
NOVAVAX
CORONAVIRUS
COVID-19
Vaccine
INJECTION ONLY

Participating in a Covid-19 Vaccination Trial

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This is a linkpost for https://eidan.substack.com/p/the-vaccine-trial-chronicles-1

I live near Stony Brook University, which has a well-known hospital and medical school. About a month ago I signed up to participate in research related to Covid-19. As a work-from-homer, this was a way I could reasonably get a vaccine without resorting to “skipping the line” or pretending I had a pre-existing condition. Today I received my first dose. Here is the story to date. I plan to post at least one follow-up to this.

The study I'm participating in is a phase III trial for the Novavax vaccine. Studies in the UK and South Africa already have demonstrated it to be safe and effective (at least to a similar standard as the Pfizer and Moderna options). Novavax also has the added advantage that it can be kept stable at higher temperatures than the mRNA vaccines. I'm not opposed in principle to studying its efficacy more, but I think it's silly that this trial has to happen before it can be distributed or used in the US. FDA Delenda Est.

Day -2: Registration

I receive a phone call from a lady calling herself Bella. Bella asks if I am still interested in participating in Covid-19 vaccine trials. I am. She takes my name, address, medical history, etc. She says to expect an email with directions to the clinic and some videos to watch.

Day -1: Orientation

In the morning there is an email from Bella with links to a required series of introductory videos. After each video there are a few questions to make sure I was paying attention. The videos are old. I can tell they are old because the second one says “There is no approved vaccine available for Covid-19.” *Unforced error count: 1.* One of the questions for this video asks if there are any approved vaccines available for Covid-19. I know what will happen if I get a question “wrong,” and I don’t want to try asking anyone to update the form, so I select “no.” *I’ve already entered a simulacrum.* I learn that if I participate in the study, I will receive the Novavax Covid-19 vaccine with probability 2/3 or a placebo with probability 1/3, and earn up to $1700 depending on how diligently I participate in follow-up. *Sounds great.*

Day 0: First Visit and Vaccination

I get in the car and drive to Stony Brook University Medical Center’s satellite clinic in Commack, NY. I walk in to a large lobby. A sign on the information desk says “COVID-19 STUDY: ROOM 201.” I go to suite 201 and enter another lobby. I walk up to the receptionist.

Am I here for a nasal swab? No, I’m here for the vaccine trial. What is my name? I say my name. I’m not on the list. She hands me the list of names. *I should not be allowed to see the list of participants, I’m just some random dude! Unforced error count: 2.* I confirm I’m not on the list. She hands me a post-it to write my name down. I write it and take a seat.

While I’m waiting my phone rings. A voice introduces herself as Kathryn and asks if I’ve found the trial. Yes I have, I’m in the waiting room right now, I just gave the woman my name. Which room am I in? 201. That’s the wrong room; that one is doing a different trial. I should wait and she’ll come get me; it should only be a minute.

I get up and explain to the receptionist that I was in the wrong room and she can forget about me. She discards the post-it. *No reason to sit in the same room with other people when there’s an empty hallway nearby. Social distancing, right?* I wait outside room 201. A woman in scrubs walks up. Are you Kathryn? Uh, no. Oops, sorry. Another woman in scrubs approaches. Are you Kathryn, here to bring me to the vaccine trial? No, I’m just getting my steps in. I grow uncomfortable accosting innocent female healthcare workers and reenter

suite 201. I sit back down to wait. Another minute passes and Kathryn arrives. She is not wearing scrubs.

Kathryn leads me down a stairway and makes some small talk. I mention that I'm interviewing later today with a startup involved in prediction markets. "Interesting!" I infer she either misunderstands what I meant by prediction markets or is politely pretending to know what they are. We reach the correct suite and go into a room. It is barren aside from two chairs, a desk, and a computer. Can I please confirm my name and birthday? I do. Do I consent to participate in the study? I do. Do I wish for the researchers to share information with my primary care doctor? *That sounds complicated.* No thanks. Do I consent to having leftover blood samples used for other research? Sure. Am I aware that they might not take blood samples even though they've asked that question? I suppose I am. Am I aware that I can answer no to either of the past two questions and still participate in the vaccine study? Yes.

