# Episode 102: Choose Your Own Path

**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. If you're confused right now about where we are in the COVID-19 pandemic, you're not alone. Though cases continue to rise across the country, last week, White House Chief Medical Advisor Dr. Anthony Fauci said the country was in a more controlled phase of the pandemic. At the same time, he declined to attend the White House Correspondents Association Dinner, an indoor event attended by roughly 2,000 unmasked people because of his assessment of the personal risk. President Biden, meanwhile, attended the dinner. This situation seems to encapsulate where we are as a country in year three of the pandemic. With few, if any, mitigation measures in place around the country, we are all in a choose your own path mode, faced with making our own decisions about what level of risk we think is acceptable. For some, that's exactly how it should be. For others, it feels irresponsible. That will be the focus of our discussion here on this May 5th episode of the podcast as we assess the state of the COVID-19 pandemic in the U.S. and around the world. We'll also discuss the potential for a summer surge of COVID cases, answer a listener question about the reports of pediatric hepatitis cases in Europe and the US, 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:** [00:02:00] Thank you, Chris. And welcome back to everyone to the podcast update. For those viewers who are regular members of the podcast family, we appreciate you coming back week after week to share with us the events of the week and what might be happening going forward. And if there's anyone who's new to the podcast this week, we hope that we're able to provide you with the information that you're looking for, the context, the perspective that can be helpful. Let me begin by saying, as I have repeatedly in recent weeks, I'm not sure where this pandemic is going. And while others may have a more certain understanding of that, a certainty which I don't find warranted, I will try to give you a sense, I think, of where there are forks in the road ahead. And as Lewis Carroll once said, if you don't know where you're going, any road will get you there. And I do know where I want to go. I know where we all want to go. We want to get over this pandemic. But the question is, what's this virus going to do? What will we expect to see in the days ahead or might we see? So this week, I think, will be another comment on what might the road going forward look like and what can we do about it. Now this week in terms of dedicating the podcast, I've thought a lot about the time that we're in right now, and as much as we can focus on COVID, we also have to focus on those events that are impacting so many people in this country that have nothing to do with COVID. And yet the overhang of COVID is always there. What I'm referring to is the fact of graduation. You know, this has often been seen as a wonderful celebratory time for many families across the United States and for that matter, around the world. And this should be no different this year. Yet we know that if you look back in the past two years, graduations have been really disrupted in a major way. It's been hard to celebrate bringing people together, the educational accomplishments of all of those who, whether they're in grade school, junior high, high school or colleges, universities, technical schools, how to celebrate those accomplishments. So this week, I do dedicate this podcast to our graduates, not just here in the United States, but across the world. When you think about it, it's actually a pretty common event that happens in so many of our families. This year there will be 3.7 million students in public schools who will graduate from high school, 0.4 million students in private schools. And that includes the 3.2 million teachers in public schools and the half million teachers in private schools who have helped get these kids through. If you add in higher education, there will be over 4 million degrees from colleges and universities and technical schools awarded just in the next few weeks. This includes associate degrees, bachelor degrees, master's degrees and doctoral degrees. And again, many in the faculties of these various institutions have done so much to get these students through. We know how disruptive the pandemic has been on education at all levels. We know how disruptive it's been in the families of those who are supporting children in schools, whether you're parents or guardians or aunts and uncles and grandpa and grandmas. This has been a real challenge and this year I do have concerns that we will see people wanting to go back to that old days of graduation and graduation parties that we saw pre-pandemic. And we'll experience, unfortunately, some major transmission events occurring at those parties, just as we're seeing in all other aspects of life. But I don't want to diminish for a moment the importance of your educational experience and what that means going forward for all of your life. One can never, never miss out on an education investment as a wasted opportunity. And so this podcast is dedicated to you, the graduates. I want to close out, of course, my opening with my usual wonderful, wonderful assessment of light. Yes, I know some of you think it's corny. Today, May 5th, we will have 14 hours, 27 minutes and 2 seconds of sunlight in the Minneapolis, Saint Paul area. We are gaining about 2 minutes, 37 seconds a day right now in sunlight as we move towards that June 21st date. We've gained almost 21 minutes just since last week's podcast. What a wonderful feeling. And oh my, you know, we've gained almost 6 hours since that December 21st winter solstice. So I just want to acknowledge that we are in that best time of the year where it just keeps getting better. I just did a radio interview this past week with Public Radio in New Zealand and wishing them more light that we could send their way with the understanding they would reverse that fine effort come December here in Minneapolis, Saint Paul. So get on with it. The light is here. Enjoy it as much as you can.

**Chris Dall:** [00:07:02] Mike, let's start our international update this week in South Africa, where the BA.4 and BA.5 Omicron sub-variants appear to be driving an increase in COVID-19 cases. Will South Africa provides some clues about what happens next in this pandemic?

