

## Episode 76: Vaccines in the World of Delta

**Chris Dall:** [00:00:00] Hi, everybody. Before we get started with this week's episode of the Osterholm update, I want to tell you about a special event coming up. It's called "Inside the Pandemic." This is a candid conversation with CIDRAP Director Dr. Michael Osterholm and former senior adviser to the Biden administration's COVID response, Andy Slavitt, as they talk one on one about COVID-19 challenges, ripple effects, and what's next. Don't miss this conversation on November 18th at 11:30 a.m. Central Standard Time. You'll need to register for the event, and you can find a link to the registration page on our episode description. And now to this week's episode of the Osterholm update. Hello and welcome to the Osterholm update COVID-19, a podcast on the COVID-19 pandemic with Dr. Michael Osterholm. Dr. Osterholm is an internationally recognized medical detective and director of the Center for Infectious Disease Research and Policy, or CIDRAP, at the University of Minnesota. In this podcast, Dr. Osterholm will draw on more than 45 years of experience investigating infectious disease outbreaks to provide straight talk on the COVID-19 pandemic. I'm Chris Dall, reporter for CIDRAP News, and I'm your host for these conversations. Welcome back, everyone, to another episode of the Osterholm Update podcast. As of Monday this week, the official global death toll from COVID-19 surpassed five million. Even though that number is likely a significant undercount, it's still stunning. As The New York Times pointed out, such a loss would wipe out almost the entire population of Melbourne, Australia or most of the nation of Singapore. The Times went on to note that the pace of confirmed deaths, however, has slowed slightly since the world reached four million deaths in July, a sign that vaccines are having an impact, at least in some parts of the world. But a million people have died since July, and in many parts of the world, only a fraction of the population has received even one dose of vaccine. And even in more highly vaccinated countries, cases are rising once again as the Delta forest fire continues to find new wood to burn. And that seems to sum up where we are in the global battle against COVID-19. We're getting to a better place, slowly. Vaccines are helping to lessen the impact of COVID-19, but the virus is still having a devastating impact, and we need to get vaccines to more people around the world to truly get this pandemic under control. On this November 4th episode of the Osterholm update, we'll assess where we are in this pandemic as we take a look at the international situation and what's going on here in the United States. We'll also discuss the evolving science on vaccine protection, breakthrough infections and booster shots, answer a COVID

query and give you the latest on vaccines for young children. But first, we'll begin with Dr. Osterholm's opening comments and dedication.

**Michael Osterholm:** [00:02:53] Thanks, Chris, and welcome to all of you to another episode of this podcast. I hope that today's podcast will provide you with the information you're looking for. I think this podcast can probably be best characterized as the crystal ball with five inches of crusted mud on it podcast. I'm going to try to do my best today to wade through a number of complicated topics involving where the pandemic is going, what are we seeing with the impact of the vaccines and where this may take us. And as we ask more questions, we're getting more questions, and I wish I could say we are coming to a place where with more information, we understood more. I think with more information, we're being more challenged by what we understand. So from that perspective, hold on. Fasten your seatbelts. The second thing I just want to say is thank you again to all of you who continue to share with us your feedback. It is incredibly, incredibly helpful to us to hear from you what it is you're needing, wanting and what you appreciate and what you find challenging. And so I just ask that you continue to send those along. And most of all, I want to just say that on behalf of the CIDRAP podcast team, we value this feedback very, very much. And it has been a very sustaining force in all of these activities as we continue to march along with our podcast. I also want to just add that in a previous podcast, I noted that hopefully I would be able to end them by the 100th podcast, and we're now approaching close to 80, meaning about 20 more weeks. Let me put that really clearly on the table as to what I meant. That's an aspirational goal. I don't believe that this pandemic will be over by then. However, I do believe that we can hopefully have more answers that will give us a much better direction as to where we're going, what we need to do to deal with this pandemic. So don't think that I've predicted that, you know, in 20 weeks, we're done. I just hope by then we have a much better sense of where we're going. In terms of my dedication today, I want to acknowledge a very critical aspect of this podcast, which often is missed. I receive a lot of attention around this podcast from you, the listeners, and I know you understand that it takes more than me to put this together. I'm just the mouthpiece, you might say. So today I dedicate this podcast to the CIDRAP podcast crew, starting right here, first and foremost with Chris Dall, the moderator of voice that also is so key in helping to frame the topics that we address. In addition, Maya Peters, who has added tremendous expertise in terms of the technical aspects of these podcasts, and Cory Anderson, Angela Ulrich, Meredith Arpey, and Sydney

Redepinning are all members of this team that every week work hard to try to get you the most current, comprehensive and authoritative information. If we don't do that, that's my fault. I haven't interpreted it as I should have and could have. It's not theirs. They've done an amazing job week after week preparing this information for your use. So I want to thank you so much for all you do to make this possible, and I wish if I could, I would call it the Osterholm, Dall, Peters, Anderson, Ulrich, Arpey, Redepinning Podcast as opposed to the Osterholm podcast. So thank you.

**Chris Dall:** [00:06:24] And thank you, Mike. Before we get started, we have a few quick housekeeping items to take care of. First, a lot of listeners have found the podcast transcripts very useful. You can find those on the episode description page on the CIDRAP website, and they typically are posted on the Monday after each episode. Also, we've gotten feedback that some listeners are having a difficult time accessing the podcast on the CIDRAP website, and we've recently learned that it's an issue if you're using the Firefox browser. You should not have problems with other web browsers or if you use Apple Podcasts or Spotify. Mike, we'll start as we always do with the international situation. As I noted in the introduction, the global impact of this virus has been immense and it's not done with us yet. What parts of the world are you keeping your eye on?

