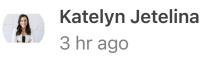
Fall bivalent boosters: Science update round 2





Lab studies assessing the preliminary impact of our updated fall boosters are trickling in. (We don't have "real world" data yet, and honestly, it may be a while.) In all, we knew boosters would help given circulating variants, but we didn't know how *much more* helpful an updated formula would be. Here is the latest science and what it means in the broader context.

Purpose of the fall booster

As a reminder, our hope with updated boosters was that they would accomplish three things:

- 1. **Greater protection** against infection and transmission, by boosting our first line of defense—neutralizing antibodies;
- 2. Longer protection against infection and severe disease, even just by a few months;
- 3. **Broader protection** or the ability to create antibodies that "see" more virus parts and "attach" more strongly compared to the antibodies we have right now.

My previous science update showed that #3 is being accomplished, which is great news. We won't know about #2 for a few months. (We are at the mercy of time.) New science out this week gives some insight on #1.

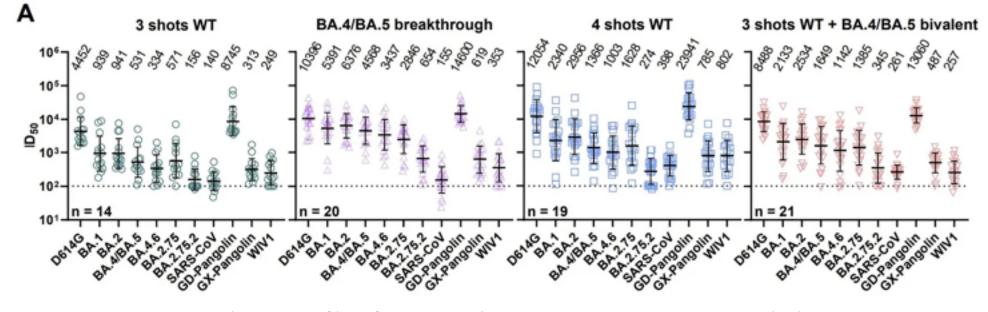
Impact on neutralizing antibodies

Two preprints were released this week (here and here) from two separate but respected labs in the U.S. Results swept mass media headlines. For example, an NPR headline stated: "Two new research papers cast doubt on the new COVID booster."

What did the studies find? Do they really cast doubt on the booster?

Overall, both labs extracted blood from vaccinated and vaccinated + infected individuals 3-5 weeks after they received the fall booster. In a petri dish, the scientists measured how many neutralizing antibodies connected to subvariants once they were introduced. (They were not the new circulating subvariants, like XBB or BQ.1.1, unfortunately). Researchers found two things:

- Neutralizing antibodies increased after the fall booster. Not surprising, but good to see.
- 2. Neutralizing antibodies were not higher after the fall booster compared to the original vaccine formula booster. *Bummer*.



Neutralization profiles of serum samples against SARS-CoV-2 variants and other sarbecoviruses. Source: <u>Wang et al., Preprint.</u>

Does this mean the fall booster isn't working?

Absolutely not.

First, an increase in neutralizing antibodies will help prevent infection and transmission in the short term. The old vaccine formula did this. The new formula does this. It's not a surprise and will help.

Second, these studies extracted blood 3-5 weeks after people got the fall booster. The timeframe is important given the intricacies of the immune system.

When we come in contact with a virus or get a vaccine for the *first time*, our immune system develops B cells, which are antibody factories. Each B cell makes a single antibody shape, and they can pump out huge quantities of antibodies if needed. If you come in contact with another variant (or another vaccine formula), B cells can evolve and modify the antibodies they create for a new variant. This is just like factories that can modify their product on the line.

When the immune system sees a threat (like a fall booster) it wants to clear the threat in the fastest way possible. Responses based on memory work fastest, so instead of modifying the factory line, B cells get to work pumping out antibodies of shapes they've seen before. This is called "B cell memory." It's not until later that the B cells update their factory line and start pumping out updated antibodies. Research shows that, for COVID-19, this factory update happens at about 2 months after exposure (here, here). So, as shown in the figure below, an updated booster's benefit may be marginal in the beginning, but better over time.

Fig. 1

Orange=updated Beta booster; blue=original formula. Source: Nature Medicine

Bottom line

The two preprints this week offered fantastic insight into the short-term impact of fall boosters. However, don't be swayed by the headlines, as one or two preprints are not the whole story. We already have data showing the fall boosters provide *broader* protection. We have studies showing boosters boost neutralizing antibodies. We just may need time to see the full potential of an updated booster formula compared to the original.

Bottom bottom line

Go get your fall booster (when the timing make sense).

Love, YLE

"Your Local Epidemiologist (YLE)" is written by Dr. Katelyn Jetelina, MPH PhD—an epidemiologist, data scientist, wife, and mom of two little girls. During the day she works at a nonpartisan health policy think tank, and at night she writes this newsletter. Her main goal is to "translate" the ever-evolving public health science so that people will be well equipped to make evidence-based decisions. This newsletter is free thanks to the generous support of fellow YLE community members. To support this effort, subscribe below:





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22 Comments

Write a comment

lisa 29 min ago

Thanks for this! Very helpful. I am curious how these studies deal with the mix of immune conditions of the subjects - ie, some people have still never have covid, some had Wuhan, some had Delta, some had Omicron, and so on - plus some were boosted regularly and some were not, etc. I would think all that would make it harder to make sense of the results.

Relatedly, I have been confused by what I've read about how soon one should get the booster after

infection. The CDC says 3 months, but I saw a small study that found that those who'd had covid less than 6 months before getting the booster had a "muted" B-cell response compared to those who had never been infected, suggesting that waiting longer would be better. The study was small and only followed subjects for 60 days. In my area, a lot of people are getting sick right now, so the idea boosting is appealing. But if one's current immunity is still very good 5 months out (especially after a bad bout), the boost might be counterproductive - the last thing one wants! [study link: https://www.medrxiv.org/content/10.1101/2022.08.30.22279344v1.full]

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Tim Klein	58 min ago	

Thank you for the explanation about B cells' "factory update" that happens over time rather than

instantly.

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