# Neutralising antibody concentrations following 2 doses of Pfizer and AstraZeneca COVID vaccines

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COM-COV
Comparing COVID-19 Vaccine Schedule Combinations




























https://comcovstudy.org.uk/

COM-COV

Comparing COVID-19 Vaccine Schedule Combinations

‘COM-COV 2’

Enrolled those

- immunized with a single dose of Pfizer or Oxford/AZ between 25th January and 20th March
- Randomisation at 2nd dose

Non-inferiority of immune response to ‘alternate’ vs ‘same’ 2nd dose

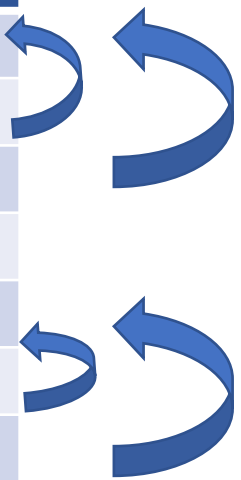
1070 > 50 year olds

Purpose was to assess flexibility of the primary immunisation schedule

Co-Funded by NIHR/Vaccine Task Force and CEPI

CEPI

| General and Immunology cohort | | number | Enrolment |
|---|---|---|---|
| 1 | primed with **Pfizer** at 8 to 12 weeks previously | 175 | Pfizer (‘BNT’) |
| 2 | | 175 | Moderna (m1273) |
| 3 | | 175 | Novavax (NVX) |
| | | | |
| 4 | Primed with **Oxford/AZ** 8 to 12 weeks previously | 175 | Oxford/AZ (ChAd) |
| 5 | | 175 | Moderna (m1273) |
| 6 | | 175 | Novavax (NVX) |
| Total | | 1050 | |



# Immunogenicity, safety, and reactogenicity of heterologous COVID-19 primary vaccination incorporating mRNA, viral-vector, and protein-adjuvant vaccines in the UK (Com-COV2): a single-blind, randomised, phase 2, non-inferiority trial

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Lancet Dec 2021

Focused on vaccine response in those with no previous infection

# Baseline demographics

| | Prime with ChAd | | | | Prime with BNT | | | |
|---|---|---|---|---|---|---|---|---|
| | ChAd (n=180) | m1273 (n=181) | NVX (n=179) | Overall (n=540) | BNT (n=175) | m1273 (n=177) | NVX (n=180) | Overall (n=532) |
| **Age** | | | | | | | | |
| Mean (SD) | 63·0 (5·51) | 63·3 (5·55) | 63·1 (5·76) | 63·2 (5·60) | 61·9 (5·37) | 62·0 (5·92) | 62·2 (5·56) | 62·0 (5·61) |
| Median (range) | 64·4 (50·1–74·2) | 64·1 (50·2–74·4) | 64·2 (50·1–74·6) | 64·2 (50·1–74·6) | 62·3 (50·4–77·1) | 62·4 (50·0–77·7) | 62·7 (50·2–78·1) | 62·4 (50·0–78·1) |
| **Gender** | | | | | | | | |
| Female | 87 (48%) | 80 (44%) | 74 (41%) | 241 (45%) | 80 (46%) | 68 (38%) | 62 (34%) | 210 (40%) |
| Male | 93 (52%) | 101 (56%) | 105 (59%) | 299 (55%) | 95 (54%) | 109 (62%) | 118 (66%) | 322 (61%) |
| **Ethnicity** | | | | | | | | |
| White | 169 (94%) | 159 (88%) | 162 (91%) | 490 (91%) | 166 (95%) | 166 (94%) | 172 (96%) | 504 (95%) |
| Black | 1 (1%) | 1 (1%) | 3 (2%) | 5 (1%) | 3 (2%) | 2 (1%) | 3 (2%) | 8 (2%) |
| Asian | 4 (2%) | 11 (6%) | 9 (5%) | 24 (4%) | 3 (2%) | 5 (3%) | 2 (1%) | 10 (2%) |
| Mixed | 3 (2%) | 7 (4%) | 3 (2%) | 13 (2%) | 1 (1%) | 1 (1%) | 2 (1%) | 4 (1%) |
| Other | 3 (2%) | 3 (2%) | 2 (1%) | 8 (2%) | 2 (1%) | 3 (2%) | 1 (1%) | 6 (1%) |
| **Comorbidities*** | | | | | | | | |
| Cardiovascular | 49 (27%) | 55 (30%) | 40 (22%) | 144 (27%) | 63 (36%) | 46 (26%) | 57 (32%) | 166 (31%) |
| Respiratory | 15 (8%) | 18 (10%) | 19 (11%) | 52 (10%) | 30 (17%) | 34 (19%) | 31 (17%) | 95 (18%) | |
| Diabetes | 9 (5%) | 10 (6%) | 14 (8%) | 33 (6%) | 22 (13%) | 21 (12%) | 24 (13%) | 67 (13%) |
| **Prime-boost interval (weeks)** | | | | | | | | |
| Mean (SD) | 9·4 (0·96) | 9·5 (0·95) | 9·5 (1·01) | 9·5 (0·97) | 9·5 (0·98) | 9·5 (0·95) | 9·6 (0·96) | 9·5 (0·96) |
| Median (range) | 9·4 (8·0–12·0) | 9·4 (8·0–12·0) | 9·4 (4·7†–11·9) | 9·4 (4·7–12·0) | 9·6 (8·0–11·9) | 9·4 (8·0–12·0) | 9·6 (8·0–11·9) | 9·6 (8·0–12·0) |

