

Vaccination after previous SARS-CoV-2 infection

Prepared by NCIRS for ATAGI COVID-19 Working Group
Thursday 27 January 2022

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Current advice



- ATAGI has decreased the time allowable for deferral of vaccination after prior SARS-CoV-2 infection to 4 months. This is due to the increased risk of re-infection with the Omicron variant, particularly for those who had a Delta variant infection in 2021.
- ATAGI continues to advise that previous infection is not a contraindication to vaccination and that vaccination can occur following recovery of acute illness from COVID-19.
- Currently advice states that vaccination can occur following resolution of acute illness. A precaution for all vaccination is acute illness. This may be acute systemic signs of illness or fever. This is to avoid adverse events (including common side effects of vaccination) in an already ill person or to avoid attributing illness symptoms to vaccination.
- Those with prolonged symptoms of COVID-19 should be vaccinated on a case-by-case basis.

Policy questions



- Any change to current advice?
- Any variation for:
 - 5-11yo with prior SARS-CoV-2 infection?
 - People eligible for a booster?
 - Special risk groups e.g. severe immunocompromised, medically-at-risk?
 - Those infected with Delta vs Omicron?

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UK advice



- As clinical deterioration can occur up to two weeks after infection, vaccination of adults and high risk children should be **deferred until clinical recovery to around four weeks** after onset of symptoms or four weeks from the first confirmed positive specimen in those who are asymptomatic.
- This interval may be reduced in periods of high incidence or where there is concern about vaccine effectiveness (for example a new variant).
- In younger people, protection from natural infection is likely to be high for a period of months, and vaccination in those recently infected may increase the chance of side effects. Therefore, vaccination should ideally be **deferred till at least twelve weeks from onset (or sample date) in children and young people under 18 years** who are not in high risk groups.
- This interval may be reduced to eight weeks in healthy under 18 year olds in periods of high incidence or where there is concern about vaccine effectiveness (for example a new variant).

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045288/20220105CominatyCovid-19VaccineProtocolV06.00.docx#:~:text=As%20clinical%20deterioration%20can%20occur,in%20those%20who%20are%20asymptomatic.

Other countries



<u>USA</u>	Defer until recovery from acute illness and completion of isolation
<u>Israel</u>	Those who recovered from COVID-19 can get vaccinated if at least 3 months have passed since their date of recovery or the date of their positive result on a serologic test.
<u>Canada</u>	Quebec: wait until symptoms resolve (previously 8 week interval recommended) Ontario: wait 30 days <u>BC</u> : after self-isolation period and at least 10 days since onset of symptoms, or for those without symptoms, the date of a positive test result
<u>NZ</u>	In a person who has had a previous SARS-CoV-2 infection, an individual is considered fully vaccinated after two doses of mRNA-CV (or another COVID-19 vaccine, see section 5.8.2). In these individuals, vaccination is recommended to be given from four weeks after recovery, or four weeks from the first confirmed positive PCR test if asymptomatic, and when cleared to leave isolation by a clinician. This also applies to the second dose for individuals who have SARS-CoV-2 infection after their first dose.

Review of evidence

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Protective immunity from infection



- Pre-Omicron RR of reinfection was 0.15 in previously infected vs uninfected¹
- Omicron: RR of reinfection 0.81 [95%CI: 0.73-1.00]
- Omicron had 5.41 (95% CI: 4.87-6.00) fold higher risk of reinfection compared with Delta²
- Multiple pre-Omicron studies show prior infection and vaccination provided similar levels of protection against subsequent infection³⁻⁶
- One CDC study suggested vaccination was more effective than prior infection⁷

1. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00675-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00675-9/fulltext)
2. <https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2021-12-16-COVID19-Report-49.pdf>
3. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac022/6507165>
4. <https://jamanetwork.com/journals/jama/fullarticle/2781112>
5. <https://www.medrxiv.org/content/10.1101/2021.07.03.21259976v2>
6. <https://www.medrxiv.org/content/10.1101/2021.04.20.21255670v1>
7. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7044e1.htm>

Protective immunity against Omicron from prior infection



Shrestha et al

- >50,000 employees of Cleveland Clinic
- 7851 infections, 37% during Omicron wave
- Among previously infected, vaccination was associated with a lower risk of COVID-19 in both
 - Pre-Omicron period: HR 0.6 (95% CI 0.4 – 0.9)
 - Omicron period: HR 0.36 (95% CI 0.23 – 0.57)

