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Hello, and welcome to the Osterholm Update: COVID-19, a weekly 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. It's been another busy week, Mike, and we have a lot to get to on this week's episode of the Osterholm Update, including a look at the muddled pandemic picture in the United States, but before we get started is there someone you'd like to dedicate this episode to?
DR. OSTERHOLM: Thank you, Chris it's good to be with you again. Yes.
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When we think of, today, about the front line health care workers, you know we often talk about the doctors and nurses, particularly those in intensive care, who are incredible heroes in this entire war against this virus, and we can never not remember, day after day, all the heroic things they do, but I think sometimes, us the professionals, myself included, forget about those support staff that don't necessarily fit into what is often seen as the professional staff as such, and that includes, I think today in intensive care, of the area of orderlies and nurses aides. Who, anybody who knows what goes on inside a hospital or a long-term care facility, know that they are often the backbone of every response that occurs, they're the ones that are there, in some very tough jobs,
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and so today I dedicate this to all the orderlies, nurses aides, and the staff who provide the kind of care that doesn't often get captured when we talk about the heroic doctors and nurses who are in our facilities. So today, this one's for you.
CHRIS DALL: So over the past week there's been a rising concern over the surge of COVID-19 cases in states that reopened early. States like Arizona, Texas, and Florida are among the more than 20 states where infections are rising, but we haven't seen an increase in some other states that reopened early, and cases are actually declining in several states. What's going on?
DR. OSTERHOLM: Well, if I could answer that question with accuracy and precision, I could probably hang up my shingle and say, "I'm done for the day." It is, at best, very confusing, and this is one where I'm a little concerned that I see people getting, I think, too far ahead of their headlights, or at least over their skis, in terms of trying to come up with answers of what's happening.
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Let's just take a step back and think about what we're seeing. Right now in the United States, if you look at the 50 states and the District of Columbia, we have 20 states where cases are increasing over the past seven days in measurable ways. We have 11 where they're actually staying the same, not changing over the past seven days, and we have 20 where they're continuing to drop. This is almost the Tale of Two Countries, and it's not just isolated to one geographic area, although the south and the west seems to be, by far, more affected than the rest of the country, and to even give you some sense of just how confusing this has been, is that

if you look at June 1st, two weeks ago, on the seven day average, which is a better way to look at this.
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You take the last seven days and average those numbers, because we get these peaks and valleys that sometimes, just within a week can give you very different data. If you look at June 1st, we reported 22,238 cases per day on average. If you look at the cases as of June 15th, for that same seven day average, it's 22,351. So the only difference is less, a little more than a hundred cases. Hasn't changed. If you look at deaths on June 1st, again, seven day average, there were 1,019 deaths per day in the United States. If you look at June 15th, it's now 747, a reduction, on average, of almost 250 deaths a day. Now, if you look at those numbers you'd say, "Well, it looks like it's pretty flat. The deaths are coming down," although we know that they reflect activity that usually is anywhere from two to three weeks before that in terms of transmission,
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and you'd say, "Well, it's kind of like what we're seeing in the country. 20 up, 20 down, 11 kind of, you know, just level," and yet, where we see the cases increasing, places like Florida, Texas, certain places in North Carolina, they are really almost on fire. There is really substantial transmission occurring, and I think that what this reflects again, is our lack of understanding of what we're dealing with with this virus, and we just have to be honest and say that. We don't know. We put forward, several months ago, our scenario planning document, in which, if you go to The CIDRAP Viewpoint, you'll find it and it lays out how are we going to get from that five percent of the population that have been infected to the 60 or 70 percent that likely will be required before you see herd immunity kick in, or the slowing down of transmission,
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and you know, we lay out scenarios, no models, because i don't think there's any models that statistically can tell you what's going to happen, but in those scenarios we include two different coronavirus scenarios. Something that we just made up, because no one's ever seen a coronavirus like this do what it's doing, and we said, "Well, what if in this case the pandemic coronaviru was actually just in slow burn. Just keeps going, week after week, month after month, and what would that look like?" We also said, "Well, what if it's more dramatic than that, but you have these peaks and valleys, almost like the foothills, where basically one month it may be more prominent in one region of the country or one country in the world, and then next month it's this one over here, and it's that country over there,
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and, but the key thing is it just keeps marching along accumulating new cases, serious illnesses, and deaths, and trying to get towards that 60 to 70 percent level we talk about." We didn't know. We said, "Well, what if it's a virus that ends up acting like a pandemic influenza virus, where we do have quite good information about what they typically do when they arrive." Often in the first wave, and I'll define that in a moment, you'll see sporadic cases, and what I mean by that, not that they were just a few cases, some areas got hit quite hard, but it was not widespread throughout all the countries, even within states, and then if you look at those, typically they lasted up to several months, and then for reasons we have no idea why, basically the cases begin to disappear. There's very little activity. This is what defines a wave.

