# COVID-19 Correlates of Risk Analysis Report

MockCOVE Study

USG COVID-19 Response Biostatistics Team

October 15, 2021

# Contents

# List of Tables

# List of Figures

# Chapter 1

# Disclaimers

The data presented in the analysis are provided to NIAID in accordance with Clinical Trial Agreement between the parties. The study was funded in part by BARDA under Government Contract No. 75A50120C00034.



**Statistical Analysis Plan**

The SAP is available at https://doi.org/10.6084/m9.figshare.13198595

**Reproducibility Notice**

This project integrates the virtual environments framework provided by the `renv` package for computational reproducibility. By taking this approach, all results are generated using a consistent versioning of both R and several R packages. This version of the report was built with R version 4.0.4 (2021-02-15), pandoc version 2.2, and the following R packages:

| package | version | source |
|---|---|---|
| bookdown | 0.21.7 | Github (rstudio/bookdown@0cec2fd) |
| bslib | 0.2.4.9002 | Github (rstudio/bslib@c7835c2) |
| data.table | 1.14.0 | CRAN (R 4.0.4) |
| delayed | 0.4.0 | Github (tlverse/delayed@f415340) |
| devtools | 2.3.2 | CRAN (R 4.0.4) |
| dplyr | 1.0.5 | CRAN (R 4.0.4) |
| ggplot2 | 3.3.3 | CRAN (R 4.0.4) |
| hal9001 | 0.4.0 | Github (tlverse/hal9001@b41ed5d) |
| haldensify | 0.1.5 | Github (nhejazi/haldensify@16350cc) |
| here | 1.0.1 | CRAN (R 4.0.4) |
| kableExtra | 1.3.4 | CRAN (R 4.0.4) |
| knitr | 1.31 | CRAN (R 4.0.4) |
| latex2exp | 0.5.0 | CRAN (R 4.0.4) |
| mvtnorm | 1.1-1 | CRAN (R 4.0.4) |
| origami | 1.0.3 | CRAN (R 4.0.4) |
| readr | 1.4.0 | CRAN (R 4.0.4) |
| rmarkdown | 2.7.4 | Github (rstudio/rmarkdown@a11240d) |
| skimr | 2.1.3 | CRAN (R 4.0.4) |
| sl3 | 1.4.3 | Github (tlverse/sl3@982f4d6) |
| stringr | 1.4.0 | CRAN (R 4.0.4) |
| SuperLearner | 2.0-28 | CRAN (R 4.0.4) |
| svyVGAM | 1.0 | CRAN (R 4.0.4) |
| tibble | 3.1.1 | CRAN (R 4.0.4) |

| package | version | source |
|---|---|---|
| tidyr | 1.1.3 | CRAN (R 4.0.4) |
| txshift | 0.3.6 | Github (nhejazi/txshift@c0f572a) |
| VGAM | 1.1-5 | CRAN (R 4.0.4) |
| xtable | 1.8-4 | CRAN (R 4.0.4) |

To get started with using this project and its `renv` package library, we first recommend briefly reviewing the `renv` collaboration guide.

# Chapter 2

# Summary Tables

## 2.1 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Negative Per-Protocol Cohort



Table 2.1: Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Negative Per-Protocol Cohort

| Characteristics | Vaccine (N = 731) | Placebo (N = 126) | Total (N = 857) |
|---|---|---|---|
| **Age** | | | |
| Age < 65 | 365 (49.9%) | 62 (49.2%) | 427 (49.8%) |
| Age ≥ 65 | 366 (50.1%) | 64 (50.8%) | 430 (50.2%) |
| Mean (Range) | 57.7 (18.0, 85.0) | 60.0 (18.0, 85.0) | 58.1 (18.0, 85.0) |
| **BMI** | | | |
| Mean ± SD | 30.1 ± 6.8 | 30.5 ± 6.8 | 30.2 ± 6.8 |
| **Risk for Severe Covid-19** | | | |
| At-risk | 369 (50.5%) | 63 (50.0%) | 432 (50.4%) |
| Not at-risk | 362 (49.5%) | 63 (50.0%) | 425 (49.6%) |
| **Age, Risk for Severe Covid-19** | | | |
| Age < 65 At-risk | 183 (25.0%) | 35 (27.8%) | 218 (25.4%) |
| Age < 65 Not at-risk | 182 (24.9%) | 27 (21.4%) | 209 (24.4%) |
| Age ≥ 65 | 366 (50.1%) | 64 (50.8%) | 430 (50.2%) |
| **Sex** | | | |
| Female | 422 (57.7%) | 72 (57.1%) | 494 (57.6%) |
| Male | 309 (42.3%) | 54 (42.9%) | 363 (42.4%) |
| **Hispanic or Latino ethnicity** | | | |
| Hispanic or Latino | 121 (16.6%) | 27 (21.4%) | 148 (17.3%) |
| Not Hispanic or Latino | 584 (79.9%) | 95 (75.4%) | 679 (79.2%) |
| Not reported and unknown | 26 (3.6%) | 4 (3.2%) | 30 (3.5%) |
| **Race** | | | |
| White | 383 (52.4%) | 69 (54.8%) | 452 (52.7%) |
| Black or African American | 174 (23.8%) | 25 (19.8%) | 199 (23.2%) |
| Asian | 54 (7.4%) | 11 (8.7%) | 65 (7.6%) |
| American Indian or Alaska Native | 25 (3.4%) | 1 (0.8%) | 26 (3.0%) |
| Native Hawaiian or Other Pacific Islander | 7 (1.0%) | 4 (3.2%) | 11 (1.3%) |

Table 2.1: *(continued)*

| Characteristics | Vaccine (N = 731) | Placebo (N = 126) | Total (N = 857) |
|---|---|---|---|
| Multiracial | 54 (7.4%) | 9 (7.1%) | 63 (7.4%) |
| Other | 28 (3.8%) | 7 (5.6%) | 35 (4.1%) |
| Not reported and unknown | 6 (0.8%) | | 6 (0.7%) |
| White Non-Hispanic | 349 (47.7%) | 59 (46.8%) | 408 (47.6%) |
| Communities of Color | 382 (52.3%) | 67 (53.2%) | 449 (52.4%) |

This table summarizes the random subcohort, which was randomly sampled from the per-protocol cohort. The sampling was stratified by 24 strata defined by enrollment characteristics: Assigned treatment arm $\times$ Baseline SARS-CoV-2 naïve vs. non-naïve status (defined by serostatus and NAAT testing) $\times$ Randomization strata (Age $<$ 65 and at-risk, Age $<$ 65 and not at-risk, Age $\geq$ 65)$\times$ Communities of color (Yes/No) defined by White Non-Hispanic vs. all others (following the primary COVE trial paper).

## 2.2 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Positive Per-Protocol Cohort

Table 2.2: Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Positive Per-Protocol Cohort

| Characteristics | Vaccine (N = 223) | Placebo (N = 249) | Total (N = 472) |
|---|---|---|---|
| **Age** | | | |
| Age < 65 | 120 (53.8%) | 127 (51.0%) | 247 (52.3%) |
| Age ≥ 65 | 103 (46.2%) | 122 (49.0%) | 225 (47.7%) |
| Mean (Range) | 55.6 (18.0, 85.0) | 57.4 (18.0, 85.0) | 56.5 (18.0, 85.0) |
| **BMI** | | | |
| Mean ± SD | 29.8 ± 6.5 | 29.8 ± 6.9 | 29.8 ± 6.7 |
| **Risk for Severe Covid-19** | | | |
| At-risk | 101 (45.3%) | 121 (48.6%) | 222 (47.0%) |
| Not at-risk | 122 (54.7%) | 128 (51.4%) | 250 (53.0%) |
| **Age, Risk for Severe Covid-19** | | | |
| Age < 65 At-risk | 59 (26.5%) | 64 (25.7%) | 123 (26.1%) |
| Age < 65 Not at-risk | 61 (27.4%) | 63 (25.3%) | 124 (26.3%) |
| Age ≥ 65 | 103 (46.2%) | 122 (49.0%) | 225 (47.7%) |
| **Sex** | | | |
| Female | 118 (52.9%) | 138 (55.4%) | 256 (54.2%) |
| Male | 105 (47.1%) | 111 (44.6%) | 216 (45.8%) |
| **Hispanic or Latino ethnicity** | | | |
| Hispanic or Latino | 31 (13.9%) | 31 (12.4%) | 62 (13.1%) |
| Not Hispanic or Latino | 184 (82.5%) | 209 (83.9%) | 393 (83.3%) |
| Not reported and unknown | 8 (3.6%) | 9 (3.6%) | 17 (3.6%) |
| **Race** | | | |
| White | 126 (56.5%) | 135 (54.2%) | 261 (55.3%) |
| Black or African American | 49 (22.0%) | 63 (25.3%) | 112 (23.7%) |
| Asian | 18 (8.1%) | 21 (8.4%) | 39 (8.3%) |
| American Indian or Alaska Native | 5 (2.2%) | 8 (3.2%) | 13 (2.8%) |
| Native Hawaiian or Other Pacific Islander | 7 (3.1%) | 4 (1.6%) | 11 (2.3%) |
| Multiracial | 14 (6.3%) | 12 (4.8%) | 26 (5.5%) |
| Other | 2 (0.9%) | 5 (2.0%) | 7 (1.5%) |
| Not reported and unknown | 2 (0.9%) | 1 (0.4%) | 3 (0.6%) |
| White Non-Hispanic | 116 (52.0%) | 125 (50.2%) | 241 (51.1%) |
| Communities of Color | 107 (48.0%) | 124 (49.8%) | 231 (48.9%) |

This table summarizes the random subcohort, which was randomly sampled from the per-protocol cohort. The sampling was stratified by 24 strata defined by enrollment characteristics: Assigned treatment arm × Baseline SARS-CoV-2 naïve vs. non-naïve status (defined by serostatus and NAAT testing) × Randomization strata (Age < 65 and at-risk, Age < 65 and not at-risk, Age ≥ 65)× Communities of color (Yes/No) defined by White Non-Hispanic vs. all others (following the primary COVE trial paper).

## 2.3 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort

Table 2.3: Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort

Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort
Sample Sizes (N=1329 Participants) (Moderna Trial)

| | Baseline SARS-CoV-2 Negative | | | | | | | | | Baseline SARS-CoV-2 Positive | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| **Vaccine** | | | | | | | | | | | | | | | | | | |
| Day 29 Cases | 8 | 2 | 6 | 15 | 5 | 10 | 5 | 1 | 3 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 |
| Day 57 Cases | 7 | 2 | 4 | 15 | 4 | 9 | 5 | 0 | 2 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 |
| Non-Cases | 155 | 78 | 77 | 210 | 105 | 105 | 95 | 35 | 31 | 35 | 23 | 26 | 67 | 36 | 35 | 31 | 12 | 11 |
| **Placebo** | | | | | | | | | | | | | | | | | | |
| Day 29 Cases | 143 | 51 | 99 | 316 | 116 | 214 | 94 | 30 | 63 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| Day 57 Cases | 128 | 44 | 79 | 297 | 88 | 174 | 90 | 25 | 50 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| Non-Cases | 19 | 12 | 10 | 32 | 18 | 13 | 16 | 4 | 8 | 49 | 23 | 24 | 72 | 41 | 39 | 18 | 12 | 11 |

Demographic covariate strata:
1. Age $\geq$ 65, Minority
2. Age < 65, At risk, Minority
3. Age < 65, Not at risk, Minority
4. Age $\geq$ 65, Non-Minority
5. Age < 65, At risk, Non-Minority
6. Age < 65, Not at risk, Non-Minority
7. Age $\geq$ 65, Unknown
8. Age < 65, At risk, Unknown
9. Age < 65, Not at risk, Unknown

Minority includes Blacks or African Americans, Hispanics or Latinos, American Indians or Alaska Natives, Native Hawaiians, and other Pacific Islanders.
Non-Minority includes all other races with observed race (Asian, Multiracial, White, Other) and observed ethnicity Not Hispanic or Latino. Participants not classifiable as Minority or Non-Minority because of unknown, unreported or missing were not included.

Observed = Numbers of participants sampled into the subcohort within baseline covariate strata.
Estimated = Estimated numbers of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

## 2.4 Availability of immunogenicity data by case status

Table 2.4: Availability of immunogenicity data by case status

| Case | $---$ | $--+$ | $-+-$ | $-++$ | $+--$ | $+-+$ | $++-$ | $+++$ |
|---|---|---|---|---|---|---|---|---|
| **Vaccine** | | | | | | | | |
| Day 29 Cases | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 55 |
| Day 57 Cases | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 48 |
| Intercurrent Cases | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 |
| **Placebo** | | | | | | | | |
| Day 29 Cases | 47 | 0 | 0 | 0 | 0 | 0 | 0 | 1126 |
| Day 57 Cases | 42 | 0 | 0 | 0 | 0 | 0 | 0 | 975 |
| Intercurrent Cases | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 136 |

The + (available) and − (unavailable) in the column labels refer to the availability of the baseline, D29 and D57 markers, respectively.

## 2.5 Antibody levels in the baseline SARS-CoV-2 negative per-protocol cohort (vaccine recipients)

Table 2.5: Antibody levels in the baseline SARS-CoV-2 negative per-protocol cohort (vaccine recipients)

| | | Baseline SARS-CoV-2 Negative Vaccine Recipients | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Cases* | | | Non-Cases/Control | | | Comparison | |
| Visit | Marker | N | Resp rate | GMT/GMC | N | Resp rate | GMT/GMC | Resp Rate Difference | GMTR/GMCR |
| Day 29 | Pseudovirus-nAb cID80 | 55 | 31.6/58 = 54.5% (41.1%, 67.4%) | 20.02 (16.24, 24.67) | 730 | 6582.6/11114.3 = 59.2% (54.7%, 63.6%) | 25.10 (23.23, 27.13) | -0.05 (-0.19, 0.09) | 0.80 (0.64, 1.00) |
| Day 29 | Pseudovirus-nAb cID50 | 55 | 51.7/58 = 89.1% (77.4%, 95.1%) | 15.45 (11.80, 20.22) | 730 | 10330.5/11114.3 = 92.9% (89.9%, 95.1%) | 18.14 (16.67, 19.75) | -0.04 (-0.16, 0.03) | 0.85 (0.64, 1.13) |
| Day 29 | Anti RBD IgG (BAU/ml) | 55 | 58/58 = 100.0% (100.0%, 100.0%) | 417.16 (261.39, 665.77) | 730 | 11011.6/11114.3 = 99.1% (97.5%, 99.7%) | 499.41 (437.47, 570.12) | 0.01 (0, 0.03) | 0.84 (0.51, 1.36) |
| Day 29 | Anti Spike IgG (BAU/ml) | 55 | 58/58 = 100.0% (100.0%, 100.0%) | 192.02 (135.69, 271.72) | 730 | 11002.1/11114.3 = 99.0% (97.1%, 99.6%) | 267.74 (240.38, 298.22) | 0.01 (0, 0.03) | 0.72 (0.50, 1.03) |
| Day 29 | Anti N IgG (BAU/ml) | 55 | 32.7/58 = 56.4% (42.8%, 69.0%) | 34.75 (21.47, 56.25) | 730 | 7060.5/11114.3 = 63.5% (59.0%, 67.8%) | 39.55 (33.99, 46.03) | -0.07 (-0.21, 0.06) | 0.88 (0.53, 1.46) |
| Day 57 | Pseudovirus-nAb cID80 | 48 | 51/51 = 100.0% (100.0%, 100.0%) | 378.93 (284.93, 503.95) | 728 | 11049.6/11112 = 99.4% (97.7%, 99.9%) | 562.59 (509.18, 621.61) | 0.01 (0, 0.02) | 0.67 (0.50, 0.91) |
| Day 57 | Pseudovirus-nAb cID50 | 48 | 51/51 = 100.0% (100.0%, 100.0%) | 281.62 (200.94, 394.69) | 728 | 11112/11112 = 100.0% (100.0%, 100.0%) | 423.23 (381.49, 469.52) | 0 (0, 0) | 0.67 (0.47, 0.95) |
| Day 57 | Anti RBD IgG (BAU/ml) | 48 | 51/51 = 100.0% (100.0%, 100.0%) | 3030.89 (1995.48, 4603.55) | 728 | 11076/11112 = 99.7% (98.6%, 99.9%) | 3712.65 (3236.69, 4258.59) | 0 (0, 0.01) | 0.82 (0.53, 1.27) |
| Day 57 | Anti Spike IgG (BAU/ml) | 48 | 51/51 = 100.0% (100.0%, 100.0%) | 1697.56 (1221.51, 2359.15) | 728 | 11112/11112 = 100.0% (100.0%, 100.0%) | 2695.30 (2409.29, 3015.27) | 0 (0, 0) | 0.63 (0.44, 0.89) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Day 57 | Anti N IgG (BAU/ml) | 48 | 35.1/51 = 68.7% (54.0%, 80.5%) | 64.51 (38.74, 107.43) | 728 | 8984/11112 = 80.8% (76.8%, 84.4%) | 106.15 (90.74, 124.18) | -0.12 (-0.27, 0) | 0.61 (0.36, 1.04) |

Cases for Day 29 markers are baseline negative per-protocol vaccine recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 29 study visit. Cases for Day 57 markers are baseline negative per-protocol vaccine recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 57 study visit. Non-cases/Controls are baseline negative per-protocol vaccine recipients sampled into the random subcohort with no COVID-19 endpoint diagnosis by the time of data-cut.

N is the number of cases sampled into the subcohort within baseline covariate strata.

The denominator in Resp Rate is the number of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

## 2.6 Antibody levels in the baseline SARS-CoV-2 positive per-protocol cohort (vaccine recipients)

Table 2.6: Antibody levels in the baseline SARS-CoV-2 positive per-protocol cohort (vaccine recipients)



| | | Baseline SARS-CoV-2 Positive Vaccine Recipients | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Cases* | | | Non-Cases/Control | | | Comparison | |
| Visit | Marker | N | Resp rate | GMT/GMC | N | Resp rate | GMT/GMC | Resp Rate Difference | GMTR/GMCR |
| Day 29 | Pseudovirus-nAb cID80 | 5 | 3/5 = 60.0% (10.6%, 95.0%) | 31.84 (19.25, 52.65) | 222 | 742.7/1143 = 65.0% (56.7%, 72.4%) | 38.39 (32.96, 44.70) | -0.05 (-0.55, 0.31) | 0.83 (0.49, 1.40) |
| Day 29 | Pseudovirus-nAb cID50 | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 35.88 (21.61, 59.58) | 222 | 1076.9/1143 = 94.2% (88.3%, 97.2%) | 28.02 (24.68, 31.80) | 0.06 (0.03, 0.12) | 1.28 (0.76, 2.16) |
| Day 29 | Anti RBD IgG (BAU/ml) | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 240.20 (51.93, 1111.05) | 222 | 1143/1143 = 100.0% (100.0%, 100.0%) | 737.72 (569.78, 955.14) | 0 (0, 0) | 0.33 (0.07, 1.54) |
| Day 29 | Anti Spike IgG (BAU/ml) | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 157.52 (102.73, 241.52) | 222 | 1130.6/1143 = 98.9% (92.6%, 99.9%) | 373.34 (307.38, 453.46) | 0.01 (0, 0.07) | 0.42 (0.26, 0.67) |
| Day 29 | Anti N IgG (BAU/ml) | 5 | 4/5 = 80.0% (15.2%, 98.9%) | 141.72 (55.78, 360.09) | 222 | 807.8/1143 = 70.7% (62.4%, 77.7%) | 53.39 (41.91, 68.01) | 0.09 (-0.56, 0.3) | 2.65 (1.01, 6.96) |
| Day 57 | Pseudovirus-nAb cID80 | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 1053.93 (647.80, 1714.67) | 222 | 1142/1142 = 100.0% (100.0%, 100.0%) | 1296.05 (1119.96, 1499.82) | 0 (0, 0) | 0.81 (0.49, 1.35) |
| Day 57 | Pseudovirus-nAb cID50 | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 856.91 (410.78, 1787.56) | 222 | 1142/1142 = 100.0% (100.0%, 100.0%) | 969.91 (799.89, 1176.06) | 0 (0, 0) | 0.88 (0.41, 1.89) |
| Day 57 | Anti RBD IgG (BAU/ml) | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 9233.11 (4223.97, 20182.51) | 222 | 1142/1142 = 100.0% (100.0%, 100.0%) | 6267.55 (5093.73, 7711.87) | 0 (0, 0) | 1.47 (0.66, 3.31) |
| Day 57 | Anti Spike IgG (BAU/ml) | 5 | 5/5 = 100.0% (100.0%, 100.0%) | 4654.13 (2835.42, 7639.39) | 222 | 1142/1142 = 100.0% (100.0%, 100.0%) | 4731.83 (4037.27, 5545.88) | 0 (0, 0) | 0.98 (0.58, 1.66) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Day 57 | Anti N IgG (BAU/ml) | 5 | 4/5 = 80.0% (15.2%, 98.9%) | 182.40 (54.59, 609.44) | 222 | 1046.2/1142 = 91.6% (85.7%, 95.2%) | 199.80 (159.94, 249.59) | -0.12 (-0.76, 0.08) | 0.91 (0.27, 3.11) |

The SAP does not specify correlates analyses in baseline positive vaccine recipients. This table summarizes descriptively the same information for baseline positive vaccine recipients that was summarized for baseline negative vaccine recipients. Cases for Day 29 markers are baseline positive per-protocol vaccine recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 29 study visit. Cases for Day 57 markers are baseline positive per-protocol vaccine recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 57 study visit. Non-cases/Controls are baseline positive per-protocol vaccine recipients sampled into the random subcohort with no COVID-19 endpoint diagnosis by the time of data-cut.

N is the number of cases sampled into the subcohort within baseline covariate strata.

The denominator in Resp Rate is the number of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

## 2.7 Antibody levels in the baseline SARS-CoV-2 positive per-protocol cohort (placebo recipients)

Table 2.7: Antibody levels in the baseline SARS-CoV-2 positive per-protocol cohort (placebo recipients)

| | | Baseline SARS-CoV-2 Positive Placebo Recipients | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Cases* | | | Non-Cases/Control | | | Comparison | |
| Visit | Marker | N | Resp rate | GMT/GMC | N | Resp rate | GMT/GMC | Resp Rate Difference | GMTR/GMCR |
| Day 29 | Pseudovirus-nAb cID80 | 4 | 3/4 = 75.0% (7.1%, 99.2%) | 24.88 (12.18, 50.82) | 248 | 373.4/1070 = 34.9% (28.2%, 42.3%) | 17.97 (15.65, 20.62) | 0.4 (-0.28, 0.65) | 1.38 (0.67, 2.87) |
| Day 29 | Pseudovirus-nAb cID50 | 4 | 2/4 = 50.0% (4.0%, 96.0%) | 6.18 (1.94, 19.74) | 248 | 777.3/1070 = 72.6% (64.8%, 79.3%) | 11.64 (9.99, 13.58) | -0.23 (-0.69, 0.24) | 0.53 (0.16, 1.71) |
| Day 29 | Anti RBD IgG (BAU/ml) | 4 | 4/4 = 100.0% (100.0%, 100.0%) | 756.08 (88.88, 6431.90) | 248 | 1040.9/1070 = 97.3% (92.9%, 99.0%) | 306.72 (235.69, 399.17) | 0.03 (0.01, 0.07) | 2.47 (0.29, 21.31) |
| Day 29 | Anti Spike IgG (BAU/ml) | 4 | 4/4 = 100.0% (100.0%, 100.0%) | 450.29 (151.38, 1339.45) | 248 | 1053.8/1070 = 98.5% (96.0%, 99.4%) | 180.26 (145.92, 222.69) | 0.02 (0.01, 0.04) | 2.50 (0.82, 7.58) |
| Day 29 | Anti N IgG (BAU/ml) | 4 | 3/4 = 75.0% (7.1%, 99.2%) | 22.00 (3.94, 122.96) | 248 | 575.6/1070 = 53.8% (45.8%, 61.6%) | 23.47 (17.64, 31.22) | 0.21 (-0.47, 0.47) | 0.94 (0.16, 5.36) |
| Day 57 | Pseudovirus-nAb cID80 | 4 | 4/4 = 100.0% (100.0%, 100.0%) | 351.66 (121.28, 1019.68) | 248 | 1063.8/1068 = 99.6% (97.2%, 99.9%) | 444.55 (373.10, 529.69) | 0 (0, 0.03) | 0.79 (0.27, 2.33) |
| Day 57 | Pseudovirus-nAb cID50 | 4 | 4/4 = 100.0% (100.0%, 100.0%) | 664.06 (91.64, 4811.88) | 248 | 1068/1068 = 100.0% (100.0%, 100.0%) | 292.71 (241.83, 354.30) | 0 (0, 0) | 2.27 (0.31, 16.59) |
| Day 57 | Anti RBD IgG (BAU/ml) | 4 | 4/4 = 100.0% (100.0%, 100.0%) | 2249.67 (224.78, 22514.92) | 248 | 1068/1068 = 100.0% (100.0%, 100.0%) | 2787.04 (2188.97, 3548.52) | 0 (0, 0) | 0.81 (0.08, 8.18) |
| Day 57 | Anti Spike IgG (BAU/ml) | 4 | 4/4 = 100.0% (100.0%, 100.0%) | 2622.60 (468.45, 14682.50) | 248 | 1068/1068 = 100.0% (100.0%, 100.0%) | 2100.42 (1718.79, 2566.79) | 0 (0, 0) | 1.25 (0.22, 7.07) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Day 57 | Anti N IgG (BAU/ml) | 4 | 3/4 = 75.0% (7.1%, 99.2%) | 145.45 (14.12, 1498.21) | 248 | 794.2/1068 = 74.4% (66.6%, 80.8%) | 79.56 (60.82, 104.09) | 0.01 (-0.68, 0.26) | 1.83 (0.17, 19.12) |

Cases for Day 29 markers are baseline positive per-protocol placebo recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 29 study visit. Cases for Day 57 markers are baseline positive per-protocol placebo recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 57 study visit. Non-cases/Controls are baseline positive per-protocol placebo recipients sampled into the random subcohort with no COVID-19 endpoint diagnosis by the time of data-cut.

N is the number of cases sampled into the subcohort within baseline covariate strata.