The entire time we're in the room the door is closed. I presume this is required to protect my privacy, but I notice that the reduced ventilation increases the chance of SARS-CoV-2 transmission. I'm wearing an n95 under a surgical mask and Kathryn is wearing a face shield over a surgical mask, so I decide it's not worth raising the issue. I conclude opening the door wouldn't meaningfully affect my privacy but only slightly reduce infection risk. *Still, unforced error count: 3.*

After scheduling my next appointment, Kathryn gets up and exits, returning a few moments later with an iPad. I sign a form on the screen. On the next page I sign again. Kathryn takes the iPad and passes me a clipboard with more consent forms and an emergency contact information form. As I'm filling those out Kathryn asks how involved I am in trading stocks. *Huh? Oh, right, I talked about prediction markets.* The conversation takes a brief detour through the recent GameStop and AMC short squeezes. I give a basic explanation of prediction markets, and say I am interested in how prediction markets can affect the future. I propose that if prediction markets were a normal thing, then (for example) perhaps back in January of last year, when the WHO was still really hesitant to sound the alarm on Covid-19, a bunch of private citizens/experts could have made bets that large numbers of Coronavirus cases would arise. Then, maybe people and governments could have reacted somewhat faster, inferring from the bets that despite the WHO's assurances a pandemic was likely. Kathryn's eyes go wide. *Wait, did I just rationality-pill this lady?* I hand her the completed forms.

Kathryn leads me through a hallway to another room with your standard doctor's office furniture. I sit on the exam chair. Kathryn leaves and is replaced by a young nurse. Her name is Rose and she takes my medical history. (Of course, she closes the door first). Can I confirm my name and birthday? I do. What prescriptions am I on? I tell her. Do I take any vitamins? D and B12. Herbal supplements? None. Do I have cancer? No. Have I done any drugs? "No, I'm a very good boy," I answer. Rose giggles; we have a rapport. Have I been in contact with any confirmed cases of Covid-19 in the past 10 weeks? No.

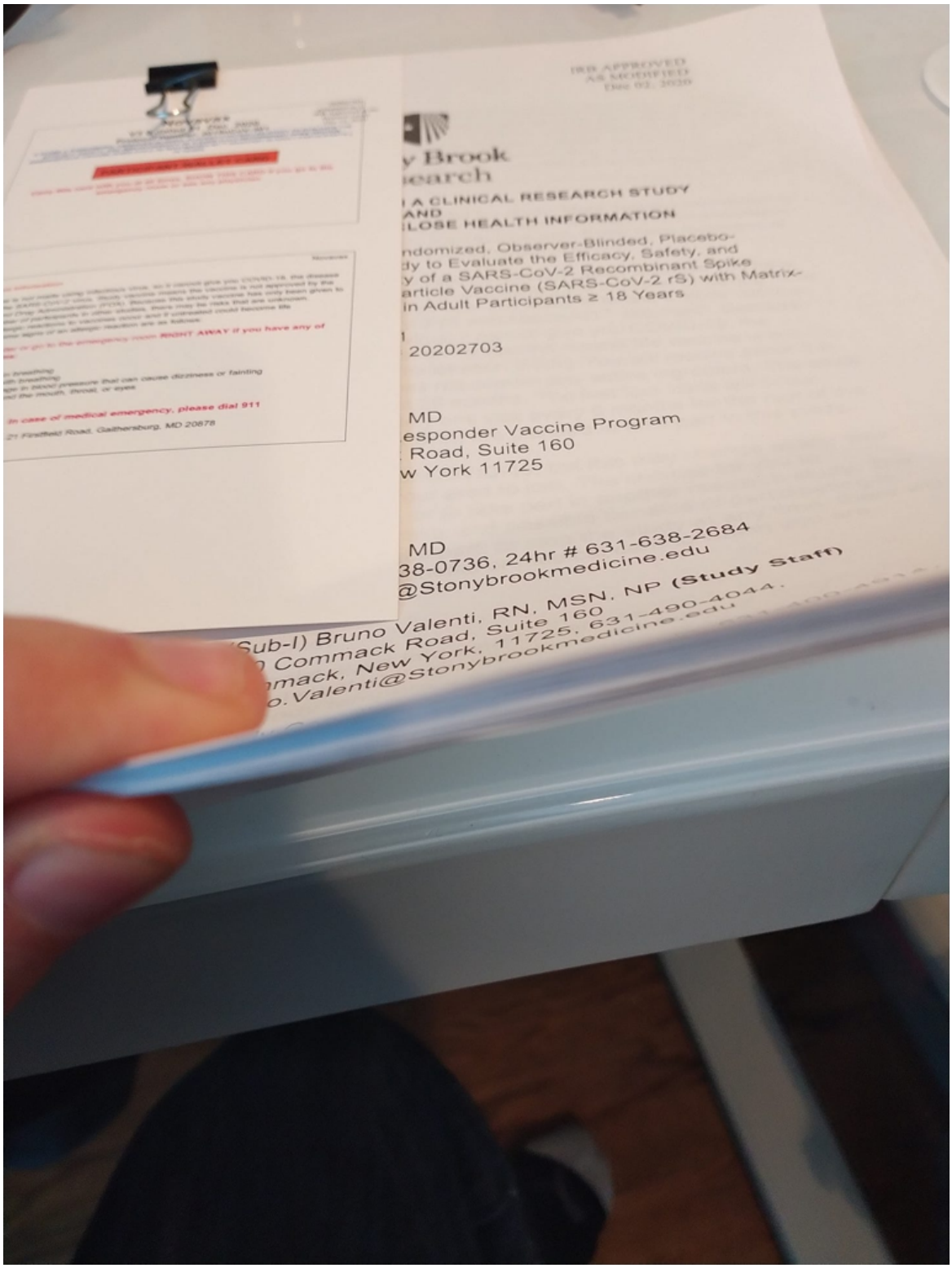
Then some demographic questions. Am I hispanic or latino? No. (It occurs to me later I accidentally answered that question in Spanish, which may have been confusing). What is my race? I'm a bit complicated. I prefer to write "Jewish" if the question allows, but I basically look White.