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It's when you have an increase in cases, with a trough, where the cases, on their own, not a vaccine, in some cases you can say not even an intervention, just literally disappear. I just can't emphasize enough: we don't know why. Then they come back after two or three months, in some cases with a vengeance, like we saw in 1918. Even in 2009 with H1N1, if you go back and look at those data, for the emergence of this virus in March into April, early May, and then we saw the case numbers decreased substantially, went through much of the summer without major activity, and then only in late August did we see a big uptick in cases, with a very large second wave far exceeding out of the first wave, that lasted from the end of August until basically the middle of October, well before vaccine arrived and had any impact, and remember back in 2009, we weren't telling people to social or physical distance.
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It was one of those situations where this is just what the virus did. We don't know why it did it. We did not have control over that, and so one of the challenges we have here is what's happening here. How much of it is what we're doing to basically reduce the virus activity in our communities? And I have no doubt, and I think the data will bear this out over time, that in those areas that have been on fire, it was really only through the physical distancing activities that it probably shaved cases off the top of that curve, that could have very well taken that event over what I call the case cliff, where there are more cases needing ICU care than are beds or staff available, and that's what we want to avoid at all cost, at all cost. So, you know, I look at this on an international level, and you see, what's happening right now. First of all in places like China, and I know we'll talk more about that later, but we're seeing resurgence of the virus there where everyone thought they had it under control.
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When we look at the hot spots right now, you know, we will, we're waiting for more data, but what we have right now suggests that New Delhi, India may be the hottest spot that's been on the earth, meaning exceeding that of Wuhan, New York City, the Lombardi region of Italy, Madrid, I mean, London, really a substantial activity going on there right now, and just two months ago everybody was saying, "Well, whatever India is doing,they're doing it right, because there's no activity here." We're seeing cases in Brazil that are, in some ways, almost like that that we're seeing in India right now, and I can go through the laundry list of other places. So the virus continues to move around the world, I'm not so sure that this still isn't all a first wave. Meaning that it's just an accumulation of different cases, different times, different places, but ultimately could result in what we would see in like 2009, or 1918.
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Time will tell.This is one where, again, I'm sure glad I don't get paid for being right, because I don't know what right is here. It's more a matter of what we know and what we don't know. So, I urge everyone who's listening, if you have experts out there telling you exactly what's happening, where it's going what will happen, I would urge that you probably not take into consideration much of the rest of their information, and I think also this situation really helps us understand the kinds of predictions I've made in the past. You may recall on this very podcast I had to address several times people who were adamant about the fact that there would be a summer reduction in cases. The seasonality would kick in. Some of the more prominent experts

said this. Well, I got to tell you right now, if you're in these 21 states that are getting hot, if you're in parts of the world right now where you're seeing this increased transmission, there's nothing here that would suggest to you that, in fact this is a, you know, seasonal virus.
12:00
It's defying all of that, and so humility is the word, intense study is a word, or words, for what we need to do here, and you know, we'll know a little in a few weeks. I think that frankly I may be ready to move my metaphor from second inning, to third inning, and maybe even quickly through fourth or fifth, depending on what we see over the next month. I think we'll know if we're going to have a wave. If we are, what that likely means. If we're not gonna have a wave, that'll be borne out too, and that will tell us then, more what it is that we're likely to see for the next 6, 10, 12, 18 months.
CHRIS DALL: I want to read to you a quote from Christine Petersen, an epidemiologist at the University of Iowa that I think speaks to the mood in the country right now. She told the political news website The Hill, quote, "I don't think there will be new shutdowns.
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There isn't the political will to do it any longer, it seems. Now we're in the pandemic wild west." Do you agree with that?
DR. OSTERHOLM: Well, I think that Christine's observation was very astute. She has put her finger on the pulse of America, and for that matter, I think, many parts of the world. I have to remind people constantly that, you know, we're just at the beginning of this situation. We're not anywhere close even to the middle. It was interesting. I was on a national talk show this morning, and I'd been on this show multiple times. I've talked over and over again about this five percent to get to 60 or 70 percent, and one of the interviewers who's been on with me in previous ones when I said that this time, he said, "Wow that's eye-popping!" He said, "I think people are really going to pay attention to that," and I thought, well, you've heard it multiple times from me before, what finally hit home?