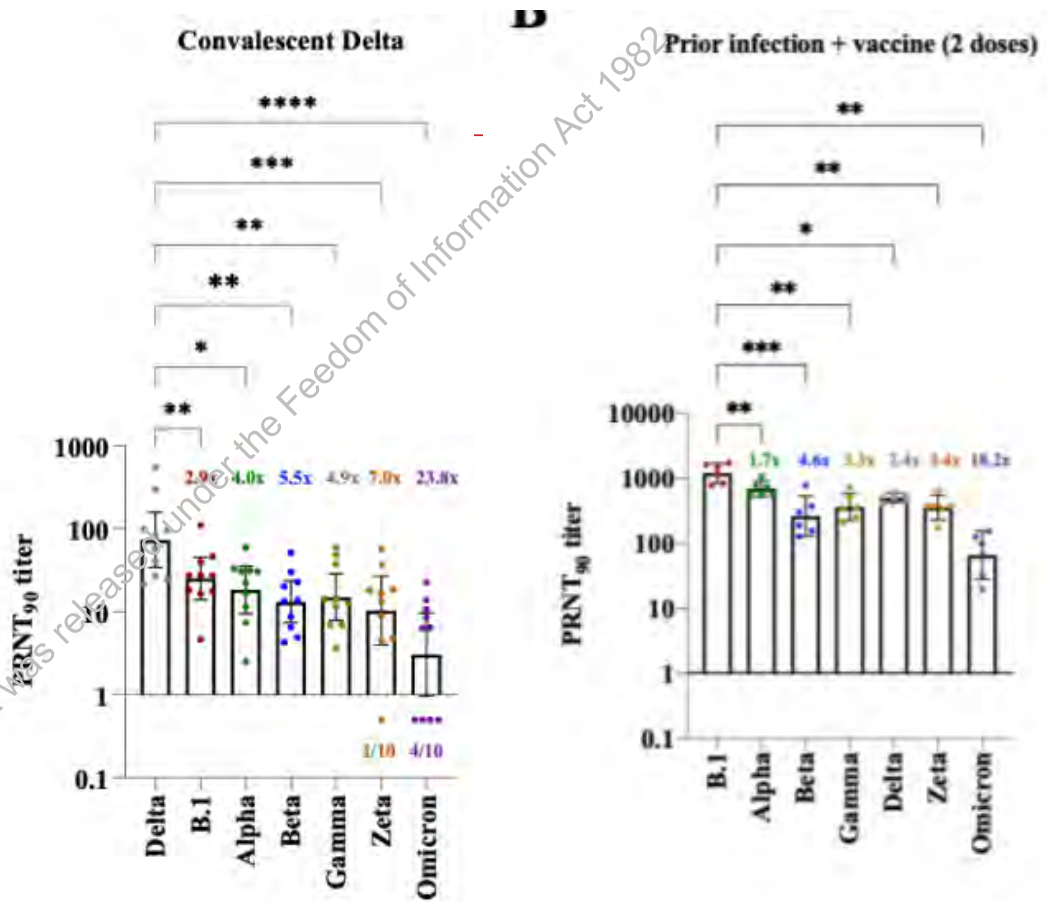
<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac022/6507165>

Variant cross-neutralisation

Omicron evades Delta-induced immunity

104 convalescent samples

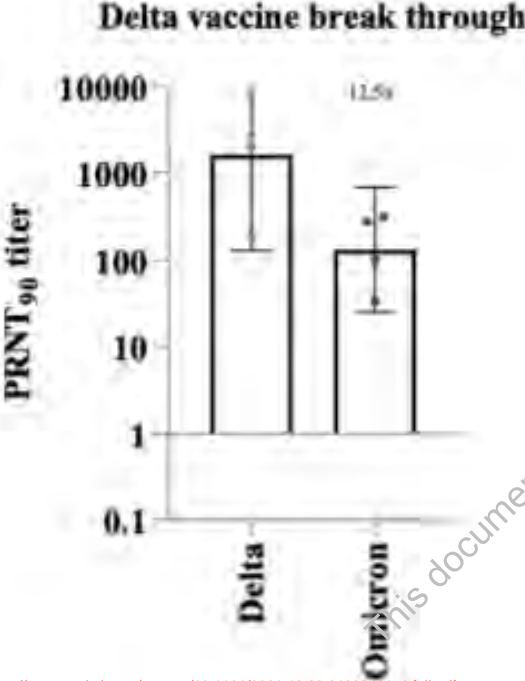
<https://www.medrxiv.org/content/10.1101/2021.12.28.21268491v1.full.pdf>



