# Episode 117: A Positive Note

**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. We're now well into our third autumn of the pandemic, and while we still have a few months to see whether colder weather, holiday gatherings, and new SARS-CoV-2 variants will bring a significant wave of COVID-19 cases, the early returns are hopeful. A surge that appeared to be building across Europe a month ago now appears to have tapered off, and U.S. COVID cases and hospitalizations are holding steady. At the same time, influenza and respiratory syncytial virus or RSV cases in the U.S. are spiking and emergency departments are filling up across the country. And a surge in COVID cases, if it does come, will put even more strain in our hospitals. On this November 10th episode of the podcast, we're going to discuss some of the positive signs that we're seeing in the current trajectory of the COVID-19 pandemic and how a surge in other respiratory viruses could complicate matters. We'll also discuss the variant situation, look at a recent study on Paxlovid and long COVID, examine the latest efficacy data on the COVID-19 booster shots, and answer COVID query about how to protect yourself and loved ones at holiday gatherings. But before we get started, as always, we'll begin with Dr. Osterholm's opening comments and dedication.

**Michael Osterholm:** [00:01:57] Thanks, Chris, and welcome back to all of you, a part of the podcast family, and welcome to those who may be coming to us for the first time. As we always start out the podcast, we want to make certain that, you know, that we hear you, that we listen to you, and that we hopefully are providing you with the kind of information that you find helpful as we all try to get through this pandemic. Well, if I could, Chris, I just want to start out by taking a step back and reflect a little bit on this pandemic. You know, right now we're closing in on the day that will mark our third year with this virus. Three exhausting, challenging, and unfortunately, often painful years. And of course, that also means we've been doing this podcast for nearly just as long. In fact, it's been about two years and eight months since we shared that very first episode titled "How We Got Here" on March 24th, 2020. I just want to say that the team and myself have always done our very best to try to provide listeners to this podcast with straight talk and to call balls and strikes as I see them. So that being the case, I know that there are times where information I've shared hasn't necessarily been cheery or lighthearted. Some of you found it very difficult. Still, whether you believe me or not, or the podcast team, we are always looking for ways or opportunities to share uplifting items. Now, obviously with the topics related to COVID, that can sometimes be quite difficult, but that's where you listeners of this podcast, the podcast family, have stepped in and proved time and time again what a wonderful gift you are to us. All the encouragement, words of support, suggestions, questions, acts of kindness, beautiful places, and so many other things you share with us are simply remarkable. We even welcome your criticism. And while we do our best to share some of your messages with everyone tuning in, I wish we had much more time to share even more. Regardless, just know that we read all of your incoming messages and never take for granted how lucky we are to have you as part of this podcast family. Remember, we're going to get through this. In fact, we are getting through this. And just for us here at CIDRAP, we owe a lot of that to you. So thank you. Now, having said that, where are we today? Well, I think you're going to hear a somewhat different tone to this podcast, because I think that the facts merit that. And this will be, I believe, welcome news. I also want to add that we don't live in isolation with COVID as the only thing happening in the world. And I know this week has been challenging for those of us living here in the United States. At the time of this recording, however, I must say that I think our country has met its moment and done it with greatness, not with the fear that so many of us had might be the outcome. And so we deal with this podcast episode, we are not unaware of what's happening out there. But I hope the tone of the podcast today will give us all a sense that today is the first day of the rest of our lives, and hopefully that will allow us to understand what our opportunities are given what we've just gone through. Now, let me just point out that despite the fact that there are some in the podcast family that would like to have me stick straight with the science, just cut to the chase. You know, if you've been listening at all, you know, that's not me. I can't do that. I'm sorry. First of all, I want to dedicate this podcast and I'm dedicating it to all of us who have not given up, to all of us who still are taking the kinds of steps that we need to protect ourselves, but at the same time allowing ourselves to become part of, in a sense, a type of post-pandemic life. And so as we go through the podcast today, I think you'll get a sense of what I'm talking about. We are not just ignoring this virus. When you have 325 deaths a day, over 2,300 a week, you can't ignore it. But we are learning to live with it. And today we'll talk about that. So I dedicate this to all of us who are learning to live with this virus in a way that's responsible, that is safer than not, and one where we do recognize that pain and suffering still continues. I wouldn't do justice to this opening if I didn't, of course, come back to that one point of happiness in so many of our lives, the concept of the light. And I'm happy to report today in Auckland, New Zealand, one of my favorite cities, that they will have 13 hours and 57 minutes and 23 seconds of sunlight, 6:06 sunrise 8:03 sunset. They're gaining almost 2 minutes of light a day. Now that's up by 23 minutes from our last podcast just two weeks ago. And so I know that you're sharing that light with us as we in the Northern Hemisphere are experiencing darker and darker days. Thank you for that. And I also want to do a shout out for my friends and colleagues at the Occidental Belgium Beer Huis on Vulcan Lane in Auckland, and please share some of that light with us as we proceed into the darkest days of the Northern Hemisphere at this time. So welcome back, everyone. We look forward to talking to you for those who are with us for the first time. And thank you for joining us.

**Chris Dall:** [00:07:19] Mike, let's start with the international situation. As I mentioned in the introduction, things are looking a little brighter in Europe. Now, does that suggest that the variants that we've been discussing in recent episodes may not be the game changers that some have feared they could be?