The denominator in Resp Rate is the number of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

# Chapter 3

# Graphical Descriptions of Antibody Marker Data



## 3.1 Boxplots

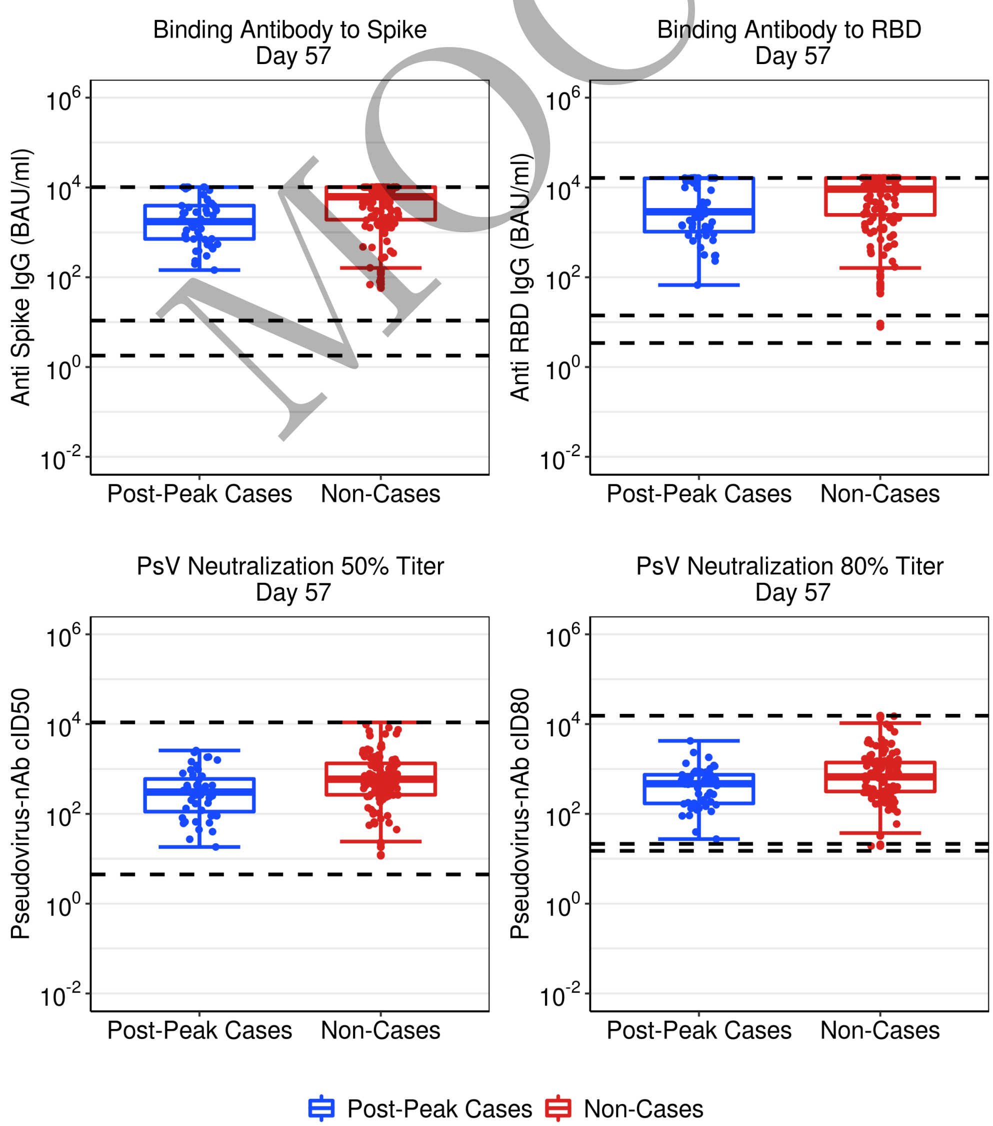



Figure 3.1: Boxplots of D57 Ab markers: vaccine arm. The three dashed lines in each figure are ULOQ, LLOQ, and LLOD, from top to bottom respectively.

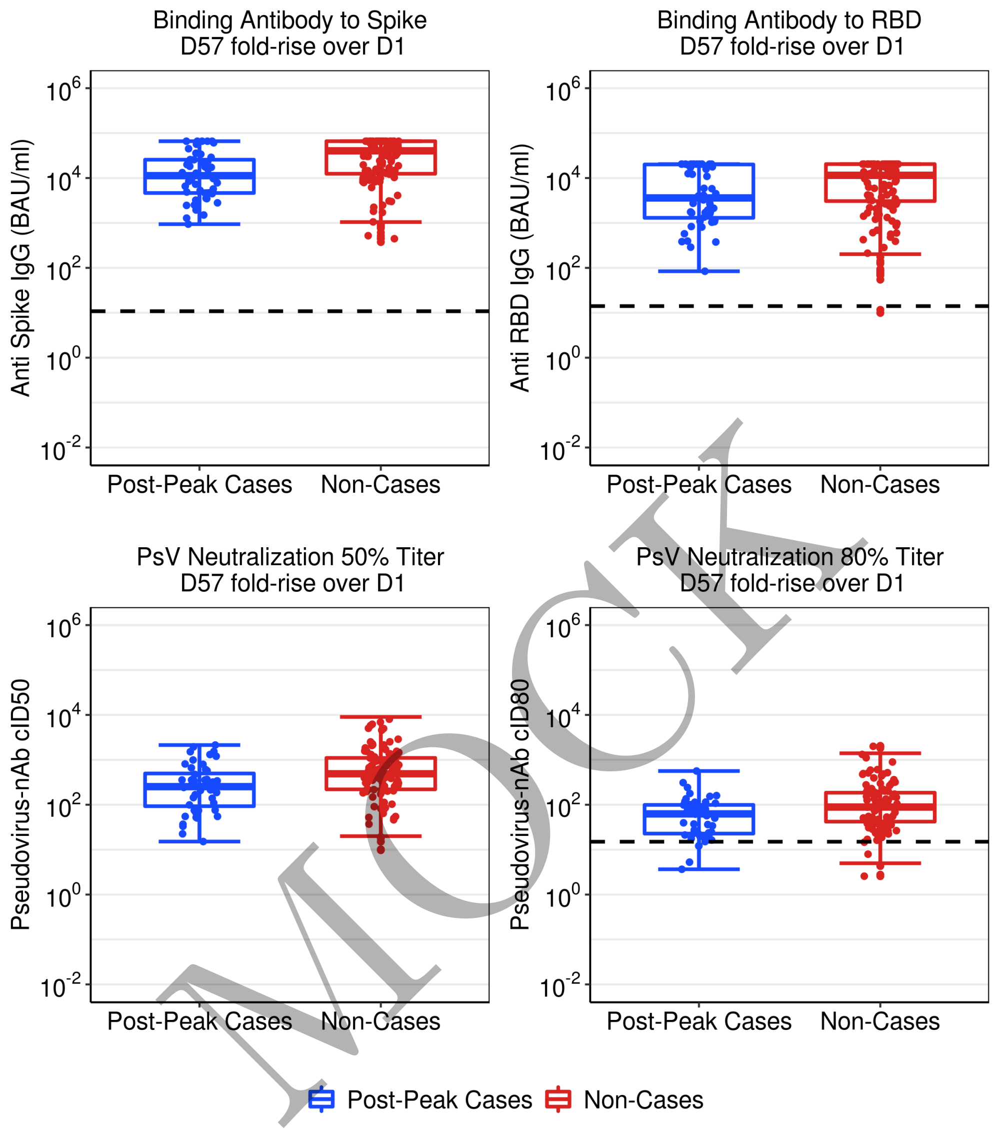



Figure 3.2: Boxplots of D57 fold-rise over D1 Ab markers: vaccine arm.

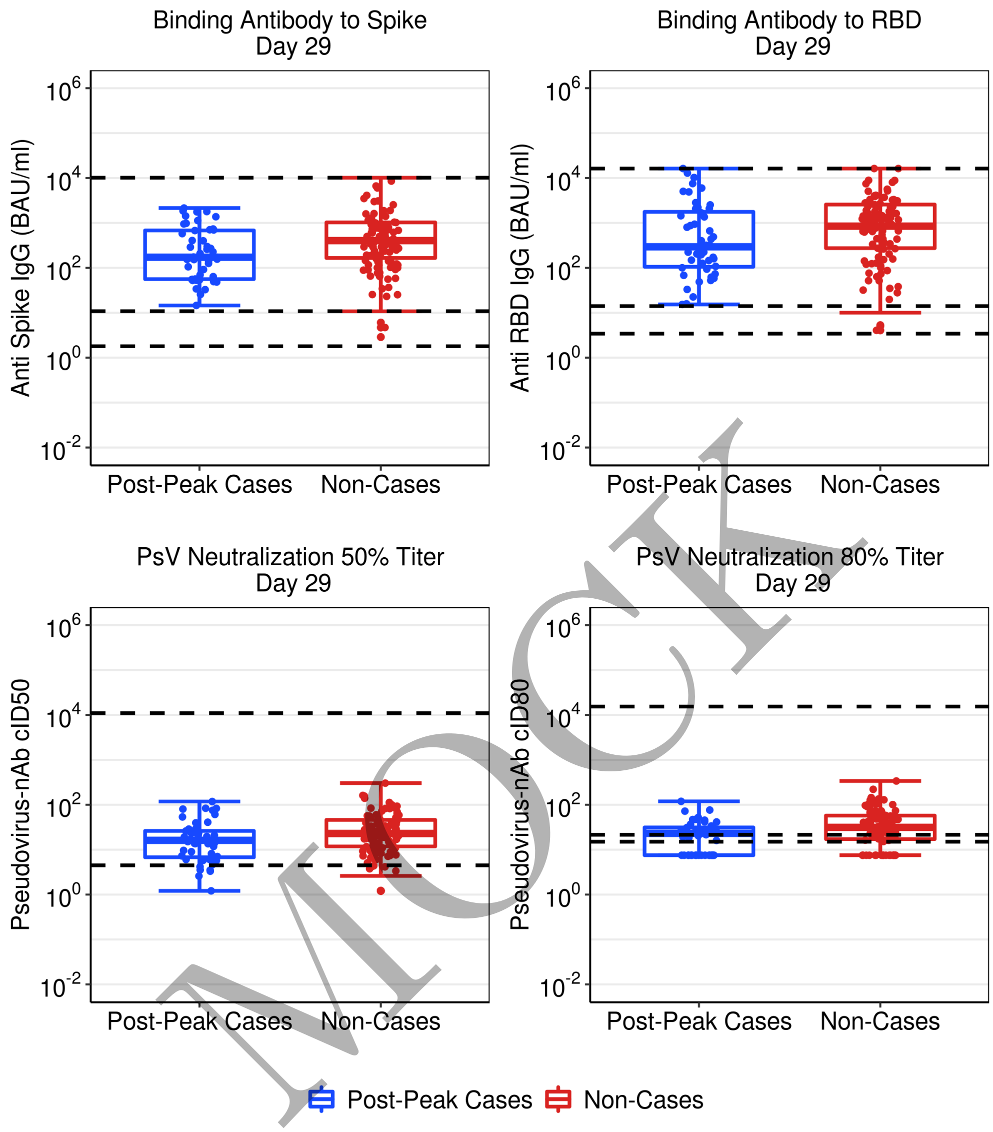



Figure 3.3: Boxplots of D29 Ab markers: vaccine arm. The three dashed lines in each figure are ULOQ, LLOQ, and LLOD, from top to bottom respectively.

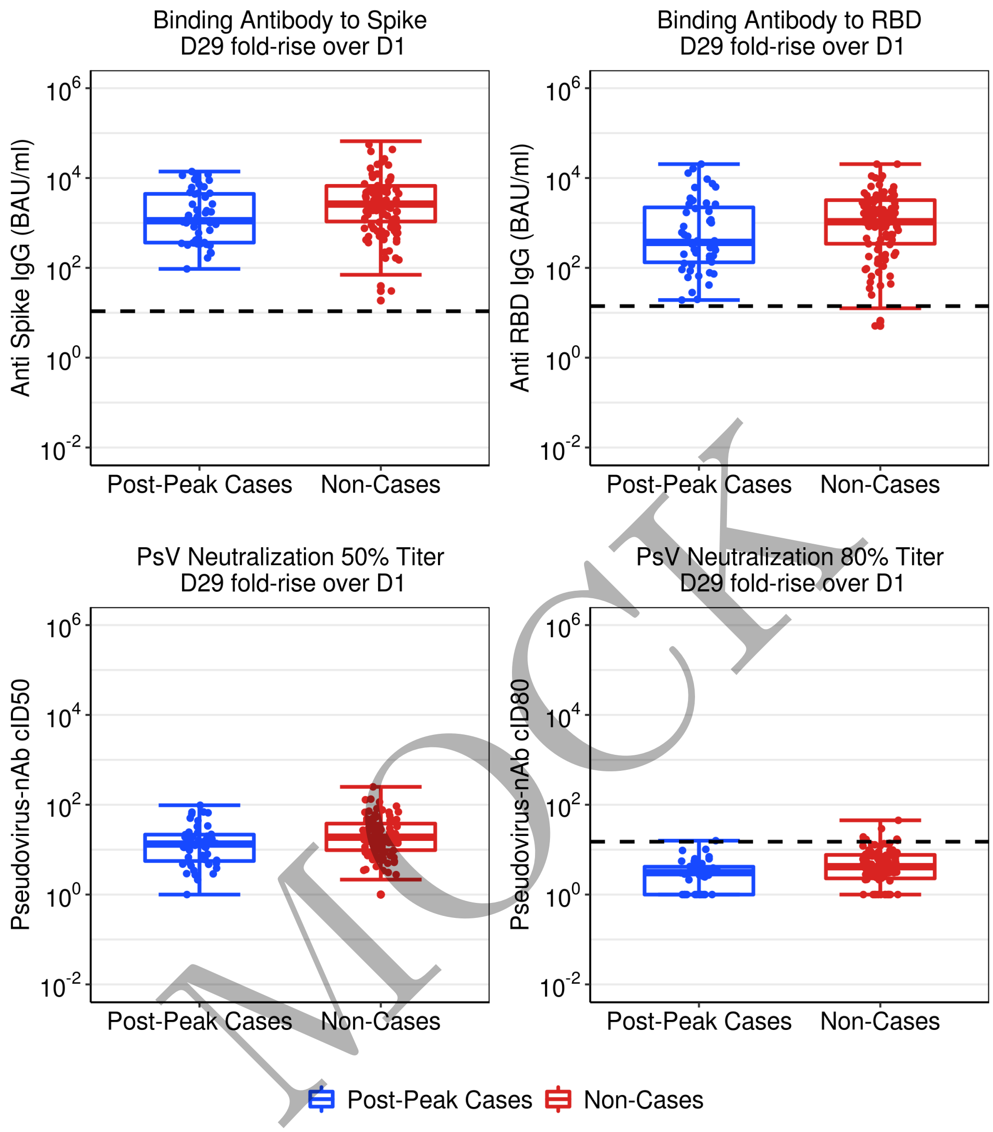



Figure 3.4: Boxplots of D29 fold-rise over D1 Ab markers: vaccine arm.

## 3.2 Weighted RCDF plots

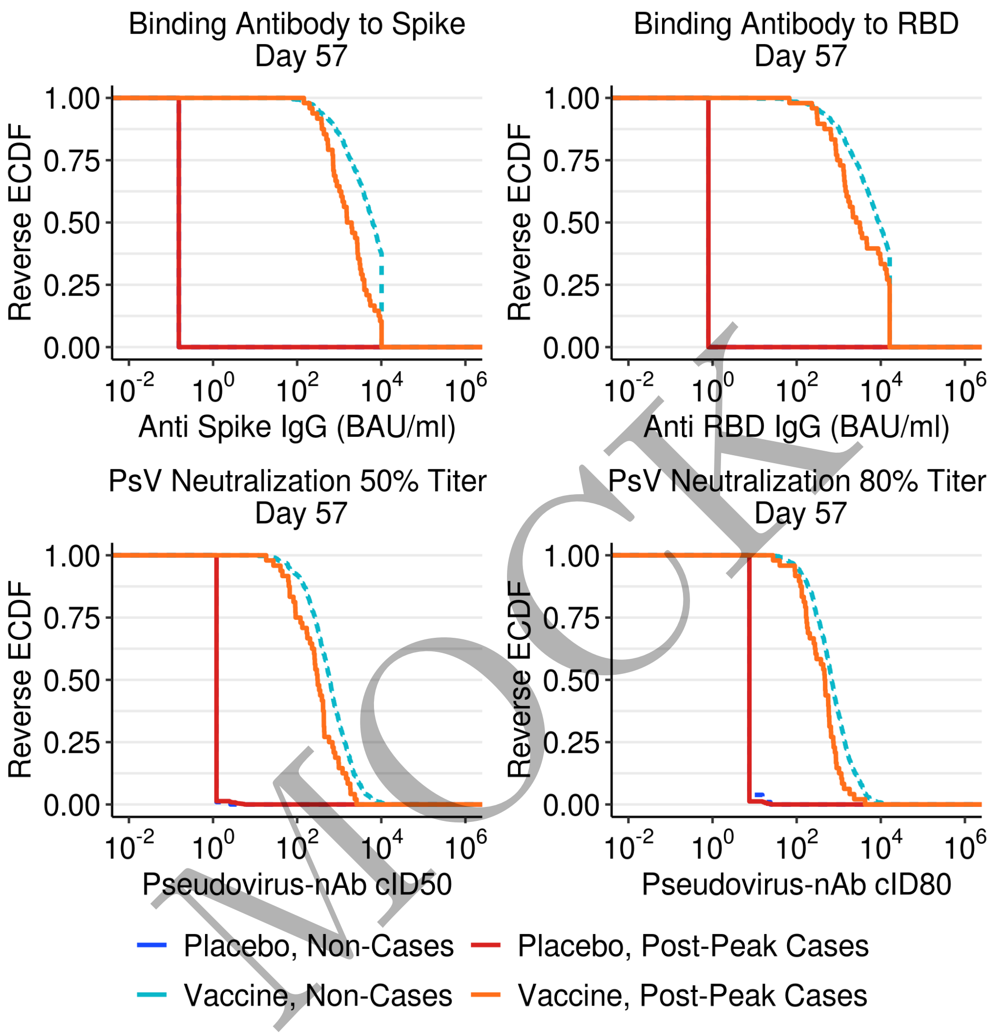



Figure 3.5: RCDF plots for D57 Ab markers by treatment arm.

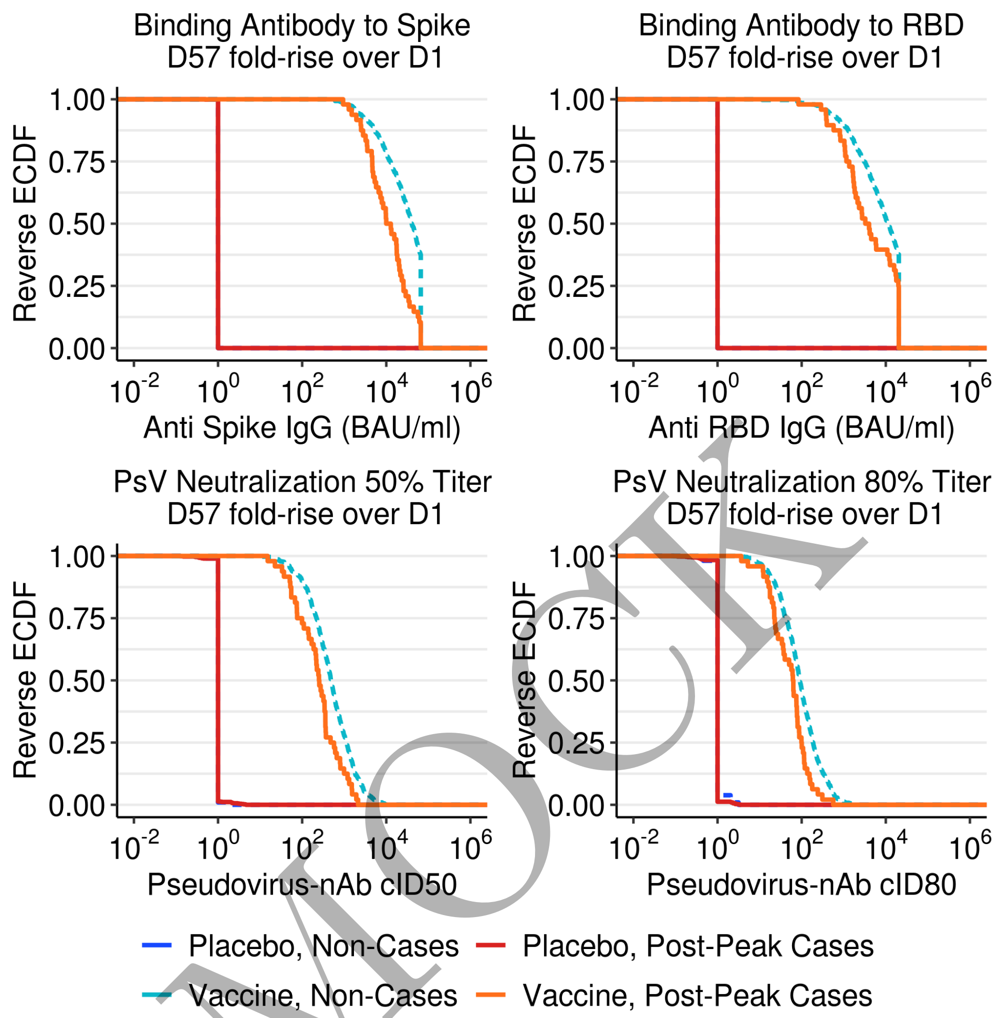



Figure 3.6: RCDF plots for D57 fold-rise over D1 Ab markers by treatment arm.

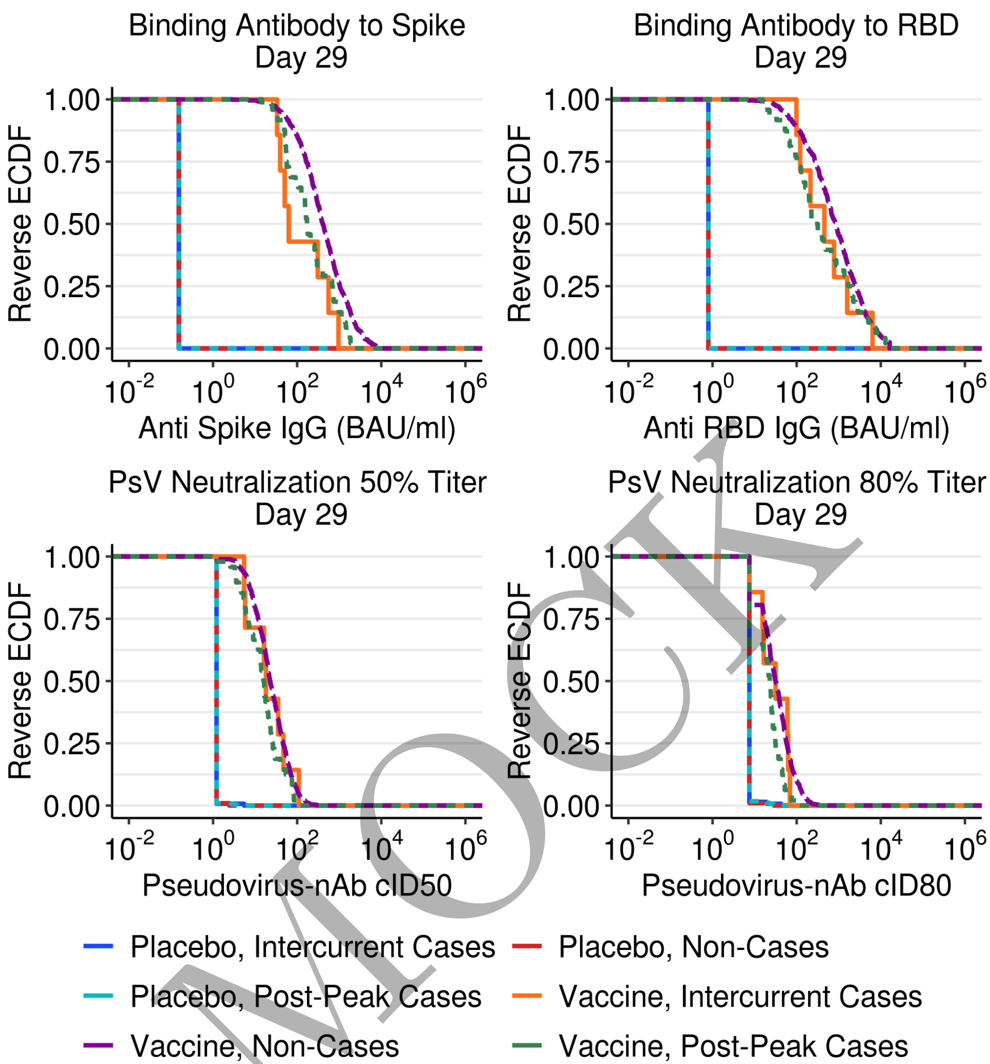



Figure 3.7: RCDF plots for D29 Ab markers by treatment arm.

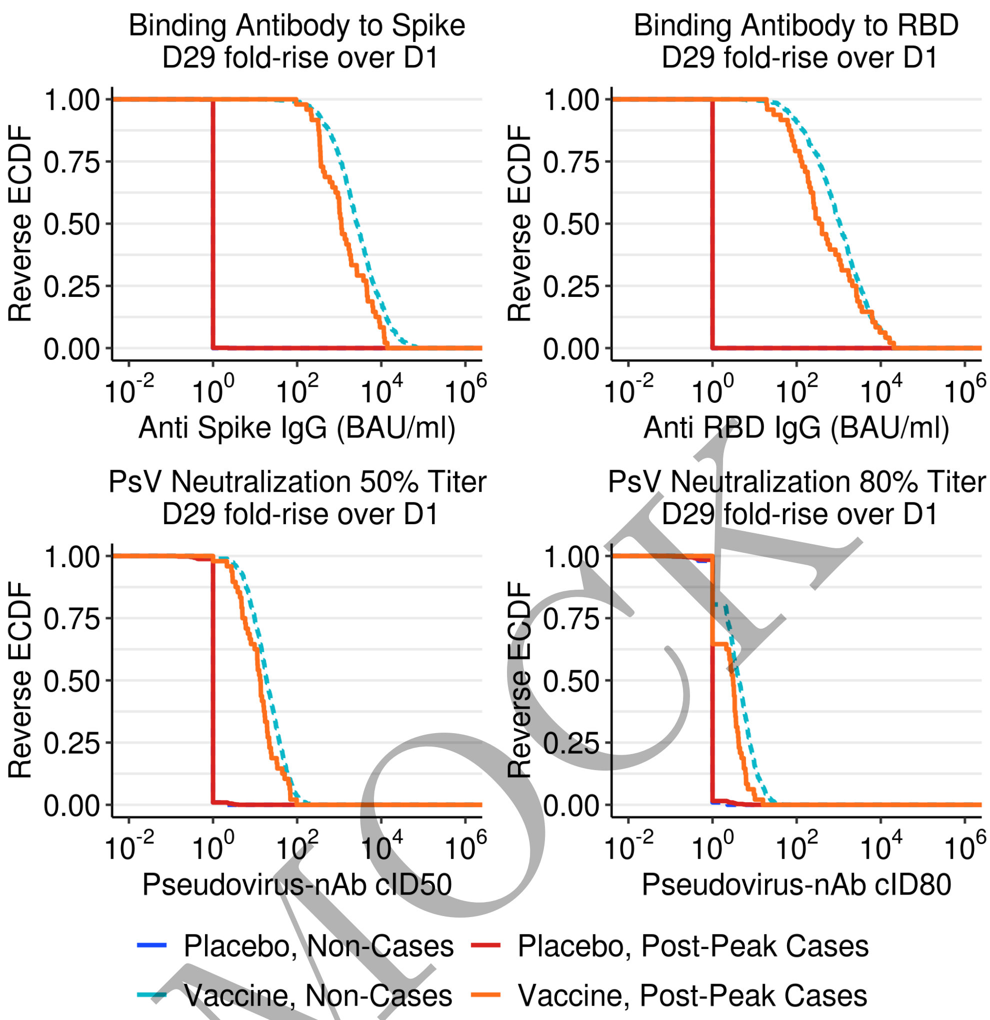



Figure 3.8: RCDF plots for D29 fold-rise over D1 Ab markers by treatment arm.

