Exhibit 176

Why did Dr. Offit vote NO on Omicron-specific boosters at the FDA Advisory meeting? What's up with the vaccine for the youngest kids?

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[Why did Dr. Offit vote NO on Omicron-specific boosters at the FDA advisory meeting? What's up with vaccine for the youngest kids? AND MUCH MORE…

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– ZDoggMD] Dr. Paul Offit, P. Diddy, if you're nasty. Welcome back to the show, man.

– [Paul] Thank you, it's so good to see you Z, it's been too long.

– [ZDoggMD] It's been like six months or something. You know, I feel like there's a pandemic between us. Every time I tell my audience, I go, you know, I'm getting Paul back on the show this week, they go crazy. They've got a million questions for you. They actually, I don't know why, but they actually trust you because you've kind of, co-invented a vaccine, you're a vaccine expert, but you don't, in many ways I think of you as the Peewee Herman of our time. Kind of a loner, a rebel. And the reason I bring that up is that recently, and I wanna get into a buncha stuff. We're gonna talk about kids vaccines. We're gonna talk about Omicron specific boosters. We're gonna talk about the state of vaccines currently, the state of the pandemic, all the things. But recently you were part of the FDA vaccine advisory committee, the VRBPAC if you will, and you were one of two dissenting votes about an Omicron specific updated vaccine in the fall. Let's start with that, maybe.

– [Paul] Okay, so lemme put it in context. I'll start from the beginning in October, November of 2019, a strain, a bat coronavirus made its debut in the human population, right, the so-called Wuhan-1 strain. That's the strain against which all vaccines are made. The mRNA vaccines, the vector virus vaccines, NOVA vaccines, purified protein vaccines, for that original strain. That's not the strain that left China. The strain that left China had a mutation at this, the amino acid number 614. It was called the D-1614-G strain. That stabilized the virus and allowed it to become much more contagious. So that's the virus that swept through Asia, swept through Europe, swept through the United States, killed a couple hundred thousand people here. That was replaced by the alpha variant, because it was more contagious. It was replaced by the Delta variant because it was more contagious. All of those viruses, those three variant viruses are well covered by that original vaccine that was made from that Wuhan strain. But then Omicron hit. And Omicron, unlike the others where you had sort of a handful of mutations, Omicron had 30 mutations in the spike protein, either receptor binding domain or N-terminal domain. That made it immune evasive. Even if you'd been vaccinated, even if you'd been naturally infected, you could get a mild illness, that was clear. And then what followed from there were the Omicron sub-variants, which were somewhat distant from Omicron. Omicron is so-called BA.1 variant. And then you have, you know, the BA.2, BA2.1.2.1, BA.4, BA.5, and that's where we are now. Where we are now is BA.4-5 represents a little more than 1/2 of the circulating strains in this country. So reasonably the FDA has considered trying to broaden our immunity. 'Cause now that we sort of cross the Omicron threshold, wouldn't it make sense to broaden our immunity by including Omicron or an Omicron sub-variant in the vaccine, in a bivalent vaccine. So you still get the ancestral strain, which some people call the original recipe strain, which I like, plus this, you know, the Omicron variant.

– [ZDoggMD] Wait, so not to interrupt, but you're saying that BA.5 is like New Coke.

– [Paul] Exactly.

– [ZDoggMD] Like maybe we, can we actually send it back and go back to the ancestral Coke?
– [Paul] Which would be Classic Coke, right?
– [ZDoggMD] Classic Coke, yes, exactly. Anyway, so back to you. So now we're up to BA.5 and we're talking about this bivalent vaccine where you're including the older strain that we started this thing with, and now the BA.5, that's the proposal.
– [Paul] Right, and so reasonable, reasonable argument. So let's look at the data. So Moderna and Pfizer both presented at our meeting last Tuesday, which was, I think was June 28th, so a week ago, and the data were not compelling. And here's why. They did the studies the right way. So they took people who had already received three doses of the ancestral strain and then gotten a fourth dose with the ancestral strain and compared that to three doses of the ancestral strain, plus the fourth dose is the bivalent strain, which can contains the Omicron mRNA vaccine, as well as the ancestral vaccine. That's the right way to do the study. Then what they did was they looked for a neutralizing antibody, its virus specific neutralizing antibodies against Omicron. And what they found was that when you got the Omicron boost, you had a 1.75 fold increase in neutralizing antibodies against Omicron. Well, the question is, what does that mean? What does that number mean? And the answer is, I think while statistically significant is I don't think that's a clinically significant difference. The reason I say that is because if you look at the original vaccines when they were authorized back in December 2020 Pfizer, Moderna, back in mid-December 2020, there was a twofold difference between Moderna and Pfizer regarding neutralizing antibodies. And Moderna had about a twofold increase in neutralizing antibodies compared to Pfizer. That did not translate into a clinically significant difference in terms of protection against severe disease, which is the goal of this vaccine. The goal of this vaccine is protecting against severe disease. Keep you out of the hospital. Keep you outta the ICU, keep you outta the morgue. So I think that that 1.75 number was not significant. Secondly it's, Omicron's gone. So the real question is, does this protect against BA.4, BA.5. Now both companies, interestingly took presented data on, now that you've gotten the fourth dose of this Omicron containing vaccine, they showed you what the neutralizing antibody titer was to BA.4, BA.5. What they didn't show you was what the neutralizing antibody titer to BA.4, BA.5 was, if your fourth dose was the ancestral strain. They never showed those data. That's the obvious thing to do because that's why you have control groups is to control for your experiment. And I just found it odd that neither presented that. That bothered me. The other thing is that that if you look at say experimental animal model studies, there was a nonhuman primate study done by Bob Cedar's lab at the NIH, was published in "Cell". Matthew Gagne, G-A-G-N-E, was the first author. But what they did was what you wanted, what you wanna see from an experimental animal model. I mean they had three doses of the ancestral strain versus two doses of the ancestral strain then the Omicron boost with an Omicron challenge, right? No difference, no difference, okay. So you don't really have animal model studies that support this. You don't have, as far as I'm concerned, neutralizing antibody study data that supports this. And I guess the thing that is most upsetting to me is normally when you get something from the FDA, when we have these meetings, so you usually get it a few days before you meet, you usually get a couple hundred pages. And actually before the June 14th meeting about pediatric vaccines, we got 440 pages to read about three days before the meeting. They assume that you don't have a life, which

