TWiV 1368 Clinical Update

Host: Vincent Racaniello

Guest: Daniel Griffin

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Vincent Racaniello: *This Week in Virology*, the podcast about viruses, the kind that make you sick.

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VR: From *MicrobeTV*, this is *TWiV*, *This Week in Virology*, Episode 1368, recorded on October 21, 2026. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from Washington, DC, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: IDWeek, right, Daniel?

DG: I am down here at IDWeek. I just arrived about an hour ago, took the train down, and so our recording's a little bit thrown. We're recording *TWiV* on a Wednesday night. We'll do a *TWiP* paper on a Thursday night, and hopefully, I'm going to learn a lot here down in DC.

VR: What's on your tie, Daniel?

DG: Actually, I think it's a coronavirus. It's got spikes sticking out like in a corona pattern.

VR: Looks colorful.

DG: I'm going with that. It might actually be the flu, for all I know. [chuckles] Tomorrow, I'm going to end up with an STD tie, because I only brought so many bow ties, right? I can't travel anywhere where I might be required to wear a bow tie on a Friday, so without an STD bow tie. Since I'm in Washington, I thought, why don't I quote one of the founding fathers? Alexander Hamilton. Am I becoming a pessimist? I don't know. His quotation, "Men are reasoning rather than reasonable animals."

VR: Hey, this is a long time ago. Men and women, people were screwed up from the start, really.

DG: I'm going to try to just disparage the men, but OK. [laughs]

VR: I think everybody falls under that category, Daniel. Sorry.

DG: We've got a bunch of things to talk about that made that seem appropriate. One, and really frustrating, but we read in the news, read the article as well, but Kennedy's vaccine plan could cause surge in hepatitis B, study finds. Not OK just killing kids with the measles efforts, but ending the practice of immunizing all newborns against hepatitis B, as Health Secretary Robert F. Kennedy has recommended, would sharply increase the number of chronic infections and put more than half of Americans at risk of disease by age 20,

according to a new study published.

Here's the study in *Annals of Internal Medicine.* We have the article "Projected Effect of 2026 Federal Changes to the Childhood Immunization Schedule on Chronic Hepatitis B Virus Infections in the United States." Here we have analysis where they determine that compared with the universal birth dose strategy, 255 childhood infections, the deferred and shared decision-making strategies would increase chronic HPV infections in the 2026 birth cohort by 19% from that 255 to 303 and by 83% to 467, if you follow that.

These strategies would also increase the number of hepatitis B virus-susceptible people at age 20. This is actually 474,000 and 1,806,000 compared with this universal birth strategy where you'd only have 232. Pretty dramatic increases if we go down this road.

VR: This from a man who knows nothing about science. There's no reason to change this schedule.

DG: He has no proper medical training. It's really unfortunate. Also, HPV vaccines. From the WHO, we have, “Highlights from the Meeting of the Strategic Advisory Group of Experts, SAGE, on Immunization, 5-8 October 2026.” This is something that we brought up a little bit before. This is the concept of a single-dose schedule. In this meeting of the WHO, they're actually going to hit three bullet points here. One is they're suggesting that a single-dose schedule is the most efficient immunization strategy for cervical cancer prevention in girls age 9 to 14.

Based on review of updated evidence, SAGE recommends HPV vaccination of girls age 9 to 14 years using a single-dose schedule. This was identified as the most efficient approach to achieve the primary goals of the global strategy for cervical cancer elimination. I'm going to stop there because maybe you and I can talk about this a little. One of my first thoughts is that this is talking about a global strategy. I do think it's important in high-resource situations like the United States that we ask ourselves, what is the most efficient strategy for us here in the U.S.?

VR: I think efficient is an interesting word. It's not the same as effective.

DG: Yes.

VR: One dose, yes, you can probably get more people. The current dosing, at least in the U.S., is three doses. I can't imagine that one is going to be clinically as effective.

DG: I think that's the issue, like we thought about MMR. "Oh, everyone gets one dose. That's great. If everyone gets two doses, that's better." I think that's important to look at the context. This is a WHO recommendation. This is not necessarily a U.S. recommendation. We have really a lot more resources here than a lot of places in the world. Some of the stuff I did like - I'll leave in a link to this, is they talk a lot about catch-up vaccination in women aged up to 25, catch-up vaccination in women aged up to 30. There's also a discussion about targeting other groups, such as young men and men in general. I just want to make sure we just talked about that a little bit.

VR: You can go up to 45 based on the clinical trial data. They're way below that, and I don't think that's fair. Also, we saw in that meta-analysis that it can help older people as well. I think studies need to be done to formalize that.

DG: Yes, I think, you look at the relationship between HPV and a lot of head and neck cancers. Also, as we saw, the idea that you can get a vaccination after infection. If anything, instead of restricting, we probably want to be expanding HPV vaccination for all the benefits that we're seeing.

VR: Sure.

