COVID-19 Vaccine Questions Answered by Virtual Panel of Healthcare Experts

Leading Pandemic Voices Dr. Bob Wachter and Dr. Ashish Jha Share Perspectives at Executive Advisory Board Meeting

As healthcare leaders around the country make decisions to guide the COVID-19 vaccine rollout, renowned physician experts Robert M. Wachter, MD, and Ashish K. Jha, MD, MPH, discussed how the pandemic is reshaping the future of medicine and healthcare delivery during a virtual meeting hosted by the TDC Group of companies (TDC Group) on February 3. These two longtime collaborators compared ideas and answered questions regarding the timing of doses, when vaccinated individuals can relax pandemic safety measures a bit, and other vital topics. At the heart of the discussion was how lessons learned so far will help the nation navigate the months ahead of the rollout.

Their unscripted conversation was the keynote for The Doctors Company's first Executive Advisory Board meeting of 2021, a virtual gathering of the nation's top healthcare providers and medical society leaders.

In the interactive session, Drs. Wachter and Jha took questions from fellow keynote speaker Richard E. Anderson, MD, FACP, chairman and chief executive officer of The Doctors Company and leader of TDC Group; from moderator David L. Feldman, MD, MBA, FACS, chief medical officer for The Doctors Company and TDC Group; and from the audience.

Both doctors have become public figures since the start of the pandemic, coauthoring editorials for major print news outlets, making frequent appearances for television news, and generating social media attention to keep facts in the spotlight.

The following are the key questions about the vaccine asked of the two experts and their responses:

How certain is it that if everyone "hunkers down" during the vaccine rollout, in a couple of months, we'll be good?

Dr. Jha: Not a certainty. But here's why I feel reasonably confident. By the end of March, I feel like we should have 80 to 100 million Americans with at least a single dose in their arms. We're at 32 million right now. That's an additional 68 million in the next two months, easy, if not more than that. And that is about 30 percent of the population. Throw in the fact that about 25 to 30 percent of the population has been infected, with obviously some chunk of overlap between the two. I would not be surprised if at the end of March, we're close to 50 percent of the American people having some level of immunity against this virus, including the variants. Assuming that nothing catastrophic happens to the vaccine rollout, I think you're going to have a lot of population immunity, though not herd immunity. But it's hard for me to imagine that things won't start looking better. And maybe April slips into May, but I don't think April slips into July.

Dr. Wachter: I guess what you're saying is that at 50 percent, you actually will influence the curve quite a bit. Not down to the point where the virus has no toehold to do its mischief, but to a point where it really exerts a significant downward pressure on spread?

Dr. Jha: I think we have some evidence of that from places like the Dakotas, for instance. I actually think North Dakota right now probably is in the mid-40s in terms of the proportion of its population that has immunity. I wouldn't take the North Dakota approach, because they got most of the way there by letting the infections run really wild for a while.

Of course, the one big piece of uncertainty is, what does happen with some of these variants, and do they end up really wreaking a lot of mischief? I don't think that's impossible, but I'm hopeful that the vaccines will stand up to these variants in reasonably good ways.

Dr. Wachter, you postulated it would not be unscientific and would not be unreasonable to delay the second dose. How did you think about that as a scientific issue? What was the reaction you got as an academic leader pushing the boundaries of what was there in the clinical trial?

Dr. Wachter: When you look at the data in the trials, one of the most interesting things I heard was, “This is anti-science.” The science was to do this trial and to give vaccine one, and then give vaccine two either three or four weeks later, depending on Pfizer versus Moderna. Well, the science is all of the information that comes out of that trial—if that was the endpoint, science was what happens when you get people two doses.

But sometimes, the science is serendipity. Sometimes, the science is something that comes out that you weren't looking carefully for, but it's as clearly shown as anything. And what the science, to me, showed was that your level of protection was between 80 and 92 percent before the second dose. That science was distorted a little bit. Sometimes, you heard people say, "Well, Pfizer was only 50 percent protective until dose two." That is integrated over the entire period from the moment you got dose one until you got the second dose. So that's not the relevant question. The relevant question is, what level of protection did you have 10 seconds before you got dose two, and the answer is close to 90 percent. So if you do the math—and some people have done modeling on this—it says that you would actually save far more lives if you got more people their first dose and got them from 0 to 80 or 90 percent protected than taking the same amount of vaccine in the same distribution process and got more people from 80 to 95 percent protected.

I ran that idea by several colleagues—immunologists and epidemiologists at UCSF and elsewhere. And they basically said, "Yeah, there's an argument to be made there." I wasn't hearing that argument, but I was hearing the argument that we have the plan, and we should stick with the plan because it's the plan. That didn't sound particularly compelling to me. So it wasn't like I thought it was a slam dunk that we should switch to this. I thought it was important to have a national conversation.

