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# Supplementary Table 1. Com-COV3 Study Group.

|  |  |
| --- | --- |
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# Supplementary Table 2. Baseline characteristics by study arm.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **BNT-30  (N=48)** | **BNT-10  (N=47)** | **NVX  (N=37)** | **Total randomised to second dose\*  (N=132)** | **Not randomised to receive second dose (N=16)** | **All enrolled†  (N=148)** |
| Age (years) |  |  |  |  |  |  |
| Mean (SD) | 14.6 (1.3) | 14.4 (1.4) | 14.6 (1.4) | 14.5 (1.4) | 14.0 (1.3) | 14.5 (1.4) |
| Median (range) | 15 (12, 17) | 14 (12, 17) | 14 (12, 17) | 14 (12, 17) | 14 (12, 16) | 14 (12, 17) |
| Sex |  |  |  |  |  |  |
| Female | 28 (58.3%) | 28 (59.6%) | 24 (64.9%) | 80 (60.6%) | 11 (68.8%) | 91 (61.5%) |
| Male | 20 (41.7%) | 19 (40.4%) | 13 (35.1%) | 52 (39.4%) | 5 (31.3%) | 57 (38.5%) |
| Ethnicity |  |  |  |  |  |  |
| White | 44 (91.7%) | 47 (100%) | 36 (97.3%) | 127 (96.2%) | 15 (93.8%) | 142 (95.9%) |
| Asian | 1 (2.1%) | 0 (0%) | 0 (0%) | 1 (0.8%) | 1 (6.3%) | 2 (1.4%) |
| Mixed | 3 (6.3%) | 0 (0%) | 1 (2.7%) | 4 (3.0%) | 0 (0%) | 4 (2.7%) |
| Anti-nucleocapsid IgG serostatus pre-first dose\***†** |  |  |  |  |  |  |
| Seropositive | 5 (19.2%) | 5 (19.2%) | 2 (15.4%) | 12 (18.5%) | 2 (12.5%) | 14 (17.3%) |
| Seronegative | 20 (76.9%) | 21 (80.8%) | 11 (84.6%) | 52 (80%) | 13 (81.3%) | 65 (80.3%) |
| Unknown | 1 (3.8%) | 0 (0%) | 0 (0%) | 1 (1.5%) | 1 (6.3%) | 2 (2.5%) |
| Anti-nucleocapsid IgG serostatus pre-second dose |  |  |  |  |  |  |
| Seropositive | 15 (31.3%) | 14 (29.8%) | 10 (27.0%) | 39 (29.5%) | - | 39 (26.4%) |
| Seronegative | 32 (66.7%) | 32 (68.1%) | 27 (73.0%) | 91 (68.9%) | - | 91 (61.5%) |
| Unknown | 1 (2.1%) | 1 (2.1%) | 0 (0%) | 2 (1.5%) | 16 (100%) | 18 (12.2%) |
| Days between two doses, median (range) | 58 (56, 95) | 61 (56, 105) | 59 (56, 109) | 59 (56, 109) | - | 59 (56, 109) |

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373; SD: standard deviation.

\* Anti-nucleocapsid IgG serostatus pre-first dose includes participants who received their first and second doses in the study (denominator of 65).

† Anti-nucleocapsid IgG serostatus pre-first dose includes participants who received their first dose in the study (denominator of 81).

# Supplementary Table 3. Paracetamol usage in days 0-7 following vaccination by study arm.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Post second dose (N=132)** | | |
| **BNT-30 (N=48)** | **BNT-10 (N=47)** | **NVX (N=37)** |
| Number with complete diary data | 47 | 45 | 37 |
| Day 0 | 4 (8.5%) | 5 (11.1%) | 7 (18.9%) |
| Day 1 | 18 (38.3%) | 5 (11.1%) | 11 (29.7%) |
| Day 2 | 12 (25.5%) | 5 (11.1%) | 2 (5.4%) |
| Day 3 | 3 (6.4%) | 3 (6.7%) | 0 (0%) |
| Day 4 | 2 (4.2%) | 0 (0%) | 3 (8.1%) |
| Day 5 | 3 (6.4%) | 1 (2.2%) | 3 (8.1%) |
| Day 6 | 1 (2.1%) | 0 (0%) | 2 (5.4%) |
| Day 7 | 2 (4.3%) | 0 (0%) | 1 (2.7%) |
| Any in days 0-7 | 22 (46.8%) | 13 (28.9%) | 16 (43.2%) |
| Any in days 0-1 | 19 (40.4%) | 9 (20.0%) | 13 (35.1%) |
| Any in days 0-2 | 20 (42.6%) | 12 (26.7%) | 13 (35.1%) |

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

# Supplementary Table 4. Serious adverse events.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Days since first dose** | **Days since second dose** | **Study arm** | **Description** | **Start date** | **Resolution date** | **Severity** | **Causality** | **SAE** |
| 177 | 121 | BNT-30 | Intentional self-harm | 28/03/2022 | 29/03/2022 | Grade 4 | No relationship | Yes - hospitalisation |
| 243\* | 185 | NVX | Anorexia Nervosa | 01/06/2022 | Ongoing | Grade 3 | No relationship | Yes – important medical event |

BNT-30: BNT162b2 30µg; NVX: NVXCoV2373.

\*First dose received in the community.

# Supplementary Table 5. Self-reported SARS-CoV-2 infections cases.

|  | **BNT-30 (N=48)** | **BNT-10 (N=47)** | **NVX (N=37)** | **Not randomised to receive second dose (N=16)** | **Overall (N=148)** |
| --- | --- | --- | --- | --- | --- |
| **Number of self-reported infections** | **24** | **25** | **12** | **4** | **65** |
| Number of unique participants with at least one self-reported infection\* | 23 (47.9%) | 24 (51.1%) | 12 (32.4%) | 4 (25.0%) | 63 (42.6%) |
| Severity |  |  |  |  |  |
| Grade 1 | 20 (83.3%) | 23 (92.0%) | 10 (83.3%) | 3 (75.0%) | 56 (86.2%) |
| Grade 2 | 4 (16.7%) | 1 (4.0%) | 1 (8.3%) | 1 (25.0%) | 7 (10.8%) |
| Grade 3 | 0 (0%) | 1 (4.0%) | 1 (8.3%) | 0 (0%) | 2 (3.1%) |
| Month of infection start date |  |  |  |  |  |
| October 2021 | 5 (20.8%) | 0 (0%) | 1 (8.3%) | 3 (75.0%) | 9 (13.8%) |
| November 2021 | 1 (4.2%) | 2 (8.0%) | 0 (0%) | 1 (25.0%) | 4 (6.2%) |
| December 2021 | 1 (4.2%) | 1 (4.0%) | 2 (16.7%) | 0 (0%) | 4 (6.2%) |
| January 2022 | 3 (12.5%) | 8 (32.0%) | 2 (16.7%) | 0 (0%) | 13 (20.0%) |
| February 2022 | 3 (12.5%) | 3 (12.0%) | 0 (0%) | 0 (0%) | 6 (9.2%) |
| March 2022 | 7 (29.2%) | 6 (24.0%) | 2 (16.7%) | 0 (0%) | 15 (23.1%) |
| April 2022 | 0 (0%) | 3 (12.0%) | 0 (0%) | 0 (0%) | 3 (4.6%) |
| May 2022 | 0 (0%) | 0 (0%) | 1 (8.3%) | 0 (0%) | 1 (1.5%) |
| June 2022 | 3 (12.5%) | 1 (4.0%) | 1 (8.3%) | 0 (0%) | 5 (7.7%) |
| July 2022 | 1 (4.2%) | 0 (0%) | 3 (25.0%) | 0 (0%) | 4 (6.2%) |
| August 2022 | 0 (0%) | 1 (4.0%) | 0 (0%) | 0 (0%) | 1 (1.5%) |
| Timing of infection start date relating to visit dates |  |  |  |  |  |
| Before second vaccination/did not receive second vaccination | 7 (29.2%) | 2 (8.0%) | 1 (8.3%) | 4 (100.0%) | 14 (21.5%) |
| >0 and ≤7 days after second vaccination | 0 (%) | 0 (%) | 2 (16.7%) | 0 (%) | 2 (3.1%) |
| >7 and ≤14 days after second vaccination | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| >14 and ≤28 days after second vaccination | 0 (%) | 3 (12.0%) | 0 (%) | 0 (%) | 3 (4.6%) |
| >28 and ≤132 days after second vaccination | 13 (54.2%) | 16 (64.0%) | 4 (33.3%) | 0 (%) | 33 (50.8%) |
| >132 days after second vaccination | 4 (16.7%) | 4 (16.0%) | 5 (41.7%) | 0 (%) | 13 (20.0%) |

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

\*Denominators are the number of participants in the study arm.

Percentages are column percentages and the denominator is the number of infections.   
Two participants each self-reported two infections during the study period: one participant in the BNT-30 study arm and one participant in the BNT-10 study arm.

# Supplementary Table 6. Summary of unsolicited adverse events up to 28 days post second dose by study arm.

|  | **BNT-30 (N=48)** | **BNT-10 (N=47)** | **NVX (N=37)** | **Not randomised to receive second dose (N=16)** | **Overall (N=148)** |
| --- | --- | --- | --- | --- | --- |
| Number of adverse events | 45 | 31 | 22 | 12 | 110 |
| Number of unique participants with at least one adverse event\* | 24 (50.0%) | 16 (34.0%) | 13 (35.1%) | 5 (31.3%) | 58 (39.2%) |
| Timing |  |  |  |  |  |
| Between first and second dose | 25 (55.6%) | 16 (51.6%) | 4 (18.2%) | - | 45 (40.9%) |
| Within 28 days after second dose | 20 (44.4%) | 15 (48.4%) | 18 (81.8%) | - | 53 (48.2%) |
| Did not receive a second dose | - | - | - | 12 (100%) | 12 (10.9%) |
| Severity |  |  |  |  |  |
| Grade 1 | 24 (53.3%) | 19 (61.3%) | 11 (50.0%) | 8 (66.7%) | 62 (56.4%) |
| Grade 2 | 18 (40.0%) | 9 (29.0%) | 10 (45.5%) | 4 (33.3%) | 41 (37.3%) |
| Grade 3 | 3 (6.7%) | 3 (9.7%) | 1 (4.5%) | 0 (0%) | 7 (6.4%) |
| Causality |  |  |  |  |  |
| No relationship | 26 (57.8%) | 22 (71.0%) | 17 (77.3%) | 4 (33.3%) | 69 (62.7%) |
| Unlikely | 12 (26.7%) | 6 (19.4%) | 2 (9.1%) | 7 (58.3%) | 27 (24.5%) |
| Possible | 7 (15.6%) | 1 (3.2%) | 3 (13.6%) | 1 (8.3%) | 12 (10.9%) |
| Definite | 0 (0%) | 2 (6.5%) | 0 (0%) | 0 (0%) | 2 (1.8%) |

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

Percentages are column percentages and the denominator is the number of adverse events.   
\*Denominators are the number of participants in the study arm.

