Vaccine effectiveness against Omicron

WHO meeting on COVID-19 Vaccines Research (28 Jan 2022)

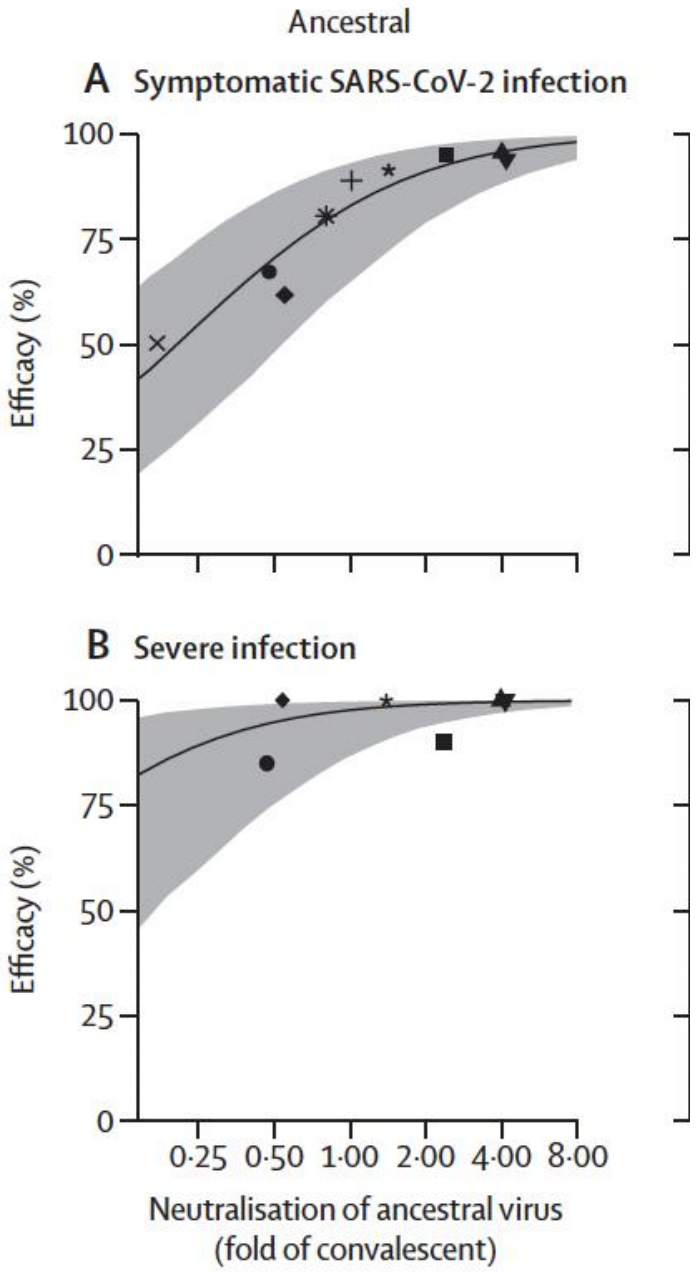
Anurag Agrawal

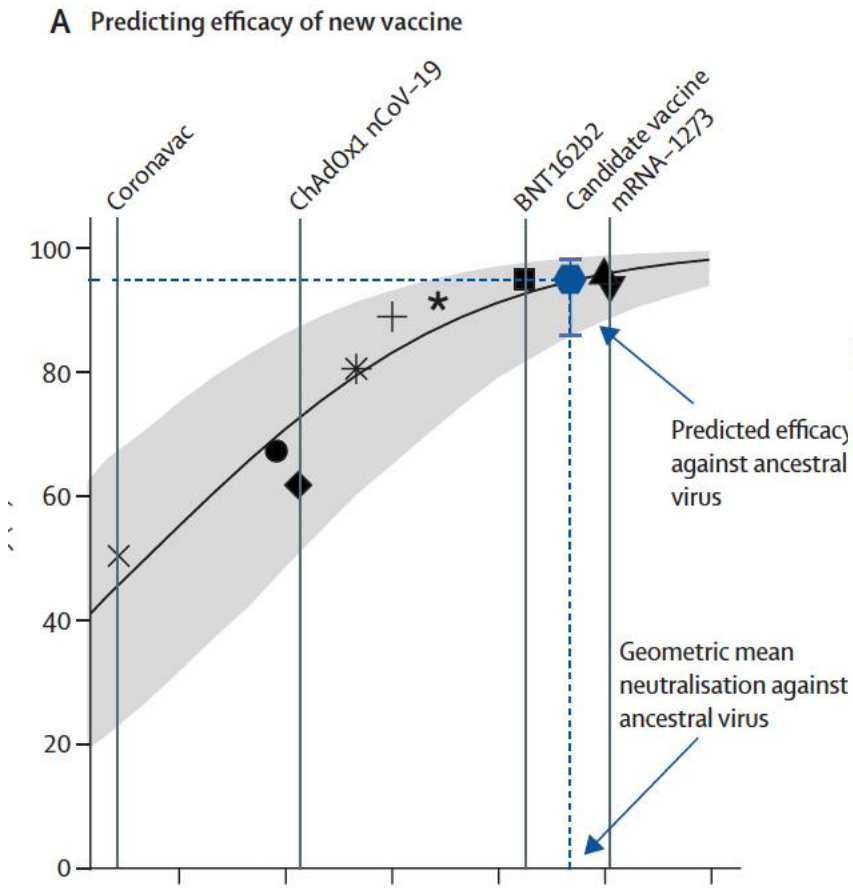
Vaccine effectiveness

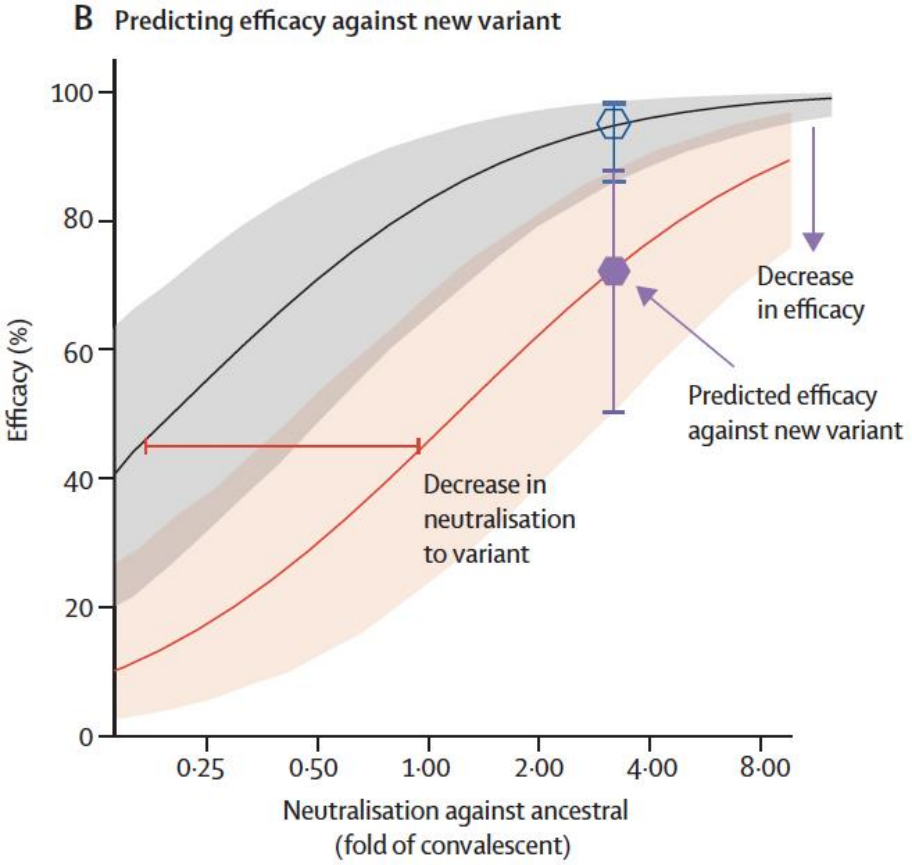
- Preventing infection
  - Clinical VE is highly correlated with neutralizing antibody titres
  - Decline in nAb titre predicts fall in VE
    - Time
    - Variant
  - Rise in nAb titre predicts increase in VE
    - Infection
    - Boost doses
- Preventing severe disease
  - Less correlated with nAb titre
  - Cellular immunity plays an important role