**Michael Osterholm:** [00:07:17] Well, as I've said many times, Chris, the more I learn about this virus, the less I know. And anyone I think who is really being intellectually honest would agree with that statement. As some may recall, we touched on South Africa a bit in last week's episode mentioning that cases there had climbed from around 1,200 a day in mid-April to almost 3,300 as of last Tuesday. In other words, the country's case levels almost tripled in the span of just a couple of weeks. Well, they've continued to grow since then, approaching 4,800 as of this past Tuesday. Of course, the big question has been what role does BA.4 and BA.5 play in this uptick? As you know, these are two of the variants from Omicron that have been of real concern. As I mentioned last week, if you look at the timing of when exactly South Africa's cases started climbing, you'll notice that it seemed to coincide with BA.4 and BA.5 becoming the dominant sub-lineages. So at least at face value, we had some early evidence that they can outcompete BA.2 and potentially drive up case numbers. However, the eye test alone doesn't always provide the complete story. In fact, sometimes it can actually be quite deceiving. Fortunately, a few studies have been shared over the past week, although they are only in preprint form. And these studies provide a little more insight on the BA.4 and BA.5 sub-lineages. According to one of the studies, while the two sub-lineages have a number of mutations that distinguish them from one another, these differences are located outside of the spike protein. In other words, the spikes of BA.4 and BA.5 are structured the same. The same study found that both were similarly capable of outcompeting BA.2. And when you look at the spike protein of BA.2, you can see that it differs from BA.4 and BA.5 in a few locations. So these mutations do appear to confer some type of an advantage. Now, before I move on, I think it's important to note that these advantages aren't always universal. In fact, the specific context or setting in which a variant or sub-lineages emerge can play a big role in determining its success or failure. For example, if you look back at Alpha, Beta, Gamma, Delta, Omicron, each one of these, in a way, were kind of quirky. And what I mean by that is if you look, Alpha did real damage in parts of Europe a little over 14 to 16 months ago. Yet a year ago, when it really hit the United States, it was only in Michigan and Minnesota that we saw the real increase in cases. The rest of the country was largely spared. Beta and Gamma, the same thing. We had major concerns about their appearance in South America and Africa and they became non-existent issues in the United States. Why? Then of course we got on with the Delta. I could go into a laundry list of unusual aspects of Delta, the rapid emergence in India, bell shaped curve like case numbers, coming down quickly after hitting a very high peak. The same thing happened in the southern sunbelt states and I'll comment more on that later. But look at what Delta did in Europe? A year ago we saw the first aspects of Delta hitting Europe. By early July, in the U.K., cases were at 1,500 a day and then rapidly climbed to over 52,000 cases a day, all largely associated with Delta. The case numbers came down by the end of July into the high 20,000 cases a day. And then rather than going back to baseline of 1,500, it stayed high. It actually increased and then it persisted in the U.K. right up until Omicron emerged much later. Well, the same thing happened in the United States with the upper Midwest, with the areas of southern Canada, Ontario into Maine, Vermont and New Hampshire. It never once hit New York. It never once hit LA. Why? So we have to be very careful about trying to describe certainty to what these variants and sub-variants will do. The one exception really was Omicron itself. That was a viral blizzard. When that took off last November and December from South Africa to the rest of the world, it did spread like a viral blizzard everywhere. No one was left out, but that was the exception. And we're even seeing that now with these sub-variants. And the reason I bring this up isn't to make things more complicated than they need to be. Instead, I say that because South Africa is in a position with COVID that is somewhat unique or different compared to other countries, largely due to their very high levels of previous infections across the population and relatively low vaccination rates. As a reminder, just 31% of South Africa's population are fully vaccinated and less than 5% have received an additional dose. Meanwhile, some estimates suggest that 90% of the country's population have likely been infected. Whether that's completely accurate or not is anyone's guess. But the overall point is that a sizable chunk of South Africa's population is relying solely on the protection conferred by a previous infection. Why might this matter? Well, it's still a bit early to know for sure, but a recent lab based study that measured neutralization of BA.4 and BA.5 using sera from individuals in South Africa offers some potential insight. According to the study, previous infections with BA.1 or the original Omicron lineage we saw, led to some neutralization of BA.4 and BA.5, but there was a pretty notable reduction overall. However, based on their results, this reduction was much more pronounced among those who were infected with BA.1 and unvaccinated, compared to those who had been vaccinated and had a BA.1 breakthrough infection. Overall, individuals who are vaccinated and had recovered from a breakthrough infection neutralized BA.4 and BA.5 at a level that was fivefold higher than those who are unvaccinated. In other words, people relying on the protection from previous infection with BA.1 alone, those who are unvaccinated might still be at pretty high risk of reinfection with BA.4 or BA.5. Thus, it's possible that South Africa's rise in cases is being driven by reinfections, particularly among those who are unvaccinated. We need more epidemiologic data to know exactly what's going on. However, I'd be very cautious about concluding what is happening in South Africa is a harbinger of things to come for many other countries where the vaccination rates are substantially higher. Of course, at this point we really don't know how large a wave of cases we'll see in South Africa or how long it'll go on. As for now, the trajectory isn't as steep as previous waves, but high test positivity rates suggest that a lot of cases aren't being picked up right now in South Africa. That being said, although it's very early, the rise in cases across South Africa hasn't been accompanied by a similar rise in hospitalizations or deaths. If you look, COVID hospitalizations there have grown a bit climbing from around 2,100 in mid-April to 2,230 as of Monday. A net increase of 130 hospitalizations. And the number of patients in the ICU has gone from 160 to 211. However, they remain at levels far below what the country has experienced during previous surges. The same thing remains true with deaths from this latest wave, or at least so far. If you look, average daily deaths from COVID in South Africa are reportedly at their lowest level since the start of the pandemic. In fact, as of this Tuesday, the average number of daily deaths stood at six. For comparison, the peak average reached during the height of their original Omicron Surge was 233 deaths per day. So the good news is that as of right now, they aren't seeing any signs of BA.4 or BA.5 causing higher rates of severe disease and subsequent deaths. Overall, this could be a situation where these sub lineages have a better ability to sidestep protection against infection. But the defenses against severe disease remain largely intact. If that's the case, then we might expect some other countries, particularly those with lower vaccination rates, to see a growing number of infections spurred by either of these sub-lineages. However, they'd hopefully avoid a subsequent wave of hospitalizations and deaths. Chris, at this point, I think it's just still a bit too early to know the implications of this and what it means moving forward. Basically we have one country as a potential model in South Africa. And while some preliminary data has offered a bit of insight, there's a lot we simply do not know. We'll have to stay tuned until we get some additional data, including better Epi. data that characterizes more clearly what exactly is being affected by BA.4 and BA.5. Taking just the information of South Africa, you can begin to understand the complexity of knowing what this pandemic is doing and where it is going, particularly as we deal with the Omicron sub-lineages.