# Supplementary Table 7. Summary of high sensitivity troponin cardiac marker by study arm for participants in the safety analysis population.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **BNT-30** | **BNT-10** | **NVX** |
| Pre-first dose |  |  |  |
| N | 25 | 26 | 13 |
| Proportion below the LLOD | 24 (96.0%) | 25 (96.2%) | 12 (92.3%) |
| Mean (SD) | 18.2 (-) [n=1] | 2.3 (-) [n=1] | 3.8 (-) [n=1] |
| Missing | 1 | - | - |
| Pre-second dose |  |  |  |
| N | 41 | 41 | 36 |
| Proportion below the LLOD | 38 (92.7%) | 37 (90.2%) | 28 (77.8%) |
| Mean (SD) | 6.6 (2.6) [n=3] | 40.2 (56.0) [n=4] | 44.0 (96.3) [n=8] |
| Missing | 7 | 6 | 1 |
| 14 days post second dose |  |  |  |
| N | 46 | 43 | 34 |
| Proportion below the LLOD | 44 (95.7%) | 40 (93.0%) | 32 (94.1%) |
| Mean (SD) | 3.0 (0.7) [n=2] | 52.4 (80.3) [n=3] | 13.8 (14.6) [n=2] |
| Missing | 2 | 4 | 3 |
| 28 days post second dose |  |  |  |
| N | 46 | 42 | 37 |
| Proportion below the LLOD | 43 (93.5%) | 41 (97.6%) | 31 (83.8%) |
| Mean (SD) | 3.2 (1.2) [n=3] | 166.3 (-) [n=1] | 28.8 (44.5) [n=6] |
| Missing | 2 | 5 | - |

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373; LLOD: lower limit of detection.

Lower limit of detection is 2. Troponin adult ranges are: Female: 0-17 ng/L, Male: 0-34 ng/L. Where tests were rerun, the latest result was used. Where there were repeated tests for each sample, the first record was used. Reproducibility of the troponin analysis was 5.1% at 17.5 ng/L, 4.5% at 71 ng/L and 3.2% at 1311 ng/L with a reported limit of detection of 1.2 ng/L (1) and standard local reporting in our laboratory was to report troponin I values results at low concentrations as <2ng/L. Manufacturers data on the 99th centile in an adult population are 34 ng/L in men and 16 ng/L in women (2).

# Supplementary Table 8. Individual vigorous activity in the 14 days post second dose relating to raised high sensitivity troponin at 14 days after second dose.

| **ID** | **Study arm** | **Troponin at first dose** | **Troponin at second dose** | **Troponin at 14 days after second dose** | **Troponin at 28 days after second dose** | **Days since second vaccination** | **Details of vigorous exercise in the 14 days post second dose** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | BNT-30 | - | 5.2 | 2.5 | - | 1 | Football training (45 mins) |
|  |  |  |  |  |  | 11 | Football match (90 mins) |
|  |  |  |  |  |  | 13 | Football training (120 mins) |
| 2 | BNT-30 | - | - | 3.5 | - | - | No episodes of vigorous exercise |
| 3 | BNT-10 | - | - | 6.0 | - | 10 | 2 km run on treadmill – 9 mins |
|  |  |  |  |  |  | 11 | 5km run – 25 mins |
|  |  |  |  |  |  | 14 | 2.5k run – 12 mins |
| 4\* | BNT-10 | - | 126.0 | 146.7 | 166.3 | 1 | HIIT workout - 30 mins |
|  |  |  |  |  |  | 2 | Run - 30 mins |
|  |  |  |  |  |  | 7 | Run – 106 mins |
|  |  |  |  |  |  | 13 | Run – 60 mins |
| 5 | BNT-10 | - | - | 6.1 | - | 0 | 9.30am Sunday morning. 30 minutes training followed by 70 mins competitive football match (Duration: 100 mins) |
|  |  |  |  |  |  | 1 | Badminton before school (Duration: 60 mins) |
|  |  |  |  |  |  | 4 | Basketball (60 mins), football training (75 mins), badminton (120 mins) |
|  |  |  |  |  |  | 5 | Badminton (50 mins), Handball (60 mins) |
|  |  |  |  |  |  | 6 | Football training (90 mins) |
|  |  |  |  |  |  | 8 | Football training followed by match (100 mins) |
|  |  |  |  |  |  | 10 | Rowing machine and exercise bike (60 mins) |
|  |  |  |  |  |  | 11 | PE (60 mins), badminton (120 mins) |
|  |  |  |  |  |  | 12 | Badminton (60 mins) |
|  |  |  |  |  |  | 13 | Football training (90 mins) |
| 6 | NVX | - | 2.4 | 3.4 | 21.2 | 0 | Swimming 120 mins |
|  |  |  |  |  |  | 2 | Swimming 90 mins |
|  |  |  |  |  |  | 3 | Swimming 90 mins |
|  |  |  |  |  |  | 4 | Swimming 60 mins |
|  |  |  |  |  |  | 5 | Swimming 50 mins |
|  |  |  |  |  |  | 6 | Swimming 40 mins |
|  |  |  |  |  |  | 7 | Swimming 40 mins |
|  |  |  |  |  |  | 9 | Swimming 90 mins |
|  |  |  |  |  |  | 10 | Swimming 120 mins |
|  |  |  |  |  |  | 13 | Swimming 120 mins |
| 7 | NVX | - | 271.0 | 26.6 | 4.9 | 3 | Rugby – 90 mins |
|  |  |  |  |  |  | 9 | Gym (weights) + cycle + 5k run – 150 mins |
|  |  |  |  |  |  | 10 | Rugby – 90 mins |
|  |  |  |  |  |  | 11 | Gym – 120 mins |
|  |  |  |  |  |  | 14 | Rugby – 120 mins |

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

\*No unsolicited symptoms entered in diary after second vaccination.

# Supplementary Table 9. Sensitivity and secondary analyses - summary of anti-spike Ig (ELU/ml) at 28 days post second vaccination by study arm and serostatus pre-second dose.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Seropositive pre-second dose (N=39)** | | |  | **Seronegative pre-second dose (N=93)** | | |  | **Total (N=132)** | | |
|  | **BNT-30**  **(N=15)** | **BNT-10**  **(N=14)** | **NVX**  **(N=10)** |  | **BNT-30**  **(N=33)** | **BNT-10**  **(N=33)** | **NVX**  **(N=27)** |  | **BNT-30**  **(N=48)** | **BNT-10**  **(N=47)** | **NVX**  **(N=37)** |
| Sensitivity analysis - per-protocol population | | | | | | | | | | | |
| GMC  (95% CI) | 19963 (14443, 27592) [n=12] | 17846 (13247, 24040) [n=12] | 10450 (7004, 15591) [n=9] |  | 18972 (15099, 23840) [n=31] | 13421 (11186, 16104) [n=26] | 25149 (19547, 32355) [n=22] |  | 19244 (16060, 23059) [n=43] | 14685 (12583, 17138) [n=38] | 19489 (15186, 25010) [n=31] |
| GMR\* | REF | 0.90 (0.64, 1.26) | 0.49 (0.33, 0.74) |  | REF | 0.72 (0.53, 0.98) | 1.33 (0.96, 1.84) |  | REF | 0.79 (0.61, 1.02) | 1.06 (0.81, 1.39) |
| GMFR | 5 (2, 13) [n=12] | 2 (1, 5) [n=12] | 3 (1, 8) [n=9] |  | 104 (68, 158) [n=30] | 69 (51, 95) [n=25] | 112 (77, 163) [n=22] |  | 43 (24, 78) [n=42] | 23 (13, 43) [n=37] | 38 (18, 79) [n=31] |
| Sensitivity analysis - participants randomised to three study arms | | | | | | | | | | | |
| GMC  (95% CI) | 18054 (12417, 26249) [n=11] | 18398 (13070, 25899) [n=11] | 11723 (7573, 18146) [n=10] |  | 18209 (14357, 23095) [n=30] | 11966 (10154, 14101) [n=24] | 25063 (20074, 31292) [n=25] |  | 18167 (14988, 22021) [n=41] | 13698 (11662, 16090) [n=35] | 20172 (16128, 25230) [n=35] |
| GMR\* | REF | 1.07 (0.66, 1.71) | 0.66 (0.39, 1.12) |  | REF | 0.67 (0.49, 0.91) | 1.38 (1.01, 1.87) |  | REF | 0.78 (0.60, 1.01) | 1.15 (0.88, 1.50) |
| GMFR | 5 (2, 14) [n=11] | 3 (1, 6) [n=11] | 3 (1, 6) [n=10] |  | 103 (67, 159) [n=29] | 63 (47, 85) [n=24] | 111 (79, 154) [n=25] |  | 44 (24, 80) [n=40] | 23 (13, 42) [n=35] | 38 (19, 74) [n=35] |
| Sensitivity analysis - excluding participants with SARS-CoV-2 infection during 28 days post second vaccination† | | | | | | | | | | | |
| GMC  (95% CI) | 21707 (16161, 29156) [n=11] | 18541 (13959, 24626) [n=13] | 11723 (7573, 18146) [n=10] |  | 18596 (14855, 23278) [n=32] | 12262 (10530, 14277) [n=26] | 25063 (20074, 31292) [n=25] |  | 19346 (16181, 23130) [n=43] | 14074 (12165, 16282) [n=39] | 20172 (16128, 25230) [n=35] |
| GMR\* | REF | 0.92 (0.60, 1.41) | 0.57 (0.36, 0.92) |  | REF | 0.67 (0.50, 0.89) | 1.33 (0.99, 1.78) |  |  | 0.74 (0.58, 0.95) | 1.07 (0.83, 1.39) |
| GMFR | 4 (1, 13) [n=11] | 2 (1, 5) [n=13] | 3 (1, 6) [n=10] |  | 104 (69, 156) [n=31] | 58 (45, 76) [n=25] | 111 (79, 154) [n=25] |  | 45 (25, 81) [n=42] | 19 (11, 34) [n=38] | 38 (19, 74) [n=35] |
| Secondary analyses - modified intention to treat population‡ | | | | | | | | | | | |
| GMR | REF | 0.85 (0.59, 1.22) | 0.59 (0.39, 0.90) |  | REF | 0.70 (0.53, 0.91) | 1.30 (0.98, 1.72) |  | REF | 0.75 (0.60, 0.95) | 1.06 (0.82, 1.36) |

CI, confidence interval; D, day; GMC, geometric mean concentration; GMR, geometric mean ratio; GMFR, geometric mean of fold rise; REF, reference; BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.   
Data presented are geometric mean concentrations and 95% confidence intervals (CI). GMFRs are for 28 days post second dose over prior to second dose.