**Michael Osterholm:** [00:07:10] Well, Chris, before I get into the international piece, I wanted to start out by just acknowledging that grim milestone of five million confirmed deaths from COVID worldwide that you mentioned. It's a death toll so large that I think it's inherently difficult for us to fully comprehend what it means. I know it's a challenge for me. As I've said before, my job has always involved numbers. Frankly since this podcast began, we've all kept our eyes on these numbers, which are constantly changing. For many of us, it's almost turned into a force of habit or a routine. What's happening with cases, hospitalizations, deaths? How does that compare to the previous time points? Over and over again, we use them in our search for clues or answers to a whole litany of questions. And unfortunately, this continuous cycle and repetition can make it all too easy to overlook the fact that each of these numbers represents a person, as I have said week after week. They are our loved ones friends, family, parents, grandparents, sisters, brothers, aunts, uncles, cousins, children. The list goes on. I know I've said this before, but I really hope we never, ever, ever forget that. Just think of this, and I do often. If you were to state each and every name of the five million

individuals we've lost to COVID and you spent three seconds on each name. Michael T. Osterholm, it would take almost 174 days of uninterrupted speaking to go through that entire list. That's almost half of year of speaking around the clock with no breaks for eating, drinking or sleeping. That should be a subtle reminder of what this virus has done. And of course, those are just the confirmed deaths. The true death toll is believed to be much higher. For example, The Economist has a group regularly analyzing global excess deaths, and their latest estimate is closer to 16.8 million COVID related deaths, which is much more than three times the official number. Nonetheless, it's a testament of the pain and suffering that this virus has dealt in less than two years time. And we must never lose sight of that. Now that being said, the pandemic clearly isn't over yet, either. Globally, we're seeing cases and deaths move back up. Over the past week, global cases have climbed above three million for the week and more than 50,000 deaths were confirmed. It is in that cycle that I've talked about so many times of the peaks and valleys of case numbers. Looking regionally, it's obvious that the situation in Europe continues to account for most of this overall upward trend we're seeing. However, both the Americas and Western Pacific regions are also now reporting slight upticks this past week. Otherwise, Africa, Eastern Mediterranean region and the Southeast Asia area are all again once again reporting case declines. While I'm doing my best to keep an eye on what's happening in most regions of the world, I've been especially interested in what we're seeing play out in Europe because I think it really illustrates the message that we've been trying to get across to our audience. Clearly, Eastern Europe is the epicenter of the region's growth. We've touched on what's been happening there several times over the past month or two, and unfortunately, things remain hot. Once again, nearly every country with the highest average number of per capita cases and deaths in the past week is located in or near Eastern Europe. In fact, in countries such as Armenia, Bulgaria, Latvia, Romania, Russia and the Ukraine, the reported death rate is at an all time high. Unfortunately, it's a tragedy that wasn't unexpected due to the relatively low vaccination rates in so many of these locations. However, what seems to be unraveling in growing parts of Western Europe lends support to my position that so many places in the world can and should expect future surges, including the US. Why do I say that? Well, just look at what's happening in places like Germany. In just the past two weeks, the average number of daily cases in the country has more than doubled, climbing from less than 9,000 cases in mid-October to nearly 19,000 cases a day as of Monday. It's not just cases, either. An article published this past Thursday featured a quote from the head of the German Hospital

Association, who warned that the country had entered a critical pandemic situation. They're seeing a growing number of COVID patients, which have pushed some ICUs in the country to full capacity. And although the total number of current ICU patients with COVID in Germany remains well below peak levels reached last winter, health care systems there are beginning to be strained to the point where normal and sometimes urgent, non-COVID related operations are having to be postponed. Remember, this is a country that has fully vaccinated 67% of its population. Remember, the United States still sits at 58%. A similar situation is unfolding in the Netherlands. Average daily cases there have grown from 1,600 cases a day in early October to more than 7,400 cases a day now. Remember that 1,600 cases a day in early October, 7,400 cases a day now. Hospitalizations in the country have increased by more than 30% just in the past week. This sharp rise prompted officials there to announce the return of a nationwide mask mandate and its expansion of their vaccine passport. I just have to keep emphasizing. The Netherlands has fully vaccinated 68% of its entire population, versus 58% of U.S. residents. Belgium, which has fully vaccinated 74% of its population, has also seen cases grow to their highest levels in almost a year. In response, they too have decided to reimplement a mask mandate and expand the vaccine passport requirements. I could go down a laundry list of countries in Western Europe facing similar situations. Cases are on the rise in Norway, where 70% of the residents are vaccinated. The Czech Republic is seeing a clear surge. Ireland is reporting their most activity since January, despite 76% of its residents reported as fully vaccinated. Even Denmark, which has received so much attention for supposedly having reached a sweet spot in terms of the number of people vaccinated so as to avoid any future surge activity with Delta. They have also vaccinated 76% of their entire population, and yet they're seeing a clear rise, with cases at their highest level since last December and hospitalizations now reaching their highest total since February. Now, as always, I want to make it very clear that the relatively high vaccination rates in each of these countries is obviously limiting a lot of the severe disease and death we saw during previous waves. If you need proof of that, I'd encourage you to look at the data and the clear differences in rates for these metrics based on vaccine status. It follows what we've seen before in places like Israel, the U.K. and Singapore, which is still in this case in the midst of its own surge. The vaccines are very effective in preventing severe disease and death. In fact, a report out of the UK's Office for National Statistics published this past Monday analyzed countrywide data spanning from early January to late September and determined that the age adjusted risk of death from COVID was 32 times higher in unvaccinated people than in fully

