TURNER:

Hello, and welcome back to Wisconsin Law In Action, a podcast where we discuss new and forthcoming scholarship with University of Wisconsin Law School professors. I'm your host Kris Turner, and today we have a very special guest, Professor Alta Charo is the Warren P. Knowles Professor of Law and Bioethics at the UW Madison Law School, and has written over 100 articles, book chapters and government reports on law and policy related to environmental protection, reproductive health, medical genetics, stem cell research, I could go on and on about all the different expertise and areas that she is involved in. She has also served, volunteered, advised and [inaudible 00:00:46] to work on numerous advisory boards, served on President Obama's transition team and worked on committees focusing on a number of topics ranging from stem cell research to the use of chimpanzees in National Institute of Health funded research. That doesn't even scratch the surface of her work. But today, we're going to talk about a very important topic, the development and allocation of the COVID vaccine as well as approved therapeutics. Thank you for joining the podcast today Professor Charo.

PROF. CHARO:

It's a real pleasure to be here, Kris, thank you for asking me.

TURNER:

Oh, absolutely, I wouldn't miss this opportunity for the world.

PROF. CHARO:

And before we get started, I do have to give a caveat here. I'm going to be talking at times today about some of the recommendations that came out of the US National Academy of Medicine committee on vaccine allocation, and also the Wisconsin State subcommittee of the Disaster Medical Advisory Committee, which worked on principles for allocation here in Wisconsin. I served on both those committees, and I endorsed the recommendations that we came up with, but my comments today are my own and I don't represent those committees on this podcast.

TURNER:

Great, thank you. We're just happy to have your expertise on this very complicated, but also very interesting area of law and bioethics and public health. Before we get into our COVID questions, let's learn a little bit more about your professional backgrounds. What are your primary research areas and what first drew you to law?

PROF. CHARO:

I think broadly speaking, I'd say it's anything having to do with life sciences in the law. So it is a wide range of topics in the areas of genetics in the law, began with things like genetic screening, but moved on to genetic engineering, which is where I spend a lot of my time now. Human genetic engineering, animal and plant, as well as a variety of topics having to do with either public health and public health ethics, or doctor patient medical ethics. I was drawn to law originally, because I wanted to save animals. And I was interested in doing Environmental Protection Policy. As a biology major, interesting, I was studying evolutionary theory and animal behavior. But I realized that if you want to become an advocate, a law degree can be much more valuable than a simple masters in the biology. It really became PhD in biology versus law and I found myself just more drawn to the more action oriented aspects of law. But environmental law turned into biomedical law because of the connection of genetics.

TURNER:

One of our recent podcasts was with Professor Stuart Macaulay, who talked extensively about law in action. And that kind of sounds very similar to what you were thinking about how to apply law in the real world when you're talking about saving animals and other genetic developments.

PROF. CHARO:

Yeah. And in fact, one of my earlier jobs only about five years out of law school, I was working for a congressional agency as a legal analyst, where we offered science policy advice to Congress. And I discovered there that law in action can also mean law that's silence, because when you work for Congress, you had to be incredibly... This particular agency, incredibly neutral in your own opinions. You were there as a resource, but not as a policy advisor. That was incredibly frustrating. So I went to academe so I can actually say what I think personally. But in academe, I realized that you could be writing to nobody or you could be trying to use your law in a real sense. So it's hard to find that middle ground where you can be your own person, which is what academe allows, but also become an effective advocate for policy, working in a government setting.

TURNER:

It seems like you've struck a very happy balance between the two so far, just looking back on your career. So, that's really great to hear and to see.

PROF. CHARO:

Yeah. Well, Wisconsin is unique I think, in it's, not only tolerance, but it's encouragement for people that want to move in and out of public life, working in government agencies on leave periodically or in advisory committees. And takes that seriously as an aspect of scholarship and academic achievement.

TURNER:

So over the past several months, you've discussed the therapeutics that have been approved for COVID, what has been approved so far and what does it take for a treatment to gain approval for COVID to be treated?

PROF. CHARO:

Okay. So for treatment as opposed to a vaccine, right?

TURNER:

Yes.

PROF. CHARO:

So there's a there's a process for approving new drugs that has existed in pretty much the same form since about 1938. Although we've tightened it up considerably, particularly in the 60s and then the 1990s. Basically, anybody who wants to start with a brand new drug never been used in any other setting, has to first approach the Food and Drug Administration, which is an agency within the Department of Health and Human Services, and ask permission to try testing it on humans. They have to present evidence that they think it's going to be safe and effective in humans based on laboratory work and animal work. If the FDA gives permission to start human trials, then there are phases of research, starting with phase one tiny numbers of people and moving up through phases two and three. And

moving from looking purely for signs of danger to signs of safety and effectiveness as you move up through those numbers.