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And this is a very bright individual, and I appreciate his observation of it, but I don't think people really have understood what this pandemic means. They thought that this was going to be like a Minnesota blizzard, not a Minnesota winter. If we just could get through the next two days, everything will get plowed, all the roads will be open, all the venues back, you know, not a concern, and they've planned for it that way. They've anticipated for that way, and so they were ready to get that blizzard over with. When in fact, we're in a very, very long Minnesota winter right now, and this just happened to be the first late October blizzard of the long winter, and I think that what we have to figure out right now, is how do we better communicate to the public that this is the case, particularly when we have those in public leadership positions who will continue to say it's over with, you know, we're in recovery, we're about to, you know, get out of this mode, the post pandemic era,
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you know, we're going to have vaccines, we're going to have drugs, etc, etc, and you know, we don't want to tell people that they're in the beginning of this, just for the sake of telling them that, upsetting them. It goes to the very heart of how we're going to get through this. As a society, as a world, and it's going to mean that we have to understand the reality of what's before us. I have

found over and over again in all my years in this business that people can take hard truth if you just tell it to them with all the honesty, all the information you have so that they can understand how you got there. Then they can get through almost anything, because they're not surprised. They're internalizing it, and this is, I think, when sometimes the human spirit is the very best.
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It's when you mislead them, or tell them it's going to be different, and it's not what they are told, that's when I think you have people who then have doubt, and when they have doubt they become hypercritical, which they surely should, and that's what leads them to distrust, and so what we need to do right now is help share that sense of where things are at, and I think that Christine's comments are right on the mark for right now. I think she's right on. My concern is how do we help change that, and I don't know what the shutdowns or lockups or you know, all these things we call, you know, the society being limited in what it can do and where it can go, but I do know that we are going to have situations that will occur with this virus that could far, far exceed anything we've seen. You know, I've said it enough times, but maybe it'll be ear-popping, eye-popping I don't know which,
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but the matter of fact is that for five percent of the population having been infected, think how much pain, suffering, death, and economic disruption we've had, and we have to understand that we got a lot more to go, so that means we have to harden our result. We got to start planning. So, what are we going to do? You know, I worry, again, as I've said time and time again if we have another big wave, or we see a substantial increase in cases around the world, our PPE supplies are going to be further drawn down. I mean, I sit here today at this particular recording, and at least 680 American healthcare workers have died as a result of their COVID infections. Now we don't believe all of those were acquired at work but largely, the majority, if not up to two-thirds probably were.
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Now think of that if this were army, military, police, any number of people that were in harm's way, which they are every day and that kind of number occurred in that group. You know, there would be an all-out investigation, what can we do, how do we deal with it, and I almost hear nothing but a whimper about all these healthcare workers who are giving their lives to help take care of us, That's why we can't let this pandemic go on. You know, in the sense of saying, "well, we're not going to lock down again," or "we're not going to do this," because when we overrun our healthcare systems, we do increase substantially, not only bad outcomes for the patients, but also for the healthcare workers who work there. So I think, I would like to invite Christine to work with us, in her astute comments, to say, "You're right, but let's not be right like that forever. What can we do to engage the public, knowing that there will be a sizable number of people who will disagree, up front, that this is even a problem?
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Who will disagree that any kind of intervention we use is far too much, and that we're damaging not only the economy, but society, which frankly I agree with, but we've got to find that way to thread the rope through the needle," and so one of the things that we're going to be doing in the near term, for CIDRAP, is actually we're developing a set of scenarios, where we will describe in very plain language exactly what many of us are thinking about every day. Is it safe for me to go

to my kids house this weekend for father's day? To actually have a picnic with my grandchildren who I've not seen since March, just because of this problem? And if I do, what are my risks? I'm an old man. What are my concerns about if I get infected? What if I should bring it to them? Although, I've been sequestered so hopefully that's not going to put me at increased risk to transmit to them, and what we're going to do with these scenarios is then play them out.
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You know, can I go to a restaurant for dinner? And just say, what do we know about the risk? What do we know about what you can do to reduce that risk? And how do you want to relate to that risk as it, as an individual? Meaning, am I at increased likelihood of having a severe illness if I get this? You know, what are my risk factors? And so, hopefully, that will also help lay out the reality of what people will want to do, or not want to do, and help maybe soften that wild, wild west issue of the pandemic.
CHRIS DALL: Well look forward to discussing that work from CIDRAP more in future podcasts. I want to get back to China which you mentioned earlier. So Chinese health officials are now investigating a cluster of new infections in Beijing, the first in more than 50 days in that city, linked to a large wholesale market, and just today, in fact, Chinese officials imposed what they're calling a soft lockdown on the city in response.
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As you've noted, we've seen this pattern playing out in places that seem to have the virus under control, does this surprise you at all, Mike?