vaccinated individuals. However, we're seeing these countries, some of which have 70 or 80% of their entire populations fully vaccinated continue to be challenged by this virus and its surge. Are there challenges as significant as those in countries with lower vaccination rates? No. But their paths out of the pandemic haven't been simple, smooth sailing. And it's a reminder to the rest of the world that any relief felt from the virus at this point shouldn't be misinterpreted as ultimate victory if surges can happen in places like Singapore, Germany and Denmark. Why wouldn't we expect to see them in places like Africa, Latin America and even the U.S. all areas with substantially lower number of people vaccinated? I want to discuss one last country as it relates to what's happening in the global picture because I think it represents a challenge to the entire world's economy. China has continued to be the only country in the world that is maintaining a zero COVID policy. They believe that they can with their very extensive public health response activities, some would call draconian, be able to contain those fires to a zero level. Right now, more provinces in China are dealing with COVID-19 than at any time since this virus first emerged in Wuhan in 2019. Despite the increasing aggressive measures the Chinese officials have taken, the Delta virus continues to flare up and expand its reach. More than 600 locally transmitted infections have been found in 19 of 31 provinces in this latest outbreak. That may seem like a small number, but when you see the kind of steps that have been taken to respond to it, you understand what the Chinese are actually trying to accomplish. They are committed to maintaining a so-called COVID zero approach, even though these flare ups are coming faster, spreading further and evading many of the measures that previously controlled the virus. Their dramatic responses needed to respond to this are having a fundamental impact on the everyday lives of all of China. The question will remain can they continue to deal with these flare ups as they are in such a way as to not halt the everyday business of China? The China's Ministry of Commerce urged residents Tuesday to stock up on necessities for the fall and winter to be prepared for future outbreaks that could trigger snap and, in some cases, massive lockdowns. Let me give you an example of some of the things that China's recently done. On Sunday, more than 30,000 people were held in quarantine and tested at the Shanghai Disneyland after a single visitor inside the park was found to be infected. They held these people until well past midnight before they were able to release them as they were all tested. They are doing the same kind of thing with their ports. We're seeing that in cities with transportation. We're seeing that in the schools. I raise this issue because the business community is starting to pay attention. I've had more media recently from the business community ask me about

COVID than from the public health or general news side of the house and what they're asking about how will this ongoing transmission of the virus in China likely affect what will happen to everyday Chinese life? And I think the Chinese are going to be very challenged to keep much of their operating activity going on, manufacturing, all the things that they've been doing to supply the world with their global supply chains. Watch this one. This is going to be an interesting study, and at this point, I think that the Chinese are not going to be able to continue doing this. They are too going to have to accept a non zero COVID policy or they will shut themselves down and the world will know a much more challenged economy and business response to this pandemic. Well, let me just conclude from an international perspective in terms of where we're at, what we're doing and saying that I welcome any relief we can manage to get from this virus. But I think it would be a mistake right now to take the international picture and assume that that supports that in fact, many countries around the world are invulnerable to this virus. The lack of activity we see in Africa and parts of the Americas, parts of Asia is not, we're done. It's until it arrives. And we're going to continue to see this and we have to understand that. And I hope that the European experience I just talked about is clear and compelling and the fact that in areas of the world much better prepared to deal with this virus from a population based vaccination standpoint are still having major major challenges.

**Chris Dall:** [00:20:13] Here in the United States, the decline we've been seeing from the peak of the Delta Surge seems to have leveled off nationally at around 73,000, 74,000 new cases a day, while deaths and hospitalizations are still declining. So Mike, is this our new baseline? And as more people get vaccinated, will daily cases become less of a meaningful metric?

**Michael Osterholm:** [00:20:36] Well, Chris, first of all, let me start off with my customary and somewhat unsatisfying disclaimer, while I'm confident there are a lot of people in this country still vulnerable to this virus. I don't really know where we will find ourselves in the coming weeks. That crusted mud is getting harder and harder to scrape off that crystal ball. The initial pattern we were seeing play out in countries hit by Delta with that dramatic surge followed by a precipitous drop, has seemed to hold true in some places, including India, Iran, Indonesia. But it also has materialized in a number of other countries. In certain instances, the initial drop is being interrupted by this apparent plateau, which we're now seeing signs of here in the U.S.. South Africa saw a similar

phenomenon, with their plateau lasting for nearly a month. Before then, additional declines brought them back to pre delta levels. On the other hand, countries like Russia and the U.K. had case surges back up again after experiencing relatively short term plateaus. So I'm not sure there's an exact model we can really use to predict what's going to happen. I certainly hope we will see eventual declines like in South Africa or India, but we could also just as easily head in the other direction. And let me just emphasize again, anyone who comes out with modeling that's more than 30 days out from today is basing that on pixie dust. And as I'll point out in a moment, I'll give you examples of where just four weeks ago, no model could pick up the kind of activity that we're actually witnessing today. Overall, as you mentioned, average daily cases in this country sit at about 74,000. That's well below where we were at the height of the Delta surge, but it's still six times higher than the level reported in late June. As expected with the drop in cases, we've also seen hospitalizations fall from nearly 104,000 to around 47,000. And average daily deaths have dipped from more than 2,000 to 1,300 deaths a day. Again, real and welcome declines, but they're still sitting at levels well above where we were pre delta. So if this does end up becoming our new baseline, it's not a good omen. Even if we take a look at what's happening at regional or statewide levels, it's hard to decipher where we're headed. While we're seeing persistent declines in many of the southern Sunbelt states that were just red hot a couple of months ago, some states in the West, Midwest and Northeast are ticking upwards. For example, if you look at cases reported over the last week, as reported in The Washington Post, there are 24 states reporting increasing cases and 27 states reporting declines. Some recent hotspots like Alaska, Idaho, Montana and Wyoming are reporting declines, but overall activity there still remains high. Let me just help paint this picture of the confusion around what's happening in this country. Today, the overall national rate of cases in this country is about 22 per 100,000 population. If you look at what's happened over the past two weeks, there's been an 8% decrease in cases. However, if you look at the last seven days, that's almost been a zero decrease. It appears to be clearly plateauing. Alaska, which is at 82 cases per 100,000 almost four times higher than the national average, has seen a 30% reduction in cases over these past two weeks. But now we're seeing something emerge in the Four Corners area we had not seen before. Arizona is at 45 cases per 100,000, twice the national average, and that is a 50% increase over the past two weeks. New Mexico is at 45 cases per 100,000, a 38% increase in the last two weeks. Colorado is at 51 cases per 100,000, a 23% increase in cases. And in fact, in a state where the governor just earlier this week declared that hospitals could defer