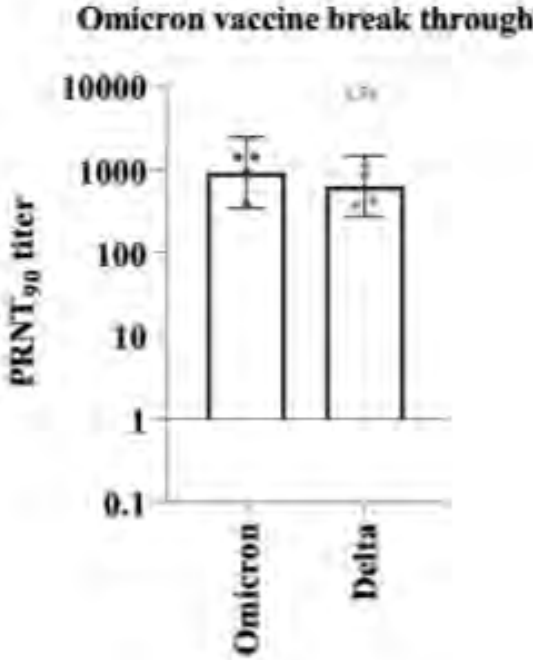
Variant cross neutralisation



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<https://www.medrxiv.org/content/10.1101/2021.12.28.21268491v1.full.pdf>

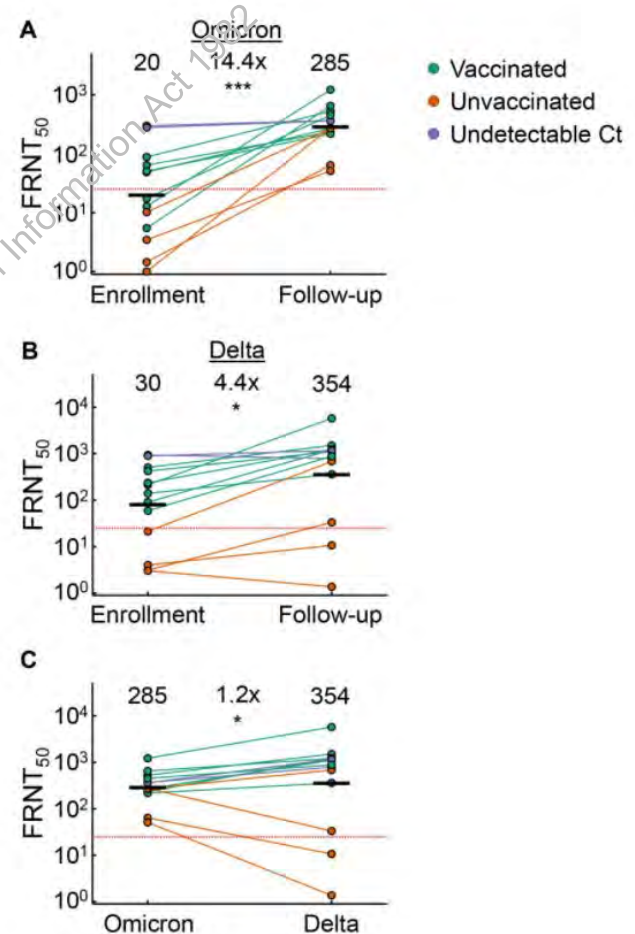
Variant cross-neutralisation

Omicron infection enhances neutralising immunity against Delta

15 participants infected with Omicron in SA

Neutralization of Delta increased 4.4-fold (95% CI 2.1-9.2), from FRNT₅₀ of 80 to 354, over 14 day enrolment period

Khan, Khadija, Farina Karim, Sandile Cele, James Emmanuel San, Gila Lustig, Houriyah Tegally, Mallory Bernstein et al. "Omicron infection enhances neutralizing immunity against the Delta variant." *medRxiv* (2021).
<https://www.medrxiv.org/content/10.1101/2021.12.27.21268439v1.full>

