

# VRBPAC Meeting

June 15, 2023



# Agenda

## **Presentation Focus:**

- Reverting to monovalent COVID-19 vaccines based on XBB 1.5.
- Allowing Novavax's Nuvaxovid COVID-19 vaccine access regardless of previous mRNA doses.
- Creating regulations that allow individuals a new primary series to overcome imprinting.
- Facilitating clinical trials of Novavax for the treatment of long COVID.
- Altering recruitment criteria for Novavax clinical trials to bring a pediatric vaccine to market.

# Aligning with WHO and EU Recommendations

- The WHO and the EU recommend a Monovalent COVID-19 vaccine based on the XBB 1.5 variant.
- If we go higher than that, we run into the BA.1, BA.2, and BA.5 debacle with XBB being a BA.2 subvariant—leaving the public without a targeted vaccine.

As of May 2023, XBB.1 descendent lineages predominate SARS-CoV-2 circulation globally. In order to improve protection, in particular against symptomatic disease, new formulations of COVID-19 vaccines should aim to induce antibody responses that neutralize XBB descendent lineages. One approach recommended by TAG-CO-VAC is the use of a **monovalent XBB.1 descendent lineage, such as XBB.1.5** (e.g., hCoV-19/USA/RI-CDC-2-6647173/2022, GenBank: OQ054680.1, GISAID: EPI\_ISL\_16134259 or WHO Biohub: 2023-WHO-LS-01, GenBank: OQ983940, GISAID EPI\_ISL\_16760602) as the vaccine antigen. Given the small genetic and antigenic differences from XBB.1.5, XBB.1.16 (e.g., hCoV-19/USA/MI-CDC-LC1038976/2023, GenBank: OQ931660 GISAID: EPI\_ISL\_17619088) may be an alternative. The spike antigens of both of these lineages are genetically and antigenically very closely related, with only two amino acid differences between XBB.1.5 and XBB.1.16 (E180V and K478R). Other formulations and/or platforms that achieve robust neutralizing antibody responses against XBB descendent lineages can be considered.

Statement on the antigen composition of COVID-19 vaccines, WHO

<https://www.who.int/news/item/18-05-2023-statement-on-the-antigen-composition-of-covid-19-vaccines>



# The FDA should recommend a Monovalent COVID-19 vaccine

Multiple analyses of these results, including antigenic mapping, made clear that inclusion of the ancestral spike prevents the broadening of antibodies to the BA.5 component in the bivalent vaccine, thereby defeating its intended goal. Our findings suggest that the ancestral spike in the current bivalent COVID-19 vaccine is the cause of deep immunological imprinting. Its removal from future vaccine compositions is therefore strongly recommended.

Deep immunological imprinting due to the ancestral spike in the current bivalent COVID-19 vaccine