PROF. CHARO:

By the time you get through phase three, you may be looking at thousands of people who are in trials. And the classic trial, there are other forms, but the classic trial has the new drug tested against a placebo or nothing with groups that have been matched in every other possible way in terms of their health status, so that if you see a difference between these two groups, you are pretty sure it's attributable to the experimental drug. There are other exceptions, but we can talk about them if needed. Once the drug has shown this kind of evidence, and the FDA is persuaded, it can be approved for marketing to the general public, it'll be marketed for a particular use, that's called an indication, and for a particular population at particular dosages. So, that's what goes on the "label." But once it's out there, any doctor in his or her discretion may choose to use it for another purpose. That's so called off label prescribing. Entirely legal, it depends upon the professionals own knowledge.

PROF. CHARO:

And certainly there are lots of drugs that turn out to have many uses that are discovered and discussed in medical journals without having gone through a formal approval process. So for COVID-19, we have seen a number of things that have been touted as cures, for example, there was a period of time when the President was touting a particular drug, hydroxychloroquine, which was already used for other purposes, and he was touting it for an off label use. So this is an approved drug for a different context, and he's saying we should use it for COVID-19. The problem here was that we really didn't have the evidence to support that off label use. So it was legal to prescribe it and use it, but it wasn't legal to market it for that use. That is, a company couldn't advertise it for this secondary use until it had proven to the FDA that it really was worthy of it. And in that case, it over time has been shown not to be worthy of it, it doesn't seem to be effective and it does have dangers.

PROF. CHARO:

On the other hand, we're looking now at these very interesting, very modernistic drugs, the monoclonal and polyclonal antibodies. Basically, these are drugs that are designed to stimulate your own immune system, so that your own immune system can now respond to this invading virus. The polyclonal antibody created by Regeneron, was the one that was used when the President was in the hospital. The monoclonal antibody that is now being proposed to the FDA comes from a different company, Eli Lilly. I think that both of them have an excellent chance of getting approved at the end. But they are going to have to get through this process of showing the data from all the trials, having it evaluated by the FDA as an independent agency and then again, they will be marketed only for a certain dose, certain kinds of people, certain diseases, and then after that may get expanded to other indications.

PROF. CHARO:

So I would suspect they'll get approved at first only for adults, not for children. They'll only get approved for people at certain stages of disease. For example, the monoclonal antibody from Eli Lilly works best in people who have the early, less severe symptoms. It doesn't help a lot for people that are getting on to the end of life and it doesn't seem to help the asymptomatic. But once it's out for people that are in the indicated area, it may expand and over time may become usable for this wider group of people.

TURNER:

It's nice to get this layer of context for the treatments that are being developed. When you hear the word treatment and you think, "Okay, this is a good sign that someone with COVID has a treatment out there." But there are more shades of gray involved here obviously because, first it has to be approved for population, age, type of COVID they might have, all that. So that's really helpful for me to shade in that context for sure.

PROF. CHARO:

Yeah, it's been very tricky in particular, to get across the information that some drugs work better at certain stages of the disease and worse at different stages. Because that affects tremendously whether the drug will be particularly useful. The other thing that is not widely understood sometimes are the complications of administering some of these drugs. These monoclonal antibody, polyclonal antibodies, they need to be given only once, but it's by intravenous, by an IV, and it takes an hour to infuse it. So it's not like you can just go in and get a shot. So where do you bring in people who are COVID positive and are already showing symptoms, so that they can sit for an hour getting an infusion. They can't go to the usual infusion centers, there are cancer patients that are there who are very vulnerable to infection, and you can't mix COVID positive and negative people. But you can't really do it easily at home either. So just figuring out the logistics of how you would deliver some of these drugs can also have an important role to play in figuring out how useful they'll be.

TURNER:

Logistics, I think is the key word there as we start to see both treatments and the vaccine spun up as trying to get this out to who needs it the most. We'll get back to that in a minute. But first, I want to shift gears a little bit to see what level of international cooperation has been out there among the legal community as these treatments have been developed?

PROF. CHARO:

Well, we've actually seen some very interesting experiments in how to speed up the development of interventions in particularly the vaccines. We've seen companies that have basically brokered a deal. In exchange for the government having provided funding that helps take away the investment risk of developing a vaccine, the companies have agreed to work not only flat out, but also to work testing multiple vaccines simultaneously, instead of just one at a time, to making larger amounts of it. Usually a company is very much aware that most drugs are going to fail. And so they're very careful to only very slowly, carefully, incrementally increase their investment so that when, as will often happen it fails, the amount of money that they lose from this research and development is minimized. But here, we wanted them to test a whole portfolio of vaccines all at once knowing most will fail and invest all that money, the government had de-risked it by saying, "We will cover those costs and give you then the economic freedom to go and push forward faster than you would."