DR. OSTERHOLM: You know, I have to be a little bit, how should I say introspective, here, because it's one of those things where I don't want it to come off like "I told you so," but I'm sure you've already thought that. The fact of the matter is that we've been talking for months about if you believe that some place has the magic bullet, if you believe that some place has found the way to respond to this virus such that it won't come back, just wait a couple weeks, and what we have here is a situation where there is likely no country in the world that has more control over its population, in terms of their movements, in terms of their monitoring, in terms of the sampling that goes on to look for influenza, and looking for coronavirus,
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so they can distinguish between the two and actually know what's circulated in their communities, and yet look at what's happening in Beijing right now, as of this time right now there are over 106 cases. They're concerned that it has already spread in other locations, that they are not yet well aware of. Do I think that they're probably going to get a handle on this? I think they will. It's remarkable what they can do, and how they can lock people down, how they can mandate testing, and restrict movements. So I think that this will happen. What I'm a little bit concerned about is something I think that's starting to develop here, which will be a terribly unfortunate in result of this particular situation here, that is the public health officials in China actually did some sampling in the market looking by PCR for virus activity, which, of course, as you and I both know is not the full virus,
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PCR just denotes that there's genetic material from the virus there, and they actually found a positive sample in the market on salmon that had been imported, as we understand it, from Australia. That initially was shared with the idea that "see, it wasn't from us. It wasn't our fault. It

was imported back into China." You know, which is, in a sense, almost a kind of a way of saying, "don't blame us this time," and I worry that the inference it'll come across is that somehow food is involved, and that would be a real shame because we already have people who have a fear of this virus that is not at all commiserate to how it's transmitted, but rather they're worried you know about the environment, anything that you know is a surface is therefore likely a virus culture dish, and so I think that I just want to emphasize to the audience here that there is no reason at all to believe that food is involved,
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that it could very well be a sneeze that landed on that, and even then if you consume that salmon raw, the likelihood of getting infected from that is still very, very, very, very low, and what we have to do at this point is understand how this virus got there. They're going to be doing the genetics on the virus to try to place it into some context of what source might have been responsible for it but I think the real message is number one: Beijing is an example of this virus is a leaky bucket virus. If there is one microscopic leak in that bucket, it'll find a way to get out, and it'll come get us. I even have to raise the issue, and again to their credit, I'll have to say this, we had an event that happened the last several days in New Zealand. You know, just over the past two weeks we've touted the fact that, you know, they've done everything they can to eliminate the virus as an island country, a little over 5.2 million people.
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You know, it's much easier to protect your borders that way, and control who comes in and out, and what you can do to stop the virus transmission. There was actually two individuals from London who had come to New Zealand for the purposes of visiting a dying person, and the government officials allowed them to get out of quarantine early to make sure that they made it. They had to drive five hours across New Zealand to get to this location, and only after they were gone, and at the location of this person who was dying, did they find out that they were actually infected, and, you know, hopefully everything that they've done in New Zealand will continue to contain this virus, but here's a country like New Zealand has to be on guard 24/7, and so I just want to point out just how challenging this is. We can do a lot better in this country than we're doing, but when you have the sizable numbers of cases we have contact tracing and follow-up is just going to be very, very difficult.
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It's one thing to think about planting your petunias in a three mile an hour wind. It's other things about thinking about planting those same petunias in a force five hurricane, and I think that, you know, right now trying to control this virus in places like the United States, is a real challenge with the terms of numbers of people who are infected, who need follow-up, et cetera, and so we'll have to see where all these go, and next week we'll report again on what's happening in China.
CHRIS DALL: In the WHO's press conference on Monday, the WHO Director General warned that the COVID-19 pandemic is creating challenges for global flu surveillance. I bring this up because you co-authored an article in Science last week on the potential of a fall surge in COVID-19 cases coinciding with the flu season. What's the main takeaway message from that piece?
27:00

DR. OSTERHOLM: Well, another common theme here with COVID-19 and influenza: we don't know what we don't know. In this piece that Ed Belongia and I did in Science, we do talk about how can we prepare for this convergence of the two? It is likely going to happen. We're trying to get as much information as possible right now from the southern hemisphere, particularly in places like South Africa, where we're seeing a substantial number of cases of COVID-19, as well as potential for influenza. New Zealand and Australia, which often contribute information, as well as South America, we're not getting much in the way of influenza data, per the fact that it has been such a major effort around COVID-19, but there are a few things that we have to be mindful of.
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If, in fact, we do see both circulating, we want to understand what kind of testing should be done, so that we can appropriately treat influenza which we have drugs for that should someone be infected could be very important in keeping them from having severe disease. We also want to make sure that people understand that getting vaccinated for influenza this year is probably as important as you've ever had. You know, we don't know how effective the vaccine will be. You know, we some years get not very good or great protection, some years we get moderate protection, but every year we virtually get some protection, and that's important that people should get vaccinated, but how do you bring people together to get vaccinated if it's in the age of COVID where we're seeing so much transmission in communities. Do we want to bring people together in that kind of setting? And so one of the things we need to be really thoughtful about is: when and where and how do we vaccinate the public for this vaccine? This is going to be an important consideration.