is true, but I don't think that they should assume that. So in any case here on the other hand, normally you get the EUA submission from the company, which is 85 to 100 pages long, and then you get the FDA's review of all those data. It really, really is heartening. I mean, it is a very thorough review. Not here, here it was 22 pages from the FDA, which included 1/2 a page on Pfizer's data and 1/2 a page on Moderna's data. You could get that from the press release. In fact, it was no more detailed frankly than the press release. So I just thought the question we're being asked is in the end always, is do the benefits outweigh the risks, even though the risks are generally small and sometimes unknown, that's always the question. Do the benefits of this vaccine outweigh the risk? I didn't see the benefits. I was surprised actually, frankly, that of the 21 voting members, 19 voted yes, 'cause I just didn't see the evidence for that. And we'll see how this plays out. I mean, this was something that I think they, that was desired by this administration. I could be wrong, but the way that this, the other thing that was odd about this meeting was that we're an advisory committee. We're being asked for our advice. So normally what happens is they just present the data. Here's the data, what's your advice? And people can ignore our advice. I mean I'm in academic medicine, people ignore my advice all the time, but to make the best advice. So here on the other hand, however, they had somebody from the WHO, Kanta Subbarao, who presented their opinion about this. And their opinion was they thought this was a good idea. And then you had the FDA presenting where they also had an opinion. That's unusual. And then the next day, you know, you read a public health announcement from the, a press release from HHS Health and Human Services that says that the government has decided to purchase at least 105 million doses from Pfizer with up to 300 million doses. It was a little unclear from that press release, but they mentioned that we had just made this decision the day before. So you just sort of felt like the fix was in a little bit here. Maybe that's not the right phrase, but it was something that they wanted. And I felt like we were being led here with a critical lack of information. So we'll see how this turns out. But I didn't like this.
– [ZDoggMD] Well, you know, this is, I mean, this is a… You remember Paul in the early days of the pandemic, when we were talking about the possibility of a vaccine happening in a year, and you and I were both skeptical. And part of the skepticism was, we were worried that it was gonna get kind of steamrolled through in a politicized way that was gonna sacrifice the integrity of the process of review, the science, and potentially vaccine uptake across other vaccines if you screw this one up. And there was concern that Trump was gonna try to rush it through, et cetera. Then the vaccine happens and now we're expressing concern that, well it just seems like it doesn't matter what politician's in office, there's always some kind of agenda, and there's always a concern that is it influencing how we actually process these FDA type strategies. And everything you said is, so let me just recap a little bit. Number one, they're looking at just neutralizing antibody levels in a way that doesn't even really quite take into account the control group the way you pointed out. The idea that, okay so it makes 1.75 the levels of neutral neutralizing antibodies, but so did Moderna relative to Pfizer in the early days and that did not translate into a nearly 2x fold improvement in prevention of severe disease or even infection. So these numbers do not necessarily correlate to efficacy. We're asking now for a logistic shift where potentially billions of dollars are at stake to transform a vaccine from the ancestral strain to a new bivalent strain, including these Omicron specific boosters, without clear and compelling evidence that it's actually gonna improve

the outcome we care about most, which is protection against severe disease. And yet it seems like the burden of proof for FDA seems to be going down and down and down instead of being at a level that you're comfortable with. Am I, is that an accurate summary of what you said?
– [Paul] No, exactly. And I think what has to be taken into account, which is why they have control groups, is the fact that if you look, for example, if you get two doses of the ancestral strain, and then you get a third dose of the ancestral strain, you clearly get a boost in Omicron specific neutralizing antibodies. So that third dose does that for you. Now, you could argue that in terms of protection against severe disease, if you're a healthy young person, two doses may still well have been enough, but you can't ignore the fact that that third dose does increase neutralizing antibodies against Omicron as well as BA.4 and BA.5. So that's why you have those control groups. And the fact that they didn't do that part of the study where they show you those neutralizing antibodies against BA.4, BA.5 with the Omicron boost, and then compared that to the pre-boost in that group, instead of comparing it to the boost with the ancestral strain. I mean, Linda Safe, just published recently an article in New England Journal of Medicine, showing that if you look at healthcare workers and they get two doses of vaccine as compared to three dose of vaccine, they clearly get a boost not only against BA.1, but against BA.4, BA.5. So what are you gaining by giving Omicron or BA.4, BA.5? Because remember it's a new product. And I think, you know, that we don't have a bivalent vaccine. And I think if anything, if we've been taught anything over the last 2 1/2 years, it's the humility of introducing a new product. I mean, no one would've predicted myocarditis associated with mRNA vaccines. I don't think anybody would've predicted this clotting problem, so-called thrombosis with thrombocytopenia syndrome. So be humble. And if you, if you're gonna, you know, if you clearly have evidence of benefit, great. But if you clearly don't have evidence of benefit then say no. And it just surprised me that we were willing to go forward with this with such scant evidence of benefit. I think that the phrase that I used was uncomfortably scant was what I said during the meeting.
– [ZDoggMD] And you're one of just two dissenters out of the 19 votes.
– [Paul] 21 votes, so it was 19-2.
– [ZDoggMD] Yeah. I see, I see, so, you know, this is, I mean that is concerning. And you point at the humility. So with Johnson and Johnson, like you said, no one would've really predicted this very unusual clotting syndrome that, what 10 fatalities, I think, documented. I think you have a "Stat" news article opinion piece on all of this that I'm gonna link to, that's very, very well done with a colleague you wrote. And I think what's interesting is, so there's a couple things I wanna dive into that you were talking about. One is this idea of the booster versus is this actually a third dose? In other words, is it necessary to get an Omicron, a more Omicron specific and robust response for the general population, or is it just in particular subgroups, like high risk people, people that are older that would require, where we would cause call that third dose, a third dose instead of a booster that just tops off your neutralizing antibodies, so you get some short-lived protection against infection, but you've already got protection against severe disease. Curious on your thoughts on that.
– [Paul] And that's the question of the day? I think when in December of 2020, we launched those two vaccines, Pfizer and Moderna, I got calls from two people who are very prominent in this field, I mean people who I really respect, who said to me, this is a