**Chris Dall:** [00:16:40] Are there any other parts of the world that you're keeping an eye on?

**Michael Osterholm:** [00:16:44] Well, quite honestly, I keep my eye on the entire world, which means that now I have to sleep not just with one eye open, but with toothpicks in my eyelids. And I actually, given what this virus has done and seems to be continuing to do, some days I think I need to be looking at the moon or Mars to really understand what's going on. Having said that, Chris, I do my best to at least try and keep tabs on what's happening worldwide with COVID. And although I'll admit that this approach can be a bit overwhelming at times, I believe that maintaining at least some understanding of the global picture is critically important. Of course, on the other hand, the very definition of a pandemic itself should elicit the global view. However, I'm certainly aware of and actually occasionally fall victim to the tendency to focus primarily on what's happening in our own backyard. In fact, that approach in and of itself can also be overwhelming at times. But ultimately, I think some of the best lessons and early insights has actually come from outside of the United States. Now, there are always those areas of concern or hotspots which we monitor or focus in on. For example, I just got done discussing South Africa, which some might say as an area of concern and what that might mean moving forward. Otherwise, anyone who's listened to this podcast over the past month or two likely knows that I'm concerned about what's happening in China right now. Just briefly, if you look at official reports out of the country, there were recent claims that all locally acquired infections in Shanghai were in quarantine or isolation facilities. However, after two days with zero cases reported outside of the areas, the number climbed to 58 this past Sunday and 73 on Monday. Of course, this is the latest news that city residents want to hear since most have been confined to their homes for at least a month. So Shanghai is clearly not out of the woods. And quite honestly, I continue to have major concerns about the accuracy of the numbers that are being reported by the Chinese public health officials with regard to outbreaks in these cities. In addition, we do know there is an ongoing outbreak in Beijing where schools have been closed, movement has been restricted and mass testing is underway. And dozens of other cities are either in partial or full lockdown throughout China. So whether you're talking about the pandemic trajectory globally, potential impacts on humanitarian levels, or the integrity of supply chains, I think it's wise for all of us to keep an eye on what's happening in China. That being said, I also want to acknowledge our current position with this virus globally. If you look at the latest numbers from the W.H.O., you can see that the weekly cases have decreased for the sixth consecutive week, falling below 4 million, which is our lowest tally since mid-November, so prior to Omicron's arrival. In addition, weekly deaths continue to decline and as of last week, sit around 15,500. Once again, these are the lowest levels since the start of the pandemic. Of course, there's plenty of room for more progress, and I hope that's what we all continue to strive for. Otherwise, there are still plenty of opportunities for this virus to regain ground. And of course, we must never forget that even with these lower numbers being reported, it's likely that they are missing a growing number of cases as testing is being reduced in many countries around the world. So overall, the view is better from a global perspective for now, and I'll come back to that again, the for now piece, and we must temper our enthusiasm for the dropping numbers a bit and realize we don't quite understand to the extent that which underreporting is still a major challenge.

**Chris Dall:** [00:20:32] Now to the US. We're continuing to see a nationwide uptick in COVID-19 cases, with the seven day average of daily cases now up by roughly 50% compared with two weeks ago. But we've yet to see a significant increase in hospitalizations and deaths are still declining. So, Mike, what do you make of this current wave, if that's what we can call it?