Data are n (%), mean (SD), or median (range). BNT=BNT162b2 vaccine, Pfizer–BioNTech. ChAd=ChAdOx1 nCoV-19 vaccine, AstraZeneca. m1273=mRNA-1273 vaccine, Moderna. NVX=NVXCoV2373 vaccine, Novavax. *Comorbidities were self-reported by participants, with review by study team doctor for assessment of severity. General practitioner confirmation was sought where needed. Included severities were those classified as mild, moderate, or well controlled. †Single participant boosted in error at 33 days, protocol deviation.

***Table 1:*** **Baseline characteristics by study arm**

Mean age 61 to 63 years

Predominantly white

Significant minority with co-morbidities

Mean interval 9.4 to 9.6 weeks

# Immunogenicity: Neutralising activity against variants of concern

| | Prime with ChAd | | | Prime with BNT | | |
|---|---|---|---|---|---|---|
| | ChAd/ChAd (n=47) | ChAd/m1273 (n=48) | ChAd/NVX (n=51) | BNT/BNT (n=46) | BNT/m1273 (n=48) | BNT/NVX (n=49) |
| **Live virus neutralising antibody (Victoria*), $FRNT_{50}$** | | | | | | |
| n | 47 | 48 | 51 | 46 | 48 | 49 |
| GMC | 109 (70–168) | 1684 (1313–2162) | 432 (301–618) | 1501 (1188–1896) | 1883 (1546–2294) | 1109 (805–1529) |
| GMR† | Ref | 16·9 (10·1–28·0) | 4·2 (2·4–7·2) | Ref | 1·3 (1·0–1·8) | 0·8 (0·6–1·2) |
| **Live virus neutralising antibody (beta), $FRNT_{50}$** | | | | | | |
| n | 47 | 48 | 51 | 46 | 48 | 49 |
| GMC | 25 (18–34) | 376 (260–545) | 109 (71–167) | 405 (290–565) | 603 (442–822) | 451 (305–666) |
| GMR† | Ref | 15·8 (9·6–26·1) | 4·2 (2·4–7·4) | Ref | 1·6 (1·0–2·5) | 1·3 (0·8–2·2) |
| **Live virus neutralising antibody (delta), $FRNT_{50}$** | | | | | | |
| n | 47 | 48 | 51 | 46 | 48 | 49 |
| GMC | 41 (27–64) | 672 (506–891) | 153 (99–237) | 697 (520–933) | 873 (688–1107) | 629 (444–891) |
| GMR† | Ref | 17·4 (10·2–29·5) | 3·7 (2·0–6·9) | Ref | 1·3 (0·9–2·0) | 1 (0·7–1·6) |