And so we wrote the piece. It did get a lot of pushback, some of it quite reasonable. Most of the vaccinologists that I know who have looked at it really are not all that afraid of the clinical problems with it. And the clinical problems, theoretically, are that the second dose won't work as well. But that’s not an issue: It's actually probably going to work better the longer you wait. That your immunity from dose one is going to wane as you wait an extra month or two is probably not an issue.

That having people, quote, "partly vaccinated" will encourage mutation—that's a scary issue. But I have a hard time getting a feel for how real that is, and it's almost a trump card. It's like people hear, "Oh, my God, mutations," and everybody kind of goes crazy. I think it's a relatively small, more-theoretical-than-real issue. I think the real issue is: Will people hear the messaging that if I can delay dose two, maybe I don't need dose two? That's bad. And we've made clear, every second that we've had the opportunity to say, you do need dose two. But delaying it for a

month or two is probably not a big deal, particularly given the dynamics of the vaccine distribution, which is this major bottleneck. We just don't have enough now, and we will later. The real practical question is what do we do today, so I'm glad we wrote it. I think it has generated a conversation. I think it encouraged what has happened, which is releasing dose two, not storing doses and waiting. I think it's encouraged the Centers for Disease Control and Prevention to liberalize that it's OK if you get dose two a month late. So I think making that argument did what we intended. But the pushback was pretty impressive.

Dr. Jha: Not only has it generated a lot of conversation, I would be surprised if we don't keep moving towards: Get the first dose out early and worry about the second dose a little bit later.

Dr. Wachter: In fact, this is what the UK has done. And the UK, they have very smart people and smart epidemiologists and virologists, and they did it under the pressure of the variants. So for them, the variants were not a theoretical problem. This was, "We discovered a couple of these nasty bugs south of London, and now 70 percent of the cases in London are that variant." So it is like a wartime footing. What do you do with a limited resource to get something under control as quickly as possible? And so I still think it's a reasonable idea to debate, and as you say, I think the system has moved somewhat in that direction, if not going completely to the UK's stance.

Dr. Jha: It does remind us that science is not dogma. Science is a process. And scientific information is far more holistic than the final sentence of the conclusion line of a paper.

If you are going to get vaccinated versus what's happening with the spread, how does that impact what you do and do not do?

Dr. Jha: Before vaccination, the most high-risk event that you could be engaged in is when you're hanging out with other people indoors and not wearing masks. That's the highest risk, and it sort of goes down from there. Over the next couple of months, we should really try to minimize this. But what happens when you get vaccinated? How much should you think about community factors?

What I have said to folks is, even if you get a Moderna or a Pfizer vaccine—I guess those are the only choices right now—it's 95 percent effective at preventing infections. So there's a 5 percent chance you might still get infected, and 5 percent of a big number is still a big number. Meaning, if it's 5 percent and you're in a place with large outbreaks happening, I don't know that being vaccinated makes me that much more comfortable. It's only when the infection numbers come dramatically down that that 95 percent reduction really starts having this huge safety effect, and a psychological effect on me, when I've gotten fully vaccinated.

I got my first dose about 10 days ago. And I feel like even after I get my second, as long as Massachusetts has a lot of cases happening, I'm going to stay pretty careful. I go to the grocery store not that frequently. I try to spend very little time in it. You might be able to tell, I haven't gotten a haircut in a little while. I probably will after my second dose—that might make me a little more comfortable, but I'll still wear a high-quality mask. All of that is my way of saying, as long as the numbers are bad, I'm not changing behavior that much. But once the numbers start moving down in the right direction, my behavior will change, because the vaccine really does offer quite a bit of protection.

Dr. Wachter: My big three are getting a haircut, seeing the dentist, and flying if I need to fly somewhere. And I have 90 and 84-year-old parents in Florida, so I will think about doing that.

But it's very much tempered, as Ashish says, by the community prevalence rate. I think people don't get that. The same activity, being in the same room with someone with no mask, has a certain rate of infection—but it has to be then multiplied by the probability that the person you're with actually has COVID-19.

The number I look at every single day is from UCSF: We test all of our patients, including people coming in for a cardiac catheterization. And it's that number, which is basically the probability that someone in San Francisco who is asymptomatic has COVID-19, that I use a lot in determining the chances that the person next to me at the Safeway is infected.

During the light parts of COVID-19, over the past year, that number has been 0.3 percent, meaning a 1 in 300 chance, and today it's 2 percent, so a 1 in 50 chance. So even though I have 95 percent protection against getting infected from them, by virtue of being vaccinated, that's a significant difference in terms of the risk that the person I'm coming close to has it and could theoretically give it to me.