<https://www.biorxiv.org/content/10.1101/2023.05.03.539268v1.full>

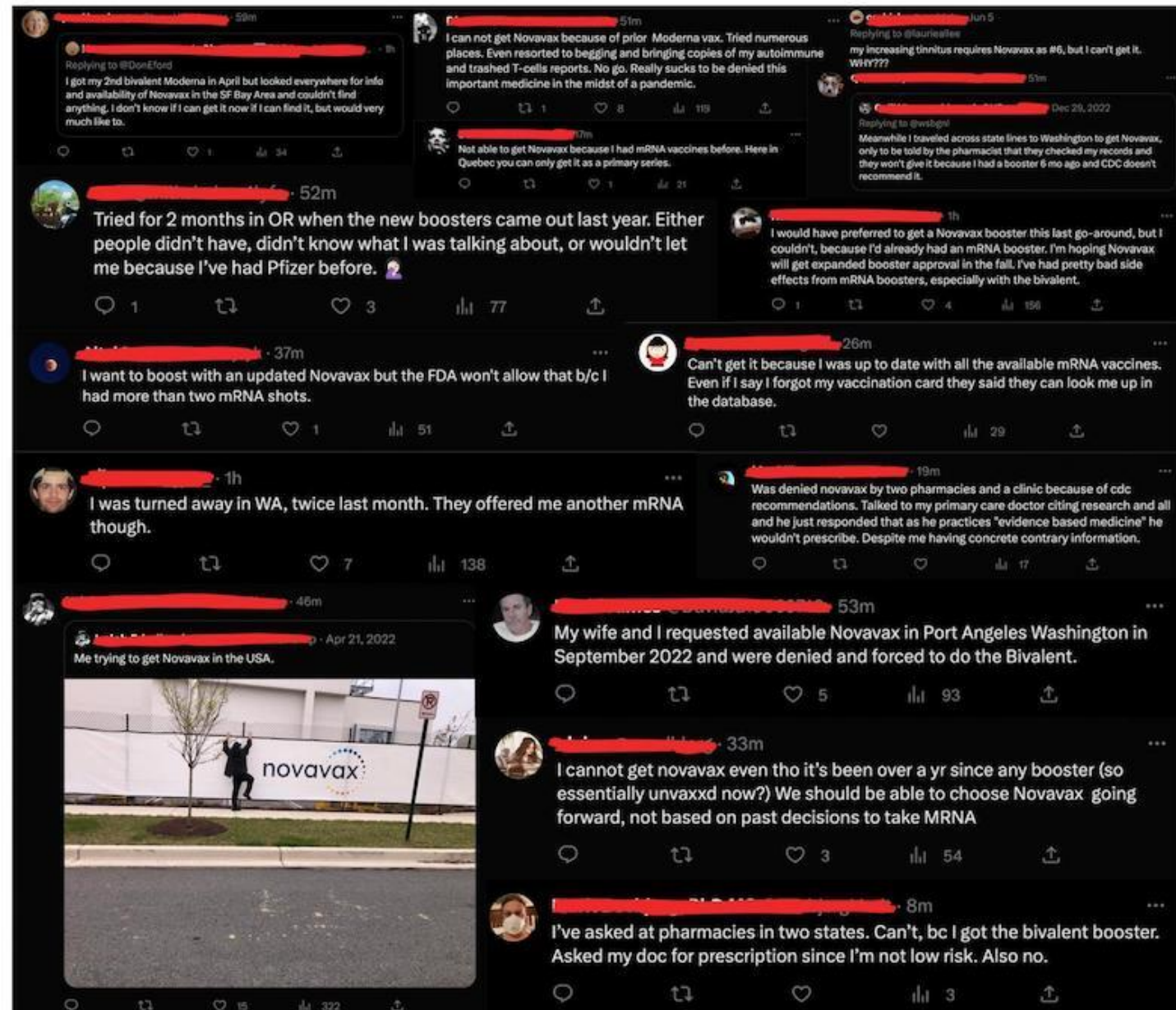
## Bivalent COVID-19 Vaccine

- Bivalent vaccines have been shown to dilute the antigen, weakening the response while also suffering from immune imprinting.
- The concern is that this will limit vaccine effectiveness and booster uptake.

## High Demand for Novavax but Access is Restricted

## Americans Restricted from Novavax

- High demand exists, but FDA's rules punish people for following its guidelines and getting mRNA first.
- No data supports the concept that it is unsafe to switch from mRNA to Novavax.
- Many countries already allow it.
- Gatekeeping access to Novavax is damaging the perception of the state of Public Health in America.



# Israel and Novavax

- Allows full access regardless of previous vaccination status.
- This includes a new primary series.
- Across multiple clinical trials, Novavax has been shown to be safe and effective when used as a heterologous booster after mRNA vaccination.

Sep 16, 2022

- *The Israeli Advisory Committee on Epidemics has recommended that Nuvaxovid™ be approved for ages 12 and older as a primary series and as a heterologous booster for those previously vaccinated with mRNA vaccines*

Novavax Nuvaxovid™ COVID-19 Vaccine Now Available in Israel for Individuals Aged 12 and Older

<https://ir.novavax.com/2022-09-16-Novavax-Nuvaxovid-TM-COVID-19-Vaccine-Now-Available-in-Israel-for-Individuals-Aged-12-and-Older>

# New Alarming Data has Come to Light: COVID-19 can Cause Brain Cells to Fuse.

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RESEARCH ARTICLE | NEUROSCIENCE f 🐦 in 🍷 🗨️ ✉️

