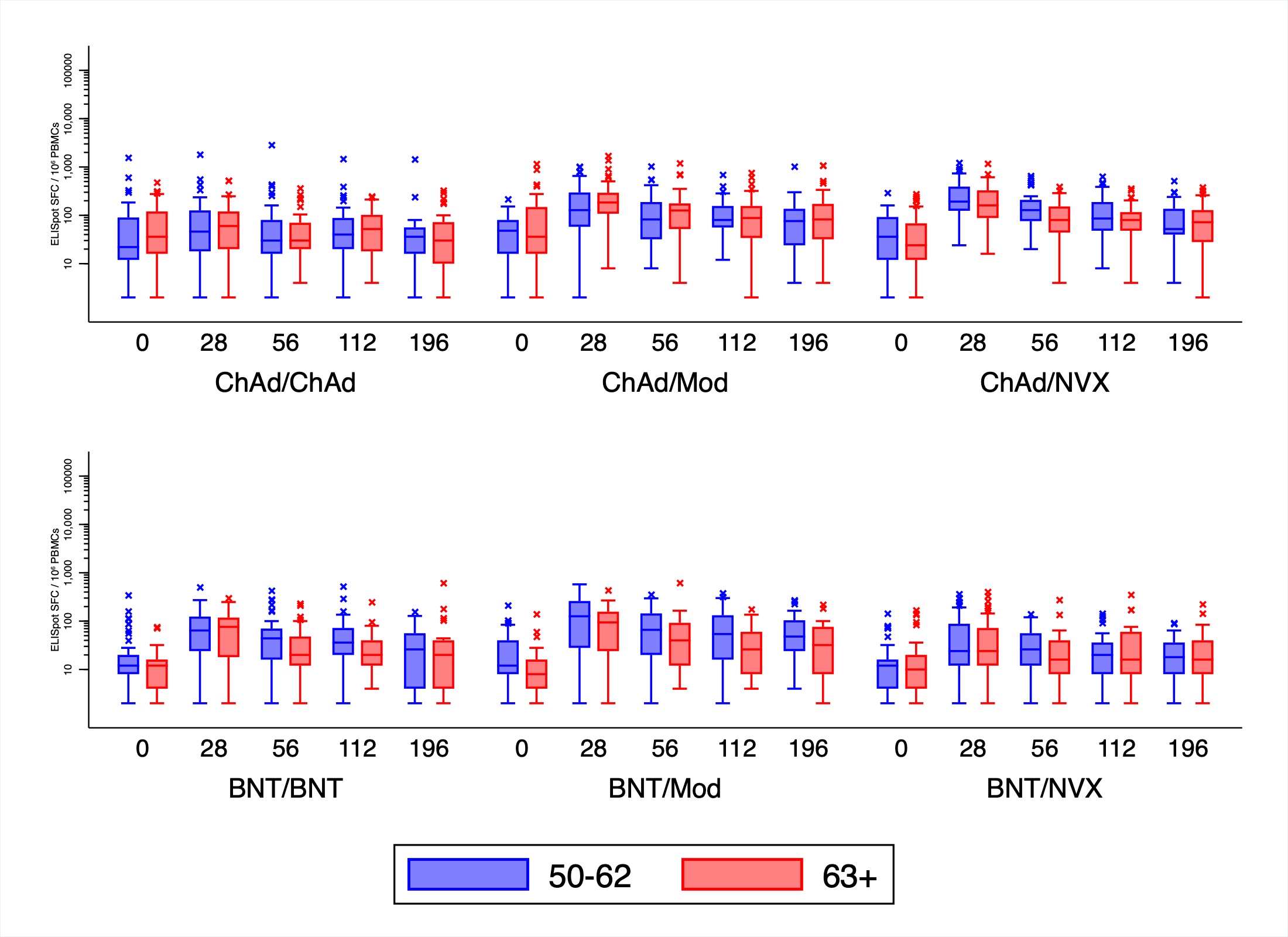
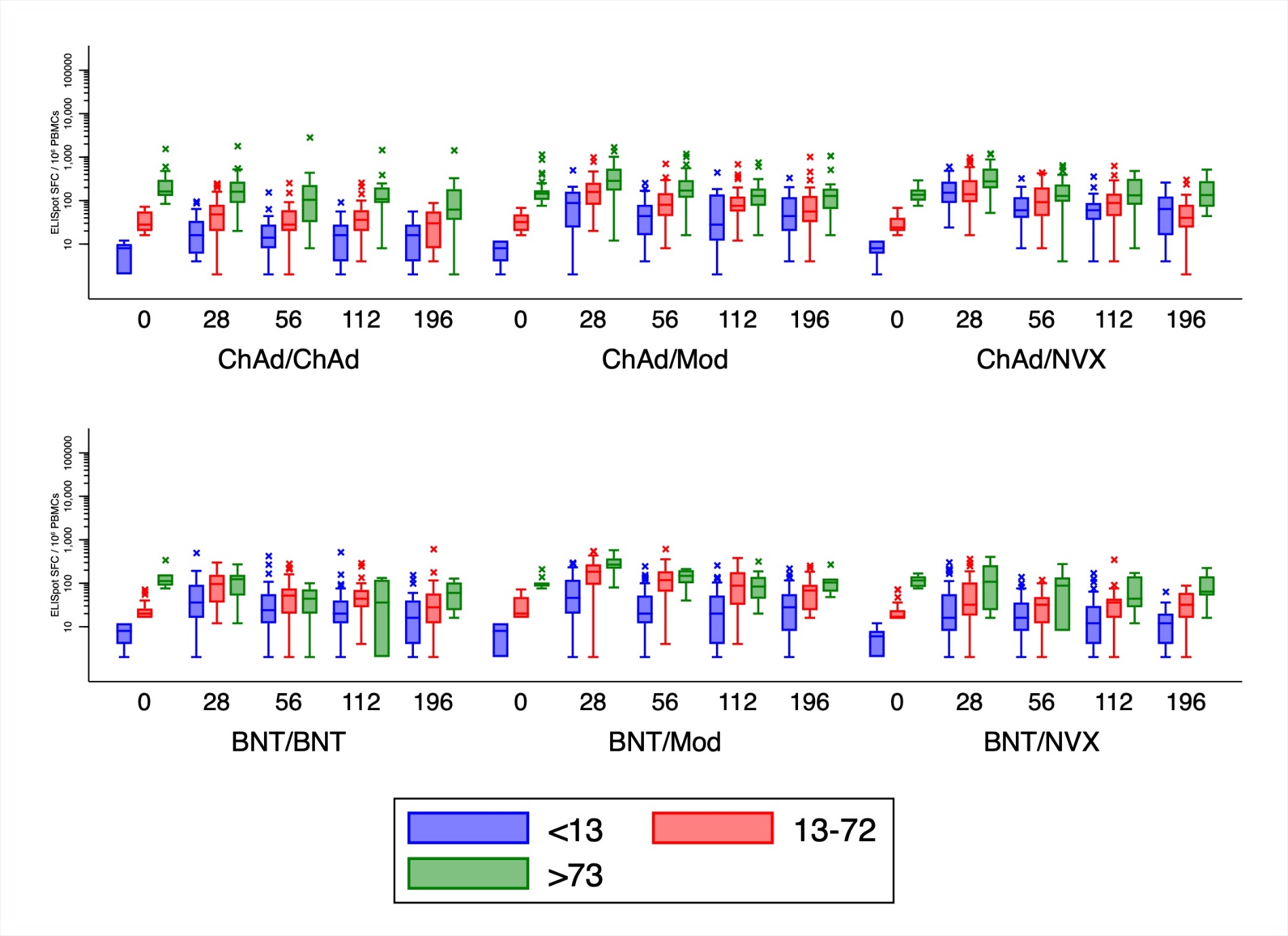
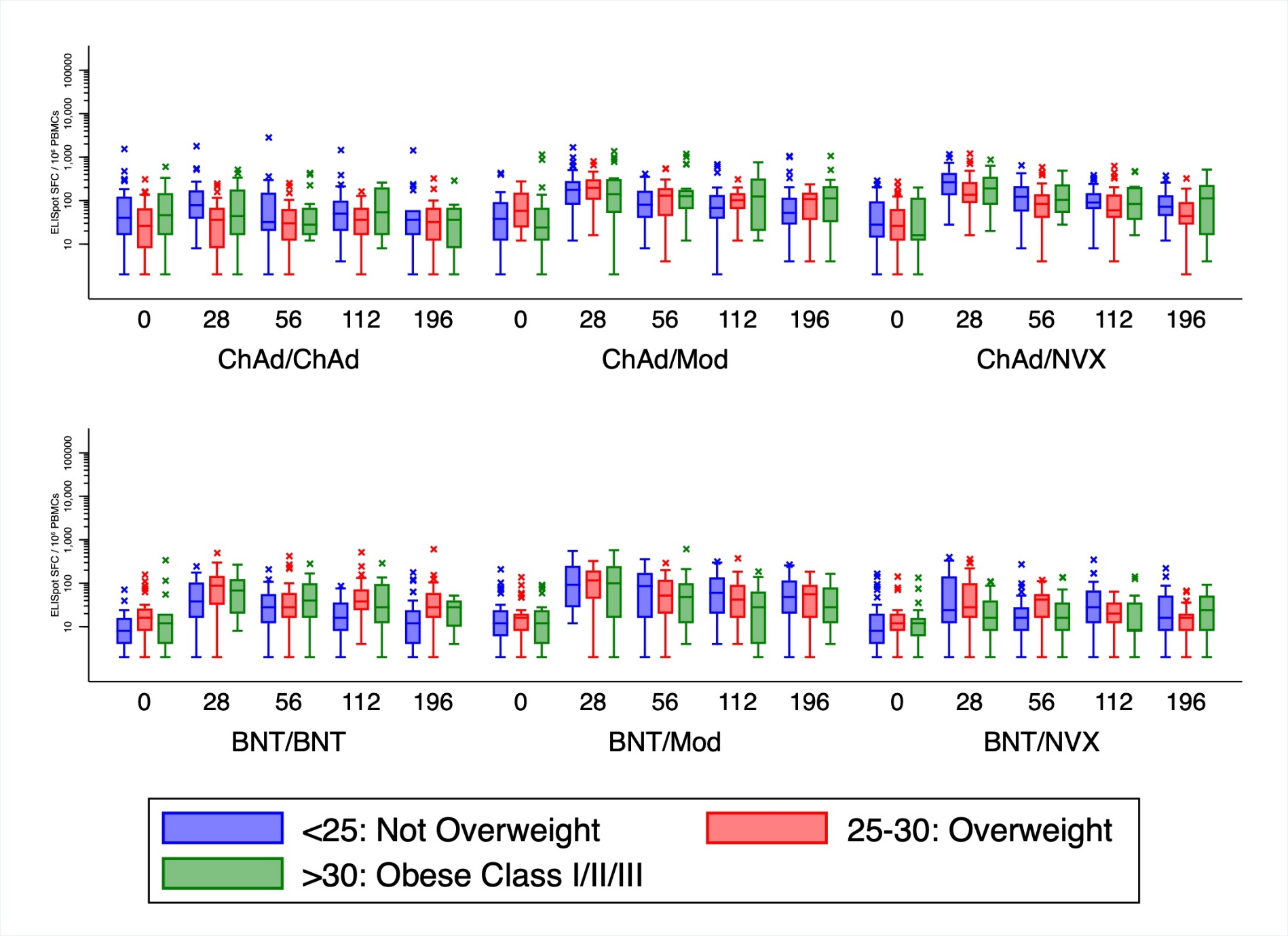
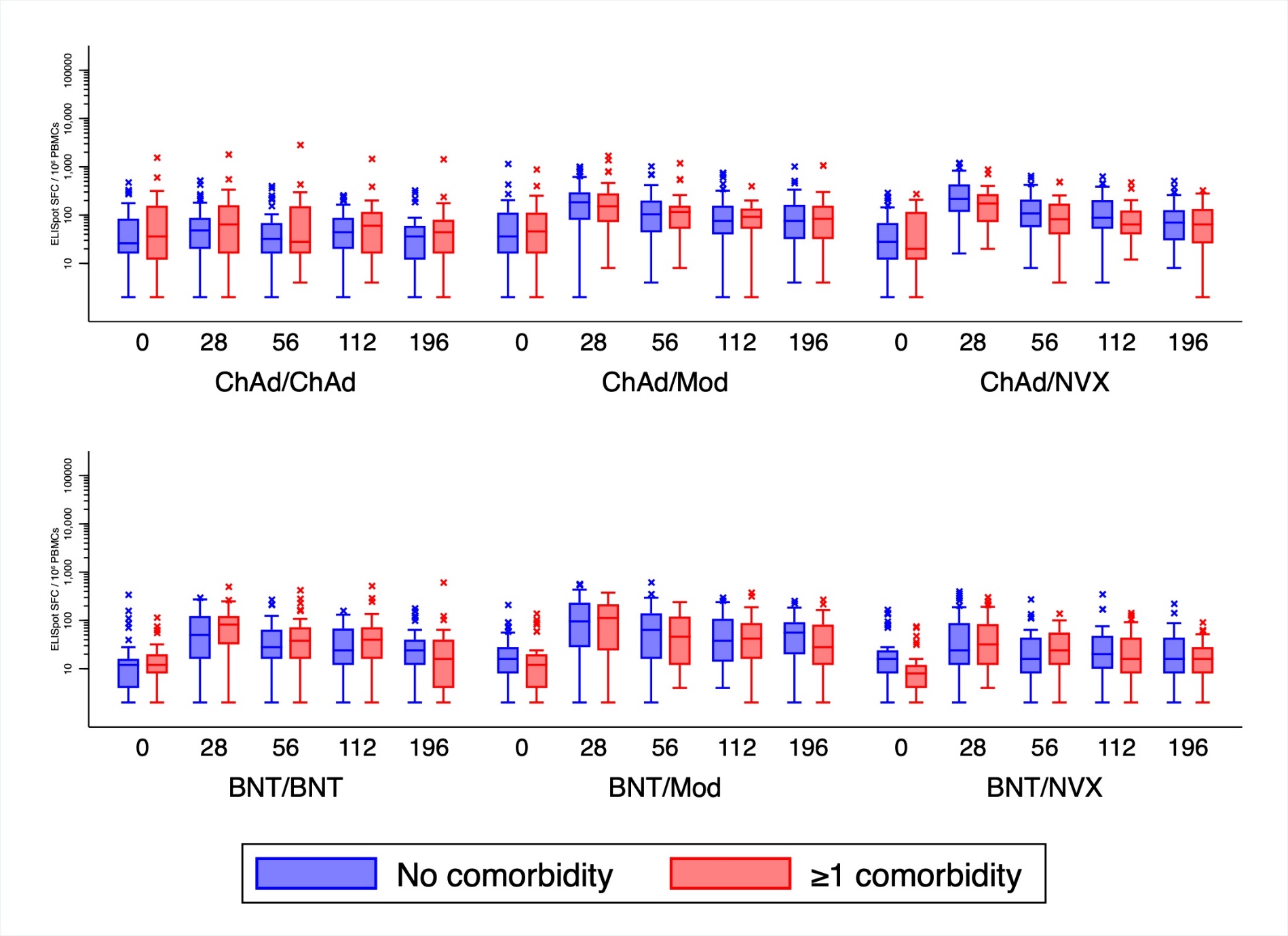
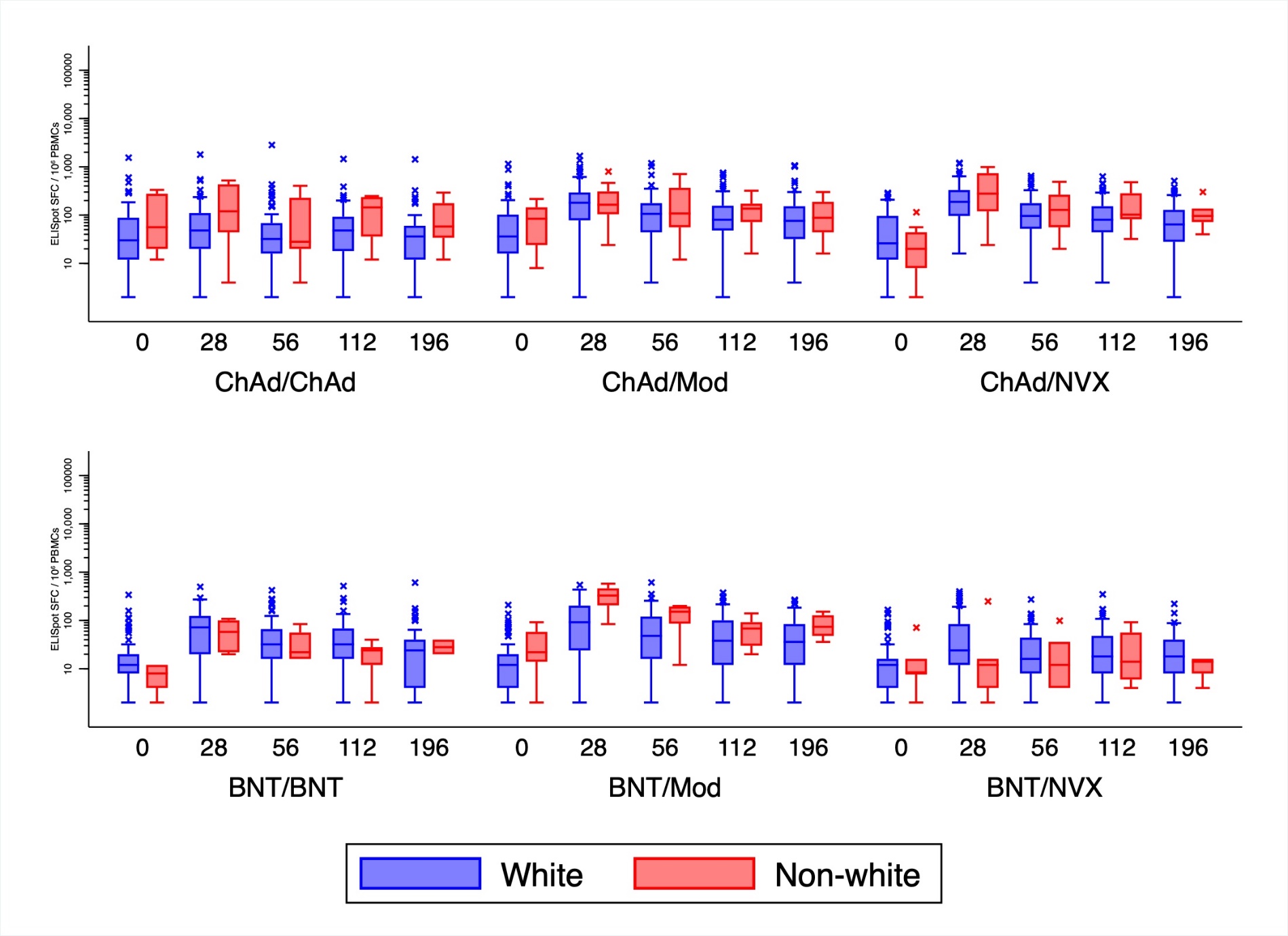
Supplementary Figure 6 - Boxplots of raw, unadjusted T-cell ELISpot counts by subgroup of covariates in mixed effects model A) Age, B) Sex, C) BMI, D) Comorbidity, E) Ethnicity, F) Interval, G) Baseline