**Michael Osterholm:** [00:07:36] Well, first of all, Chris, as you know, one of the most important priorities for us in doing these podcasts is to be current, comprehensive and to the point of authoritative as we can be. What are the data? What are the facts? And so keeping that in mind and based on my opening comments, I think it's only fitting to start this episode with some reassuring news of our own regarding COVID from an international perspective. If you're a long time listener, you'll know that's not exactly the norm. In fact, if you've listened to some of our more recent episodes in particular where we've discussed the volatility of the overall global situation, given the context of these emerging Omicron subvariants, this may even come as somewhat of a surprise. Well, suffice to say we've been watching very closely and waiting to see what the real world impact of these variants like the BQ and XBB could have. Up to this point, we've documented their ability to better evade some of the immune protection that existed based on experiments conducted in various labs. At the same time, we've watched them outcompete BA.5 and increase in prevalence throughout the numerous countries and regions of the world. Honestly, it's a story not unlike what we've seen in the past. And more often than not, this progression eventually leads to a resurgence in activity. So that's been our concern for places seeing variants like BQ.1.1 or XBB take off in frequency. But on top of that, there have been a number of countries, particularly in Europe, where this displacement has been playing out at a time when activity already happened to be quite elevated. So for these places there was even more concern since they'd basically be dealing with a surge on top of a surge. Well, after looking at the latest data and estimates made available from some of these countries, I'm becoming more and more optimistic that a transition from BA.5 to BQ.1.1 won't necessarily be synonymous with a wave of activity. One of the places that helped alleviate some of that anxiety up to this point has been France. Again, from the standpoint of cases which we already know are major undercounts, we watched France go from reporting around 1,600 cases a day in early September to almost 57,000 cases a day by mid-October. Again, 16,000 cases a day in September, 57,000 cases a day by mid-October. Around that same time, the number of patients hospitalized with COVID in the country climbed from less than 13,000 to more than 20,000. And COVID patients in the ICU rose from 700 to 1,100, all in a matter of just a few weeks time. Meanwhile, as I mentioned before, the sequencing data coming out of France at this time made it quite clear that the surge wasn't the result of the new variant. BA.5 still accounted for the vast majority of cases. However, you could also see that the BQ variants, in other words, BQ.1, BQ.1.1 biting into more and more of the overall share. So the realization that they would overtake BA.5 as a dominant variant in France during the weeks ahead brought with it the possibility of another wave, and particularly the potential for severe illness. Well, as it turns out, BQ particularly BQ.1.1 did overtake BA.5 in France. In fact, according to some estimates, that might have happened around the same time that our last episode was released. However, what's been reassuring up to this point is that the activity report out of France has largely continued to decline. Again, decline. If you look at the time of our last episode, which was released on October 27th, they were reported an average of 38,000 cases a day. So not quite as high as the 57,000 cases a day they were at in the previous week, but still an elevated baseline for a potential BQ driven surge. But fortunately, the surge has yet to happen in France. Instead, cases have dropped below 21,000 and hospitalizations have started to decline. Remember again, back in mid October, France was seeing 57,000 cases a day. Now we're dropping below 21,000. So that's what's been good to see. Now, I do want to mention that it's still somewhat early to draw firm conclusions about BQ's impact in France. In fact, there's even been some potential signs of a slight rise in cases there as of this podcast recording, going from 21,000 to 22,500 over the past few days, which could be real or could just be a blip in the data. So we'll have to see. Either way, I'm still pleased that we didn't see a situation where BQ built off much higher base lines in France, which is what we were worried about. And I'm hopeful that the other countries in Europe looking to recover from recent surges of their own, like Germany and Greece, will also manage to get by without BQ changing the situation. Otherwise, right now in Germany it's growing in frequency and outcompeting BA.5. But there are signs that it's still losing some of its momentum with regard to cases. What that means ideally is that BQ will become dominant but won't transmit at levels high enough to actually drive up activity and surely not cause more increased numbers of severe cases. At the end of the day Chris, we'll just have to wait and see what happens. Now, some might argue that it took far too long for it to sink in, but I've learned firsthand just how difficult it is to anticipate what this virus will do next. And make no mistake, it is still changing. In fact, we're seeing more and more descendants emerge from the latest batch of variants. At the same time, I think it's critical that we evaluate and understand what our toolkit for effective treatments look like moving forward, since there's data indicating that certain monoclonal antibodies like Evusheld aren't all that effective anymore against BQ and XBB variants. But at least for the time being, I view each passing day without a variant driven surge as a real positive and something that we have to celebrate.

**Chris Dall:** [00:13:54] So before we get to what this all means for the United States, let's talk briefly about China, where the situation appears to be getting worse despite the Chinese government's zero COVID strategy.