## SARS-CoV-2 infection and viral fusogens cause neuronal and glial fusion that compromises neuronal activity

RAMÓN MARTÍNEZ-MÁRMOL <sup>ID</sup>, ROSINA GIORDANO-SANTINI <sup>ID</sup>, EVA KAULICH <sup>ID</sup>, ANN-NA CHO <sup>ID</sup>, MAGDALENA PRZYBYLA <sup>ID</sup>, MD ASRAFUZZAMAN RIYADH <sup>ID</sup>,  
EMILIJA ROBINSON, KENG YIH CHEW, RUMELO AMOR <sup>ID</sup>, [...], AND MASSIMO A. HILLIARD <sup>ID</sup> +5 authors [Authors Info & Affiliations](#)

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<https://www.science.org/doi/10.1126/sciadv.adg2248>



# Novavax Reduces Nasal Viral Replication at Exposure

Having established that SARS-CoV-2 creates syncytia in the brain, inhibiting viral replication in nasopharynx is of the utmost importance.

It is critical to stop virions from reaching the brain.

Unfortunately, mRNA only offers limited protection in this capacity.

One of the important findings of our study is that NVX vaccines blunt virus replication in the upper respiratory airway early post-infection. Importantly, all three vaccines showed a profound control of virus replication in the upper respiratory airway by 7–10 days, while the control animals showed high levels of persisting viral loads. Consistent with previous studies (24–26), the mRNA-1273 booster offered only limited protection early post-infection (at Days 2 and 4) in the upper airways. However, both NVX vaccines showed significant control of viral load in the upper airways starting from Day 2 until necropsy. Nasopharyngeal viral loads correlate with the presence and quantity of infectious viruses (48); thus, vaccines that reduce viral loads early during infection are likely to help reduce transmission to other individuals. Our results highlight the need

SARS-CoV-2 infection and viral fusogens cause neuronal and glial fusion that compromises neuronal activity

<https://www.science.org/doi/10.1126/sciadv.adg2248>



# Study: Vaccine Effectiveness in South Korean Adults

A large study in South Korea used a balanced cohort to challenge hospitalization protection of both Novavax and mRNA (Pfizer)...

Though protection was high for both vaccines, Novavax was shown to be twice as protective against hospitalization in a balanced cohort.

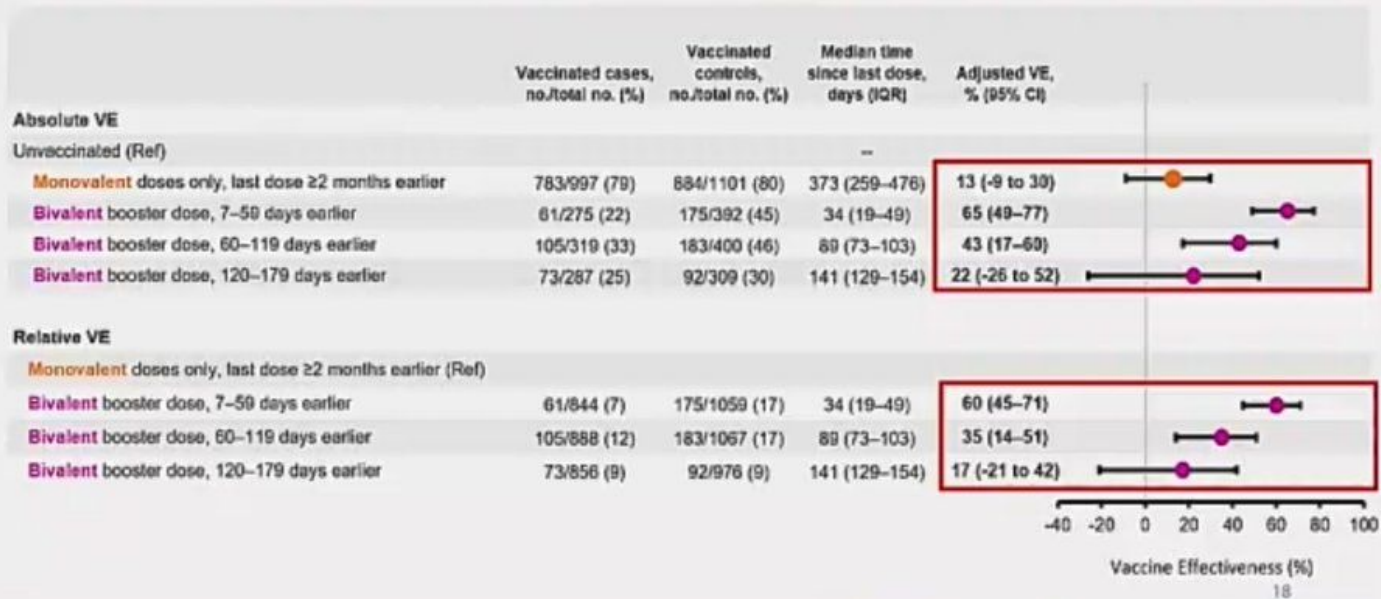
2.014) for severe SARS-CoV-2 infection. Estimated risk of severe infection was 0.001 events per 1000 persons (95% CI, 0 to 0.003) for the NVX-CoV2373 vaccine and 0.002 events per 1000 persons (95% CI, 0.001 to 0.006) for BNT162b2 vaccine.

