Mixing and matching vaccines could help solve many rollout problems

May 31 2021, by Fiona Russell, John Hart

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In the face of changing eligibility for the AstraZeneca vaccine, new variants of the coronavirus and supply constraints, many people are wondering whether they can "mix and match" COVID-19 vaccines.

This means, for example, having the AstraZeneca vaccine as the first dose, followed by a different vaccine such as Pfizer as the second dose, and boosters with other vaccines later on.

While many studies are ongoing, data has recently been released from mix and match trials in Spain and the United Kingdom.

This data is very promising, and suggests mix and match schedules may give higher antibody levels than two doses of a single vaccine.

While Australia's drug regulator, the Therapeutic Goods Administration (TGA), hasn't yet approved a mix and match COVID-19 vaccination schedule, some countries are already doing this.

So how does this work, and why might it be a good idea?

What's the benefit of mixing and matching?

If the COVID-19 vaccine rollout can mix and match vaccines, this will greatly increase flexibility.

Having a flexible immunization program allows us to be nimble in the face of global supply constraints. If there's a shortage of one vaccine, instead of halting the entire program to wait for supply, the program can continue with a different vaccine, regardless of which one has been given as a first dose.

If one vaccine is less effective than another against a certain variant, mix and match schedules could ensure people who've already received one dose of a vaccine with lower effectiveness could get a booster with a vaccine that's more effective against the variant.

Some countries are already using mix and match vaccine schedules

following changing recommendations regarding the AstraZeneca vaccine because of a very rare side effect of a blood clotting/bleeding condition.

Several countries in Europe are now advising younger people previously given this vaccine as a first dose should receive an alternative vaccine as their second dose, most commonly mRNA vaccines such as Pfizer's.

Germany, France, Sweden, Norway and Denmark are among those advising mixed vaccination schedules due to this reason.

Is it safe?

In a UK mix and match study published in The Lancet in May, 830 adults over 50 were randomized to get either the Pfizer or AstraZeneca vaccines first, then the other vaccine later.

It found people who received mixed doses were more likely to develop mild to moderate symptoms from the second dose of the vaccine including chills, fatigue, fever, headache, joint pain, malaise, muscle ache and pain at the injection site, compared to those on the standard non-mixed schedule.

However, these reactions were short-lived and there were no other safety concerns. The researchers have now adapted this study to see whether early and regular use of paracetamol reduces the frequency of these reactions.

Another similar study (not-peer reviewed) in Spain found most side effects were mild or moderate and short-lived (two to three days), and were similar to the side effects from getting two doses of the same vaccine.

Is it effective?

The Spanish study found people had a vastly higher antibody response 14 days after receiving the Pfizer booster, following an initial dose of AstraZeneca.

These antibodies were able to recognize and inactivate the coronavirus in lab tests.

This response to the Pfizer boost seems to be stronger than the response after receiving two doses of the AstraZeneca vaccine, according to earlier trial data. The immune response of getting Pfizer followed by AstraZeneca isn't known yet, but the UK will have results available soon.

There's no data yet on how effective mix and match schedules are in preventing COVID-19. But they're likely to work well as the immune response is similar, or even better, compared with studies using the same vaccine as the first and second dose. This indicates they will work well in preventing disease.

Might this be one way to help resolve Australia's slow rollout?

In Australia, we've seen many people wanting to "wait for Pfizer" and not have the AstraZeneca vaccine. This is despite the UK's recent real-world findings that, following two doses, both vaccines are similarly effective against the variants circulating in the UK.

Delays in vaccine uptake have also been due to concerns regarding the very rare but serious blood clotting/bleeding syndrome after the first dose of AstraZeneca, as well as changing age restrictions in terms of who can receive this vaccine.

This caused widespread uncertainty and meant some younger people in some countries in Europe who had already received a first dose were excluded from getting a second dose.

The results from these mix and match studies support the possibility of vaccinating people who have received the first dose from AstraZeneca, with a different booster, if the need arises.

Further studies are underway to evaluate mix and match schedules with Moderna and Novavax vaccines, both of which Australia has supply deals with.

Don't delay getting vaccinated

As Victoria tackles its current outbreak, many other countries in our region are experiencing a surge in cases too. These include Fiji, Taiwan and Singapore, countries previously hailed as excellent examples of how to manage COVID-19.

These examples highlight the difficulty of sustained suppression in the absence of high vaccination coverage. This will be further exacerbated by the new, more transmissible variants.

The current cases in Victoria are caused by the B.1.617.1 ("Indian") variant. Both vaccines are effective against the closely related B.1.617.2 variant (albeit a bit lower than against B.1.1.7) and we would expect similar effectiveness against B.1.617.1.

It's not clear what kind of evidence regulatory authorities, like Australia's TGA, would require for a mixed schedule to be approved for use.

While we are waiting, it's critical eligible people don't delay getting

vaccinated with the vaccine that's offered to them now. Vaccination is an essential part of the pandemic exit strategy.

It's likely the vaccination schedule will be modified in the future as boosters may be needed. This is normal for vaccination programs—we already do this each year with the influenza vaccine. This shouldn't be seen as a policy failure, but instead an evidence-based response to new information.

Provided by The Conversation