## 3.3 Weighted RCDF plots of threshold correlate concentration for vaccine efficacy

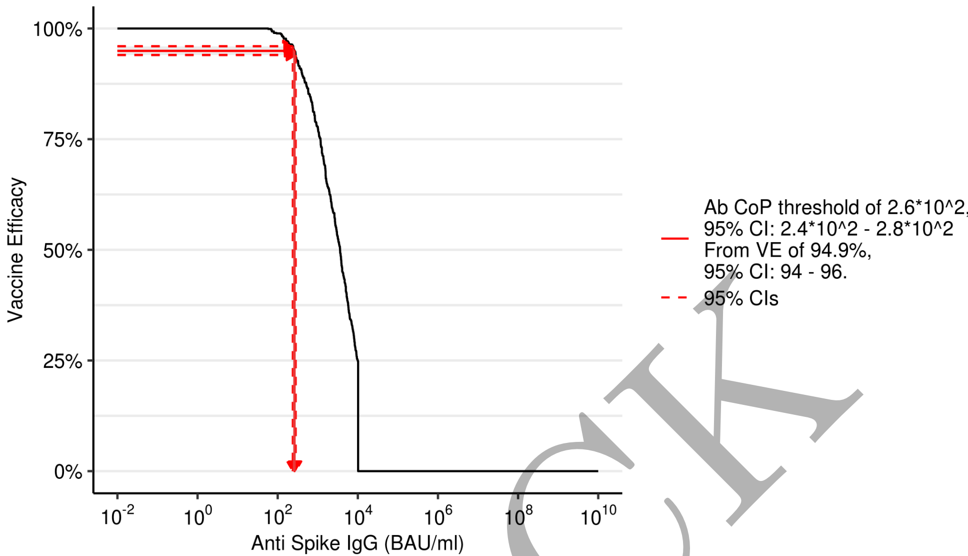



Figure 3.9: Marker RCDF of D57 anti-Spike binding Ab: vaccine arm

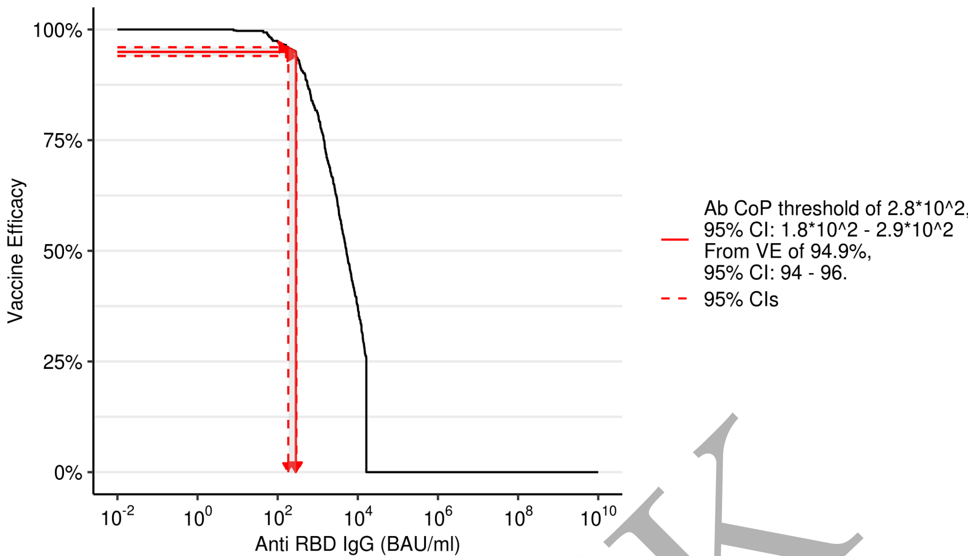



Figure 3.10: Marker RCDF of D57 anti-RBD binding Ab: vaccine arm

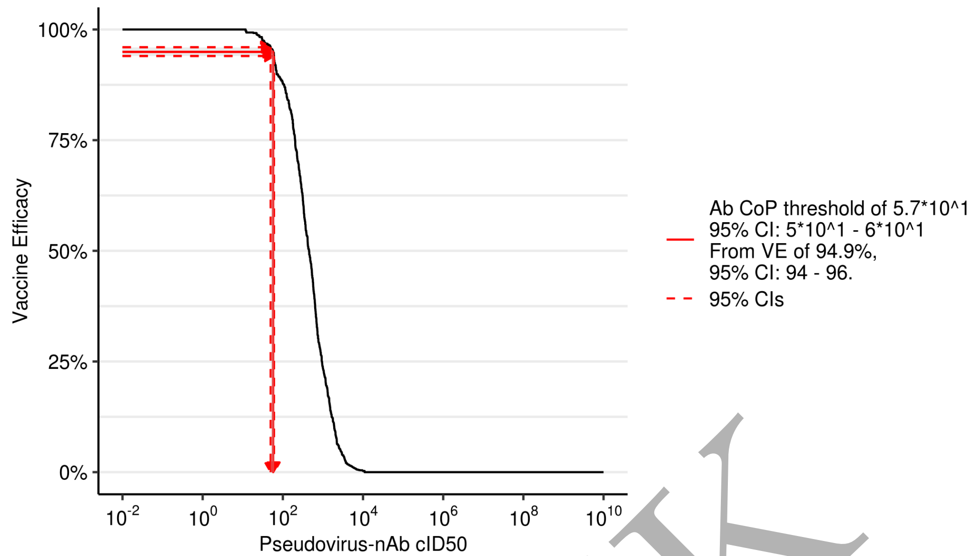



Figure 3.11: Marker RCDF of D57 PsV-nAb ID50: vaccine arm

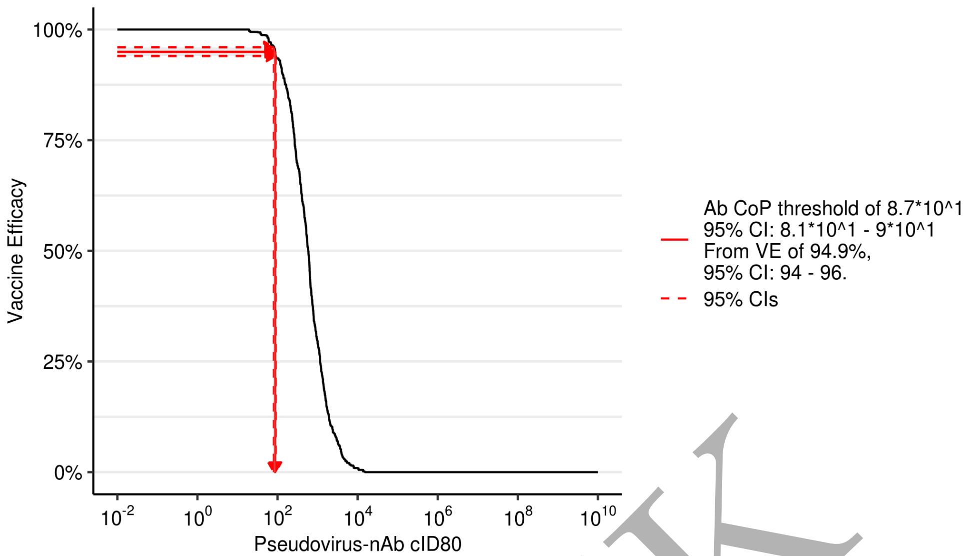



Figure 3.12: Marker RCDF of D57 PsV-nAb ID80: vaccine arm

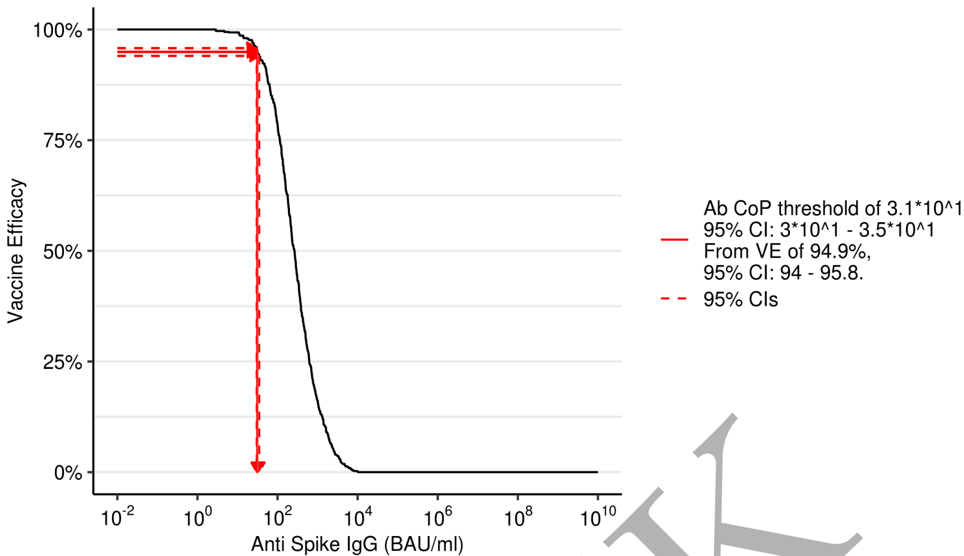



Figure 3.13: Marker RCDF of D29 anti-Spike binding Ab: vaccine arm

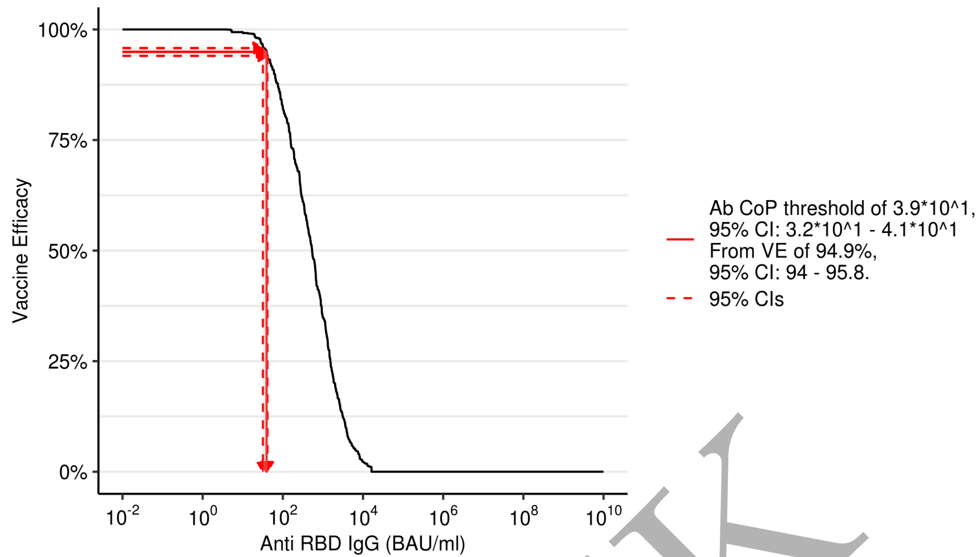



Figure 3.14: Marker RCDF of D29 anti-RBD binding Ab: vaccine arm

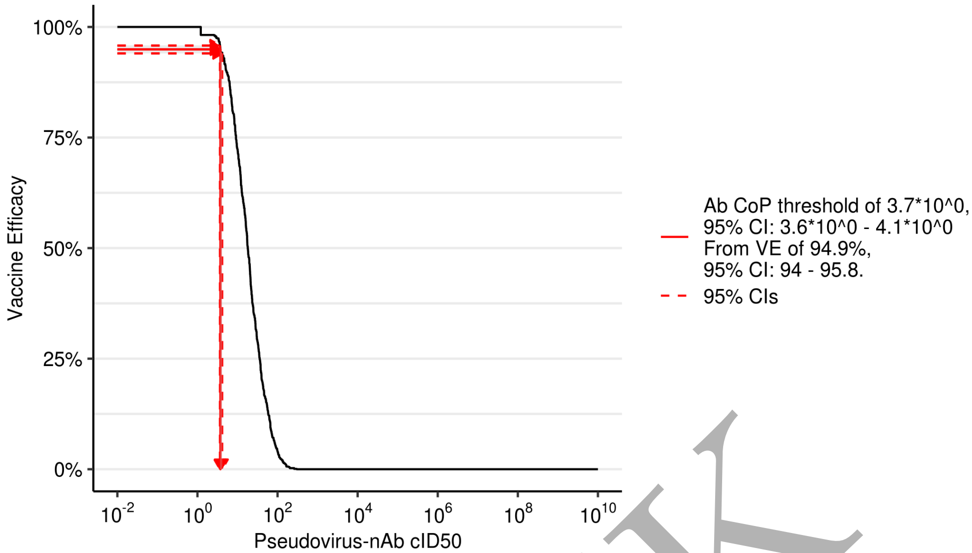



Figure 3.15: Marker RCDF of D29 PsV-nAb ID50: vaccine arm

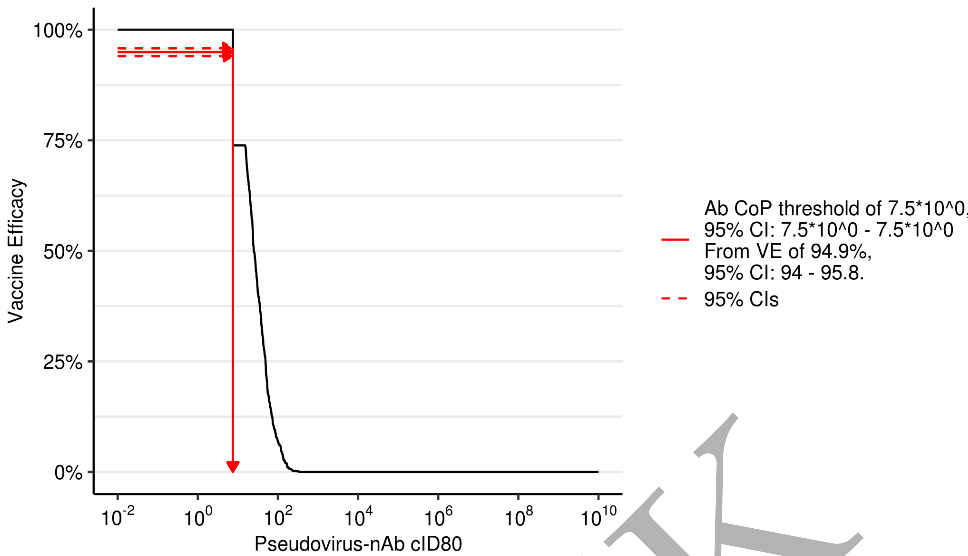



Figure 3.16: Marker RCDF of D29 PsV-nAb ID80: vaccine arm

## 3.4 Spaghetti plots

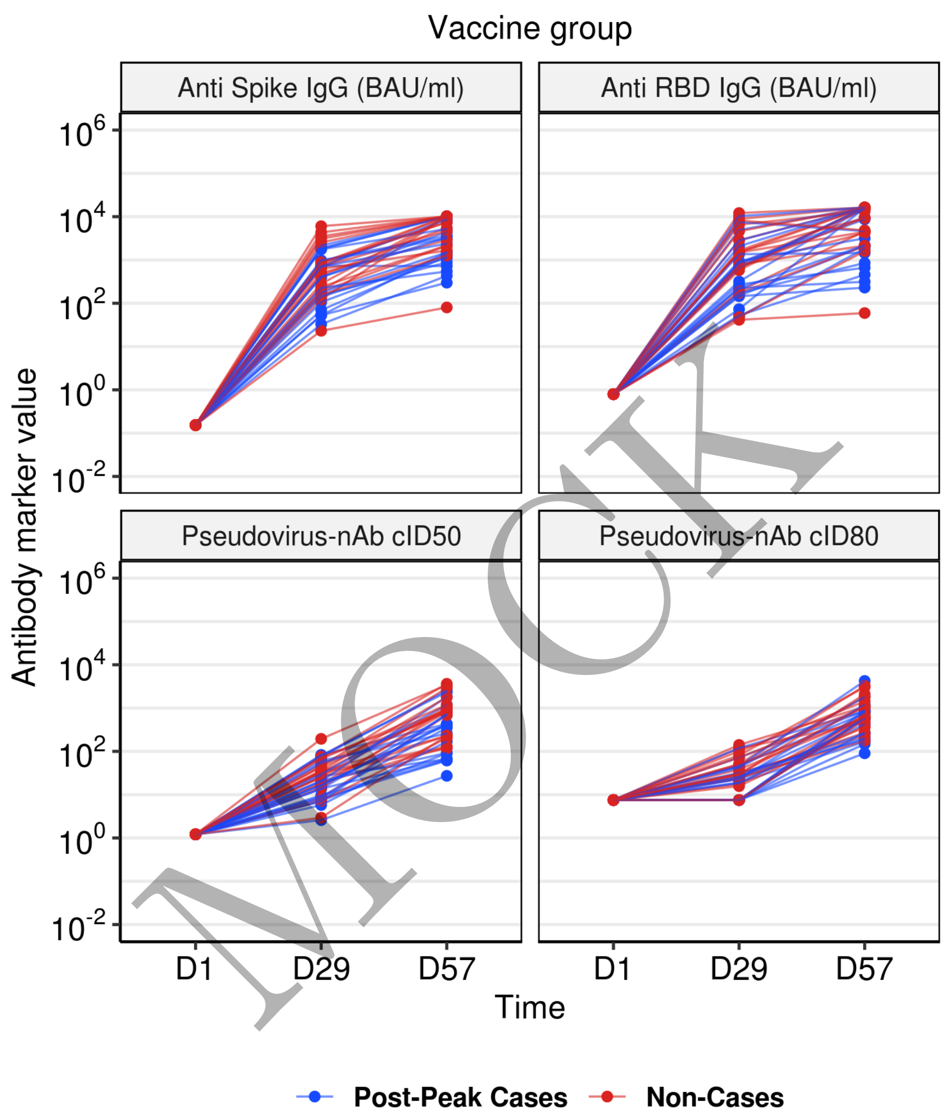


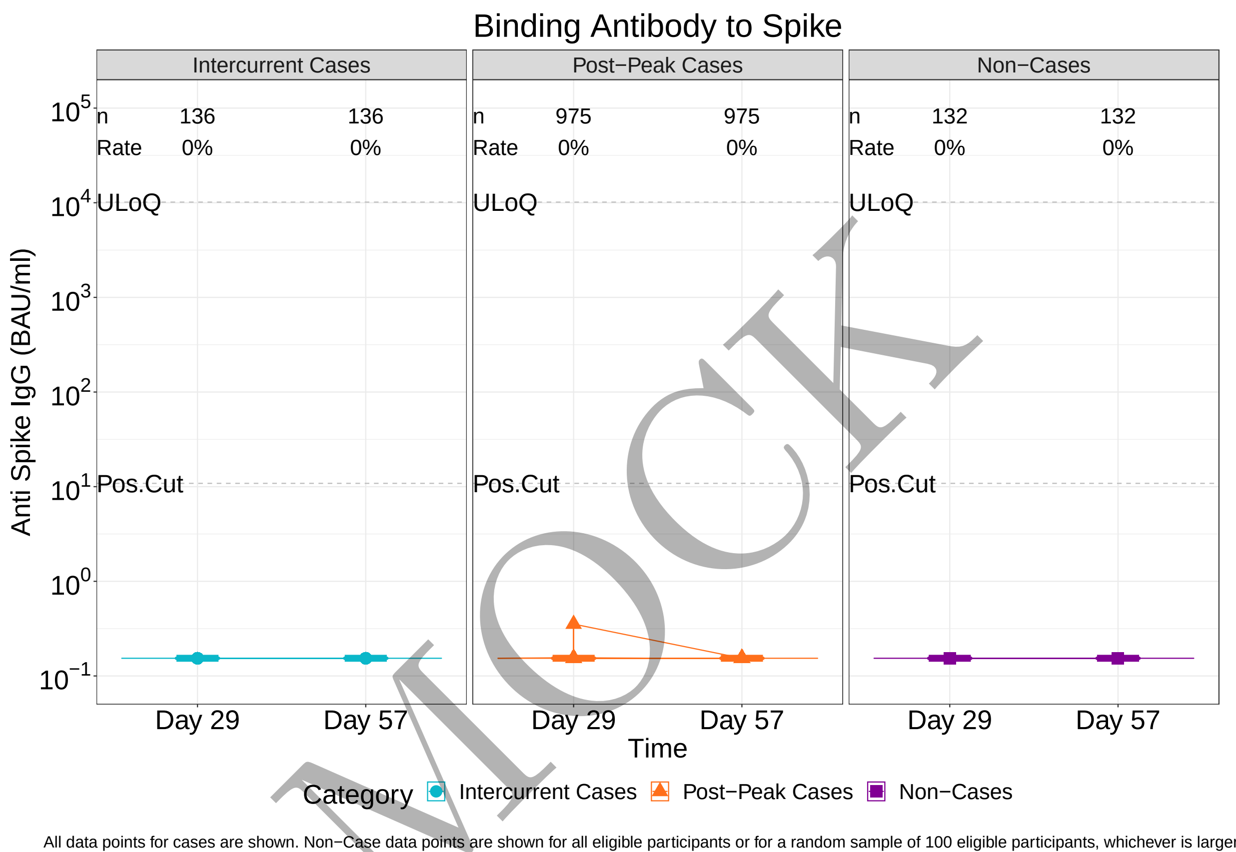


Figure 3.17: Spaghetti Plots of Marker Trajectory: vaccine arm

## 3.5 Violin and line plots

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}



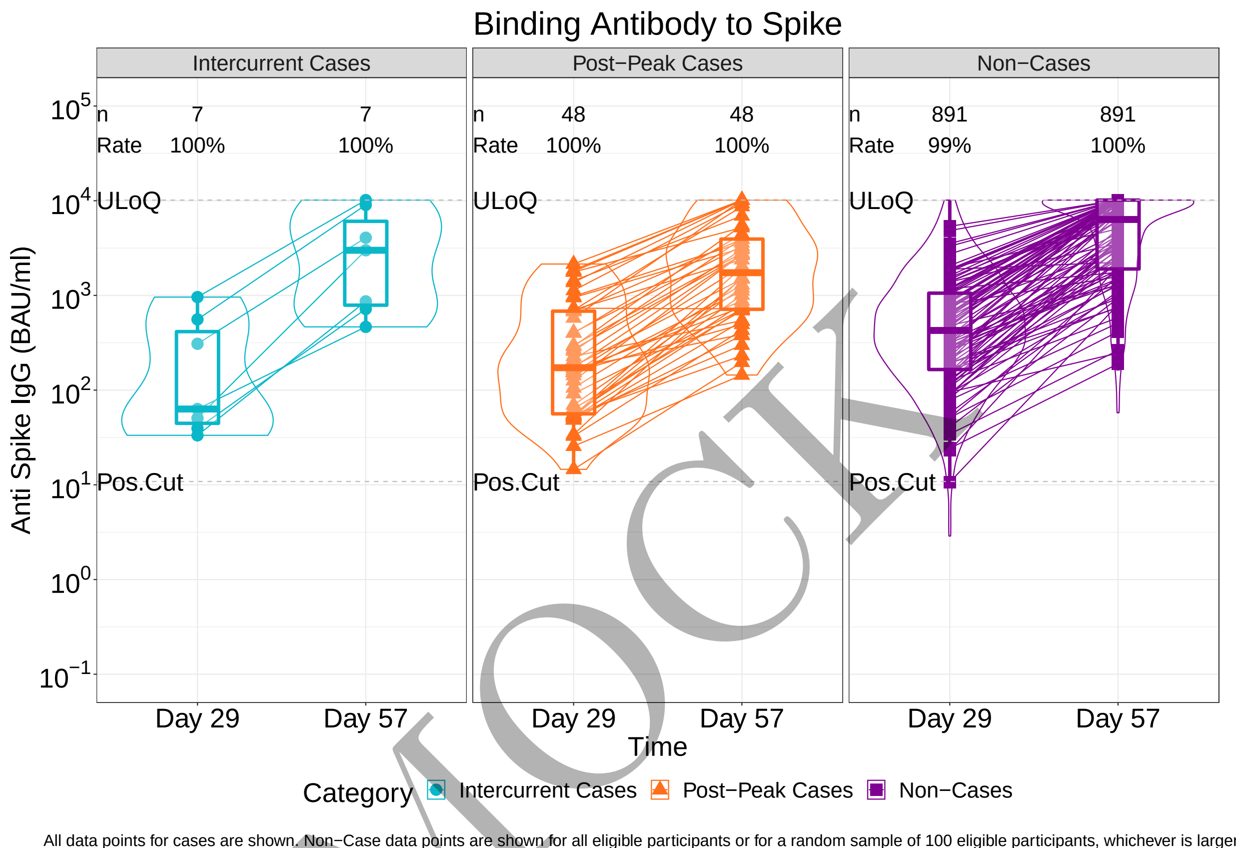

\caption{

Figure 2.5.1: lineplots of Binding Antibody to Spike: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





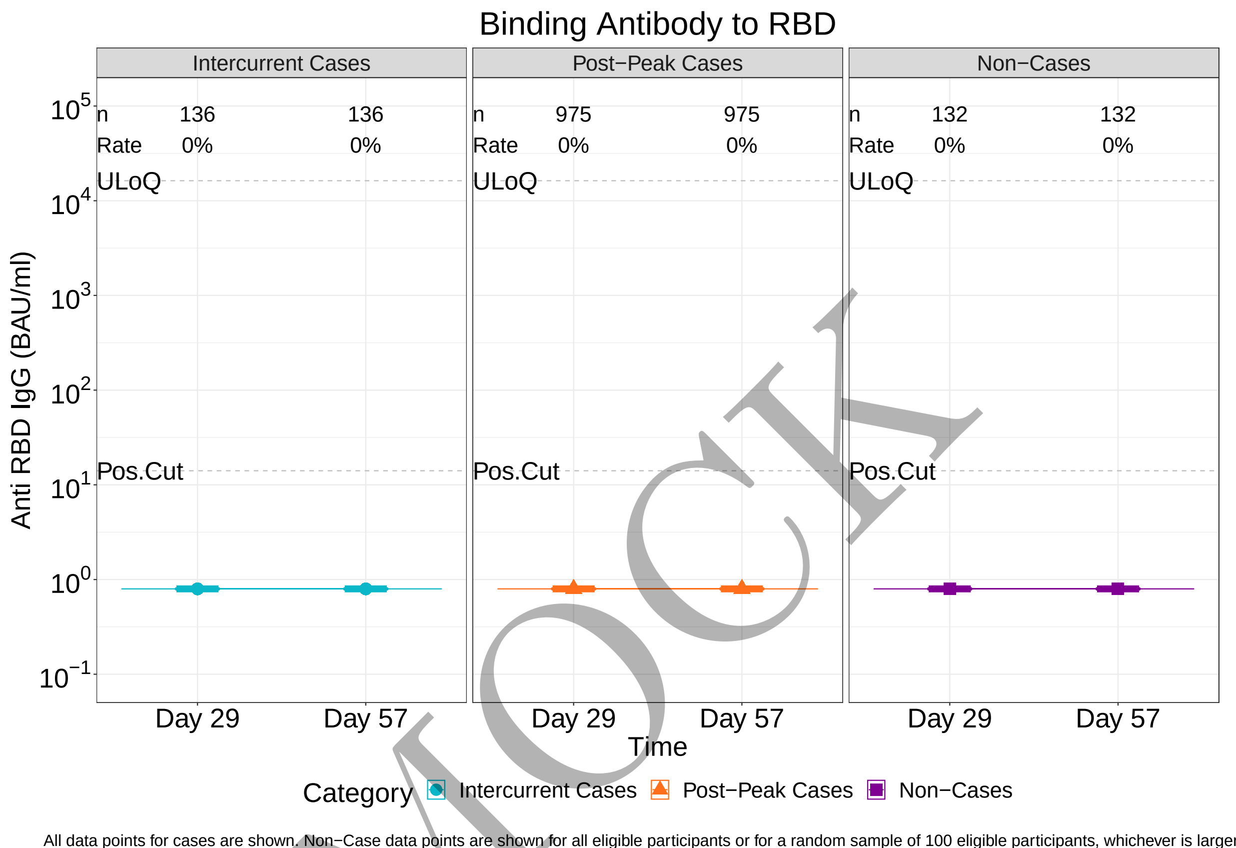

\caption{

Figure 2.5.2: lineplots of Binding Antibody to Spike: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