**Michael Osterholm:** [00:20:54] Well, you're right, Chris. Cases in the US continue to rise, and that's even in the face of what I would consider to be a significant increase in under-testing, meaning testing not available or home testing where people's results are not being reported to state or local health departments. But here are the numbers. Cases are up 50% over the last two weeks in this country, averaging almost 62,500 per day as of Wednesday. On Tuesday, according to the Johns Hopkins Tracker, the US reported more than 61,700 cases. BA.2.12.1 cases are also on the rise, now making up 37% of cases in the past week. BA.2 made up 62% of the cases last week. Again, that is different than BA.2.12.1. However, BA.2.12.1 is now dominant in CDC's Region two, which includes New York and New Jersey. Why is that important? 47 states have seen an increase in COVID-19 cases in the past two weeks, and 31 of these 47 states have seen more than a 50% increase. Only Oklahoma, Arizona, Colorado and D.C. have seen their cases decrease over the past two weeks. 24 states and the District of Columbia are seeing more than 15 cases per 100,000, compared to 14 states and the District of Columbia last week. Rhode Island and Vermont are seeing the highest daily average of about 50 cases per 100,000. Maine is not far behind at 47 cases per 100,000. Massachusetts 42 per 100,000. New York State 39 per 100,000. The District of Columbia now at 33 per 100,000. And New Jersey at 33 per 100,000. As you can see, this really makes up a large part of the northeast corridor area of the country. This is why when we talked about BA.2.12.1 now being dominant in CDC's Region two, which is the Northeast, make some sense. I think it's really critical, I have been emphasizing for some weeks now that this particular disease we're seeing at this point is different than what we saw in the earlier days of the pandemic, where individuals were much more likely, if infected, to actually experience serious disease, be hospitalized and even die. I have continued to emphasize hospitalizations as a lagging indicator. And interestingly, hospitalizations are not showing us all that much right now. We continue to see a rise in hospitalizations which have increased 18% over the past two weeks in the US. And they are sitting at a daily average of just slightly more than 17,500 daily hospitalizations, or about five per 100,000. 40 states are seeing increases in hospitalizations over the past two weeks, but they've really only been limited increases. Fortunately, only three states Delaware, Maine and New York and the District of Columbia are seeing double digit hospitalizations per 100,000. These hospitalization numbers continue to remain low, as you mentioned in your question, Chris, and we haven't seen a major spike. We'll have to wait and see what is going to happen with these numbers and hope that we will continue to see much less severe illness with these new variants and the likelihood that preexisting immunity plays some role. And of course, when we think about the worst of all outcomes, it's about death. Deaths continue to decline as they have over the past several weeks, but we continue to slowly inch towards the grim milestone of 1 million Americans lives lost throughout this pandemic. Even then, as those being official numbers, there have been several studies suggesting we actually passed a million deaths some time ago, just deaths that were not yet counted as being related to COVID. With 340 daily average deaths as of Wednesday, which is 17% lower than two weeks ago, we are now sitting at just under 995,000 deaths, according to Johns Hopkins. I fully expect this next week when we actually get close to hitting 1 million, more and more people will be talking about that. That will be the big news story. I hope that this put into the context. However, though, the number of deaths have been reduced substantially from the earliest days of the pandemic. New York City announced on Monday that they're increasing their COVID-19 risk level to yellow or medium risk. This is based on a new system that considers cases and hospitalizations per 100,000 over the past seven days, as well as the percentage of hospital beds being utilized by patients with COVID. The new metrics consider 200 new cases per 100,000 a week, or at least ten new COVID hospital admissions per 100,000 as a means to increase the risk level. New York State has seen a 26% increase in cases over the past two weeks, averaging 38 cases per 100,000 and a 36% increase in hospitalizations averaging 11 daily hospitalizations per 100,000. However, New York City, not the whole state, but New York City itself, is seeing an average of 2,500 new cases per day. Monday's announcement will do little to change things in the city. The yellow or medium threat level means that individuals should consider taking preventative measures, but there would not be any significant changes as far as mandates are concerned. The mayor may consider implementing mask mandates in schools, but he has yet to indicate that he intends to do so. So this is a stay tuned issue, and as the pattern that we've been talking about unfolds over the course of the past weeks, we are seeing increasing cases, only marginal increase in hospitalizations and really almost level incidence of deaths among those with COVID. Let me just close by commenting on what is now becoming almost the news of the day in this country, and that is superspreading events associated with big, large public gatherings. I think we're all aware of the fact that the White House Correspondents Dinner was held Saturday. And now we have had at least several COVID cases that have been reported as of yesterday. And it's thought that they may have very well been associated with the dinner itself. One, a notable news reporter. The more than 2,000 attendees required to be boosted and show proof of a negative test within 24 hours of the event. We are not out of the woods on this one yet. It's still early and it's still just three days post event. This week will be very telling about how well the safety measures worked in this case and if there will be a model for events in the future. I think there are going to be more cases here associated with this event. Testing on the day of with a antigen test hardly tells you that you are not infected or infectious. And of course, we've already discussed the issue about breakthrough infections among those who have been vaccinated. It's going to be a challenge going forward as we talk about events like graduation, we talk about concerts. We talk about so many different public gatherings, including transportation and what will happen. I predict that we will continue to see a growing number of superspreading events in these particular settings, and the question will be, what does that mean? Are we all going to go to these masked? I don't think so. Will we accept that this is the normal level of cases we will expect to see? Well, with these with this variant I think that may be possible. If we don't see major increases in hospitalizations, I think people will just say eh, this is part of everyday life, just like we're influenza. We'll wait to see and we'll also wait to see who might yet still be infected, having attended the White House Correspondents Dinner on Saturday.

**Chris Dall:** [00:28:42] Over the weekend, former White House Coronavirus Task Force Coordinator, Dr. Deborah Birx, said in a TV interview that the U.S. should prepare for a potential summer surge, given that we've seen surges the last two summers. So Mike, what did you think of these comments? Can we expect this constantly evolving virus to follow the patterns we've seen over the last two years?

**Michael Osterholm:** [00:29:04] Well, let me be perfectly clear. And hopefully, as I noted in a previous answer, this virus will remain unpredictable for both the foreseeable future and the long term future. And so, I don't know. As an epidemiologist, I study disease patterns and unfortunately, like the weather, I can generally get them right within the season of saying it's going to snow or it's not going to snow. But can I give one five months notice, tell you whether it's going to snow or not on a certain day five months from now? No. I think that the comments that were made by Deborah Birx are based on, at best a faulty understanding of what this pandemic is all about. And I think this has been a challenge with a number of individuals who have gone so far as to project this as what will occur. As you heard me say time and time again, we need to be far more humble with the comments about what this virus is going to do next. All of us, but especially anyone considering themselves an expert, need to be more comfortable saying, I don't know. The only thing that the patterns over the last two years can tell us at this point is that this virus is unpredictable. We have numerous examples of people speculating about when and where cases will rise and fall. In almost every instance of a pattern, we have run into counterexamples. For example, as I noted earlier in today's podcast, in the winter of 2020-2021, we saw the Alpha variant create chaos in the United Kingdom. However, when Alpha did become the dominant strain in the United States, we didn't see widespread severity similar to that seen at all in the U.K. Even within the United States, we see unexplained differences by region. Last spring into summer, Michigan and Minnesota experienced large surgeons in cases, hospitalizations, and even deaths. And yet the rest of the country did not follow suit. Whether you're a public health expert or a supercomputer, you can't predict the future with this virus. You just can't. I do acknowledge that in terms of Dr. Birx's comments, for the past two summers, we have seen a major summer surge in the southern sunbelt states. You cannot attribute that to seasonality. Some say, well, it's a hotter weather and people indoors will then explain to me what happened to the desert southwest. They, too, had hot temperatures. We didn't see the same big peak in cases. What does it mean in terms of Delta, for example, which was the cause of the last surge and the fact that it never impacted New York, never impacted L.A.? As I discussed a moment ago, it did impact the upper Midwest and Southern Canada substantially well into the Northeast. What was that all about? Why? And so I surely don't want to suggest that we couldn't see a peak next summer. But I just remind people over and over again, a broken clock is right twice a day. And just because something has happened twice doesn't mean automatically it will happen a third time. It might. This is where I think the humility really becomes important. So let me just say, what is it that we often get from our academic and even government colleagues? Well, we see them developing complex epidemiologic models, and they even use machine learning methods that rely on historical data and assumptions about each variable's impact in a forecasting equation. Variables we commonly discuss like weather and holidays, influencing social interactions, population vaccination rates, and changes in public policy and mandates surely may all contribute to an effect. The problem is, we don't truly have enough evidence to estimate the impact of each of these variables and their interactions with each other. Moreover, each new variant is scrapping everything we thought we knew, bringing us back to the drawing board. What I do want to emphasize is that while we can't make statements about when or where surges will happen, that doesn't mean we shouldn't be preparing. During times the case counts are lower and our hospitals are a more reasonable capacity, that's not when we sit back and say we beat this thing. Instead, those are the times we should be building our public health infrastructure, ensuring that the next time things start heating up, we're able to respond and not just react. Better testing, better hospitalization care. We can be doing more to improve indoor air quality. How can we develop even better vaccines and therapies that will reduce hospitalizations and deaths? What measures are we taking to support our health care workforce from completely burning out? We can take action without knowing an exact time or place the virus will strike next. And let me just conclude by saying, remember, the focus of all of this discussion today has been on Omicron and the sub-variants of Omicron. What happens when Pi or Sigma shows up, a brand new variant? Will that rewrite all the information that I've just shared with you? Will it have the ability to evade immune protection even more than anything we've seen with the previous variants? Will it be more infectious? I can't imagine it being more benign and actually surviving and outcompeting a more aggressive and infectious virus. So to me, the evolutionary tree says, at least for now, we can expect major new variants to arise. So I put this into the context of just sharing that where we're at right now is by itself confusing. But imagine if a whole new variant shows up. I know no one wants to hear this. No one wants to hear this. They didn't want to hear it a year ago when I talked about what Alpha might mean in the US and the new variants after that. And then along comes Delta and Omicron. I know they don't want to hear it. I don't want to hear it. I'm ready to move on. I'm tired like all of you. But I think we have to, again, keep our eyes wide open. What I'm sharing with you now is that the sub-variants of Omicron are causing more infections, but fewer hospitalizations and deaths. That is good news. That is good news. And there may be some super spreader events tied into all of those. But again, if we can reduce serious illness, hospitalizations and deaths, that's good news. But I can't tell you for the life of me what it might be like if a new variant or a brand new variant emerges that changes that equation. That's going to be important, and that's data I wish that all of us could acknowledge as we are talking heads on TV or in the print media making comments about what will or won't happen.