PROF. CHARO:

It also meant though, that there was going to be a quid pro quo having to do with advantageous pricing at the end of the day for anything that succeeded. We also saw a lot more sharing of data that is typical in an area where intellectual property is a very, very valuable commodity. So we may see that this opens up our imaginations to new ways to incentivize the development of new therapeutics in the future, especially for areas where the market is not working well. If you're making a blockbuster cholesterol drug, a company may risk a lot of money and lose a lot of money on failures, but when it hits, it has a blockbuster, it makes back all of its money. And there are marketing advantages, you get to being the

first one out with this blockbuster drug. But if what you're talking about is a drug that's only usable for small population, it's a rare disease, or it's an economic orphan. This disease only hits poor people, right? Like some of the tropical diseases do. Or interestingly, it's a drug that you want to develop, but never use.

PROF. CHARO:

New antibiotics that you want to keep in reserve, when somebody becomes resistant to all the standard, so you want to spend all this money to develop a new antibiotic and then never sell it. These are places where the market fails and where this is a moment where the government needs to have some imagination about other ways to incentivize the industry. And I think the COVID-19 experience may help us do that.

TURNER:

Right. So to put a thumb on the scale of the cost benefit analysis here to say that this is... Even if it's going to cost you a lot of money, we try to encourage you to get ahead of some of the viruses that really have the antibodies if something were to mutate, it would still be possible that something would be... You'd be maybe ahead of the game a little bit.

PROF. CHARO:

And there are other things. For all of these things, we've already got some kind of program. There're marketing advantages if you invest in orphan disease drugs, et cetera. But What really made a difference in COVID-19 truly, was the research that wasn't on COVID-19. It was the basic science research in genomics that made it possible to very, very rapidly understand the genetics of this virus, which was the key to developing some of the most forward looking kinds of vaccines that we're now talking about, including the Pfizer, Moderna and type. So the government's role is both way behind the scenes in the continued funding of basic research, which has a serendipitous quality. But when it turns out to matter, it's often profound in its effects, as well as the more practical interventions to provide a financial insurance policy for companies when you want them to invest in something that's risky, but nonetheless important.

TURNER:

Mm-hmm (affirmative). So again, we're going to shift around because there's so many different areas I would like to get your input on. So this time, I want to turn towards the legal challenges we've seen about stay at home orders and about mask mandates. Are there any precedents in the legal world to keep people at home, to quarantine them during a pandemic? Or is this breaking new grounds?

PROF. CHARO:

Well, you're going to laugh because the answer is a classic law professor answer, which is it depends.

TURNER:

I will laugh, yes.

PROF. CHARO:

So, yes. We have a long history in the United States of having legal powers, primarily at the state level, not the federal level, shifted somewhat over the years. To enact various kinds of restrictions on

businesses and on personal freedom in the name of protecting the community's health. But it is not unlimited. So what we're seeing is a constant testing of the boundaries. If you go back to the beginning of the 20th century, the seminal case, you'll see quoted all the time, is going to be the Jacobson versus Massachusetts case about somebody who refused to take a smallpox vaccine and didn't want to have to pay the $5 penalty if you refuse to take the vaccine. And it was a seminal case, because it really set the stage for this idea that there are areas in which there is expert knowledge. And in the area of public health, we need to have a fair amount of deference to that expert knowledge in that case in the form of the public health authorities.

PROF. CHARO:

In addition, we have specific statutory authority for states and also in some cases for the federal government to isolate people who are known to be sick with something that's infectious, to quarantine people who've been exposed to an infectious agent and who may or may not be infected themselves, we're not yet sure. But if you do that, it has to be done in a way that balances these burdens you're imposing on people with the public health needs. So for example, the quarantine can't be endless and it has to be restricted to only those people who realistically are potentially a threat. It has to be administered in a way that is not discriminatory, very famous early case, the Jew Ho versus Williamson case in California, in which the court said you can't just quarantine only the people who are of Chinese descent in this particular neighborhood while letting all of the European, Americans continue to go about their business. So we know that there are limits on government power. And of course, you can yes, shut down businesses temporarily.

PROF. CHARO:

States have generally passed statutes that lay out the range of ordinary powers under public health with regard to closures and contact tracing and privacy invasions of that sort, as well as quarantine. And then a separate statute usually that defines what is a public health emergency and what special rules will apply during the time of that emergency. It may be that you relax certain procedural rules like having to put out a competitive bidding for a procurement. It could be that you can bypass notice and comment for the issuance of a kind of order or rule. It may be that you can force businesses to close in ways that you couldn't ordinarily. And these emergency statutes will usually set out limits on the time that the declaration can last and what it would take to have re-opt. Does it have to change? Or the criteria have to be met? You need the legislature to buy into it. What we've seen is that we have 50 states and a few common jurisdictions like DC and every one of them has a different statute.

PROF. CHARO:

So when you asked about precedents, the answer is we got tons of precedents, but precedential value is limited because they're based on idiosyncratic differences among the statutes. There's also federal power under the Commerce Clause, but it tends to work only for the interstate issues or for border control issues. The intrastate issues are primarily the subject of state power.