Cromer et al, Lancet Microbe 2022

nAb titre to predict VE against variants



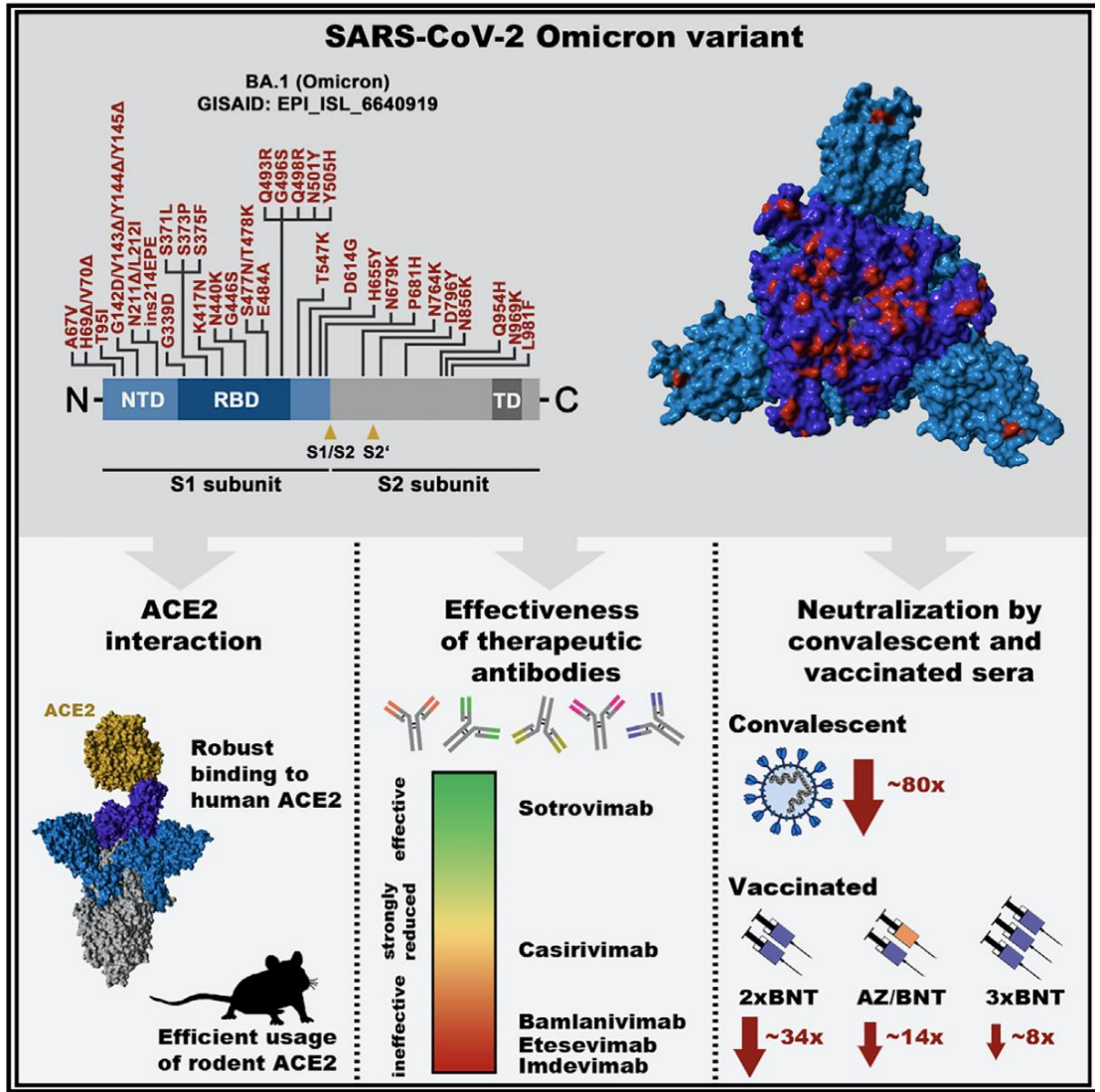




Cromer et al, Lancet Microbe 2022

Omicron

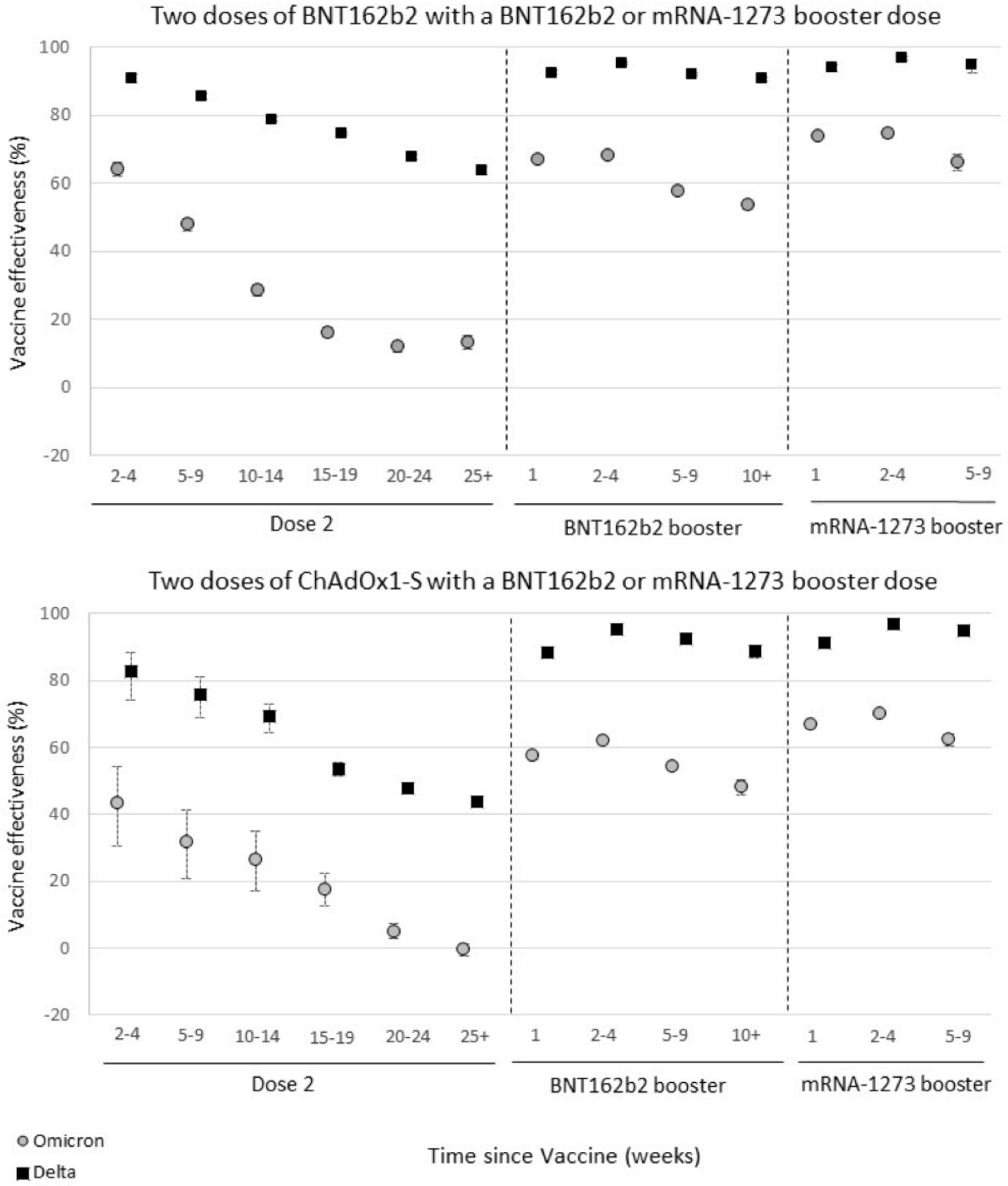
- Severe loss of nAb titre, for 2 doses of all vaccines (20-50- fold reduction)
  - Preserved neutralization in infection + 2 dose vaccination independent of order (hybrid immunity)
- Rise in neutralization to moderately effective levels with 3rd dose for most vaccines tested so far
- Preserved T-cell (CD4 and CD8) responsiveness for all vaccines tested so far, with about 50% loss at most