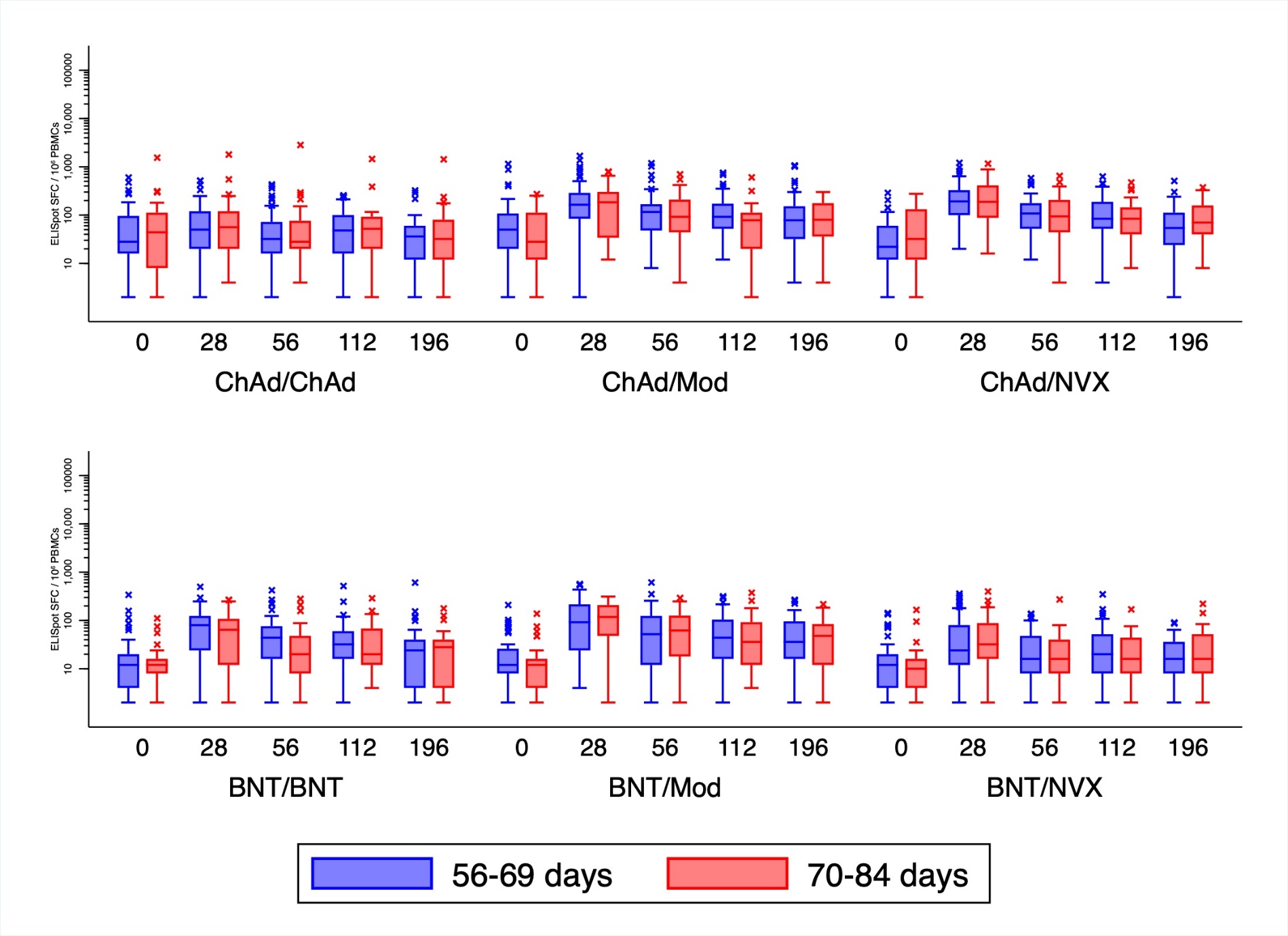


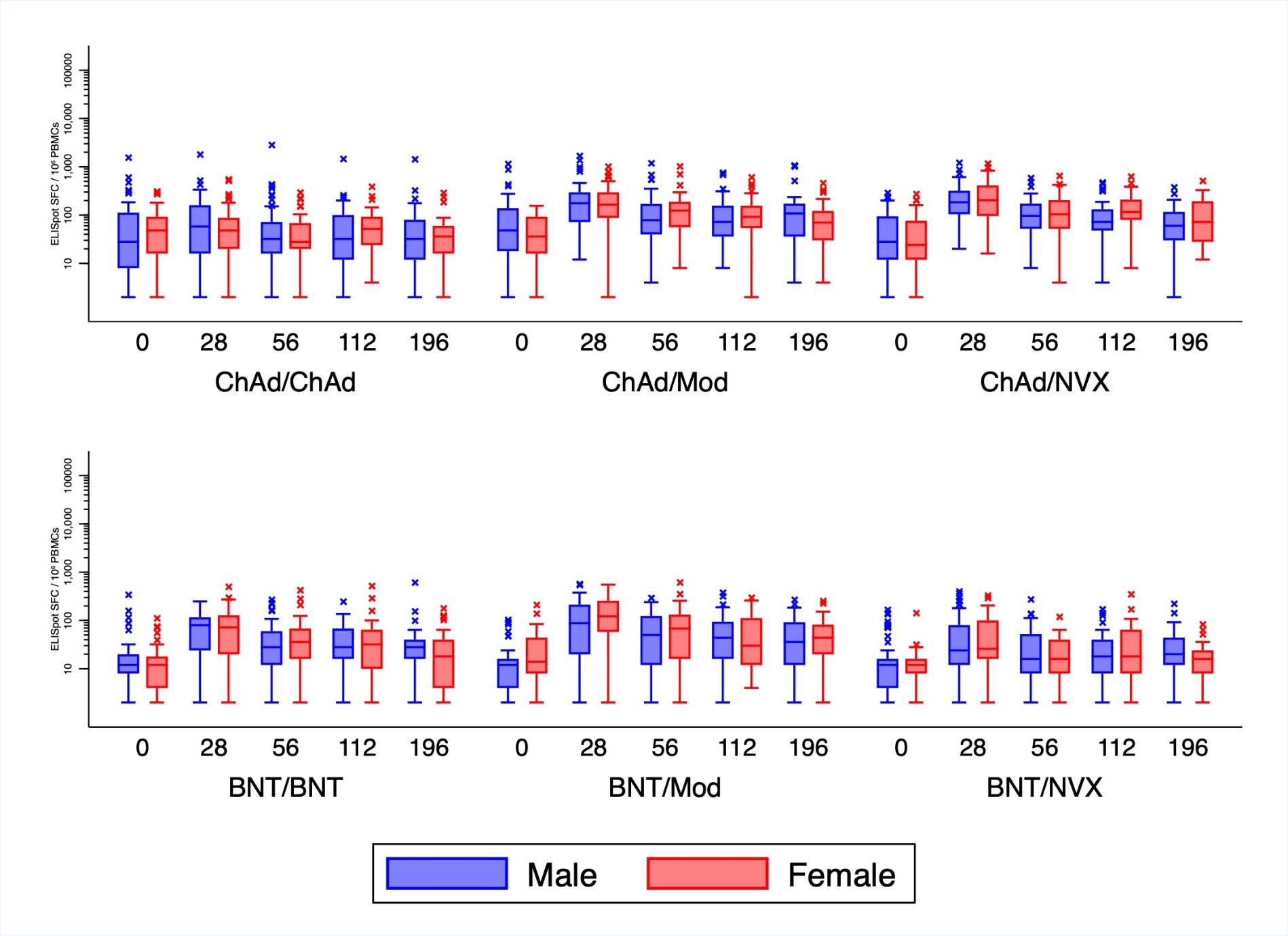




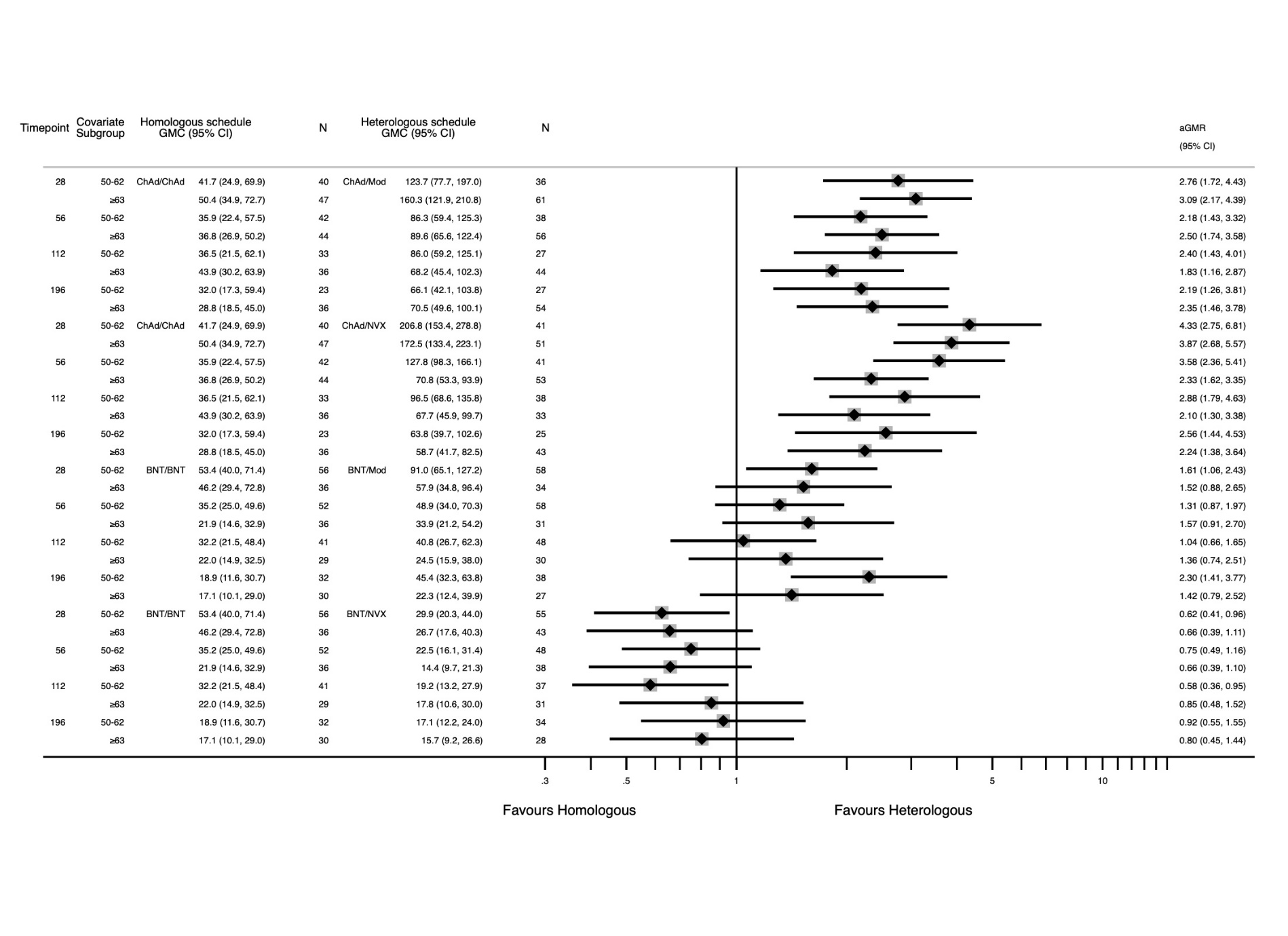


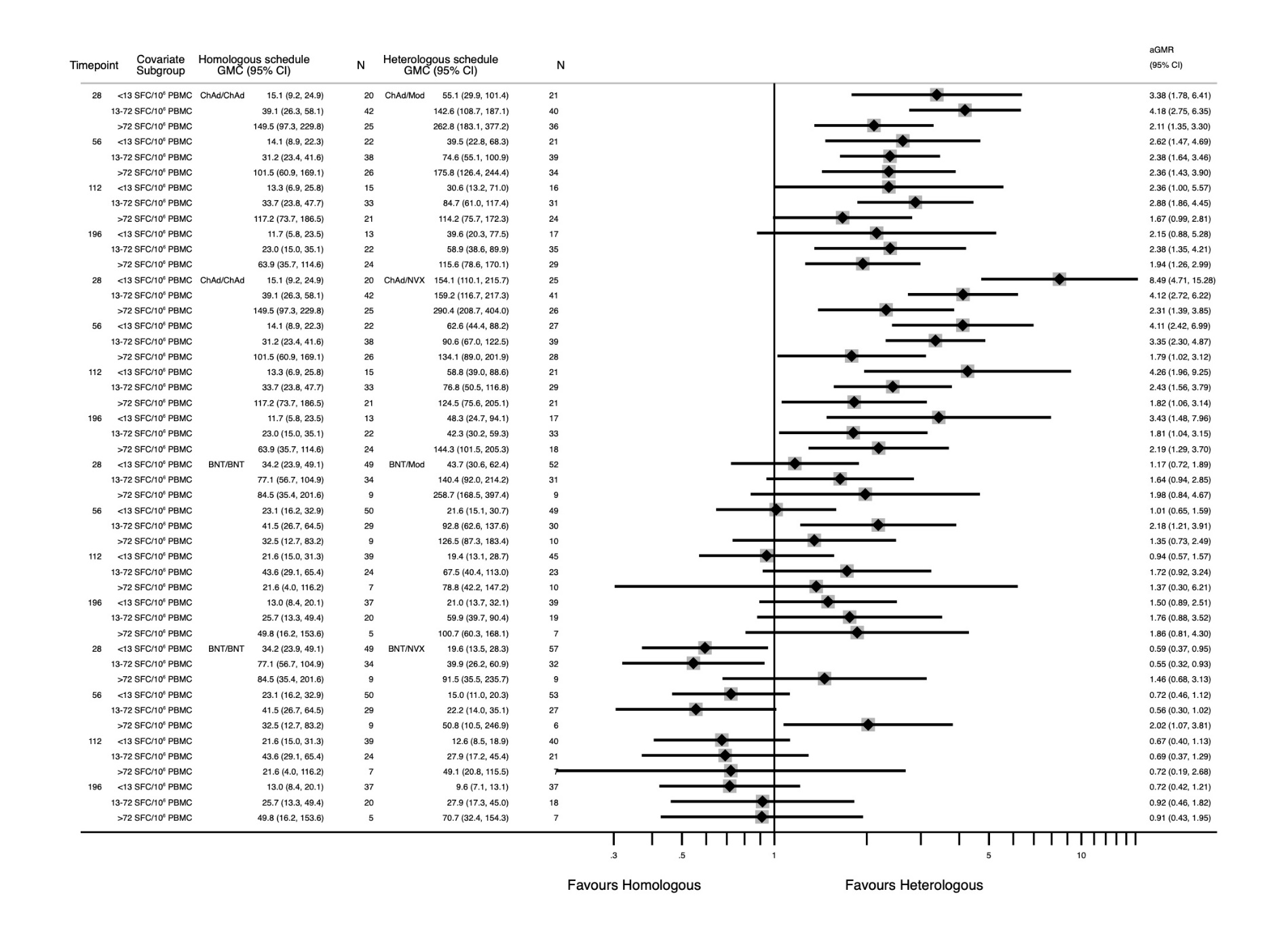


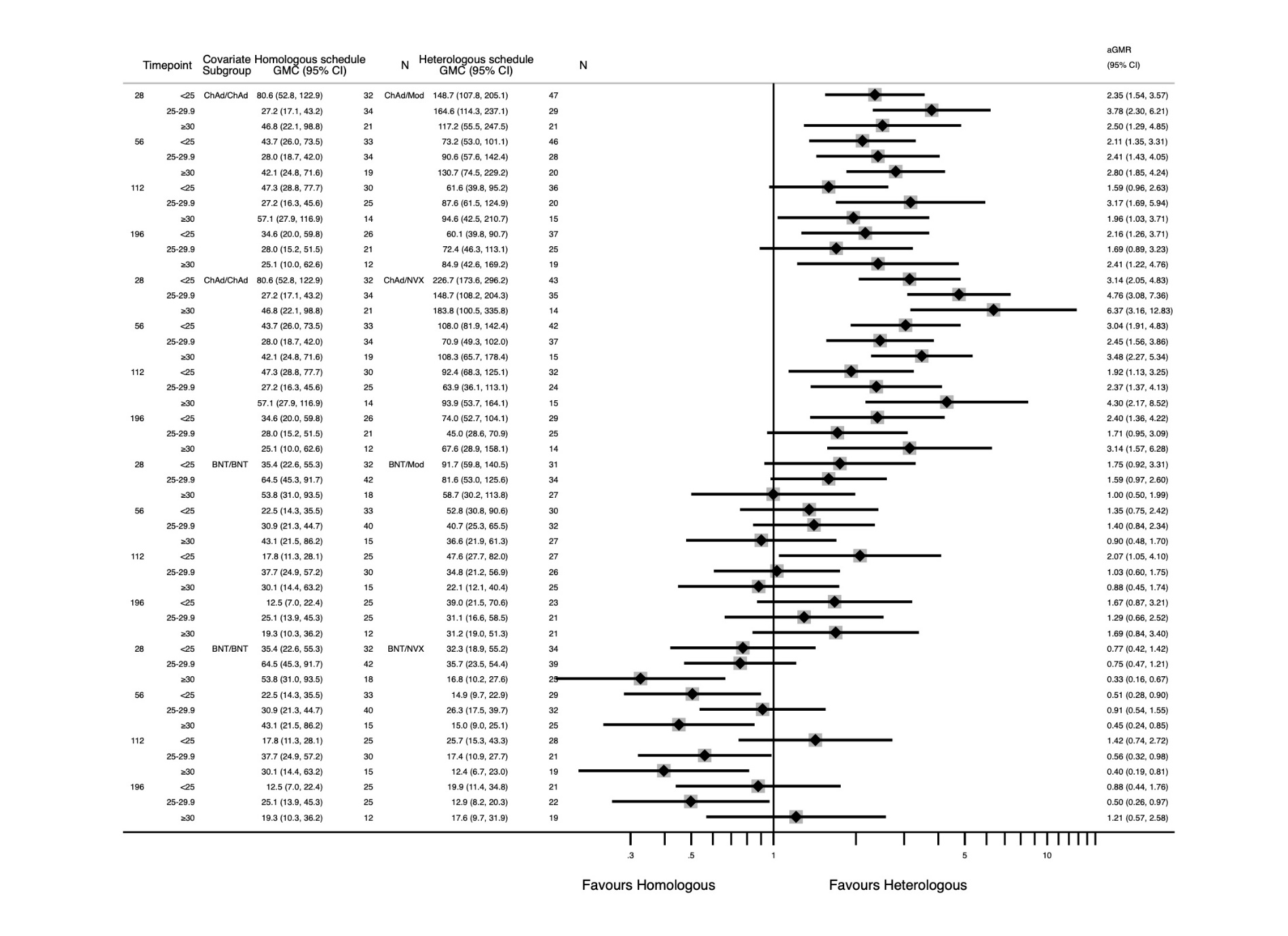


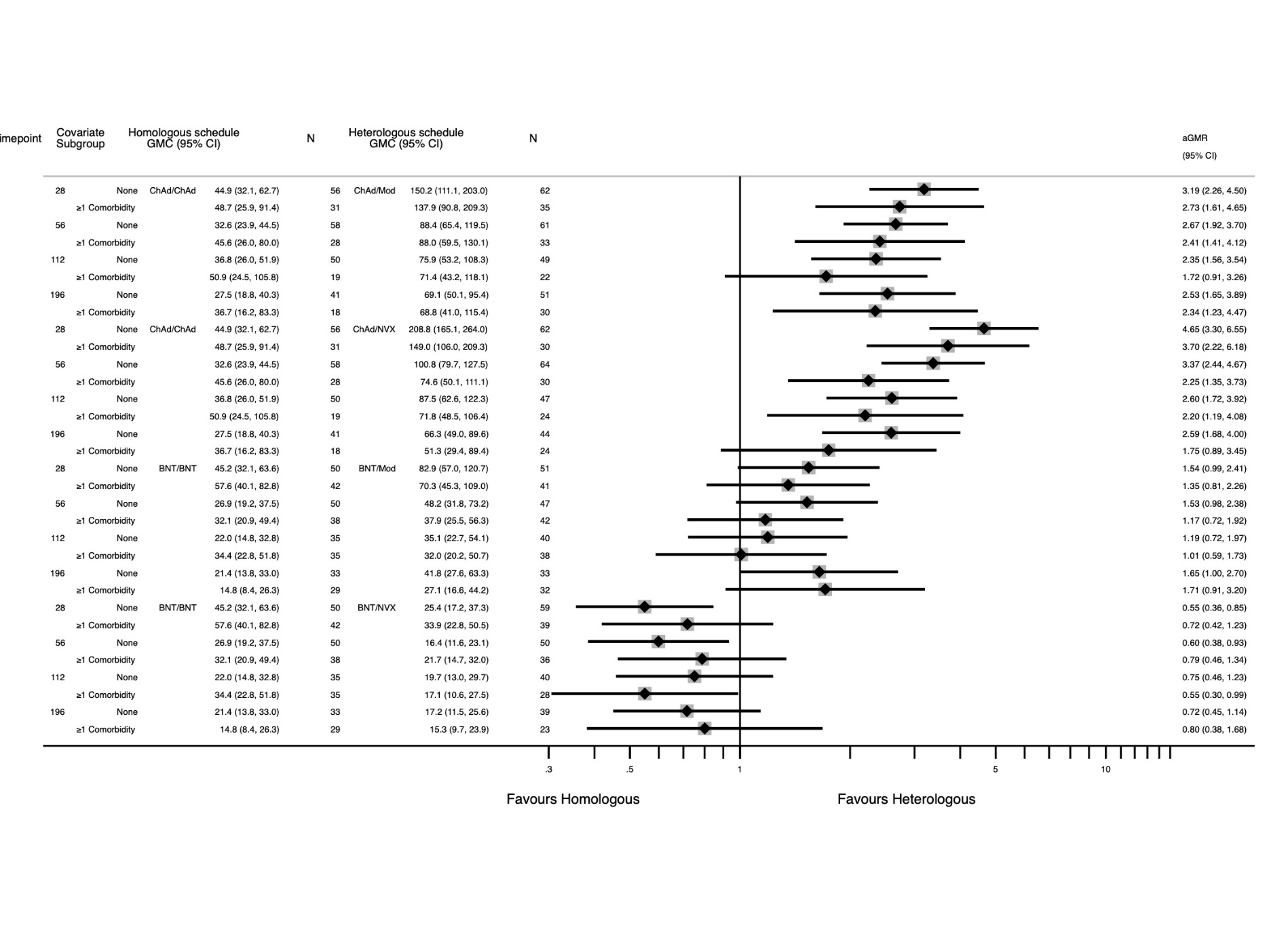