Comparative Effectiveness of BNT162b2 and NVX-CoV2373 Vaccines in Korean Adults

<https://www.medrxiv.org/content/10.1101/2023.02.18.23286136v1>

# Unreleased Vaccine Effectiveness Data, CDC (presented at ACIP)

**Absolute and relative VE against COVID-19 hospitalizations among immunocompetent adults aged ≥65 years — IVY Network, September 8, 2022 – April 1, 2023**



ACIP Meeting, April 2023

<https://youtu.be/1r8UMABcHmY?t=5594>

## Waning of mRNA Vaccine Effectiveness

- Internal CDC/FDA data presented at ACIP demonstrated that bivalent mRNA only offers protection against hospitalization for 110 to 170 days.
- Protecting against COVID for a limited time is not sufficient for a virus that can fuse brain cells.
- As it stands, the mRNA vaccine alone is not satisfactory to protect the American people.

# Study: mRNA Needs a Cool-Down Period



The screenshot shows the AACC website header with the logo and tagline "Better health through laboratory medicine." Below the header is a navigation menu with categories: COMMUNITY, SCIENCE & RESEARCH, CLINICAL LABORATORY NEWS, EDUCATION, MEETINGS, and ADVOCACY & OUTREACH. A search bar is located in the top right corner. The main content area features a breadcrumb trail: "AACC.org // Media // AACC Press Releases // Increasing the Time Gap Between COVID-19 Vaccine Doses Leads to a Stronger Antibody Response". The article title is "Increasing the Time Gap Between COVID-19 Vaccine Doses Leads to a Stronger Antibody Response". Below the title is the text "Breaking research published today in AACC's The Journal of Applied Laboratory Medicine". The date is "Date: AUG.3.2021" and there is a "MEDIA CONTACTS" link.

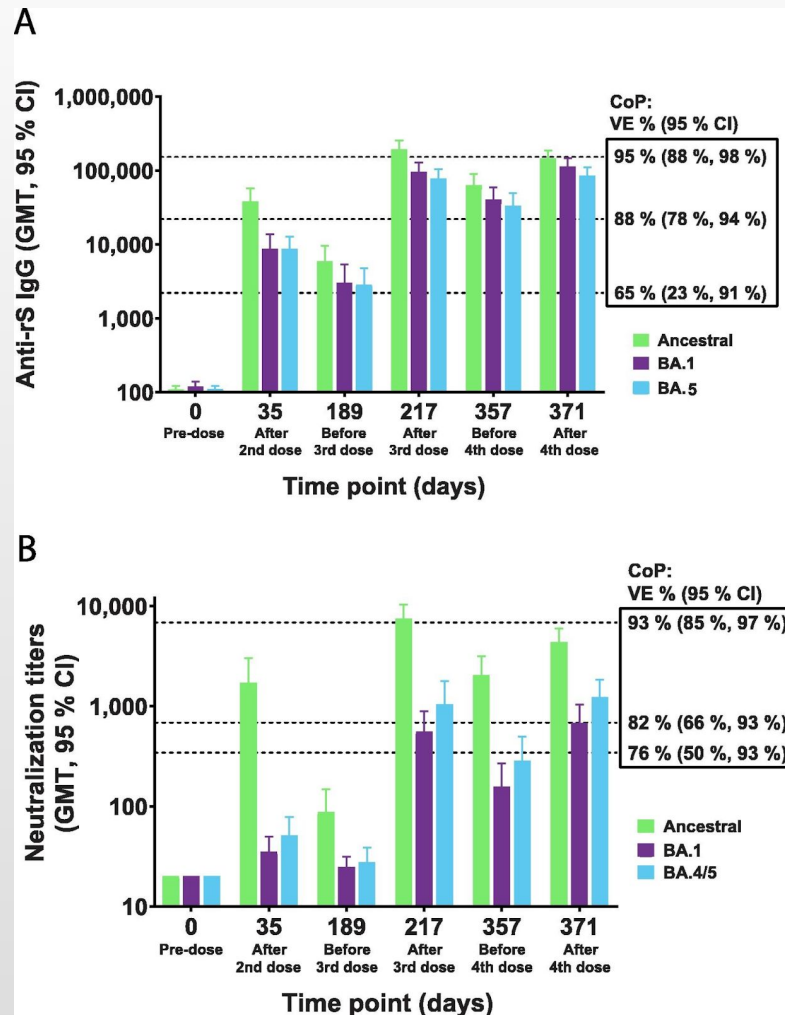
<https://www.aacc.org/media/press-release-archive/2021/08-aug/increasing-the-time-gap-between-covid19-vaccine-doses-leads-to-a-stronger-antibody-response>