DG: The article, "The Effect of Pertussis Vaccination During Pregnancy on Pertussis and Diphtheria Immunity in Children at 3 and 4 Years of Age," published in *JID*. Let's talk a little bit about pertussis. We're seeing significant problems with pertussis, and there's a couple different strategies. We talk about cocooning or ring vaccination. This is where not only a pregnant woman gets vaccinated, but everyone around them gets vaccinated.

Here is a tough one. This group followed children born to tetanus, diphtheria, acellular pertussis vaccinated, and unvaccinated mothers to 4 years of age. At both 3 and 4 years, children born to the Tdap-vaccinated mothers, so that's the tetanus, diphtheria, acellular pertussis, Tdap-vaccinated mothers, had lower anti-pertussis toxin and anti-diphtheria toxin IgG concentrations than control children, and pertussis toxin seropositivity and diphtheria seroprotection rates were low in both groups. After a preschool acellular pertussis booster at 4 years, antibody concentrations increased to comparable levels in both groups.

Now, is this a concerning difference? We can look at the numbers and discuss this a little bit. You can see, right? Vincent and I, and for those on YouTube, we're looking at the actual data right now, and you see these levels, you see them go down, and you see these rises. Now, I think there's a couple comments. I spent a little time trying to think about them. One of the ones is that this is data from Finland, and they have a different Tdap schedule.

Now, they're giving this combination vaccine at 3, 5, and 12 months, and then a booster at age 4. If you look at the data, you can see, "Oh, we're seeing these low numbers right before those boosters in Finland." Now, in the US, we're doing boosters at 2 months, 4 months, 6 months, then another at 15 to 18 months, and another at 4 to 6.

VR: Yes, there's a reason for that because you can't depend on maternal antibodies for four years, right?

DG: Yes. I think that you look at this, and we're seeing something we've described where sometimes the maternal antibodies can interfere with the early vaccination, but if you're getting a 2-month, a 4-month, a 6-month, and then a 15 to 18, I think I would want to see the data here in the U.S., and that's data we can certainly get, to see if it really is concerning in any way here in the United States.

VR: I also think we need to know if this is clinically relevant. Do we see an increase in pertussis in Finland, for example, not just the antibody titers going down, right?

DG: I don't think we're seeing a problem. I think that's an important comment. We do know that pertussis vaccines work. We have some really great data from the CDC, the *MMWR*, "Effectiveness of Diphtheria and Tetanus Toxoids and a Cellular Pertussis Vaccine in Children aged 6 Months to 6 Years During a Statewide Pertussis Outbreak - Alaska, May through November 2024." Pertussis vaccines, like so many of our vaccines, are pretty incredible in what they've done.

"Widespread use of pertussis vaccines in children has resulted in a greater than 90% reduction in the number of annual pertussis cases in the United States after a period of low U.S. pertussis incidence during and shortly after the COVID-19 pandemic incidence increased in 2024. Data on the real-world effectiveness of diphtheria and tetanus toxoids and a cellular pertussis vaccine against pertussis during this disease resurgence are limited.

In response to documentation of a record high pertussis incidence in Alaska during May through November 2024, the DTaP vaccine effectiveness against pertussis in Alaska children aged 6 months to 6 years was evaluated. Now, the adjusted VE, vaccine effectiveness, was 96.2% among children who completed the three-dose primary DTaP series, and 85.3% among those who were partially vaccinated. Compared with children who received three or more of those doses, the odds of lab-confirmed pertussis was 26 times as high in unvaccinated children," 26 times, "and about four times as high in those who only got one or two doses."

These findings really reinforce the importance of following the pertussis vaccine recommendations to protect the children. I actually brought up for our YouTube watchers to see what is the current vaccine schedule from the American Academy of Pediatrics. You can see the birth dose of hepatitis B still recommended by our professional pediatric society, protecting the little kids against RSV. You can see a lot of these other doses in here.

I'll just bring up that it was a recent survey that has me a little troubled. It's this rhetoric about, "Oh, all these vaccines, it's just too much." I even hear this. I was in the hospital the other day, and so I was talking about what vaccine should they get. I was like, "You should get your flu. You should get your COVID shot this fall." They're like, "Oh, so many vaccines." I'm like, "What are you talking about? So many vaccines. Two? Is that so much?" They're just like, "Well, this and that." I'm like, "Do you get dressed every morning?" Like, "Oh, my left sock, my right sock, my underwear, my pants, my shirt."

VR: Too much clothes.

DG: It's too much. A jacket or a hat. "Oh, let's just stop with the sock. That's enough. That's two."

VR: Daniel, I'm looking at this. The tetanus doesn't show up until 7 to 10 years. What's going on there?

DG: Oh, actually, so go down. We're looking at it all together. One, 2, 3, 4. Here you see diphtheria, tetanus, acilia, pertussis. First dose, 2 months, 4 months, 6 months, and then the fourth dose, the fifth dose.