Screaton Laboratory, Oxford

# Immunogenicity: Cellular immune response against variants of concern

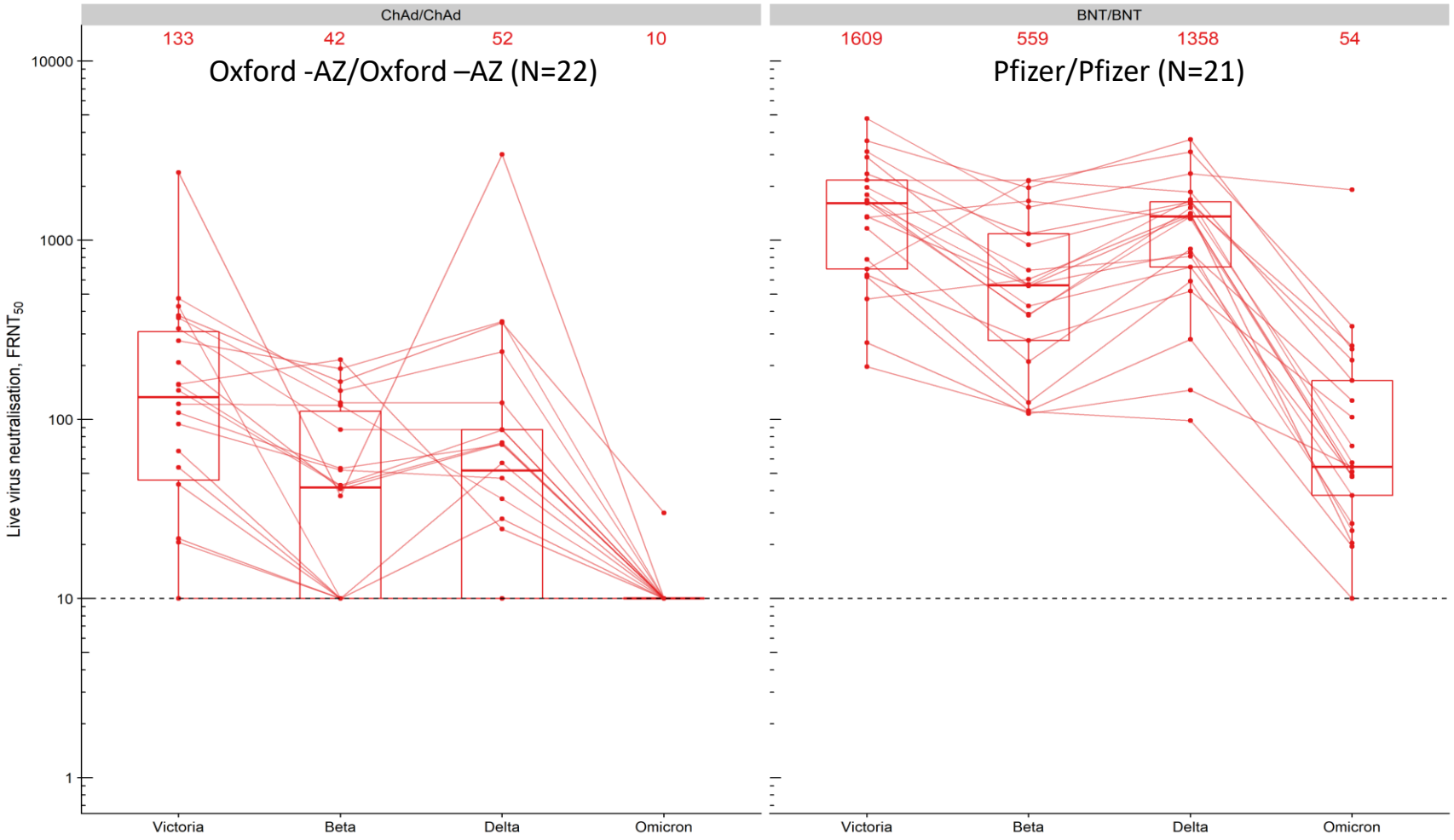
| | Prime with ChAd | | | Prime with BNT | | |
|---|---|---|---|---|---|---|
| | ChAd/ChAd (n=47) | ChAd/m1273 (n=48) | ChAd/NVX (n=51) | BNT/BNT (n=46) | BNT/m1273 (n=48) | BNT/NVX (n=49) |
| **Cellular response (wild-type, frozen samples), SFC per million PBMCs** | | | | | | |
| n | 44 | 47 | 50 | 44 | 44 | 46 |
| GMC | 41 (27–62) | 100 (73–136) | 160 (129–198) | 35 (25–49) | 71 (52–97) | 20 (14–29) |
| GMR† | Ref | 2·9 (1·8–4·6) | 4·5 (3·0–6·8) | Ref | 1·9 (1·2–3·0) | 0·60 (0·4–1·0) |
| **Cellular response (beta, frozen samples), SFC per million PBMCs** | | | | | | |
| n | 44 | 47 | 50 | 44 | 44 | 46 |
| GMC | 41 (28–60) | 104 (77–141) | 150 (120–187) | 34 (23–48) | 69 (52–92) | 22 (17–30) |
| GMR† | Ref | 3·1 (2·0–4·7) | 4·2 (2·9–6·0) | Ref | 2·0 (1·2–3·1) | 0·72 (0·46–1·1) |
| **Cellular response (delta, frozen samples), SFC per million PBMCs** | | | | | | |
| n | 44 | 47 | 50 | 44 | 44 | 46 |
| GMC | 35 (23–54) | 102 (76–136) | 155 (123–196) | 36 (26–51) | 64 (47–86) | 19 (13–28) |
| GMR† | Ref | 3·4 (2·1–5·4) | 5·0 (3·3–7·6) | Ref | 1·6 (1·0–2·5) | 0·56 (0·3–0·9) |