**Michael Osterholm:** [00:14:06] Well, Chris, it's almost become routine to talk about China at some point during these podcast episodes. And there are probably some listeners who are thinking to themselves, oh, no, here he goes again. But the truth of the matter is what happens in China can and it will have implications that stretch far beyond its boundaries. It's a reality that's tied directly to the way our entire global economy operates. Many of the things that we use on a daily basis and sometimes even depend upon are sourced from China. One example I shared several times is the issue around prescription drug supplies, particularly those that are critical and life saving. For many of them, China is the world's primary and in some cases only supplier. And so, as I've mentioned in the past, as China goes, so could go the world. Just ask the folks at Apple and the availability of their iPhones for Christmas. That being said, if you're only talking exclusively about COVID activity, what's happening in China doesn't seem at all that significant. In fact, when you measure their official numbers against the entire backdrop of global activity, where we're reporting nearly 341,000 cases and 1,700 deaths on a daily basis, China is basically a drop in the bucket. But we all know it's not that simple. And that's because of their continued commitment to the whole zero COVID strategy. Remember, I've talked about this a number of times. Last February, I wrote an op ed in The New York Times saying that the zero COVID policy of China was fraught with all kinds of challenges and it would never work. Well, as we all know, it's not that simple as to say that China's COVID policy doesn't affect us, and that's because of their continued commitment to the whole zero COVID strategy. Even though it's only been a few weeks since China's congressional meetings took place, which included several instances where officials lauded the zero COVID approach, the country has been seeing more and more cases crop up. For example, at the time of our last episode two weeks ago, the overall number of locally transmitted infections reported out of China stood at just over 1,000. Again, from the standpoint of absolute numbers, that's not a lot, especially for a country that's home to 1.4 billion residents. But when you're talking about a place that might implement a lockdown in response to even a single detection, even a 1,000 could seem plenty high. However, things have only continued to grow since that time 1,000 eventually turned into 2,000. By last Wednesday, the total grew to 3,000. On Saturday, it climbed to 4,400, Sunday 5,500. And finally, as the time that this podcast is being recorded, the latest daily total for total cases in China sits at more than 7,500, the highest it's been since Shanghai's outbreak almost six months ago. Also with this latest total, it's worth noting that each of the country's 31 provincial level regions are now reporting cases and many reporting lockdowns. Otherwise, more than a third of the detections came out of the Guangdong Province, which happens to be one of the world's largest manufacturing hubs. In fact, a lot of the activity being documented there is in the province's capital city, a place that some consider the factory floor of the world, resulting in lockdowns across numerous districts. Another notable outbreak has been unfolding in China's Henan province. Again, most of the cases there have been reported in the province's capital of Zhengzhou, otherwise known as iPhone City. As I just mentioned, it is home to the world's largest assembly plant of Apple iPhones. This facility, which has a total of 200,000 employees, has been dealing with an outbreak since mid-October. Despite the plant's implementation of a closed loop system, the situation actually led to Apple releasing a statement this past weekend saying that production of the new iPhones 14 has been severely impacted. And these are just a couple of the examples. There are many others. Even in Beijing, a total of 64 cases in a single day was reported up from recent totals that were in the single digits. So once again, Chris, China is being put to the test and with no clear indication that they'll be changing their approach any time soon. I'm not sure what the days ahead might bring, but as I said in February, and I'll repeat here again in November, zero COVID policy will not work against the Omicron version of this virus. And until they understand that in China, I believe that their entire economy will be ever increasing at risk for failure.

**Chris Dall:** [00:18:53] Now to the US. While we know official case numbers are relatively meaningless at this point, hospitalizations have remained steady and deaths appear to be declining. At the same time, we're seeing the BQ.1 and BQ.1.1 subvariants accounting for more COVID-19 cases. So, Mike, is it too soon to make any predictions about how these next few months will play out?

**Michael Osterholm:** [00:19:13] Well, like you said, Chris, the national picture has remained pretty steady. Hospitalizations are up 2% over the past two weeks. And while it is nothing to celebrate, we are now seeing an average of 325 deaths per day, down 15% from two weeks ago and down from the numbers we were seeing during the high plains plateau of around 450 deaths a day. I want to be really clear, however, when we think about 325 deaths a day, we're still talking about over 2,300 deaths a week. That is a remarkable number. And as I have said so many times, I really don't like talking about these numbers as numbers because it's in a sense, does not pay the kind of respect to what all of these deaths meant to the individuals, to the families, to the friends and colleagues. But today, we have to at least acknowledge 325 deaths per day is a lot better than the numbers we've previously seen. As I've said, episode after episode, COVID just hasn't gone away because the public has moved on. It isn't going anywhere in the near future. We're finding the three roads to navigate our way through this virus. Today, we will talk more about the issues of vaccines and drugs and what they can do to lessen this number. I do believe if everything were to stay stable with the virus, we can significantly lower the incidence of deaths even further by just targeting our vaccines and our drugs to those who are particularly older over age 50. Clearly, this virus isn't going anywhere anytime soon and it has proven itself unpredictable yet again, with several new variants making a name for themselves. As I just noted in the international section, the BA.5, which has been dominant for months, is finding itself being outperformed by several new variants. The BQ variants are growing in prevalence fastest around the world, but they are not yet dominant here. BA.5 now makes up just under 40% of new US cases, while BQ.1.1 is at 18.8%. BQ.1 itself is at 16.5%, totaling 35% of the new cases combined. In the last episode, we discussed the concerning trend in New York City, where we are seeing steady case rates but increasing hospitalizations and higher prevalence of the new BQ.1, BQ 1.1 variants. Since that episode, cases have increased nearly 25% and hospitalizations have increased 11%. Fortunately, we have not seen this become the case across the country, despite the rise in BQ.1.1 and BQ.1. So we will continue to follow this closely, particularly in New York. But right now for the country, I'm hopeful that these variants will not drive new surges. As far as making predictions about the next few months, I don't know. And as you've heard me say time and time again, despite the fact I have colleagues out there saying with some specificity what will happen. All I can tell you is that anybody that does say that, be careful, because they probably also have a bridge to sell you. The variant picture alone illustrates the unpredictability of this virus, and I just can't tell you what comes next. Right now, the news looks better than it has in some time. I am hopeful we can keep our COVID hospitalizations low to not overwhelm our already overwhelmed hospitals. And I'm also really excited about the bivalent booster data, which we'll talk about in a moment. Finally, we're going to talk about the potential role that that Paxlovid may have in reducing severe illness, hospitalizations and deaths. All good news. But overall, Chris, while it's not time to celebrate victory or let our guards down, I think it might be a moment to take a quick breath and prepare for the unknown and do it with a smile.

**Chris Dall:** [00:23:02] So, Mike, let's talk about the other respiratory viruses we're seeing in the US right now. Last week, the CDC held a press briefing to warn about the rise in influenza and RSV cases. How concerned are you about what we're seeing with flu and RSV?