VR: I see. Then the other one is greater than 7 years.

DG: It's interesting with tetanus. There's a couple shots. Actually, this tetanus one's perfect because it's got the tetanus and the pertussis. There are certain shots when you're on something of a scheduled series. You get first shot, second shot, third shot, fourth shot, fifth shot. Oh, my gosh. Then there's this idea that you could extend the schedule and say every 10 years, you should probably be getting a booster there.

Then you have these unscheduled boosts. You go, and you step. It's always a rusty nail. I don't know how many people are stepping on rusty nails, but it's a dirty wound. Then you

get another tetanus shot. And year later, you step on another rusty nail. You're like, "I've already had them. I don't need any more of those. I'm overwhelmed." The same as we talked about pertussis, these unscheduled additional boosters might be thrown in there.

VR: If you are getting your second month, you're going to get one, two, three, four, five. Would you get those all in one visit, or would they space them out?

DG: They actually have a shot, which is really nice. A big thing is getting poked all these times. If anything, our vaccines have gotten better. You can actually get these pentavalents. You actually get shots with five different protections in there. The nice thing, think about we used to give people smallpox, and it was like the whole thing, and you get horrible reactions.

VR: I'm just thinking about a mom is not going to bring the kid in more than once a month.

DG: I think that's the challenge is this whole idea, like, "Let's just spread them out." It's like, "Oh my gosh, you're going to live at the pediatric office? You're going to be there every month?"

VR: Or dad. Mom or dad. Not just mom.

DG: Let's be honest. Actually, I should ask you. When our kids got vaccinated, my wife would go wait in the car, and I would be the bad guy hanging out with the kids when they got their vaccines.

VR: I'd go in too, sure.

DG: "Global, Regional, and National Burden of Pertussis in 1990 through 2023: A Global Burden of Disease Study." This is a *Nature* paper. "Despite longstanding immunization programs, pertussis remains a major cause of vaccine preventable mortality, particularly among infants." I will point out pertussis, it's a bacterial infection. It's not a virus. This is a clinical update, so we're hitting pertussis hard this time. Here we present a primary assessment of global pertussis incidence, mortality, disability, adjusted life years across 204 countries, territories, 1990 to 2004.

Now, the reason I think I included this was just the number of deaths. In 2023 alone, there were 18.9 million cases, 115,000 deaths. This is not equally distributed. A lot of this is concentrated in sub-Saharan Africa where we're seeing about 65% of the global deaths. Really pointing out pertussis is a horrible disease. Not only can it kill over 100,000 people a year, but it's disaffectionately termed the 100-day cough. You just keep coughing and sometimes the coughing can be so profound, you actually end up vomiting this post-tussive vomiting that occurs.

"Is Rabies Making a Comeback?" This is *New York Times*. "A handful of unusual outbreaks have made headlines. Rabid beavers at a Maryland state park, a cluster of goat cases at a North Carolina petting zoo, officials in several states including Idaho and Alabama flag surges in animal cases. California set an annual record for rabid bats." I guess they'll get in the *Guinness Book* with that. "Last month, the CDC issued a national health advisory citing reports of local increases in human rabies exposures."

It's OK, because - oh, wait, it's not OK. "The CDC has lost about 30% of its staff since last year, including members of the rabies team, which no longer has the capacity to advise

state officials after hours." If you're going to get bit by rabid animal, do it between 9:00 to 5:00 Eastern Standard Time because they're in Georgia there. "'All paused rabies tests came back online by August 2026,' Dr. Ryan Wallace, a veterinary epidemiologist at the agency's rabies and poxvirus branch, said in an email. Dr. Wallace did not directly answer questions about the current size of the rabies team but said that it was 'fully equipped to respond to rabies questions and requests for technical assistance.'" I think with the caveat, as long as it's between 9:00 to 5:00, Monday through Friday.

VR: I read this article and there have been no cases of human rabies confirmed this year so far.

DG: That's actually good.

VR: The headline, “Is Rabies Making a Comeback?” This is all about animal, non-human rabies, right?

DG: This is true.

VR: Although you could argue that there have been human cases that haven't been diagnosed because the CDC - I mean, the guy won't say how many people work on it. Maybe it's just one.

DG: [laughs] We've definitely had a lot of - well, personally been involved in a number of exposures this last year where we've jumped in. I'm getting a little worried about those foxes which torture my dog. They've decided this is what they do. I think I mentioned this. I don't think the foxes are rabid, but you do worry about them. They come to the back door and then freak out my dog, and then they just hang out on the other side of the fence because they know she can't get out.

VR: That's where the word foxy behavior came from, right?

DG: [laughs] Maybe. Screwworm. I keep an eye on this, but oh my gosh, I saw a bunch of cases so far. Already another five cases in October. It's up to 56 cases. This is all in the U.S., is in animals, but we did have our first fly trap detection. Do you see that, Vincent?

VR: Yes, look at that. First time all year, yes.