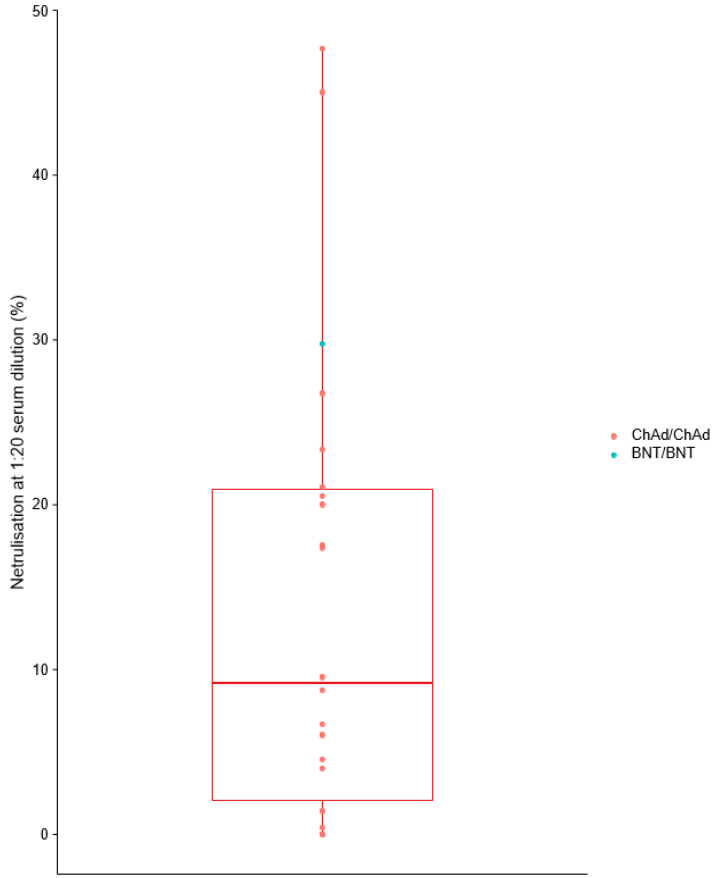
Data shown are geometric mean (95% CI), unless otherwise specified. BNT=BNT162b2 vaccine, Pfizer–BioNTech. ChAd=ChAdOx1 nCoV-19 vaccine, AstraZeneca. ELU=ELISA laboratory units. $FRNT_{50}$=50% focus reduction neutralising antibody titre. GMC=geometric mean concentration. GMR=geometric mean ratio. m1273=mRNA-1273 vaccine, Moderna. NVX=NVXCoV2373 vaccine, Novavax. PBMCs=peripheral blood mononuclear cells. SFC=spot-forming cells. *A Wuhan-related strain isolated early in the pandemic from Australia. †The two-sided 95% CIs of GMRs were adjusted for study site, cohort, interval between first and second dose, and baseline immunogenicity.