all elective surgeries because of the strain that was starting to be experienced by Colorado hospitals. In the last of the four corner area states, Utah is also a rate of 45 cases per 100,000 has seen a 13% increase in the last two weeks. We know that we're seeing right now an ever increasing number of cases in the Navajo Nation, a group that has over a 70% vaccination rate. We don't know how much of this in the Four Corners area is being accounted for by that. It surely appears to be more. Let me take another area, one that is obviously near and dear to my heart. The Upper Midwest. If you look at what had been happening in our area, we had this initial surge that seemed to have peaked in late September, early October, started to come down and now that's changing. North Dakota, which is at 65 cases per 100,000, almost three times the rate of the national average. The number of new cases is flat. It's not decreasing anymore, even at that high level. Minnesota is at 43 cases per 100,000, we're flat. Michigan's at 43 cases per 100,000. It's flat. Wisconsin's at 38 cases per 100,000, with only a 2% decrease in the last two weeks. Iowa is at 35 cases per 100,000, but a 14% increase in the last two weeks. And finally, Nebraska is also at 35 per 100,000, with a 17% increase over the past two weeks. What's happening here? This is bucking the national trend. We don't know. So I have to say we seem to have found ourselves in a holding pattern. And the overall U.S. trajectory will depend on what plays out in some of these pockets of smoldering activity that are scattered around a number of different regions of the country. I hear people all the time wanting to talk about national numbers. We can't do that here because of what we're seeing is truly emerging differences by region. If overall activity does ultimately end up declining in the weeks ahead, I couldn't tell you why. As I mentioned during the international update, I think most of this country still has wide gaps in the protection at the population level. It's only a matter of time until we see the virus take off in other areas, which still includes major population centers like Los Angeles and New York. I keep hearing about the success of New York City. Yet, in fact, only 67% of all individuals in New York City are vaccinated, and even only 78% of those 65 years of age and older. They are simply ripe for another surge. That being said, I keep coming back to the idea of floodplain management and the importance of preparing for additional rises. You may recall in last week's podcast, I talk about how when the heavy rains come, you can't predict them. They're here. What can we do about them? We can't stop them. When this virus decides to surge, we can't stop it, but we can do a lot to mitigate its impact. The vaccines are what will ultimately rescue us from a lot of the damage we could expect to see during future surges. So just like we manage our flood plains, make sure we don't have buildings in the way of floods, make

sure we don't increase the runoff quickly into our rivers, that we have water holding capacity and also make sure that we have ways to rapidly evacuate people from a flood area if we should see an emerging flood from this new precipitation. That's kind of what our vaccines are. When this virus unleashes its power, hopefully, we've done everything to be prepared to respond to it. And despite news covering the announcement of approval for vaccines in children or mandates in certain workplaces, we still have a lot of progress to make in this area. An average of less than 1.3 million doses of vaccine are being administered each day in this country, and nearly two thirds of these are booster doses. In addition, there are still 14 states that haven't fully vaccinated more than half of their population. Even the states with the highest rates, such as Vermont, Rhode Island, Connecticut, Maine and Massachusetts, each of which have fully vaccinated 70 to 71% of their populations remain below the levels of vaccination we're seeing in some of those western European countries reporting these current surges. So for now, I think the cases will serve as an important role as a bellwether. Eventually, we could reach a point where the inevitable wave of hospitalizations and deaths that trail behind cases becomes much less pronounced. But I think case counts will continue to be meaningful for the foreseeable future in most places.

**Chris Dall:** [00:29:28] So let's talk about the vaccines. We got some new data last week on breakthrough infections with the Pfizer vaccine, on household transmission among fully vaccinated individuals, and on the impact of booster shots. So what does this data add to the evolving science of the vaccines and our understanding of how protective they are and how long they are protective for?

**Michael Osterholm:** [00:29:51] Well, let me begin by saying that if you think that my inability to predict what's going to happen with cases is a challenge, then you're going to really be in for an interesting time with this one. I will cover six different issues related to vaccines. And I will tell you now in advance, that with the most current information we have, none of these are going to be satisfying for you. So just get ready now, just fasten your seatbelt, lock in, and let's go for it. I want to start out, however, by reminding ourselves over and over and over again, these vaccines are remarkable. But they're not perfect. They're remarkable, but not perfect. The second thing I want to remind everyone is that we are living in a world of evolving science. I have to come back to this, I know for some of you, you've heard this so many times you're bored with it, but it's very important for everybody to keep remembering that had we five, six, seven years to