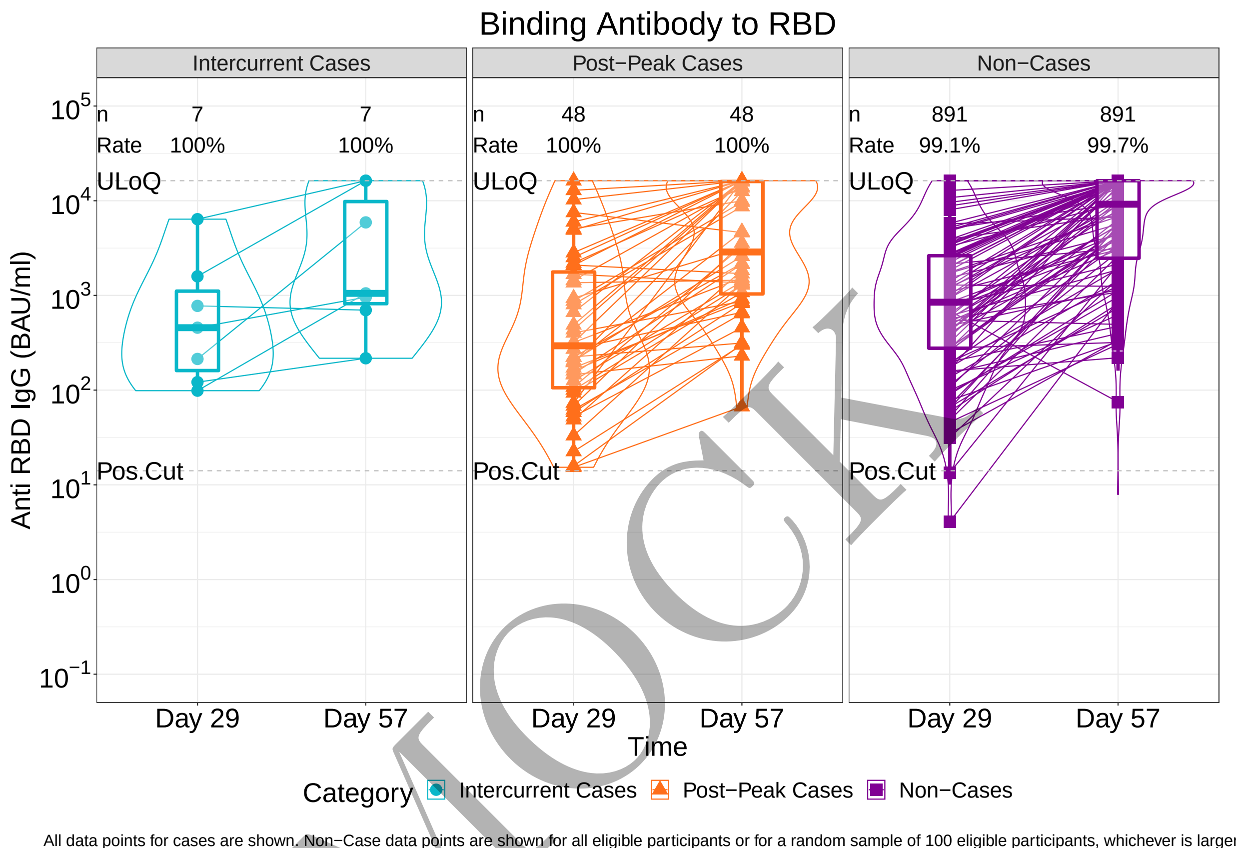

\caption{

Figure 2.5.3: lineplots of Binding Antibody to RBD: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





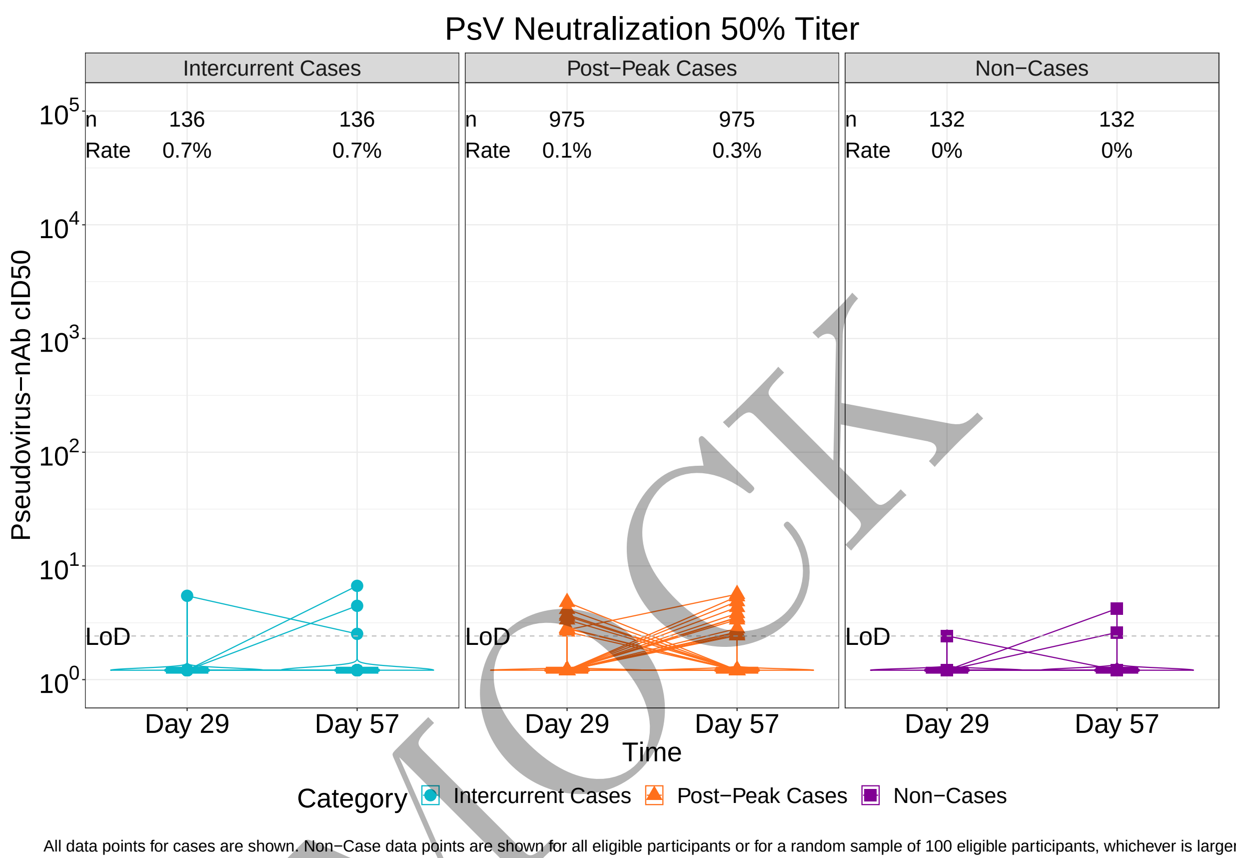

\caption{

Figure 2.5.4: lineplots of Binding Antibody to RBD: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



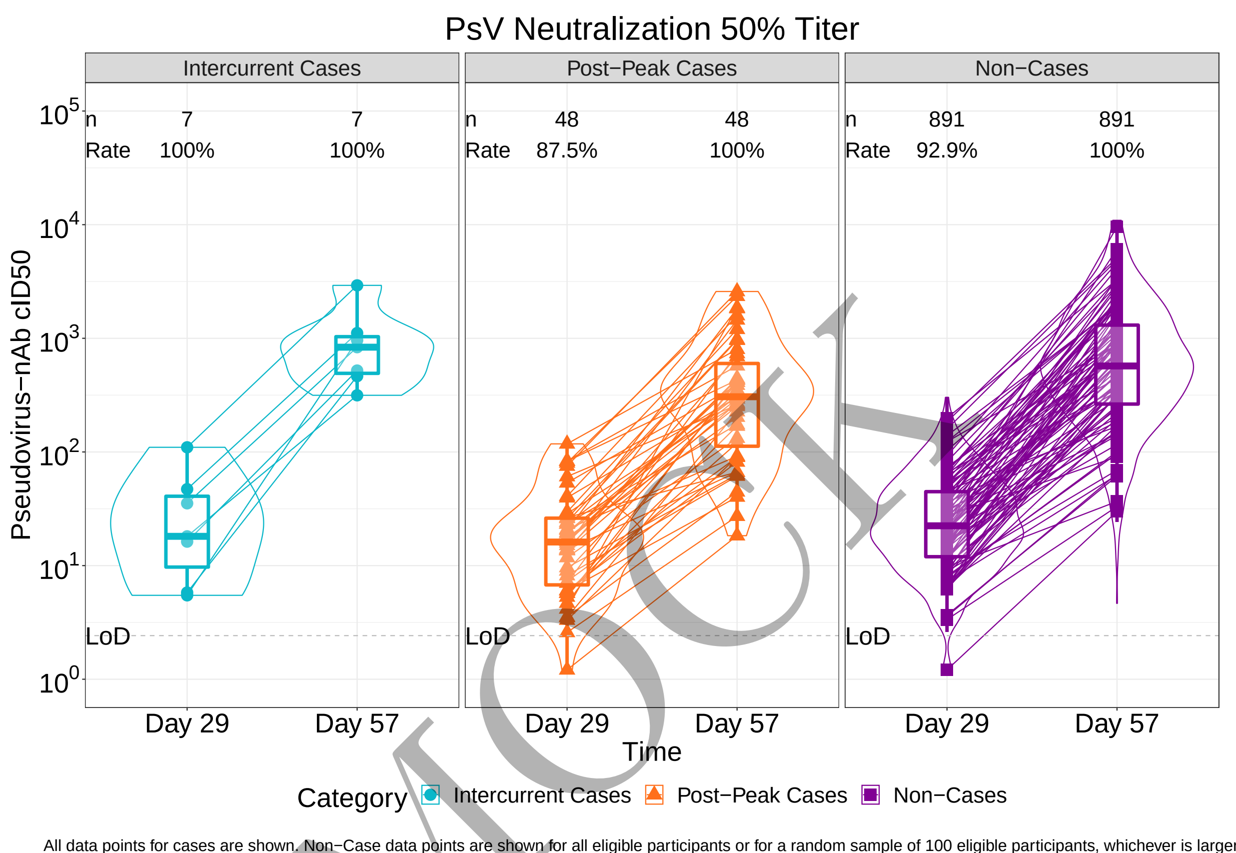

\caption{

Figure 2.5.5: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



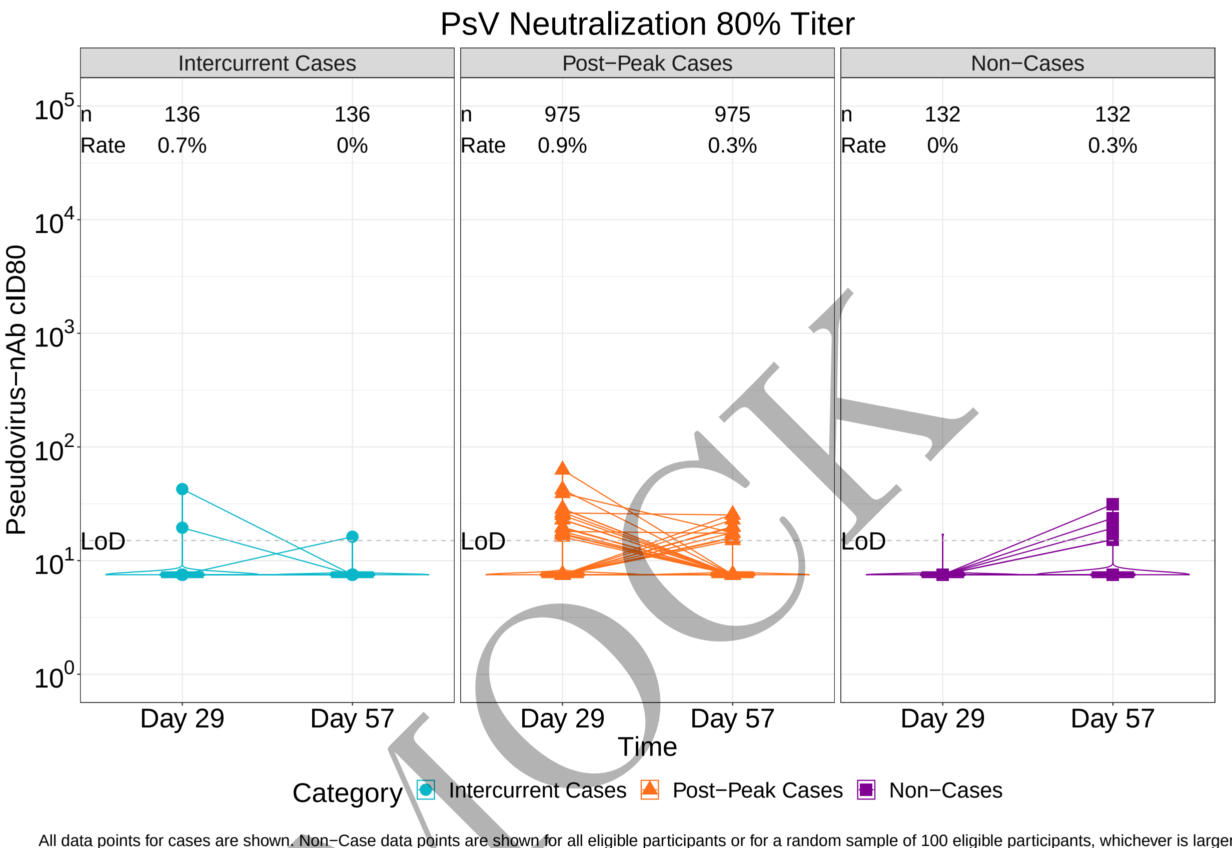

\caption{

Figure 2.5.6: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



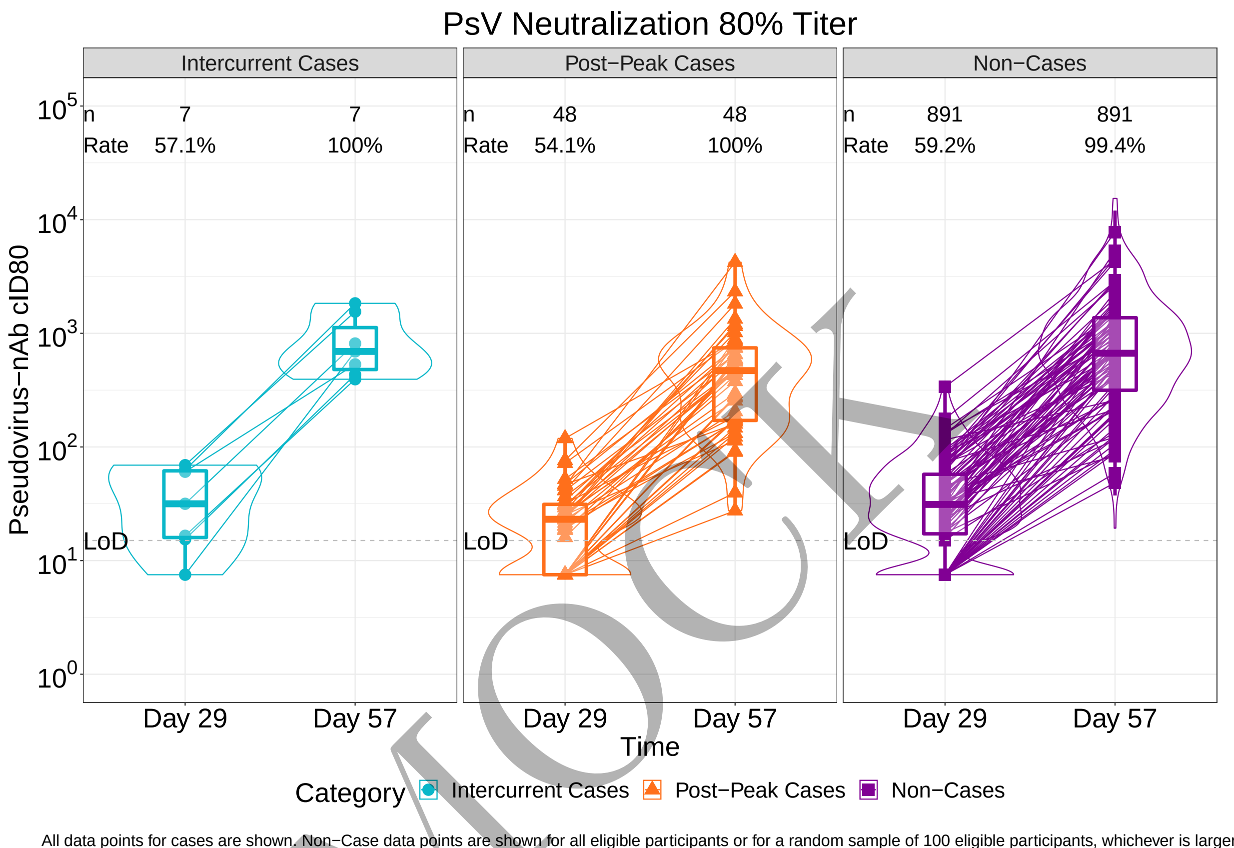

\caption{

Figure 2.5.7: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





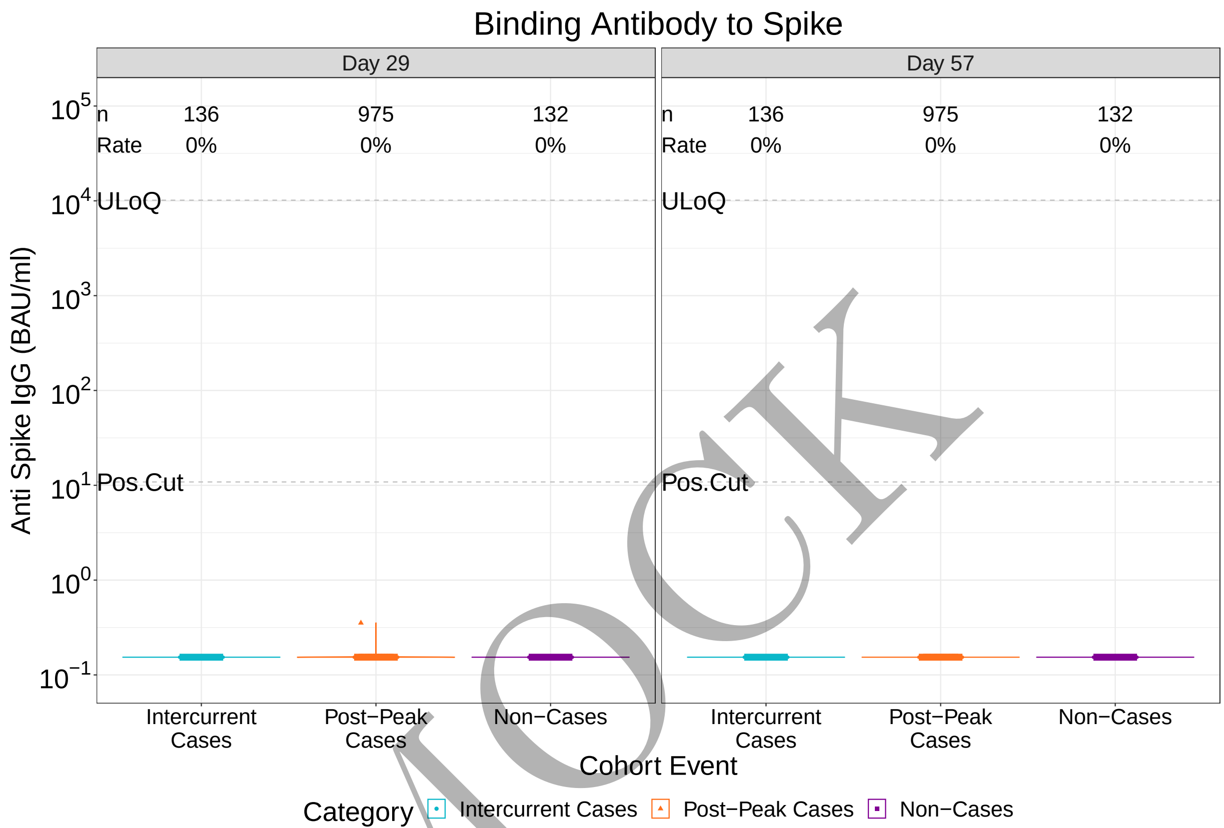

\caption{

Figure 2.5.8: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



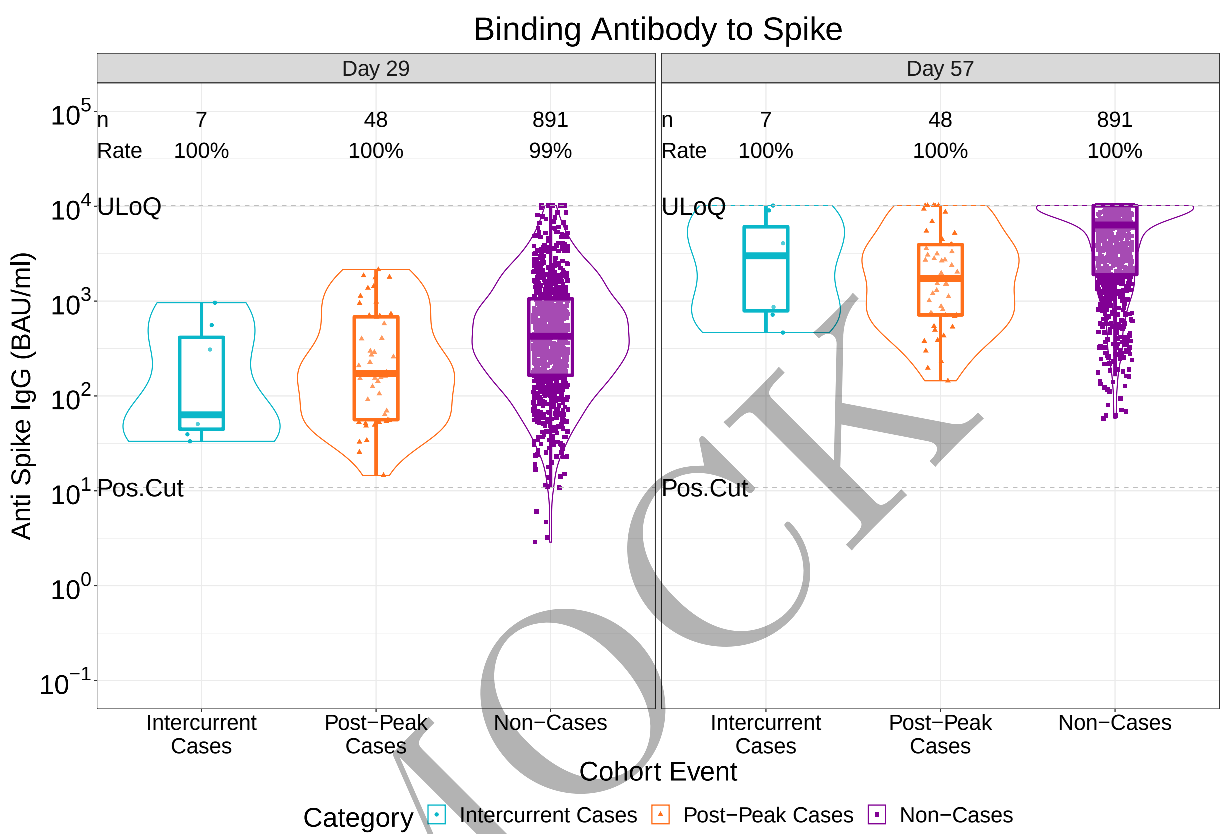

\caption{

Figure 2.5.9: violinplots of Binding Antibody to Spike: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



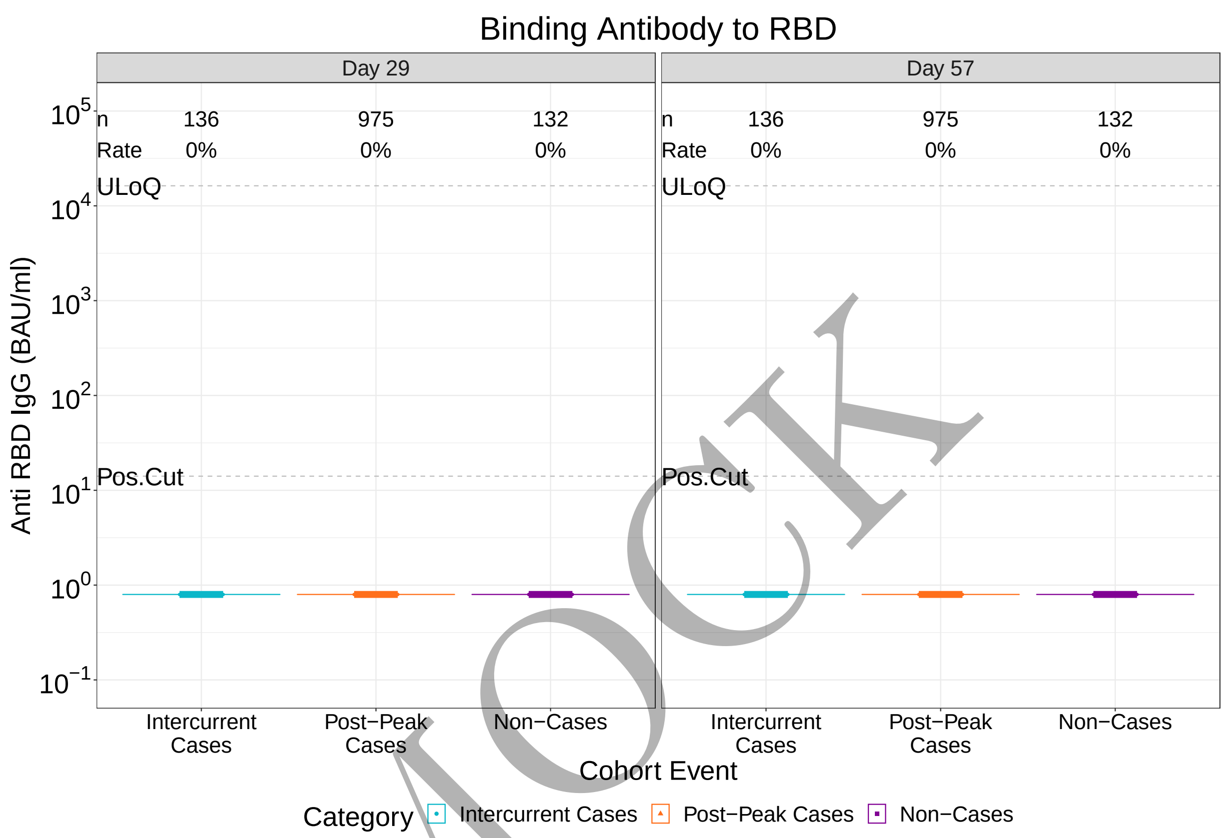

\caption{

Figure 2.5.10: violinplots of Binding Antibody to Spike: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