Halfway through Rose is joined by an older nurse. She doesn't introduce herself and starts prepping a blood draw kit. Rose takes my blood pressure and pulse. Older Nurse turns to me and asks me to confirm my name and birthday, which I do. She begins to repeat other questions that Rose has already asked, but Rose interrupts and tells her she has already covered it. *Thank god.* Rose removes the blood pressure cuff and Older Nurse wraps a tourniquet around the freed arm. She fills a few vials while Rose is typing away at a computer.

I know from experience I don’t react well (purely psychosomatically, probably) to blood draws, but I also know this volume is smaller than a normal blood test so I don’t expect to react too strongly. I am wrong. Once the needle is removed, I have my usual minute or two of dizziness, nausea, and sweating, which promptly causes Rose to overreact. I’m handed multiple cups of water, a juice box, and a granola bar. By the time they come back to check on me I am completely recovered.

I’m pretty hairy, so for small wounds (like needle holes) I prefer not to use tape or sticky bandages. Older Nurse doesn’t let me refuse for some reason. I’ve never had this happen before. I wonder if I’ve offended her for some reason that she wants to cause me such a petty amount of pain.

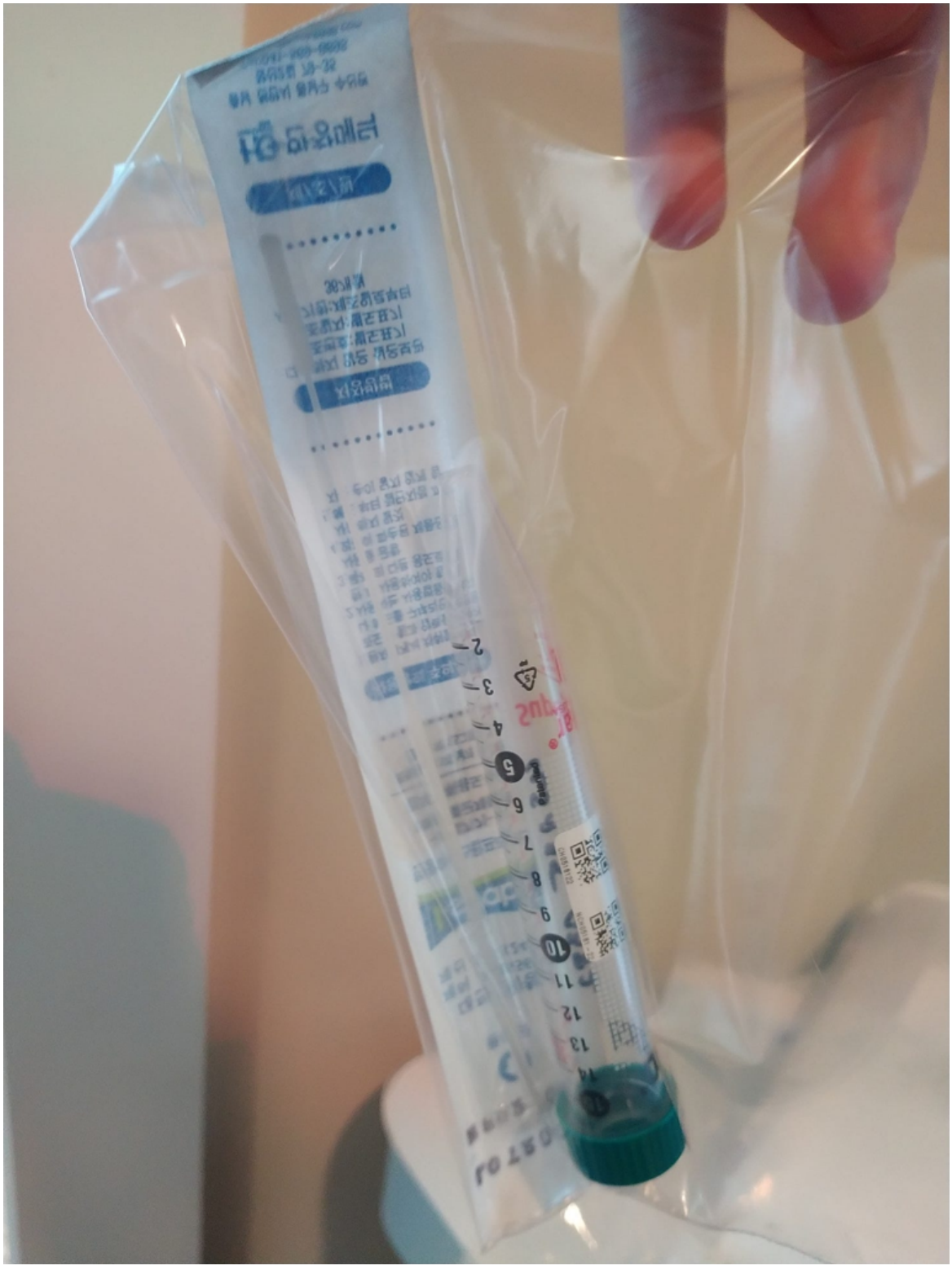
Rose leaves. Older Nurse gives me a Covid-19 nasal swab, collects her blood samples, and follows. She returns a few minutes later and hands me a thick stack of copied consent forms.



Did I really consent to this much stuff?

She also has a bag of three testing kits, a clear ruler, and a thermometer. The ruler is for measuring any redness around the injection site. She demonstrates to me how to use a ruler. “Each of these lines is .1, or 1/16 of an inch. So if you were to measure something as 1 and 11/16ths, you should write 1.11.” This system of mathematics is beyond my understanding.

Unforced error count: 4. She explains how I would swab myself and take my temperature. If I have symptoms, I may be asked to swab once a day for three days after I report them. Older Nurse asks if I understand. I do. Have I received the vaccine shot yet? No, they must be saving the fun part, I answer. She doesn't laugh. Why doesn't Older Nurse like me? Rose liked me. I miss Rose.



One of the supplied nasal swab kits.