## Waning of mRNA Vaccine Effectiveness

- mRNA only achieves its best reaction if there is a gap between shots.
- The gap is greater than the window of protection.
- These gaps in protection leave Americans vulnerable to hospitalization from COVID infections.



# Data on 4th Novavax Shot Shows Efficacy of Successive Doses



Immunogenicity and safety of a fourth homologous dose of NVX-CoV2373

<https://www.sciencedirect.com/science/article/pii/S0264410X23006126>

## Novavax Protection

- Vaccine can be taken successively to maintain protection with no gaps.
- It provides consistent protection.
- Response continues to increase beyond anything mRNA has achieved.

# Immunogenicity and safety of a fourth homologous dose of NVX-CoV2373

In studies, Novavax consistently demonstrates that their protection extends beyond the testing windows. This stands in contrast to mRNA.

titers (ID<sub>50</sub>) to the ancestral strain increased to 4367 (637IU<sub>50</sub>/mL) by day 371. While this titer was somewhat lower than that seen after the third booster dose, antibody titers were only assessed 14 days after the fourth booster as compared with 28 days after the third dose, and it is possible that further increases would have been seen over the next 2 weeks. Consistent with other approved vaccines [19], lower antibody levels were noted

Immunogenicity and safety of a fourth homologous dose of NVX-CoV2373

<https://www.sciencedirect.com/science/article/pii/S0264410X23006126>

## Extended Protection

- In contrast to mRNA, Novavax has demonstrated that protection from hospitalization has no clear endpoint, extending beyond testing windows.
- This provides consistent protection with no gaps.

# Novavax Received Funding For Its COVID-19 Vaccine As Part of Operation Warp Speed

July 7: HHS [announced](#) \$1.6 billion in funds to support the large-scale manufacturing of Novavax's vaccine candidate. By funding Novavax's manufacturing effort, the federal government will own the 100 million doses expected to result from the demonstration project.

Explaining Operation Warp Speed

<https://www.nihb.org/covid-19/wp-content/uploads/2020/08/Fact-sheet-operation-warp-speed.pdf>

## Funded By Americans

- Novavax was a product of Operation Warp Speed and paid for with US American Tax Dollars.
- Yet Americans have extremely limited access to the product they funded development of.



# CDC Recommendations Don't Even Suggest Offering Novavax Boosters on top of Novavax

## COVID-19 Vaccine

Interim COVID-19 Immunization Schedule for Persons 6 Months of Age and Older



Table 1c. For Most People (those who are NOT moderately to severely immunocompromised)

| Novavax* (Monovalent vaccine)<br>Type: Protein Sub-Unit |   |  |   |
|---|---|--|---|
| Age   | Vaccination History                           | Vaccine Schedule <sup>†</sup>  | Administer  |
| 12 years and older                                      | 1 or more doses of monovalent Novavax vaccine | 1 dose bivalent mRNA vaccine at least 8 weeks (2 months) after Dose 2 <sup>‡</sup> | <b>Moderna:</b> 0.50 mL/50 $\mu$ g from the vial with a blue cap and gray label border.<br><b>OR</b><br><b>Pfizer-BioNTech:</b> 0.3 mL/30 $\mu$ g from the vial with a gray cap |
|   | At least 1 dose of bivalent vaccine           | No dose <sup>‡</sup>   | No dose <sup>‡</sup>  |