three dose vaccine. The reason it's a three dose vaccine is if you look at say the purified protein vaccines, like the hepatitis B vaccine or the human papilloma virus vaccine, or you look at the whole killed viral vaccines, like polio or hepatitis A, you really need a four to six month interval between doses to get the kind of frequencies of memory B and T cells that will give you long lived protection against serious illness. I believed that, but was waiting for evidence to see it because we don't have any experience with this vaccine. mRNA technology is a new technology, and what you saw six months after that vaccine came out, like June, July was that the epidemiologically protection against severe disease was holding up. And with the clinical, the immunological studies by people like John Wherry and Shane Crotty, you saw that the frequencies memory B and T cells was holding up. Then 12 months later, i.e. December of 2021, you still saw, this was a Mark Telford paper that was published in "Clinical Infectious Disease" out of the CDC that at least through the Delta wave, that you still had excellent protection against severe disease, and you still had high levels of memory B and T Cells. So therefore that that advice early on wasn't holding up. Then Omicron hit and that sort of threw a wrench into things because now you had a lot of people who were getting infected, who were otherwise vaccinated. And so then the question is, why? Because there was an increase in hospitalization and there was an increase in deaths. And the question was who? And Z you said it, I think if you looked at who that was, it was primarily people who were the elderly and I mean, really elderly, even more elderly than me and people who were, who had, you know, really the kinds of comorbidity or were immune compromised or had, you know, the kinds of comorbidities that really do put you at high risk. And I think what was happening there was not that they needed a boost in memory, because not easy to boost memory, I think what was happening there is they just couldn't handle that infection because they didn't, let's say they didn't make adequate cytotoxic T-cell responses. So a milder, moderate infection to them was a problem. And so therefore you could help them by boosting neutralizing antibodies for a short period of time, three to six months, and then help them at least get through the period of that Omicron wave. So that's different. And so I'm still not sure that, you know, I still wish you could still argue that a healthy young person, a person less than say 60 years of age still has long term protection against serious illness, because still you're protected. There's enough memory to protect you against serious illness, even with these variants. And that's the good news. I mean, you haven't yet had what you most fear, what I most fear is a variant that is resistant, even if you're vaccinated or naturally infected, or both, that you're still, that you're still at risk of serious illness and that variant hasn't happened yet. So you could make an argument that that's when you need to add a variant specific vaccine, but we're not there yet.

– [ZDoggMD] Okay this is very important. What you just said is crucial for people's understanding. The idea that when Omicron hit, 'cause you and I were both kind of booster skeptics early on in the sense that we needed to see the data about severe disease. And what you're saying is when Omicron hit, so many people were infected because Omicron does kind of escape the, you know, again, it's not a breakthrough, even that term, like you said, early on, it's a terrible term. The vaccine is not really designed to prevent infection, it's designed to prevent severe, I mean, that's the goal of the vaccine. So people were getting infected and this is the deal. And I'll use my dad as an example. So my dad is 82. He was admitted to the hospital this year because he has COPD from

living in polluted environments. He never smoked. Has restrictive lung disease from kyphosis and has a paralyzed hemidiaphragm from a hiatal hernia surgery years ago. And on top of that, he has AFib and some hypertension and is on blood thinners. So he's not the best protoplasm. He got sick with hyponatremia, something got admitted, ended up going to a nursing home. I go to visit him in the nursing home and he just looks terrible and he hadn't, he'd been getting better. And I asked the staff, I go, you know, was he tested on admission? Yeah, he was. Can you test him again? They test him he's positive for COVID. And that COVID infection with presumably Omicron, he's been boosted. He didn't get a fourth dose, but he had three doses and a booster, and that infection itself was not, it did not seem to be causing the havoc. It just was enough to push a guy in that degree of infirmity over the edge to require rehospitalization. He never needed Paxlovid or anything. He got some dexamethasone, but he did fine, it was the other diseases that were thrown out of equilibrium. And I think a bad cold, a mild flu could have done the same thing. So where would a fourth dose have been helpful there? Well, right before if his neutralizing antibodies might have been topped up, he might have had more resistance to infection that might have prevented that. So that's the case study I think, where that thing really makes sense, but, and tell me, am I wrong or am I crazy?
– [Paul] I think that's exactly right. And I think that's what the CDC can help us most, is instead of showing us, for example, they have in a recent publication that you see they look at sort of two doses versus three doses for Omicron, and you see clearly better protection against serious illness in those who got the third as compared to just two doses. Who are those people? Who are they? And because we need to define them. Because if we don't and we don't do a very good job of this, then everybody gets recommended to receive it. And I just think, you know, not everybody benefits.
– [ZDoggMD] And now this and this points right back at not everybody benefits, but yet as a policy tool, many colleges have been mandating a third dose in order for kids to attend virtual graduation even. So, I mean, what are your thoughts on the sort of policy hammer of mandate with something like a booster for young people?
– No, it's hard to watch actually. I mean, my daughter's fiance, she's getting married next year.
– [ZDoggMD] Congrats.
– [Paul] You know, he was at Cornell and he's a, you know, he's a healthy 20, 20 plus year old, and he was mandated to get a third dose of vaccine before he could go back on campus. It's wrong. I mean he was protected with two doses. It's just wrong. It's not, it just was unfair.
– [ZDoggMD] You know, it's kind of heartbreaking because you're a massive vaccine advocate. I mean you've dedicated your life to this and you've written books about it. And what's interesting is it's harming, like when, when these young people email me, they say, you know, what can I do about this? Like, I've gotten two doses. I've had actually infection with COVID. They're mandating I get a third dose. I feel like my bodily autonomy is violated for no community benefit. Like these are idealistic young people. They're willing to take, you know, a hit to their own autonomous decision if it's gonna help other people, but they don't see the evidence for that, and that's where it just gets ugly.
– [Paul] I agree.