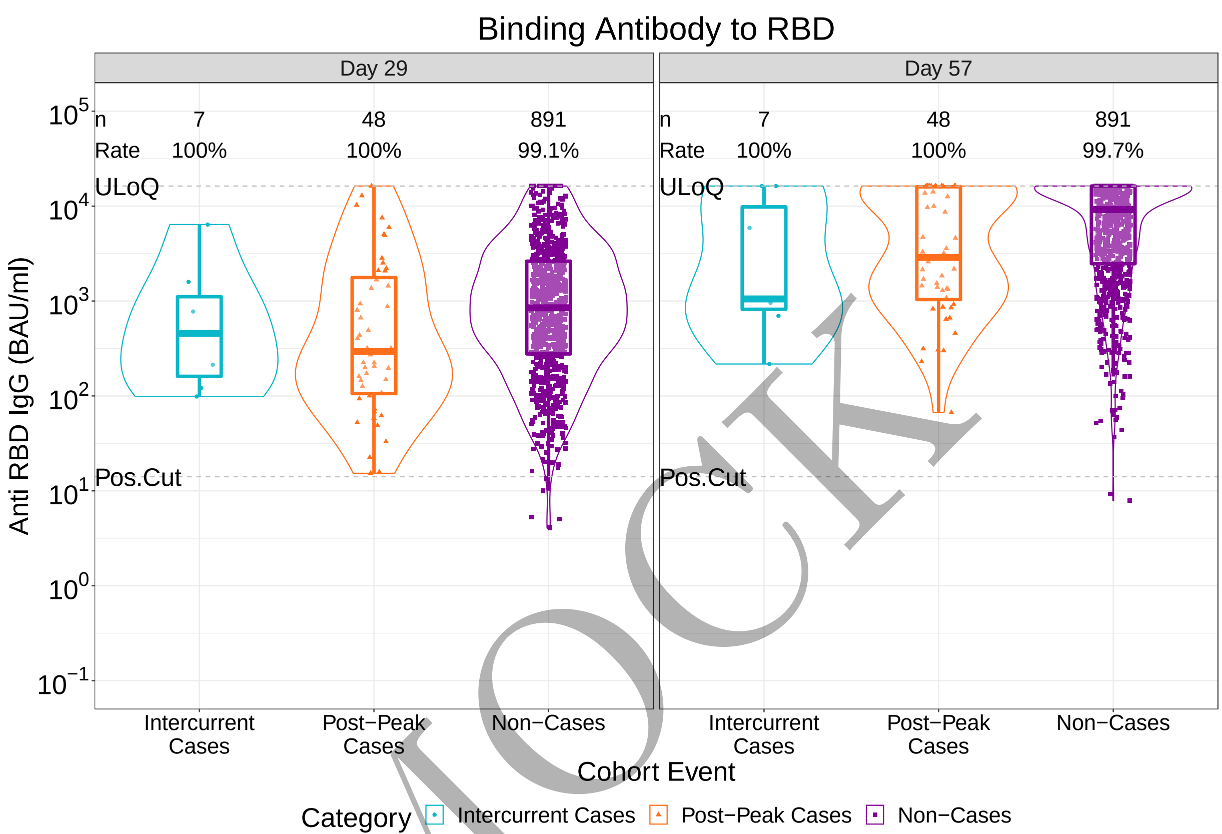

\caption{

Figure 2.5.11: violinplots of Binding Antibody to RBD: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



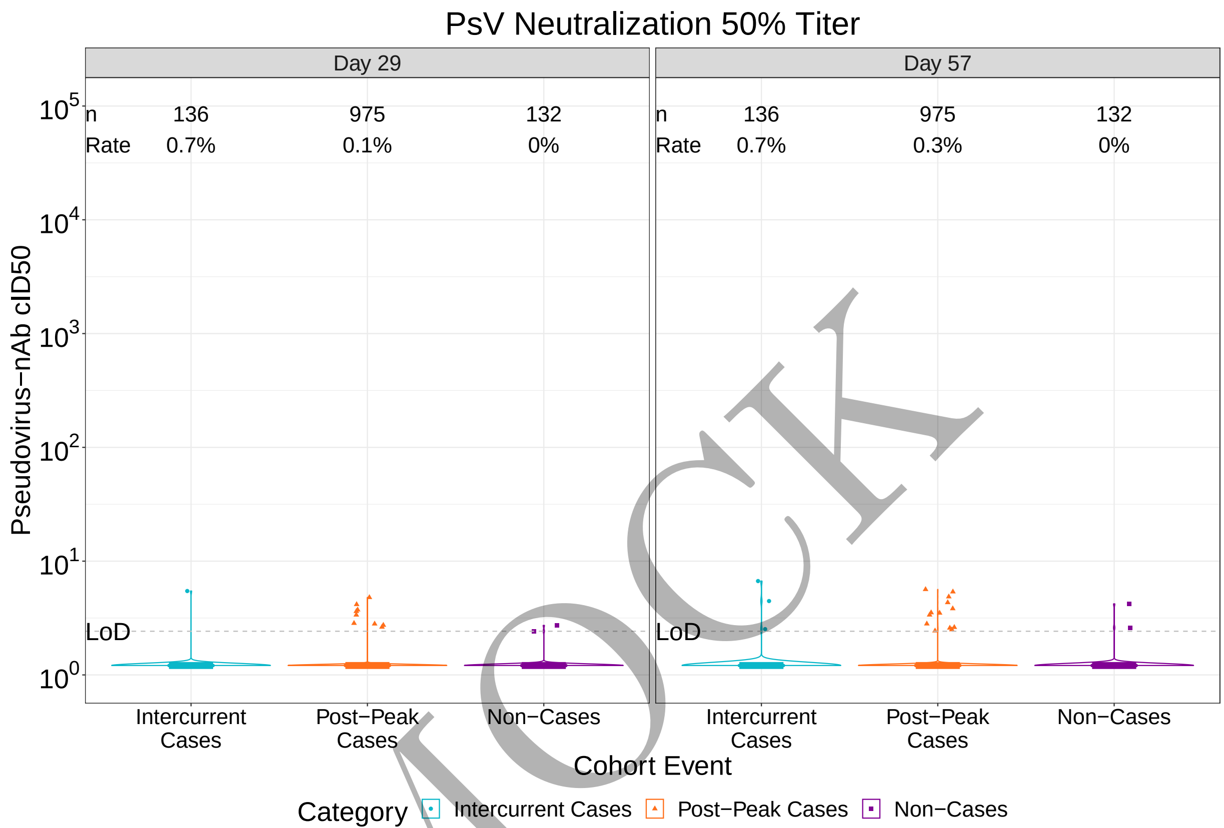

\caption{

Figure 2.5.12: violinplots of Binding Antibody to RBD: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



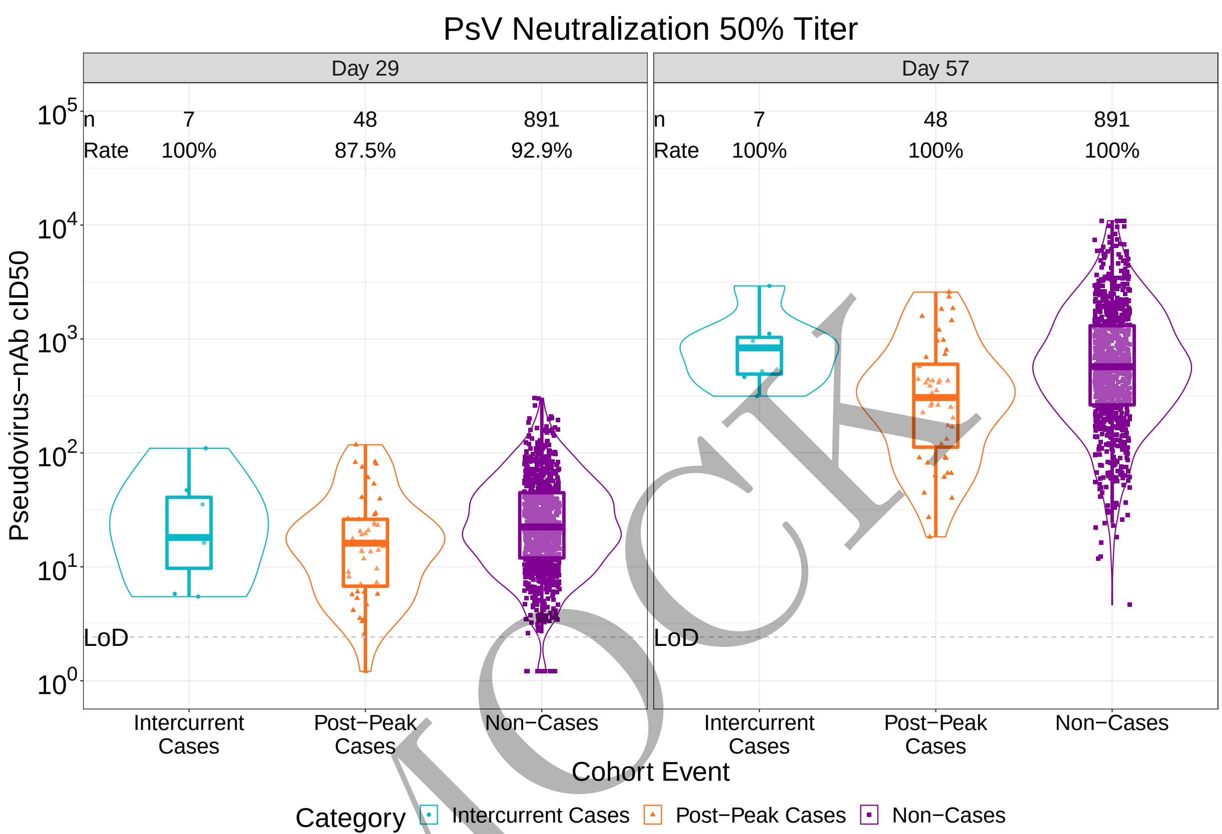

\caption{

Figure 2.5.13: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



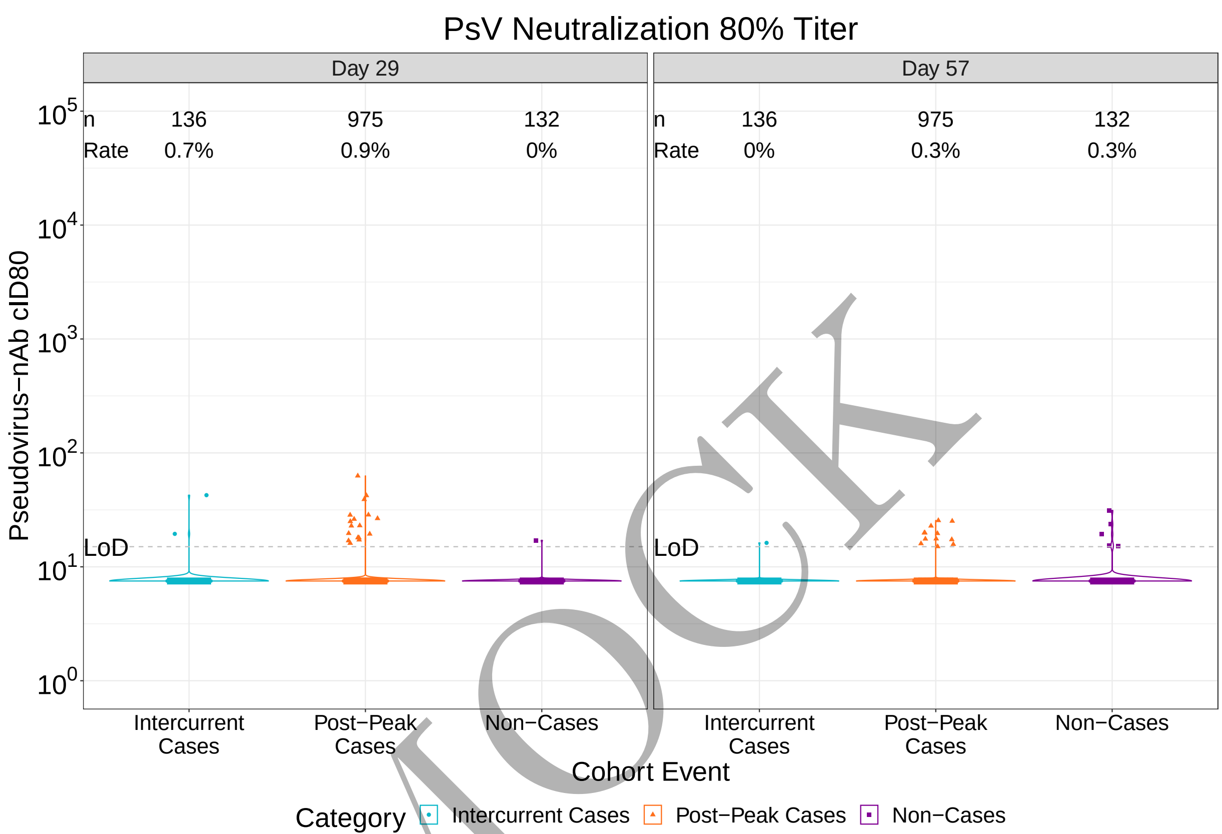

\caption{

Figure 2.5.14: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



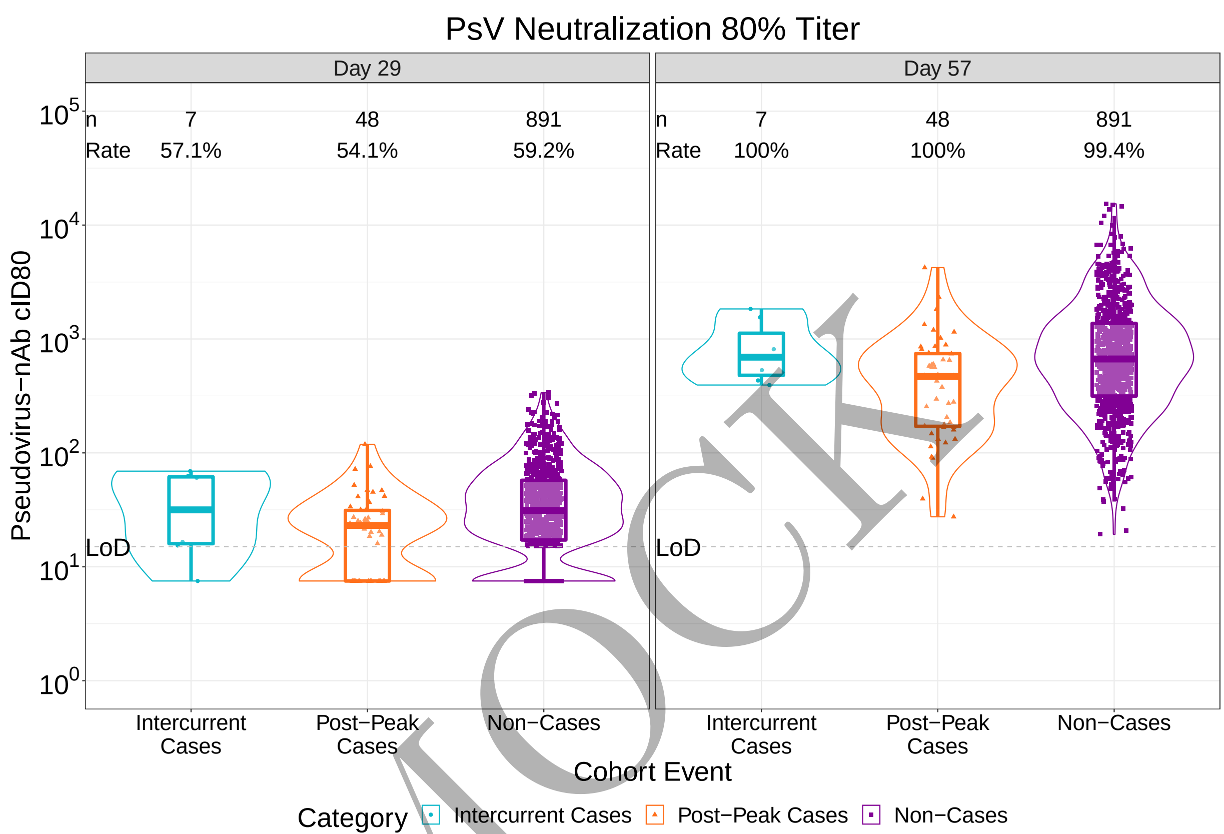

\caption{

Figure 2.5.15: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





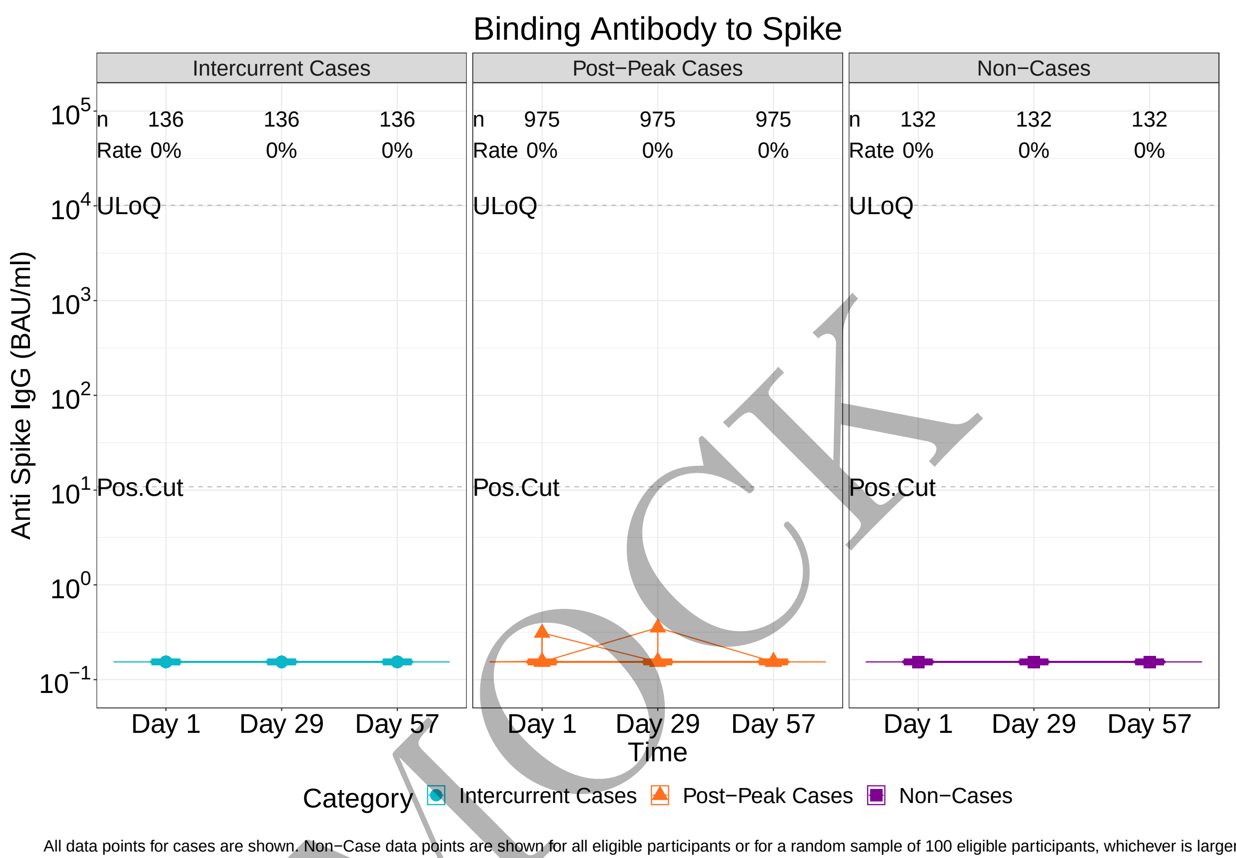
\caption{

Figure 2.5.16: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



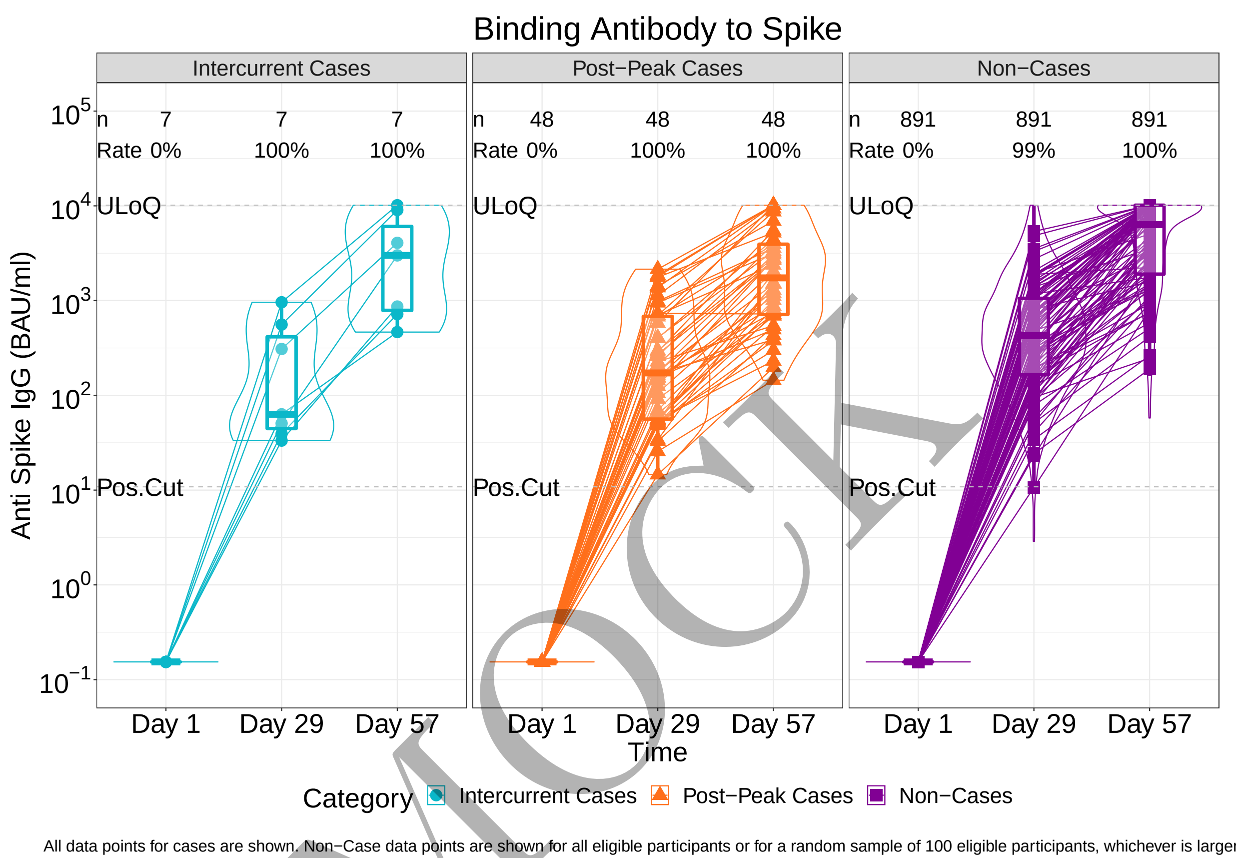

\caption{

Figure 2.5.17: lineplots of Binding Antibody to Spike: baseline negative placebo arm (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



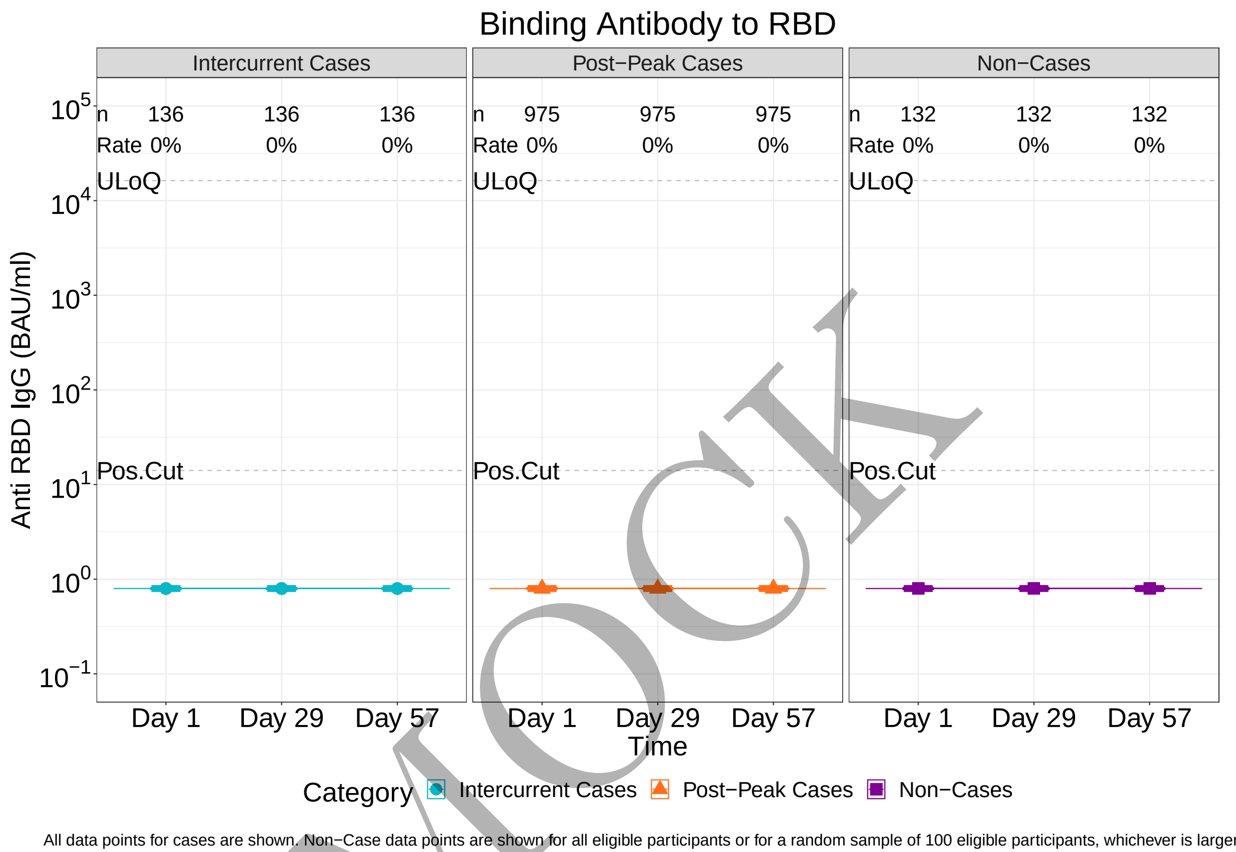

\caption{

Figure 2.5.18: lineplots of Binding Antibody to Spike: baseline negative vaccine arm (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