**Chris Dall:** [00:35:51] In the introduction, I said that we are in a choose your own path phase of this pandemic, which is perfectly fine for some people and pretty disconcerting for others. But unless a totally new variant that can completely evade vaccine protection comes along, a Pi or a Sigma, as you just noted, is this the way it's going to be forward with these Omicron sub-variants? And how are you approaching things like large gatherings and travel in this moment?

**Michael Osterholm:** [00:36:19] Well, I do approach the current situation as a improvement from where we were a year ago. In terms of my risk as an old man who might surely be at increased risk of serious illness or hospitalization, should I get infected. To my knowledge, to this point, I have not been infected. I've had four doses of vaccine and I am very conscious of exposures in the public setting. And even though today I don't worry nearly as much about serious illness, because with my four doses of vaccine, I do believe that I will have substantial protection against serious illness, hospitalizations and deaths. And also I can avail myself to the antivirals that are available. And fortunately for someone like me, I wish that were the case for everyone, and it's not. But at least I have access to those antivirals, but given my age and the country I live in. So from that perspective, I actually feel positive about my experience with this virus. With one major exception. I worry a lot about getting infected and developing long-COVID. I'm watching what Long-COVID is doing. It's hell. There are a number of people who listen to this podcast can attest to what the long COVID is like the brain fog, the fatigue, the heart, the lung problems. All of the things that we're seeing with this and anywhere from 5 to 35, 40% of people who get infected with SARS-CoV-2 are experiencing long term. And it's not just those who are severely ill. It's also includes those who actually had mild illnesses initially who then go on and develop long COVID. So this scares me. It does. I have to acknowledge it. I don't want to get long COVID. And there's nothing right now about my vaccines necessarily, or even antivirals that means I won't get long COVID if I get infected. So while I'm not taking steps today, literally out of the fear of dying, although that surely could happen, I don't think that's the likely outcome of an infection. I do worry about long COVID a lot. As I pointed out a moment ago, to my knowledge, I've not yet been infected and I want to keep it that way. But I'm trying to live life like everybody else. How do I go back into public places? How do I go to locations where lots of people have just taken every aspect of control around COVID and thrown them out the window? You've heard me say time and time again, I was never all that impressed with a lot of the masking mandate issues just because of the fact that people were using inadequate masking protection to begin with which which didn't do much to protect them or protect me from them. And in addition to that, now everybody's back into the crowds, they're back into large gatherings indoors. I mean, it's notable what happened, for example, at the White House Correspondents Dinner that I just talked about and the fact now we appear to be seeing cases that are actually resulting from attending that particular event. And that was, again, remembering people had to be fully vaccinated and had to be test negative the day of. And it was interesting that Trevor Noah, the host of The Daily Show and who is the evening's host for the event, joked about the likelihood that many of attendants would contract COVID. People were expecting that, he said, and I quote, "This is my great honor to be speaking tonight at the nation's most distinguished Superspreading event," Noah said. He went on to say, like, "Do you read any of your own newspapers? I mean, I expect this from Sean Hannity. But the rest of you, what are you doing here? You guys spent the last two years telling everyone the importance of wearing masks and avoiding large indoor gatherings. Then the second segment offers you a free dinner, you all turn into a Joe Rogan, huh?" That is a very fair analysis of where we're at. And I don't know yet how I personally am balancing that idea of I don't worry as much about severe illness, hospitalizations and deaths, and yet I still worry about long COVID. So, Chris, I'm still wearing my N95 respirator in public places. I don't wear it around my family. I've moved on to that point. Do I have objective data for that? Not at all. My family could clearly bring the virus home. They could. It's my way of saying I'll accept this much risk here, but I won't accept it over there. And that over there is with large groups. And I think that that's becoming a real challenge for many of us. Where is the line? Is it a bright line? Is it a blurry line? What does it mean if it's with friends? Well, gosh, your friends can't infect you, right? No, they can. Your family can't infect you. No, they can. But I got to live life. And so I am in that place where I think many of the listeners are what to do. So here's my advice. One, do take Long-COVID seriously. And if you have risk factors for serious illness, make certain you've had your four doses of vaccine and that you have ready access to testing and antiviral therapy if you should become infected. Big, big dos right now. Get those done. Then basically limit to the extent you can these large groups where you're seeing more and more outbreaks. I continue to hear about superspreading events all the time, which tell me that there's a lot of unrecognized transmission going on in our communities. And right now I will continue to wear my N95 respirator in large gatherings and not in smaller gatherings. And I don't have one lick of good data to say that's okay. It's the way I've come to rationalize me living with this virus, and I'm acknowledging that up front. So if anybody wants to write in and criticize me and say, well, you're inconsistent, you're right. But that's where I've come to in my life. And I hope we all can have an honest conversation about that. Do I expect that I might get infected someday? I do. I hope not. But I do. Will I intentionally just throw caution to the wind and go out there and large public settings and just say, well, it doesn't matter, it doesn't count? No, I won't. I don't have any magic answers. I'm struggling like everybody else. I don't want to get long COVID. I don't want to get COVID, period. I don't want to get long COVID. And I understand where all of us are at right now and we're in a transition time. The one thing that will change that is if we see a new variant, that fundamentally changes the risk of serious illness, hospitalizations and deaths. And nobody wants to think about that option. Meaning we'll have to go back to where we were a year ago. But that's where I'm at right now.