**Michael Osterholm:** [00:23:17] Chris, I am concerned about the rise in influenza and RSV cases in combination with COVID-19 continuing to circulate. I'm worried about what this may mean for health systems that are exhausted after having been strained for nearly three years. The CDC just recently issued a health alert network health advisory about elevated respiratory disease incidents caused by the co-circulation of RSV, influenza, and SARS-CoV-2, among others, especially among children. They are placing an immense strain on the health care system. This could be the early warning shot of a challenging fall and winter ahead. Let me specifically address each of these virus illnesses. In terms of influenza, the US officially crossed the flu epidemic threshold last week. The US is now experiencing the highest levels of influenza hospital admission rates for week 43 since the 2010-2011 season. In this case, this is the earliest activity. So I don't want to suggest this is the highest activity we've seen since 2010-2011, but it's the earliest we've seen the increase reach this level since that time period. So far this season, the CDC estimates there have been 1.6 million illnesses, 13,000 hospital admissions, and 730 deaths from flu. We're seeing a difference in influenza virus activity by region in the US. The southeast and the south central states are reporting the highest levels of flu activity, followed by the mid-Atlantic and south central west coast regions. Two weeks ago, ten states were reporting high levels of flu activity. This week, ten states and the District of Columbia are experiencing very high levels, and an additional eight states are what we call high levels. Southern states are reporting flu test positivity rates as high as 20%, mostly involving H3N2, a subtype known to cause more severe illness in young children and seniors. Meanwhile, the mid-Atlantic and Midwestern states are seeing rises in 2009 H1N1 Activity. RSV levels continue to increase in all regions except those that include the southeast and south central states, areas that were the first to see a rise from flu. RSV activity appears to be declining in the northwestern regions that include Colorado, Montana, North Dakota, South Dakota, Utah and Wyoming. Keep in mind that we're still early in the RSV season, and although activity appears to be plateauing or declining in some places, the overall timing, intensity, and severity of the current RSV season are still quite uncertain. Any of these three viral respiratory illnesses alone at the levels we're currently seen would be a challenge. But all three together, in combination with a rise in staffing shortages and delayed care for other illnesses during the pandemic, are simply overwhelming hospitals and emergency rooms around the country. For example, emergency departments in Massachusetts are reporting nearly an eight hour wait time. Children's specialty hospitals and emergency rooms are being currently overwhelmed by RSV in many cities around the country. Boston's Children's Hospital has postponed some elective surgeries to make room for more patients with respiratory illnesses. Pediatric specialty hospitals in Orange County, California, Seattle, Lubbock, Texas and Baltimore are at full capacity. As we saw during the COVID surges, as a side effect of the surge in respiratory infections, is that children who visit the emergency room for non-life threatening conditions or injuries will have to wait longer to be seen because they are lower on the triage scale. Fortunately, there are some things you can do to minimize your risk of influenza and COVID-19 during this time. You already all know what I'm going to say, but it bears repeating. If you haven't gotten your flu shot yet this year, or if you haven't gotten your COVID bivalent booster and are eligible, now is the time. Your annual flu vaccine is the best way to protect against flu, and particularly in preventing serious illness, hospitalizations and deaths. In addition, there are also prescription flu antiviral drugs that can be used to treat flu illnesses. Again, particularly among those who are most likely to have severe illness, older individuals, people with underlying immune conditions. But remember, these drugs need to be started right away, just as we talked about with Paxlovid. And finally, the methods to help protect you from COVID-19, like high quality respiratory protection, will also help protect you from the flu. Now, having said all of this, I still am challenged to understand how will these three interact in our communities? Meaning will one of the viruses dominate? We've already seen the difference with flu in the south and southeast versus the upper Midwest, where we have seen more RSV. I don't know what's going to happen here, but the three of them together surely are a toxic mix. And we'll follow this very carefully over the days and weeks ahead.

**Chris Dall:** [00:28:24] One of the questions we've gotten from several listeners is whether the mitigation measures that have been used for COVID-19 over the last two years, namely masking and social distancing, have helped fuel the current surge in RSV cases. And of course, there are some people who are using that to criticize those mitigation measures. Is there any credence to this, Mike?