– [ZDoggMD] Yeah, so I have a question. So as we get these BA.5, you know, we're up to BA.5, BA.4/5 is the predominant strain in the country right now, where do the old variants go? 'Cause many people ask these questions. Are they extinct? Are they hiding somewhere? Are they in an animal reservoir? What's going on with that?
– They're just outcompeted. I think, so they become just less and less as a circulating strain. This virus out competes them. I mean, it's interesting that it doesn't appear that, well, it's hard to know whether these viruses are more virulent, because you're up to now like 80 to 90% population immunity. So it's not where we were two years ago, where it was much easier to say virulence, because you didn't have, you had people who truly were naive. It's the rare person who's naive. I think what's gonna be really interesting is what happens this winter. Because although the virus can clearly circulate year round and cause harm the year round, if you look at the last two winters, there clearly is a bump, once you start to get to November, December, January in terms of hospitalizations and deaths. And so now you have such a high level of population immunity, I suspect there'll be a bump, but I think it's gonna be a little bump. I'm really curious to see how this virus plays out, because no one predicted that it would mutate to the degree that it does. I mean, I know it's a single stranded RNA virus, but you know, there's other single stranded RNA viruses that don't mutate like this. I mean measles is a single stranded RNA virus. We could eliminate it with vaccination. Rubella is a single stranded RNA virus. We could eliminate it with vaccination. They're not all the same. This one is different than I think what would've been predicted.
– [ZDoggMD] Yeah, and you know what's interesting about this whole dynamic, is it is a dynamic. We can't take COVID and pull it out of isolation. You have to put it in the context of, you have a, it's now almost like a constant flu pressure on the elderly infirm population or the people with multiple comorbidities, where it's year round, there's like a new variant that's so contagious that everybody's getting it. And we don't really normally have that. We have our normal compliment of viruses that we're quite used to, and we have some immunity to, and they're quite seasonal. And this has kind of thrown us for a loop in that sense. So it wouldn't surprise me if we see some uptake in deaths in that population, even with 90 plus percent population immunity between natural infection and vaccine infection. It wouldn't be a surprise. And one related question to that, so now with kids, which we're gonna get into kids vaccination and all of that, with kids because of our behavioral changes, we've masked young kids, we've taken them out of school for a bit, put them back in. We've kind of been quite cautious with kids, especially parents that are worried since there wasn't a vaccine and so on. And have we, and now we see changes in patterns of viral infections that have been quite standard for years, like RSV, influenza. What are your thoughts on this in the context of whether it's hygiene hypothesis or just the general viral milieu that we're around, how has COVID thrown that into disarray?
– [Paul] Well, it certainly did the first year. I mean, when we just, you know, closed businesses, shut down, you know, closed schools, you know, restricted travel, everybody wears masks, social distance, we didn't, you know, sporting events were not attended by groups of people, I mean, large groups of people. That first year flu disappeared. I mean, you know, we normally have about 75 to 150 pediatric deaths from influenza every year. One, one pediatric death that year. I mean, our hospital is loaded with respiratory syncytial virus, you know, associated with bronchiolitis, none. I mean, so that's it. If you

wanna stop respiratory viruses, it's not that hard, just never leave your house. As soon as you leave your house, they've come back. I don't think, I think the hygiene hypothesis, I really don't think applies to this, because it's always been brought up with regard to vaccines, right? We're now eliminating certain viruses, therefore, because of that, you know, we're sort of biasing our immune system towards this TH2 rather than TH1 response and therefore we're more likely to have these allergic phenomena, asthma, et cetera. I don't think that that really applies to vaccines. And I don't think it applies to this. But I think what'll be really interesting is how this plays out. Because, and you alluded this earlier, this virus isn't going anywhere. I mean, we are gonna be dealing with this virus for decades. Remember the first two human coronaviruses that were isolated in the early 1960s, we were both derived from bats. One of them probably came into the human population in the late 1700s, the other in the late 1800s. I think we're gonna be dealing with virus for decades if not centuries. And the question is, how will it play out? Knowing that every year 3 1/2 to 4 million children are born in this country who are completely susceptible to the virus and knowing that there are people who are immune compromised, because we have such a variety of immune compromising agents now much more so than we did 30 years ago. So, those are gonna be the people that are gonna need to be protected as we move forward, depending on what this virus does. I mean, the four strains of human coronavirus that circulate probably account for about 15 to 20% of the respiratory infections that come into our hospital every winter. Will this virus settle into that? Because this virus is different. I mean, this so-called, multi-system inflammatory disease of children where the virus basically teaches your immune system to react against the cells that line blood vessels, so you see children come in with not just lung disease, but heart disease, liver disease, kidney disease, these other viruses don't do that. But will this virus evolve away away from that? I mean, multisystem inflammatory disease in children has virtually disappeared. So we'll see what happens.

– [ZDoggMD] Now, this is really interesting because you answered the question I was gonna ask, which is, is this just the natural, are we watching in a modern context with modern tools and modern susceptibilities and strengths, the introduction of a coronavirus, which has happened historically, you know, three other times, right? Or is it four? How many circulating coronavirus? Four. That includes SARS-CoV-2 or without SARS-CoV-2?

– [Paul] No, SARS-CoV-2 would be the, well there's other ones too, but in terms of common circulating, this would be the fifth.

– [ZDoggMD] Got it. So are we now seeing like the, you know, was there, MIS-C in those times, and we just never knew what that was, you know?

– [Paul] I don't think so. It's a pretty, I mean, MIS-C in our hospital is striking. I mean, many of those kids have to go to the intensive care unit. It is striking.

– [ZDoggMD] Yeah.

– [Paul] Although the problem is right now it's like every child who comes into our emergency department who has fever, who was COVID positive in the past month is considered to be having MIS-C. So it's whereas it's often not true. And so it's frustrating.