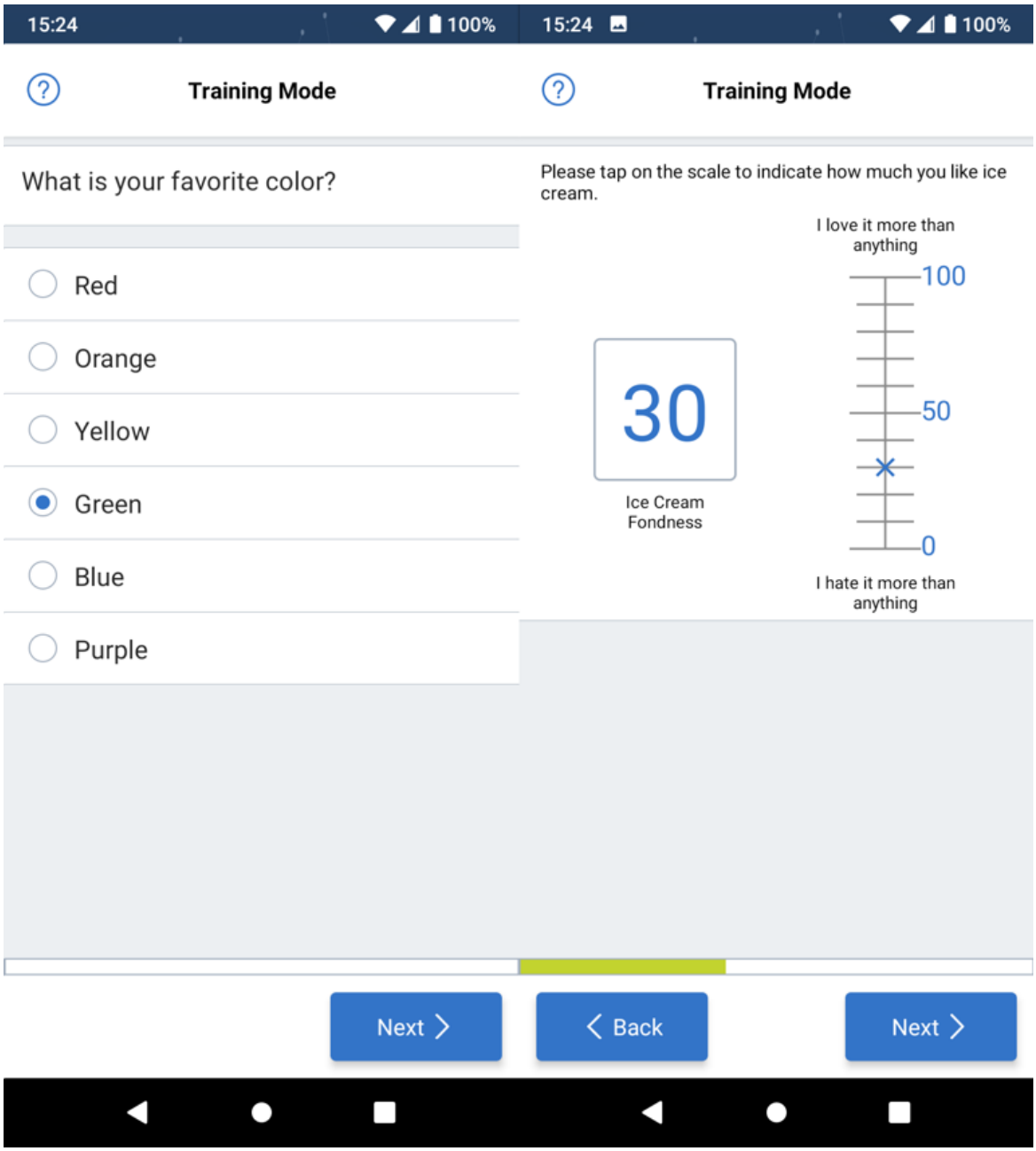
Older Nurse leaves and I’m alone for a minute or two. Then a man walks in. He is a nurse practitioner and is going to give me a brief physical exam. Can I confirm my name and birthday?

Nurse Practitioner asks me some medical history questions that are largely redundant with the ones Rose asked. I consider mentioning this, but I realize that Rose must have been taking my medical history for the hospital, but Nurse Practitioner is taking my medical history for the experiment, and of course I shouldn’t expect them to talk to each other. *More of an unforced inconvenience than an unforced error, I guess.* New questions include: Do I have any allergies to phosphate-enhanced saline? Do I have any allergies to saponin, a.k.a. Soap Bark? He also asks about who I live with and their occupations. I deduce he is trying to get an idea of my risk of coronavirus exposure. NP asks me to stand up and touch my toes, checks my ears and throat, and does the normal physical exam ritual. Then he asks me to smile, frown, puff out my cheeks, and raise my eyebrows. I think he’s joking at first, but then realize he’s confirming I do not have Bell’s palsy. NP is satisfied I’m in good health and leaves.

A new nurse comes in. Her name is Mary. Can I please confirm my name and birthday? I confirm for what feels like the twentieth time. Mary gives me a mystery shot, which was the Novavax vaccine with probability 2/3. Mary tells me that I have to wait at least half an hour before leaving in case of any adverse reaction and hands me a nurse call button. *Press here if too lonely.* I crack myself up. Mary leaves.

The call button and my post-blood draw resuscitation snacks. Yum.

Another woman walks in and instructs me in downloading and using a health diary app, PatientCloud. It is all very straightforward and we fly through the tutorial. She also hands me a check for $170. *Cool*. I'm all done!



Example questions from PatientCloud.