Alex Sigal group medRxiv
Hoffman et al Cell 2021
Barouch group medRxiv

Clinical VE

- 2 doses of vaccines ineffective in preventing infection, but effective against severe disease
  - Third dose provides 60-70% reduction in risk of infection and boosts protection against severe disease to high levels
  - Vaccination reduced transmission by primary case in households
- Prior infection + vaccination reduces symptomatic infection beyond vaccine alone for 2 doses



Real world Data:

UKHSA Update 34 dt 14 Jan 2022

- 2 dose VE against infection practically zero against infection at 5-6+ months
- Still over 50% protection against hospitalization

Table 2. Hazard ratios and vaccine effectiveness against hospitalisation (all vaccine brands combined). OR = odds ratio, HR = hazards ratio, VE = vaccine effectiveness

Dose	Interval after dose (weeks)	OR v symptomatic disease	HR vs hospitalisation	VE vs hospitalisation
1	4+	0.74 (0.72-0.76)	0.57 (0.38-0.85)	58% (37-72)
2	2 to 24	0.81 (0.8-0.82)	0.45 (0.36-0.56)	64% (54-71)
2	25+	0.94 (0.92-0.95)	0.6 (0.49-0.74)	44% (30-54)
3	2 to 4	0.32 (0.31-0.33)	0.26 (0.19-0.35)	92% (89-94)
3	5 to 9	0.42 (0.41-0.43)	0.29 (0.23-0.37)	88% (84-91)
3	10+	0.5 (0.49-0.51)	0.34 (0.26-0.44)	83% (78-87)

Important to consider background natural immunity

Table 3. Incidence of Omicron infections in the SIREN cohort between 1 December 2021 and 4 January 2022 by vaccination and prior infection status on 30 November 2021 (n=18,464)

Status	Number of participants	Number of days of follow up	Number of infections	Crude incidence rate (per 10,000 person days)	Vaccine effectiveness (%) (100 x1-IRR)	95% CI
No previous infection and vaccine status on 30 November 2021						
Unvaccinated	87	1,935	21	108.5	Ref	Ref
Vaccinated 2 dose	1,156	24,801	182	73.4	32%	-6%-57%
Vaccinated 3 dose	9,841	225,126	937	41.6	62%	41%-75%
Prior infection and vaccine status on 30 November 2021						
Unvaccinated	255	5,750	35	60.9	44%	4%-67%
Vaccinated 2 dose	1,333	28,255	123	43.5	60%	36%-75%
Vaccinated 3 dose	5,386	121,762	377	31.0	71%	56%-82%

Notes: IRR Incidence Rate Ratios. IRR are not adjusted.

UKHSA Report 34, dt 14 Jan 2022

Conclusions:

- Existing vaccines (and natural infection) remains effective at preventing severe disease / hospitalization
- While vaccination, with additional doses or with prior infection, can also provide moderate protection against infection, it will not stop transmission and prevent outbreaks
- Each infection is a further chance for viral evolution, so long-term strategy needs to consider how to best reduce infections and outbreaks, even if there is no healthcare stress