develop these vaccines, test them to look and see what happens over time with the immune response and potential risk for exposure and infection, we could come in with a portfolio of information that would be comprehensive and all the questions would be asked and answered. We don't have that luxury with these vaccines because of their need to be here now for this pandemic. So we're learning. And just remember that that process sometimes can be cumbersome. It's almost like watching sausage be made. But I reaffirm over and over again from a safety standpoint, we have an immense data set that provides really real satisfaction about what we know and how we can use these vaccines as safely as possible. But we're still trying to work out the piece about how do they work? What's the best way to use them? How do we take these tools and apply them? So from that perspective, I think it's really important as we look at this issue of evolving science, these six areas I'm going to talk about are only going to get more information with time. And as that happens, we will be more informed. We will be able to make more definitive statements. But in the meantime, it's not going to be a very satisfactory situation. So let's take the data first on waning immunity. As some of you know, there was an Israeli study that was just published in the New England Journal of Medicine last week looking at the use of the Pfizer vaccine in Israel. This is one that's received lots of attention, lots of comment. This study looked at the rates of COVID infection, as well as the rates of severe disease per 100,000 population in Israel during the delta wave from July 11th to July 31st. It looked particularly at when people were vaccinated, stratified by different age groups and then adjusted for confounding factors or those things that might be associated with severe disease or the vaccination. The data source included all residents of Israel who have been vaccinated about 5.8 million people, a study I wish we could do in the United States, but given our health care system or lack thereof a system, we can't do these same studies. Overall, the study found that immunity against the Delta variant waned in all age groups a few months after receiving the second dose of vaccine. With those vaccinated in earlier months, having a significant higher rate of COVID-19 infection and severe infection than those vaccinated more recently. The study concluded that protection against severe COVID for those aged 60 and over, about 1.3 million people, was markedly reduced for those vaccinated six months earlier compared to those vaccinated more recently. These data just support the sense that, yes, we do have a challenge with waning immunity. And as we look today to deliver these boosters, it's going to be unclear who will all need them. Will it be everyone? Will it be those only with certain underlying health conditions? And why will we give boosters? Is it to eliminate severe illness? Is it to eliminate

hospitalizations? Is it to eliminate even mild infections? And I think to me, the picture is becoming increasingly clear that over time, the further you get out from having had that last dose, regardless of your underlying health condition, we are going to see an increased incidence of disease and likely severe disease. So I think the challenge we have in our hands is what does this mean overall with waning immunity? I know there are still critics who think that this is a luxury to give the third dose of mRNA vaccines or second dose of J&J vaccine, given the world condition for lack of vaccine. I have to repeat again, I still believe that in fact, these are always meant to be three or two dose vaccines. And at the very least, that will be the same we will want the whole world to be able to have access to. The bigger question for me will be what happens six months from now? Will we need a booster again? If we do, how will we do that? How will we make vaccine available to the world? We're still having problems getting people, getting their booster doses now for this round of vaccination. So stay tuned. This one, I think, is a potential Achilles heel in this entire vaccine situation. And again, these are remarkable tools. They are clearly clearly preventing severe disease and deaths, but they are going to be challenged by the waning immunity. So that's number one, waning immunity.

Number two, data and transmission. A study reported this past week in *The Lancet* compared COVID transmission of the Delta variant among people with and without prior vaccination in 162 people with mild symptomatic infections. The study looked at viral load trajectories and the risk of transmission, as measured by the secondary attack rate among household contacts. In other words, by vaccination status. The peak viral load was similar for unvaccinated and vaccinated cases, but there was faster clearance in the vaccinated group versus the unvaccinated group. All breakthrough cases were mild. That's important to note, but the study also highlighted that the vaccine effect on reducing transmission is limited in the context of the Delta variant circulation. What I mean by that is the study found that vaccination reduced transmission to household contacts, but did not eliminate it. The secondary attack rate among unvaccinated household contacts was 38% compared to the secondary attack rate among vaccinated household contacts at 25%. So being vaccinated surely did reduce your risk of becoming infected in that household setting. If you look at the secondary attack rate among household contacts exposed to fully vaccinated cases, it was actually similar to the household contacts exposed to unvaccinated cases, meaning that in the end, even if you could reduce transmission, if you look at those secondary attack rates in individuals, they still have the same rate, whether they were vaccinated or not. And what this points out, I believe, is that there surely is likely less exposure to the virus from

a vaccinated person than an unvaccinated person. But does that exposure basically over time kind of get wiped out if you are in a household setting and you have the time and dose issue? So it's not a 15 minute exposure, it's a five day exposure. Does that even out? In summary, this paper found that vaccination reduces the risk of Delta variant infection and accelerates viral clearance, meaning people are less likely to get infected and are infectious for a shorter period of time. But maybe similarly likely to transmit to household contacts regardless of the vaccination status of the infected person. The study also notes an important observation in the discussion. When looking at positive versus negative, fully vaccinated contacts, there was a marked difference in the time interval between vaccination and the study recruitment. This suggests that there is an increase in susceptibility after vaccination, which the author suggests may occur as soon as two to three months following vaccination. Again, another comment on waning immunity and what does that mean? The third area that I want to cover relates to data on efficacy in immune competent versus immune compromised adults. This has been a critical issue from day one for me, trying to parse out recommendations as to what someone might have to be concerned about if they do become infected. What might be their likely outcome and how do you then proportion your risk behavior based on that particular piece of information? This is an article that was published on Tuesday in the CDC's MMWR, and it provided data on the effectiveness of the mRNA vaccines against COVID-19 hospitalization and immune competent and immune compromised adults. The data showed that the mRNA vaccines had a significantly higher rate of effectiveness protecting against COVID-19 associated hospitalizations for immune competent adults, people with normal immune systems is that 90%, and it was compared to only 77% for those who are immune compromised. The study also found that why patients are immune compromised was also very important in how well they responded. For example, the vaccine effectiveness varied across immunocompromised conditions subgroups ranging, for example, from 59% for organ or stem cell transplant recipients to 81% for persons with rheumatologic or inflammatory disorders. Immune compromised persons benefit from mRNA vaccination, but are less protected from severe COVID outcomes than the immune competent persons, and vaccine effectiveness varies among immunocompromised subgroups. This is an important piece of information that we've all along assumed and had some indirect evidence as to the fact that it existed. But now how do I advise someone who's had two or three doses of vaccine, or maybe even that fourth dose as to what they need to do for their risk behavior response? Should they, in fact, continue to keep masking under all conditions,