\* Novavax COVID-19 Vaccine remains authorized to provide a 2-dose primary series (separated by at least 3–8 weeks) to people ages 12 years and older. Administer 0.5 mL/5  $\mu$ g rS and 50  $\mu$ g of Matrix-M™ adjuvant vaccine from a vial with a royal blue cap. A booster dose is authorized in limited situations to people ages 18 years and older who completed the primary series using any COVID-19 vaccine, have not received any previous booster dose(s), and are unable (i.e., vaccine contraindicated or not available) or unwilling to receive an mRNA vaccine and would otherwise not receive a dose. This dose is administered at least 6 months after completion of any primary series.

<sup>†</sup> Persons with a recent SARS-CoV-2 infection may consider delaying vaccination by 3 months from symptom onset or positive test (if infection was asymptomatic).

<sup>‡</sup> Adults 65 years of age and older: May receive 1 additional bivalent mRNA vaccine dose at least 4 months after the first dose of a bivalent mRNA vaccine.

## CDC Recommendations

- United States is one of only a few countries using draconian restrictions that prevent access to a vaccine paid for by its citizens.
- We need greater access to Novavax, including a new primary series at least 4 months out from your last COVID vaccine.

# Bivalents Increase Immune Imprinting and Reduce Efficacy

high ACE2 binding affinity. Our findings suggest the WT component should be abandoned when updating COVID-19 vaccine antigen compositions to XBB lineages, and those who haven't been exposed to Omicron yet should receive two updated vaccine boosters.

Repeated Omicron infection alleviates SARS-CoV-2 immune imprinting

<https://www.biorxiv.org/content/10.1101/2023.05.01.538516v3>

Multiple analyses of these results, including antigenic mapping, made clear that inclusion of the ancestral spike prevents the broadening of antibodies to the BA.5 component in the bivalent vaccine, thereby defeating its intended goal. Our findings suggest that the ancestral spike in the current bivalent COVID-19 vaccine is the cause of deep immunological imprinting. Its removal from future vaccine compositions is therefore strongly recommended.

Deep immunological imprinting due to the ancestral spike in the current bivalent COVID-19 vaccine

<https://www.biorxiv.org/content/10.1101/2023.05.03.539268v1>

## Overcoming Immune Imprinting

- Recent testing has demonstrated that a new primary series is required to consistently elicit a protective immune reaction.
- Not taking this step could lead to an insufficient immune response.
- This could damage the public's perception of vaccine effectiveness and Public Health.

## Anecdotal Reports Showing Potential Benefit of Novavax for Long COVID

# Novavax for Long Covid

- There have been many anecdotal reports of long COVID patients showing signs of recovery after receiving one or more Novavax vaccines.
- We need studies from the NIH and Novavax into the anecdotal reports showing that Long COVID patients begin recovery after receiving this vaccine.

End of Feb I went and got a dose of Novavax. I got it as a booster, not as it's own primary series. My previous vaccinations were mRNA which I had no significant trouble with. 8/

Maybe 10 or 11 days later I was walking around (a big deal on its own) and realized my ears weren't ringing anymore. I do still have some tinnitus but it's gone from being so aggravating I would cry, to being something I have to actively listen for. 9/

Now, 33 days later, I am very much improved. I can sit upright for as long as I want. I'm using my kitchen stool much less because I can tolerate standing. I can even stand and sing at the same time again. For a while, I couldn't sing at all. 10/

I no longer get the "if I don't lay down right now my head is going to explode" feeling. I'm not counting the seconds to my next nap anymore and I can play video games for extended periods of time again. 11/

Palpitations are very rare, and I haven't logged chest pain on Visible in weeks. I can tolerate carbs without much trouble and can regulate my temp much better. I can shower on my feet again, and take a hot bath. 12/

The other day, I took 3300 steps before noon, which is pretty close to my normal. I was not terribly active pre Covid. "Normal" for me is mostly just household duties, playing outside with my kids and a dog walk. 13/

Not LC, but the 3rd dose of Novavax specifically helped reduce my long monkeypox.