I think that's the key point of looking at community prevalence rates on top of the individual activity, and then on top of whether you're vaccinated, to make decisions. This is why everybody's head hurts, because for an epidemiologist, this is sort of OK. You're trying to multiply three different factors to come up with the decision. But for a regular human being trying to live their life, this is brutally difficult.

What do you make of a recent article that suggests we have actually underestimated the efficacy of the vaccines?

Dr. Jha: Yes, across 75,000 studied patients, we're arguing about whether there was one or zero hospitalizations, which is a nice argument to have. While the vaccines are quite effective at preventing infections, they vary in how effective they are. But imagine I told you that I have a therapy or a vaccine that can turn the coronavirus into something that really is safer than the flu, as opposed to the rhetoric we've heard about that. You'd say, "I'll take that, even if it means I might get infected. At worst, I might have to spend two days in my bed with a fever, but I know I'm not going to get hospitalized, and God knows I'm not going to die." And we know less about this part, but we don't think you're going to have long COVID or any of that stuff. My take would be, that's a huge victory.

That's where I think we are with vaccines right now. I think with all of these—Johnson & Johnson, Novavax, and more data from AstraZeneca this morning—we are yet to see anybody who got vaccinated die from COVID-19 as a result. And I'm going to argue that not a single person has even been hospitalized, though a credible argument could be one person got hospitalized in the Moderna trial.

Dr. Wachter: There are caveats. We don't know for 100 percent sure that you can't get long COVID. And so that weighs a tiny bit on people's minds, and appropriately. And this issue of, can you spread it? So as I said, I, now, having been vaccinated, will get a haircut, will get to see the dentist. But I still am very careful around my wife, who has not been vaccinated.

But the point that Ashish made and was written up in the *Times* is really crucial. And crucially, it's all five vaccines in that calculation, including the ones whose top-line efficacy was significantly lower than 95 percent. Still, nobody died after getting a vaccine that might be only 70 percent "effective" in preventing COVID-19. But the key thing is, nobody gets seriously sick and nobody dies. It's unbelievable.

Why are we leaving healthcare's A-team on the bench with vaccine administration rollout? I.e., primary care providers. What are your thoughts about that, or is it coming?

Dr. Jha: I have mixed feelings about this, and let me just share them. A large chunk of physicians still practice in small practices, and handling these vaccines is not like handling the flu vaccine. There's a lot of infrastructure complexity around managing them, opening them up, thawing them, making sure the doses get out in time. There's no question in my mind that physicians could do it, and nurse practitioners could do it, and the clinical infrastructure of our country can manage it. But one of the questions that is on the table is: Do we want 100,000 places doing these things? Because what happens when the freezer breaks overnight?

I actually think all that sets up more risk into the system. And I have argued that we probably want to keep this to a smaller number of places and think of this as more a short-term, high-volume thing that we want to try to get done.

Even on the hospital side: Now obviously hospitals have a lot more infrastructure and capability, and there are hospitals like UCSF Medical Center that are more than capable of doing this. And they could do a chunk in their community, and I'd be game for that. But then there are small rural hospitals that have gotten these vaccines and have had a hard time managing them. They may not have enough people around to actually even give the vaccines to, and end up wasting doses.

So I have believed that for this one, employ the healthcare sector, sure. But let's keep it a little bit tighter, a little bit smaller number of places, keep it more high volume, because we have a very specific task. We've got to get lots of people vaccinated very quickly. And handling this vaccine is complicated. It's not like the flu vaccine.

Dr. Wachter: I agree with everything that Ashish said. It may change with the Johnson & Johnson vaccine, which has easier storage requirements, and it's single dose, less complex. And it certainly will change by the summer. I mean, this will get to a point where it does resemble the flu vaccine, and you can get it at Walgreens and you can get it at your doctor's office, probably. But I agree that the rollout has needed to be from high-volume places that could manage really something far more complex than physicians have done in their offices around vaccination in the past.

Any guidance on vaccines for women of childbearing age?

Dr. Jha: I'll start by saying, OK, the clinical trials did not include pregnant women. But there are two separate issues: Pregnant women versus women of childbearing age. Women of childbearing age I wouldn't worry about. There's a lot of misinformation and disinformation about how these things sterilize people, and how Bill Gates is behind all of this, but all of that is mostly just junk. These vaccines can't cause sterility. It's not like what's going on.

The issue of pregnant women is a different one, just because we don't have very good clinical data. And this is where it actually comes back to a conversation that we started with, where I asked Bob about the one dose delayed versus not, and this whole issue of what is science.

