at the beginning of the pandemic. His stay lasted three months as we navigated learning online at home so his mother could work. Landon, his uncle Caleb, and I hiked at the Ludington State Park to gain and maintain our sanity. There are so many beautiful places in our park, including the area Landon called his playground the dunes, since he wasn't allowed to play on the play structures in the park due to COVID restrictions. In 2021, he came again during spring break. That visit turned into three weeks as Landon's mother contracted COVID. We continued our hiking together. This week, Landon is here again for spring break and we have had our first hike. I have hiked the park regularly throughout the pandemic. It has been a balm for my soul. I've taken thousands of pictures during the pandemic and posted my hikes on my Facebook page. I have continued hiking with friends who are inspired by my pictures and stories and will continue my hikes for as long as I'm able. It's hard to pick a few pictures because the park is large and diverse and I have hiked every trail in every season, Idy." I'm happy to share with you Idy's beautiful pictures. They're on the website for the podcast. Please go back and take a look. And I can only imagine what it was like to have her grandson with her through this park. What a special, special gift. I hope Landon's mother is doing well after her COVID case and that Idy, you are safe and protected against COVID, too. So thank you very much for this wonderful, beautiful place.

**Chris Dall:** [01:14:13] And just a reminder to our listeners that if you have a beautiful place you want to share with us, a place that has provided solace and comfort for you during the pandemic, and it does not have to be a physical place, please email us at osterholmupdate@umn.edu. Also, as the nation nears 1 million deaths from COVID-19, we'd love for you to tell us something about a special person, a loved one, or a friend or coworker that you lost during the pandemic. We're calling these messages celebrations of life. Again. You can share those with us at osterholmupdate@umn.edu. Mike, what are your take home messages for today?

**Michael Osterholm:** [01:14:47] Well, this is a challenge to kind of hone down the messages to three summary points since there were a number of messages. But let me share with you what I think really are the three take homes. First of all, there is good news for much of the world. As well case numbers are going up, severe cases and deaths are actually going down. And will it be what the future of the pandemic will look like? I don't know. But for now, we're enjoying this and we should. And we have to be prepared for anywhere from 1 to 10 as a possibility in terms of the challenges going ahead. But right now, we've got good news. Number two, we can't know the future of COVID, and we shouldn't use speculation to support future challenges. We should use the best data we have and logic. So as I've said on many occasions, we're somewhere between a one and a ten in terms of how bad it is or how good it is. And we don't know yet. I think the modeling concept going out months and months maybe looks good on paper. It may sound really very sophisticated in the minds of many, but largely it is based on pixie dust. And I just can't say that enough times. The media continues to make major pronouncements about these studies that come out like this. I just wish once they'd go back and actually look at all these previous projections that were put out there and ask, how often were they right? How often did they actually turn out to be what had been purported that would happen, and I think they'd be very surprised. So again, we can't know about the future. I can only hope that things stay like they are now. But as you've heard me say many times, hope is not a strategy. But I also do recognize the inevitability of another variant arising, and I don't know what that's going to do. Finally, vaccines and drug research remain so important. I think it's critical that we not feel like we're over the pandemic and all regards many people do in terms of what they're doing publicly and all the celebrations, all the graduations, etc.. But we still need critical, critical support for vaccine and drug research. We need support for getting new improved vaccines out the door. And in that same context, we need much more research on Long-COVID. I keep coming back to that issue over and over and over again. For all of you that are suffering from Long-Covid, we hear you. We see you at CIDRAP and we have so much more we have to do with long-COVID. So we've got our work cut out for us right now.

**Chris Dall:** [01:17:32] And is there a closing song for the week?

**Michael Osterholm:** [01:17:36] Yes, there is. And it's one that from my favorite group of all times, I think for many people listening to this, they would agree with that. This is a song from The Beatles. They will continue, I think, to define the finest of pop music, at least in my generation surely experienced. This is a song that was the title song for their 1965 film and its soundtrack album. It was released as a single in July 1965, and it was number one for three weeks in the United States and the United Kingdom. It was credited to both Lennon and McCartney, but most will say it was primarily written by John Lennon with some help from Paul McCartney. During an interview with Playboy in 1980, Lennon recounted, "The whole Beatle thing was just beyond comprehensive. I was subconsciously crying out for help." So I'm sure for any of you who have a love of the Beatles, you know what song I'm talking about here it's "Help." I would also point out that John Lennon noted in an interview with Rolling Stone in 1970, he said he felt that "Help" and "Strawberry Fields Forever" were his most honest, genuine Beatle songs and not just songs written to order. Today I share that song. In that sense, this is really a statement to all of us about where we're at and what we need to be doing to get us through this pandemic. "Help" by John Lennon and Paul McCartney. "Help. I need somebody. Help. Not just anybody. Help. You know I need someone. Help. When I was younger, so much younger than today, I never needed anybody's help in any way. But now these days are gone. I'm not so self-assured. Now I find I've changed my mind and opened up the doors. Help me if you can. I'm feeling down. And I do appreciate you being round. Help me get my feet back on the ground. Won't you please, please help me. And now my life has changed in oh so many ways. My independence seems to vanish in the haze. But every now and then, I feel so insecure. I know that I just need you like I've never done before. Help me if you can. I'm feeling down. And I do appreciate you being round. Help me get my feet back on the ground. Won't you please, please help me? When I was younger, so much younger than today, I never needed anyone's help in any way. But now these days are gone. I'm not so self-assured. Now I find I've changed my mind and opened up the doors. Help me if you can. I'm feeling down. And I do appreciate you being round. Help me get my feet back on the ground. Won't you please, please help me? Help me. Help me, ooo." Thank you very much. John Lennon and Paul McCartney. And I think it's fair to say we all very much want help today in living our lives in this world of the pandemic. So thank you to all of you for being with us again today. I know we covered a lot of territory. I hope it was helpful. I wish we had more answers for you. As I started out the podcast also, for all of you with mental health challenges right now, I hope you're able to get the help you need. I know this is a very, very tough time and we think about you a lot. This is not something that will be solved overnight. But we need to do everything we can to help support the mental health of all of our population from young children right up through late years of life. I also want to thank all of you for the letters and cards, emails that we continue to get the provider of such important feedback. You know yes, we like to hear that you like what we're doing, but we also very much welcome ways that we can improve what we're doing. And so from that regard, please know how important these are. I want to thank the podcast team today. Again, this is really a work of a team, not me. I'm just a simple voice here. Thank you so much for being with us. Be kind. Right now boy, it's tough. It's hard. Particularly as we see more cases occur in our families and our friends. But at the same time, I feel positive about the fact that we're making a difference in severe illness. So have a good week. We'll see you next week. Thank you so much for being with us again. Thank you, Chris. And be kind. Be safe. Be kind. Thank you.

**Chris Dall:** [01:22:13] 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.