DG: Human cases, in 2025, 837 human cases, including four deaths in eight countries. This year, though, January 1 to September 2026, 1,355 cases, including five deaths in six countries. Mexico had 592, up from 117. Guatemala, Honduras, Panama. We're having a number of cases there in human beings.

Ebola. Things are not going well. It was a series of Kenya reports second Ebola case. Kenya confirms third Ebola case. Now we're actually up to nine Ebola cases in Kenya. We actually got an imported case in Nigeria that was confirmed by the WHO. If you look at the CDC trajectory, it is just rising. Apparently, on the ground there in the DRC, it's actually spreading to new districts. The majority of these people are not being actively tracked. We're up to 9,666 total confirmed cases, 4,649 total confirmed deaths.

VR: Wow. The curve keeps going up.

DG: Yes. It isn't even starting to level at all. It's just shooting up. We are hearing a little bit

about the vaccine trial, the TUMAINI or Swahili for Hope vaccine trial. This the Ebola. This is the Zaire vaccine. We're going to see how well that does.

VR: They have some Bundibugyo-specific ones for November too, it looks like.

DG: Yes. I got through that whole section without even saying that.

VR: I did it for you.

DG: [chuckles] Thank you. We've got our own viral epidemic here in the U.S. "U.S. Measles Cases Grow by 8% One Week for a Total of 4,410." That's out of *CIDRAP*. I'll just read from *CIDRAP*. "Measles continues to rip through unvaccinated communities across the United States." I do want to point out, this continues to be a disease of the unvaccinated. In *The New York Times*, we have a pretty interesting article. "The Amish Families Pushed to Undo a Vaccine Law. Then Measles Arrived."

This is an article that's also in *The New York Times*. "For five years, New York State Health Department has been locked in a battle with three tiny Amish schools upstate to dispute whether students must be vaccinated. Amish families say that New York's immunization rules, which allow no religious exemptions, threaten their religious freedom and way of life." There's a whole discussion about this tight-knit religious community and their interaction with the world.

There's even some sort of first person. "David Leslein, a 33-year-old furniture maker who is Amish, said that his seven children were vaccinated against tetanus but had not received the MMR because he feared they would be stricken by terrible side effects." So much of this is, who is telling them that? Who is misinforming them? Who is giving them this fear? There's a lawyer here involved, a Mr. Sasser, who's a lawyer at the First Liberty Institute. He focuses on these religious liberty cases.

That going on, but now we've got the context of just all these people actually getting measles. This next article is going to help put this in context because we hear the numbers of measles. We hear the number of 10% to 20% end up in the hospital. A lot of these little kids are in the ICU struggling to breathe. Then they survive, but now you've got this ticking time bomb. I was actually talking to a nurse from the Philippines about this earlier this week because in the Philippines, they had some pretty significant outbreaks. There's this idea that six to 10 years later, you might then develop this devastating, fatal encephalitis.

This is the, “Subacute Sclerosing Panencephalitis after Measles Outbreaks, the Philippines, 2007 to 2022,” published in *EIS*. Subacute sclerosing panencephalitis, this is a delayed, almost uniformly fatal complication of measles. The Philippines had measles outbreaks in 2010 to 2011, 2013, 2018 to 2019. The last was the largest in the WHO Western Pacific region. Now published SSPE data from the Philippines ended in 2015. This group reviewed all 20 children admitted with SSPE to a tertiary pediatric hospital in Quezon City during 2007 to 2022, an estimated year of measles infection.

There's some nice data where you can actually see the periods of time when, you see ivory bands mark the periods of reported nationwide measles outbreaks. Then you can actually see the SSPE admissions by year in blue, the number of cases in measles are in maroon. The authors point out that because SSPE is latent for years after initial infection, those cases most likely represent the leading edge of a post-outbreak wave, and additional cases may

emerge over the coming years. With continued measles outbreaks in the U.S., we've got to anticipate that we're going to see a number of these little kids dying of SSPE in the years to come.

VR: Of course. No question.

DG: I got that book, Vincent, that book about the Faroe Islands. I think it's over there on that. Let me grab it. I'm going to grab it. [silence] All right, I'm back. Back with my book.

VR: There you go.

DG: It's little. It's a paperback. You can get it through Amazon. You get the paperback. They even spent twice as much on a hardcover copy if you want. It really, it's pretty impressive about that lifelong immunity described. Based on the folks who had measles when they were little, when measles came back, they didn't get it, though.

VR: This is great that they're still selling this book.

DG: I think it's this new print-on-demand. With this new print-on-demand, you can just--well, it says published by Legare Street Press. Yes, no, they're still publishing it, which I think is really great. There's a nice article. I'm going to leave a link to the article in *The New England Journal of Medicine*. This you can actually go through. It really gives some really interesting - really, it recaps the whole book about the folks who ended up getting the measles there in the Faroes.

VR: It's great. Did you start reading it?