**Chris Dall:** [00:43:21] That brings us to this week's Non-COVID query, which is from Carrie, who has a question about the clusters of pediatric hepatitis cases being reported in Europe and the US. She wrote, "I'm reading and hearing reports of pediatric hepatitis cases, some severe, and investigations into potential causes. Some initial research points to adenovirus as a potential common link between many cases. Some researchers question whether or not the methods of investigation are considering all likely correlations or potential causes. What are your thoughts as to how researchers might be able to proceed as effectively as possible? What is known to date about the novel coronavirus' effects on liver health and what may be reasonable questions to consider, if any, regarding the novel coronavirus and pediatric hepatitis?"

**Michael Osterholm:** [00:44:07] Well, let me start out on a personal note. As a father and a grandfather. I understand the pain of having a child with serious illness. I will never forget those days that I sat in that intensive care bed next to my 16 year-old son at that time who was experiencing La Crosse encephalitis. Nothing prepared me as a professional for what it felt like personally to watch your young child desperately ill. And so my heart goes out to these parents, these family members who are experiencing this situation right now with their kids. It's truly, truly painful to know what's happening. This unexpected rise in pediatric hepatitis cases is certainly a mystery, something that those of us in infectious disease epidemiology basically trained for to understand and try to respond to our entire careers. It's a sad situation. About 200 children in at least 16 countries and ten US states have been affected so far, with about 10% of these children requiring liver transplants. And fortunately, only one child has died so far. And I say only even that's painful. One, but I expect that there surely could be more in the future. Hepatitis, which is an inflammation of the liver, can have a variety of causes. There are some viruses that are commonly known to trigger hepatitis, hepatitis A, B, C, D and E and certain medications, heavy drinking, exposure to toxic substances can also trigger the condition. The children impacted by this mysterious outbreak do not have any of the five viruses that commonly trigger hepatitis, nor do they have any known medications or toxic substance exposures that could explain their illnesses. These children also do not have any known co-morbidities or other health conditions that might put them at increased risk of developing hepatitis, making this situation even more unusual. And though 200 cases may not seem like a lot, unexplained hepatitis in otherwise healthy children is extremely rare. And given the seriousness of this condition, it's very concerning. In fact, some pediatric liver units in the U.K., where many of these cases have occurred, have seen more unexplained pediatric hepatitis cases so far in 2022, than they would expect to see in an entire year. As you mentioned in your question, Chris, this is mostly a non-COVID query, and that is because we do not have any reason to believe that COVID is the primary or even a contributing cause to this situation. We know that this is not a reaction to COVID vaccines for a number of reasons, but the main one being the most of the children being affected have not received any doses of vaccine since they are too young to qualify. For example, in the U.K., none of the 74 children involved in the outbreak have been vaccinated. We can also rule out the impact of in utero effects from maternal infection or vaccination, since many of the children impacted are older than age two, meaning that their mother's pregnancy has occurred before the COVID-19 pandemic was even here. The larger concern is whether current or prior COVID infections could be involved. 20 out of the 169 patients identified by the World Health Organization were infected with COVID at the time of their hepatitis. However, given the levels of transmission of the virus we're seeing right now, we would expect that some of the children would be infected. This is a point we've talked about many times, that life happens. And when you have such a very prevalent disease like COVID, where 50 or 60% of the population may be infected, at some point you're going to see a lot of coincidental health issues or activities take place at the same time. Most of the children have not had known previous COVID infection, however. Though it is possible that they may have been infected and were not just tested either due to being asymptomatic, not having access to sensitive testing or other barriers. The fact that we are over two years into this pandemic and only started to see this rise in hepatitis in late 2021, means that this is not likely the explanation. The timing of these cases has led some to speculate that this could be an Omicron specific consequence of COVID infection. But there is not a lot of data to support this theory other than the timing of these cases. More data will need to be collected before we can entirely rule out COVID infection or other previous COVID infections as a contributing culprit. But as of right now, it's not even close to a likely explanation for these cases. So of course, the question then becomes if this is not likely caused by COVID, then what is causing it? Well, the short answer is that we still don't know, but there are a few non-COVID theories that are being evaluated. As Carrie noted in her question, one of these theories is based on a link between these hepatitis cases and an adenovirus infection, specifically an adenovirus called adenovirus 41. Adenovirus is very common and there are several types which typically cause respiratory common cold like symptoms or gastrointestinal symptoms. Most children will have had at least one adenovirus infection before their 10th birthday. Adenovirus have not been known to cause hepatitis in otherwise healthy children. At least 74 of the 169 cases reported to the World Health Organization were confirmed to have tested positive for adenovirus infection, and at least 18 of them tested positive for adenovirus type 41. This does not necessarily mean that we can jump to the conclusion that these adenovirus infections alone must be the cause of these hepatitis cases. And there are a few reasons for that. Notably, remember, this is not widespread in anyone given area, so we're not seeing hundreds and hundreds of cases in a region of a country. And however, the spread is worldwide, we're seeing cases in many, many countries, which then speaks to the fact that this likely is some kind of an infectious disease that actually also has some other factor involved with it. As I pointed out, adenovirus infections are very common in children, just as we expected that some of the children would have had COVID infection during their hepatitis case, we would also expect that some would have an adenovirus infection. That said, the incidence is higher than we would have expected. Since only about 11% of healthy, asymptomatic children at this particular age in life are positive for adenovirus, and at least 43% of the children with hepatitis have tested positive. The second reason that we cannot view adenovirus infection as a simple explanation is that I said earlier, adenoviruses including adenovirus type 41, which was the strain found in many of these cases, typically cause mild respiratory and gastrointestinal symptoms. In very rare cases, adenoviruses have caused hepatitis, but not in healthy children without significant co-morbidities or underlying health problems. There are numerous other theories for what is causing this phenomenon. It's possible that an adenovirus infection, in addition to another factor, could be responsible for these hepatitis cases such as a co-infection with another infectious agent, or even exposure to a toxin, a drug, or some other environmental exposure. Children may be experiencing increased susceptibility to severe adenovirus infection due to a lack of adenovirus exposure from reduced social interactions during the pandemic. This explanation is fairly unlikely, considering it would still not explain why these children are experiencing hepatitis rather than just more severe versions of the symptoms typically associated with adenovirus infections. It is possible that this adenovirus linked hepatitis could be the result of a novel strain of adenovirus that does cause hepatitis. But if that were the case, we would expect to see cases be epidemiologically linked, which so far has not been the case. Of course, it's also possible there is another cause entirely separate from both COVID and adenoviruses. It's possible that a new novel pathogen could be behind this. And as I said before, it's also possible we're seeing an interaction of multiple factors at play here, including unique genetic features of these individual patients. It is too soon to rule out anything, aside from conspiracy theories surrounding the potential role of COVID vaccines. We hope to learn more about these cases as more studies are done to identify common exposures or factors between these cases. As I stated before, this is a concerning issue and one I wish we had better answers for, but we can't be overconfident in stating cause and effect, especially when the stakes are so high. This is yet another example of why saying I don't know is the most responsible statement in these scenarios where we lack data. We follow that up with continued research and sharing more information as it comes forward, and we will share that information with you as it becomes available to us. And so, Carrie, thank you very much for your very thoughtful question. I hope this gives you some insight as to what the current state of affairs are with these hepatitis cases. And as I pointed out, we will keep you informed over time as we learn more about them.