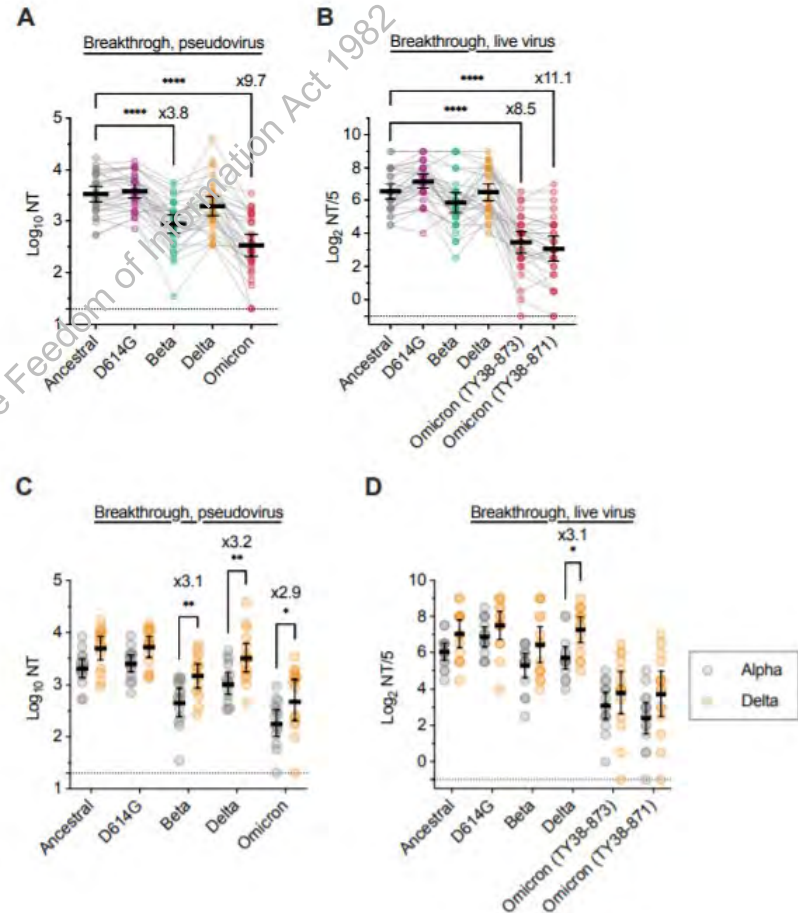




Impact of interval between vaccination and breakthrough infection

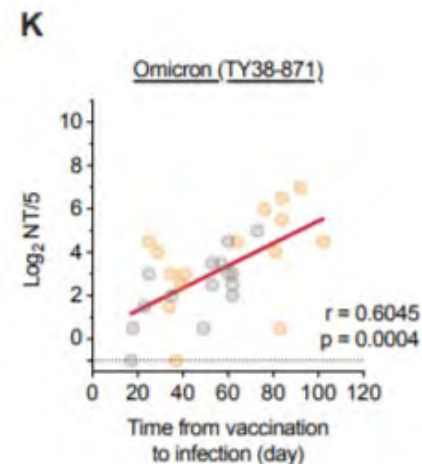
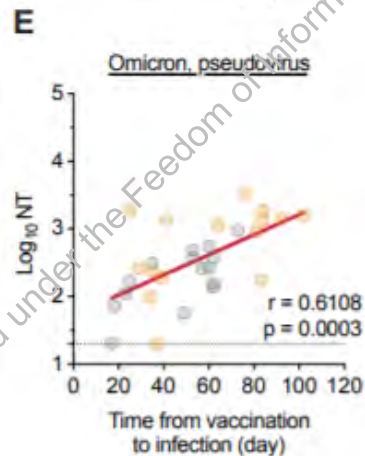
- Cross-neutralisation of Omicron in mRNA-vaccinated individuals with Alpha or Delta breakthrough infection

<https://www.medrxiv.org/content/10.1101/2021.12.28.21268451v1.full.pdf>





Correlation between interval from vaccination to breakthrough infection (with Alpha or Delta) and neutralisation titres against Omicron pseudovirus (E) and live virus (K)



<https://www.medrxiv.org/content/10.1101/2021.12.28.21268481v1.full.pdf>

Summary



- Omicron invades immunity induced by infection with prior variants
- Compared with prior variants, Omicron is resistant to neutralisation from antibodies induced by prior vaccination or infection
 - Better in those with longer interval between vaccination and breakthrough infection
- Conversely, Omicron induces strong neutralising activity against Delta variant

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