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The other thing that we have to do is best respond to what has been a growing misinformation campaign in social media that indicates that influenza vaccines increase the risk of SARS-CoV infection, and there is absolutely no data to support that, and yet, if you look on social media it has really taken off. So, everyone who's listening to this podcast: please know there are no data, and we've looked for anyone that would suggest that a influenza vaccination will make your SARS-CoV infection more severe should you get it. So one of the things we're going to be looking at very carefully over the course of the next months is just trying to develop the kinds of recommendations that one, facilitate influenza vaccination in a timely and safe way, number two, is that if we do have close circulation during the season, how can we best target getting effective drug treatments to the people with influenza,
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since there is something we can do about that one early on, and three, just trying to understand what kinds of impacts does SARS-CoV-2 virus and influenza virus infections have on each other? What does it do? We'll not know, and this is going to be one of those challenges where we may not even see flu virus transmission. They may actually get cancelled out like we've seen when a pandemic strain of influenza comes along and cancels out other influenza strains, or it could exacerbate it, and make it worse. We just don't know.
CHRIS DALL: In our previous discussions about masks, one of the issues you've covered is aerosol versus droplet versus airborne transmission of SARS-CoV-2. Where are we in our understanding of how the coronavirus is transmitted?

DR. OSTERHOLM: Well, I think one of the things that I have come to appreciate and learn that there are always those hot button items in public health and medicine,
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if you get five professionals in a room you can probably get seven different opinions on what's going on, and this is clearly one of those areas where, you know again, I have no claim on expertise here. I would never consider myself an expert on aerosol science. You know, I've taken graduate classes on the issue of industrial hygiene and air and so forth, have surely spent a lot of time with people who do specialize in this area, but I find the challenge is that so often we have misunderstandings about what people are talking about, and it's because there is a confusing set of definitions that depending on which organization you're talking to or with, you may find very different meanings for those same definitions.
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So the concept, for example, of whether we're talking about airborne contact or droplet, and what that means, sometimes means something very different to different people, and so one of the suggestions that came to me here through listeners is they'd like more information on how can I learn about this? What can I understand? And you know, I'm not going to spend the time today to go through an entire lecture from a novice on aerosol transmission infectious diseases, but I have a series of three articles that will be in our reference list that I think you would be well to go take a look at if you have more questions or issues, because they do really provide a good framework. One of them is by Rachel Jones and Lisa Brousseau, from Lisa's from CIDRAP now,
and it's called "The aerosol transmission of infectious disease," and it's really a very nice overview of what do we know about the issue of airborne contact and droplet transmission,
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how different viruses in particular actually are transmitted and what the implications are for understanding this combination. There's another article including from Jan Gralton and colleagues entitled "Respiratory virus RNA is detectable in airborne and droplet particles," and really describes more, here, of the kinds of transmission considerations, and what it might mean to actually have, in this case, virus RNA and the implication of virus itself in these drop in these airborne and droplet particles, and then the final one is just understanding how we generate aerosols and droplet particles, and this is an article by Lindsley and colleagues, and it's entitled, "Quantity and size distribution of cough generated aerosol particles produced by influenza patients during and after illness,"
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and none of these are heavy reads. I mean, they're, if you're not as aerosol particle technology expert you can still read these and get a lot out of them, so I would urge from a homework standpoint as we have these discussions about mass respiratory protection, you know N95s versus surgical masks, versus cloth face coverings, what can we ascertain from what we know about how viruses, in this case the coronaviruses, are likely transmitted. I think this would be very helpful. So, we can discuss these more in another episode, but I think right now those three papers on our resource list that accompanies this podcast I think will give you a good opportunity to really understand some of the definitions and some of the issues behind the science.

CHRIS DALL: CIDRAP has begun an effort to better understand infectious dose of SARS-CoV-2, and how it informs our decisions about exposures and controls for preventing SARS-CoV-2 transmission.
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What is that effort going to entail, Mike?
DR. OSTERHOLM: Well, I'm very excited about this, you know, I'm kind of one of those people, that I always say, you know, either kind of put up or go home. Okay, you know, you all know, on this podcast I've been raising issues around the relative effectiveness of respiratory protection, and what we need to do about it. Well, one of the challenges is, what do we know, just in general, about the transmission of the SARS-CoV-2 virus, and how does infectious dose and issues related to exposure, including the actual concentration of the virus and say, for example, air in your exposure time?