DG: I have not. I'm so excited. That's what I'm going to do after. Everyone else will go to sleep, but I have got my reading.

VR: Yes, and you can report on it in the future.

DG: I think we're doing some talks up at Weill Cornell, and I might talk a little bit about this when I'm up there.

VR: Yes, in a couple of weeks, we're doing an update there.

DG: Yes, I'm looking forward to that. I'm going to leave in a link to, we also have the, "Global and Regional Burden of Measles and Vaccine Coverage: A Global Burden of Disease Study." This was published in *The New England Journal of Medicine.* I'm going to leave that in. We just have so much to cover that I don't want to drown everybody. Pennsylvania, things are not going well there. It's actually gotten to the point now where there was a Pennsylvania State Department issue this Guidance for Measles and Pregnancy and Congenital Measles. I'll leave a link into that.

It walks through, like, "What do you do?" One, ideally, you get everyone vaccinated ahead of time. If you don't, what happens when a pregnant woman gets measles? What happens as far as what you might do? These are replication-competent, attenuated vaccines. We don't actually vaccinate someone while they're pregnant. Then what to do? Really, a warning for everybody, but also some guidance for patients and physicians on what to do.

"CDC Ignored Requests From States to Validate a New Measles test." That's helpful. "Health

officials in California and Washington facing outbreaks in measles this past spring asked the CDC to validate a test that could diagnose 500 cases in eight hours. They did not hear back for two months." Next time you're on, waiting for the cable guy, at least it's not two months, right? "Officials from the West Coast Health Alliance, California, Washington, Oregon, Hawaii, recounted the experience this week in a letter to Dr. Erica Schwartz, the CDC's new director." This is just - yes.

VR: They said CDC response was they had other competing priorities. Really? Measles outbreak it's not a priority? It would be if you had enough people because the jerk didn't fire so many of them. Folks, what are you thinking? Please. I'm talking to you, voters. There's no reason to keep this guy in office.

DG: Johns Hopkins Measles Tracker. We are up to 4,603. Those of you watching on YouTube can see the map, see we're a huge cluster right in Pennsylvania, really driving a lot of this. If you look specifically, another 108 cases in Pennsylvania. You're up to 1,317 in Pennsylvania. New York, we got our own measles problem going here. We got 162. Actually, a couple cases out in Nassau County. That's why I had to go to Washington. I had to run down south.

I really like New York City. Look at this banner. "Spread the truth, not measles."

VR: That's good.

"The measles vaccine is safe and effective," because we've got seven confirmed cases in New York City so far.

The flu, just starting to get some activity. We're just starting to see a little bit down in Louisiana. We're already starting. If you look at the epidemic trend from the CDC, we're just starting to have that flu activity start to come up. It looks like it's a little early this year. You still have that opportunity to get your flu vaccines.

If you're 65 and over, then you're going to want to get one of the high-dose or the senior-specific vaccines. Make sure you ask. We've got our egg-based vaccines. We've got our cell culture, recombinant protein, nucleic acid-based vaccines. They're all dry this year. They've got a couple different A lineages, and they've got one B. They've only got the Victoria lineage because the Yamaguchi, is that how that is?

VR: Yamagata.

DG: Yamagata. Yamaguchi is the restaurant in town. I'm going to end up at the wrong place. I'm going to end up getting a vaccine instead of a good Japanese dinner.

VR: Daniel, on this epidemic trend, COVID is going down, but in the wastewater, it's going up.

DG: Yes, it's interesting. This is the percent of positive tests. It's interesting. People don't want to get tested for COVID. You can't get a positive test if you don't consent to get tested.

VR: That's true.

DG: Yes, it's a bit of an issue. We're going to get to COVID here in a second. I say in just a second because we're really not much going on. RSV is still quiet, which, usually, by this time of year, we start to see activity in Florida. We'll keep an eye on that. Yes, let's look at our

COVID. I have to say, I had a number of folks in the hospital this weekend, this early part of this week. Yes, we look like we're bouncing all around, but we're bouncing all around on our way up.

VR: We're down.

DG: We're down.

VR: I don't know. I can imagine this being the midpoint of this little outbreak, and now it's going down.

DG: Yes, you know what the hardest thing to predict is, Vincent?

VR: The future.

DG: You got it. You got it. If you look at our map, you can see that the activity is concentrated in certain parts of our country. Yes, the 50 somewhat United States. Remember, all the things we've talked about, masking, avoiding high-risk situations. We now have, if you actually end up in one of those situations, we have Xocova, ensitrelvir, post-exposure prophylaxis. In general, about a 50% reduction in getting COVID. If you take post-exposure prophylaxis, that's a SCORPIO-PEPtrial. It's up to almost 70% in the high-risk folks. We've got things to do there. They charge too much, I should mention.

The early viral phase, we still have early antivirals that we can be doing. Let's get to late phase, PASC/Long COVID, because we actually have, I'm going to say, an interesting trial. We'll tell you how interesting it is. Vincent, are you ready for this?

