Scientists are wrong to claim the AstraZeneca vaccine is a "second-best option" and its rollout should be paused. They claim its effectiveness is too low to generate herd immunity and this vaccine could not meet public expectations of getting Australia to the point where "the virus dies out". But it is unlikely that SARS-CoV-2 will **ever** die out - it is already everywhere. And it is silently infectious before symptoms even start.

The evidence does not allow us to say that the AstraZeneca vaccine is inferior. Yes, its effectiveness at protecting against any infections stands at 62 per cent, a figure that looks obviously inferior to 95 per cent for the Pfizer mRNA vaccine. But it is not a second-rate vaccine. To understand why, we have to go beyond the headlines.

First, results for both trials were reported at warp speed, so numbers were limited. This affects how confident we can be that the percentages are accurate. The AstraZeneca trial also started early and had a complicated "rolling" design – again, warp speed – such that adjustments to manufacturing processes **during delivery** and vaccine availability led to lower amounts of the viral vector **in one group of vaccine recipients (1),** who also typically had a longer interval between doses. Third, the Astra Zeneca trial mainly recruited people directly involved in health care, who have a higher risk of more severe disease.

Looking at severe cases in the AstraZeneca trial, of about 20,000 who received at least one dose, there were two hospitalisations in the vaccine group and 16 in control group, an efficacy against severe disease **of 88 per cent. (2)** Of about 42,000 in the Pfizer trial, there was one severe case in the vaccine group and nine in the control group, an efficacy against severe disease of **89 per cent**. **(3,4)** So, more severe cases in the AstraZeneca trial but not many severe in either trial, due to the young age of participants.

Looking at all cases, efficacy among about 2,600 early AstraZeneca recruits who received a lower first dose was 90 per cent, compared with 62 per cent among the 8,800 who received two standard doses. However, these results carry greater uncertainty than those from the Pfizer trial, due to smaller numbers. Importantly, **some of those** in the AstraZeneca were tested weekly for COVID-19, with or without symptoms; efficacy against asymptomatic infection in the group who received a low first dose was 59 per cent, compared to 4 per cent in the standard dose group.

Was it the lower first dose or the time between doses that mattered in the AstraZeneca trial? According to data given to the UK regulator, the Medicines and Healthcare products Regulatory Agency, levels of the neutralising antibody **in the blood** (what is used to see if it kills the virus in the test tube) were about three times higher if the second dose was given 12 weeks after the first, rather than six weeks, regardless of whether one dose was low or both were standard. **(5)** This suggests that a later second dose is better and makes sense because it is what we see with other vaccines. Also puts debate about the evils of delaying the second dose into context, but is a preliminary result needing confirmation with bigger numbers.

Looking ALL the details results from vaccine trials, not just the headline numbers, is the hard work that expert advisory committees like the Australian Technical Advisory Group on Immunisation do **before any vaccine is rolled out across the population**. Putting

more timely, detailed information about this group's work in the public domain would reassure people, especially at this time of understandable public anxiety.

Elimination? Globally, I suspect what is achievable is strong protection against severe disease by vaccination, with reduced, but continuing, virus circulation. The protection seen in reported trials of COVID-19 vaccines, especially for the elderly, is far superior to current influenza vaccines, even in a good year. The silver lining is that global efforts on COVID vaccines have resulted in a quantum leap forward for vaccine development generally, which is likely to translate into improvements in protection against other respiratory pathogens, even if boosters are required.

Peter McIntyre is a former director of the National Centre for Immunisation Research and Surveillance and sits on the World Health Organisation's Strategic Advisory Group of Experts for vaccines. The views in this piece are his alone and do not necessarily reflect those of either NCIRS or WHO

(1) AZ trial full paper

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext

(2) AZ trial supplementary materials

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext#supplementaryMaterial

(3) Pfizer trial full paper

https://www.nejm.org/doi/10.1056/NEJMoa2034577?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

(4) Pfizer trial supplementary materials

https://www.nejm.org/doi/10.1056/NEJMoa2034577?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed#article_supplementary_material

(5) (5) UK MHRA agency report with immune response details

https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca/information-for-healthcare-professionals-on-covid-19-vaccine-astrazeneca