The results generated for antibodies against the SARS-CoV-2 receptor binding domain measured using the Roche Elecsys anti-SARS-CoV-2 spike assay are reported in binding antibody units per ml (BAU/ml). This assay has been calibrated to the NIBSC first WHO international SARS-CoV-2 immunoglobulin standard allowing reporting in BAU/ml. The assigned units for the WHO IS are IU/ml for neutralising antibody activity and BAU/ml for binding antibody activity.  
\* GMRs and 95% CIs were adjusted for study site as a fixed effect.  
† Excluding participants with a SARS-CoV-2 infection defined as either: a self-reported infection, a change in serostatus prior to second dose to 28 days post second dose from seronegative to seropositive, or a 2-fold increase in anti-nucleocapsid value prior to second dose to 28 days post second dose.  
‡ GMRs and 95% CIs adjusted for study site, logarithm of pre-second dose immunogenicity value and interval between first and second dose as fixed effects.

# Supplementary Table 10. SARS-CoV-2 infections following second dose for participants randomised to three study arms before 29th November 2021 in the day 236 modified intention-to-treat population.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **BNT-30** | **BNT-10** | **NVX** | **Total** |
| **All participants in the day 236 modified intention-to-treat population** | **N=38** | **N=29** | **N=26** | **N=93** |
| Self-reported infection up to day 132 | 9 (24%) | 13 (45%) | 3 (12%) | 25 (27%) |
| Self-reported infection up to day 236 | 13 (34%) | 15 (52%) | 8 (31%) | 36 (39%) |
| Seroconversion of anti-n status from second dose to day 132 post second dose | 9 (24%) | 13 (45%) | 5 (19%) | 27 (29%) |
| Seroconversion of anti-n status from day 132 to day 236 post second dose | 8 (21%) | 2 (6.9%) | 4 (15%) | 14 (15%) |
| 2-fold rise in anti-n value from second dose to day 132 post second dose | 12 (32%) | 16 (55%) | 7 (27%) | 35 (38%) |
| 2-fold rise in anti-n value from day 132 to day 236 post second dose | 16 (42%) | 6 (21%) | 6 (23%) | 28 (30%) |
| 2-fold rise in anti-s value from day 28 to day 132 post second dose | 3 (7.9%) | 4 (14%) | 0 (0%) | 7 (7.5%) |
| 2-fold rise in anti-s value from day 132 to day 236 post second dose | 10 (26%) | 3 (10%) | 7 (27%) | 20 (22%) |
| Infection by any definition up to day 132 | 13 (34%) | 16 (55%) | 7 (27%) | 36 (39%) |
| Infection by any definition up to day 236 | 25 (66%) | 20 (69%) | 16 (62%) | 61 (66%) |
|  |  |  |  |  |
| **Seronegative participants in the day 236 modified intention-to-treat population** | **N=26** | **N=18** | **N=18** | **N=62** |
| Self-reported infection up to day 132 | 9 (35%) | 13 (72%) | 1 (5.6%) | 23 (37%) |
| Self-reported infection up to day 236 | 13 (50%) | 14 (78%) | 6 (33%) | 33 (53%) |
| Seroconversion of anti-n status from second dose to day 132 post second dose | 9 (35%) | 13 (72%) | 5 (28%) | 27 (44%) |
| Seroconversion of anti-n status from day 132 to day 236 post second dose | 8 (31%) | 2 (11%) | 4 (22%) | 14 (23%) |
| 2-fold rise in anti-n value from second dose to day 132 post second dose | 10 (38%) | 14 (78%) | 5 (28%) | 29 (47%) |
| 2-fold rise in anti-n value from day 132 to day 236 post second dose | 14 (54%) | 5 (28%) | 5 (28%) | 24 (39%) |
| 2-fold rise in anti-s value from day 28 to day 132 post second dose | 3 (12%) | 4 (22%) | 0 (0%) | 7 (11%) |
| 2-fold rise in anti-s value from day 132 to day 236 post second dose | 9 (35%) | 3 (17%) | 7 (39%) | 19 (31%) |
| Infection by any definition up to day 132 | 11 (42%) | 14 (78%) | 5 (28%) | 30 (48%) |
| Infection by any definition up to day 236 | 21 (81%) | 16 (89%) | 13 (72%) | 50 (81%) |

Events are >14 days after second dose.

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

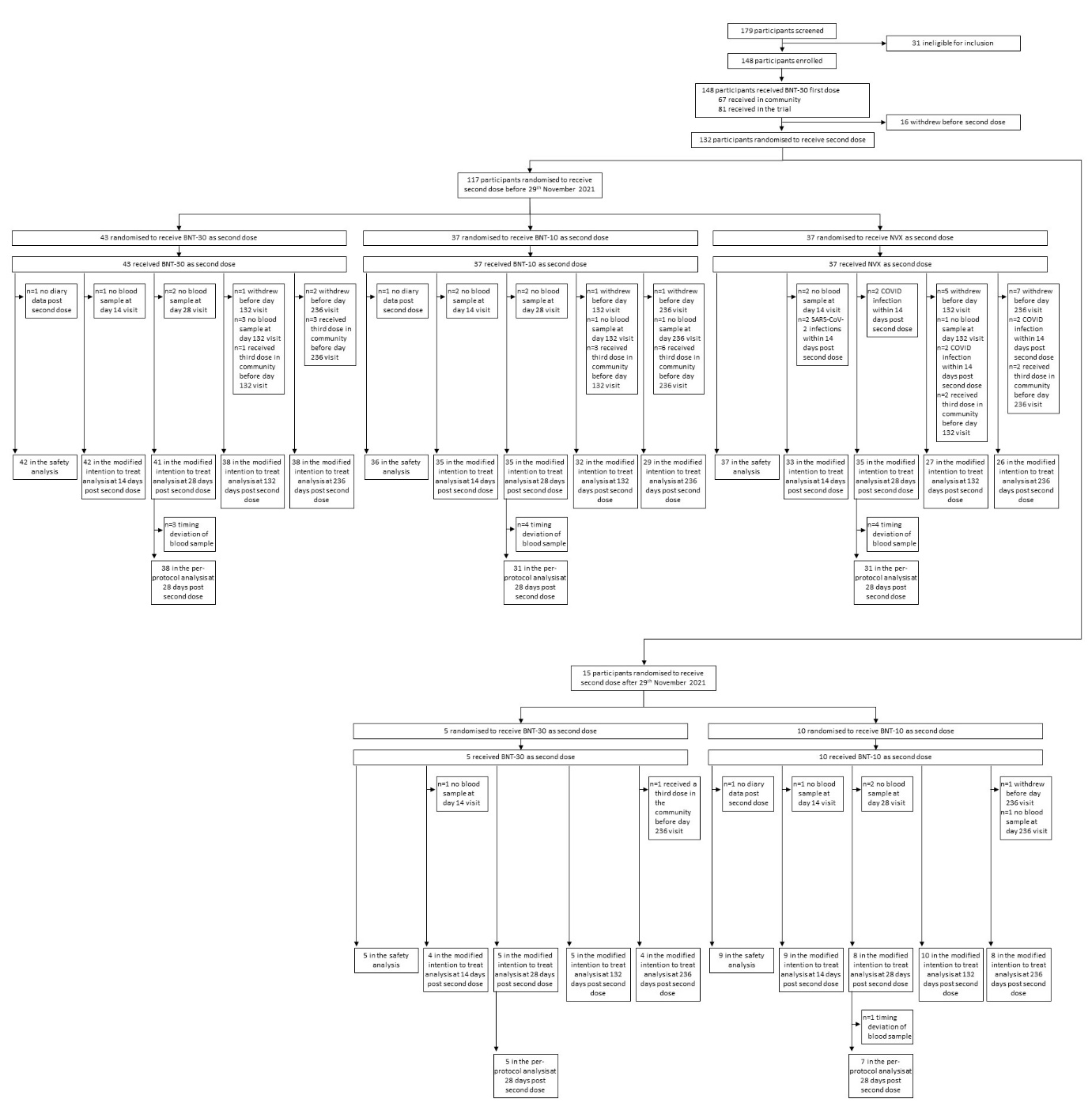
# Supplementary Table 11. SARS-CoV-2 infections following second dose for participants randomised to BNT-30 or BNT-10 over entire recruitment period in the day 236 modified intention-to-treat population.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **BNT-30** | **BNT-10** | **Total** |
| **All participants in the day 236 modified intention-to-treat population** | **N=42** | **N=37** | **N=79** |
| Self-reported infection up to day 132 | 9 (21%) | 17 (46%) | 26 (33%) |
| Self-reported infection up to day 236 | 14 (33%) | 21 (57%) | 35 (44%) |
| Seroconversion of anti-n status from second dose to day 132 post second dose | 10 (24%) | 17 (46%) | 27 (34%) |
| Seroconversion of anti-n status from day 132 to day 236 post second dose | 9 (21%) | 2 (5.4%) | 11 (14%) |
| 2-fold rise in anti-n value from second dose to day 132 post second dose | 13 (31%) | 20 (54%) | 33 (42%) |
| 2-fold rise in anti-n value from day 132 to 236 post second dose | 17 (40%) | 9 (24%) | 26 (33%) |
| 2-fold rise in anti-s value from day 28 to day 132 post second dose | 3 (7.1%) | 4 (11%) | 7 (8.9%) |
| 2-fold rise in anti-s value from day 132 to day 236 post second dose | 11 (26%) | 5 (14%) | 16 (20%) |
| Infection by any definition up to day 132 | 14 (33%) | 20 (54%) | 34 (43%) |
| Infection by any definition up to day 236 | 27 (64%) | 27 (73%) | 54 (68%) |
|  |  |  |  |
| **Seronegative participants in the day 236 modified intention-to-treat population** | **N=28** | **N=24** | **N=52** |
| Self-reported infection up to day 132 | 9 (32%) | 17 (71%) | 26 (50%) |
| Self-reported infection up to day 236 | 14 (50%) | 18 (75%) | 32 (62%) |
| Seroconversion of anti-n status from second dose to day 132 post second dose | 10 (36%) | 17 (71%) | 27 (52%) |
| Seroconversion of anti-n status from day 132 to day 236 post second dose | 9 (32%) | 2 (8.3%) | 11 (21%) |
| 2-fold rise in anti-n value from second dose to day 132 post second dose | 11 (39%) | 18 (75%) | 29 (56%) |
| 2-fold rise in anti-n value from day 132 to 236 post second dose | 15 (54%) | 6 (25%) | 21 (40%) |
| 2-fold rise in anti-s value from day 28 to day 132 post second dose | 3 (11%) | 4 (17%) | 7 (13%) |
| 2-fold rise in anti-s value from day 132 to day 236 post second dose | 10 (36%) | 4 (17%) | 14 (27%) |
| Infection by any definition up to day 132 | 12 (43%) | 18 (75%) | 30 (58%) |
| Infection by any definition up to day 236 | 23 (82%) | 21 (88%) | 44 (85%) |

Events are >14 days after second dose.