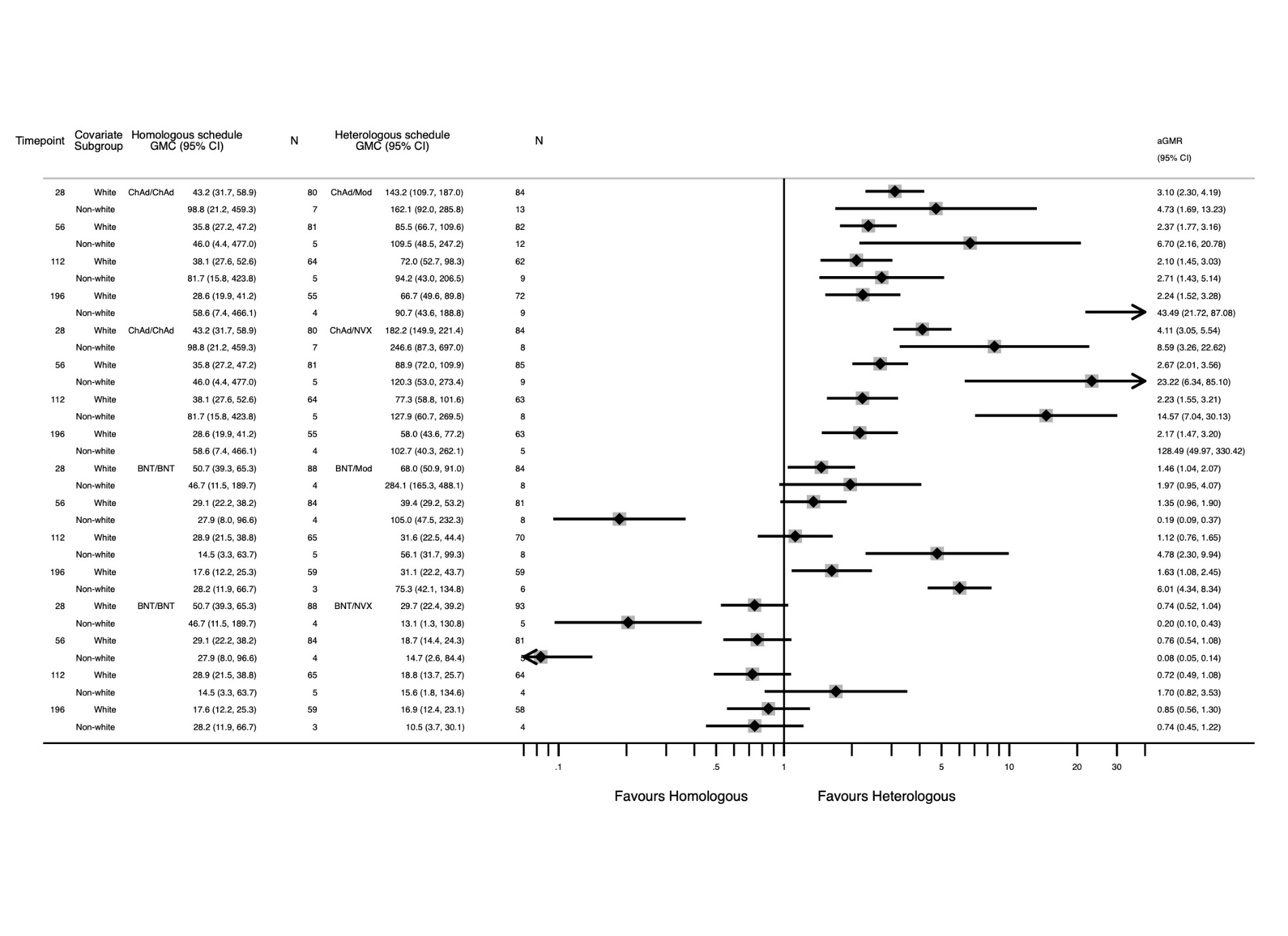
Supplementary Figure 7 - Forest plots comparing T-cell ELISpot counts over time between heterologous and homologous schedules by subgroup of covariates in mixed effects model A) Age, B) Sex, C) BMI, D) Comorbidity, E) Ethnicity, F) Interval, G) Baseline