***Table 3:*** **Summary of immunogenicity against variants of concern between heterologous and homologous prime-boost schedules at 28 days after boost**

Oxford Immunotech

# Neutralising antibodies against Omicron: 1 month post second dose (uninfected at enrolment)



# COV-BOOST

Evaluating COVID-19 vaccine boosters

University of Southampton | NHS University Hospital Southampton NHS Foundation Trust

Chief Investigator Saul Faust
Munro et al, Lancet Dec 2021

Neutralising antibodies

Wild type

Delta

| | Prime with ChAd/ChAd | | | | | Prime with BNT/BNT | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control (n=93) | BNT (n=95) | VLA (n=95) | VLA half (n=107) | Ad26 (n=101) | Control (n=97) | BNT (n=96) | VLA (n=99) | VLA half (n=98) | Ad26 (n=89) |
| **SARS-CoV-2 anti-spike IgG, ELU/mL** | | | | | | | | | | |
| GMC* | 763 (630–924; n=91) | 20 517 (17 718–23 757; n=93) | 1835 (1514–2224; n=93) | 1430 (1198–1707; n=103) | 5517 (4647–6548; n=98) | 3197 (2714–3767; n=94) | 27 242 (24148–30 731; n=96) | 4204 (3640–4856; n=98) | 3721 (3200–4326; n=98) | 17 079 (14 488–20 133; n=87) |
| GMR† | Ref | 24·48 (19·5–30·79) | 2·20 (1·75–2·77) | 1·81 (1·45–2·27) | 5·84 (4·65–7·33) | Ref | 8·11 (6·59–9·99) | 1·31 (1·07–1·62) | 1·25 (1·01–1·54) | 5·63 (4·55–6·97) |
| **Pseudotype virus neutralising antibody (wild-type), $NT_{50}$** | | | | | | | | | | |
| GMT* | 69·6 (57·2–84·6; n=91) | 1621 (1314–1998; n=93) | 202 (166–247; n=89) | 147 (124–174; n=95) | 563 (454–698; n=95) | 205 (167–253; n=93) | 1789 (1520–2107; n=95) | 289 (244–342; n=91) | 234 (200–272; n=87) | 1441 (1188–1749; n=75) |
| GMR† | Ref | 21·58 (16·93–27·51) | 2·68 (2·10–3·43) | 2·01 (1·57–2·55) | 6·85 (5·37–8·73) | Ref | 8·35 (6·88–10·14) | 1·38 (1·14–1·68) | 1·22 (1·00–1·49) | 7·84 (6·37–9·64) |
| **Pseudotype virus neutralising antibody (delta), $NT_{50}$** | | | | | | | | | | |
| GMT* | 20·4 (16·4–25·5; n=91) | 315 (254–391; n=93) | 35·2 (28·4–43·7; n=89) | 31·1 (25·6–37·7; n=95) | 125 (99–159; n=90) | 56·5 (43·6–73·3; n=92) | 392 (320–479; n=95) | 67·1 (55·4–81·2; n=94) | 54·7 (45·1–66·4; n=92) | 418 (330–530; n=78) |
| GMR† | Ref | 14·43 (10·97–18·98) | 1·65 (1·25–2·17) | 1·50 (1·14–1·96) | 5·33 (4·04–7·03) | Ref | 6·60 (5·10–8·53) | 1·19 (0·92–1·54) | 1·02 (0·79–1·32) | 8·02 (6·12–10·50) |
| **Live virus neutralising antibody, normalised $NT_{50}$** | | | | | | | | | | |
| GMT* | 174 (139–218; n=30) | 4899 (3955–6069; n=38) | 354 (215–584; n=21) | 301 (212–427; n=25) | 1053 (691–1605; n=23) | 756 (568–1007; n=34) | 4603 (3685–5749; n=36) | 836 (580–1207; n=20) | 555 (407–756; n=23) | 3535 (2459–5080; n=19) |
| GMR† | Ref | 25·61 (18·07–36·31) | 2·04 (1·37–3·05) | 1·81 (1·23–2·65) | 5·97 (4·03–8·84) | Ref | 5·79 (4·25–7·90) | 1·42 (0·98–2·06) | 0·93 (0·65–1·33) | 5·36 (3·67–7·83) |