The big problem is still access. I've gone online and searched with all the tool both public and from Twitter links and no luck in two different states (NC and IL). Heading home to Thailand where they manufacture it but don't provide it! 🇹🇭

After my 3rd dose of Novavax in February 2023 I felt significantly better within a couple days and all my lingering Covid symptoms( elevated Bp, weird stuff going on internally, fatigue) from 06/22 infection were gone. I bought the stock so I'm a believer.

After first Novavax I seemed to wake up. Felt as though I could go on. After second Novavax I was off inhaler for lungs, no longer registered diabetic, fatigue dramatically less, chest pain reduced. Third Novavax next week

My wife had LC from early 2020. Each time she's had a novavax the words she describes to use the outcomes are "I feel like my baseline health and strength have jumped up each time".

A couple weeks ago, I finally got novavax in san jose california just eight months after a bivalent booster. But pretty sure i've never had covid, Including a blood test for antibodies some months ago.

I realized novavax has helped 5 things: allowed my shoulders 2 move again after 16 mos & took 80% of the pain away in 48 hrs. 2nd jab made them back 2 norm. It got rid of 95% of internal tremors, my painful GI flare ups, 80% heart pain gone, & heartburn basically gone. #novavax

My memory has declined significantly. But I am getting towards middle age so it's hard to attribute that.

Certainly what I did have was thumping heartbeat - out of my neck thumping. My legs were like concrete to move and I had short breath.

That all resolved after Novavax.



## Demand For Novavax Remains High in Spite of Restrictions

# Novavax for Long Covid

- These are just a few examples; there are many similar reports.
- Due to time constraints we can't show them all here.

Oct 27, 2022

Replying to @CovidDataReport

Guys I took my Novavax booster last week and all of my long covid/mRNA symptoms faded away. I felt like my old self before I was infected with covid and vaxed with Moderna . I will never take a mRNA again.

1 6 479

Aug 27, 2022

I feel that @Novavax cured my long Covid! I can run more and I feel like I can manage my nystagmus (dizziness) more. I been feeling better ever since I got @Novavax I had my Brain Injury 3 years ago around when Covid-19 hit. I fell like my symptoms were worse before @Novavax

1 6 410

Aug 28, 2022

Replying to @DonEford

I am just 1 person and I am only a week from first of Novavax vaccine but after covid I had daily knee pain, maybe arthritis, heat and aching treated by Advil. I have not had to treat since morning after Novavax.

1 5 373

Aug 28, 2022

Replying to @BryanIverson5 and @Novavax

Same. I started to feel better a week after and completely better 3 weeks after. Weird heart beat dizziness and fatigue are gone now.

1 4 330

Sep 5, 2022

Woke up the next day better than pre-Novavax baseline, with my lingering Covid brain fog resolved. If it's viral reservoirs clearing, I believe it, if it's placebo, I'll take that too—I feel really good in the head for the first time since July. 23/

[Show this thread](#)

1 5 318

Oct 20, 2022

Replying to @DonEford

I recieved novavax as 4th booster 2 weeks ago, LC symptoms have improved in the past week.

1 7 293

Dec 20, 2022

Update on yesterday's @Novavax shot! Slept well, no fever, my lingering cough gone! So strange. But there you have it. No arm pain. [twitter.com/elizavetaka/st...](https://twitter.com/elizavetaka/st...)

1 4 273

Nov 6, 2022

Replying to @organichemusic

When I was infected with covid, I immediately experienced inflammation in my lower back/buttock area, it would wake me up at night. Once I got Novavax 5 months later, my symptoms disappeared. I can only relate it to the vax, no other explanation. No side effects from Nova either.

1 4 264

Jan 8

Replying to @Rivkatweets @ExiledNoMo and @Elyzium13

the third Novavax shot has improved my son's #MyalgicEncephalomyelitis This was 6 months ago