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

# Supplementary Figure 1. Consolidated Standards of Reporting Trials (CONSORT) Flow Diagram and Study Design.

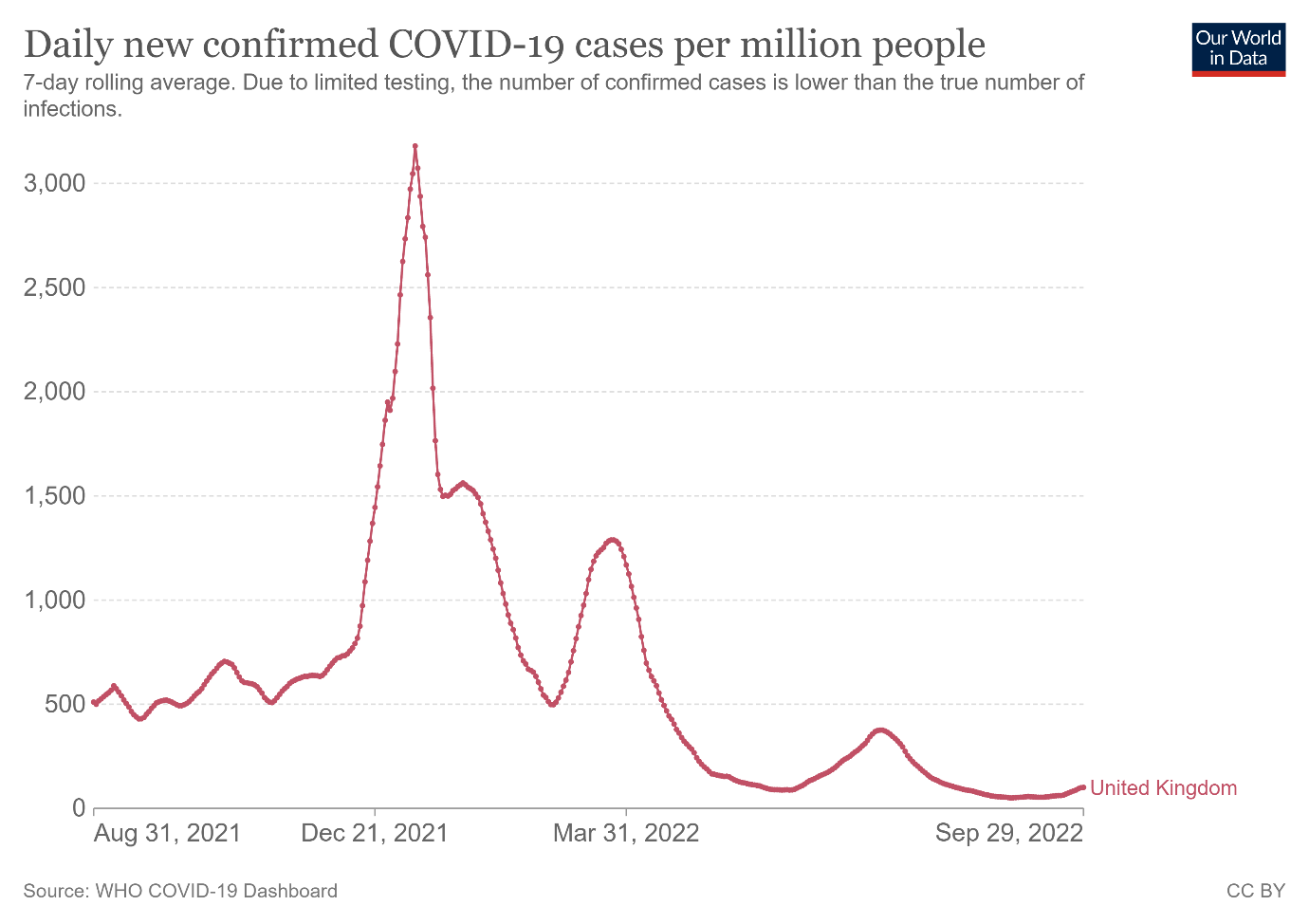


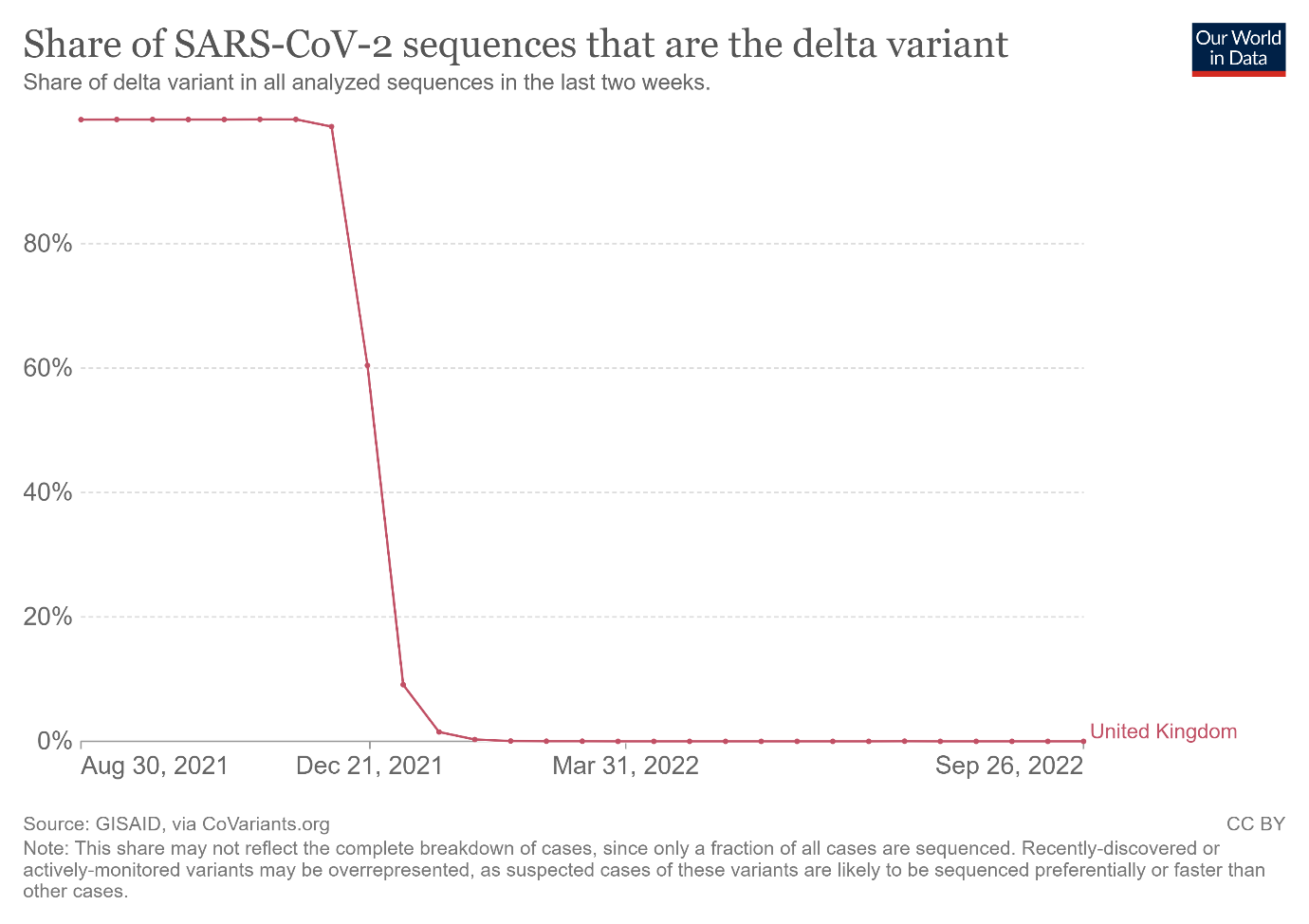
BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

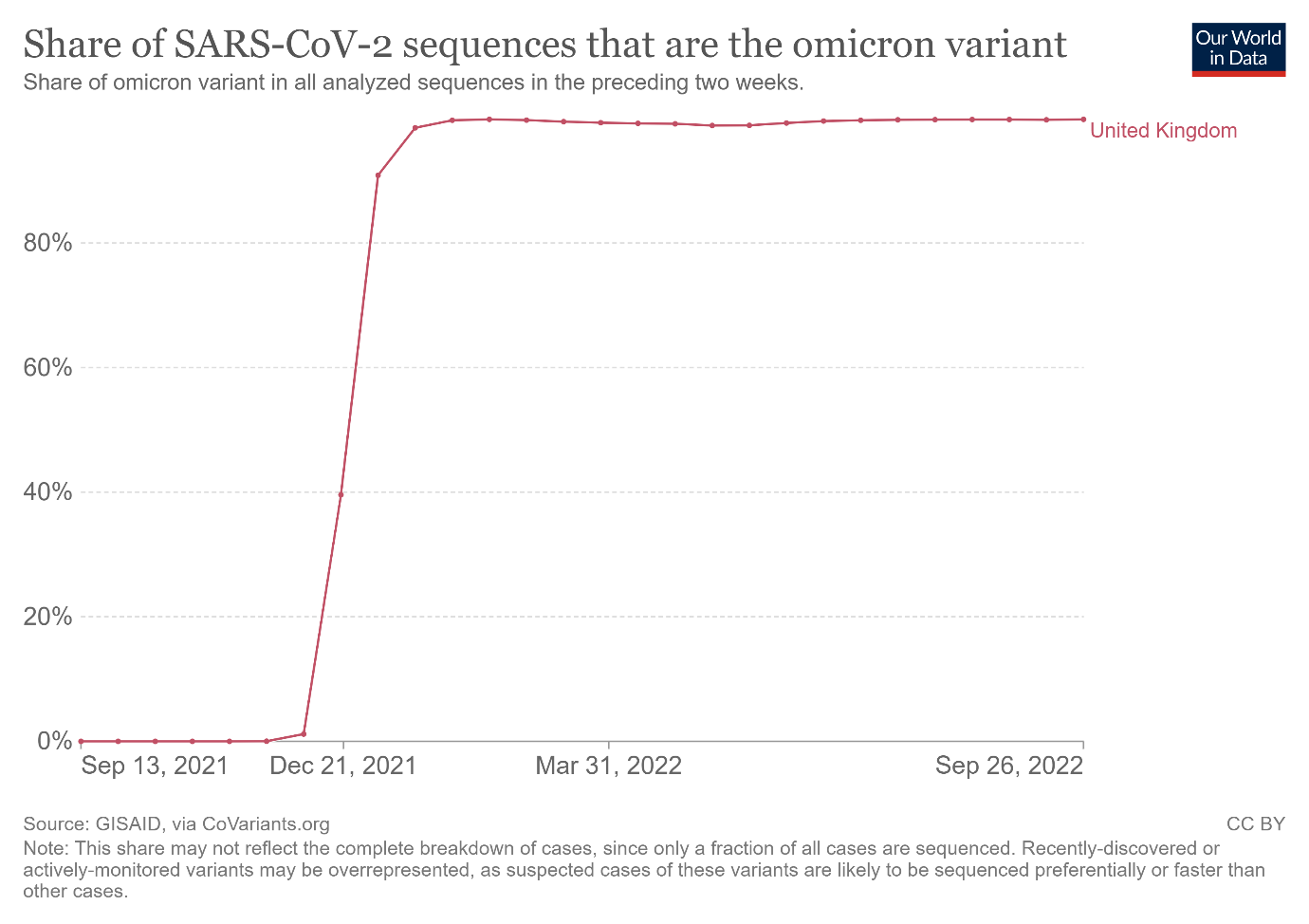
Participants were randomised 1:1:1 at the time of their second vaccination to BNT-30, BNT-10, or NVX. After 29th November 2021, when UK national immunisation policy changed to offer all 12-to-15-year-olds a second dose of BNT, recruitment stopped and participants who had already received their first dose of BNT within the study were randomised 1:1 to receive 30µg BNT162b2 or 10µg BNT162b2 as a second dose. Sixteen participants withdrew before the second vaccination because of needle phobia, difficult phlebotomy, lost to follow up, or change of mind.