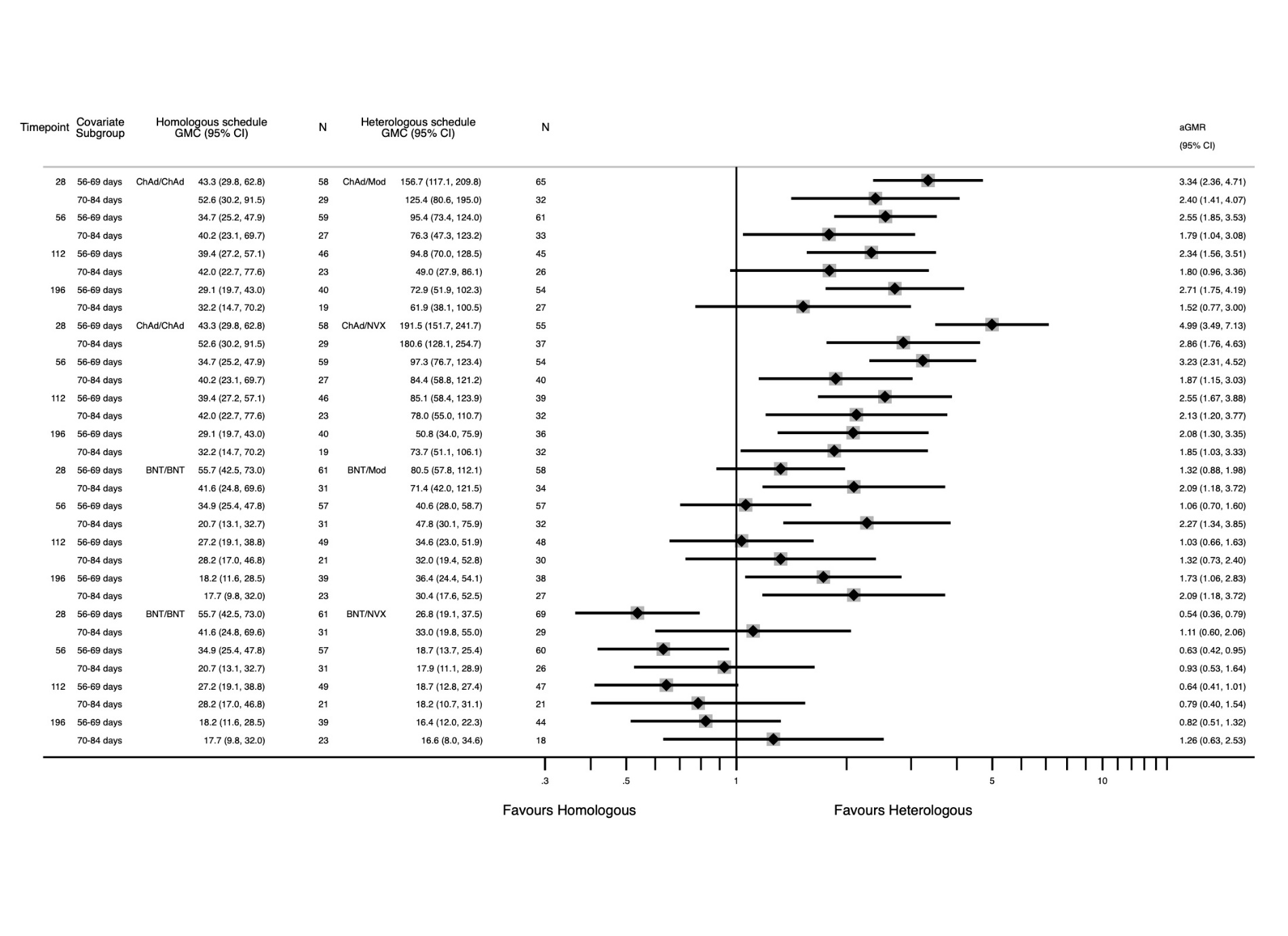


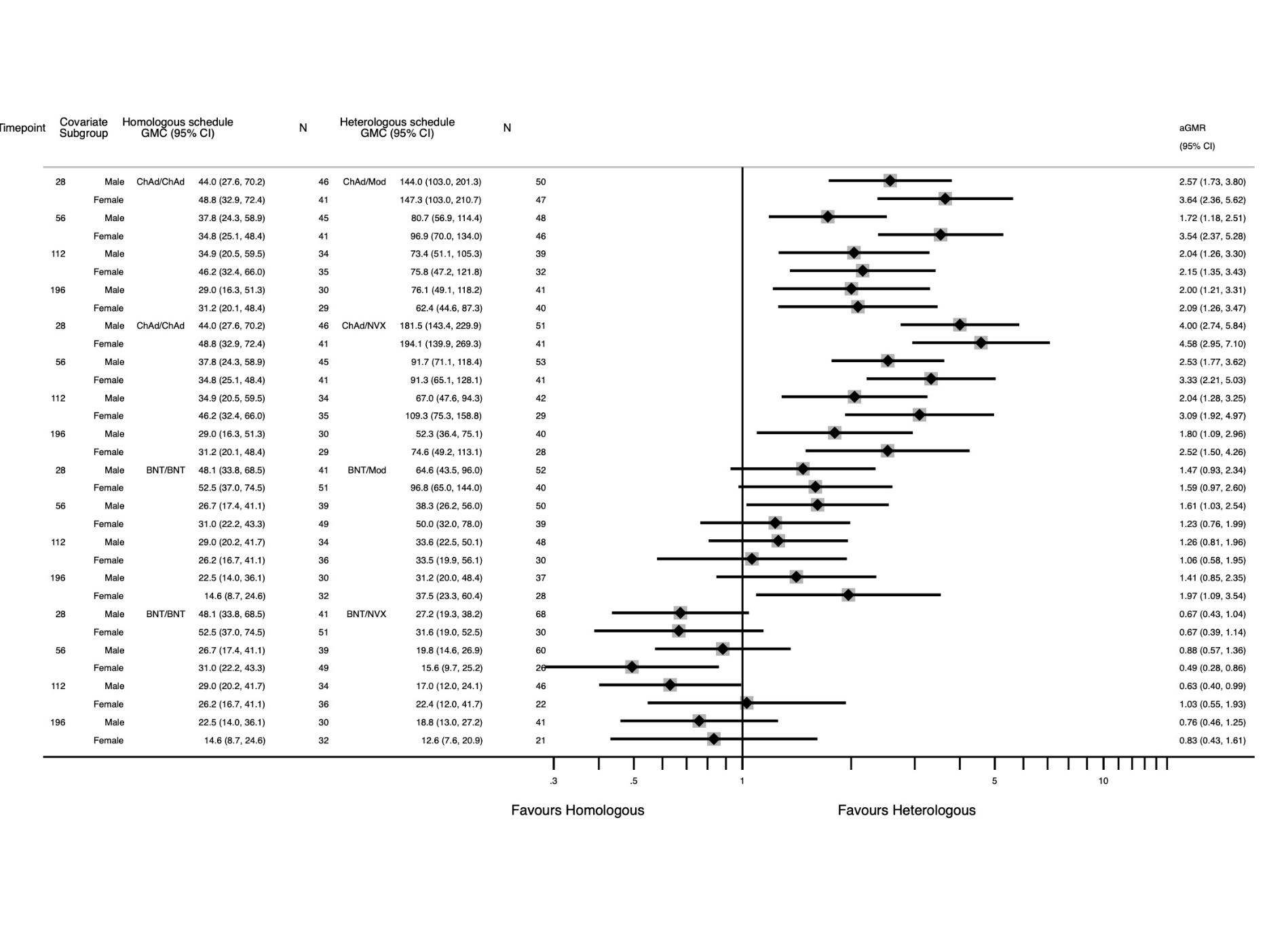












Supplementary Table 1 – Baseline characteristics of analysis population

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Prime with ChAd** | | | | **Prime with BNT** | | | |
| **ChAd (N=180)** | **mRNA-1273 (N=181)** | **NVX-CoV2373 (N=179)** | **Overall (N=540)** | **BNT (N=175)** | **mRNA-1273 (N=177)** | **NVX-CoV2373 (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 (48.3%) | 80 (44.2%) | 74 (41.3%) | 241 (44.6%) | 80 (45.7%) | 68 (38.4%) | 62 (34.4%) | 210 (39.5%) |
| Male | 93 (51.7%) | 101 (55.8%) | 105 (58.7%) | 299 (55.4%) | 95 (54.3%) | 109 (61.6%) | 118 (65.6%) | 322 (60.5%) |
| Ethnicity |  |  |  |  |  |  |  |  |
| White | 169 (93.9%) | 159 (87.8%) | 162 (90.5%) | 490 (90.7%) | 166 (94.9%) | 166 (93.8%) | 172 (95.6%) | 504 (94.7%) |
| Black | 1 (0.6%) | 1 (0.6%) | 3 (1.7%) | 5 (0.9%) | 3 (1.7%) | 2 (1.1%) | 3 (1.7%) | 8 (1.5%) |
| Asian | 4 (2.2%) | 11 (6.1%) | 9 (5.0%) | 24 (4.4%) | 3 (1.7%) | 5 (2.8%) | 2 (1.1%) | 10 (1.9%) |
| Mixed | 3 (1.7%) | 7 (3.9%) | 3 (1.7%) | 13 (2.4%) | 1 (0.6%) | 1 (0.6%) | 2 (1.1%) | 4 (0.8%) |
| Other | 3 (1.7%) | 3 (1.7%) | 2 (1.1%) | 8 (1.5%) | 2 (1.1%) | 3 (1.7%) | 1 (0.6%) | 6 (1.1%) |
| Comorbidities |  |  |  |  |  |  |  |  |
| Cardiovascular | 49 (27.2%) | 55 (30.4%) | 40 (22.3%) | 144 (26.7%) | 63 (36.0%) | 46 (26.0%) | 57 (31.7%) | 166 (31.2%) |
| Respiratory | 15 (8.3%) | 18 (9.9%) | 19 (10.6%) | 52 (9.6%) | 30 (17.1%) | 34 (19.2%) | 31 (17.2%) | 95 (17.9%) |
| Diabetes | 9 (5.0%) | 10 (5.5%) | 14 (7.8%) | 33 (6.1%) | 22 (12.6%) | 21 (11.9%) | 24 (13.3%) | 67 (12.6%) |
| 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) |