1 5 240

Feb 10

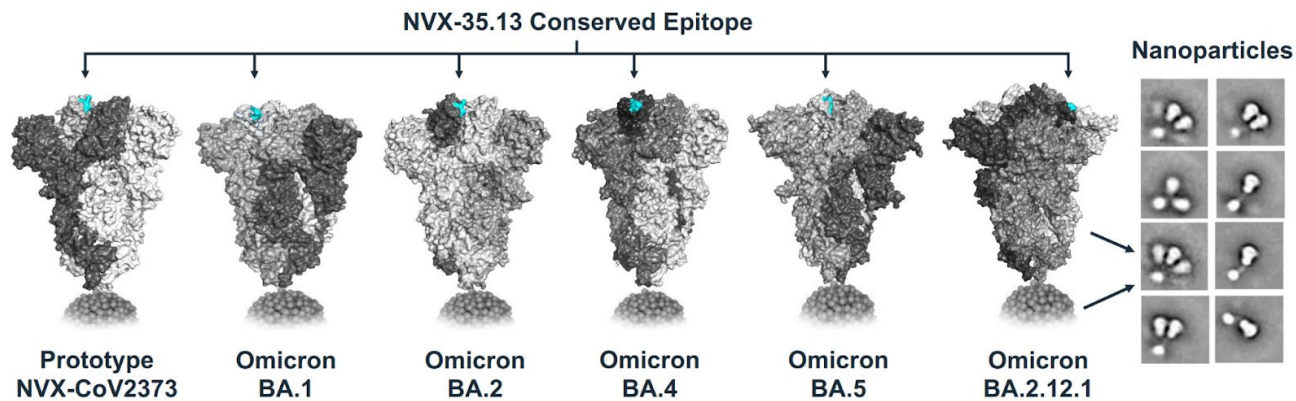
Just want to put it out for anyone else looking for a sign - take the Covavax (Novavax). Coupled with some exercise every other day, it has helped me recover from what I believe to be long covid effects. A month & a half was enough to feel the change

1 5 251

# Novavax Fights Every Variant Because of Conserved Epitopes

NV-5

## Novavax NVX-CoV2373 and Omicron Variant Vaccines: Full Length Spike Protein Trimers



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## Long-lasting Potential

- Novavax is designed to target conserved epitopes.
- This effect provides a broad spectrum immune response against variants of concern.
- It is likely that it assists the immune system in finding and targeting persistent virus, which is a primary driver of Long COVID.

# Changes are Needed to the Novavax Pediatric Vaccine Trial Recruitment Criteria

- The requirements for Novavax to bring a pediatric vaccine to market are unreasonable and outdated.
- Specifically, regulations requiring that pediatric cohorts be infection or vaccine-naïve must be updated.
- The population that they will be vaccinating will not fit that model, and will only delay protection for children.

**These restrictions are wholly inappropriate for the situation.**

# Project NextGen Funding Saved from the Debt Ceiling Deal

The recent deal to raise the debt ceiling preserved about \$5 billion in funding for Project NextGen, which aims to develop new Covid vaccines and treatments.

<https://www.politico.com/newsletters/future-pulse/2023/06/08/project-nextgen-has-no-warp-speed-00100956>

The outcome of the Debt Ceiling Deal is that Project NextGen may provide the only funding for COVID-19 vaccines in the foreseeable future.

## Project NextGen

- Funding needs to be allocated from Project NextGen to expedite the production of the Novavax pediatric COVID vaccine.
- Spending caps created during the debt ceiling deal will limit the ability of Congress to make new investments in treatments and vaccines for at least the next two years.
- We cannot wait that long to protect our children.



## More Tweets From Individuals Denied Novavax



## Novavax Restrictions are an Unresolved Vaccine Equity Issue

- Limiting access to Novavax is preventing Americans from being protected against COVID-19.
- It is cruel to limit the tools at hand, especially when vials are going wasted and unused because of outdated regulations.
- Demand exists but the current FDA recommendations artificially limit access; this is unique to America.

# Americans Want Novavax



## Novavax Restrictions are an Unresolved Vaccine Equity Issue

- There are many more examples of Americans that want access to Novavax, but are restricted by this committee's recommendations.

# Issues to address:

- Next year's COVID-19 vaccine must be a monovalent vaccine targeting XBB.1.5, but no higher.
- Novavax access must be extended to any Americans who would like to get a new primary series. This is a requirement to avoid immune imprinting.
- Allocate NextGen funding and re-assess the trial recruitment criteria so Novavax can expedite a pediatric vaccine to market.
- Remove the regulation stating that Novavax is only used as a secondary vaccine in cases of refusal.
- Limiting access is a vaccine equity issue, and the FDA is not rising to the moment, but we could fix that today.

Please take the necessary steps to protect the American people.

We need leadership; we need you to be those leaders.