**Michael Osterholm:** [00:28:45] Chris, as you know, I have addressed this time and time again on this podcast as to saying that we don't understand the interactions of these viruses when they are together in the community. I come back to the issue of people talking about mitigation as having given us what some people call the immunity debt immunity where in fact people were not subjected to this virus infection such as RSV or influenza while COVID was really running rampant. And therefore the amount of immunity in the community from previous infections has dropped. Well, first of all, remember, if you get that kind of immunity, you will have had to have the infection of the past. So if you have it then or now, I'm not sure quite the difference, but more importantly is the fact that as I've shared time and time again, if you go back and look at, say, for example, the 2009 H1N1 pandemic where there the virus emerged in Mexico in late January, early February of 2009. It took off around the world in April and early May, causing a large peak of cases in many countries. There were no mitigation strategies put into place anywhere, no closings, no lockdowns, no recommended masking, nothing. And then the virus virtually disappeared. We went through much of the summer throughout the world, our summer in the northern hemisphere, but in the winter, even in the southern hemisphere and didn't see this H1N1 new virus activity. Well, then along comes mid-August, particularly in the northern hemisphere, and we saw H1N1 take off for the big peak, the one that really was the by far the most concerning with H1N1 in 2009. That ran roughly from mid-August until early October, and then it dropped precipitously again, as just with the previous peak, there were no mitigation strategies put into place. There was no effort made to limit people's contacts with others, etc.. Why the peaks went up and down, we don't know. Vaccine didn't arrive largely till mid to late October. And so it didn't have really any material impact on the actual occurrence of cases. But what was interesting is then we get into the fall and winter and we did see some additional H1N1 activity. But for the first time in years, we didn't see other influenza strains like H3N2 and or any of the RSV activity. It just disappeared. Well, it can't be because of mitigation, because we didn't do mitigation. The only thing that was operative at the time was this pandemic strain of H1N1. So I use that as a backdrop just to say, think about that now. Why Mother Nature had this happen like this, I don't know. Well, now fast forward to COVID, and we saw the very same thing in the early days of COVID where we saw COVID activity, but with depressed influenza and RSV activity, particularly in the winter of 2020, 2021. But then we get to 2021 summer and we see RSV activity, which we had never seen before like that. People say the winter season didn't happen because we were mitigating. Well, I don't buy that at all because COVID transmission was doing just fine. Thank you. If we were really doing effective mitigation, why would we have had 80 to 90% of kids get infected with COVID, with Delta and Omicron? It just doesn't make sense. So I don't think we did effective mitigation. I'm not sure that the efforts we made to lock down locations or to recommend cloth masks really had any material impact. There's something inherent going on with regard to our immune status. Maybe it's innate immunity. Certain chemicals that we produce and response to the infection with a virus carries over, such as interferon to other potential virus infections so we don't get them. So, no, I don't buy the fact that it's all about mitigation. If everyone were wearing N95s that were highly effective, then I would say, you know what? If you see activity, that's really a challenge because I don't know how it's getting through the effective use of N95s. But more importantly, if you don't wear them, I don't know what is the impact of the virus itself, as well as the impact of making these mitigation strategies more common. So my answer is, yeah, you're going to see a lot of my colleagues out there making statements that, oh, my was seeing a lot of influenza and respiratory syncytial virus because of previous mitigation strategies. I'd like to have them show me some data that supports that and addresses the challenge that I just raised and they can't. And so what it really comes back to is the ultimate act of humility to say, I don't know. I just don't know why this what's happening is happening. I will be very curious to see how over the next 3 to 4 months, this combination of influenza, respiratory syncytial virus, and COVID play out in our communities. Will one dominate? Will all three happen at the same time? I don't think that will be the case all three, but I don't know. So to answer the question, I don't know.

**Chris Dall:** [00:34:18] Pfizer and Biontech said in a press release last week that new clinical trial data showed their bivalent booster shot produced a greater immune response in recipients one month later, compared with the original vaccine. This is some of the good news you were mentioning earlier, but there have also been some studies suggesting the updated boosters may not be much better than the original shot. So what do you take away from all these data?

**Michael Osterholm:** [00:34:41] We do have some possible positive news here, which is something we haven't been able to say lately. We now have some preprint studies and a Pfizer press release with clinical data showing that these bivalent boosters are producing very effective immune responses. Now, again, let me add the caveat they are of limited time following vaccination, i.e. 30 days or so. So we have to be very careful about assuming that that will last long term. To understand the whole picture, I want to take a step back and remind us what boosters in general, not just the newest bivalent versions are able to offer. The primary series of vaccination is typically responsible for helping our bodies produce a T cell response that protects us from severe disease and death. We've talked about that, and some of us have experienced how immunity from that primary series wanes over time, resulting in breakthrough infections. According to a recent study in Science Immunology, our COVID-19 booster doses do not appear to further expand T cell response. However, they do specifically boost antibodies that act specifically against the spike protein. Without diving too deeply into the science of immunology, boosters are playing a very important role overall in keeping our immune system up to date, especially against severe disease. Now, to improve on the positive effects of the original formulation of these boosters, the bivalent boosters are now proving to be even more effective. Chris, as you mentioned, Pfizer released additional clinical data this week. In addition, there have been five preprint studies looking at the impact of bivalent boosters in comparison with the original mRNA vaccine formulations. There were some differences across the studies methodology. However, all six of these studies show that the bivalent booster is at least equally as effective as the original formulation. Four out of the six studies showed a significant increase in the production of neutralizing antibodies against the BA.5 variant compared to the original formulation. In the three studies that compared the bivalent booster to one of our latest variants taking hold in the US, BQ.1.1, the bivalent booster proved more effective than the original formulation. The one study that assessed effectiveness against BA.2.75.2 a variant we've seen taking off in other areas of the world has also shown to be very promising. Data from the live virus studies show an immune response that was 3 to 4 fold higher than the original formulation. Significant results that make the latest formulation worth celebrating. Now, again, I want to emphasize one more time that these data are early in terms of the time period from vaccination to assessment. I want to know what they look like, not at 30 days, but at 60 days, 180 days, 365 days. That will be very, very important. The frustrating closing remarks of the exciting news, however, is that regardless of how well the vaccines work, our latest uptake data of these bivalent boosters is incredibly discouraging as it is so low. In the United States, less than 10% of people who are eligible have received it. We absolutely have to change our messaging to ensure that this valuable resource isn't wasted, especially coming into the holiday season and a new wave of variants. For those at risk for serious illness, hospitalizations and deaths, particularly those over age 50, or who have an underlying health condition, getting this dose of vaccine can be a lifesaver. I hope that you take very seriously this information if you haven't been vaccinated yet and go out and get it, it is not too late.

**Chris Dall:** [00:38:38] Mike, there is also an interesting preprint study that came out last week that showed the antiviral Paxlovid appears to ease symptoms of long COVID. What can you tell us about this study?