Testing against Omicron pending

# COV-BOOST

Evaluating COVID-19 vaccine boosters

University of Southampton | NHS University Hospital Southampton NHS Foundation Trust

Chief Investigator Saul Faust
Munro et al, Lancet Dec 2021

Wild type

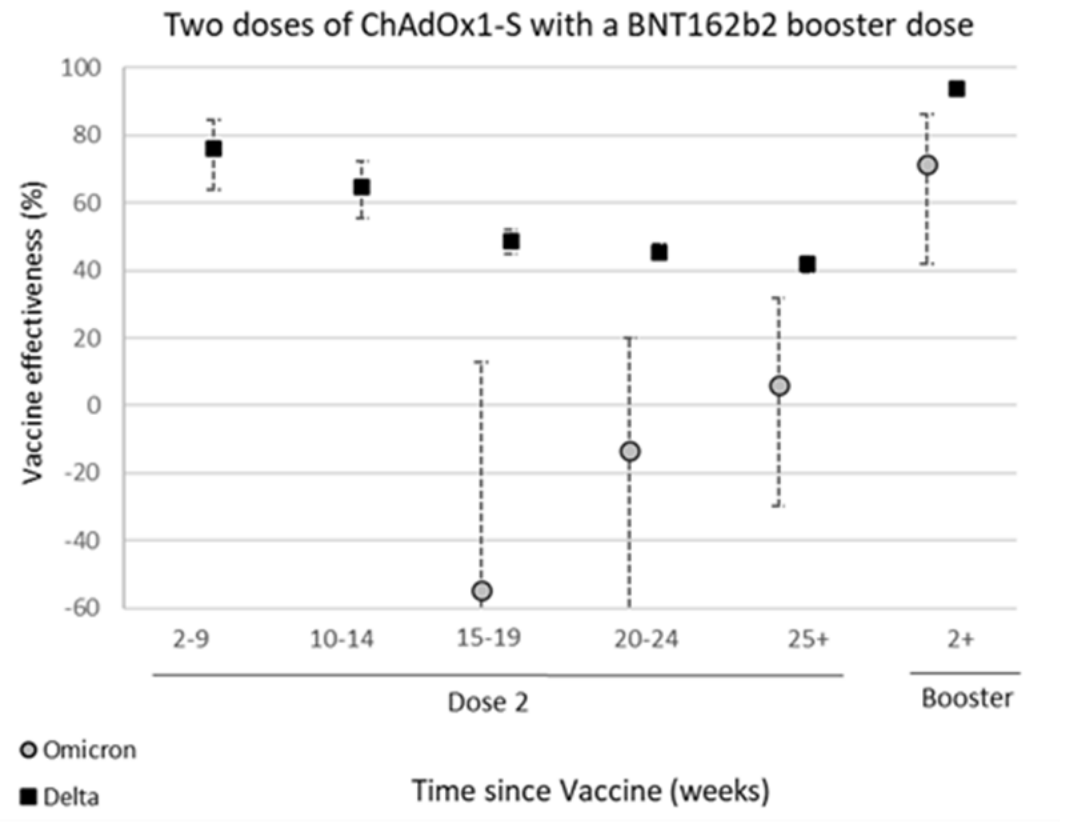
Delta

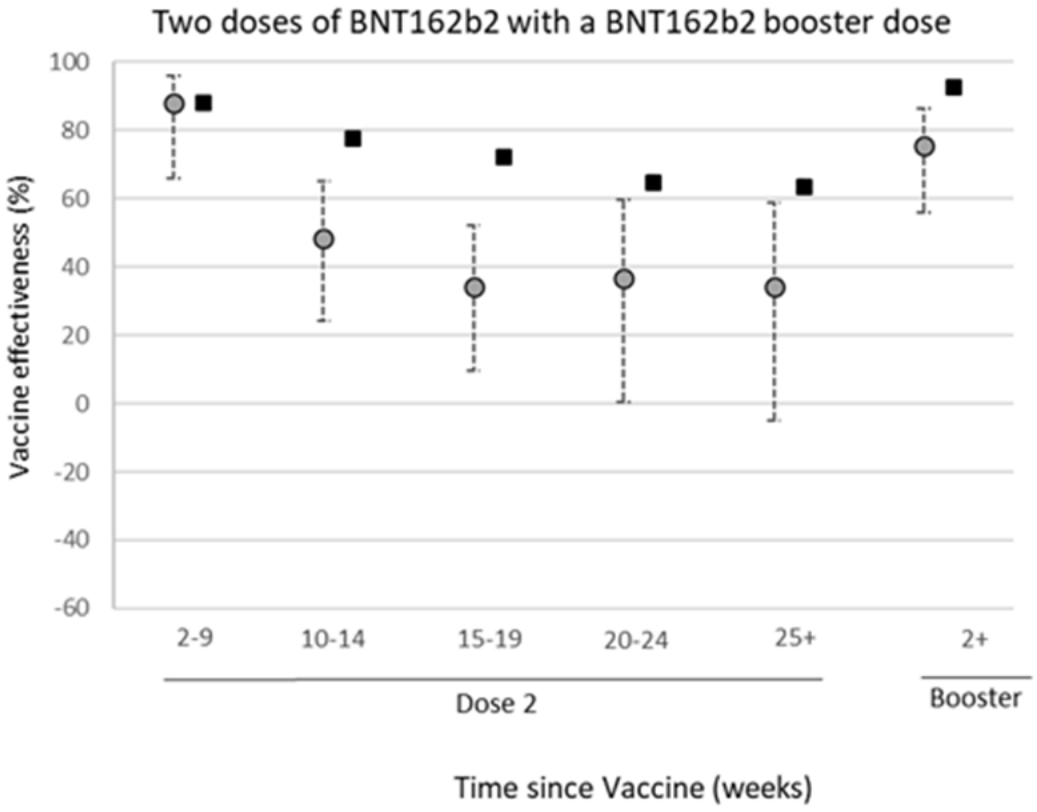
| | Prime with ChAd/ChAd | | | | | Prime with BNT/BNT | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control (n=93) | BNT (n=95) | VLA (n=95) | VLA half (n=107) | Ad26 (n=101) | Control (n=97) | BNT (n=96) | VLA (n=99) | VLA half (n=98) | Ad26 (n=89) |
| **Cellular response (wild-type), spot forming cells per $10^6$ peripheral blood mononuclear cells** | | | | | | | | | | |
| GM* | 42·6 (30·9–58·8; n=49) | 115·5 (81·7–163·3; n=50) | 52·2 (36·3–75; n=47) | 55·5 (40·4–76·3; n=53) | 106·0 (80·1–140·4; n=53) | 29·4 (21·0–41·2; n=50) | 83·8 (65·4–107·2; n=49) | 33·5 (24·7–45·4; n=51) | 38·1 (26·1–55·5; n=51) | 111·0 (71·8–171·6; n=43) |
| GMR‡ | Ref | 3·15 (2·08–4·76) | 1·39 (0·92–2·11) | 1·40 (0·93–2·11) | 2·74 (1·82–4·12) | Ref | 2·65 (1·78–3·95) | 1·04 (0·69–1·55) | 1·12 (0·75–1·66) | 2·93 (1·93–4·44) |