– [ZDoggMD] Right, right, so there may be a little bit of hypervigilance going on. And that kind of relates too to the idea of, and we'll is a good segue into children, right, because you said, you know, two to 3 million kids are gonna be born into the world with total susceptibility to this new coronavirus. But in many ways, that's how it's been for the

other coronaviruses too, right? Because when you're born, you get that maternal immunity for what about six months, and then it's gone. So, but yet there's some modulation of disease. Or is there? Because you're also pointing out that 15 to 20% of your respiratory infections that are getting admitted are these old school coronaviruses.
– [Paul] That's right.
– [ZDoggMD] So yeah, just curious, you know, what you think.
– [Paul] Yeah, so we'll see how this virus settles out. You know, you don't, viruses can evolve to become more virulent or less virulent. This virus may be evolving to become less virulent. We'll see. You would think from the virus's standpoint that it's always the virus's advantage to be less virulent because it's never an advantage of the virus to kill you because then it can't do what it wants to do, which is just continue to live and spread from one person to the next. So there are, there's some evidence that Omicron was less virulent. So we'll see how this plays out. And I'm really curious, this winter, I think will tell all about where we stand in terms of population immunity.
– [ZDoggMD] Yeah, and one thing I want to double down on that you said earlier is we're trying to figure out how virulent a virus is or a new variant is, it's difficult to do in the context of the changing level of population immunity. So that's the, and that's why, like you say, in the winter, let's see what happens as some of the neutralizing antibodies wane, but we still have these memory B and T cells from previous infection and from vaccination. And again, it comes back to, do you really need a booster for most levels of population versus those elders and those younger people with multiple chronic diseases that are at risk. And now back back to kids. So I wanna kind of set a stage about what are kids at risk for with this virus? What's at stake? And then where does vaccine fit into this picture? We talked about, MIS-C, and that's largely disappearing now, which is interesting, right? What about severe disease and death in kids? And then what about long COVID and what is that and how do we think about that and what's going on there?
– [Paul] Right, so on June 15th, the FDA, our FDA's vaccine advisory committee meant to discuss Pfizer and Moderna's vaccine for children less than five. And so the first issue that the CDC addresses, what's the burden of illness? And they argued that for the past, previous two years, that if you look in that age group, that there's been roughly 45,000 hospitalizations. Of those hospitalizations, 10,000 of those hospitalizations resulted in ICU admissions, intensive care unit admissions. There were about 420 to 430 deaths in that age group. Now there's a couple limitations there. One is that was the previous two years. So that doesn't necessarily predict what's gonna happen in the next two years where there's a much higher level of population immunity. Two is it's, oh the other point they made was that about 2/3 of those children had no known risk factors. So one only 1/3 had high risk factors. But the other issue is, and it really is important for us to separate children who are admitted with, or for COVID. And 'cause you see some of these studies now where they're looking just at a simple metric like oxygen requirement, and that eliminates a lot of people who are just being eliminated with COVID and not for it, not for the treatment of it. 'Cause we will screen everyone who comes into our hospital will be screened to see whether they have COVID and I think those statistics can get mixed up. So that's also important. And I think as we move forward and knowing that there are certain groups that are susceptible, when will be the best time to immunize? And I think that that we're gonna learn about that over time. I mean, you know, with HPV we immunize in the adolescent age group, even though arguably you know, there

are certainly children who are born to women who are HPV, who have HPV, who will then get this so-called re recurrent respiratory papillomatosis, you know, that they'll get in the first two months of life. So when you immunize is gonna be an issue and I'm really interested to learn how this plays out. Children certainly can get this virus and they certainly can get it severely. I was on service last week, we had a child who had a pretty severe COVID pneumonia. I mean he had it for a couple weeks. I mean when you saw his chest x-ray and his CT of his chest, it was brutal and he was really struggling to breathe. So if this disease can be prevented safely, then it should be prevented. But when is the best time to do that? I think we'll find that out as we move forward.
– [ZDoggMD] Yeah, it's really interesting because I've thought about this quite a bit, even in the context of the preventable childhood illnesses that we use vaccines for now, measles, mumps, rubella, et cetera, because a lot of people will push back and say, well, this particular syndrome really hurts the elders and people with multiple chronic diseases, but it's so unusual to harm a child. But what you're pointing at is, well, okay, but let's say the child, that the children that are harmed, it's terrible and a lot and a fair number of them have no preexisting conditions, so you're not, you don't have a good warning that that child is at risk. If you have something that is very safe and you can administer in a mass vaccination, why wouldn't you do it, if you can prevent even, you know, 400 deaths of children a year? Those are children that would have had a whole life ahead of them. Am I understanding that calculus correctly?
– [Paul] Exactly. So there's been what, you know, there's been a million deaths roughly in this country, from that virus, from this virus. and about 1,000 roughly in children, depends somewhere between 1,000, 1,500, that's 0.1%. So obviously you're much, much worse off if you're an older person than if you're a younger person. But you know, if the virus can cause harm and it can, I mean, same with flu, I mean there's 75 to 150 flu deaths a year, whereas, you know, sometimes there's many thousands of flu deaths, so that's a small percentage again. But if it can be prevented safely, then it should be, then it should be prevented. I think that's where people, I mean, if you look for example, at the 12 to 15 year old, what percentage of 12 to 15 year olds are vaccinated? About 60%. That vaccine's been out since last May, more than a year. If you look at the five to 11 year old, about 30%, a little more than 30% have been vaccinated, for a vaccine that's been out since last November. So you're already, you know, seven months into this. And now we have this vaccine, which is out for the less than five year old. I'm sure it's gonna be well less than 30%. I'd be surprised if it was 15% of parents of that, in that age group vaccinated. And so why? Why do they choose not to do that? I think two reasons. I think one is because they just don't see their children as likely to get this disease or suffer, 'cause that's not what they hear. They hear it correctly, that it's mostly the older people who die. And two, because we're always a little hesitant about inoculating our child with a biological agent that we don't understand very well. And we assume that a choice to do nothing is a risk free choice when it's not, it's just a choice to take a different risk. I mean, so that's your goal as a parent is take the lesser risk. That's our job.
– [ZDoggMD] Yeah, now that's key. You're you're always taking a risk no matter what you do. And so the question is what's the risk you're comfortable with or the risk that's lesser in your mind or in your calculation of risk. So let's then dive into the less than five year old vaccines, which are… This has been very tough on a lot. So there are a lot of parents that really have been desperate for this, and they'll take almost any level of

evidence that says, okay, it's not gonna hurt my kid, I wanna give it to them. I'm quite anxious about this. And then there's groups of parents that are like, you gotta show me a multi-thousand person, randomized trial, where I don't see cases of, you know, myocarditis or anything unusual. And I wanna see outcomes that show that it's actually preventing severe disease. And then there's people in between that are just don't quite know what to do with it. And so I'm curious how you kind of think about this and you've seen the data, you sit on the committee, like what are your thoughts on the less than five year old vaccine.