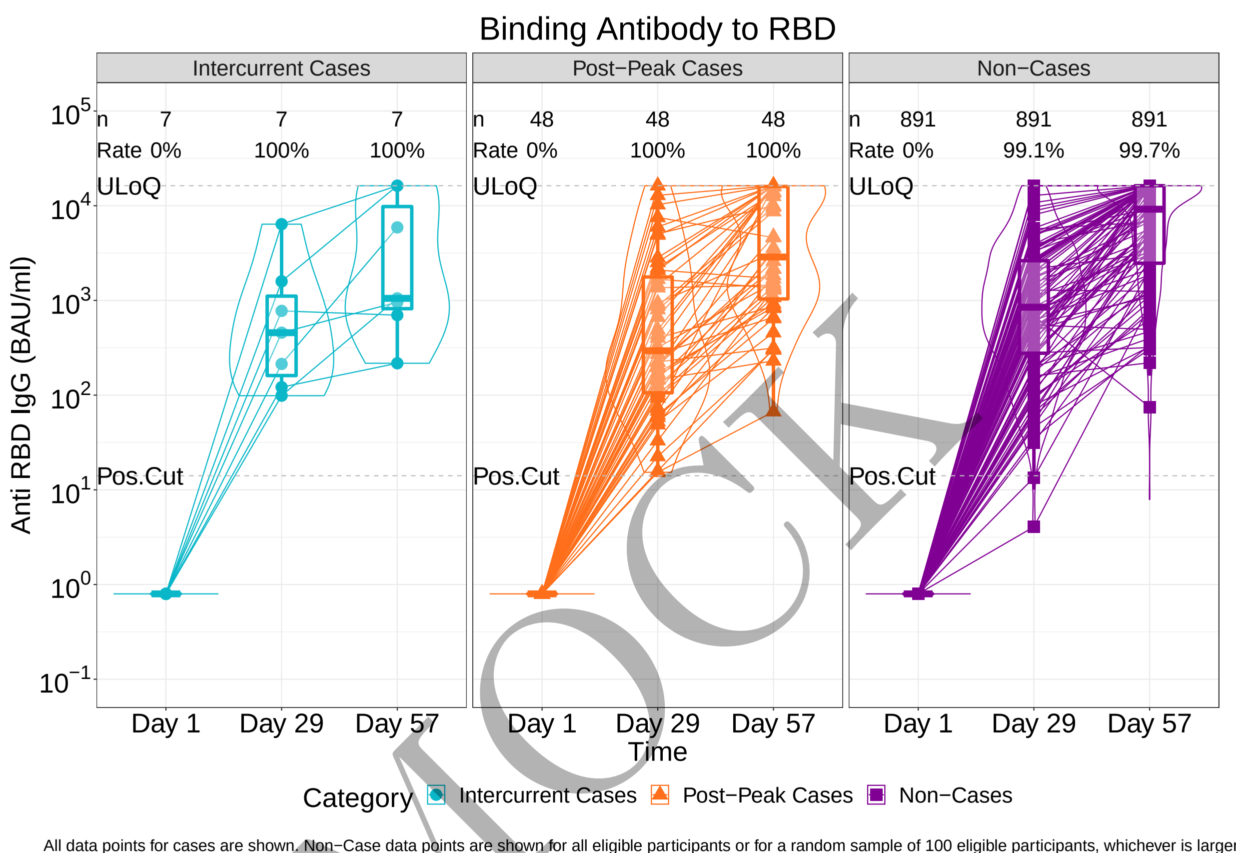

\caption{

Figure 2.5.19: lineplots of Binding Antibody to RBD: baseline negative placebo arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



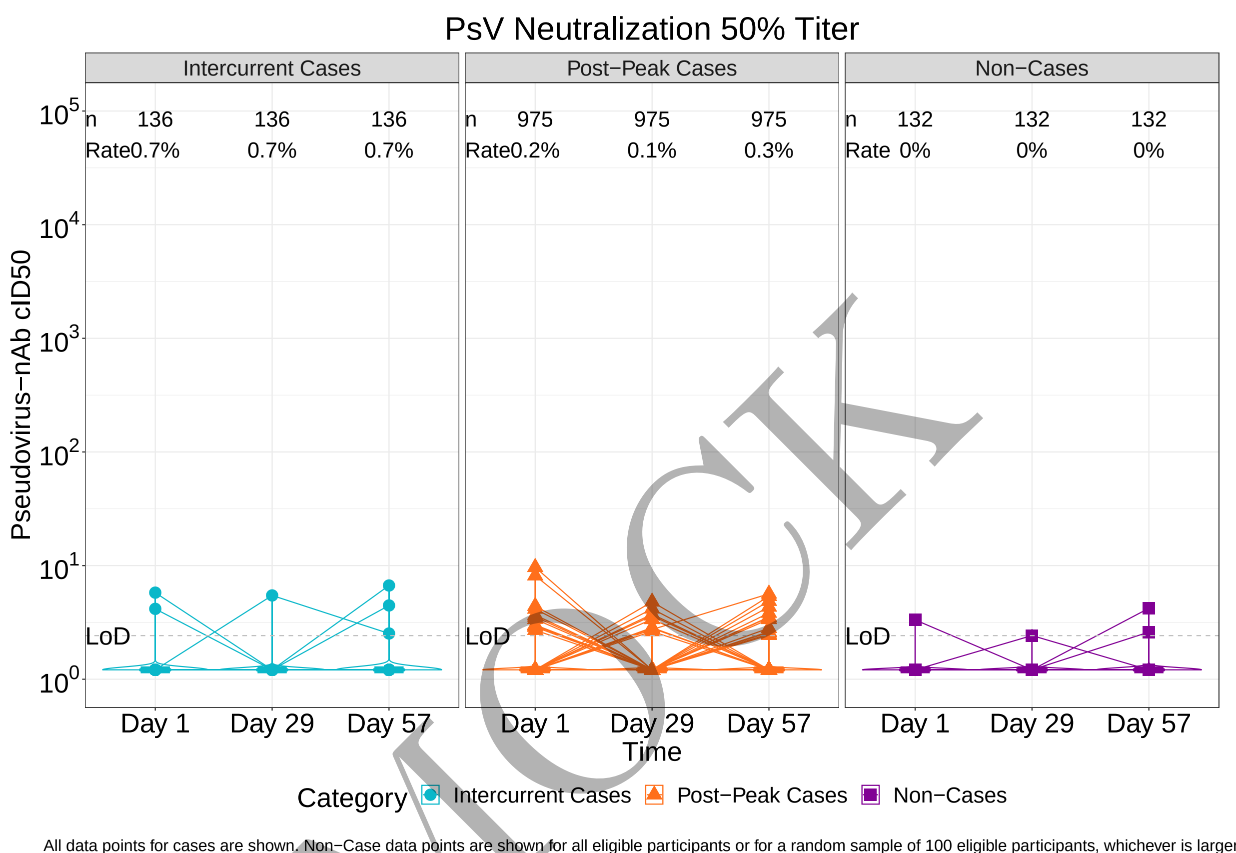



\caption{

Figure 2.5.20: lineplots of Binding Antibody to RBD: baseline negative vaccine arm (version 2)

} \end{figure}

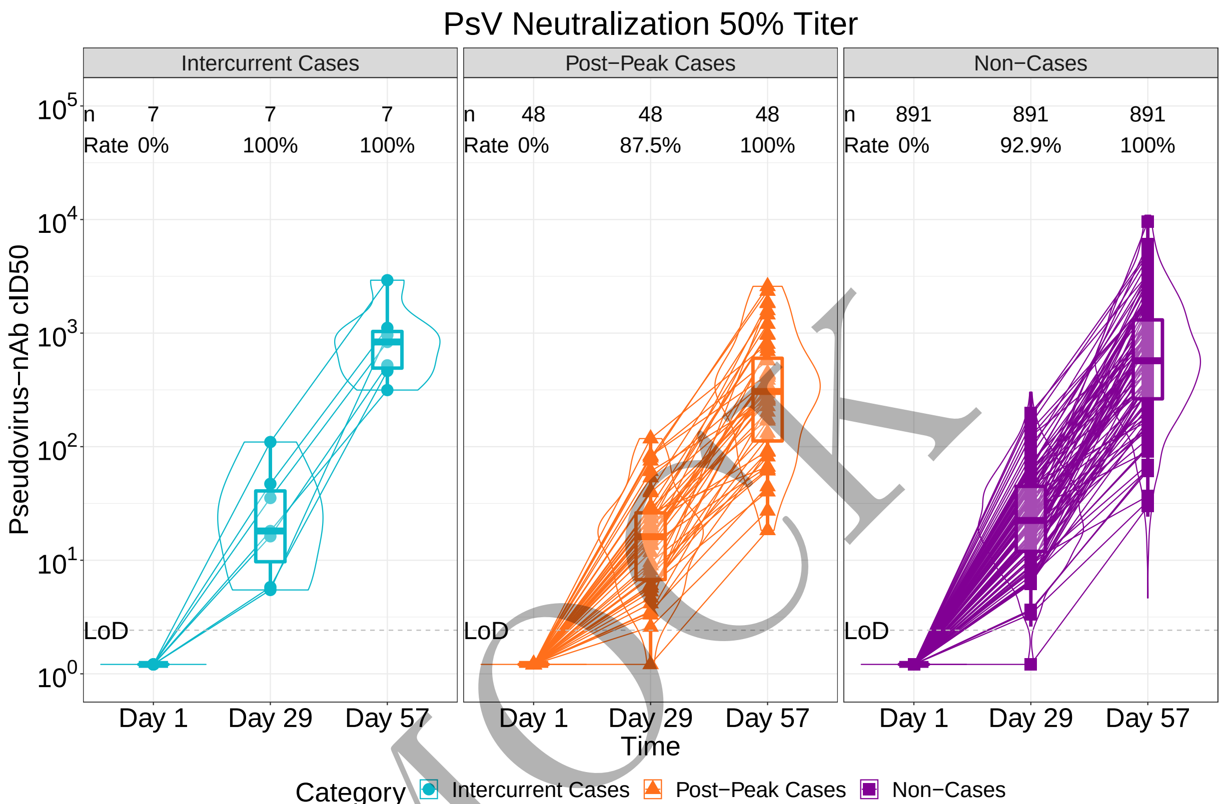
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
\begin{figure}




\caption{
Figure 2.5.21: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm (version 2)
} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}




All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

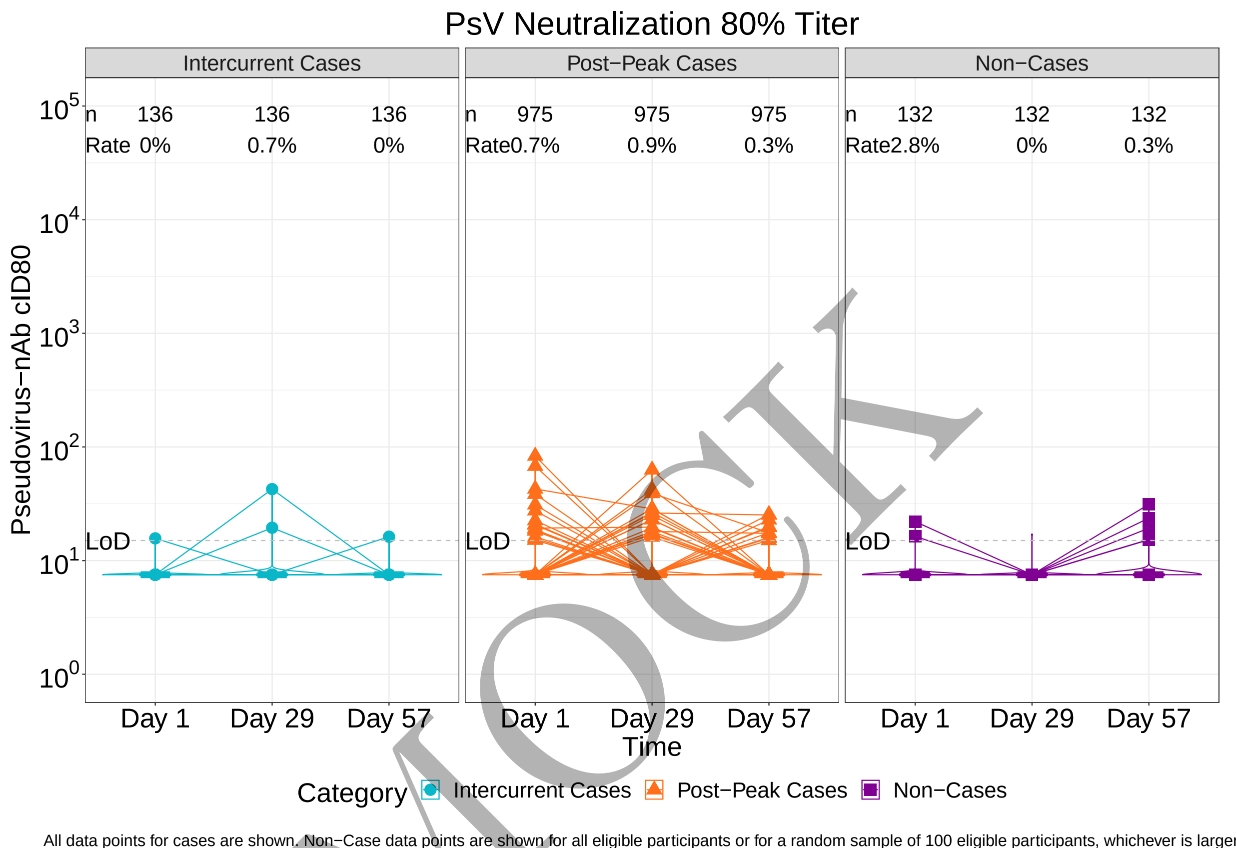
\caption{

Figure 2.5.22: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



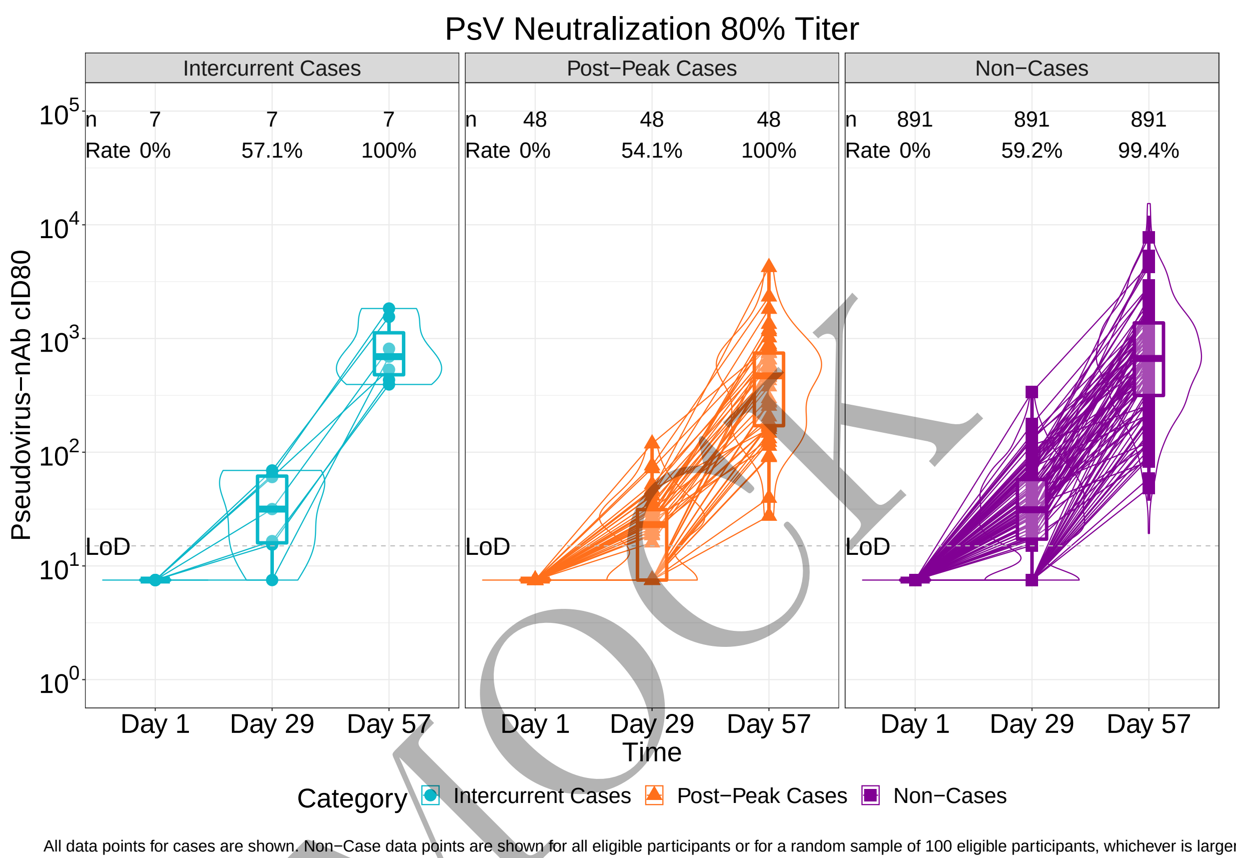

\caption{

Figure 2.5.23: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



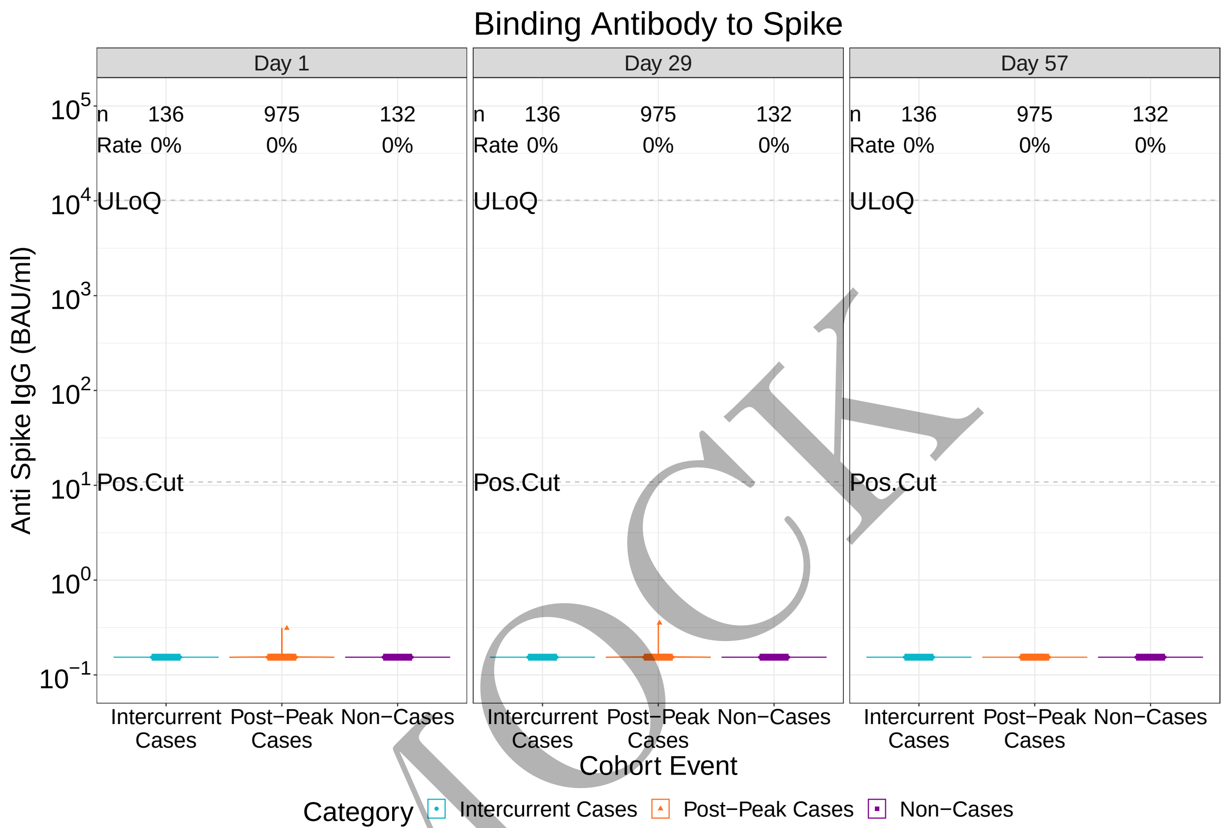

\caption{

Figure 2.5.24: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



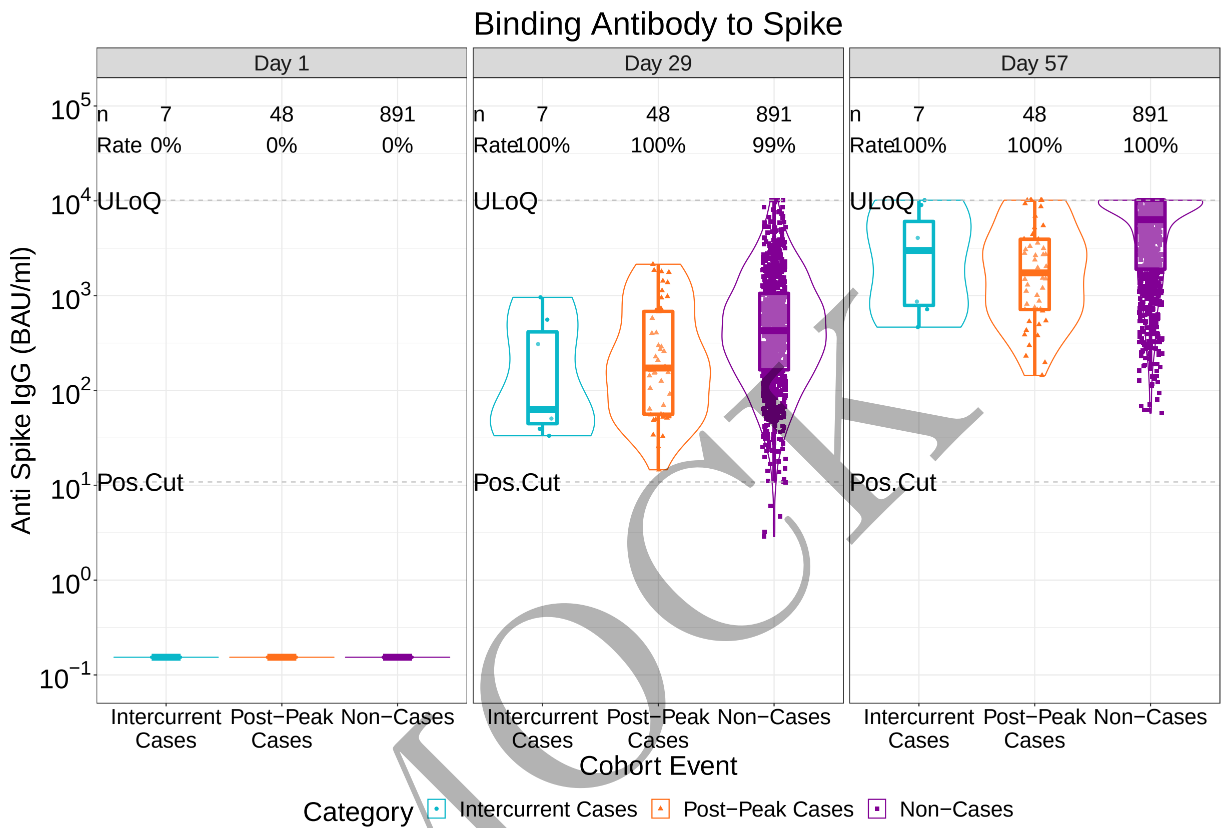

\caption{

Figure 2.5.25: violinplots of Binding Antibody to Spike: baseline negative placebo arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



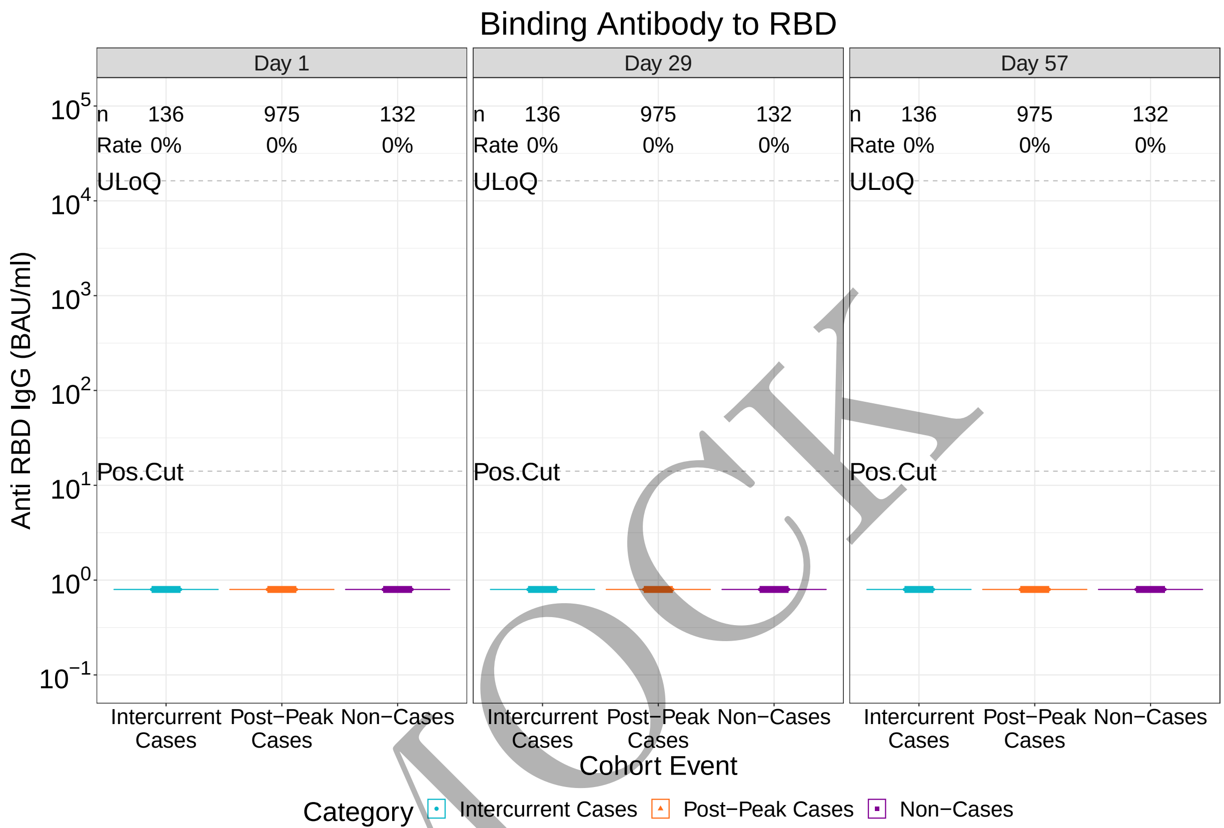

\caption{

Figure 2.5.26: violinplots of Binding Antibody to Spike: baseline negative vaccine arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