| **Cellular response (delta), spot forming cells per $10^6$ peripheral blood mononuclear cells** | | | | | | | | | | |
| GM* | 42·2 (30·5–58·3; n=49) | 123·2 (93·0–163·3; n=50) | 52·8 (36·9–75·6; n=47) | 54·7 (41·5–72·0; n=53) | 102·1 (74·4–140·2; n=53) | 28·2 (19·9–39·9; n=50) | 82·1 (65·7–102·7; n=49) | 29·6 (20·9–42·0; n=51) | 39·2 (27·2–56·6; n=51) | 121·5 (78·9–187·0; n=43) |
| GMR‡ | Ref | 3·23 (2·15–4·86) | 1·40 (0·93–2·12) | 1·39 (0·93–2·08) | 2·67 (1·79–4·00) | Ref | 2·71 (1·78–4·13) | 0·96 (0·63–1·47) | 1·22 (0·80–1·85) | 3·29 (2·12–5·11) |
| **Cellular response (beta), spot forming cells per $10^6$ peripheral blood mononuclear cells** | | | | | | | | | | |
| GM* | 47·6 (35·2–64·4; n=49) | 120·5 (88·0–165·0; n=50) | 52·6 (36·3–76·3; n=47) | 56·8 (41·0–78·7; n=53) | 99·9 (72·6–137·6; n=53) | 27·6 (19·9–38·5; n=50) | 85·2 (69·8–103·9; n=49) | 31·1 (22·5–42·9; n=51) | 40·3 (28·1–57·7; n=51) | 118·6 (78·3–179·7; n=43) |
| GMR‡ | Ref | 2·88 (1·89–4·38) | 1·25 (0·82–1·90) | 1·28 (0·85–1·94) | 2·30 (1·52–3·48) | Ref | 2·86 (1·92–4·28) | 1·05 (0·70–1·56) | 1·27 (0·85–1·89) | 3·36 (2·21–5·10) |