# 

# Supplementary Figure 2. COVID-19 cases in the UK from August 2021 to September 2022.



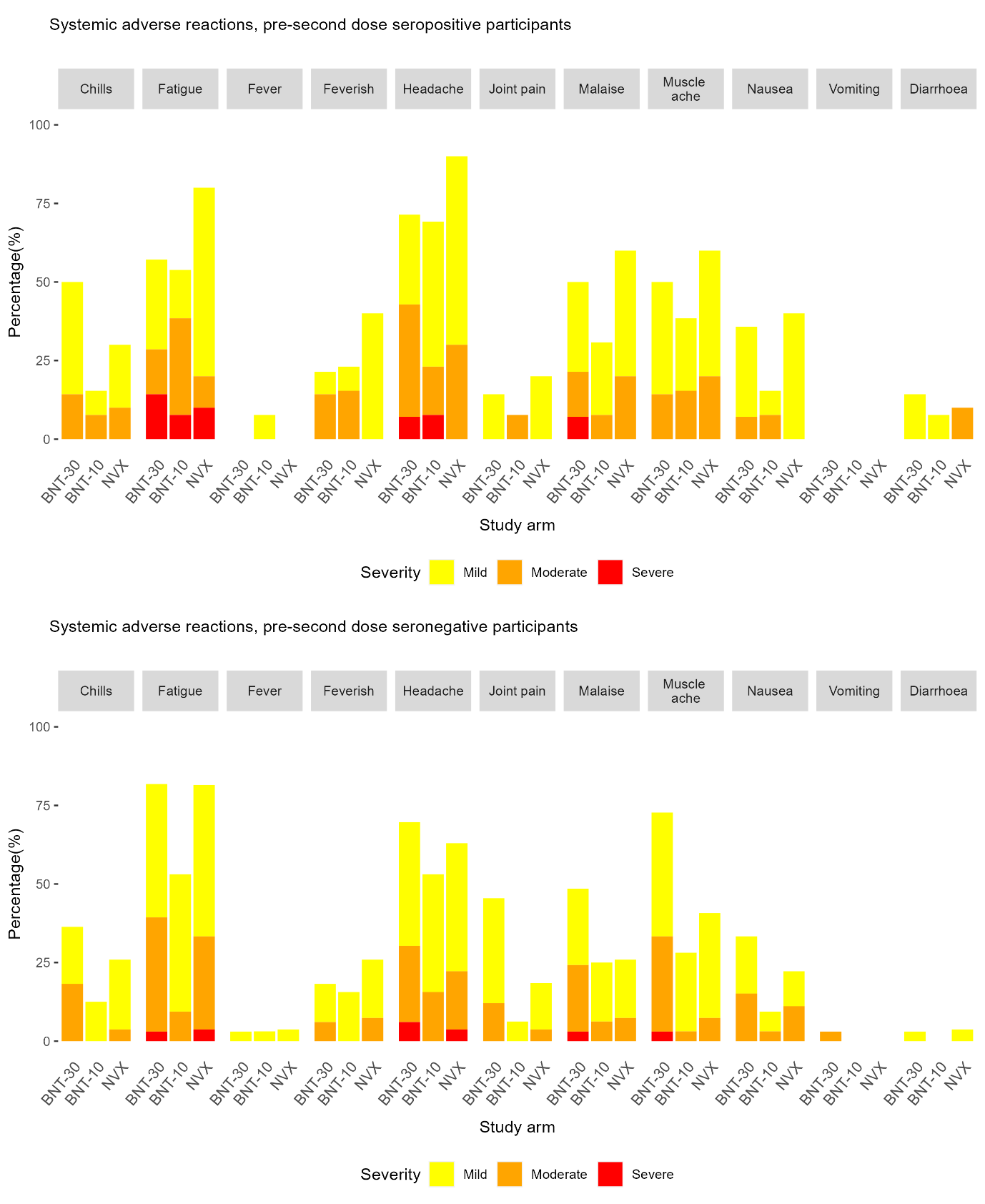


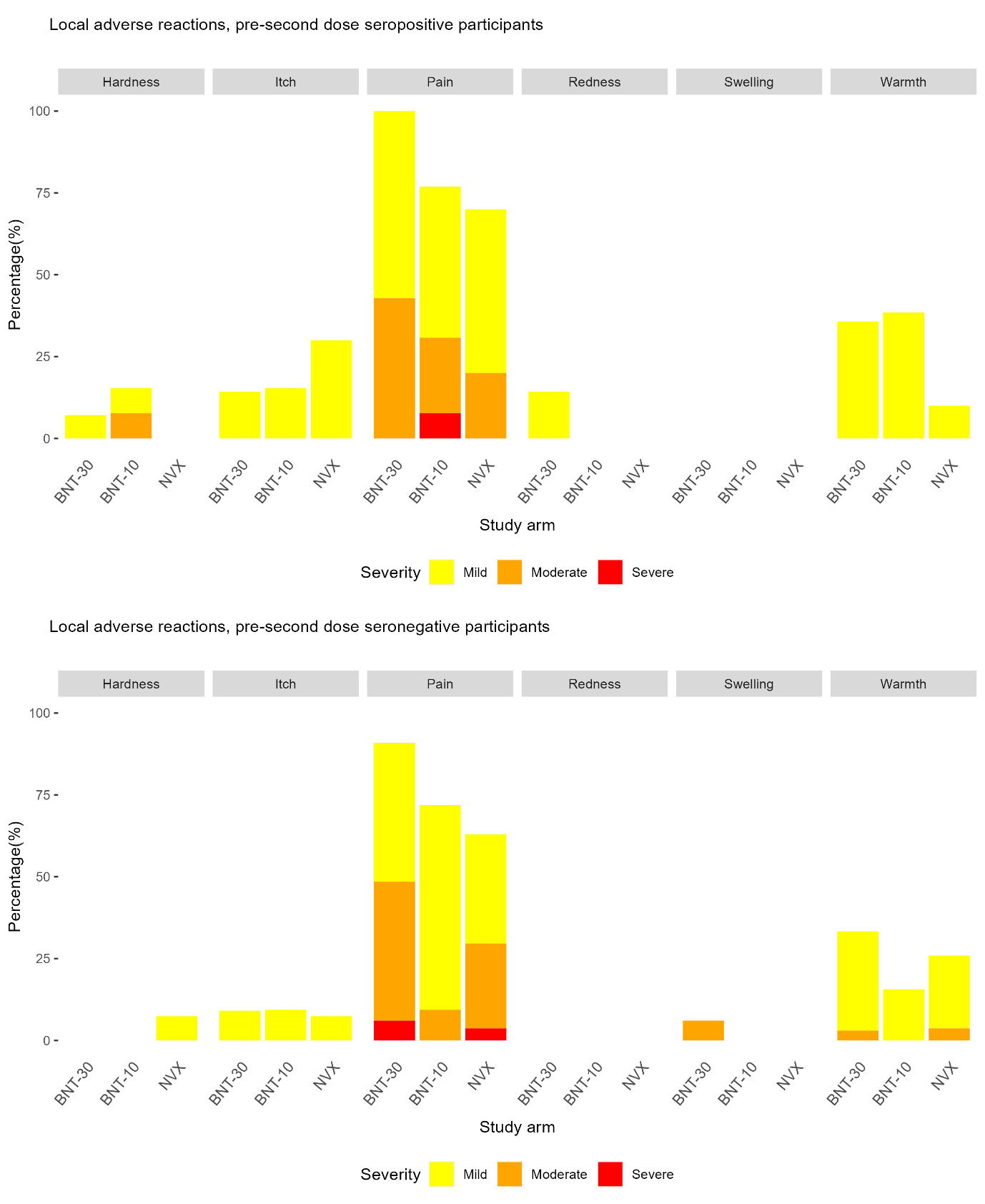


Recruitment commenced in September 2021 and ended November 2021. JCVI recommended first dose of BNT162b2 in September 2021 and second dose of BNT162b2 in November 2021 for all UK 12-17-year olds. The final day 236 visit took place on 5th September 2022.

Charts are open access and were downloaded from Our World In Data (3).

# Supplementary Figure 3. Severity of solicited adverse reactions in days 0-7 after second vaccination by study arm and pre-second dose serostatus as self-reported in participant electronic diaries in the safety analysis population.