**Chris Dall:** [00:53:31] Mike, what can you tell us about our latest beautiful place submission?

**Michael Osterholm:** [00:53:37] Well, this is one that is all about fair play, okay. We clearly, clearly have touched a very wonderful nerve in people around beautiful places when we several weeks ago first talked about the companion animals. And it's almost been a race and a kind of an adventure here as to who has the best companion animals and the beautiful places that go with them. And I was reminded this past week that there are many, many people in this country that have wonderfully, wonderfully loving companion animals that are not dogs. And so I know we've had a number of animal beautiful places. Please audience, if you're not an animal lover, think about that. But if you are not an animal lover, just know that we will move on eventually here. But for now, we are sharing the love of animal lovers. And this week's beautiful place comes from Vivian. And she wanted to talk about the feline beautiful place in contrast to our canine, beautiful places of the past. So, Vivian, this is for you and for all the feline lovers out there, your beautiful place, she wrote "Dear Dr. Osterholm and CIDRAP team, I think of the Weekly Osterholm update as the eye in the pandemic storm. Each Thursday I find solid footing and calm in the midst of what can feel like a storm of worry and questionable information. I also appreciate the humanity that you bring to the science from the reminders of the lives behind the numbers to the personal life experiences that you share with us. On March 10th, 2020, our family canceled our spring break trip to visit college campuses and to take a vacation during my son's junior year of high school. As a consolation of sorts, we reached out to our local animal shelter to see if they had any mom cats and kittens that needed fostering. Our son has fostered mom cats and kittens for years and he has dutifully taken care of them and watched with joy and pride as they were placed with forever homes. Our local shelter had a mom cat with four day old kittens born on March 2nd, 2020. We immediately went to pick them up. For the next eight weeks as my son finished the remainder of his junior year online and my husband and I worked from home, these kittens brought our family joy during the lockdown, giving us something to focus, love and attention on as the pandemic storm swirled around us. When it came time to place the kittens in adoptive homes, we had grown so attached to that litter that we kept one kitten Butterscotch, even though we already had two cats and a dog. Butterscotch has come to symbolize the passage of time during the pandemic. He was born on March 2nd, 2020, is now a strapping two year old furball. One objective of fostering parenting kittens is to socialize them so they can hopefully seamlessly adapt to a new adoptive home. My son exposes them to new experiences and people while he foster parents them, but unique to this litter Butterscotch also reminds us of the deprivations of the pandemic. For the first 18 months of his life, he only knew our family and our home. Aside from vet visits mostly conducted in our garage, no one came into our home and everything stayed quiet and the same in our home as we isolated and tried to follow the science to protect ourselves and others. Of all of the pets and foster cats and kittens that we've had, Butterscotch remains extremely nervous with anyone new or new experiences. We think this is because the beginning of his life was so limited and consistent day in and day out. His days were filled with love, but he still grew up in a bit of artificial suspended pandemic animation. He reminds me that we all have been affected by the pandemic in ways we are still learning about. I'm attaching a photo of Butterscotch on the day we got him when he was four days old, as well as a photo with his litter mates as they learn to navigate stairs. There's an adolescent photo as well as a current photo. Our family is grateful for all the foster kittens we have had during the pandemic and encourage others to seek out foster parenting opportunities with local rescue organizations, if you have an interest and a safe home to provide. It can be a truly rewarding experience. Again, thank you for providing guidance and educated humility and humanity over the last 101 episodes of the Osterholm Update. Vivian." Well, I must tell you, thank you, Vivian. It was a wonderful experience seeing those pictures. I would urge all of you to go take a look at them whether you are a cat lover or not. Butterscotch is a personality, there's no question about that. And I do so much appreciate and respect the beautiful place that you have provided for Butterscotch and in turn, the beautiful place that you have experienced because Butterscotch was there. Thank you very, very much. Now, if anyone wants to send in any more beautiful places about kangaroos or boa constrictors or whatever. We're open to a reading and to considering them, so we look forward to hearing from you.