**Michael Osterholm:** [00:38:49] As you know Chris, long COVID has been a very important topic to our listeners, both those who have had long COVID and those who are terrified of getting it. We've covered in previous episodes how vaccines provide some protection against developing long COVID, but they aren't nearly as effective as we'd like them to be. And many of us are rightfully still worried about getting long COVID. I'm at the top of the list. A lot of the discussions we've had about long COVID in previous episodes have not been very hopeful. But this week I'm pleased to report that we actually have some good news. As you mentioned, a preprint from the Veterans Administration here in the United States, which we will link in our episode description was released last week that looked at the effectiveness of Paxlovid in preventing long COVID symptoms. I might add that these studies from the VA have been remarkably well done, and provide us with critical information that we can actually use. The study looked at over 56,000 individuals who had at least one risk factor for developing severe COVID illness, about 9,000 of whom received Paxlovid within five days of testing positive for COVID and about 47,000 of whom did not receive any antiviral or antibiotic treatment for their COVID infection. The study found a significant reduction in the absolute risk of developing ten long COVID symptoms: dysrhythmia, ischemic heart disease, pulmonary embolism, deep vein thrombosis, fatigue, liver disease, acute kidney injury, muscle pain, neurocognitive impairment and shortness of breath, in those who took Paxlovid compared to those who did not take Paxlovid. The study looked at two other symptoms diabetes and cough. But the absolute risk reduction for those symptoms was not statistically significant. What this is really telling us is that, in fact, in this population, we did see a reduction in long COVID symptom development by just merely taking Paxlovid during the acute illness. Paxlovid significantly reduced the absolute risk for long COVID in vaccinated, partially vaccinated and fully vaccinated and boosted individuals in the study, as well as those who were experiencing a reinfection with COVID and those who are infected for the first time. In addition to the ten long COVID symptoms mentioned earlier, those who took Paxlovid also had a reduced risk of hospitalization and death after their acute infection. We've already known for some time that Paxlovid would reduce the risk of hospitalization and death during the acute phase of a COVID infection. So it is really exciting to see that it may also reduce the risk of developing long COVID. If you are uncertain whether it was worth discussing Paxlovid with your health care provider, please see this as another reason to have that conversation. Yes, there has been discussion about Paxlovid and rebounds, but Eric Topol and colleagues will soon be releasing data showing that the increased risk of rebound is minimal with the use of Paxlovid. And it occurs regardless of whether you use Paxlovid or not. So from my perspective right now, the benefits of reducing the risk of hospitalization, death and long COVID far outweigh any concerns that you should have about taking Paxlovid. I hope that we continue to see more good news like this, both regarding Paxlovid and the prevention and treatment of long COVID in the months ahead. And as always, we'll keep you updated as that data emerges. I also have to add, just as I did in the previous issue with the vaccines Paxlovid cannot be helpful to you if you don't take it. And today we see a unfortunate number of people who are seriously ill and dying from COVID who were never offered or did not take Paxlovid early in the course of their illness. So we want to do, as we might say, a double whammy promotion here for both vaccine and use of Paxlovid. Those two together surely, surely can make a big difference for those who are still at increased risk for dying of COVID or who at least have a risk of serious illness.

**Chris Dall:** [00:43:03] Now for our COVID query segment, which this week addresses upcoming holiday gatherings. Here's an email we received from Karen, who wrote "My dilemma is the upcoming holiday gatherings. How can we gather safely with these differing behaviors and beliefs without further distancing or putting up barriers? The good news is, while my extended family are not interested in changing their daily behavior, they are willing to listen to me and do what I might ask them to do during a gathering. It is a lot of responsibility on me and it is stressful and fills me with anxiety. So what I'm asking is, how do we gather safely?" So, Mike, what can you tell Karen and how are you approaching the upcoming holidays?