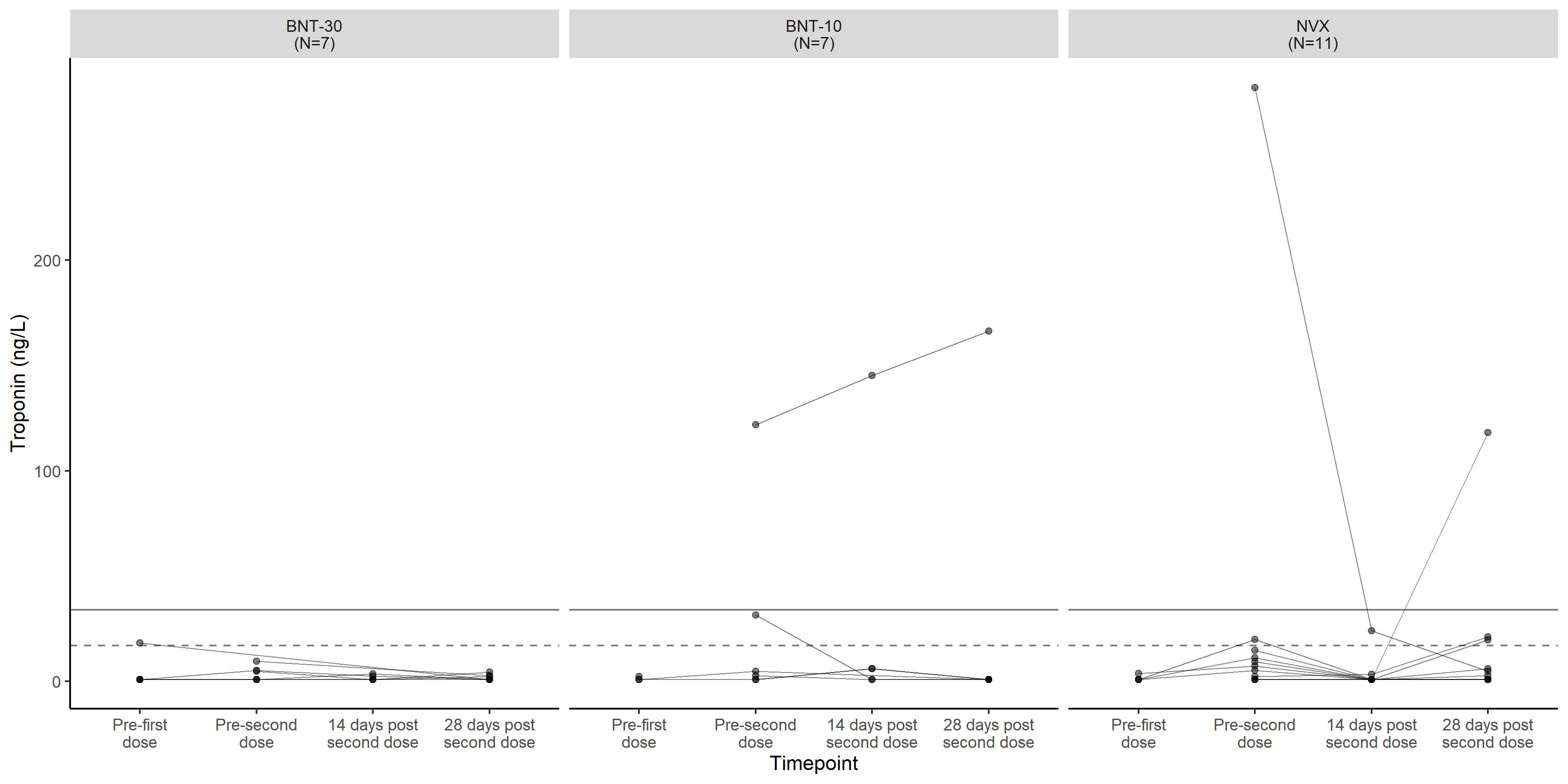




BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

The severity presented is the participant’s highest severity across 7 days post vaccination for each solicited adverse event. Fever: Mild: 38·0°C to <38·5°C; moderate: 38·5°C to <39°C; severe: ≥39·0°C. Feverish: Self-reported feeling of feverishness. For systemic symptoms, grading was classified as: Mild – easily tolerated with no limitation on normal activity; Moderate – some limitation of daily activity; Severe – unable to perform normal daily activity. There were two self-reported SARS-CoV-2 infections in days 0-7 after second vaccination both occurring in the NVX-CoV2373 study arm. The first participant self-reported 6 days after second vaccination had a grade 1 headache on day 6. The second participant self-reported 7 days after second vaccination had a grade 1 headache and grade 1 fatigue on day 5.

# Supplementary Figure 4. Individual profiles high sensitivity troponin for those with values above the lower limit of detection by study arm in the safety analysis population.

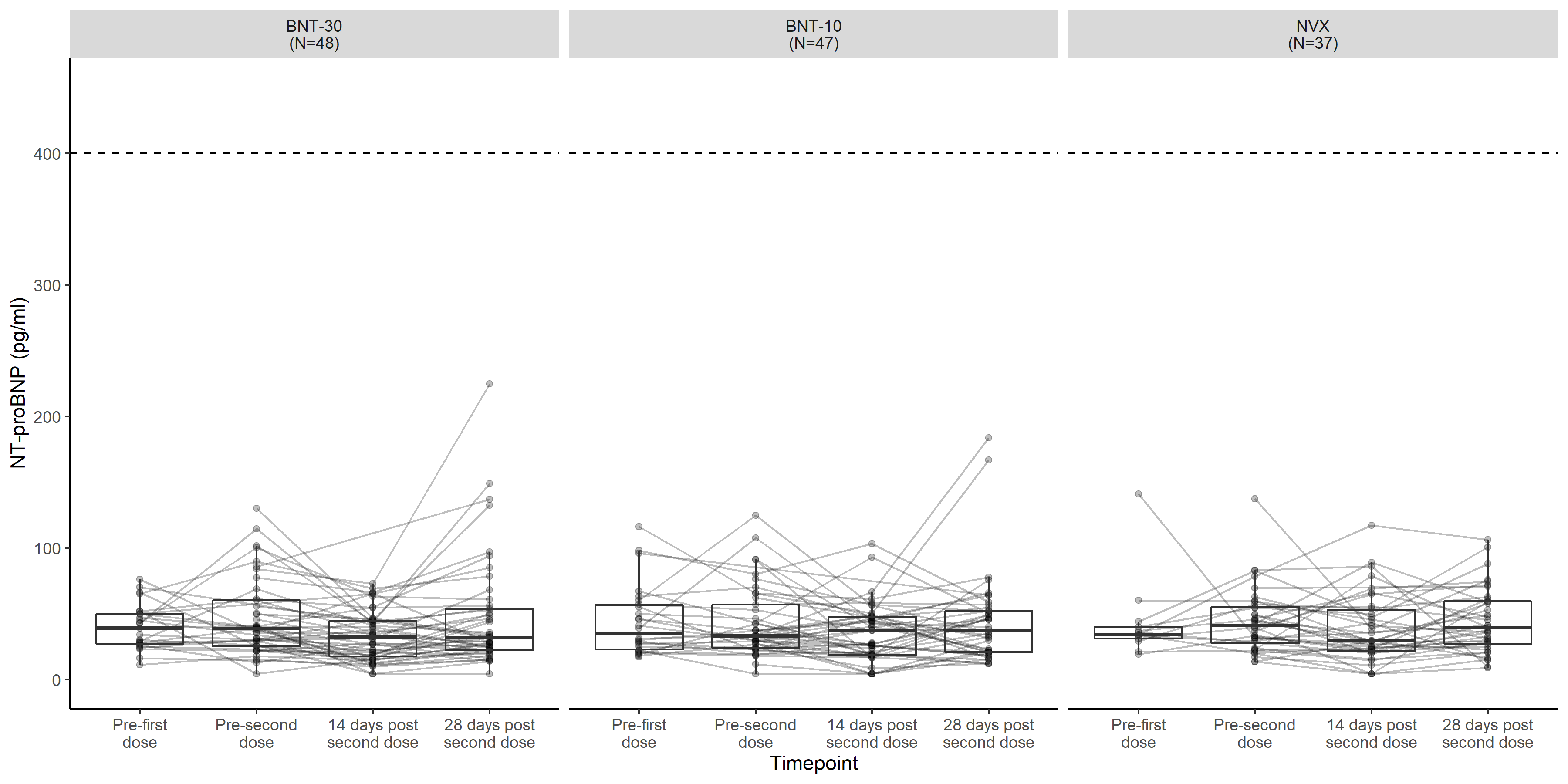


BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

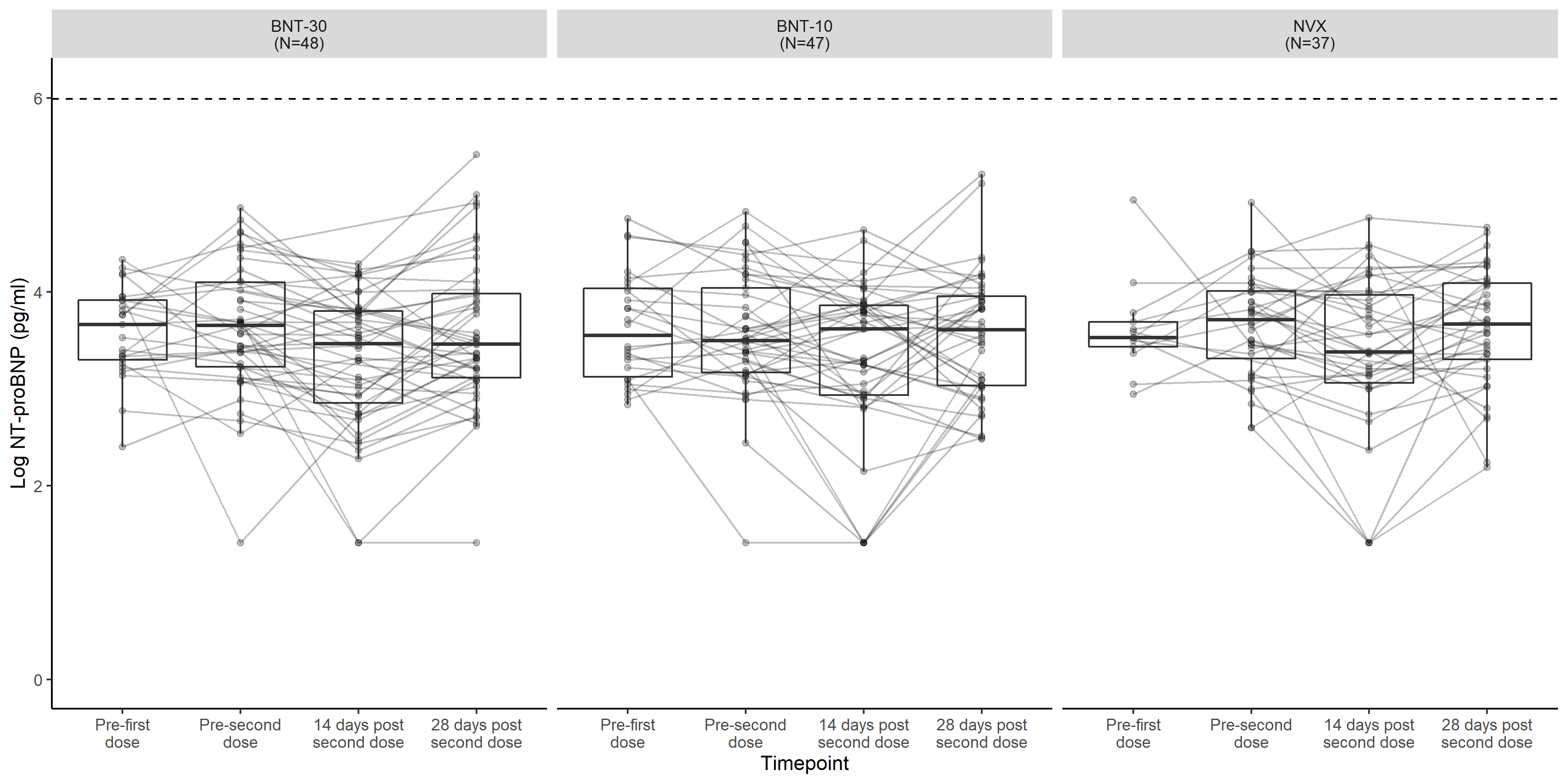
Where there were repeated tests for each sample, the first record was used. The lower limit of detection is 2, records below 2 were imputed with 1. The lines indicate the maximum value for troponin adult ranges: female range 0-17 ng/L (dashed line), male range 0-34 ng/L (solid line).