– [Paul] Right. It's interesting, it's exactly what you said. When the 12 to 15 year old vaccine was available, there was a huge spike in uptake and then it immediately came down and really never recovered. Same thing with the five to 12, huge. So those parents who wanna get it, they're gonna get it the minute it comes out and that's it, then we're done. And I'm sure that that's probably gonna be what happens here, spike, come right back down again. It's interesting. It's the first time I would say we ever considered vaccines for any age group, whether it was the adults back in December of 2020, or then the 12 to 15 year old, and then the five to 11 year old, where there was a divergence between those two vaccines, the Moderna and Pfizer mRNA vaccines. I mean the Moderna vaccine is a two dose vaccine. The Pfizer vaccine is a three dose vaccine. Now we were supposed to meet actually, we the FDA vaccine advisory committee were supposed to meet in February, so towards the end of February of this year to discuss Pfizer's vaccine, I think, as a two dose vaccine. And then we didn't meet. And I think it's because the data were so poor after the second dose, both in terms of immune response, as well as protective efficacy that they were gonna wait till they finished their third dose trial, and with that, you saw that there clearly was a boost in immunity that if you look at the immunobridging studies, meaning the neutralizing antibody levels that were seen in those children was essentially identical to what was seen in the 16 to 25 year old group, where you knew there was protection. And there was, you know, protection, again, the numbers were really, really small, like 10 total kids had actually symptomatic illness, so you couldn't say anything about efficacy. But you were reassured by the immunobridging data and same thing with Moderna. Because see right now, the protection against mild disease, which is what most kids get is not very good with these vaccines because they're, because of Omicron, and now the Omicron variants. You know, when the studies were done way back, you know, for the adults and even the 12 to 15 year old, and even to some extent, no, not so much the five 11 year old, but the 12 to 15 year old, then, you know, Delta was still the circulating strain. So even efficacy against mild disease look good. It doesn't look good now. But I'm trying to figure out a nice way to say this, who cares? The goal is preventing severe illness. It's okay, we're gonna have to get used to mild illness. This is a short incubation period, mucosal, respiratory infection. It has an incubation period of whatever, four to six days. That is short, and so while you may have great memory responses, it takes too much time for activation of those memory cells to become, say, in the case of memory, B cells, antibody screening cells, to prevent a mild infection. I mean, you need a long incubation period, two to three weeks in order to, for that to happen, which is what happens with measles. You can eliminate measles because it has a long incubation period, meaning two to three weeks. You can eliminate small pox. You can, which we've done. We actually eliminate measles from this country by 2000, until a critical percentage of parents chose not to vaccinate their children anymore.

We eliminated rubella by 2005. Why? Because it's a long incubation period disease. You will never eliminate this virus because it's a short incubation period. If 100% of this country and this world is vaccinated, this virus will still circulate and it will still cause mild disease, and at some point we're gonna have to get used to that. 'Cause we're coming off this sort of zero tolerance with this virus, no asymptomatic infection, no mild asymptomatic infection, test, test, test, quarantine, quarantine, quarantine, and at some point we're, and it's happening. I mean, you are already seeing sort of an arose where people are willing to accept the fact that we're gonna be living with mild illness for this, for my lifetime, my children's lifetime and their children's lifetime.
– [ZDoggMD] And so, I mean, this is what I think you and I, and others have been advocating for a while, that eventually we're gonna get to a equilibrium point where this thing, like you said, because of the incubation period, because of the fact that you cannot prevent infection, it's not going away, and there's animal reservoirs. So on top of all that, unless you wanna murder all the deer and all the cats and all that, which, you know, there's some allure to a mass murder of animals. I believe we do it when we eat our burgers it's not gonna work. And so one of the questions then becomes Paul, because you said, you know, it becomes a tipping point of the community benefit of the vaccination versus the individual benefit. And where do mandates as a public policy tool come in? Early on, we were talking about mandates and this was in the early days of vaccine. And it was like, you know, people were dying, people weren't getting vaccinated, and so employers were throwing in mandates, schools were throwing in mandates, et cetera. What is the role of the mandate for a, 'cause we don't mandate influenza vaccine except for healthcare workers generally. Do we continue to put in mandates for the coronavirus vaccine in this new setting of population immunity and living with the virus or is it now not a useful policy tool, relative to say measles where if you stop immunizing children, that disease comes back with a vengeance?
– [Paul] I guess I put it right now in the category of flu where I think it's reasonable to mandate it for healthcare workers as we do at our hospital, because we take care of people with COVID and you can transmit that virus from one person to the next, as we do with flu. So I think it's reasonable there. I guess I'm not at mandates for yet for this virus for, let's say for school entry. I'm not there. We'll see how it plays out, but I'm not there.
– [ZDoggMD] Right, so for the kids vaccine, I think one of the concerns a lot of people have is if it's approved, even as a UA, schools are gonna start mandating it, and–
– [Paul] Oh, you mean if it's approved for UA that they would mandate.
– [ZDoggMD] That's right.
– [Paul] I'd be surprised actually. First of all, you know, we're just, I feel like you're leaning into a left hook right now if you mandate it, given sort of the attitudes that people have about this vaccine. It's just what scares me more frankly, is that this sort of, you know, government off my back don't tell me what to do is gonna spill over into other vaccines. And you're gonna see an erosion in mandates in general and do that and these vaccines will come back. I'm sorry, these diseases will come back.
– [ZDoggMD] Agree, and I think that's why our public health messaging around the COVID vaccine is so important. You know, some nuance and some the kind of way you talk about it, where actually a rather skeptical audience actually trust you about vaccine is because you're actually quite forthright and authentic about, okay, here are risks, here are benefits, here are what I would do for my kid. Here's what I, that's kind of how I think