TURNER:

And it seems like this is a topic that a lot of people have a vested interest in now obviously. Because all these 50 states plus all the territories and the districts are trying something different in some way. And how often are these emergency statutes passed at a time when there isn't an emergency and then when the rubber meets the road, there is concern or issue about what they allow the government to do?

PROF. CHARO:

Well, typically statutes like this are passed after an emergency has occurred. And we've all seen how inadequate our legal structures were. And I predict after we get past the most acute phases of this pandemic, there's going to be a fair number of, let's call it pandemic autopsies. Not to be morbid about it, but it's going to be legal autopsies. Where were we lacking? There is a model State Emergency Health Act that was published a number of years ago by academics and public health officials, but as you can see immediately, these are things that balance civil liberties with public health need. So it should not surprise you that there's a tremendous amount of controversy about exactly where that balance should lie. In fact, we've been watching lately, some cases that are being brought with federal constitutional challenges to state actions. In Pennsylvania, basically a substantive due process challenge to the power of the state to restrict movement and businesses as much as it was trying to do in Pennsylvania to control the pandemic.

PROF. CHARO:

An irony by the way, because Pennsylvania and Philadelphia in particular was where there was a real reluctance to crack down during the 1918 Spanish flu pandemic. And as a result, they had the worst outbreak in that entire region. We're also seeing specific challenges brought up in states like Nevada, and most recently, as of this past Friday in New York, where the effect of these rules has been to make it difficult for houses of worship to operate the way they ordinarily do. So those challenges are being brought under First Amendment, freedom of religion practice, or under... In some cases under state or federal Religious Freedom Restoration Act reference. So this testing of boundaries is going to continue for quite a while. And until we have more uniformity among the states in terms of the way their public health statutes layout powers and distribute those powers as among the organs of government, particularly executive and legislative and between state government and county government, we're going to still struggle state by state, county by county with challenges because every set of rules will be slightly different.

TURNER:

And there's something that you said that there's 50 different states, 50 different sets of rules. And what some people want to see is the experiments and the different levels of approaches. But when it comes to something like this, it's difficult to control a national pandemic with 50 different sets of rules.

PROF. CHARO:

It really has been and it has also meant that every state had to figure it out for themselves in an ad hoc fashion, instead of being able to draw on the lessons of other states as much as they like. That said, you can say that there's the glory of the laboratory of the states or the laboratory of the counties, but at a certain point, when you mix too many things in a laboratory, you get an explosion.

TURNER:

Very true, very true. And in some ways, we have seen an explosion.

PROF. CHARO:

Yeah. I think we have. I think we have. And we've also simply seeing too much uncertainty, which breeds a lack of public collaboration with authorities. Over and over in public health, we have found that the legal powers are only the beginning of the conversation. Often it's really about voluntary cooperation

more than anything else. Very rarely do we have to order people into isolation or quarantine, they go in on a voluntary basis, because they're advised to do so. Cooperation is always better. Fewer people resist at simply a generic resistance to being told what to do, fewer people try to evade with secretive methods or with fraudulent documents. So part of what's happened We've had very confused messages because of all these different legal challenges. Nobody's ever really sure what the advice is today.

TURNER:

Right. It's hard to be cooperative if I'm not sure what I'm being told to do. I'd want to be cooperative, but when I'm hearing different things, it's just difficult to do so. And then that generic, "I don't want to do this because I'm getting contradictory messages," is going to flare up more often.

PROF. CHARO:

That's exactly right.

TURNER:

It's just human nature there, I think.

PROF. CHARO:

Yeah, it's exactly right.

TURNER:

So let's now pivot back again to the vaccines that we were talking about a little bit earlier. We've had now three companies, I believe announce promising results for a vaccine. Are terms like encouraging and promising appropriate to use of these early test results?

PROF. CHARO:

Yes. That was a quick answer.

TURNER:

That was a quick answer. What steps remain before the vaccines are prepared for use?

PROF. CHARO:

So from a regulatory point of view, none of these have actually gotten any kind of approval for use yet. Now, the FDA does have a procedure it can use in moments of acute need, it's called an emergency use authorization. Companies still have to show the kind of statistically sound proof of safety and effectiveness before they can get an authorization just as if they were going for a regular approval. But there are some things that can be speeded up in terms of the regulatory steps that are taken to go through the process of review and decision making. In addition, these are not vaccines that will have been tested over as long a period of time now, they'll have looked for several months worth of possible adverse events or side effects. But what might be six months or 12 months after you take the vaccine, by definition we can't know, we can guess there are lots of good biological hypotheses, but you can't know. So if you put something on the market under this emergency use authorization, it's going to be accompanied by special rules about monitoring and follow up.