are they at risk if they're exposed to their grandchildren who are not yet vaccinated? Or for that matter, for any of one around in them? Who should they be around? So this is not all that satisfactory for many people who have these immune compromising conditions. I still recommend that these immune compromised individuals, particularly the organ transplants, the stem cell recipients, that they have to be extra careful about being in public places or enclosed environments with anyone who potentially could be infected. This is a real challenge, and I regret that we don't have better information on this very issue. So just to summarize it, though, these data really emphasize the importance of third doses for immunocompromised people in order to better protect them against COVID-19 hospitalization. And as the CDC has recommended recently, I think, is why these individuals should also consider that fourth dose. Now, the fourth area I want to cover is data on booster dose effect. So do booster doses actually create some level of protection that wouldn't be otherwise available? Another study published in The Lancet again from the United Kingdom. And this study compared 728,000 people had received three shots of the Pfizer vaccine and compared it to more than 728,000 matched controls who had received only two doses of the Pfizer vaccine. They found with these booster doses that there was a 93% reduction in COVID hospitalizations and an 81% reduction in deaths among those that got the three doses versus the two. I will say, however, this study may have had some challenges from study design standpoint in that they only followed people up through on average 13 days after they received their dose of vaccine, but yet they were still able to show this big difference. What would it be like in four or five and six months out? I don't know. But it surely does demonstrate that these booster doses can be very effective of not only preventing disease, but serious disease, notable an 81% reduction in deaths. The fifth study I wanted to cover is the data on natural infection versus vaccination, a point of great debate and argument. This was another study published in the MMWR on October 29th. This study examined hospitalized patients 18 years of age and older who had had COVID-19 like illness and looked just at those whose previous infection or vaccination occurred at least three to six months earlier. They found that the adjusted odds or the risk of laboratory confirmed COVID-19 among unvaccinated adults with previous SARS-CoV-2 infection were about 5.5 times higher than those who are fully vaccinated recipients with an mRNA vaccine who had had no previous documented infection. What this study really demonstrates is that, yes, natural infection does produce immunity, which can be protective. But overall vaccination is still the most important way to assure that protection. So whether you've been previously infected, whether or not, get vaccinated, and that's an important finding.

Finally, the last piece of information I would want to cover is just data on breakthrough infections. We keep hearing a lot about this. I personally have had, unfortunately far too many experiences in my personal life with breakthrough infections recently. And we do have to acknowledge they're still rare, but they're growing in number. If we look right here in Minnesota, as of November 1st, 3.2 million Minnesotans are fully vaccinated against COVID-19. Minnesota has 57,023 cases of breakthrough infection reported, 2,609 breakthrough hospitalizations, and 372 breakthrough deaths. This means that 1.8% of fully vaccinated Minnesotans have had a breakthrough infection, 0.08% have had a breakthrough hospitalization, and 0.01% have had a breakthrough death. We have to be very careful when we talk to the public about these numbers that we don't portray them as being rare. In their minds, to say that 372 breakthrough deaths have occurred is rare, doesn't sit well yet. We know from a risk perspective is that that 0.01% is in fact the number. But we're going to expect to see more breakthroughs, I really believe that this waning immunity is going to continue to be a challenge. We also are reporting more reinfection numbers here in Minnesota. In the past week, the Minnesota Department of Health has reported among Minnesota residents, more than 8,336 COVID-19 reinfections. Some have had COVID three or more times. The daily confirmed reinfections have surpassed the peak from the previous spring now. That's not surprising, given the fact that you see more people further out from their original vaccination dates. As of October 16th, Washington state has seen just over 60,000 breakthrough infections, up from over 50,000 on October 2nd. With 9% hospitalized and 568 deaths up from 493. What these data from Washington and Minnesota are telling us is while breakthrough infections are possible, vaccines are remarkable at preventing infection and at preventing severe illness, hospitalizations, and deaths if you do have a breakthrough case. So I think it's really important that we continue to understand that in fact, breakthrough infections will occur, but they should not be misinterpreted as these vaccines are failing. It's the fact that we are paying a price for waning immunity, and this is how we're going to have to continue to learn how to best use these vaccinations. Let me just conclude this piece by saying that the Kaiser Family Foundation issued a recent report that talked about just how valuable these vaccines have been, even with all the potential flaws and rough spots I just talked about. Between June 16th, when the U.S. hit 600,000 deaths and at a time when this most recent delta surge really started going, there have been an additional 140,000 deaths. Their report recently issued estimated that approximately 90,000 deaths could have been prevented between June and September with those delta surge if we had fully vaccinated our country. Think of that,

90,000 deaths could have been prevented if we had just vaccinated everyone in our country. That's a sobering number. That's what I want you to remember about these vaccines. Remarkable tools, but not perfect. So we're going to continue to work on issues around immunity. We're going to work on the issue of breakthrough infections. We're going to work on the issues of natural infection and the role of vaccination in that. But please don't forget, the most important thing you can do is get vaccinated, and that will remain the mainstay of our public health response.

**Chris Dall:** [00:48:24] So, Mike, here's a question that I'll admit, I have a personal interest in the answer to. We have a lot of people right now who are fully vaccinated, are near or at six months past their second shot of the mRNA vaccine, aren't in the categories of individuals who are eligible for boosters, and don't know when they will be eligible. So given what we know about waning protection and what you just talked about, if you're one of those people and I am, how should you be thinking about your level of protection?

**Michael Osterholm:** [00:48:52] It's a challenge, I must admit, right up front, it's a challenge. I believe that over the course of the next few months, we will see public policy continue to change from just a couple of months ago when boosters were not even really on the radar screen to where they are today. I'm convinced that within the next few months, we will see us moving towards a routine three dose mRNA vaccine and the J&J vaccine of a two dose vaccine. And I think it will cut across all ages. I think that it's one we're going to find out that waning immunity is not unique to older people. It's not unique to people who are immune compromised. It's how we roll that out. And I think the rest of the world is going to do that. And I know we'll have our concerns and legitimate concerns about what are we doing to help supply vaccine for the rest of the world. But also, what are we doing if we see this waning immunity result in more and more infections, including severe illnesses, hospitalizations and deaths? Stay tuned. I believe that booster doses are going to become more and more of a reality. What I'm continuing to look out towards knowing that it is completely a black hole right now is will there be more booster doses in the future? And what will that mean? How will we do that? Will we do that? And so this is one of those moments right now where I know less about our approach to preventing COVID-19 with vaccines than I did six months ago. And there are days I wish I was back six months ago where I was at then and could live in that bliss of ignorance of what now I know. And so we'll see. We'll do everything we



can to keep you updated here in this podcast as to what the current science tells us and what we believe is your in your best interest.