Supplementary Table 2 – Lower bound censoring of VOC assays

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **VOC** | **Timepoint** | **ChAd/ChAd** | **ChAd/Mod** | **ChAd/NVX** | **BNT/BNT** | **BNT/Mod** | **BNT/NVX** |
| **Victoria** | 28 | 7 | 0 | 1 | 0 | 0 | 0 |
| **B1351** | 28 | 22 | 2 | 8 | 1 | 1 | 2 |
| **B16171** | 28 | 15 | 0 | 6 | 0 | 0 | 1 |
| **B11529** | 28 | 18 | 0 | 0 | 1 | 0 | 0 |
| **Victoria** | 112 | 13 | 0 | 4 | 0 | 0 | 2 |
| **B1351** | 112 | 30 | 7 | 17 | 10 | 6 | 10 |
| **B16171** | 112 | 25 | 2 | 14 | 4 | 3 | 7 |
| **B11529** | 112 | 40 | 32 | 41 | 33 | 28 | 26 |

Supplementary Table 3 - Tabulation of Live virus neutralising assay results for wild type, Beta, Delta and Omicron variants

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Arm** | **Timepoint** | **Victoria** | **B1351** | **B16171** | **B11529** |
| **ChAd/ChAd** | 28 | 120.3 (75.1 - 192.6) | 26.1 (18.3 - 37.1) | 46.2 (29.0 - 73.6) | 10.6 (9.4 - 12.0) |
| **ChAd/ChAd** | 112 | 62.1 (37.4 - 103.1) | 15.9 (11.8 - 21.4) | 24.8 (15.3 - 40.2) | 10.0 (10.0 - 10.0) |
| **ChAd/Mod** | 28 | 1659.7 (1279.8 - 2152.4) | 368.2 (250.4 - 541.4) | 661.0 (492.1 - 887.9) | . (. - .) |
| **ChAd/Mod** | 112 | 589.7 (421.7 - 824.8) | 80.6 (54.0 - 120.4) | 142.9 (102.4 - 199.5) | 14.7 (12.0 - 18.0) |
| **ChAd/NVX** | 28 | 467.8 (323.7 - 676.1) | 125.1 (81.0 - 193.2) | 165.5 (104.3 - 262.7) | . (. - .) |
| **ChAd/NVX** | 112 | 182.2 (118.0 - 281.4) | 43.4 (29.1 - 64.7) | 62.6 (39.4 - 99.4) | 11.3 (10.0 - 12.7) |
| **BNT/BNT** | 28 | 1497.4 (1171.3 - 1914.3) | 401.5 (282.9 - 569.9) | 683.2 (503.9 - 926.4) | 75.7 (42.4 - 135.0) |
| **BNT/BNT** | 112 | 392.9 (298.0 - 518.0) | 57.7 (39.5 - 84.3) | 125.8 (85.4 - 185.2) | 14.3 (11.2 - 18.3) |
| **BNT/Mod** | 28 | 1926.7 (1570.6 - 2363.4) | 630.3 (454.5 - 874.1) | 930.4 (730.5 - 1185.1) | . (. - .) |
| **BNT/Mod** | 112 | 608.0 (450.9 - 819.9) | 99.3 (67.3 - 146.5) | 171.1 (118.7 - 246.5) | 16.7 (13.3 - 20.9) |
| **BNT/NVX** | 28 | 1118.0 (799.3 - 1563.6) | 449.8 (298.6 - 677.7) | 625.9 (434.6 - 901.5) | . (. - .) |
| **BNT/NVX** | 112 | 385.5 (245.6 - 604.9) | 86.0 (52.6 - 140.6) | 150.2 (89.2 - 252.8) | 17.5 (13.5 - 22.8) |

Supplementary Table 4 – Mixed regression outputs for A) ChAd-primed schedules at Day 28 for Anti-Spike IgG, B) BNT-primed schedules at Day 28 for Anti-Spike IgG, C) ChAd-primed schedules at Day 28 for T-cell ELISpot, D) BNT-primed schedules at Day 28 for T-cell ELISpot, E) ChAd-primed schedules fold change Day 196 from Day 28 (decay rate) for Anti-Spike IgG, F) BNT-primed schedules fold change Day 196 from Day 28 (decay rate) for Anti-Spike IgG, G) ChAd-primed schedules fold change Day 196 from Day 28 (decay rate) for T-cell ELISpot, F) BNT-primed schedules fold change Day 196 from Day 28 (decay rate) for T-cell ELISpot

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Peak Log10(Anti-Spike IgG) at Day 28 for ChAd-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | 0.0313 | 0.0568 | -0.0800, 0.143 | 0.581 |
| Days | -0.0118 | 0.00874 | -0.0289, 0.00537 | 0.179 |
| Baseline | 0.372 | 0.0343 | 0.304, 0.439 | <0.0001 |
| Interval | 0.00105 | 0.00243 | -0.00372, 0.00581 | 0.667 |
| BMI | -0.00858 | 0.00325 | -0.0149, -0.00221 | 0.00827 |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | -0.0303 | 0.0336 | -0.0962, 0.0357 | 0.368 |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.0689 | 0.0317 | 0.00665, 0.131 | 0.03 |
| Age | 0.000435 | 0.00302 | -0.00548, 0.00635 | 0.885 |
| ChAd/ChAd Baseline |  |  |  |  |
| ChAd/Mod | 0.987 | 0.0377 | 0.913, 1.061 | <0.0001 |
| ChAd/NVX | 0.472 | 0.0381 | 0.397, 0.546 | <0.0001 |
| Constant | 2.778 | 0.357 | 2.079, 3.478 | <0.0001 |
|  |  |  |  |  |
| Observations | 475 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Peak Log10(Anti-Spike IgG) at Day 28 for BNT-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | -0.104 | 0.065 | -0.231, 0.0236 | 0.11 |
| Days | 0.000588 | 0.00808 | -0.0153, 0.0164 | 0.942 |
| Baseline | 0.542 | 0.0304 | 0.482, 0.601 | <0.0001 |
| Interval | 0.0112 | 0.00238 | 0.00651, 0.0159 | <0.0001 |
| BMI | -0.00285 | 0.00249 | -0.00773, 0.00203 | 0.252 |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | -0.0203 | 0.0284 | -0.0760, 0.0355 | 0.476 |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.0252 | 0.0285 | -0.0306, 0.0811 | 0.376 |
| Age | -0.0105 | 0.00289 | -0.0161, -0.00479 | 0.000302 |
| BNT/BNT Baseline |  |  |  |  |
| BNT/Mod | 0.134 | 0.0336 | 0.0679, 0.200 | <0.0001 |
| BNT/NVX | -0.261 | 0.0335 | -0.326, -0.195 | <0.0001 |
| Constant | 2.718 | 0.33 | 2.071, 3.364 | <0.0001 |
|  |  |  |  |  |
| Observations | 484 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Peak Log10(T-cell ELISpot) at Day 28 for ChAd-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | 0.142 | 0.0874 | -0.0289, 0.314 | 0.103 |
| Days | -0.0326 | 0.0151 | -0.0622, -0.00306 | 0.0306 |
| Baseline | 0.476 | 0.0436 | 0.391, 0.562 | <0.0001 |
| Interval | -0.00398 | 0.00401 | -0.0118, 0.00388 | 0.321 |
| BMI | -0.0105 | 0.00568 | -0.0216, 0.000658 | 0.0652 |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | -0.0509 | 0.0568 | -0.162, 0.0603 | 0.369 |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.0261 | 0.0523 | -0.0765, 0.129 | 0.618 |
| Age | 0.00465 | 0.00496 | -0.00506, 0.0144 | 0.348 |
| ChAd/ChAd Baseline |  |  |  |  |
| ChAd/Mod | 0.473 | 0.0636 | 0.348, 0.597 | <0.0001 |
| ChAd/NVX | 0.625 | 0.0637 | 0.500, 0.749 | <0.0001 |
| Constant | 2.103 | 0.597 | 0.933, 3.273 | 0.000428 |
|  |  |  |  |  |
| Observations | 272 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Peak Log10(T-cell ELISpot) at Day 28 for BNT-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | 0.137 | 0.126 | -0.109, 0.384 | 0.275 |
| Days | -0.0212 | 0.0222 | -0.0646, 0.0222 | 0.339 |
| Baseline | 0.526 | 0.0612 | 0.406, 0.646 | <0.0001 |
| Interval | 0.00222 | 0.00515 | -0.00788, 0.0123 | 0.666 |
| BMI | -0.0178 | 0.00551 | -0.0286, -0.00695 | 0.00128 |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | 0.155 | 0.0628 | 0.0318, 0.278 | 0.0137 |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.095 | 0.0623 | -0.0271, 0.217 | 0.127 |
| Age | -0.014 | 0.0066 | -0.0269, -0.00107 | 0.0339 |
| BNT/BNT Baseline |  |  |  |  |
| BNT/Mod | 0.187 | 0.0739 | 0.0421, 0.332 | 0.0114 |
| BNT/NVX | -0.181 | 0.074 | -0.326, -0.0359 | 0.0145 |
| Constant | 2.812 | 0.803 | 1.239, 4.385 | 0.000458 |
|  |  |  |  |  |
| Observations | 277 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fold change D196 from D28 of Log10(Anti-Spike IgG) for ChAd-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | -5.77e-05 | 0.0632 | -0.124, 0.124 | 0.999 |
| Days | 0.0119 | 0.0099 | -0.00754, 0.0313 | 0.231 |
| Peak Result at D28 | -0.141 | 0.0437 | -0.226, -0.0549 | 0.0013 |
| Interval | 0.000787 | 0.0025 | -0.00412, 0.00569 | 0.753 |
| BMI | -0.00968 | 0.00335 | -0.0162, -0.00311 | 0.00388 |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | 0.0196 | (0.0345) | -0.0480 - 0.0872 | (0.570) |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.00163 | (0.0325) | -0.0620 - 0.0653 | (0.960) |
| Age | -0.00121 | (0.00330) | -0.00768 - 0.00525 | (0.713) |
| ChAd/ChAd Baseline |  |  |  |  |
| ChAd/Mod | -0.0249 | (0.0569) | -0.137 - 0.0867 | (0.661) |
| ChAd/NVX | -0.0363 | (0.0446) | -0.124 - 0.0511 | (0.416) |
| Constant | -0.228 | (0.407) | -1.026 - 0.570 | (0.576) |
|  |  |  |  |  |
| Observations | 361 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fold change D196 from D28 of Log10(Anti-Spike IgG) for BNT-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | -0.0179 | (0.0747) | -0.164 - 0.128 | (0.811) |
| Days | -0.00907 | (0.00986) | -0.0284 - 0.0102 | (0.357) |
| Peak Result at D28 | -0.18 | (0.0405) | -0.260 - -0.101 | (8.33e-06) |
| Interval | 0.00578 | (0.00274) | 0.000411 - 0.0112 | (0.0349) |
| BMI | -0.00539 | (0.00278) | -0.0108 - 5.87e-05 | (0.0525) |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | -0.0423 | (0.0333) | -0.108 - 0.0229 | (0.204) |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.0234 | (0.0325) | -0.0403 - 0.0872 | (0.471) |
| Age | -0.000390 | (0.00338) | -0.00702 - 0.00624 | (0.908) |
| BNT/BNT Baseline |  |  |  |  |
| BNT/Mod | 0.0965 | (0.0389) | 0.0202 - 0.173 | (0.0132) |
| BNT/NVX | 0.0236 | (0.0410) | -0.0568 - 0.104 | (0.565) |
| Constant | -0.0719 | (0.411) | -0.877 - 0.733 | (0.861) |
|  |  |  |  |  |
| Observations | 360 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fold change D196 from D28 of Log10(T-cell ELISpot) for ChAd-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | -0.0492 | (0.113) | -0.271 - 0.173 | (0.664) |
| Days | 0.00132 | (0.0229) | -0.0435 - 0.0461 | (0.954) |
| Peak Result at D28 | -0.382\*\*\* | (0.0613) | -0.502 - -0.262 | (4.82e-10) |
| Interval | 0.00269 | (0.00512) | -0.00734 - 0.0127 | (0.599) |
| BMI | 0.0131\*\* | (0.00665) | 7.49e-05 - 0.0261 | (0.0487) |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | -0.0364 | (0.0680) | -0.170 - 0.0970 | (0.593) |
| Male Sex Baseline |  |  |  |  |
| Female Sex | 0.0385 | (0.0629) | -0.0848 - 0.162 | (0.540) |
| Age | -0.00798 | (0.00682) | -0.0213 - 0.00538 | (0.242) |
| ChAd/ChAd Baseline |  |  |  |  |
| ChAd/Mod | 0.0818 | (0.0813) | -0.0775 - 0.241 | (0.314) |
| ChAd/NVX | 0.00183 | (0.0865) | -0.168 - 0.171 | (0.983) |
| Constant | 0.366 | (0.870) | -1.340 - 2.072 | (0.674) |
|  |  |  |  |  |
| Observations | 193 |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fold change D196 from D28 of Log10(T-cell ELISpot) for BNT-primed Schedules** | | | | |
| **Covariate** | **Beta Coefficient** | **SE** | **95% CI** | **p-value** |
| White Ethnicity Baseline |  |  |  |  |
| Non-White Ethnicity | 0.0717 | (0.143) | -0.208 - 0.352 | (0.616) |
| Days | 0.0181 | (0.0308) | -0.0422 - 0.0784 | (0.556) |
| Peak Result at D28 | -0.573\*\*\* | (0.0610) | -0.692 - -0.453 | (0) |
| Interval | 0.00390 | (0.00617) | -0.00820 - 0.0160 | (0.527) |
| BMI | 0.00350 | (0.00627) | -0.00878 - 0.0158 | (0.577) |
| No Comorbidity Baseline |  |  |  |  |
| ≥1 Comorbidity | -0.222\*\*\* | (0.0770) | -0.373 - -0.0713 | (0.00390) |
| Male Sex Baseline |  |  |  |  |
| Female Sex | -0.158\*\* | (0.0734) | -0.302 - -0.0141 | (0.0314) |
| Age | -0.0137\* | (0.00758) | -0.0286 - 0.00118 | (0.0712) |
| BNT/BNT Baseline |  |  |  |  |
| BNT/Mod | 0.205\*\* | (0.0877) | 0.0326 - 0.376 | (0.0197) |
| BNT/NVX | 0.0808 | (0.0913) | -0.0981 - 0.260 | (0.376) |
| Constant | 0.649 | (1.048) | -1.404 - 2.703 | (0.536) |
|  |  |  |  |  |
| Observations | 179 |  |  |  |