**Chris Dall:** [00:58:48] Mike, what are your take home messages for today?

**Michael Osterholm:** [00:58:52] Well, at the risk of sounding very much like a broken record over recent weeks, I just have to come back to number one, number one, number one. Welcome to uncertainty. You have to choose your own path right now in this uncertainty. Do I expand my social involvement with the world? How do I do it? Do I have concerns about what happens if I get infected not only from an illness standpoint in terms of hospitalizations and serious illness, but from long COVID. And we really are in an uncertain time. I felt totally inadequate today addressing that question you asked, Chris, about what I'm doing. I don't know for certain that I'm doing the best or the right thing. I'm trying to understand what I know, what I don't know how to internalize that and move it out of my life. How do I live with my loved ones? How do I deal with my colleagues at work? That's a real challenge. So uncertainty and knowing which path to take. I think the second point is clearly the current variant world is one that we are trying to understand. But let's not forget there could be another shoe to drop any time soon. Meaning that here we are, six months out from Omicron's emergence. Will we see Pi or Sigma or another one show up that will be very different from Omicron as it now is occurring in our communities? This is a huge issue. When I hear people say the pandemic is over or that we're in this lull in cases that's true we're in the lull in cases, but none of us have an idea what might happen next. Maybe nothing. Wouldn't that be something? But maybe something really, really difficult is ahead. We don't know. And finally, I just come back to the fact that I surely appreciate people providing insight and trying to help the world see what the future might look like. But I just have to keep coming back and saying, beware of those with all the answers or these telescopic crystal balls, because I don't think that they are at all warranted based on what we know or don't know about this virus. So I keep getting asked these questions. Somebody will make a statement, the pandemic is over or the pandemic is going to happen this way or that way. And I tell them, well, on a scale of 1 to 10, that is of somewhere between a one and a ten. You know, that's what we have to understand. What we do know is from microbial evolution and what we've seen with this virus, it is going to change, is going to continue to change. And I don't know what else is going to bring us. So beware of those with all the answers. I think these really hit at the heart of my take home for today.

**Chris Dall:** [01:01:45] And do you have a closing song for us today?

**Michael Osterholm:** [01:01:49] I do. Thank you. Trying to find lyrics that fit the moment can be very difficult. Anyone in the podcast team can tell you because we discuss these at some length. And this one today that we've chosen here is really about, I think, where we're at right now in the pandemic and the encouragement we have to have to move forward. The lyrics today that I picked are from a song by Fleetwood Mac, written by keyboard player Christine McVie, sung by guitarist Lindsey Buckingham and McVie. It was on their 1977 Rumors album, which this particular hit reached number three in the Billboard Hot 100 in October of 1977. We used this song before an episode 53, just a little more than a year ago, April 29th of 2021. That particular episode, by the way, was "Two Doses of Vaccine and One Dose of Humility," and it was dedicated to those who are immunosuppressed seeking answers on the protection from vaccines. So today we've chosen the lyrics for "Don't Stop" by Christine McVie. "If you wake up and don't want to smile. If it takes just a little while. Open your eyes and look at the day. You'll see things in a different way. Don't stop thinking about tomorrow. Don't stop. It will soon be here. It'll be better than before. Yesterday's gone. Yesterday's gone. Why not think about times to come? It's not about the things that you've done. If your life was bad to you, just think what tomorrow will do. Don't stop thinking about tomorrow. Don't stop. It will soon be here. It'll be better than before. Yesterday's gone. Yesterday's gone. All I want is to see you smile. If it takes just a little while. I know you don't believe that is true. I never meant any harm to you. Don't stop thinking about tomorrow. Don't stop. It will soon be here. It'll be better than before. Yesterday's gone. Yesterdays gone. Don't stop thinking about tomorrow. Don't stop. It will soon be here. It'll be better than before. Yesterdays gone. Yesterdays gone. Don't look back. Oh, don't look back. Don't look back." Christine McVie Well, thank you, everyone, for joining us for another edition of the podcast. I hope that the information we provided has been helpful. At least if nothing else, you get an unvarnished perspective of what we're seeing here from where we sit at CIDRAP. Again, I want to thank all of you for your support for the many, many letters, many emails we get. Thank you so much. We learn so much from you. I also want to acknowledge for all of you who are grieving this week, who have lost loved ones, who want to have someone at your child or your grandchild's graduation, but they can't be there because COVID took them away from us. We must never forget that. There will be grandpas and grandmas, moms and dads, brothers and sisters, aunts and uncles who won't be at graduations this year because of COVID. That's sad. That's so sad. So thank you so much for being with us. Be safe. Like you, I'm sure you're going to be struggling as to what to do and how to do it moving forward. Nobody has a perfect answer. We're all going to have to keep exploring that trail and we look forward to sharing that experience with you more next week. So thank you. Be kind. Be kind right now. Be safe. Be kind. Thank you.

**Chris Dall:** [01:05:34] 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.