we ought to talk. And it then doesn't create this reactance that spills over. Because it really triggers the sort of libertarian antibodies in this country, when you start mandating, say a two year old to go to a preschool, has to have a vaccine that has what, how many, 400 odd people in each trial arm and, you know, so on and so forth. Do you think so far the evidence of safety in that population is sufficient to vaccinate children?
– Yes, I think 'cause we're sort of testing, keep testing the water with one foot in a sense. I mean, you have, you know, you knew that for example, so myocarditis is what one worries about. And what you worry about, or it was what I worried about is that when you did that study saying the greater than 16 year old for Pfizer, the greater than 18 year old for Moderna, Moderna had the bigger problem. It was really the young person who had myocarditis, I mean the sort of less than 30 year old. So now you're going to the 12 to 15 year old. First of all, why was it the young person? And the thinking behind myocarditis is that it's molecular mimicry. So in other words, that you have the, that sort of the heavy chain of alpha myosin on your heart muscle, you know, mimics the SARS-CoV-2 spike protein. So while you're making an immune response to the spike protein, you're inadvertently making an immune response to your own heart muscle. Now the good news is that was a transient, short-lived, generally self resolving phenomenon. When we see it in our hospital, those children were often in the hospital for a couple days, rarely went to the ICU, virtually, never went to the ICU. We really didn't do much, and then it got better. That's good, but you have to assume that there's a spectrum of illness because that's always true. So, and you have to assume that there may be long term problems because that is certainly possible. So as you move down to the 12 to 15 year old, it was reassuring that although it could occur, it occurred less commonly. And then as you moved down to the five to 11 year old, it occurred even less commonly. So I feel that we jump into some extent with a net here. I mean, this is the most studied vaccine in history, Maurice Hilleman, who I consider to be the father of modern vaccines, and I was fortunate enough to know, you know, for the years that he was at Merck. I mean, he's, you know, the primary researcher or developer of nine of the 14 vaccines that we give to children. It's like trying to imagine, you know, another dimension, how much work he did that was successful. But he said it best, he said, I never quote, "I never breathed a sigh of relief until the first 3 million doses are out there." Well, the first 3 billion doses are out there, so we have a lot of information on this vaccine. So yeah, I mean, if I had my children or you know, of an age where they can start to have children, I would recommend that they vaccinate those children in a second.
– [ZDoggMD] And again, based on your understanding of the safety and the fact that even if you can prevent a severe disease and it's rare in those kids, why wouldn't you do it if the safety threshold's quite good?
– [Paul] Right, I mean, look at meningococcosis. How many cases of meningococcosis are there in the United States? 300. You know, but that's a severe disease and occasionally fatal disease. So yeah, I mean, I guess we'll have our biases. I work at Children's Hospital in Philadelphia and so I see some of these. I was just on service last week, and this is not a peak, you know, COVID time right now, and there was one perfectly healthy boy who really was struggling and you looked at his chest x-ray and his CT scan and it was brutal. I mean, I just felt so badly for him struggling.
– [ZDoggMD] Yeah.
– [Paul] And if it's preventable then prevent it.

– [ZDoggMD] You know, so you point out our biases and stuff, what's interesting about you Paul, this is just a meta comment on this is you know, you're a guy who went through this system, you know, you worked in conjunction with pharmaceutical companies to develop a vaccine. You're an expert on these things. And what's interesting is that you're not ideologically possessed. In other words, if something happens like this booster thing with Omicron, you're gonna question quite hard, even though it might cost that pharmaceutical company a ton of money, if they took the decision you're recommending, which is to wait and get more data. That's what you're doing because that's the integrity of the position. And again, I think we ought to have our public officials, our public scientists, when they look like they're ideologically possessed by their own bias, nobody trusts them, except for people who are possessed by the same ideology. And that's why I think it's important, your voice is so important in all this. Now, speaking of which–
– [Paul] Let me just have one thing, cause I think you really raised a really good point. It's the opposite is true for something like me. I mean, so I was fortunate enough with Stanley Block and then Fred Clark to create the strains that became the bovine human reassortant vaccine RotaTeq. So it's, so we spent 10 years doing the research to try and figure out how to create these essentially combination of viruses that could induce an immune response without causing disease. I mean, that was 10 years worth of work. And then there's like another 15 years of doing the research of development, meaning get the right buffering agent, right stabilizing agent, the right dose, the right dosing interval, the right vial. I mean the real time stability studies do all of that. It's 26 year effort, okay. And then, you know, it's as the old Chinese proverb goes when the gods are angry, they grant you your wish. Okay, so now this is a vaccine. This is a vaccine that's been licensed by the Food and Drug Administration and approved for universal use in children in the United States, it was a nauseating moment. I know you would think it would be the opposite. Because what you're scared of is what have we done? I mean, you saw what happened with the previous vaccine. I mean, there was a vaccine that was available in the late 1990s that was made by Wyeth with researchers at the NIH. It was a simian human reassortant vaccine that was found when it was out in the real world to be a cause of intestinal blockage called intussusception. That was a surprise. So Fred and I, Dr. Clark and I remember sort of pouring through gene databases. Is there anything about the surface proteins of this virus that mimics say cells that line your synovium you know, where we could be inducing arthritis. Anything that's similar that could be inducing an immune response against pancreatic eyelet cells that could cause diabetes. I mean, is there anything that would mimic say, you know, neuronal cells where you would cause any sort of dysmyelinating disease. Have we, what have we wrought? I mean you are now having your wishes coming true. You are about to put this into millions and tens of millions and hundreds of millions of children, and you just hold your breath. It is a, it's a nauseating moment in many ways to wait to see what happens. So in many ways I feel like people like me or Dr. Clark and Dr. Block are exactly the people you want doing this, because we know just what it means to do this, I think.
– [ZDoggMD] Oh man. See and, that. This is why when we talk about the death of expertise, right, it is really quite heartbreaking because there are experts and there are experts. So someone who's been through the mill, who's actually has the humility to go, this is still terrifying because we don't know what we don't know sometimes, and we've