# Supplementary Figure 5. Summary of N-terminal-pro B-type natriuretic peptide by study arm in the safety analysis population, A) raw, B) log-transformed.

A)

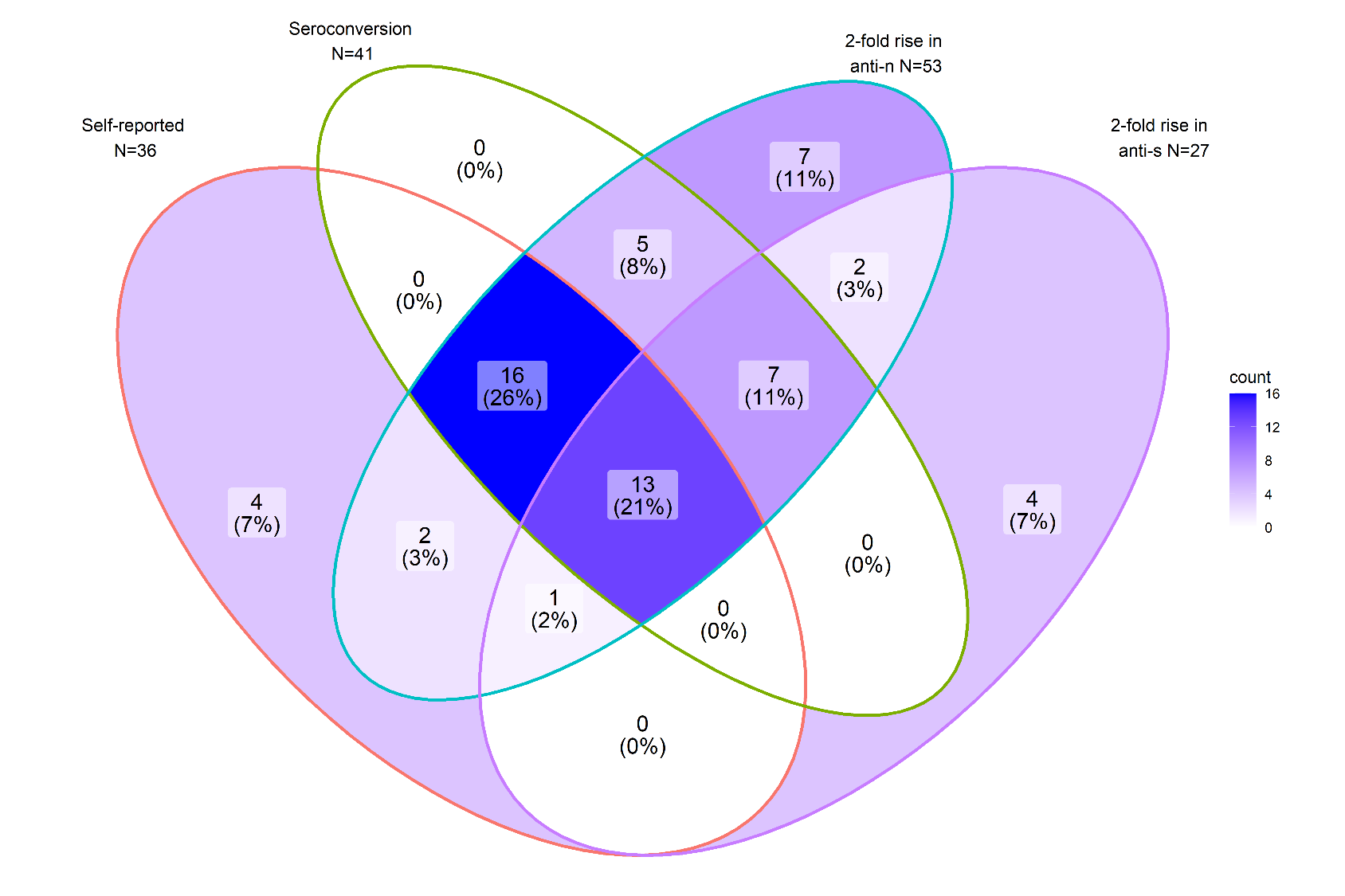


B)

  
BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373.

The dotted lines indicate the threshold for referral to cardiology (raw values >400 ng/L) from National Institute for Health and Care Excellence for heart failure. Where there were repeated tests for each sample, the first record was used. The lower limit of detection is 8.2. Records below the lower limit of detection were imputed with 4.1. Data were natural logarithm transformed. The coefficient of variation was 5.6% at a concentration of 7.9 pg/mL, 4.3% at 43.5% pg/mL, and 3.8% ag 365 pg/mL for NT-proBNP.

# Supplementary Figure 6. Venn diagram of SARS-CoV-2 ‘breakthrough infections’ in participants randomised to three study arms before 29th November 2021 in the day 236 modified intention-to-treat population.



A ‘breakthrough infection’ between second dose and day 236 visit was defined as either: a self-reported SARS-CoV-2 infection >14 days after second dose, a two-fold rise in anti-nucleocapsid IgG from second dose to 132 days after second dose or 132 to 236 days after second dose, a two-fold rise in anti-spike antibodies from 28 to 132 days after second dose or 132 to 236 days after second dose, or anti-nucleocapsid IgG seroconversion from second dose to day 132 days after second dose or 132 to 236 days after second dose.

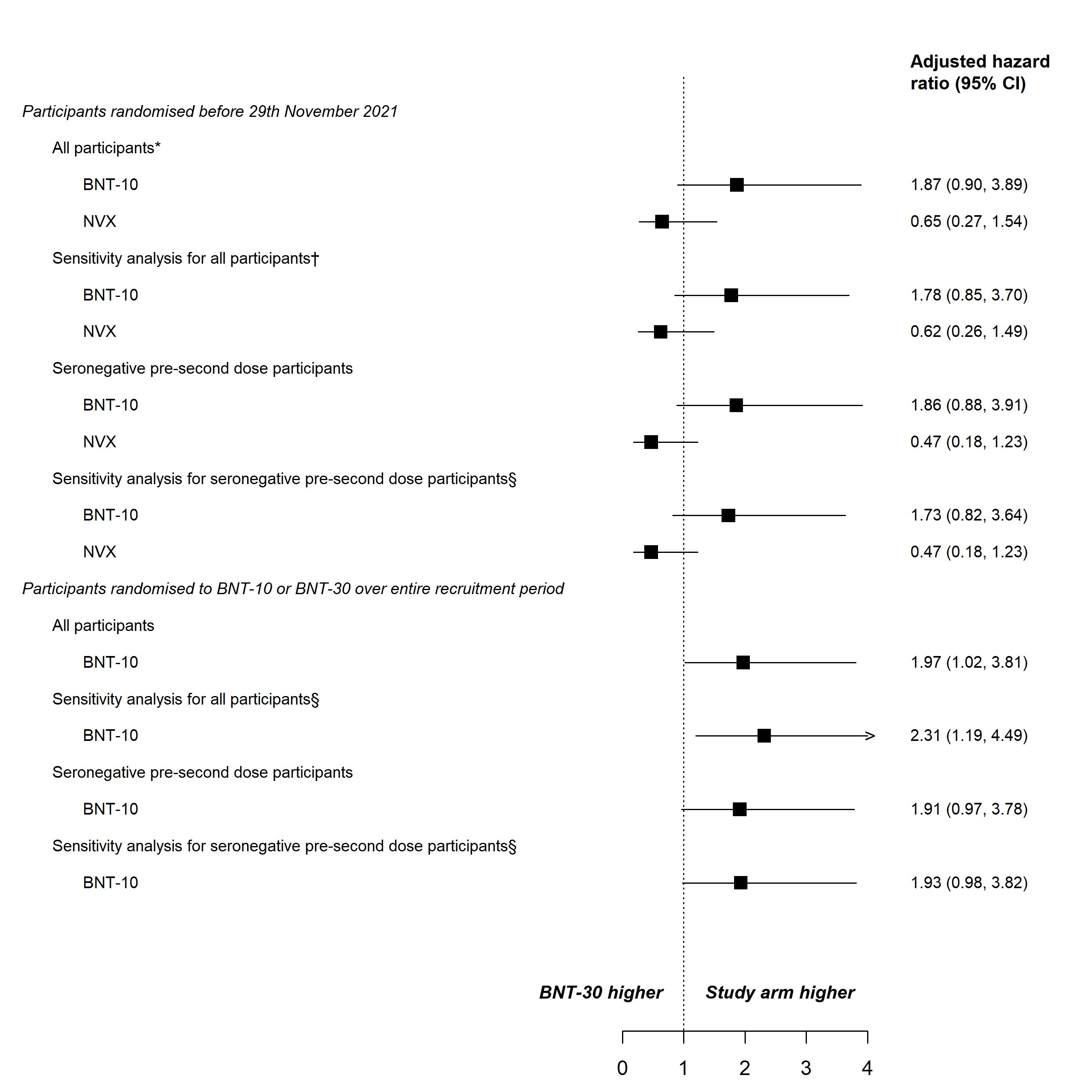
# Supplementary Figure 7. Cox regression models for risk of self-reported SARS-CoV-2 infections during follow-up.

A) Day 132 post second dose

Table

Description automatically generated

B) Day 236 post second dose



\*Adjusted for serostatus pre-second dose as a fixed effect. †Adjusted for serostatus pre-second dose and anti-spike antibodies pre-second dose as fixed effects. §Adjusted for anti-spike antibodies pre-second dose as a fixed effect.

BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373; CI: confidence interval.

Data presented are adjusted hazard ratios and 95% CIs. The boxes represent adjusted hazard ratios and the horizontal lines represent the corresponding 95% CIs. BNT-30 is the reference study arm for the adjusted hazard ratios. The vertical dashed line at one represents the line of no difference. A CI that lies completely to one side and not intersecting the line of no difference indicates a significant difference in the risk of a self-reported SARS-CoV-2 infection during follow-up between the study arm and the reference BNT-30 study arm. Self-reported SARS-CoV-2 infections occurring from >14 days were considered an event. For day 132 analyses, participants were censored at the time of either: self-reported SARS-CoV-2 infection within 14 days of second dose, third dose of COVID-19 vaccination, withdrawal, day 132 visit, or 132 days after second vaccination if day 132 visit was missed and no infection was self-reported, whichever came first. For day 236 analyses, participants were censored at the time of either: self-reported SARS-CoV-2 infection within 14 days of second dose, third dose of COVID-19 vaccination, withdrawal, day 126 visit, or 236 days after second vaccination if day 236 visit was missed and no infection was self-reported, whichever came first. Participants were randomised 1:1:1 at the time of their second vaccination to BNT-30, BNT-10, or NVX. After 29th November 2021, when UK national immunisation policy changed to offer all 12-to-15-year-olds a second dose of BNT, recruitment stopped and participants who had already received their first dose of BNT within the study were randomised 1:1 to receive 30µg BNT162b2 or 10µg BNT162b2 as a second dose.