I have about fifteen minutes before my half-hour observation period is up. I want to leave early but I'm concerned it might jeopardize my study participation or otherwise get someone in trouble. I wait, and then step outside. I remove my mask and take in the cool air on the way to my car. A flute concerto plays on NPR as I turn on Suffolk County Route 4 and head home.

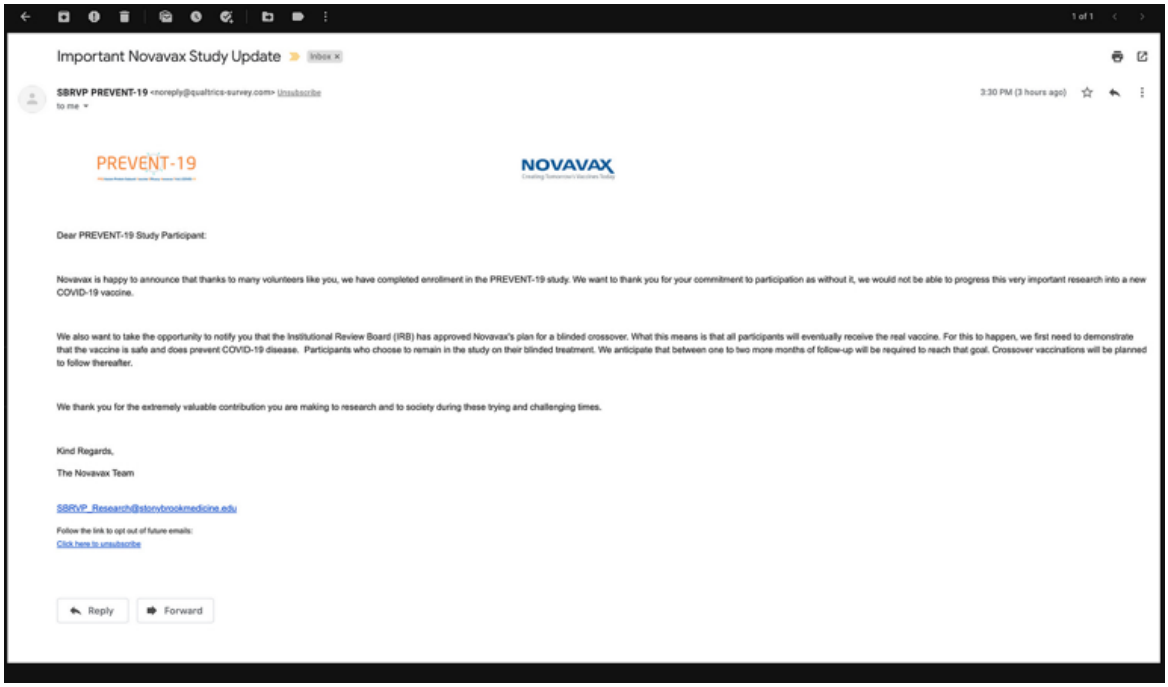
My next appointment is in March. I will receive my second dose then.

Participating in a Covid-19 Vaccine Trial #2: We pretty much knew it would work the whole time

The past few weeks have been uneventful. I spend a few minutes each day filling out a questionnaire on the Patient Cloud app I installed during my first visit. The study is interested in reactions to the injection itself: redness, swelling, pain, etc. around the injection site, and the first section of the questionnaire checks for these symptoms. The next part is a self-screen for Covid-19 itself. Using the thermometer the nurses gave me, I take and report my temperature. There's a checklist of symptoms to look out for: malaise, nausea, fatigue, etc. I've had nothing interesting to report, which I'm sure is a delight to the researchers.

I have my next injection appointment in about a week - I planned to write this second update sometime after that, since I would have a better idea of whether or not I received the placebo treatment. However, I got a very interesting email today (image below):

> Dear PREVENT-19 Study Participant:
>
> Novavax is happy to announce that thanks to many volunteers like you, we have completed enrollment in the PREVENT-19 study. We want to thank you for your commitment to participation as without it, we would not be able to progress this very important research into a new COVID-19 vaccine.
>
> We also want to take the opportunity to notify you that the Institutional Review Board (IRB) has approved Novavax's plan for a blinded crossover. What this means is that all participants will eventually receive the real vaccine. For this to happen, we first need to demonstrate that the vaccine is safe and does prevent COVID-19 disease. Participants who choose to remain in the study on their blinded treatment (sic). We anticipate that between one to two more months of follow-up will be required to reach that goal. Crossover vaccinations will be planned to follow thereafter.
>
> We thank you for the extremely valuable contribution you are making to research and to society during these trying and challenging times.
>
> Kind Regards,
>
> The Novavax Team



Important Novavax Study Update

SBRVP PREVENT-19 <noreply@qualtrics-survey.com> Unsubscribe
to me

3:30 PM (3 hours ago)

PREVENT-19

NOVAVAX

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We thank you for the extremely valuable contribution you are making to research and to society during these trying and challenging times.