There are a lot of people who say, "Well, we don't have data on pregnant women, therefore we can't make a recommendation." And my take is that pregnant women are at higher risk of complications of COVID-19. Pregnant women find themselves in high-risk situations. They are

critical care doctors. They are ER doctors. They are people who are, quote-unquote, in harm's way. And what do we say to them? You can't do this, you can't get vaccinated? My personal take is that all the evidence we have so far suggests these vaccines are going to be safe. So my recommendation to people has been: You're in a little bit of a data-free zone, but that said, it's probably quite safe to get vaccinated as a pregnant person. And certainly, we know that there are substantial risks of getting COVID-19 as a pregnant woman.

But if you're not pregnant, then I just think you're like any other person in terms of thinking about risk.

Dr. Wachter: It is somewhat of a data-free zone. But science also extrapolates from things that we do know about other vaccines and their impact on pregnancy. And we know about the safety profile of these vaccines, which are really remarkable. I mean, this allergy risk now has been downgraded slightly to about one in 200,000 people having an anaphylactic reaction. No one has died of it yet. It is interesting how we take those numbers. We say, “Oh, my God, I hear there's a risk of having an anaphylactic reaction.” But 3,000 people a day are still dying of COVID-19, so you have to keep them in proportion.

Should we just give the second dose for high-risk individuals and not everybody else? Would there be more of a reaction to a delayed second dose?

Dr. Wachter: There’s no evidence of more of a reaction to it. The question is whether to give the full vaccination to people on the sort of clinical trials–based timetable who are at high risk. You could easily say that for people above a certain age, for example, we're going to go ahead and give them the two doses, not that large a population. And if you look at the numbers, people over 70 or 75 represent a wildly disproportionate number of the deaths. That's a perfectly reasonable way of looking at the data, to say, "We will give the two doses on the normal schedule to people over age 70 or age 75, and people who are younger will wait on the second dose.” That would be reasonable. You may have heard the results of a preprint that came out yesterday that makes it look like, if you've had a prior case of COVID-19, you may only need one dose. So that may be another way of saving vaccine doses. The challenge there is going to be another operational challenge: How do we do that? Or do we test everybody for antibodies?

Dr. Jha: I've been pretty involved in trying to help Rhode Island think about a strategy for ramping up. It's been doing OK, but not great. I actually sent that to the head of the Department of Health, as well as somebody in the governor's office, and said, "How hard would it be for us to operationalize this?" We're not going to start doing it until we get some more guidance from the Food and Drug Administration on this. But at least we could start. Could we start by getting a high-quality antibody test, testing people, and then people who are positive, giving them their dose, but then really trying to work with the FDA to say, how do they feel about forgoing the second dose? I'd like to try to figure out, can we operationalize this—but I'm very confident it's going to be hard to operationalize. It's a really important and interesting idea. But I just don't know that we have enough capacity to do it.

Dr. Wachter: I hadn't realized that what we could theoretically do is, when they get their first dose, you take their blood at that time, and then they either get invited back for a second dose or they get told they have antibodies and they don't need it. I thought you'd have to test them before they come in for their first dose. But there's really no reason you need to do that.

There have been discussions of having a booster or an "updated" vaccine to deal with the variants. Which is the more realistic option that we should pursue as a country?

Dr. Wachter: There will likely be a reformulated vaccine out in the fall, which will have more activity against the variants. Since most people will have been vaccinated by then, this will likely be given as another booster. The FDA approval process for this will be shorter, more akin to the approval process for the flu vaccine—which simply needs to show the appropriate antibody response, rather than effectiveness in a large clinical trial.

What are you currently seeing with respect to antibodies and the variants? Do people with antibodies from a prior COVID-19 infection have any degree of resistance or immunity to the new variants?

Dr. Wachter: We are presuming, for now, that immunity from the native coronavirus, whether obtained from prior infection or vaccination, works against the UK variant, which is the most prevalent one in the U.S. Whether this works against the South African and Brazilian variants is more uncertain; preliminary evidence points to lower efficacy for vaccines and a higher rate of reinfections.

Who should not get the vaccine?

Dr. Wachter: The CDC has provided and is updating guidelines.

Dr. Wachter, an internist, is professor and chair of the Department of Medicine at the University of California, San Francisco, a member of The Doctors Company's Board of Governors, and a thought leader in care quality, patient safety, and digital health. He has published more than 250 articles and six books and is the best-selling author of The Digital Doctor: Hope, Hype, and Harm at the Dawn of Medicine's Computer Age*.*

Dr. Jha, a practicing physician, is dean of Brown University School of Public Health and professor of health services, policy, and practice. He is recognized globally as an expert on pandemic preparedness and response as well as on health policy research and practice, has published more than 200 pieces of original research, and is a frequent contributor to a range of public media platforms.