**Chris Dall:** [00:50:49] So as you noted earlier on Tuesday, the CDC's Advisory Committee on Immunization Practices recommended the Pfizer vaccine for children ages five to 11, and CDC Director Rochelle Walensky quickly endorsed that recommendation. But the hard part, turning these vaccines into vaccinations comes now. Now, let's first acknowledge that there are millions of parents and grandparents out there who are thrilled with this news. But we've already seen that vaccine uptake in adolescents hasn't been as robust as hoped. So how much of a challenge is it going to be to get younger children vaccinated?

**Michael Osterholm:** [00:51:24] Let me just make it very clear it is very important from a personal health standpoint and from a public health perspective, to get these kids vaccinated as quickly as possible. The data presented at the ACIP meeting this week painted a very compelling picture of why these kids need to be protected. We know that severe disease, while considered by some to be relatively rare with this virus, has fundamentally changed with the Delta variant presence. Overall, 94 American children ages five to 11 have died during the pandemic due to the virus, and more than 8,300 have been hospitalized. But that has changed fundamentally with the advent of Delta. During that time period of the Delta surge in August and September, COVID became the number six killer of kids in this age group. Absolutely remarkable and scary. Of the kids who are admitted to the hospital right now, over a third of the five to 11 year olds require intensive care. And it was shown that overall vaccinating these kids will also reduce transmission in the community substantially. In one study in which they presented modeling data showing how vaccinated children ages five to 11 would reduce transmission of the virus by 80% between November and next March. So I can go on and on why all the reasons why you want to vaccinate kids. The challenge has been safety, and there were data discussed there about the risk of myocarditis and how it continues to dominate the discussion. And again, in another study presented from the CDC, it was very clear that getting COVID is much riskier to a child's heart than getting the vaccine, much riskier. So in this sense, it should be every reason why a parent wants to get their child vaccinated. So I'm hopeful that at this point, we will see parents willing to do that. Now, do I think that will happen? The answer is no. And it's a challenge for me. If you look at the vaccination rates of those 12 to 17 years old, which

kind of serves us the model, what we might see with their younger sibs, only 47.5% of 12 to 15 year olds are currently vaccinated, less than half. Only 54.8% of those 16 to 17 are fully vaccinated. If you use these data and then extrapolate to what might happen with younger kids, it becomes more discouraging. The Kaiser Family Foundation has recently done a survey which roughly shows that one third of parents can't wait to get their children vaccinated in that five to 11 year old age group. About a third are kind of waiting and watching, and a third are saying absolutely not. I will be very surprised if by early next year, even 40% of kids in this age group are fully vaccinated, which will be a very unfortunate situation because these vaccines may be the critical element in preventing transmission to a grandpa or a grandma or a mom or a dad, particularly ones who may have immune compromising conditions. So we can only hope that our strategies of trying to reach out to families as to why they should get vaccinated is just like we're trying to reach out to pregnant women, why they should get vaccinated will hopefully persuade them not to wait and see, or to just categorically reject the vaccines but get them. And it will be a test of our public health and medical care systems to see what we can do to get these kids vaccinated.

**Chris Dall:** [00:55:16] Now to this week's COVID query, this one is from Dolores and it regards booster shots. She writes, "Would you be able to provide any more thoughts and analysis to inform the decisions those of us over 65 and others have to make and choosing which booster to schedule since the mix and match approach is now authorized?" Mike, I know you get a lot of questions on this. What can you tell, Dolores?

**Michael Osterholm:** [00:55:38] Thank you, Dolores, for that very thoughtful question. It is front and center for many individuals in our community today, and I hope that I can provide you a very simple answer that basically says, don't worry, you're going to be in good shape with whatever you do. Well, let me start out by saying what I did. I had received two doses of Pfizer vaccine earlier in the year, and I got my third booster dose of Pfizer vaccine. And I think that this mix and match study that was done that so many individuals have cited as providing definitive data on what to do or not to do did not do that at all. When we think about the number of people included in these studies, a little over 500 participants and looking at all the different combinations of vaccines from which one you got first, which one you got second, among the three vaccines didn't leave a lot of data for each of these different categories of what's first, what second. Now, it surely did show across the board that was without regard to which of the

additional vaccines you got, you still had a boost. The question was how much? And some people are interpreting these numbers that came out of this study as like the Dow Jones or like a temperature, an exact number of some kind of measure. We don't know what they mean. We don't have a correlate of protection. Meaning what is it that about the immune response? Which kinds of antibody? How much antibody? How much does your cellular immunity? The T cells play a role. We don't know any of that. So I think that to make a decision that somehow there was some secret that we now have discovered about how to use these vaccines just isn't the case. I continue to just follow, I think, the old rule of thumb, you know, keep it simple, stupid and in my mind, from an immunologic standpoint, I would stick with the vaccine you got before, if you can. And if you can't still get a booster, just get it and don't feel somehow that you have cheated yourself or you game the system, just get it. And if you can get the same one, do it. I think that's the best way to approach it right now, and we'll learn over time what will be the right combination of mixing and matching. And is there one that will give a preferred type of immunity that may be more durable, that may be more protective? But right now, we don't have those data to say that we just have enough data to say if you boost with any dose, you will get a boost. And I think that's what we're trying to accomplish right now. So hopefully this is the simplest of all the answers I could have given you. You know, just go with what you got. And if that that doesn't work, get what you can.