tried everything to know what we do not know and control for that, but there's still this thing. And that's why Hilleman's quote of like, you never breathe a sigh of relief until it's in three million arms is I think the central premise. And again, let's go back to COVID.
– [Paul] You're the one who did this. You're the one who made these strains. You're the one who's now put it out there. I mean, it's your name on it at some level. Therefore, you're responsible. I mean you're not gonna be held responsible, but you are responsible for this.
– [ZDoggMD] Man, that gives me chest pain just putting myself in your shoes. And I don't easily get chest pain anymore. Wow, so okay, So let's then bring it back to real life situations. Have you yet gotten COVID?
– [Paul] Yes, I got COVID about a month ago.
– [ZDoggMD] Just a month ago, after all this time, just a month, you got COVID. So presumably an Omicron strain.
– [Paul] Right, I would assume or an Omicron sub variant, yeah.
– [ZDoggMD] And you can refuse to answer any of these questions if you like, 'cause I'm gonna ask personal questions. How many doses of the vaccine did you get and what roughly is your age and comorbidities?
– [Paul] Right, so I can actually tell you exactly my age, it's 71. But so I had three doses. The last dose that I got was a year earlier. So I got it in May of 2021 Technically because I'm over 65, I was recommended to receive a fourth dose. I felt that that didn't, that didn't make me less likely to get a severe disease. I felt that I was protected against severe disease with three doses. I didn't think I needed the fourth dose for that. I thought what the fourth dose would do for me is it would protect me against what happened to me a month ago, but for how long. And I think the answer to that is probably three to six months. So I didn't see the need for the constant booster dosing. I assumed I would likely be exposed to this virus 'cause it's just especially these viruses like BA.5, especially now, which is kind of rampant is just a highly contagious virus. And also when you have the really contagious viruses that are highly transmissible, you need even higher level of neutralizing antibodies, you know, to really prevent that. So basically my attitude was, I may well get this, I'm gonna be, you know, I went to my son's wedding, you know, which is, you know, a lot of people in. You know, I go to sporting events, which is a lot of people. And I realize that at some point I'm gonna be exposed to this virus but I'm presuming I'm gonna get a mild illness, which I got. I mean, I had it for a couple days. Technically, I also should have received Paxlovid, but I just felt like the next day I was largely better. And also Paxlovid, it's now been tested, initially it was tested just in people who were unvaccinated, now it's been tested more in people who were vaccinated. But I didn't, I just thought I was gonna get better on my own and did.
– [ZDoggMD] How about that? So you actually analyzed your own risk and made decisions based on your tolerance and understanding of your own risk. Heaven forbid.
– [Paul] I'm generally healthy. I mean, I don't take any medicine. There's nothing, I have no chronic disease. I'm not on any medicine actually. So I just assumed that even though I'm over 70, that I would survive this. And by definition I did, since we're doing this program, right?
– [ZDoggMD] Yes.
– [Paul] 'Cause otherwise we wouldn't be doing this.

– [ZDoggMD] There's a survivorship bias here. Now, so how much long COVID do you have? I need to ask that too.
– I'm good.
– [ZDoggMD] You're good.
– [Paul] Because I'm, I do think my vaccination status makes me at a lesser risk of long COVID.
– [ZDoggMD] Yeah, now and that's what question I wanted to ask too is so with things like long COVID both in children and adults, which we don't really understand well, do you think the vaccine actually has an impact on that arising? Do we have good data for that?
– [Paul] I think you're, you know, I can, I'm with and with you, I don't really understand this phenomenon. I think we're gonna explain it much better over time. I think virologically, immunologically, psychologically, I think we will have much more information over time about this particular phenomenon. I'm struck by the fact when you look at sort of these meta-analyses of long COVID the one symptom that always rises to the top is fatigue. You know, so we really need to define these things and in more objective ways and it's gonna be hard. I do think though, you're much more likely to suffer this if you were, have a severe illness than if you have a mild illness. Which is not say it's not possible, if you have a mild illness to suffer, 'cause I think it is. But, and I'm really curious to know what the basis of this is. And I think we will learn that over time. I don't think it's one thing. I think it's sort of like saying something like cancer, which is many things, I think long COVID is many things and we'll learn about that over time.
– [ZDoggMD] Yeah, I think the term biopsychosocial applies more than any other disease, it applies to all diseases, but there's a biological trigger, there's a social component and there's a psychological component and they all interact in a way that it makes it very difficult to reduce it to one answer, yeah. Wow Paul, so hey man, every six months we get together, you school us, people get either reassured or terrified or a mix of a toxic stew of both. What, is there anything we didn't talk about that you wanna make sure this audience understands before the next time we talk?
– [Paul] No, we actually talked about all the things actually that are interesting to me in this. I am curious to see how this plays out regarding the bivalent vaccine, because we really need much better data, I think before we move forward on this and I can only hope that it's coming. Because I feel very strongly about my no vote there. In fact, the only reason I voted no was because hell no was not a choice. That's how I felt about this. It's just we need more data.
– [ZDoggMD] Ah, my favorite luminary of all the things Dr. P Diddy, Paul Offit. Man, thank you brother as always. What's next on the social agenda for you, anything fun?
– No, no, no. I pretty much just work.
– Now you're living up to my ideals of what an academic leader should be. All right brother. Thanks so much guys. Share the show. If you wanna join our supporter tribe, do it. If not, no big deal. We're just gonna keep trying to speak the truth as we see it. And we are out. Peace, thanks Paul.
– Thank you, take care Z.