PROF. CHARO:

So I can see all three of these going through that process. And similar thing happening now in Europe, at least one of them has announced they're going to get a decision probably December 29 in Europe. And here in the US on December 10th we're going to have the public advisory committee meeting for the FDA, that's we're independent people not involved in the trials, not working for FDA, independent experts come in, they see the data, they see the structure of the trials to see whether or not there's some reason that the data is faulty, and they give advice to the FDA about whether they think it meets the necessary standard for sufficient effectiveness and a sufficiently low level of serious kinds of risks. At that point, the FDA can put it out under this emergency authorization with various conditions.

PROF. CHARO:

However, when the emergency ends... And this is under the Federal Public Health Emergency, which had to be declared by the secretary of HHS. When that emergency declaration expires, so does the authorization for these vaccines, at which point they need to get an ordinary approval to continue to be used. But presumably, all the data collected up until now, plus all the new information we get when it's used under the emergency use authorization, will be we hope sufficient to justify a regular approval. But it will still have to go through that new review for a general marketing outside this emergency setting.

TURNER:

Do you think that the emergency would remain declared to ensure that the emergency authorization can continue to be used or would you see some overlap there?

PROF. CHARO:

The declaration of a public health emergency by the secretary of HHS is permitted only when certain criteria are met. So you can't maintain the emergency status when the criteria no longer apply, even if you want these emergency use authorizations to continue to exist. There's always interpretive movement in any set of criteria, but these are not supposed to be manipulated that way.

TURNER:

Supposed to-

PROF. CHARO:

Supposed not to be manipulated that way. Exactly.

TURNER:

Interesting. So is it possible that you could have the authorization to send out these vaccines and the emergency is no longer met, so it's withdrawn and there's not enough data to support a regular authorization of the vaccines? Yes.

PROF. CHARO:

So in theory that could happen. Although, in fact you could start the process for asking for a regular approval now even while the emergency approval authorization has been given so that you've kind of started that long road of review already and collecting data along the way under the emergency use. The thing is that an emergency will suggest a slightly different kind of risk benefit balance. In an emergency situation, you've got for example, an infection rate of spread that's much higher than in a non emergency situation. And so what level of effectiveness you're going to require from your vaccine

may change if you've got a fast spreading virus that you might take a somewhat lower effectiveness rate just to slow the pandemic down a bit. But at a normal level, you might insist a much higher rate of effectiveness because otherwise it's not worth using it. So the standards can change a little bit depending upon the context.

PROF. CHARO:

The other thing though that's going to be interesting is that once we have a few vaccines that have actually been authorized, it does get harder and harder to test new vaccines. Because the ethics of research trials suggests that you can't put people to unreasonable risk. So in order to test a vaccine, you have to have people that are taking the new vaccine and other people that are not. Right now, the people that are not taking the experimental vaccines are getting nothing. And both populations then go out and they live their lives with masks, with social distancing, with all of that, but even with that, some people get infected and other people don't and you look for a difference between the population of vaccinated and unvaccinated.

PROF. CHARO:

Would it be ethical to have a trial in the future where you have a population that's truly not vaccinated at all? Or would you now have to run trials where you have the experimental new vaccine versus one of these already authorized vaccines? That's fine, but now you're going to have to have a trial that has many, many more people and goes on much longer before you'll get enough difference in infection rates to know for sure whether your experimental vaccine is actually better, or even just as good as the one that's already on the market. So it's just going to make the testing for new vaccines harder.

TURNER:

It would make it very difficult for a company to say, "We want you to stay away from any vaccines, because we want you to be someone that we are going to test a new vaccine on," and that person catches COVID and passes away from it. On top of an ethic standpoint, it just looks bad any which way you slice it.

PROF. CHARO:

Yeah. Making people die is always going to look bad. I completely agree.

TURNER:

Yes. I'm not a very controversial stance on my part there, Yes.

PROF. CHARO:

No, no, I shouldn't make fun because that's exactly right. That said, each vaccine is going to have a slightly different profile in terms of its risks and its benefits, its side effects. So for example, some vaccines may turn out to be more effective for people who are at ordinary weight, but when you're talking about people who are very obese, they simply don't have a comparable level of effectiveness. And yet a different kind of vaccine that's built on a different kind of biological platform may actually do better for people who are morbidly obese. That's an important thing to know, that makes a very legitimate justification for trial. When you're trying to figure out what's the best vaccine for people in your condition, you've got this existing medical problem, you're an organ transplant recipient with immune system depressant, you're morbidly obese, you're very elderly, you're very young. So we do

have to keep testing vaccines to look for the best match of the vaccines effectiveness and safety profile to each sub population.

TURNER:

For me, growing up in a society where it feels like a lot of the major diseases have either been controlled in some way, or wiped out entirely, this is just an entirely new ground for people my age and younger, especially.