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So, in that way, Lisa Brousseau, who I already referenced here, and myself, really initiated an effort to best describe what the current data that exists in terms of the infectious dose of SARS-CoV-2, and how to estimate and inform our decisions about exposure? What does it mean to go to a grocery store? What does it mean to ride in a car with someone? And then really, what can we do to control that exposure, in terms of preventing disease? And so what we've done is we've invited 19 leading experts in respiratory protection, industrial hygiene, virology, infection control, and dose response modeling to participate in an effort we're putting together. Right now we're very actively involved. All 19 experts have fully agreed to participate. They're from around the world, and what we're doing right now is identifying and reviewing all the scientific data that addresses the concept of infectious dose, and the role it may play in respiratory transmission of SARS-CoV-2.
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While we don't know what that dose is yet, we're trying to understand it from other similar respiratory transmitted viruses like H1N1 that caused the pandemic of 2009, and as well as animal studies in SARS-CoV-2 that have been conducted already in terms of vaccine challenges, and so forth, and we have already an organized set of questions that we're addressing as a group, including what does the public need to know about infectious dose that will help them better understand potential exposures and how to minimize them? So not just a matter of, "tag, you're it!" in a model, where two roving buttons bump into each other, but what do we really know about what it's going to take to get infected, and you know one of the other things we're trying to do right now, is identify what information that is available and what information do we still yet need to generate to understand what an infectious dose for SARS-CoV-2 is,
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and then from that perspective we're trying to, then in a sense, model, meaning to actually then take these data and say, so given different concentrations virus in the air, that might be reasonably encountered in a public setting, what are the interventions or control measures that we can look at and understand how well they work, whether they be face coverings, masks, or respirators, or you know, dilution ventilation barriers, such as the plexiglas we're seeing, physical distancing which always is important. Physical distancing is the one thing I have to

emphasize over and over again. It's the one thing you're in most control of, and it's the one thing that'll make the biggest difference. So, I'm really excited by this effort, I'm very appreciative of the people who agreed to participate when this comes out, and you see the names of these people.
39:00
It's names that are very familiar now in terms of in the public eye, with regard to respiratory protection, and this will be, you know, as unbiased and as comprehensive as we possibly know. This is exactly what I was calling for in a previous podcast I did on masks. You know, we just need the data. This is not about being pro or con. This is not any of that. This is just, help the public understand. What is my risk? Under what conditions can I change that risk? And how can I be in control of that risk? And so, we hopefully will have the kind of information that will really help the public, and we will get this to you as soon as possible. We're clearly working on it right now. I think we actually have a call in two days at 5:00 A.M here, just so we can make sure that our Asian collaborators are all on the call that day.
CHRIS DALL: As always we've received a ton of great email questions this week, Mike, and the one we've selected is about vaccines.
40:00
Earl writes, "I know your position is that we most likely won't have a vaccine for COVID-19 in the near future. We hear a lot about companies or institutions in phase two or phase three of clinical trials for a vaccine? What do these phases exactly mean and what is the approximate time necessary between phases to safely judge a vaccine's effectiveness? And do you feel that in the rush to find a cure, that these companies are not following proper protocol?"
DR. OSTERHOLM: Well, thank you Earl, for that very thoughtful question. The only challenge is that could be worth a podcast unto its own as a question goes, but it's a very important one. Right now, I think the public is quite confused about what's happening with these 120 plus vaccines that are all in some form of consideration or research for protecting us against SARS-CoV-2 infection, and when we talk about clinical trials, many people don't really have a sense of what this means.
41:00
You know, it's not quite like baking cookies or, you know, washing your clothes where you kind of can know step one through the final process, and so it is important to understand what's happening. When you ask the question, "how long will it take?" This is one of the areas where there is such an urgent need, that the efforts are going, and I would say with all honesty and unprecedented velocity, in terms of trying to find an answer. Now that doesn't mean that they are unsafe. It doesn't mean that we're you know going to skip over potential signals would say that there's a problem. That could happen, but we've got to guard against that. What it's saying is that, you know if I can double up on things, if I can be making more vaccine before I ever prove that it works, which financially is a big hit if it doesn't work, because then you just basically have to throw away the vaccine, but you, for a sake of a crisis you'll do that, is going to cut down a lot of time.
42:00
We'll be able to shave time off. It's not unusual for some vaccines to go many years between the time that they start getting into early trials, and before it's licensed and available to the public.

Every effort here is being made to get it as soon as possible, and I do believe there is an emphasis on safety. Now you ask, what are these phases? Well, there are basically four phases to clinical trials, as deemed by the food and drug administration, EMA, the European FDA, and how they evaluate and regulate products. Phase one, is really a, what I would call, "assess safety study," and to get some early immunogenicity data, meaning if we give somebody this vaccine, what happens with antibody?