Supplementary Table 5 – Numbers of participants per assay per timepoint

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | ChAd/ChAd | | | ChAd/Mod | | | ChAd/NVX | | | BNT/BNT | | | BNT/Mod | | | BNT/NVX | | |
| Median Timepoint (range) | Anti-spike IgG | Anti-spike IgG sensitivity | T-cell ELISpot | Anti-spike IgG | Anti-spike IgG sensitivity | T-cell ELISpot | Anti-spike IgG | Anti-spike IgG sensitivity | T-cell ELISpot | Anti-spike IgG | Anti-spike IgG sensitivity | T-cell ELISpot | Anti-spike IgG | Anti-spike IgG sensitivity | T-cell ELISpot | Anti-spike IgG | Anti-spike IgG sensitivity | T-cell ELISpot |
| 0 (0-0) | 159 | 154 | 93 | 165 | 160 | 100 | 160 | 159 | 100 | 162 | 161 | 99 | 159 | 157 | 97 | 169 | 158 | 101 |
| 28 (18-42) | 159 | 154 | 91 | 162 | 157 | 99 | 158 | 157 | 95 | 162 | 161 | 93 | 160 | 158 | 95 | 167 | 156 | 99 |
| 56 (47-77) | 157 | 153 | 87 | 161 | 156 | 95 | 159 | 158 | 95 | 159 | 158 | 89 | 157 | 155 | 92 | 161 | 150 | 87 |
| 112 (99-155) | 153 | 148 | 81 | 155 | 150 | 86 | 153 | 152 | 87 | 156 | 155 | 76 | 156 | 154 | 85 | 150 | 140 | 74 |
| 196 (168-239) | 108 | 105 | 59 | 142 | 137 | 81 | 116 | 116 | 71 | 115 | 114 | 64 | 125 | 123 | 66 | 122 | 113 | 63 |

Supplementary Table 6 - Summary of adverse events, by group and boost vaccine

|  | | **ChAd/ChAd**  **(N=180)** | | **ChAd/Mod**  **(N=181)** | | **ChAd/NVX**  **(N=179)** | | **BNT/BNT**  **(N=175)** | | **BNT/Mod**  **(N=177)** | | **BNT/NVX**  **(N=180)** | | **Total**  **(N=1072)** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Number of adverse events | 140 | | 148 | | 116 | | 122 | | 122 | | 108 | | 756 | |
| Number of unique participants | 83 (45.6%) | | 81 (44.8%) | | 65 (36.3%) | | 70 (40.0%) | | 71 (40.1%) | | 66 (36.7%) | | 436 (40.7%) | |
| AE within 28 days post boost | 96 (68.6%) | | 119 (80.4%) | | 90 (77.6%) | | 91 (74.6%) | | 93 (76.2%) | | 81 (75.0%) | | 570 (75.4%) | |
| AE within 3 months post boost | 129 (92.1%) | | 143 (96.6%) | | 112 (96.6%) | | 115 (94.3%) | | 117 (95.9%) | | 102 (94.4%) | | 718 (95.0%) | |
| Adverse of special interest | 12 (8.6%) | | 7 (4.7%) | | 6 (5.2%) | | 5 (4.1%) | | 5 (4.1%) | | 7 (6.5%) | | 42 (5.6%) | |
| Serious adverse event | 4 (2.9%) | | 5 (3.4%) | | 1 (0.9%) | | 3 (2.5%) | | 5 (4.1%) | | 3 (2.8%) | | 21 (2.8%) | |
| Severity |  | |  | |  | |  | |  | |  | |  | |
| Grade 1 | 79 (56.4%) | | 90 (60.8%) | | 62 (53.4%) | | 62 (50.8%) | | 66 (54.1%) | | 53 (49.1%) | | 412 (54.5%) | |
| Grade 2 | 46 (32.9%) | | 47 (31.8%) | | 45 (38.8%) | | 49 (40.2%) | | 43 (35.2%) | | 44 (40.7%) | | 274 (36.2%) | |
| Grade 3 | 13 (9.3%) | | 10 (6.8%) | | 8 (6.9%) | | 10 (8.2%) | | 9 (7.4%) | | 10 (9.3%) | | 60 (7.9%) | |
| Grade 4 | 2 (1.4%) | | 1 (0.7%) | | 1 (0.9%) | | 1 (0.8%) | | 4 (3.3%) | | 1 (0.9%) | | 10 (1.3%) | |
| Causality |  | |  | |  | |  | |  | |  | |  | |
| No relationship | 52 (37.1%) | | 43 (29.1%) | | 48 (41.4%) | | 52 (42.6%) | | 51 (41.8%) | | 44 (40.7%) | | 290 (38.4%) | |
| Unlikely | 52 (37.1%) | | 60 (40.5%) | | 46 (39.7%) | | 51 (41.8%) | | 43 (35.2%) | | 40 (37.0%) | | 292 (38.6%) | |
| Possible | 26 (18.6%) | | 25 (16.9%) | | 16 (13.8%) | | 9 (7.4%) | | 18 (14.8%) | | 12 (11.1%) | | 106 (14.0%) | |
| Probable | 8 (5.7%) | | 18 (12.2%) | | 4 (3.4%) | | 6 (4.9%) | | 6 (4.9%) | | 6 (5.6%) | | 48 (6.3%) | |
| Definite | 2 (1.4%) | | 2 (1.4%) | | 2 (1.7%) | | 4 (3.3%) | | 4 (3.3%) | | 6 (5.6%) | | 20 (2.6%) | |
| Type of SAE |  | |  | |  | |  | |  | |  | |  | |
| An important medical event | 1 (0.7%) | | 3 (2.0%) | |  | | 1 (0.8%) | | 1 (0.8%) | | 1 (0.9%) | | 7 (0.9%) | |
| Hospitalisation | 2 (1.4%) | | 2 (1.4%) | | 1 (0.9%) | | 2 (1.6%) | | 3 (2.5%) | | 2 (1.9%) | | 12 (1.6%) | |
| Life threatening | 1 (0.7%) | |  | |  | |  | | 1 (0.8%) | |  | | 2 (0.3%) | |
| Outcome |  | |  | |  | |  | |  | |  | |  | |
| Ongoing |  | | 2 (1.4%) | |  | | 1 (0.8%) | |  | | 1 (0.9%) | | 4 (0.5%) | |
| Recovered | 2 (1.4%) | | 3 (2.0%) | | 1 (0.9%) | | 1 (0.8%) | | 4 (3.3%) | |  | | 11 (1.5%) | |
| Recovered with sequelae | 2 (1.4%) | |  | |  | | 1 (0.8%) | | 1 (0.8%) | | 2 (1.9%) | | 6 (0.8%) | |

Supplementary Table 7 - Non-serious adverse events of grade ≥3 (excluding SAEs)