PROF. CHARO:

Well, and we haven't even begun to talk about the complexities, Kris. Let's not talk about just the delivery issues. So the first two vaccines that are coming out Pfizer and Moderna, they are built on a new kind of way of doing vaccination development. It's based on a trick by which you can create something genetically that mimics the coronavirus enough that it stimulates your body's immune system directly. As opposed to the older forms of vaccines where they'll take a virus and they'll inactivate it or kill it so that its shell remains in your body, latches on to the shell and says, "Oh, let's fight against it," but it can't actually make you sick. Okay. Very different things. Now, the problem with these new ones is that while they have incredible promise for all kinds of reasons, they also post some delivery challenges. The Pfizer vaccine requires storage at about 100 degrees below zero fahrenheit. That's a problem.

PROF. CHARO:

I was amazed when I read over the weekend that United Airlines had to waive its usual rules on the amount of dry ice it's willing to carry in order to have enough dry ice for all the boxes of all of the vials of vaccine that were being shipped from, I think it was Belgium to the United States. Now think about that when it gets here. To be transported from the central location where it's delivered in the United States to all 50 states, and then it gets to the Public Health Departments, which have to be able to receive it in this pristine condition and get it out to all the other locales, pharmacies, hospitals, clinics, all of which have to continue storing it at this incredibly low temperature, do you even have a refrigerator that will go that low? And vaccines come usually in batches. So you might get a box that has 10, 20, 30, depending on the size of these batches.

PROF. CHARO:

But if it can only be kept at ordinary refrigeration temperature for let's say five or six hours, then you need to be in a place where you're going to get enough people coming in to get the vaccine in five or six hours, that you're not going to wind up wasting some of it becomes useless because it's been stored too long at that temperature. The Moderna doesn't have to be quite as low temperature but still pretty cold. Versus I think AstraZeneca, which is coming out soon I think, is going to be much closer to the kind of ordinary refrigeration that we're used to. Second, the Pfizer and Moderna vaccines require two doses separated by several weeks in order to get the effectiveness that we're seeing in the clinical trials. And I think most of us can imagine that even if you get people in first shot, already a challenge considering how many people are vaccine hesitant, how many of them are going to forget to come back for the second shot three weeks later?

PROF. CHARO:

They get busy and they forget or the first shot gave them side effects, lots of them will get headaches or even a mild fever and it discourages them. So maybe these kinds of vaccines should only be given to

people who are going to stay in one place. People who are in nursing homes, people who are in prisons, where you know that if Joe was here today, Joe is going to be here three weeks from now and you'll make sure that the second dose gets to them, and then use one of the single dose vaccines for people in the general community. That's also going to affect your allocation decisions, right? All of these things have to be taken into account.

TURNER:

Enormous logistical challenges again. Just imagine tracking all this to see who has gotten one, but has not gotten the second one.

PROF. CHARO:

That's another thing. Registries, absolutely. What if you get one of them at Walgreens here in Madison, but then you're trying to get your second shot when for whatever reason you're now in Illinois and you had a CDS? Do they talk to one another? We've got registries, we've got state registries, no problem, but having registries talk to one another across state lines and nationally, is less perfect. And it's very easy for those records to get missed. And so you may either never get your second shot, or you may get too many shots. Even I personally was a victim of that where I forgot I had gotten a shot for something and I got another one because I was in a different state. And lo and behold, it turned out that was not a good thing to do. So, that's-

TURNER:

You're the expert there, I'll take your word for it.

PROF. CHARO:

Yeah. But this is just the beginning of some of the concerns, right?

TURNER:

Right.

PROF. CHARO:

Get the shot, you have side effects like a mild fever or aches and pains for a day or two. So if you're going to give your vaccinations let's say to your healthcare workers first because you want to make sure that they are able to take care of the rest of us, you may not want to give it to everybody on the service on the same day. Because if they do have the side effects, it may be two days from now you've got half of the people calling in asking for a sick day and you're suddenly short staffed. So you may want to have a rolling vaccination program within your OB service or in your ICU personnel, et cetera. Again, the logistics down to the kind of granularity of how many people per day is where our local public health departments really become the experts.

TURNER:

And along these same lines, we've talked about the ethics and allocation a little bit, but I want to dig in a little bit more. You've discussed this a little bit elsewhere, but there's proposed orders for who is first in line to get these vaccinations once they are available and being allocated. How is it being determined or how should it be determine perhaps?

PROF. CHARO:

There's no one way that is necessarily correct. It takes thinking through what your goals are going to be. If what you want to do is simply reduce the sheer number of people who are dying, it's pretty clear, you would vaccinate first the people who are the oldest and most medically vulnerable. Because while nursing home residents for example, are only about 1% of the population, there are about 6% of the people infected, about 39% of the people who are dying. So if that's your goal, to keep people alive, you're going to go ahead and focus on nursing home residents first, first, first. On the other hand, you may want to make sure that society continues functioning. So you may want to focus on people you consider essential. And that's why you get health care workers and meat packers and national security people or anybody in the food delivery business and people who are in transportation.

