- Vaccination

Why mixing vaccines and getting boosters are a bad idea

We still don't have all the data and enough research

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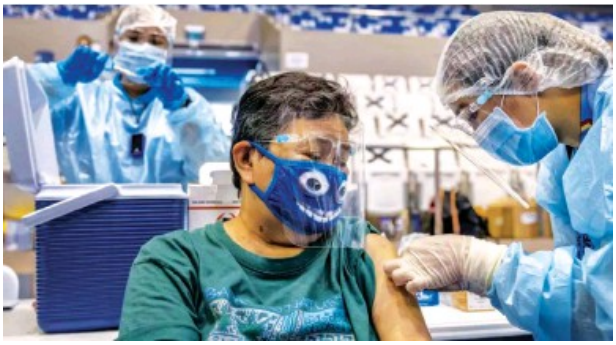
It sounds straightforward: If there are more breakthrough infections against our current vaccines, why not give a booster? Or what about giving another vaccine course? Or mixing the vaccines? Many people talk about this as if it were a simple thing, but it is much more complicated. Why do the World Health Organization, the Centers for Disease Control, and the European Medicines Agency recommend against mixing at this time? Here are some answers to the most common questions on vaccine mixing and boosting.



With the emergence of the new variants, can't we just mix vaccines to improve protection? There are many facets to this question. The first problem is safety. Any drug, before being used in a large population, goes through extensive clinical trials with thousands of participants looking for potentially harmful side effects. Phase 1 and phase 2 clinical trials are mostly concerned with safety, while phase 3 clinical trials look at safety and efficacy. Mixing two different vaccines without going through proper clinical trials is pretty much a shot in the dark.

There are already some studies showing higher adverse reactions with vaccine mixing. Doing this pre maturely on a large scale can cause a significant amount of harm without any guarantee of increased protection. There is also the question of which vaccine brands are compatible with each other and can be mixed safely. Finally, the correct sequence and interval between the two different vaccines need to be properly explored.

Vaccine sequence is not a trivial issue. The pneumococcal vaccine is a good example. For pneumococcal vaccination, giving PPSV23 followed by PCV13 is much less efficacious than giving PCV13 first followed by PPSV23. Giving the second vaccine too early also affects efficacy and duration of protection. Without doing a proper study, otherwise effective and life-saving vaccines may end up being wasted. Worse, it might cause unforeseen side effects.

There is data that mixing some vaccine brands results in higher neutralizing antibody levels. Shouldn't this be enough to recommend mixing vaccines? There is no clear data that mixing vaccines results in better clinical protection against COVID-19. There is no evidence that someone given two doses of the same vaccine is better protected against getting

sick and dying from COVID-19 compared with someone who received two kinds of vaccine. There isn't any clinical evidence that a mixed vaccine regimen has at least equivalent efficacy to two doses of the same vaccine. The mixture might give even less protection or a shorter duration of effect.

Clinical trials have already shown that using two doses of the same vaccine (except for Janssen which is only one dose) is associated with good protection from clinical and severe disease. There are no equivalent results yet for vaccine mixtures. The trials are still ongoing. What is available are measurements of neutralizing antibody levels after using some vaccine combinations. A few studies have shown that higher levels of neutralizing antibodies are generated when some types of vaccines are mixed. The problem is that no one knows what level of neutralizing antibodies is needed for protection, and whether higher levels beyond this will translate into better disease protection. This doesn't even take into account T-cell responses (more on this in question 3).

Clinical trials are currently ongoing. If these show that fewer people get sick from COVID-19 from a mix of vaccines compared with two doses of the same vaccine, and there aren't worse side effects, then health authorities will be in a better position to recommend mixing. Without these assurances, mixing vaccines potentially presents safety issues without guaranteeing better protection.

Higher titers of neutralizing antibody should mean more protection, right?

Not necessarily. Aside from the uncertainty on what levels of neutralizing antibodies are protective, neutralizing antibody activity has been going down as a result of the emergence of variants like Beta and Delta. Boosting with the same vaccine target without making changes to the spike protein may have limited effectiveness, since the generated antibodies don't work very well even if there are more of them.

Because most current vaccines have shown some T-cell activity, however, they will continue to protect against severe disease. T-cells, which include helper T-cells and cytotoxic T-cells, can prevent severe disease even if the virus gets past the neutralizing antibodies. This is because T-cell responses are not dependent on spike protein responses alone. Even if neutralizing antibodies become completely useless against new spike protein variants, a vaccine can continue to generate a good T-cell response. Cytotoxic Tcells produced as a result of vaccination can recognize virus-infected cells, and will work to decrease the severity of infection. Helper T-cells can better coordinate the immune response and generate longer-lasting immunity.

But Thailand and Indonesia are considering boosting their healthcare workers! What about us?

This is a country-based response and is not yet supported by the current data. The World Health Organization (WHO) in particular advises against this for now because it will further exacerbate vaccine shortages. Without more compelling data that categorically shows better protection with mixing or boosting, taking vaccines away from those who have not yet been vaccinated cannot be justified. It is also riskier in terms of side effects.

What about Canada which has been mixing mRNA vaccines as well as Astra and Pfizer? Can't we do the same?

This type of mixing was in response to an extraordinary situation due to acute vaccine shortages. As cases spiked in Canada, the Canadian government decided to use whatever vaccines were available to fully protect as many people as possible. Because this kind of of-flabel use violates emergency use authorization, only the government can decide if it will allow this kind of action. In the Philippines, we have avoided this situation by ensuring that the second dose of a vaccine is already secure if we decide to vaccinate an individual. In hindsight, this turned out to be a very good decision because partial vaccination is not very effective against the new variants. Being full vaccinated, defined as at least two weeks from the second dose of a COVID-19 vaccine, is the most effective way to protect against the new variants of concern.

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