VR: I'm ready, let's go.

DG: This is our last paper, and then we're going to get to emails. In the *Annals of Internal Medicine*, we have, “The Effect of Fluvoxamine and Metformin for Fatigue in Patients with Long COVID: An Adaptive Randomized Trial.” This is the REVIVE-TOGETHER. The trial was conducted at 22 participating outpatient sites in Brazil between October 23 and February 2025. We've talked about the results of several adaptive trials over the last few years. Trying to bring people up to speed on what is an adaptive clinical trial. This allows researchers to make pre-planned changes to the design, not just any, but certain pre-planned.

You can adjust the sample size. You can drop ineffective treatment arms. You might modify patient selection rules. This is all pre-specified, but then based on interim data while the trial is still running. If one of the things isn't working, you stop. You just say, "We're not going to do that anymore." Patients were randomly assigned in a 1:1:1 ratio to get fluvoxamine, metformin, or a matching placebo. You got this web-based randomization system.

Placebo tablets were manufactured, so you couldn't tell which was which. You end up getting something twice daily for 60 days. Some folks are getting extended-release metformin. Initially, it was 750 BID, but this is that adaptive. It was some issues with tolerance. They dropped it to 500 BID. Oral fluvoxamine, that was 100 BID, or placebo BID. They do this for 60 days with follow-up. They're going to do this FSS score. Basically, nine items are going to ask them about Fatigue Severity Scale. You're going to score things from one to seven. Higher levels is more fatigue.

The trial enrolls 399 participants. You end up with a number in each different set. They found fluvoxamine for Long COVID-related fatigue reduced fatigue severity as measured by the FSS with a mean treatment effect of 0.43 at day 60 and a sustained effect of 0.58 at day 90. Now, those are small. That's half of a point. Then this is the one that gets headlines. "These effects both have a posterior probability of superiority of 99% compared with placebo. Improvements in health-related quality of life assessed by the EQ-5D-5L were also observed at day 60 and 90."

Let's look at the data. Let's look at Figure 2. You've got Figure 2. They've got these box plots. They're going to show the distributions of individual items. They're doing this fatigue severity scale here. You're going to end up - and this is for folks who are looking at this on YouTube, watching the video. The placebo is in white. Fluvoxamine is light green. Metformin is medium green for the 500. It's a darker green for the 750. Then they've got it 0, 30, 60, 90 days. A lot of overlap here.

VR: What really bothers me is they have three treatment categories. They have fluvoxamine. They have metformin at 500 and at 750. The results are all the same. There's no difference.

DG: Pretty darn similar.

VR: Why is that?

DG: It's such a small difference. It's a statistically significant difference. How big is 0.5? This is like going from "I agree fatigue interferes with my work" to "I somewhat agree that fatigue interferes with my work."

VR: Daniel, the placebo goes down as well in fatigue score. You see, the open boxes are placebos. At 90 days, they are indistinguishable from the treatment arm.

DG: Except a statistician can tell them apart. I think that's what has me a little bit. Interesting. It seems like if you do something, if you get people in this trial and you meet with them and you acknowledge them. Everyone seems to be getting better, but it's really subtle. It's statistically significant.

VR: These are drugs with very different targets, right?

DG: Yes.

VR: The placebo has a very different target from both of them. It just does not make a lot of sense. Would you prescribe these based on these data?

DG: Metformin, no. Would I consider a trial of fluvoxamine? It's reasonable. Then again, each individual. Because if you're seeing this difference of 0.5, then some people are getting worse, right?

VR: Fluvoxamine is an SSRI, right?

DG: It is.

VR: Maybe part of this fatigue is depression, right?

DG: Yes. Maybe if you're better at selecting which people you're going to consider fluvoxamine, you might do that. I know this has got a lot of attention, so I want to at least just look through it.

VR: I am not impressed at all by these data.

DG: I'm not either. I'm disappointed, to be honest, which is too bad.

VR: We would like to find something that works.

DG: We really would. I'm glad this is in the news again. This should be in the news again. There was that marathoner who's now bedridden. This should be in the news. Why should it be in the news? Because there are so many people suffering. The current folks, they said that spending money researching Long COVID was a waste of money, and the money should be spent on other things.

VR: Who said that?

DG: Those are the people, Makary, and the people involved with HHS.

VR: I don't understand what you're doing, folks.

DG: Yes. All the folks out there that are struggling, having a tough time, now's your chance to vote for science. Make your vote count. As we've been saying for years now, no one is safe until everyone is safe. We're actually getting pretty close to the end of our American Society of Tropical Medicine and Hygiene fundraiser. We're hoping to double your donations because, well, this is it. October is it. August, September, October, because we're trying to raise money for the Dickson Despommier five-year One Health Lecture Series.