**Chris Dall:** [00:58:27] And just a note to all of our listeners, we thank you for all the great questions you send us week after week. We're sorry, we can't get to all of them, but please keep them coming. I also want to remind listeners that in addition to any questions that you have, if you find a special place of comfort or solace during this pandemic and want to share it with us, please email us at [osterholmupdate@umn.edu](mailto:osterholmupdate@umn.edu). We love hearing about and seeing the places that have helped you get through this difficult time. So, Mike, what are your take home messages and closing thoughts for today?

**Michael Osterholm:** [00:58:58] Chris, let me summarize the podcast, as I surely saw it from my vantage point today. There are three general conclusions I come away with. One is scraping off the five inches of a dried mud on my crystal ball is going to be something that I will have to do every day. And I realize that and accept that is the challenge going forward. My concern is when that mud turns into concrete and it makes it even more complicated. I want to emphasize right now that if you have others out

there who are telling you exactly what will happen more than 30 days out with this pandemic. Be careful. As I've said, time and time again, they probably have a bridge to sell you. You know what? Not one of the models, not one of those prognosticators, including myself, would have told you four weeks ago that was about to happen in the Four Corners area. Based on our experience, what we saw in Europe as well as Asia. We might have said maybe the Upper Midwest will be different than the South. Maybe the South will have their big surge and case numbers dropped precipitously back to baseline. But you know, that's not going to happen in the Midwest or at least in northern Midwest, as I just shared with you today. Something's happening here where we're flattening out. We're more like what we've seen in the UK. We couldn't have predicted that. So I think it's very important that we understand that we will continue to observe this virus. We will continue to make every effort. To give a sense of where we think it's going, but know there's a tremendous amount of uncertainty. The only thing I can say with certainty is when cases occur in any area of the world and the more people that are vaccinated, the less impact this virus will have. The surges will be in fact lower and hopefully they won't extend to nearly as long. Secondly, these vaccines are remarkable tools, but they're not perfect. I worry that we've set the world up for an expectation when they were first researched to say, look at, you're going to get 90 to 95% protection forever and ever. And a lot of people came away with that. And I can understand why. We need to be much more humble in how we talk about these. Don't for a moment back off about the fact they're remarkable. But be clear in laying out the potential limitations and what we know and don't know. And what we're going to learn. So we have to appreciate this evolving science. We still have a lot of questions about the protection from these vaccines, about how long it will last, how long will it work? How will it work in certain people who may have underlying immune compromising conditions, etcetera, etcetera? The third conclusion from this podcast, I hope, is the kids. Love them, love them, and the way you love them is you get them vaccinated. I can't say that any more straightforward than that. If you're grandparents, if you're friends, you're neighbors, you're aunts and uncles, you're godparents, please help assure that these kids get vaccinated. It's not going to be perfect. Remember, I didn't say that all diseases would go away in these kids. I can't say for certain all the deaths in these kids will go away. But I can tell you, getting these kids vaccinated is the best chance we have of protecting their lives. Not getting a child vaccinated today when you can is a lot like carelessly not caring, if in fact there are seatbelts in the back seat of your car when you're running through red lights at 40 miles an hour. You know who would do that? Get your kids

vaccinated, I can't say it enough. There are two conclusions I want to leave you with today. The first note I want to leave you on is a quote from Madam Curie. I think most everyone is familiar with her. Born in 1867, died in 1934. She was Polish and a naturalized French physicist and chemist who conducted pioneering work on radioactivity. She was the first woman to win a Nobel Prize. The first person and only woman to win the Nobel Prize twice and the only person to win the Nobel Prize in two scientific fields. She once said, "Nothing in life is to be feared. It is only to be understood. Now is the time to understand more so that we may fear less." Powerful. That's where we're at right now in this COVID pandemic. We have to understand more. And we should not fear that. And as we do understand more, we will fear less, and I'm confident of that very piece. Think about that. Finally, I want to leave you with one last verse. This plays together with the previous quote I just shared with you. I want to share with you the lyrics for a song that I've previously used on this podcast. Back on November 6th, Episode 30: A New Dialog, I shared with you the words of "Tomorrow." This song comes from the musical Annie, and it was written by Charles Strouse and the lyrics by Martin Chernin in 1977. I think it strikes the note that we all want to leave on today. "The sun will come out tomorrow, tomorrow, bet your bottom dollar that tomorrow there'll be sun. Just thinking about tomorrow clears away the cobwebs and the sorrow till there's none. When I'm stuck with a day that's gray and lonely, I just stick out my chin and grin and say, Oh, the sun will come out tomorrow, so you got to hang on till tomorrow. Come what may. Tomorrow, tomorrow, I love you, tomorrow, you're only a day away." Thank you again for joining us. We appreciate your time and again, I want to thank my podcast crew members who make this possible to do this each and every week. They are a remarkable team of people and I hope you all understand this wouldn't happen but for them. And I just want to leave you on one last note, as it gets confusing, it gets challenging as the unknown continues to seem to grow bigger than the known. It's a time where one can lead to dark and bleak places. Now's the time to have hope in tomorrow. Now is the time to find the answers so that we don't have fear and we're going to do that. Evolving science. In the meantime, that's not very satisfying if you're wondering, given my health condition, what happens if I get infected? Can I go to work or not now? Will there be breakthrough infections that might expose me? What will happen? We have a lot of work to do, but we're dedicated here, at least in this center to doing that work. I leave you with that. One last thought that, I hope, is what carries us all through the week. Be kind. Please be kind. It's hard right now on

some days to be kind, but it was never more needed than ever. Be kind. Be thoughtful. Be safe and thank you.

**Chris Dall:** [01:06:50] 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](https://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](https://CIDRAP.umn.edu/donate-now). The Osterholm update is produced by Maya Peters, Cory Anderson, Angela Ulrich, Meredith Arpey, and Sydney Redepenning.