| **Prime vaccine** | **Study arm** | **Days to onset from boost** | **MedDRA Preferred Term** | **MedDRA System Order Class** | **Duration (days)** | **Severity** | **Causality assessment** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ChAd | ChAd | 9 | Wrist fracture | Musculoskeletal and connective tissue disorders | 39 | Grade 3 | No relationship |
| ChAd | ChAd | 0 | Hyperkalaemia^ | Metabolism and nutrition disorders | 2 | Grade 3 | No relationship |
| ChAd | ChAd | 9 | Dental caries | Gastrointestinal disorders | 49 | Grade 3 | No relationship |
| ChAd | ChAd | 65 | Polytrauma | Injury, poisoning and procedural complications | 107 | Grade 3 | No relationship |
| ChAd | ChAd | 2 | Vertigo | Ear and labyrinth disorders | 1 | Grade 3 | Probable |
| ChAd | ChAd | 39 | Lower respiratory tract infection bacterial~ | Infections and infestations | 13 | Grade 3 | Unlikely |
| ChAd | ChAd | 3 | Fatigue | General disorders and administration site conditions | 9 | Grade 3 | Probable |
| ChAd | ChAd | 0 | Headache | Nervous system disorders | 2 | Grade 3 | Definite |
| ChAd | ChAd | 1 | Musculoskeletal chest pain | Musculoskeletal and connective tissue disorders | 35 | Grade 3 | Possible |
| ChAd | ChAd | 7 | Sleep apnoea syndrome | Respiratory, thoracic and mediastinal disorders | 29 | Grade 3 | Unlikely |
| ChAd | ChAd | 126 | COVID-19\* | Infections and infestations | 62 | Grade 3 | No relationship |
| ChAd | mRNA-1273 | 9 | Headache | Nervous system disorders | 1 | Grade 3 | Possible |
| ChAd | mRNA-1273 | 11 | Prostate cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 178 | Grade 3 | Unlikely |
| ChAd | mRNA-1273 | 0 | Fever | General disorders and administration site conditions | 2 | Grade 3 | Definite |
| ChAd | mRNA-1273 | 23 | Limb injury | Injury, poisoning and procedural complications | . | Grade 3 | No relationship |
| ChAd | mRNA-1273 | 1 | Fever | General disorders and administration site conditions | 2 | Grade 3 | Probable |
| ChAd | mRNA-1273 | 58 | UTI | Infections and infestations | 4 | Grade 3 | No relationship |
| ChAd | NVX-CoV237 | 48 | Pacemaker insertion (cardiac) | Surgical and medical procedures | 1 | Grade 3 | Unlikely |
| ChAd | NVX-CoV237 | 27 | Fatigue | General disorders and administration site conditions | 2 | Grade 3 | Unlikely |
| ChAd | NVX-CoV237 | 65 | Dizziness | Nervous system disorders | 4 | Grade 4 | No relationship |
| ChAd | NVX-CoV237 | 1 | Menopausal symptoms | Reproductive system and breast disorders | 31 | Grade 3 | Possible |
| ChAd | NVX-CoV237 | 91 | Head injury | Injury, poisoning and procedural complications | . | Grade 3 | Unlikely |
| ChAd | NVX-CoV237 | 26 | Chest pain | General disorders and administration site conditions | . | Grade 3 | Unlikely |
| ChAd | NVX-CoV237 | 52 | Urinary tract infection | Infections and infestations | 4 | Grade 3 | No relationship |
| ChAd | NVX-CoV237 | 43 | Cystitis | Renal and urinary disorders | 8 | Grade 3 | No relationship |
| BNT | BNT | 5 | Tooth repair | Surgical and medical procedures | 1 | Grade 3 | No relationship |
| BNT | BNT | 11 | Back pain | Musculoskeletal and connective tissue disorders | 17 | Grade 3 | Unlikely |
| BNT | BNT | 64 | Eyelid operation | Surgical and medical procedures | 1 | Grade 3 | No relationship |
| BNT | BNT | 0 | Hypomagnesaemia | Metabolism and nutrition disorders | 15 | Grade 3 | No relationship |
| BNT | BNT | 42 | Back injury | Injury, poisoning and procedural complications | 2 | Grade 3 | No relationship |
| BNT | BNT | 21 | Tooth extraction | Surgical and medical procedures | 4 | Grade 3 | No relationship |
| BNT | BNT | 74 | Orthostatic hypotension | Vascular disorders | 40 | Grade 3 | Unlikely |
| BNT | BNT | 27 | Labyrinthitis | Ear and labyrinth disorders | 8 | Grade 3 | Unlikely |
| BNT | BNT | 16 | Muscle spasms | Musculoskeletal and connective tissue disorders | 3 | Grade 3 | Unlikely |
| BNT | mRNA-1273 | 10 | Tooth extraction | Surgical and medical procedures | 16 | Grade 3 | No relationship |
| BNT | mRNA-1273 | 9 | Tooth extraction | Surgical and medical procedures | 6 | Grade 3 | No relationship |
| BNT | mRNA-1273 | 24 | Fatigue | General disorders and administration site conditions | 7 | Grade 3 | Possible |
| BNT | mRNA-1273 | 19 | Chest pain | General disorders and administration site conditions | 2 | Grade 4 | Unlikely |
| BNT | mRNA-1273 | 24 | Joint injury | Injury, poisoning and procedural complications | 4 | Grade 3 | No relationship |
| BNT | mRNA-1273 | 5 | Joint dislocation | Musculoskeletal and connective tissue disorders | 5 | Grade 4 | No relationship |
| BNT | mRNA-1273 | 11 | Back pain | Musculoskeletal and connective tissue disorders | 3 | Grade 3 | Unlikely |
| BNT | mRNA-1273 | 1 | Fever | General disorders and administration site conditions | 2 | Grade 3 | Definite |
| BNT | NVX-CoV237 | 12 | Oropharyngeal pain | Respiratory, thoracic and mediastinal disorders | 3 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 12 | Fatigue | General disorders and administration site conditions | 1 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 12 | Abdominal discomfort | Gastrointestinal disorders | 3 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 12 | Myalgia | Musculoskeletal and connective tissue disorders | 3 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 16 | Fatigue | General disorders and administration site conditions | 4 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 16 | Abdominal discomfort | Gastrointestinal disorders | 4 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 77 | Basal cell carcinoma | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 33 | Grade 3 | Unlikely |
| BNT | NVX-CoV237 | 37 | Tendon sheath incision | Surgical and medical procedures | 1 | Grade 3 | No relationship |

\*COVID-19 Grade 3 AE is also included in Supplementary Table 9 as a COVID-19 AESI, but Supplementary Table 6 containing the summary data does not double count this.

Supplementary Table 8 - Adverse events of special interest\* in all study arms

| **Prime vaccine** | **Study arm** | **Days to onset from boost** | **MedDRA Preferred Term** | **MedDRA System Order Class** | **Duration (days)** | **Severity** | **Causality assessment** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ChAd | mRNA-1273 | 75 | Seizure | Nervous system disorders | 1 | Grade 2 | Unlikely |
| ChAd | NVX-CoV237 | 28 | Acute kidney injury | Renal and urinary disorders | 12 | Grade 1 | Unlikely |
| BNT | mRNA-1273 | 29 | Eosinophilia | Blood and lymphatic system disorders | 105 | Grade 2 | Possible |
| BNT | NVX-CoV237 | 105 | Contusion | Vascular disorders | Ongoing | Grade 1 | Unlikely |
| BNT | NVX-CoV237 | 83 | Retinal vein thrombosis | Eye disorders | Ongoing | Grade 2 | Unlikely |

\* Excluding SAEs

Supplementary Table 9 - Adverse events of special interest - COVID-19 cases, by study arm

| **Prime vaccine** | **Study arm** | **Days to onset from boost** | **Severity** |
| --- | --- | --- | --- |
| ChAd | ChAd | 174 | Grade 2 |
| ChAd | ChAd | 130 | Grade 1 |
| ChAd | ChAd | 68 | Grade 1 |
| ChAd | ChAd | 183 | Grade 2 |
| ChAd | ChAd | 96 | Grade 1 |
| ChAd | ChAd | 67 | Grade 2 |
| ChAd | ChAd | 84 | Grade 1 |
| ChAd | ChAd | 151 | Grade 1 |
| ChAd | ChAd | 104 | Grade 1 |
| ChAd | ChAd | 118 | Grade 1 |
| ChAd | ChAd | 126 | Grade 3 |
| ChAd | mRNA-1273 | 77 | Grade 1 |
| ChAd | mRNA-1273 | 134 | Grade 2 |
| ChAd | mRNA-1273 | 108 | Grade 1 |
| ChAd | mRNA-1273 | 180 | Grade 2 |
| ChAd | mRNA-1273 | 173 | Grade 1 |
| ChAd | mRNA-1273 | 70 | Grade 2 |
| ChAd | NVX-CoV237 | 168 | Grade 1 |
| ChAd | NVX-CoV237 | 148 | Grade 1 |
| ChAd | NVX-CoV237 | 91 | Grade 2 |
| ChAd | NVX-CoV237 | 109 | Grade 2 |
| ChAd | NVX-CoV237 | 117 | Grade 2 |
| BNT | BNT | 137 | Grade 1 |
| BNT | BNT | 82 | Grade 1 |
| BNT | BNT | 177 | Grade 2 |
| BNT | BNT | 217 | Grade 2 |
| BNT | BNT | 155 | Grade 2 |
| BNT | mRNA-1273 | 76 | Grade 1 |
| BNT | mRNA-1273 | 165 | Grade 2 |
| BNT | mRNA-1273 | 144 | Grade 1 |
| BNT | mRNA-1273 | 142 | Grade 1 |
| BNT | NVX-CoV237 | 197 | Grade 2 |
| BNT | NVX-CoV237 | 194 | Grade 1 |
| BNT | NVX-CoV237 | 166 | Grade 2 |

Supplementary Table 10 - Serious adverse events

| **Prime vaccine** | **Study arm** | **Days to onset from boost** | **MedDRA Preferred Term** | **MedDRA System Organ Class** | **Duration (days)** | **Severity** | **Causality assessment** | **SAE Type** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ChAd | mRNA-1273 | 28 | Neutropaenia | Blood and lymphatic system disorders | 10 | Grade 4 | No relationship | An important medical event |
| ChAd | ChAd | 142 | Diverticulitis | Gastrointestinal disorders | 8 | Grade 3 | No relationship | Hospitalisation |
| BNT | mRNA-1273 | 84 | Renal colic | Renal and urinary tract disorders | 2 | Grade 3 | Unlikely | Hospitalisation |
| BNT | mRNA-1273 | 183 | Dog bite | Injury, poisoning and procedural complications | 3 | Grade 3 | No relationship | Hospitalisation |
| BNT | mRNA-1273 | 184 | Penicillin allergy | Immune system disorders | 1 | Grade 3 | No relationship | An important medical event |
| BNT | NVX-CoV237 | 94 | Intervertebral disc protrusion  Intervertebral disc operation | Musculoskeletal and connective tissue disorders  Surgical and medical procedures | . | Grade 3 | Unlikely | Hospitalisation |
| ChAd | mRNA-1273 | 39 | Coronary arterial stent insertion | Surgical and medical procedures | 143 | Grade 3 | Unlikely | An important medical event |
| ChAd | mRNA-1273 | 67 | Jaw fracture | Injury, poisoning and procedural complications | 133 | Grade 3 | Unlikely | Hospitalisation |
| ChAd | NVX-CoV237 | 56 | Sebaceous cyst excision | Surgical and medical procedures | 3 | Grade 3 | No relationship | Hospitalisation |
| ChAd | ChAd | 109 | Humerus fracture | Injury, poisoning and procedural complications | 22 | Grade 3 | No relationship | Hospitalisation |
| ChAd | mRNA-1273 | 21 | Headache | Nervous system disorders | . | Grade 3 | Unlikely | Hospitalisation |
| BNT | BNT | 179 | Hysterectomy | Surgical and medical procedures | 42 | Grade 2 | No relationship | Hospitalisation |
| BNT | NVX-CoV237 | 18 | Transient ischaemic attack\*\* | Nervous system disorders | 1 | Grade 3 | Unlikely | An important medical event |
| BNT | mRNA-1273 | 45 | Aortic dissection | Vascular disorders | 33 | Grade 4 | No relationship | Life threatening |
| BNT | BNT | 133 | Hysteroscopy | Investigations | . | Grade 3 | Unlikely | Hospitalisation |
| ChAd | ChAd | 52 | Acute myocardial infarction\*\* | Cardiac disorders | 10 | Grade 4 | Unlikely | Life threatening |
| ChAd | ChAd | 111 | Breast cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 77 | Grade 4 | No relationship | An important medical event |
| BNT | mRNA-1273 | 0 | Cholecystitis | Hepatobiliary disorders | 4 | Grade 4 | Unlikely | Hospitalisation |
| BNT | BNT | 94 | Retinal detachment | Eye disorders | . | Grade 4 | No relationship | An important medical event |
| BNT | NVX-CoV237 | 134 | COVID-19\*\* | Infections and infestations | 14 | Grade 4 | No relationship | Hospitalisation |
| ChAd | mRNA-1273 | 179 | Varices oesophageal | Gastrointestinal disorders | . | Grade 3 | No relationship | An important medical event |

\* See protocol for causality assessment guidance \*\* Also AESI