We also want to support American Society of Tropical Medicine and Hygiene and help bring folks from those lower and middle-income countries so they can come to the annual meeting, they can network, and they can move their careers forward. Go to parasiteswithoutborders.com and click the Donate button.

VR: It's time for your questions for Daniel. You can send yours to Daniel@microbe.tv. Allan writes, "What the [redacted] is going on with the medical community in this country? I have an undergraduate degree in microbiology from University of Florida. While there, I spent three years in infectious disease research at the School of Medicine. While in dental school at Emory, I worked at the CDC the summer between my freshman and sophomore year. The summer Legionnaires broke out in Philadelphia.

I've been listening to your podcast for the past five years, as well as others. I've also been writing a regular infectious disease update for the past five years at the facility I provide volunteer services 16, 17 years now. I'm hearing from neighbors that their physicians nationwide, and especially in the New York area, are not recommending anyone receive the current COVID vaccines. In addition, there was a super-spreader event in my community a couple of weeks ago where more than a dozen people caught COVID from a neighbor at their home during a particular small event.

A friend of ours who attended the event tested positive. She followed the advice I previously gave her and her husband and called her HCP's office for Paxlovid. The doc was out of town, and the nurse practitioner called in the prescription immediately for her. Her

husband did not test positive, so I suggested they get a Xocova prescription. The NP refused as she had never heard of this medication. Since he and his wife were both due for their COVID vaccines, I suggested he go ahead and immediately receive the vaccine, which he did.

Both our friend and her husband did great. However, she told us that none of the other people were able to get Paxlovid prescription from their PCPs because the doctors didn't think it was necessary or said it wasn't done anymore. Please tell me what's going on out there, doctors. Thank you in advance. I really enjoy listening to your broadcasts and find them extremely informative."

DG: Yes, Allan, this is really frustrating. One of the things I'm going to be doing here at *IDWeek*, and actually by the time this drops, I will have done this at IDWeek. It's five hours on Thursday and two and a half hours on Friday as a Lucy booth, information booth, where you can just come up, and we can talk about COVID. I'm hoping this is an opportunity to educate, get people up to speed on COVID.

There seems to be this, "I'm done with COVID," but COVID's not done with you. We want to just think that COVID is now a simple cold, but it's not. We had tens of thousands of people die last year from COVID. I ended up with a number of people in the hospital this week for COVID. People just, they want it. "Oh, but it's mild." I'm like, "They're in the hospital. They're on oxygen. I don't know what's mild about that." You don't end up in the hospital on oxygen from the cold, from a common cold. Not only is there that.

Not only do we see over a million people seeking medical attention each year for COVID, not only do we see hundreds of thousands of people end up in the hospital, not only do we see tens of thousands of people die each year from COVID, but we have Long COVID, which we talked about. People, marathon runners, who now are bedridden, and their dreams and their life are destroyed. We have people who get COVID, and now your chance of getting diabetes is more than doubled. It's about 2.5 when you look at all the data put together.

We've talked about increased risks of strokes and heart attacks. You know what? If you get a vaccine, you can prevent the disease. You can reduce your risk of COVID-19, symptomatic disease, in half. You can reduce your risk of a stroke, of a heart attack, of ending up in the hospital. You can reduce your risk of dying. It's quick. They poke you with the needle. You get your vaccine. They're incredibly safe. If you don't like the mRNA, you've got the Novavax, the Sanofi, Novavax, Nuvaxovid. We've got options out there.

I worry that a lot of physicians, rather than following the scientific literature, rather than talking to experts and physician thought leaders, they're just watching the news and following what everyone else is doing.

VR: Ruth writes, "Currently shivering after having just had flu and COVID vaccines and an immune response. Odd question from me. My cardiologist called my cholesterol levels very generous, and I'm contemplating taking statins. The only downside for me is that apparently they kill off all the archaea that are lurking in my guts, which I've learned from various *TWiV*s and a great program from BBC Radio, “In Our Time.” Anyway, should I take statins, and as a side effect, kill off my own personal archaea of rare and ancient origin? It feels like a sad step to take."

DG: Ruth is probably a meat-eater if she had this significant shivering response. We talked about that last time.

VR: Yes, it's right. [chuckles]

DG: It's also probably why her cholesterol is so high, because she switches to a plant-based diet. It's really interesting. Yes, you are correct. There is some data that statins can affect the microbiome. There's the other interesting that the microbiome can actually impact how well the statins work. That's why we talk about, if you're going to take statins, you also should consider making those "lifestyle changes." I think that, in the scheme of things, there's good data that statins are going to reduce your risk of a heart attack, your risk of a stroke. It might be worth sacrificing some of your personal archaea for the increased quantity and quality of life you might get from that.

VR: Ruth says they kill off all the archaea. I don't think it kills all of them off. I think this -

DG: Not all your own personal archaea.