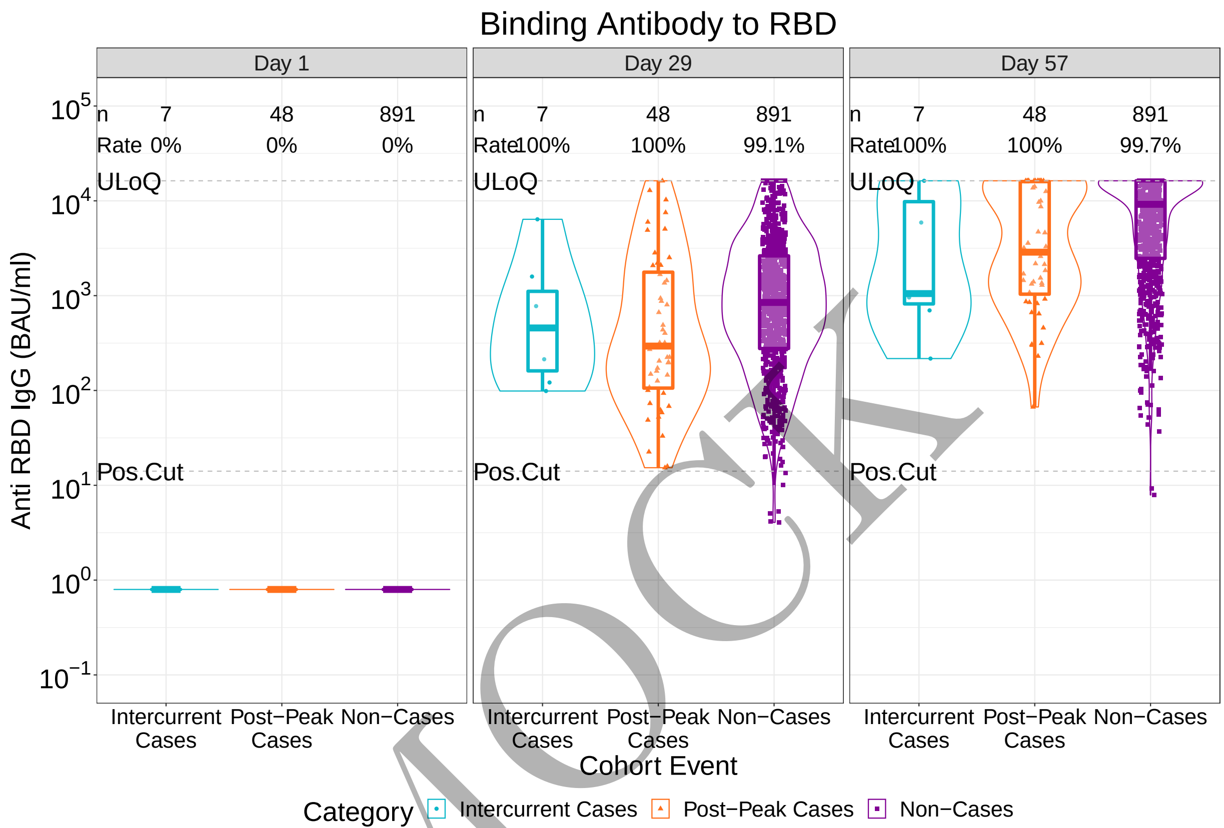

\caption{

Figure 2.5.27: violinplots of Binding Antibody to RBD: baseline negative placebo arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



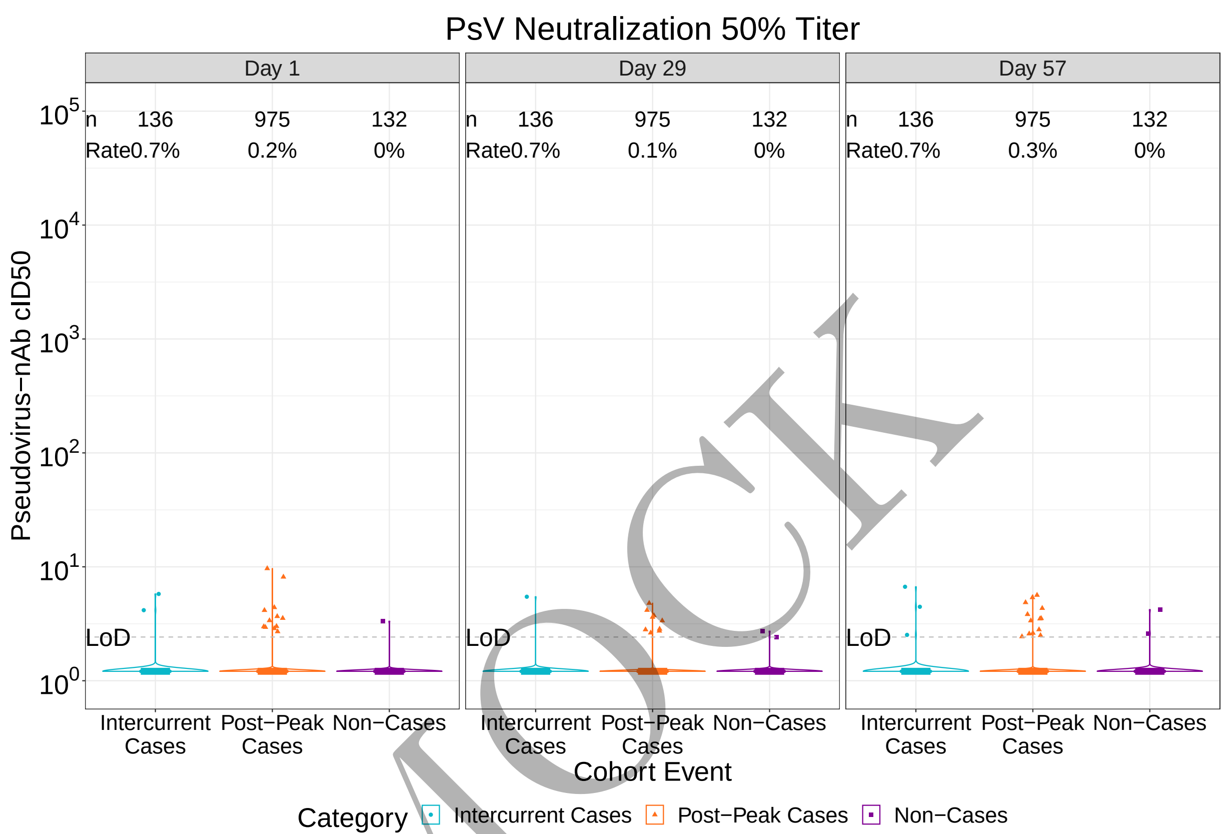

\caption{

Figure 2.5.28: violinplots of Binding Antibody to RBD: baseline negative vaccine arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



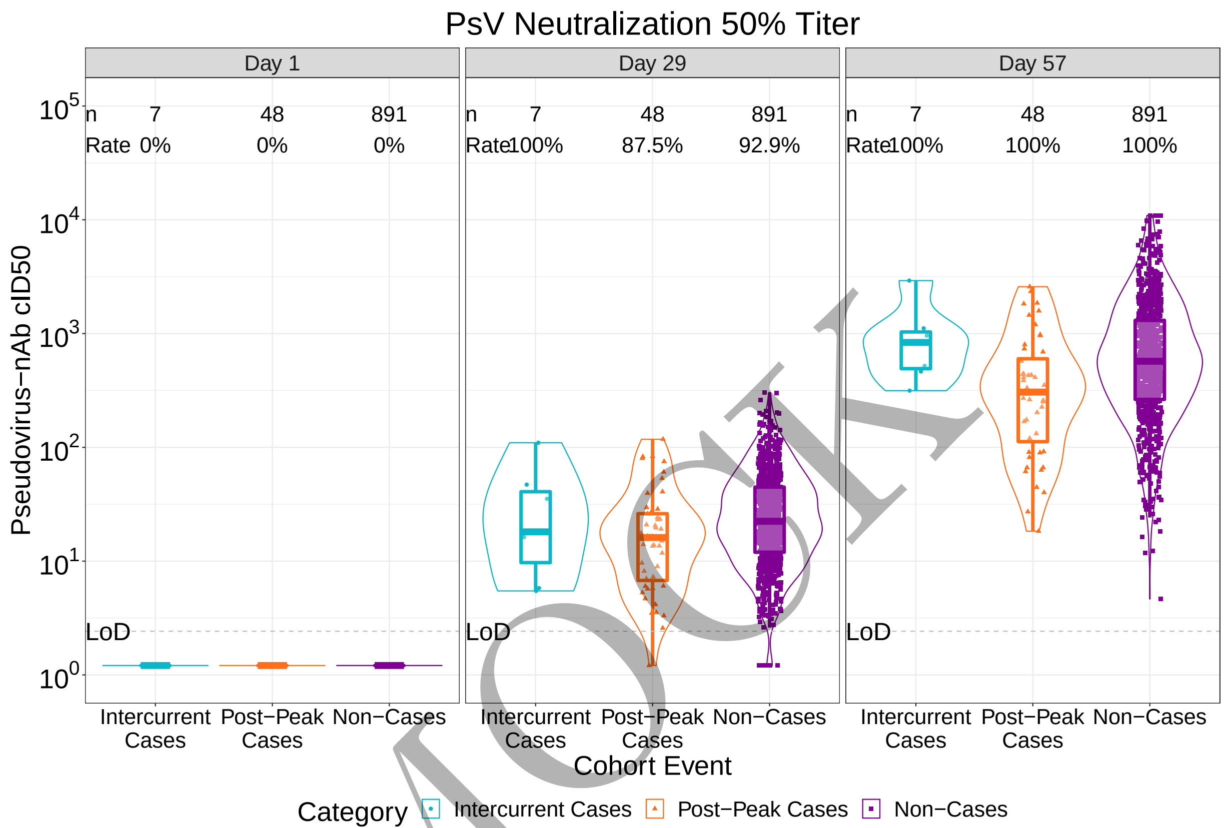

\caption{

Figure 2.5.29: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



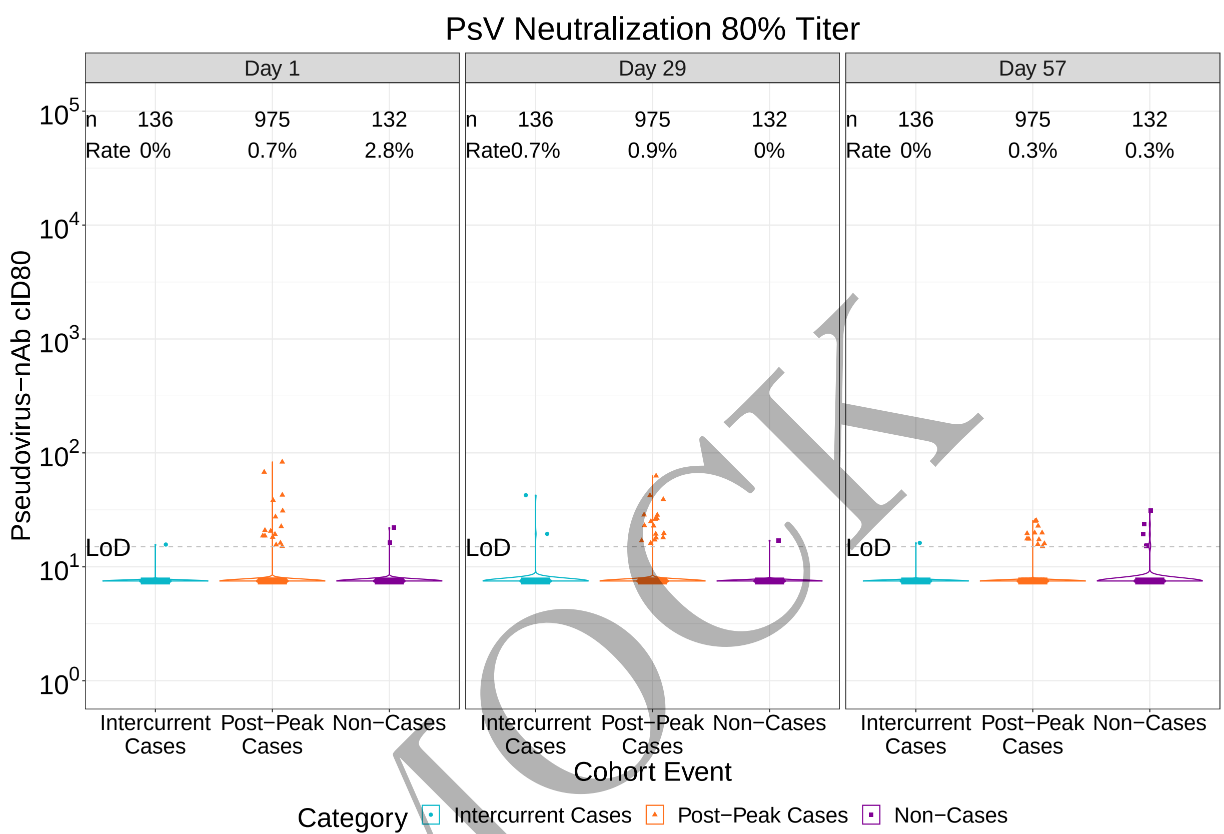

\caption{

Figure 2.5.30: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



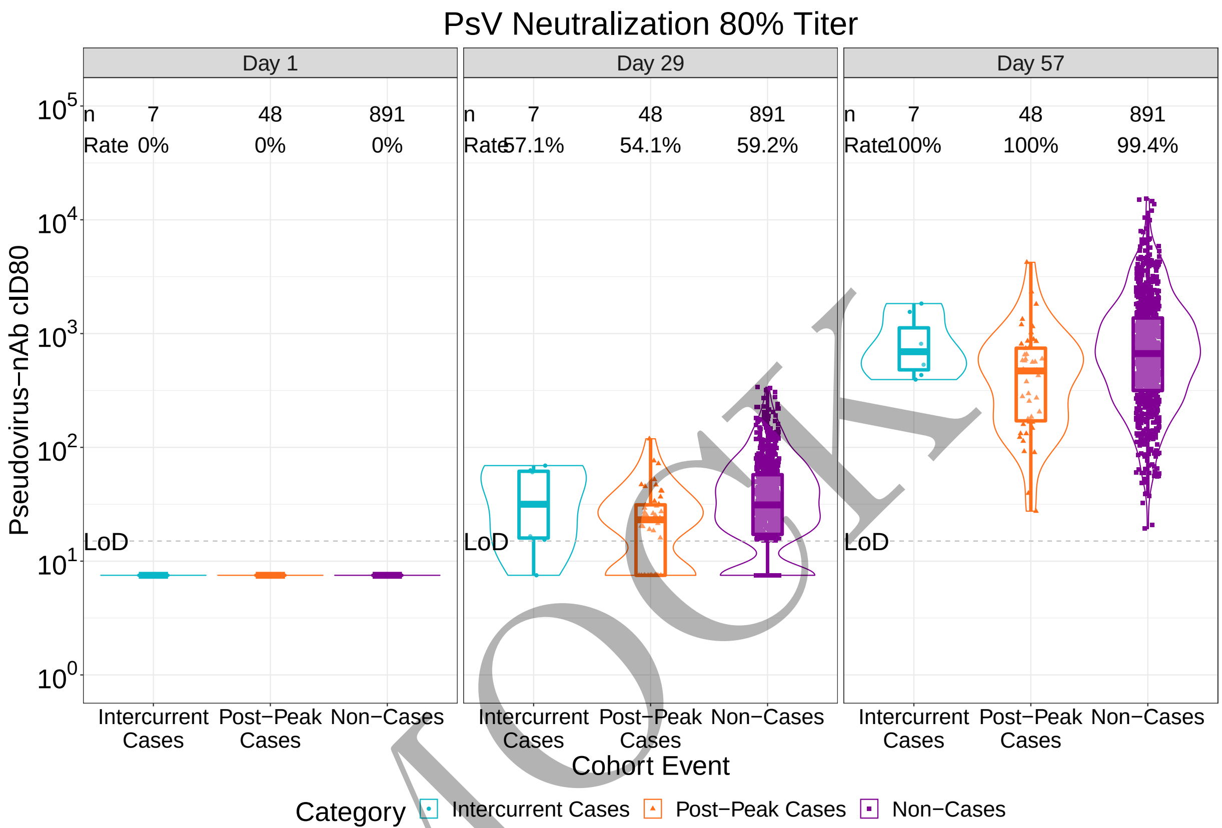

\caption{

Figure 2.5.31: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



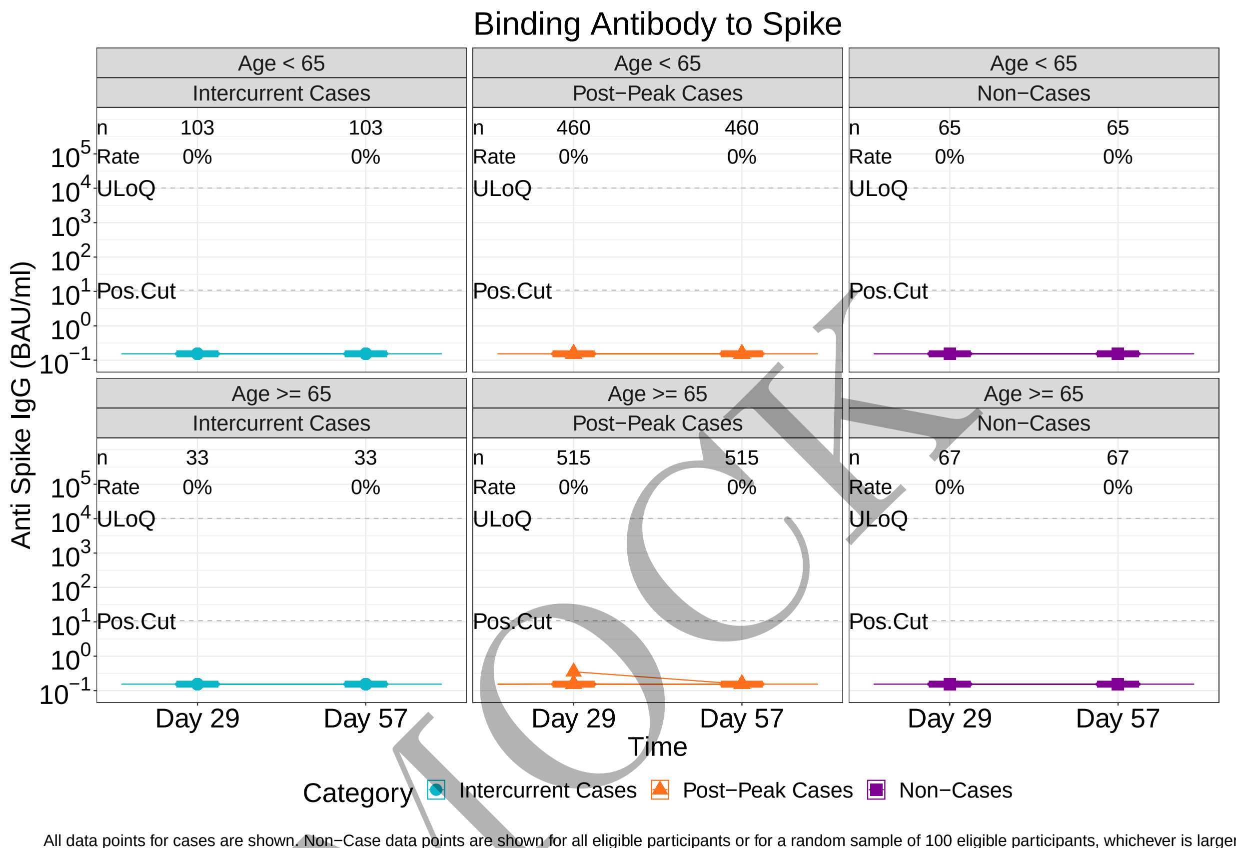

\caption{

Figure 2.5.32: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





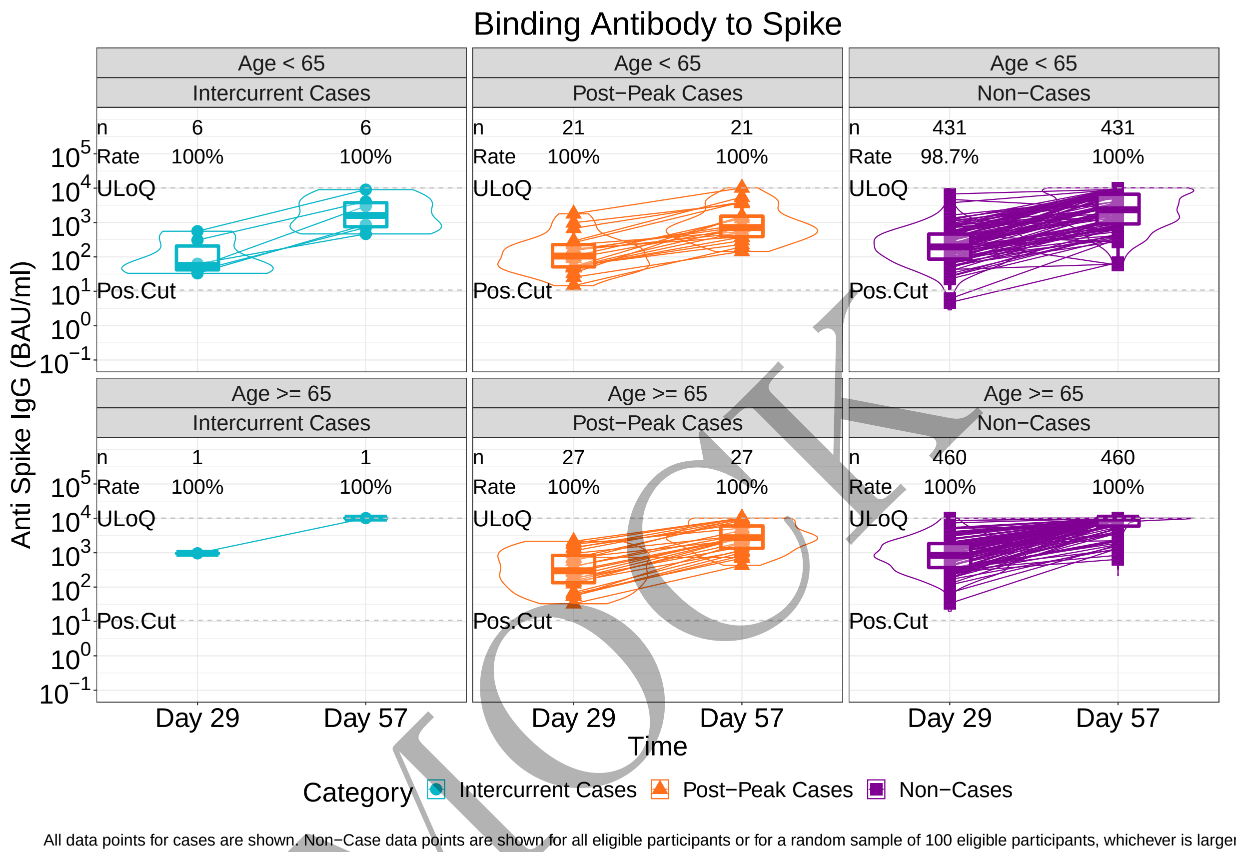
\caption{

Figure 2.5.33: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



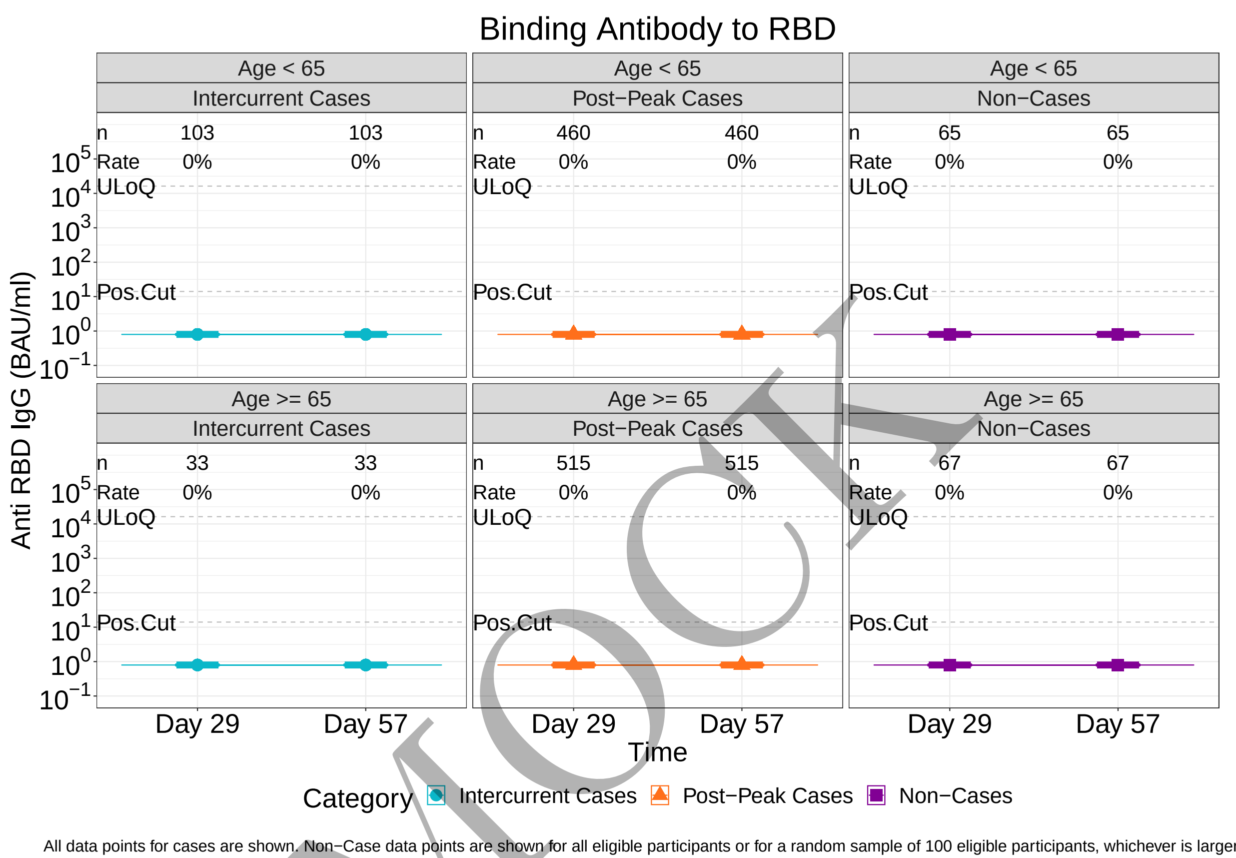

\caption{

Figure 2.5.34: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



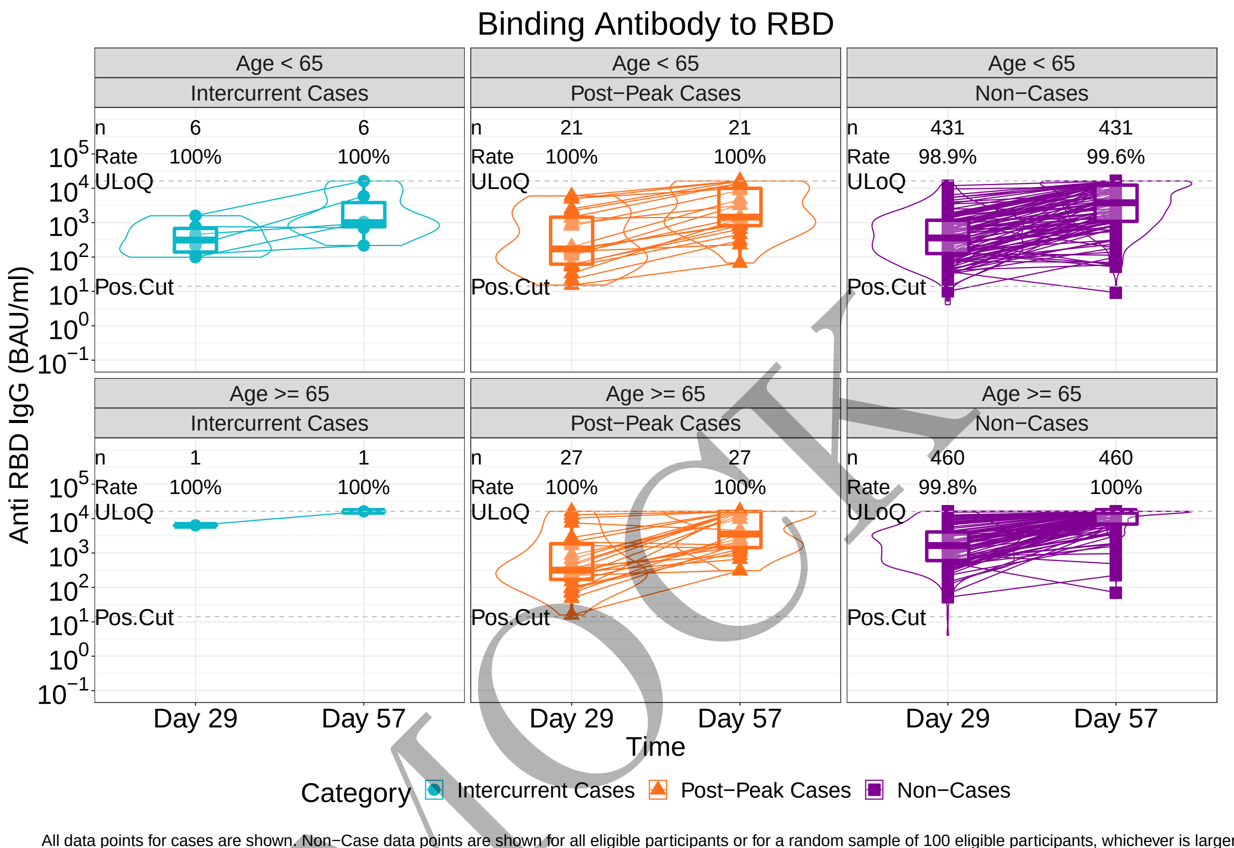

\caption{

Figure 2.5.35: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 1)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