**Michael Osterholm:** [00:43:42] Karen, I applaud you for taking the initiative to put some precautions in place to benefit everyone in your family. I don't have a foolproof plan for a perfect, safe gathering. I don't really think there is such a thing. But as we've talked about in the past, there are things we can do to reduce the risk and still enjoy family, friends and community that make life worth living. Let me share with you specifically two instances in my personal life that help illustrate what I think you can do and what I do with my loved ones from a safety standpoint. Number one, I am getting together with colleagues and friends for dinners. I do them in my private home. The protocol is in the three previous days to the actual dinner, you cannot have had no in contact with someone who had a COVID case. Number two, if you have any symptoms on the day of including allergy-like symptoms, thinking that it's just ragweed, that's disqualifying. And last but not least, a lateral flow test on the day of the event. That has to be negative. Now, that's not perfect. It doesn't mean it will screen out everyone. But I have had so many wonderful moments, again, with people with no respiratory protection on, close contacts, laughing, cheering, hugging, in some cases crying. That, I think, is one way that you can, again, safely take on COVID. I just got back from an extended trip in Europe. I was actually in France and Greece, countries with increased number of cases. Both Fern and I wore N95s any time that we were in public places. Not alone. We were very careful if we were in a setting where we needed to eat, that it was outdoors, away from people or in settings where everyone had just been tested. We actually had a wonderful trip. We did not forgo that. Yes, we wore our N95s on the plane for the duration of each of the flights. We were about the only ones on the plane that did. But we did it with the knowledge that we were doing everything to protect ourselves. So I want to be clear that we should move ahead. We should engage our lives as we want to do it using these safety precautions. And again, remember, being vaccinated, fully vaccinated with the bivalent vaccine, together with if I do get symptomatic, having Paxlovid available, are all going to be part of that safe approach program. Now, I do want to add one thing. We get these wonderful, wonderful comments and stories sent to us by our listeners. And I want to give you one that I think was just remarkable and it illustrates what can be done and yet at the same time, preventing transmission, but allowing for events to take place that are so near and special. Again, as this particular event will remind me of the painful story that Rebecca shared with us some weeks ago. This one actually came from Sarah. Sarah's family hosted a recent wedding and was able to take a number of precautions to reduce risk. Let me read what she shared with us. "Our daughter got married at the end of August in a beautiful farm in the Catoctin Mountains of Maryland. She and her husband decided early on to require that everyone attending to be vaccinated and also that they take a rapid test the morning of their arrival at the venue. Five people tested positive the day that they were to arrive. One of them was a bridesmaid, two of our closest friends, the photographer, and the friend in charge of the music for the ceremony and reception. Two others stayed home because of symptoms. Our daughter was surprisingly calm about the last minute changes. Fortunately, the photographer found a substitute and a friend stepped in to do the music. Our daughter and son-in-law created a heartfelt ceremony that had many of us in happy tears. Zoe walked down the aisle to an instrumental version of a song she had written and animated for Logan when they first started dating and their wedding arbor was covered with wildflower paintings she created for the ceremony. They wrote their own vows and made beautiful pledges to one another. We ended the day with a celebratory meal in a colorful, well ventilated tent with 116 of our family and friends. It was a perfect weekend. The week after the wedding, four people tested positive. We figured out that they were all exposed before the wedding. They hadn't known they were with someone who was infected and the rapid test hadn't picked it up. Fortunately, however, no one person tested positive as a result of the wedding. We greatly missed the people who were absent. We were also so thankful that the vaccination and testing left us with only wonderful memories in a picture perfect setting." I think this is a wonderful story and it points out how a combination of creativity and concern for others can result in still having these moments. I'm sorry that there were family members and others and part of the wedding that could not be at the wedding because of this. But what if they actually had attended? If there had been transmission and someone had become seriously ill and died? That wedding would always be marred by that. So I just want to acknowledge to you, Sarah, and all of your family, particularly Zoe and Logan, for taking on this very challenging situation in such a wonderfully productive way and making it possible for such a special day. Now, for all the listeners here, I want you to know that we have linked to pictures that she sent from the wedding, and they're absolutely stunningly beautiful. And I hope that you will take a look at them and I hope that this all reminds us of what we can do. So to summarize, one, I'm out there living my life right now, but I'm taking precautions in a way that does not mean I can't live my life, but I am not putting myself at risk. I'm using my N95, I'm fully vaccinated, I have my Paxlovid. I have a protocol for family members and friends getting together, and it's surely does add another wrinkle to life. But boy, it sure a lot better than being locked up afraid of this virus.

**Chris Dall:** [00:50:22] And Mike, we also got some pictures sent to us with our latest beautiful play submission. Where is that submission from this week?

**Michael Osterholm:** [00:50:30] Well, thank you, Chris. This particular one comes to us from the White Mountain area of Maine, and it comes from Corky. And it's beautiful. The note is beautiful. The pictures are beautiful. Corky writes, "Good afternoon,CIDRAP team. First and foremost, thank you for your collective dedication informing so many of us who seek your straightforward updates each time that the podcast drops. I am mindful that this service is far from your only responsibility, and I'm grateful that it remains a priority among the team." Footnote for me, it always will. "I listen with interest to every episode and use the information to make decisions that keep us as healthy as is possible, as well as share content with many family, friends and acquaintances who are looking for a trustworthy source of information. While the information was the hook that captured me back in the earliest episodes, it is the humanity that has brought me back time and time again and become so sustaining. Several of my siblings also listen in. We often refer to the teams updates in our conversation. We also share beautiful places among ourselves. Perhaps the takeaway I appreciate most has been the beautiful places. Blessed with living in Kittery, Maine, with proximity to oceans minutes away and mountains within an hour, there is no shortage of moments that are breathtaking and beautiful. It is simply being present to see them. Attached to our recent daily walks with the local beaches and foliage in the White Mountains. Thank you for all who research, write and present these episodes in addition to your many other public health roles and a heartfelt gratitude for helping to see all the beautiful places in nature in each other. Warmly Corky." Oh my. This almost brings you to tears. Thank you so, so much for your very kind thoughts. And the pictures are stunningly beautiful and they obviously came from a beautiful person to do that. We appreciate your input and we're glad that we can be of some support to you and this whole entire pandemic. And again, I just want to emphasize, please keep sending in these beautiful places. As I started out in the introduction of this podcast, you all, as participants in this podcast family, have done so much for us. And this is one of the best ways to do it is to to read these wonderful emails and to see the picture. So thank you. Thank you, thank you, Corky, and to your family and friends for all you do.

**Chris Dall:** [00:52:59] And a reminder to our listeners that if you want to tell us about the beautiful place that has helped get you through the pandemic or share a celebration of life for a loved one friend, neighbor or coworker who died during the pandemic, please email us at osterholmupdate@umn.edu And also a scheduling note, I want to let our listeners know that we will be back with another episode of the Osterholm Update next week. Then we will be taking the week of Thanksgiving off. So our next episode will be posted November 17th, and after that we'll resume our every other week schedule. So Mike, what are your take home messages for today?