VR: Christine writes, "At the risk of being redundant, could you please provide clarification about the influenza vaccines currently available? I was disappointed to learn that all my options, I am not yet 65, were versions of a trivalent vaccine. Each option omitted one of the Flu B variants. I understand that Flublok has a higher concentration of antigen. Also, I've learned that in order to receive Fluzone high-dose, folks under 65 need a doctor's note in addition to paying out-of-pocket. I'm both a nurse and grandmother of an infant. I'd like to be as well protected as possible for the upcoming respiratory virus season."

DG: Christine, this is actually good. We were talking about this a little bit earlier. One of the things that happened during the pandemic is one of the Flu Bs is gone. The quadrivalent vaccines, you don't need them anymore. They don't make them. Everything's trivalent because the Yamagata vaccine, the Yamagata B, it's gone. It's not something you have to worry about. You don't need to vaccinate or protect yourself against something that isn't out there. The different vaccines are going to have the different A, and they're going to have the one remaining B out there.

Let's see. Yes, I think the other is the 65. Yes, let's run through all the different vaccines. that are out there. I've got that. I'm going to zip up to my notes. Here we are to the different - what is going to be in them. Depending on whether you get egg or the others, they're going to be different. The egg-based vaccines is going to have the influenza A, Missouri, the influenza A, Darwin, and the influenza B, Tokyo, which is a Victoria lineage. The other option, in addition to the egg-based or egg-attenuated, as I disparage them, the cell culture, recombinant protein, or nucleic acid. There is an mRNA vaccine out now.

These are going to have also influenza A, Missouri, influenza A, Darwin, but the one difference is these are going to have the influenza B, Pennsylvania, as their Victoria lineage. The big thing for you to ask about is if you are 65 and over, you're going to want one of the ones that are specifically for the seniors. It'd be a high dose or maybe the adjuvanted.

VR: Barb writes, "I was hoping you could review the COVID vaccine options. As I understand, there are four, Comirnaty, Spikevax, mNEXSPIKE, Nuvaxovid." She writes, "I understand they're all pretty similar in terms of protection, but is there any reason I should get one over the other? They've gotten mRNA vaccines before. They don't have reactogenicity issues."

DG: Yes. In that case, you could really go with any of these options. You mentioned you laid them all out. We've got Pfizer. We've got the Moderna Spikevax, and then the Moderna

mNEXSPIKE, which when I did head-to-head with the Spikevax, was 25% better at preventing clinically identified COVID-19. It's the RB-- receptor-binding domain, RBG only. Isn't that correct with the--

VR: RBD.

DG: RBD. [chuckles] Ruth Bader Ginsburg, no, the receptor-binding domain, the RBD. Then the Nuvaxovid, it's your protein-based. Some people prefer that. If you look at all the efficacy data, it's pretty similar. I did mention the one comparison between the Spikevax and the mNEXSPIKE.

VR: Bob writes, "I've been thinking of concept of vaccine hesitancy and how it might be overcome. Childhood vaccines are protective devices for our children. I remember when my child was born in 1982, we could not bring him home from the hospital unless we had a federally approved car seat properly installed in the vehicle, and the nurse checked the car and car seat before we could put the baby in it. Our families had never heard of this, and we were thought to be overprotective when we would not let our child ride in a car without a car seat.

Ten years later, when there were many more young children in our families, it seemed everyone with children had the car seat and booster seats, and seat belts. I live in California, and here seat belts are part of the culture. I'm not sure how the rest of the country feels about the importance of car seats and seat belts. Here, I think it would be helpful to talk to a vaccine-hesitant parent, to think about vaccines like a car seat or a seat belt. You may feel you're a good driver, but is everyone else? You don't get in an accident every time you drive, but you know it can happen. Your child may not be exposed to viruses vaccines prevent every day, but it can happen." Just a thought.

DG: Maybe Paul Offit will listen to this and hear your letter.

VR: Paul Offit always says that. He's always saying, "What's this choice?" You don't have a choice about seat belts. Why do you think you need a choice about vaccines? He's bought into it.

DG: Yes. I remember the early days. It's always the uncle. There's always some uncle who's like, "I want to be thrown clear. I don't want the seat belt. It's going to bruise my chest." I'm like, "No, really?"

VR: You don't want to be thrown through a windshield.

DG: You do not want to be thrown through a windshield. You don't want to get measles. You don't want your kid to get measles. You don't want your kid to get these horrible vaccine-preventable diseases. The vaccines are safe. They're effective. Don't let people lie to you about them.

VR: Being thrown clear is like getting measles naturally instead of being vaccinated. It's the same mentality.

DG: It's the same mentality. I'm going to be thrown through the windshield, and then hopefully, six to 10 years, I don't end up dying of encephalitis. You want your child to be thrown clear. If they survive that, then you got to worry that six to 10 years, it's going to

destroy their brain. It's horrible.

VR: That's *TWiV* weekly clinical update with Daniel Griffin. Thank you, Daniel.

DG: Thank you. Everyone, be safe.

[music]

[00:55:02] [END OF AUDIO]