COVID-19 Rapid Briefing

COVID-19 Update from SAHMRI

16 December 2021

Third dose vaccine scheduling for COVID-19

Key points

- Vaccine effectiveness against COVID-19 wanes over time, particularly for AstraZeneca.
- Greater waning has been observed for the Omicron variant compared to the Delta variant
- A third dose of an mRNA vaccine increases vaccine effectiveness against infection (and transmission)
- Scheduling:
    - Australian Technical Advisory Group on Immunisation's (ATAGI) current advice is boosters at 5 months, based on data from Israel
    - A UK study (published in the Lancet) observed no safety concerns arising from providing a third dose 10-12 weeks post second dose
    - The UK Government are offering boosters at 3 months, in response to Omicron
- Reduced timing between 2nd and 3rd doses would assist with rapid, widespread uptake of 3rd doses. High uptake of third doses will help mitigate the pace of transmission of Omicron.

EVIDENCE

In-vitro studies

- To date there have been several neutralisation studies, with the overall findings suggesting a drop in neutralisation for Omicron (1-7). A greater reduction in activity was observed for AstraZeneca.
- These studies indicate that a booster dose increases antibody titres.

Case control study

- **Andrews et al**. (pre-print, not peer reviewed) (8)
    - Background: Estimated vaccine effectiveness against symptomatic disease with 2 dose courses of Pfizer and AZ, as well as booster doses of Pfizer, using a test negative case control design. Booster vaccination was introduced in Sep 2021 to adults over 50 years and those in high risk groups, and was later expanded to all adults, initially offered 6 months post 2 dose, but since reduced to 3 months with the emergence of the Omicron variant.
    - Results: There were 581 symptomatic Omicron cases, 56,439 Delta cases, and 130,867 test negative controls.
    - Vaccine effectiveness against symptomatic disease:

	Pfizer		AstraZeneca	
Weeks post dose 2	**Omicron**	**Delta**	**Omicron**	**Delta**
2-9	88% (65.9-95.8)	88.2 (86.7 to 89.5)	-	-
10-14	48.5% (24.3-65.0)	77.7 (76.3 to 79)	-	-
15-19	34.1 (9.7 to 52)	72.2 (71 to 73.4)	-54.7 (-174 to 12.6)	48.5 (44.7 to 52)
20-24	36.6 (0.4 to 59.6)	64.8 (62.6 to 66.9)	-13.2 (-60.2 to 20.1)	45.4 (43 to 47.6)
25+	34.2 (-5 to 58.7)	63.5 (61.4 to 65.5)	5.9 (-29.7 to 31.7)	41.8 (39.4 to 44.1)
Booster (Pfizer) 2+ weeks	75.5 (56.1 to 86.3)	92.6 (92 to 93.1)	71.4 (41.8 to 86)	93.8 (93.2 to 94.3)

NOTE: Only small numbers of AZ are available for 15-24 weeks post 2nd dose, giving unreliable estimates.

- Authors interpretation: vaccine effectiveness against symptomatic disease with the Omicron variant is significantly lower than with the Delta variant. We were unable to determine protection against severe forms of disease due to the small number of Omicron cases so far and the natural lag between infection and more severe outcomes. Note that there are population differences in vaccine and booster rollout (e.g. AZ given to older population with more co-morbidities)

Epidemiology

- Discovery Health, South Africa 14 Dec 2021 (not peer reviewed) – insights from data collected from private health patients (211,000 test results) during first three weeks of the Omicron-driven wave in South Africa
  - Vaccine effectiveness: 2 dose Pfizer provides 70% protection against hospital admission, and 33% protection against infection (relative to unvaccinated), during the current Omicron wave
  - Reinfection risk: The risk of re-infection following prior infection has increased over time – 40% relative risk of reinfection among those infected during the recent Delta wave, 60% relative risk of reinfection among those infected during the second wave (Beta).
  - Severity: Adults are experiencing 29% lower admission risk relative to first wave, and lower propensity to be admitted to ICU. The lesser severity could be confounded by high seroprevalence in the general population.

Safety

- **Munro et al**. **The Lancet** (2 Dec 2021) (9): Randomised trial of third dose booster vaccines given **10-12 weeks** after an initial course of Pfizer or AstraZeneca. Investigated the reactogenicity and immunogenicity of seven different COVID-19 vaccines as a third dose after two doses of ChAdOx1 nCov-19 (Oxford–AstraZeneca; hereafter referred to as ChAd) or BNT162b2 (Pfizer–BioNtech, hereafter referred to as BNT)
  - Results: The vaccines boosted antibody and neutralising responses with **no safety concerns**.

Policy

- BBC news (14 Dec 2021): UK has recently made the policy decision to move to booster doses to **3 months** post second vaccination for all adults
- ATAGI advice (12 Dec 2021): COVID-19 booster vaccination for anyone aged 18 and older who completed their primary course of COVID-19 vaccination 5 or more months ago.
  - Rationale for timing: "Although registered for use from 6 months after primary vaccination, there are considerable data on the effectiveness and safety of boosters from 5 months from the Israeli program." (10, 11)

Expert opinion

Prof Sharon Lewin, Director, Doherty Institute (The Sydney Morning Herald Dec 14 2021)

> *"The first two doses of AstraZeneca give you really good protection against hospitalisation and disease from Delta infection, probably because it gives you a good T-cell response. But there's no doubt that antibody levels are lower after two AstraZeneca vaccines compared with the mRNA vaccines."*
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> *"The Australian Technical Advisory Group on Immunisation is now recommending having it at five months. They put it at five months because there's data on safety of boosters at five months, but not much safety data on boosters at three months. Your antibodies do start falling after about two months, but you've still got protection from infection. Your risk of hospitalisation and death doesn't drop off after either AstraZeneca or Pfizer for at least six months. But with Omicron we also are currently trying to use vaccines to stop transmission and therefore aiming to reduce infection – not just hospitalisation – because that's where we are at the moment. This might change. You definitely need higher levels of antibodies in the bloodstream to protect against infection with Omicron."*

How effective are the first two doses of COVID-19 vaccine against Omicron?

"We've only got very preliminary data on that. There's only one real-world study out, which is based on 500 patients with Omicron from the UK, and that shows that your protection from getting infected is reduced down to 10 per cent with two doses of AstraZeneca and 40 per cent with Pfizer, so there's quite a big drop in protection from infection. Although this is a small study and not published, this matches other findings that the level of antibodies after two doses aren't high enough to neutralise Omicron. We don't yet know the impact and protection from hospitalisation. Once you have your third dose, your antibody levels shoot up about 25-fold, say for after three doses of Pfizer, and then your antibodies will be in the range that will be much more likely to protect against Omicron. There's about five studies now that have looked at antibody levels and how high they need to be for Omicron. The only clinical study I know on vaccine effectiveness is from the UK. It's early days. The reason why we can't just say, 'Look, you've got to get higher antibodies so just go for a booster shot now,' is because we're always balancing safety versus efficacy. And the safety data is important to know that giving the booster at two, three, four months is actually safe. So, you balance those two things: how much safety data do we have to know that this gap is safe, and then how urgent is it to get your antibodies high? There are a few loud voices in the media that don't seem to appreciate that balance, but it's critical because you're giving these boosters to millions and millions of people, you really want to know it's safe."

References

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