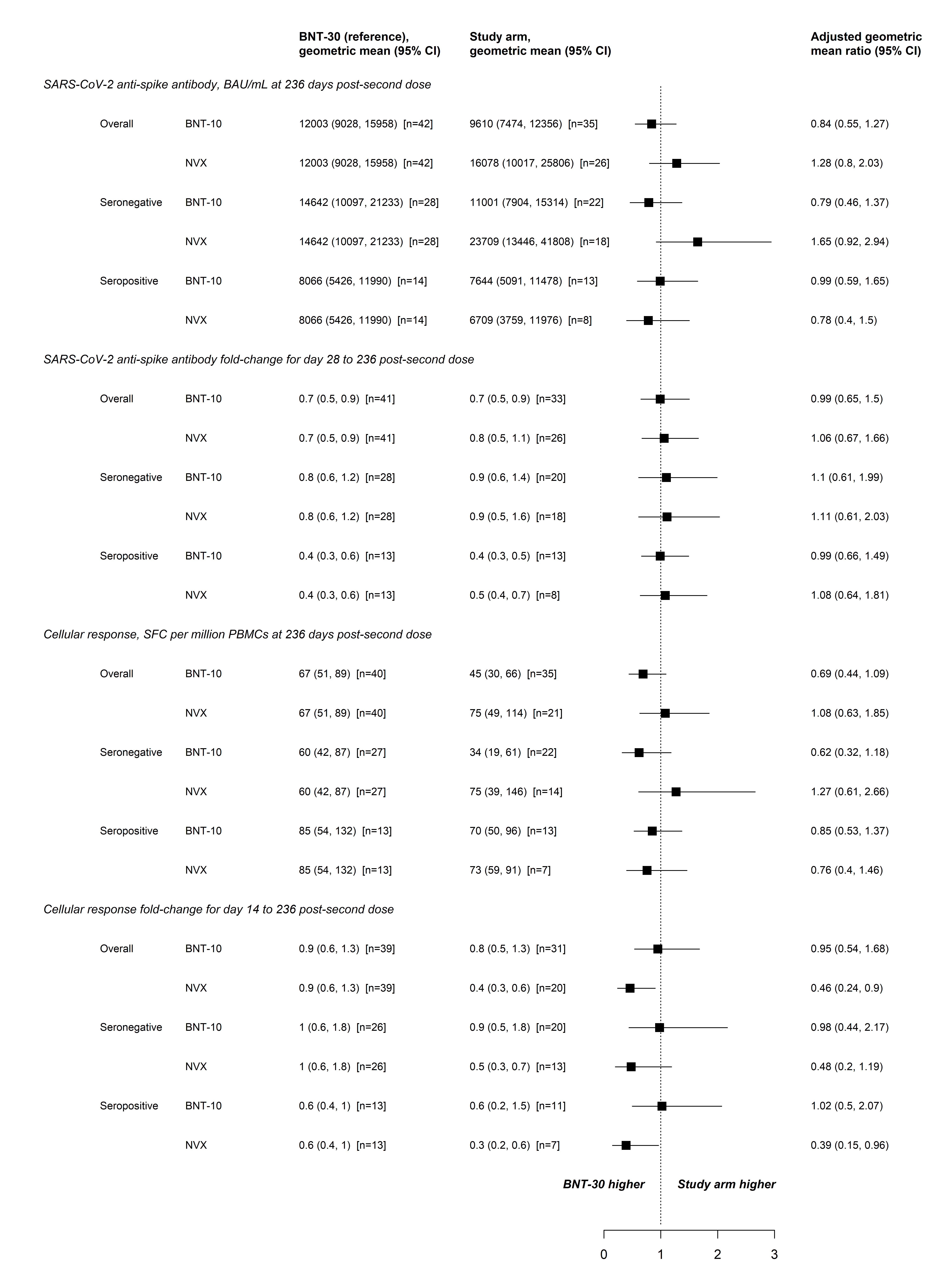
# Supplementary Figure 8. Immune responses, by study arm and pre-second dose serostatus in the modified intention-to-treat populations.

A) Day 132 post second dose

Table

Description automatically generated

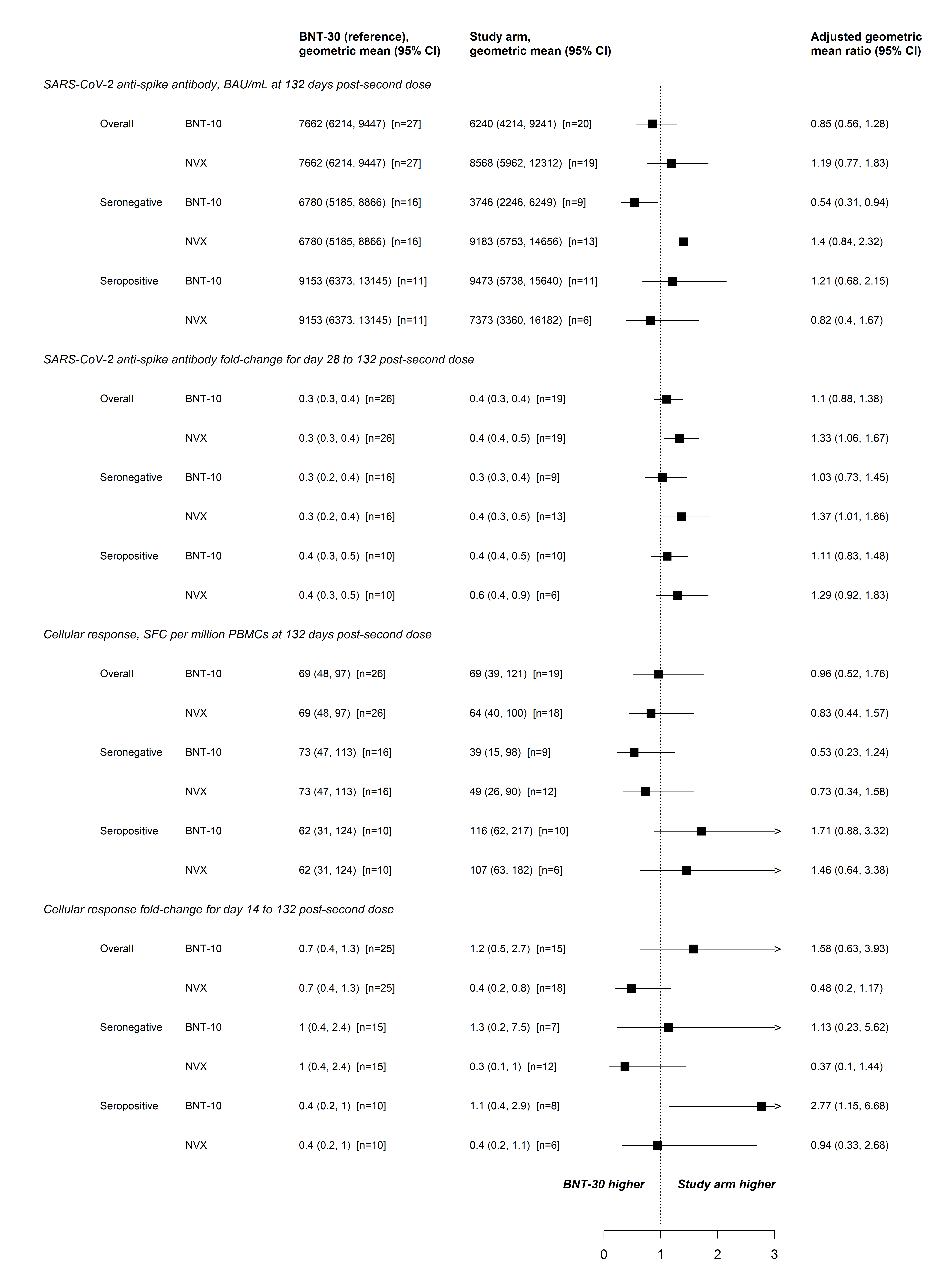
B) Day 236 post second dose



BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373; CI: confidence interval.

Data presented are the geometric means, adjusted geometric mean ratios and their corresponding 95% confidence intervals. Fold-changes were calculated by dividing the immune response at either 132 or 236 days following second dose by that at 28 days following second dose. The boxes indicate the adjusted geometric mean ratio and the horizontal lines indicate the corresponding 95% confidence intervals. The geometric mean ratios between BNT-30 and either BNT-10 or NVX are adjusted for study site as a fixed effect. The vertical dotted line refers to an adjusted geometric mean ratio of one and indicates the line of no difference. A confidence interval that lies completely to one side and not intersecting the line of no difference indicates a significant difference in the geometric mean concentrations between the study arm and the reference BNT-30 study arm.

# Supplementary Figure 9. Immune responses , by study arm and pre-second dose serostatus in the day 132 modified intention-to-treat populations excluding ‘breakthrough infections’ during follow-up.



BNT-30: BNT162b2 30µg; BNT-10: BNT162b2 10µg; NVX: NVX-CoV2373; CI: confidence interval.

Data presented are the geometric means, adjusted geometric mean ratios and their corresponding 95% confidence intervals. Fold-changes were calculated by dividing the immune response at either 132 or 236 days following second dose by that at 28 days following second dose. The boxes indicate the adjusted geometric mean ratio and the horizontal lines indicate the corresponding 95% confidence intervals. The geometric mean ratios between BNT-30 and either BNT-10 or NVX are adjusted for study site as a fixed effect. The vertical dotted line refers to an adjusted geometric mean ratio of one and indicates the line of no difference. A confidence interval that lies completely to one side and not intersecting the line of no difference indicates a significant difference in the geometric mean concentrations between the study arm and the reference BNT-30 study arm. A ‘breakthrough infection’ between second dose and day 236 visit was defined as either: a self-reported SARS-CoV-2 infection >14 days after second dose, a two-fold rise in anti-nucleocapsid IgG from second dose to 132 days after second dose or from 132 to 236 days after second dose, a two-fold rise in anti-spike antibodies from 28 to 132 days after second dose or 132 to 236 days after second dose, or a seroconversion of anti-nucleocapsid IgG from second dose to day 132 days after second dose or 132 to 236 days after second dose.

# References

1. Shah AS, Anand A, Sandoval Y, Lee KK, Smith SW, Adamson PD, et al. High-sensitivity cardiac troponin I at presentation in patients with suspected acute coronary syndrome: a cohort study. Lancet. 2015;386(10012):2481-8
2. Shah AS, Griffiths M, Lee KK, McAllister DA, Hunter AL, Ferry AV, et al. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study. BMJ. 2015; 350: g7873.
3. Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, et al. A global database of COVID-19 vaccinations. Nat Hum Behav. 2021;5(7):947-53.