**Michael Osterholm:** [00:53:34] Well, Chris, I have a lot of take home messages, some of them that make sense. Some of them are emotional statements that are all about hoping and wishing. So let me cut to the chase and say, I think the three most important things I hope people take away from today's podcast is, number one, we may be at a turning point in this pandemic, but it's still too early to know that and surely not yet done. You can protect yourself. If you're older, have underlying health conditions, please be fully vaccinated with that bivalent dose. Use your N95s when you're in public or in situations you may pose as a potential exposure. I do it all the time. I've gotten more and more comfortable with it. I can honestly say I wore it on ten hour airplane flights and not even think about it. Be prepared to get Paxlovid very quickly if you should get infected. Don't wait. Even if you aren't severely ill, which is what the whole purpose of taking the drug is supposed to do prevent that, get it even if you have mild symptoms. And one of the things you're going to need to look at is because of the data I presented today on long COVID. Would this be a benefit to even those who are younger, who aren't necessarily at increased risk for serious illness, but who are in fact at risk of long COVID? And I think you're going to hear a lot more discussion about that in the days ahead. Number two, RSV influenza, and COVID are still here, and they are, in fact, a challenge. We don't know how this is going to play out. What will be the interaction between these three? Will we see all of three of the viruses at the same time in the same communities? I don't think so. But we already know what we are seeing is challenging our health care system significantly. And so, number one, if you have a young child with respiratory symptoms and a child appears to be having difficulty breathing, please get that child into medical care as soon as possible. Even though we know the systems right now are overrun. That could be a life saving measure. Get your flu shot. Even if it does not prevent you from getting infected, it still can go a long ways like COVID vaccines to prevent you from having severe illness and hospitalizations. And finally, the third thing, We are at a critical time in this pandemic journey. But it's really important that we have to keep an eye on the future and not forget that, in fact, that could change. Also, we're at a critical time in this pandemic. And as many of you know, I have avoided at all cost political statements and will continue to do so. I've served roles in the last six presidential administrations. My job is to be a private in the public health army and do the best I can. But I want to say, as I record this podcast, to watch what's happened this past week and to see largely how as a country, we did not let ourselves devolve into the darkness around the elections, which could have an impact on the pandemic. That made me proud. I'm sorry that we ever had to get here to think that that could be a challenge to have a fair and representative election. But it gives me hope and it gives me hope that therefore, we can have really thoughtful, legitimate and real discussions about what the pandemic is about and what we need to do to be better prepared. So I just want to leave us with this critical time in the pandemic as a message of, yes, the virus is our challenge. Our whole world is a challenge. And right now we're rising to meet that challenge.

**Chris Dall:** [00:57:27] And Mike, what is your closing song for today?

**Michael Osterholm:** [00:57:32] Well, you know, again, to the audience, we actually take this closing very seriously. It is, in a sense, our message to you, maybe subliminally, maybe just so obvious that we couldn't be subliminal if we tried. But I think it's really important that we try to set the tone of what it is we're experiencing. And this particular song is very, very meaningful to me. It's something that I find both in my heart and my head has real meaning. The song is "Humble and Kind." It's a song written by Lori McKenna and first released by American country music singer Tim McGraw, someone who we have used songs from in the past. It was released on January 20th of 2016 as the second single from his 14th studio album, "Damn Country Music." Mckenna later recorded her renditions of the song for her eighth studio album. Of Note, among several other wins and nominations, the song won the award for the best country song at the 59th Annual Grammy Awards, Video of the Year at the 2016 CMT Music Awards, and Song of the Year at the 2016 CMA Awards, and the Country Song of the Year at the 2016 American Music Awards. Obviously, others have also recognized how special this song is. But the note I want to put on before I share the verses with you is that this song was written by Lori and in an interview with CMT, published in July of 2016, she revealed that the song was written for her husband and their five kids and it's her list of all the things she wanted to make sure she told them. Well, she did a remarkable job. So here it is, "Humble and Kind." Written by Lori McKenna. "You know, there's a light that glows by the front door. Don't forget the keys under the mat. When childhood stars shine. Always stay humble and kind. Go to church. Because Mama says to. Visit Grandpa, every chance that you can. It won't be wasted time. Always stay humble and kind. Hold the door. Say, please. Say thank you. Don't steal. Don't cheat. Don't lie. I know you got mountains to climb, but always stay humble and kind. When the dreams you're dreaming, come to you. When the work you put in is realized. Let yourself feel the pride. But always stay humble and kind. Don't expect a free ride from no one. Don't hold a grudge or a chip. And here's why. Bitterness keeps you from flying. Always stay humble and kind. Know the difference between sleeping with someone and sleeping with someone you love. I love you. Ain't no pickup line. So always stay humble and kind. Hold the door. Say, please. Say thank you. Don't steal, Don't cheat. Don't lie. I know you got mountains to climb, but always stay humble and kind. When those dreams you're dreaming come to you. When the work you put in is realized. Let yourself feel real pride. But always stay humble and kind. When it's hot, eat a root beer Popsicle. Shut off the AC and roll the windows down. Let the summer sun shine. Always stay humble and kind. Don't take for granted the love that this life gives you. When you get where you're going, don't forget. Turn back around and help the next one in line. Always stay humble and kind." Well, thank you all so very much for joining us again. I'm sure that many of you found this podcast and hopefully it's positive note somewhat of a difference from previous episodes. We believe that we may be at that point. So again, thank you so much for being with us. And as I noted in the dedication, this podcast is for all of us who are struggling to find that new normal, that place where we can live life and not be either captured by the virus in our homes. And most of all, I hope that all of us, as we get closer into this holiday season, can find a new note of positive of something that gives us reason to want to get up every morning with excitement. So thank you. Again, I acknowledge the fact that even though things may be getting better, we must never forget all of our loved ones. We've lost our friends, our family, our colleagues, people who are part of our lives. This pandemic has been hell that way. So thank you very much. And as Lori McKenna just said, remember, we must stay humble and kind. Today, go out and surprise friends, neighbors, whoever, with an act of kindness. It will make you feel so much better and it will clearly make your friends and neighbors also feel better.

**Chris Dall:** [01:02:39] 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. The Osterholm Update is produced by Cory Anderson, Meredith Arpey, Elise Holmes, Sydney Redepenning, and Angela Ulrich.