PROF. CHARO:

So we know who's really necessary to keep society functioning while we deal with the pandemic. And that by the way, may be different from locality to locality. Here in Wisconsin, as we enter the winter season, I would not be surprised to see snow plow operators deemed essential, because if the streets aren't clear, the ambulances can't get through. In Arizona over the summer, on the other hand, it's the air conditioning repair people who are essential because people literally die from heat stroke. So there's going to be that. What if you want to deal with the fact that some people are more likely to get infected than others? The people who work in jobs where you can't avoid personal contact, a lot of the service workers, a lot of the bus drivers. These are people that can't escape the risk of infection, because they don't have the luxury that I have of being a law professor who can teach on Zoom. So maybe they should be prioritized. What about people who are most likely to transmit?

PROF. CHARO:

So you talk about people who live in high density housing, maybe we should be talking about vaccinating people who live in apartments versus houses, because if one person gets infected, everybody in the apartment gets affected, right? There's no way to isolate. See, you got to really ask what you're trying to accomplish and model out the effect it has on deaths, on infections, on hospital burden, on the functioning of society and the economy, crucial with schools for example. And then figure out what's the best balance of these goals. So what's developing is a bit of a consensus, not perfect, but a bit of a consensus that in the very first stages, it'll probably be focused on people in the healthcare system who are the most exposed. So people who are working directly with infected patients, people who clean the rooms of infected patients. So it's not just doctors and nurses, it's also cleaning staff, catering staff, things like that.

PROF. CHARO:

After that, it's probably going to be the most medically vulnerable, who are also in highly exposed conditions like nursing homes for the elderly and sick, as well as the people who interact with them, like the caregivers in those settings, who can be a vector from community to the nursing home resident. After that, everybody seems to be moving on now to talking more broadly about essential workers, particularly those who are showing one of the other factors like a comorbidity, they're obese, they're older, they're diabetic, and that are more likely to be exposed. Some essential workers can be protected, but others are more exposed. And moving down the line that way. So basically, what you're trying to do is you're trying to merge this concern about the personal medical fragility of the individual and the risk that that individual might transmit to others and the effect on society of taking that

individual out of society because that individual is sick. All three things simultaneously. And layered over all of that are the tremendous inequities we've seen in the burden of this pandemic on some groups.

PROF. CHARO:

Because of the combination of things in which various minorities are disproportionately represented among the poor, among those who live in high density housing, among those who do service work, who had poor health insurance in the past, and so have a whole host of comorbidities now. We've seen incredibly high rates of infection and hospitalization and death in the African American, Hispanic, Alaskan Native, Native American communities. Alaskan Natives have been suffering from this at about five times the rate of the general population. Is extraordinarily high. So even with all of what I've laid out, the next thing you do is you layer on top of that what they call social vulnerability index and say, "Look, if we don't have enough for everybody who's let's say in phase two where we're looking at essential workers who are highly exposed, let's at least make sure we get this stuff to the people who are in that category and who live in one of these socially deprived areas," because then we're more likely to get people who have also, all these other co factors like the comorbidities and such.

PROF. CHARO:

It gets very hyperlocal, but you can understand why you're trying to achieve multiple things that are not completely consistent with one another all at the same time.

TURNER:

It does sound like a very well thought out plan with a lot of complicating factors in it. So it'll be interesting to see how it unfolds over the next several months, especially as these vaccines start to come online. Just today actually, the advisory committee to the CDC on vaccine allocation had an emergency meeting. What were they discussing and what came out of this?

PROF. CHARO:

So they were discussing exactly what we're just done talking about. How to phase in vaccination as these vaccines come online. And keep in mind, whatever you decide today based on the two vaccines that we may have now, might change when we have two more that come online in February and have a different profile. So it has to be a framework that's able to adapt to changing circumstances as new vaccines become available. So today, they were working only on the very first phase. Let me first give you some context about who they are and where they fit in the system. Who is this committee and what do they do? The Department of Health and Human Services has an agency, the Center for Disease Control and Prevention CDC, which is our public health agency. That agency uses advisory committees of various types, this one's called the Advisory Committee on Immunization Practices, ACIP. And one of their jobs is to advise the CDC about how to handle vaccines that the Food and Drug Administration has now approved. So one of their jobs is to help the CDC decide how to advise the country.

PROF. CHARO:

The CDC by the way, is already working with advice from our National Academies Committee. So that was step one, step two now is the ACIP. They will make a recommendation to the CDC, which will issue guidelines. And those guidelines go out to the states, but the states have the discretion to make the decision for themselves about what framework they're going to use for their own applications. And we have our own committee here, as I mentioned at the top of the podcast. So it's a lot of advisories going down the line. What happens is over time, you begin to see this kind of confluence of advice. So today,

the ACIP had an emergency meeting, because it became clear that the FDA was on the verge of making a decision about whether to give authorizations to these vaccines from Pfizer and from Moderna. And for the moment, they were focusing only on the very first stage when you've got the fewest doses available.