43:00
Often this is done in an animal first, before it ever hits a human, to see if they make some kind of antibody, or have some kind of immune response that would suggest that it has the potential to work. Also, did it kill the animals or not? Well, you hope if you vaccinate five, ten animals, it doesn't kill them, because that right there says, "oh, we got a problem," and so, phase one can involve humans also. Phase two, which is where we're at now with some of these other vaccines, is really looking at more expanded safety, in terms of the number of people enrolled, and also looking at dosing and preliminary effectiveness. Meaning that you may have some data that someone did or didn't get infected, who was in this phase two trial. What this is really, is kind of that middle place. You got enough data now to know that there's something possible here, but not enough data to say, "Do I go to a large clinical trial?" which can be very, very expensive and challenging,
44:00
and so this is kind of that mid-call, and this is going to be a very important point here to decide how do we move vaccines on to phase three, which is really looking for definitive safety and definitive effectiveness, and this can be a challenge, because safety is a relative term. What if something happens one out of a thousand times or one of the ten thousand times? How many times you have to be vaccinated in the population before you're going to pick up that particular event? So, if you're only testing and sampling among a thousand people, and it occurs once every two to five thousand, you may never pick it up, and so what we have to look at is just what the anticipated side effects could be, and how we would account for those in the study size. The second thing that's a challenge, and this happens unfortunately almost as if it's one of those omens about the vaccine world,
45:00
is if you vaccinate a population you obviously have to have disease in that population to determine whether it works or not, and you don't want to have any disease at all, but on the other hand if there's more disease in that population, the faster and more likely you are to learn did this vaccine work or not? So if you vaccinate 10,000 people, and it turns out the disease has just disappeared and there's only two cases in the entire country the next year, you're not going to be able to show anything about did that vaccine work or not. On the other hand, if you only vaccinate 100 people and half the population gets the infection in the next six months, boy you may have a real chance of showing the vaccine really worked, and so one of the challenges we have is doing vaccine trials right now is when and where do you do them? You know, we've already talked about the fact that there's big differences in case numbers in the United States right now. Well, what if you put all of your vaccine effectiveness study locations in the states that just happen to have few cases right now, or you put them in an area where they're on fire?
46:00

That's going to have a big impact on how fast and how complete the information will be in a certain time period, and so phase 3 trials can be very, very expensive, very difficult. Phase 4 trials typically are monitoring studies, where they're collecting the information continuously on vaccine usage, they're constantly looking for any adverse events, and they're trying to measure long-term immunity. This is going to be a critical issue with this vaccine. I don't want to wait to get a vaccine licensed, if I can show that after six months there is immunity there that protects me against this virus. Boy, would I love that to be 60-year immunity, 20-year immunity, heck, I'll even take two years immunity, but the bottom line is we won't know and we can't wait five years to find out how durable this community is before we license this vaccine. So one of the things we're going to be studying is, if in fact it does get licensed, how long does it last?
47:00
That's going to be a critical issue. So, and safety is going to be another important piece, you know, if we're vaccinating thousands of people, what if again, the side effects occur at a rate such that we might miss those signals about a problem, and how that works? Now, I will say at that point, you know, if you have a vaccine that has an adverse event rate of one per million, but if you get vaccinated, it'll save thousands and thousands of lives for that same million. I mean the trade-off has got to be obvious, you know, no medical technology today is perfectly safe in a sense, and so we need to look at that, so we'll be following that up too so to your very good question we have a lot going on. Now, one of the issues that we're also looking at is, how are these studies being coordinated or collaborated with, meaning that we've got these hundred and twenty some vaccines, we've got the World Health Organization involved with a number of vaccine trials,
48:00
we've got the Chinese government involved with vaccine trials, and we've got the U.S. government, and within the U.S. government we have two different locations. We have what been called Operation Warp Speed which is largely a White House Department of Defense vaccine effort, and we also have what's called the Accelerating COVID-19 Therapeutic Interventions and Vaccines Project within the NIH itself to help move this along. We're all trying to figure out what kind of collaboration, cooperation will help here. You know, we've already seen the FDA, I think misfire on the oversight of testing reagents, kits. You know, we need them to be helpful with the vaccines, but not so helpful as to miss their responsibility with oversight to make sure that they're safe.
49:00
A lot of us will be looking at that very carefully, and then we're gonna have to again, come back to asking hard questions about how will these vaccines get made? Who will have access to them first? Do we have the tools to actually make and deliver vaccines? And what I mean, I don't assume, I don't mean just the machines, but just simply glass vials? Already the world wants these glass vials, not just the United States, whether you're in China, or whether you're in Europe, wherever, and countries are now banking and getting millions and millions of doses, should have vaccine become available. Well, wouldn't that be horrible if the one thing we ran out of was glass vials or needles, and that's being looked at right now but I can tell you those are going to be challenges. You know, it would be terrible to have vaccine we can't deliver because we don't have those tools. So we have a lot of work to do, you know I think it's going as quickly

as possible, I have, you know, from my perspective, I'm not seeing to suggest that safety has been an issue.