Kind Regards,

The Novavax Team

SBRVP_Research@stonybrookmedicine.edu

Follow the link to opt out of future emails:
Click here to unsubscribe

Reply Forward

My first response was a sense of relief that, worst case, I would likely receive the real vaccine within a few months. But then my critical thinking booted up. We are still experiencing a national (and global) shortage of vaccines - If the Novavax vaccines are believed safe and effective, shouldn't they be going into the same supply of vaccines that everyone else is being served out of? I came up with two possible answers to this question. (Spoiler: both of them suck)

1. I am getting special priority because I volunteered to participate. If that is true, is that kind of kickback scheme remotely ethical? To participate in the trial, I needed to have the time, energy, and ability to sign up online, transport myself to the site, and then spend part of my day answering questions and letting the nurses poke and prod me a bit - all of which was made considerably easier by ability to speak English, access to a car, resources and free time, etc., in other words, exactly NOT the kinds of things according to which we should be allocating vaccines.
2. Novavax and the experimental team think it's safe and effective enough to do the cross-over and give the control group the real vaccine, but the Very Serious People in charge of US vaccine approvals don't. In that case, we're just back to the regular story of an abundance of caution causing senseless morbidity and mortality; blah blah blah FDA Delenda Est.

Of course this is all occurring with the backdrop of the Novavax vaccine already having been tested with great results overseas, and oh my god why haven't we been distributing this thing since last month?

If it turns out that I was randomized into the placebo group and they offer me the real treatment sometime in the future, I plan to take it despite not being particularly vulnerable - I don't think me refusing on principle would result in someone else getting the dose any faster, but it might result in a lot of wasted effort contacting me repeatedly while the dose meant for me sits in a freezer unused.

Participating in a Covid-19 Vaccine Trial #3: I Hope I feel Worse Tomorrow

Today is four weeks to the day after my first injection, and I received my second at my appointment this morning. The process was very similar to my first visit: I entered and met first with someone who led me through paperwork and asked a series of screening questions, then had a brief medical exam, got my shot, waited 30 minutes in case of any acute reaction, and left. Notable differences this time:

- The entire process seemed less repetitive and went by faster (both subjectively and objectively). I was also filling out fewer forms than last time and wasn't getting any orientation so this makes sense.
- I was told that my follow-up meeting "had to" be scheduled for two weeks from now by order of Novavax. This is sooner than was specified in the study design. I suspect they have enough data already to show that it works so they are planning to close the site.
- In the middle of my health exam, someone rang a Nurse Call button and the doctor ran out of the room. A few minutes later the Nurse Practitioner from last month came in and finished up. The building we were in is also used a clinic for World Trade Center survivors and first responders (and probably other health care I don't know about) so it's possible that this was totally unrelated, but the call would imply that someone had a reaction to the injection.
- There were specific instructions to inject the 2nd dose in the opposite arm from the first dose. I am right-handed so I used my left arm last time, which meant I had to use my dominant hand this time. The second round is more likely to have side effects though, so I wish I had known this to begin with. By word-of-mouth from a medical professional (my mom), apparently some people have reported pain in the *first* injection site after getting their *second* dose. So maybe they are looking for that.
- Doors were mostly kept open by default instead of closed by default. The first person asking me health-related questions even asked me if I wanted to close the door.

When I received my shot the NP mentioned that most people don't have side effects from the vaccine. He also said the side effects seem to have a similar profile as the Pfizer and Moderna vaccines, namely mild flu-like symptoms for a day or two. This was not exactly supported by the literature I ended up reading.

Did I get the Placebo? Using Bayes' Theorem

I would like to have a better idea of my chances at having received the real vaccine. The experiment randomized 2 people into the trial group for every 1 person in the control. This gives a **prior odds** of 2:1.

There are two pieces of **evidence:** my symptoms after the first injection (none), and my symptoms after the second injection (to be observed over the next day or so). These are obviously not independent. I need to know how much more likely I am to experience side effects from the real injection than the placebo.