ChAd=ChAdOx1 nCoV-19 vaccine, Oxford–AstraZeneca. Control=quadrivalent meningococcal conjugate vaccine. BNT=BNT162b2 vaccine, Pfizer-BioNTech. VLA=VLA2001 vaccine, Valneva. VLA half=half dose of VLA2001 vaccine. Ad26=Ad26.COV2.S vaccine, Janssen. ELU=ELISA laboratory units. GMC=geometric mean concentration. GMR=geometric mean ratio. GM=geometric mean. GMT=geometric mean titre. $NT_{50}$=50% neutralising antibody titre. $NT_{80}$=80% neutralising antibody titre. *Data are GM (95% CI; number of samples available). †GMRs of the study vaccines were calculated by comparing to their corresponding controls in group A, B, or C, after adjusting for age group, site, baseline anti-spike IgG, interval between first and second dose, and interval between second and third dose; for primary endpoint of anti-spike IgG, 99% CIs were presented to account for multiple comparisons; for the secondary endpoints, 95% CIs were presented. ‡GMRs of the study vaccines were calculated by comparing to their corresponding controls in group A, B, or C, after adjusting for age group, site, baseline cellular response against wild-type, interval between first and second dose, and interval between second and third dose; 95% CIs were presented.

*Table 6:* **Immune responses by third dose vaccine allocation and priming vaccine schedule at 28 days post boost dose among the COVID-19-naive modified intention-to-treat population, group B**

# UK -HSA data: protection against symptomatic infection



# Summary

- Suggest neutralising antibodies against Omicron lower following 2 doses of Oxford/AZ or Pfizer than against Delta

- Both groups highly likely to have increase in neutralising activity against Omicron following 3rd dose

- Ongoing testing for
  - Post 3rd dose (COV-Boost)
  - Mixed schedules
  - T cell response

- Needs to be interpreted in light of surveillance
  - Infection
  - Severe disease

  - Supports push for 3rd dose

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  - Helen Hill
  - Daniela Ferreira
  - Chris Green
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