50:00
I would welcome the fact that the manufacturers spend less time doing public relations announcements with their data, and actually give us the data in manuscript form, showing us what they really have and letting us as a scientific community look at that carefully. I always regret when it's a press release that brings the information out. We've already seen what happens with that, and how fragile those kinds of pieces of information that get everyone's hopes up can be.
CHRIS DALL: So, speaking of news put out in press releases, we had some news out of the United Kingdom today from the RECOVERY trial, which is a large randomized clinical trial with various arms looking at different COVID-19 treatments, and investigators noted a news release, that a cheap widely available steroid, dexamethasone, reduced deaths by a third in ventilated COVID-19 patients, and about a fifth in patients who needed oxygen.
51:00
What do you make of this news, Mike?
DR. OSTERHOLM: Well, having just commented on the problem with press releases and the challenges that we have in interpreting data, I also understand the need to get data out quickly to try to impact on outcomes, but I would rather not see it released like this. I think it would be better to get a very quickly prepared peer review paper that at least allows us to have a better sense of just what do these data mean. We've already been there before, you've seen that with hydroxychloroquine issues, and where we've been. So I think this is a potentially helpful improvement, but again having been here before and seeing, you know things that were supposed to be blockbuster kinds of changes not necessarily being that at all, it would be ideal if something like this could really help this much for ventilated patients. Remember this is a very small sub-segment of the overall number of patients who get COVID-19,
52:00
but yet nonetheless it's the one where people die, so if you could really reduce deaths by one-third in ventilated patients and by one-fifth in patients just receiving oxygen, that's got to help. Now, ironically one of the things that we would like to see here, is what does that do for hospitalization? Meaning that, from a planning standpoint, these patients may not only survive, but they will survive longer in intensive care, meaning that now we could see additional burden intensive care because instead of dying in six days, you stay alive for 14 days before you get out. That's a good thing, don't get me wrong, I want to see people survive, but now we have to ask ourselves if this were to happen what would this mean for our patient numbers in ICU care requiring these beds, and I didn't see anything on that in this press release, but it's one that we really need to understand what what that did to their patient population.
53:00
CHRIS DALL: So, Mike any thoughts you'd like to leave our listeners with? Any musical suggestions that you have, as you've had in the past episodes?
DR. OSTERHOLM: Well thanks Chris, I think the listeners here have become probably expecting me to come up with a little music here, this is one of the challenges I want to

offer to the group here, okay, the question of the of the week has been really helpful. Thank you, by the way. The questions we're getting have been remarkable. Numerous ones. We try to read them all and talk about them, and this has been very helpful, and it helps us understand what you'd like to have us cover, so now I'm going to challenge you to the songs, or even poetry that might end up framing the end of these podcasts, and this one, you know, we're still in a lot of hurt in this country, after the past several weeks, and rightfully so,
54:00
and also we're in that place where we're trying to navigate COVID-19 in such a way that, "what does this all mean? You know, what are we supposed to be doing? How are we supposed to be doing it?" So I have a song here that, again, has meant a lot to me in my my past, it was written in 1969 by Curt Sapaugh and Bobby Austin. It's been recorded by more than 11 artists, but the artist who really made it was Glenn Campbell and his 1969 hit was "Try a Little Kindness," and the lyrics go, "if you see your brother standing by the road, with a heavy load from the seeds he sowed, and if you see your sister falling by the way, just stop and say you're going the wrong way. You've got to try a little kindness.
55:00
Yes, show a little kindness, and shine your light for everyone to see, and if you try a little kindness, then you overlook the blindness of narrow-minded people on the narrow-minded streets. Don't walk around the down and out, lend a helping hand instead of doubt, and the kindness that you show every day, will help someone along their way. You've got to try a little kindness. Yes, show a little kindness. Just shine your light for everyone to see, and if you try a little kindness, then you'll overlook the blindness of narrow-minded people on the narrow-minded streets." I can't think of a better way to say it. So I again challenge all of you on this podcast, for your acts of kindness. Our epidemic is going to take over this pandemic, before long we'll just keep doing at it, so please be kind today, tomorrow, until next week, and again, thank you so much for joining us. I know you have many other options to get your information from, and the fact that you spend some time with Chris and me is really a gift to us.
56:00
So, thank you very much.
CHRIS DALL: Thank you, Dr. Osterholm and thanks for listening to the Osterholm Update: COVID-19, a weekly podcast from the Center for Infectious Disease Research and Policy. We'll be back next week with another episode. Until then, you can keep up with the latest COVID-19 news by visiting our website: cidrap.umn.edu.