PROF. CHARO:

They were talking about the approximately 20 million healthcare workers and how many doses are we going to have in the beginning from these vaccine manufacturers as they scale up the manufacturing process and how do we distribute them? It does seem pretty clear, it's going to be healthcare workers first. But even there, there may be a need to prioritize within that group and focus on those who have the highest degree of risk, either because of where they're working, or because of their own personal characteristics, because we won't even have enough for all the healthcare workers in the very beginning. And then they are going to incrementally continue working through the different phases that they're going to advise local governments about.

TURNER:

It's so fascinating to watch this play out in real time as it's developing. It's obviously affecting us every day of everyone's life. And so I'm glad to see that there is progress being made. But let's wrap up here a little bit. I want to know what do you most hope readers be they either researchers or a layperson, takes away from your work?

PROF. CHARO:

Well, first I want them to appreciate that there's a role for the public in this as well. So right now, it's now Tuesday, December first as we record this, until December fourth, the public is allowed to comment here in Wisconsin on the Wisconsin proposal for its first distribution of vaccines. So, that's at the Sate Disaster Medical Advisory Committee website on the wisconsin.gov website. And you can comment on their proposed first initial distribution among healthcare workers. You may think that's crazy and that the first distribution should be nursing home residents. You should write in and tell them that. So that's the first thing I want people to know, is that the public has a voice. The second is that there's been a lot of distrust of government agencies in the last year and we have certainly been the victim of the unhappy confluence of a political election season with this pandemic, so that everything that's been done instead has been seen somewhat through a political lens. The election's over, the particular pressure that November third brought on everybody has been relieved.

PROF. CHARO:

And it's time now to really listen hard to what the experts and independent, dispassionate reviewers are telling us about safety and effectiveness and believe them, because we have way too many people who are still saying that they don't trust the vaccines for some reason. And if we don't get enough people agreeing to take up the vaccine, we are not going to get the kind of widespread immunity we need to let society truly return to normal someday. We're going to have a long, awkward period where we're going to have to be taking vaccines, but still using masks, still using social distancing, because we're not out of the woods yet. And that's the worst, most difficult time for public communication. But the first step is for people to actually go ahead and get vaccinated.

TURNER:

Hopefully with the political aspect removed from this, there is more clear communication about what is required and what is coming forward. Because as you said, where people have taken a vaccination, but

they still need to wear a mask, still need to be socially distant, I absolutely agree with you, that it will be very difficult to clearly communicate the steps that we will do to go forward to get back to what will constitute normal after this is finished.

PROF. CHARO:

There're always going to be some people that can't get vaccinated because they have some medical condition that makes it unwise or because the vaccines haven't yet been tested on people that are as young as they are. So you'll have children who are unvaccinated. And one of the reasons we all get vaccinated is not just to protect ourselves, but to protect all of them. The nature of public health is that we have to remember it's about solidarity. We are all in this together. I do things to protect you as well as protect myself. I'm like a Girl Scout child of immigrants, [inaudible 00:52:14] America, I think of it as patriotism. To do things that help everybody around you. So that's going to be what we need to really communicate to people as we move into this next stage, that it's about taking the vaccine to protect yourself and others and then continuing to use these other non pharmaceutical measures, until it's safe enough for everybody to go out and about again, as they used to.

TURNER:

Where can researchers find more of your work?

PROF. CHARO:

Well, the National Academy of Sciences, Engineering and Medicine has a website that will lead you to the report on equitable allocation of vaccine, as well as the State Disaster Medical Advisory Committee website for information specifically on this. My biography page on the law school website will lead you to some links that can connect you to the various committees and journals where I've been active. And I welcome people who occasionally just write to me out of the blue to comment on or even argue with some of the things I've done. The dialogue is wonderful, and I will end by telling you that I got my favorite fan letter every yesterday from somebody who had seen me in a video and said, "Yes, she had a video very interesting." But mostly she wanted to say that she really wanted to compliment my accessories because she wears exactly the same pair of earrings when she wears the color of the suit jacket I had on.

TURNER:

Hey, I'll take a compliment any day of the week. That's nice to hear. And of course, we will link to everything that you just listed on the podcast's homepage to make sure one can find your biography very easily and find links out to the National Institute for Health as well. Thank you very much for joining us today, Professor Charo. We've been discussing the COVID pandemic, therapeutics, treatment, vaccine trials, ethics, we ran the whole gamut on COVID discussions here today. Thanks to everyone for listening. As I mentioned, you can find a link to Professor Charo's work either on SSRN or the law school repository or the law school homepage on our podcast page at wilawinaction.law.wisc.edu. I hope that by now you are subscribed to our Wisconsin Law In Action podcast, we've had a lot of great discussions beyond just the COVID pandemic with a whole bevy of UW Law School professors. You can find us on Apple iTunes Store or Stitcher or listen to our full archive at wilawinaction.law.wisc.edu. Thank you again for listening and happy researching.