After reading a few unhelpful press releases, I found my way to medrxiv.org and entered NVX-CoV2373 into the search bar. I found a few papers which seemed likely to

have the information I was looking for.

Estimating Likelihood Ratios

This first study was a phase II investigation of dose response; in simpler language, they were giving people different amounts of vaccine and seeing what happened. They also broke their study population into two age cohorts (18-59 and 60-84). Younger patients were on average more prone to react at all stages and doses. Data are not available but there are graphs (Fig. 2) and some statistics in the text. All of the numbers here are read off of graphs and are approximate.

“Local” adverse effects from the vaccine include pain, swelling, tenderness etc. at injection site, while “Systemic” adverse effects include fever, nausea, or malaise. The study had one placebo group and two pairs of dosed groups; each pair used a different dose size in their vaccines. Within each pair of dosed groups, one group received two doses and one group received a placebo shot for their second dose.

At least one local adverse effect was reported by:

- 15% of placebo participants on the first shot, 10% on the second shot
- 50% of the 5-microgram dose group participants on the first shot, 70% on the second shot
- 65% of the 25-microgram group participants on the first shot, 80% on the second shot

For the second shot, about 10% of participants who received a placebo that round reported local adverse effects, whether or not they received a real vaccine for their first dose.

Systemic adverse effects were reported by:

- Roughly 40% of people in all groups after the first shot
- 20% of people receiving the placebo for their 2nd shot
- 50% of the 5-microgram group after their 2nd shot
- 60% of the 25-microgram group after their 2nd shot

For younger participants, the gaps between placebo and treatment groups was a bit larger - younger people reacted to vaccines more often - so I’m tempted to bump all of those figures up a bit in my own calculation (I am in my 20s).

The second study I read had a very similar design, but participants generally reported more symptoms than in the first one I discussed. I suspect whichever method they used to ask participants about their symptoms was more sensitive - for example, more than a third of the placebo group reported a headache, which counts as a systemic adverse effect - so these numbers might be inflated. Even if this is true, there’s almost no reports of fever from any of the participants, which surprised me. Looking at the other systemic effects, it looks like fatigue, malaise, and muscle pain were each all about two or three times more common in the treatment groups than the control group.

Finally, I read this meta-analysis which apparently has done most of the work for me:

> For the meta-analysis, we separated the adverse events based on vaccine vs. placebo injection as reported by individual studies. In general, we observed there was an increase in total adverse events for subjects with low dose vaccine

> injection [OR: 2.86; 95% *CI*: 1.90-4.29, $P < 0.00001$]. Especially, the local reactions were significantly enhanced in subjects with low dose vaccine groups [OR: 2.07; 95% *CI*: 1.07-4.00, $P = 0.03$]. However, the systemic reactions were no significantly changed between vaccine and placebo groups [OR: 1.28; 95% *CI*: 0.67-2.43, $P = 0.46$].

The doses used by the Novavax PREVENT-19 trial are 5 micrograms, at the lowest end of the doses used in these papers. The analysis of high-dose vaccines yielded modestly higher odds ratios (there was a significant increase in systemic reactions for high-dose participants vs placebo) but the same general picture.

Integrating all of this evidence in a reasonable way is not a trivial problem, but they don't seem to disagree too much - the odds ratio for having local adverse effects seems to be about 1.5-4, and the odds ratio for systemic adverse effects a little lower than that. The systemic reaction doesn't seem to be very diagnostic and it's probably correlated to the local reaction in ways I don't understand and am uneasy guessing about. So to a first approximation I will just update on the presence or absence of local adverse effects.

Conclusion

At the time I am publishing this, it's been about 6 hours since the injection. I have a slight pain my right arm and general malaise, but not to such a degree that I am sure I'm not imagining it. Hopefully I feel worse tomorrow!

If I **do**, I'd update my posterior odds to be 2:1 times 2:1 = 4:1. I'd be about **80% confident** I received the real vaccine.

If I **don't**, I'd update my posterior odds to be 2:1 times 1:2 = 1:1. I'd be about **50% confident** I received the real vaccine.

Since I'm young, and younger people tended to have vaccine reactions more reliably, these could probably be treated as (very rough) lower and upper bounds, respectively, e.g. I would be at least 80% or at most 50% confident I received the real treatment depending on the case. In the unlikely event I wake up with crushing fatigue and nausea or aching all over, I reserve the right ignore these estimates and throw myself a party.