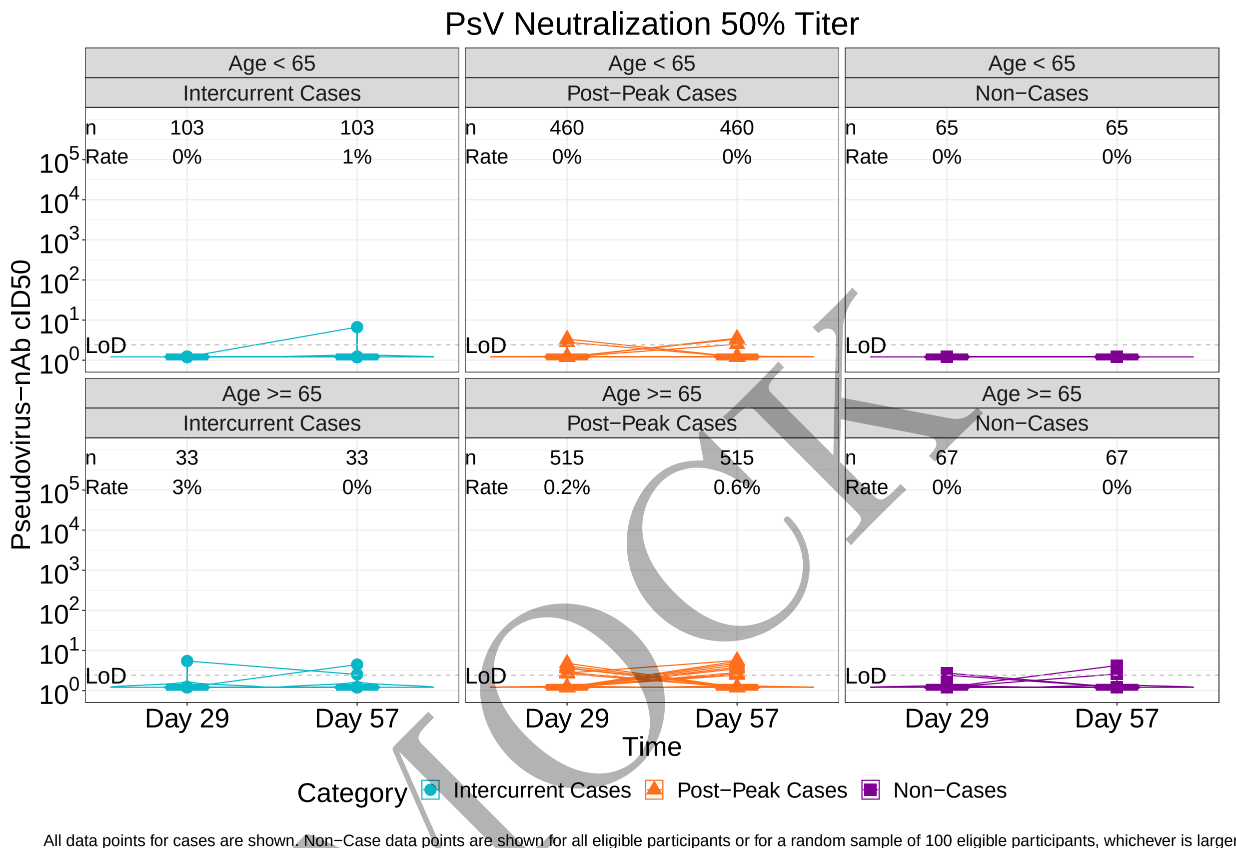
\begin{figure}




\caption{
Figure 2.5.36: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 1)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



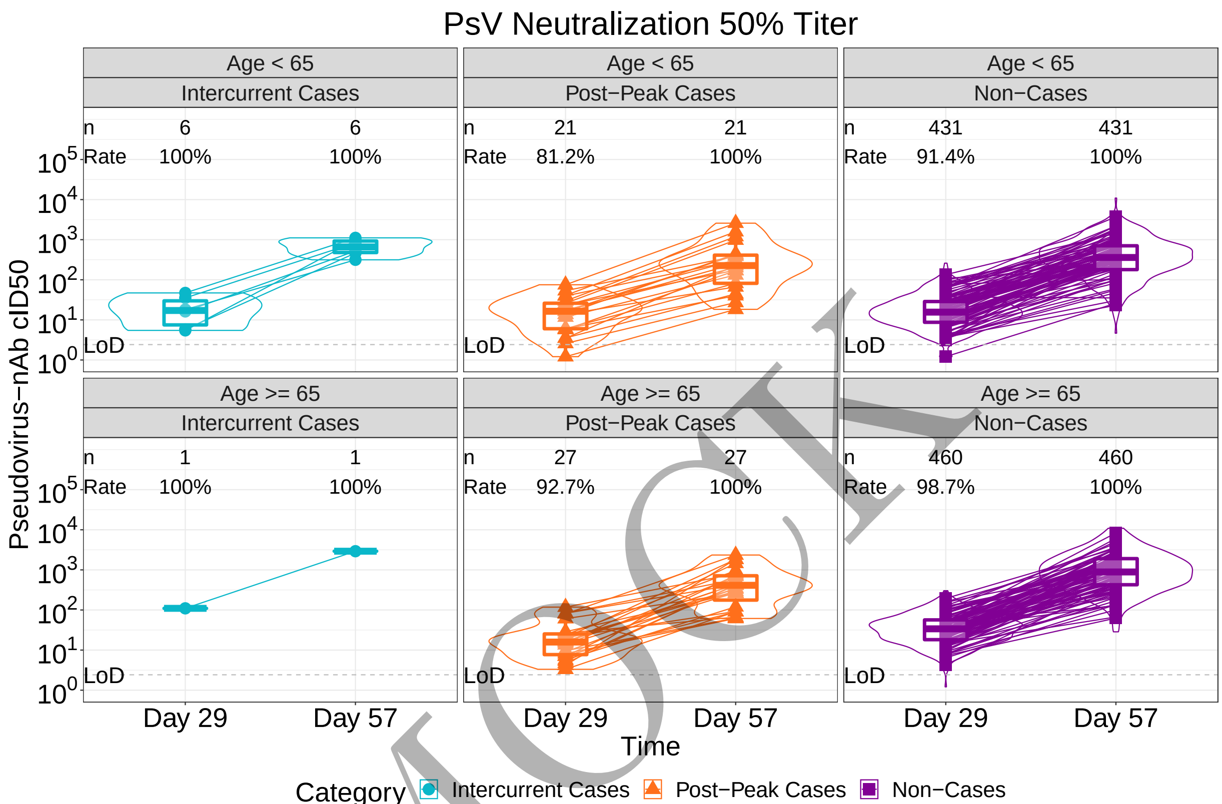

\caption{

Figure 2.5.37: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}




All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

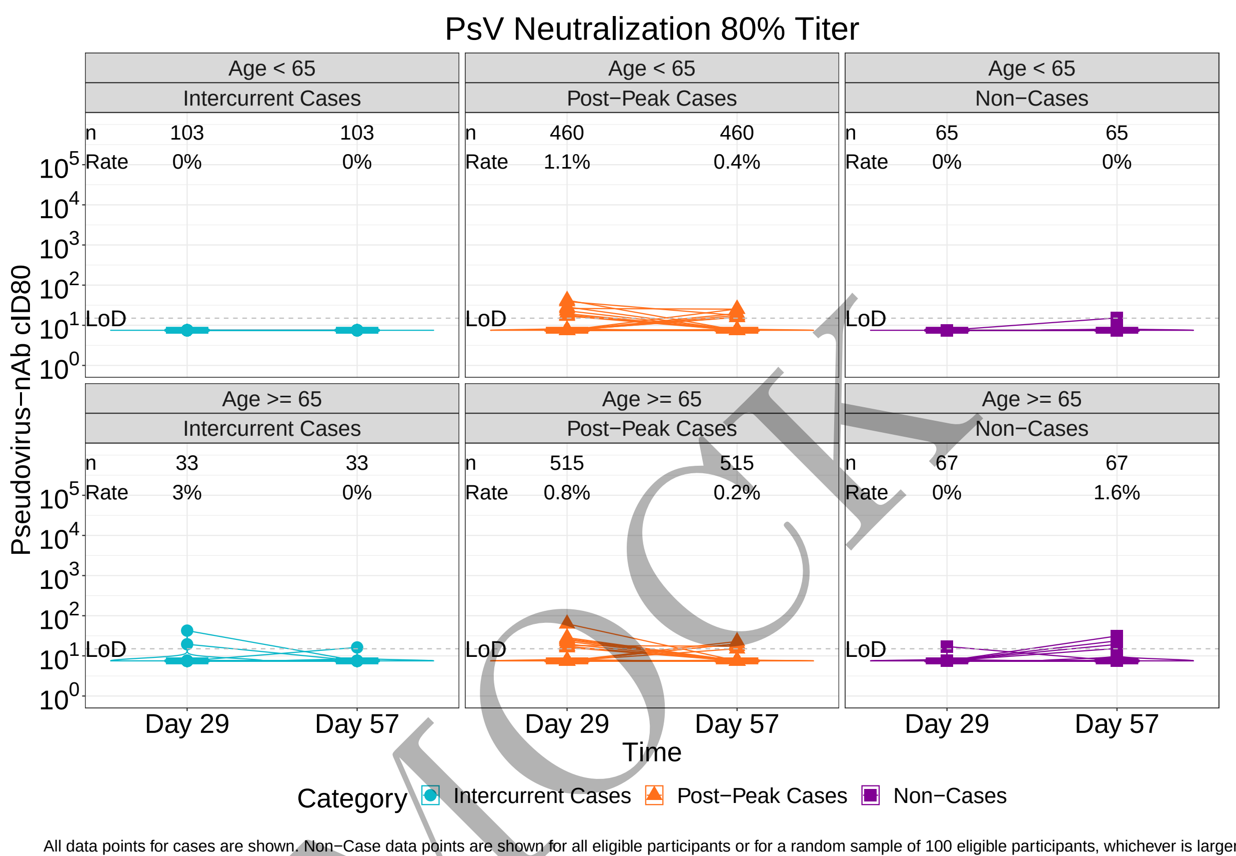
\caption{

Figure 2.5.38: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



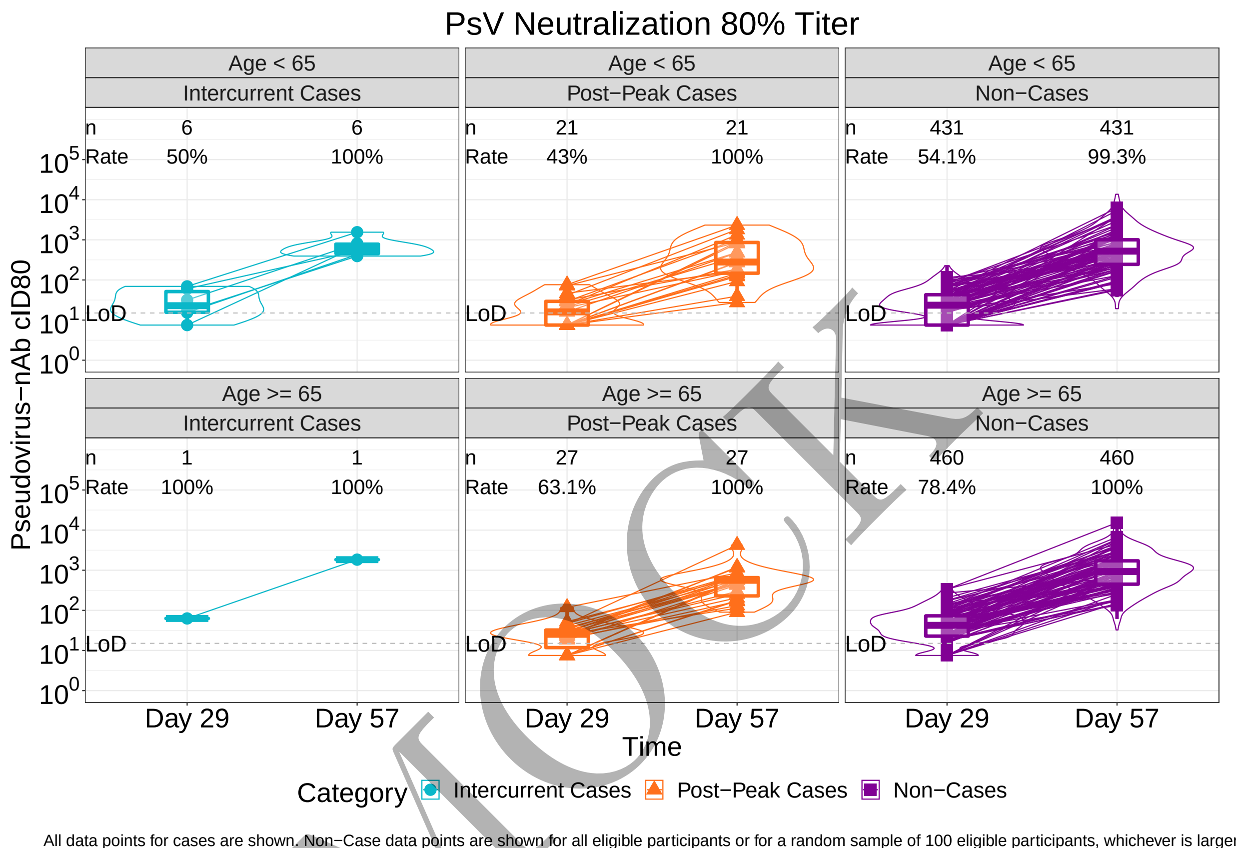

\caption{

Figure 2.5.39: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





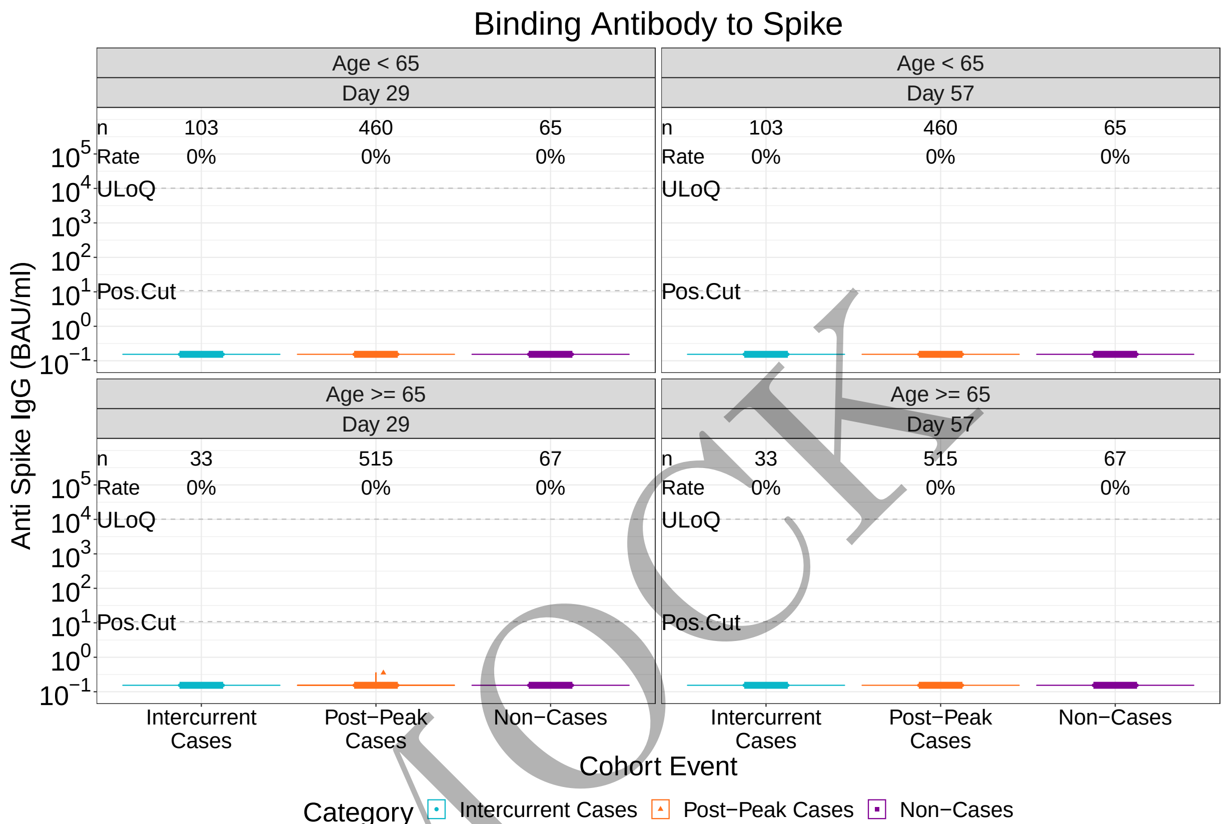

\caption{

Figure 2.5.40: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age (version 1)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

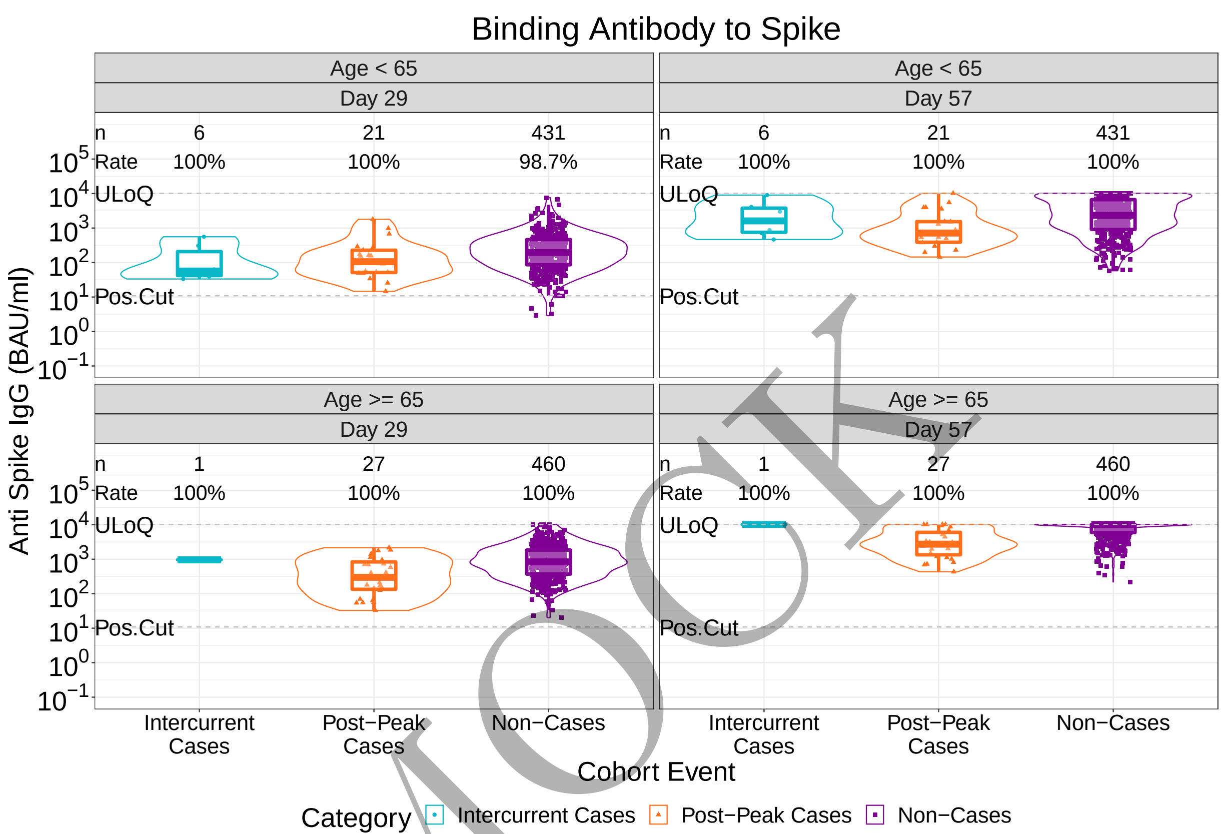
\begin{figure}




\caption{
Figure 2.5.41: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 1)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



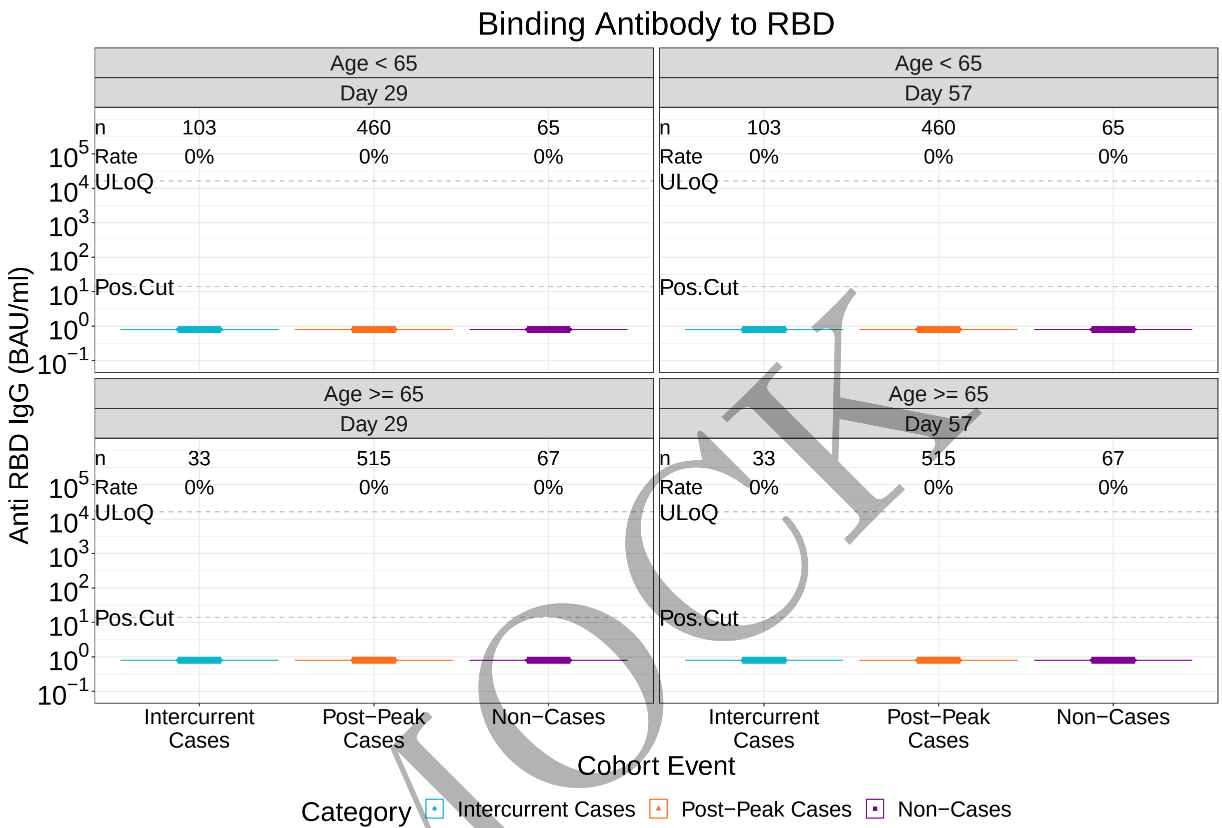

\caption{

Figure 2.5.42: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

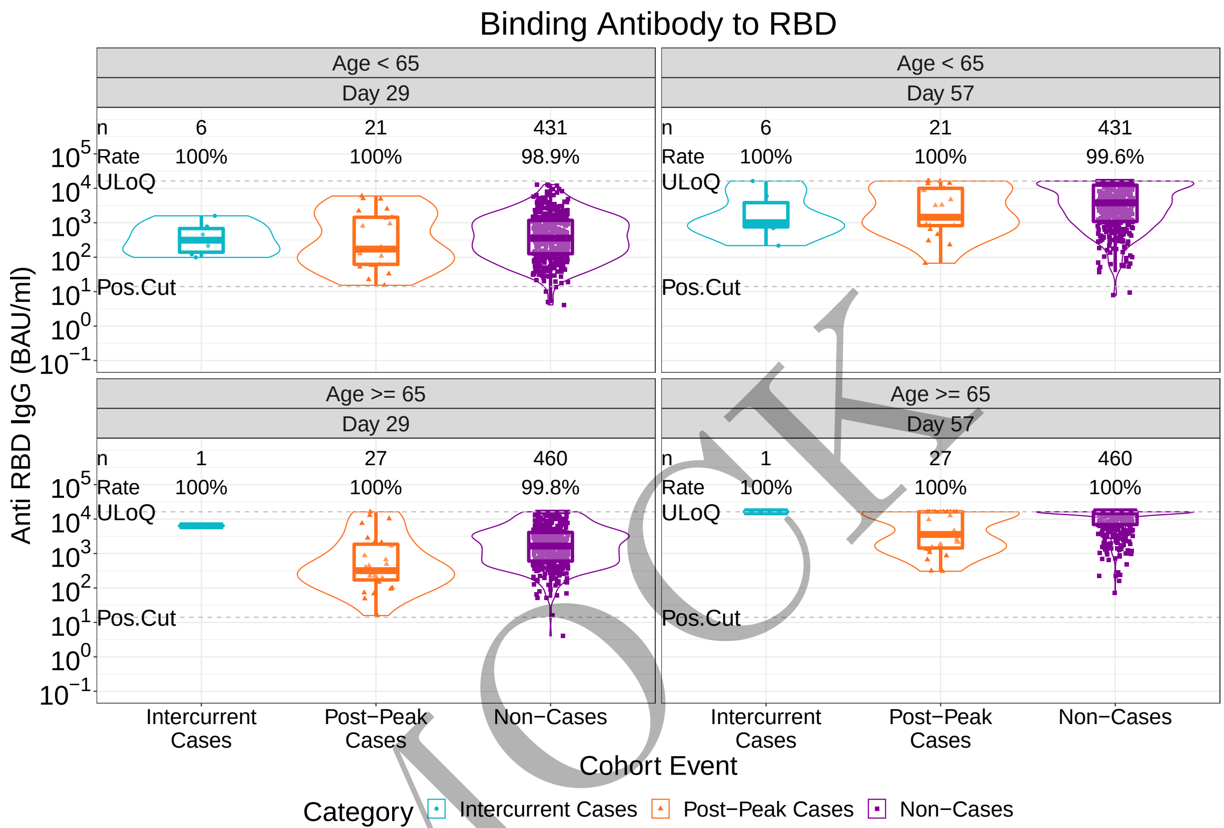
\begin{figure}




\caption{
Figure 2.5.43: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 1)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



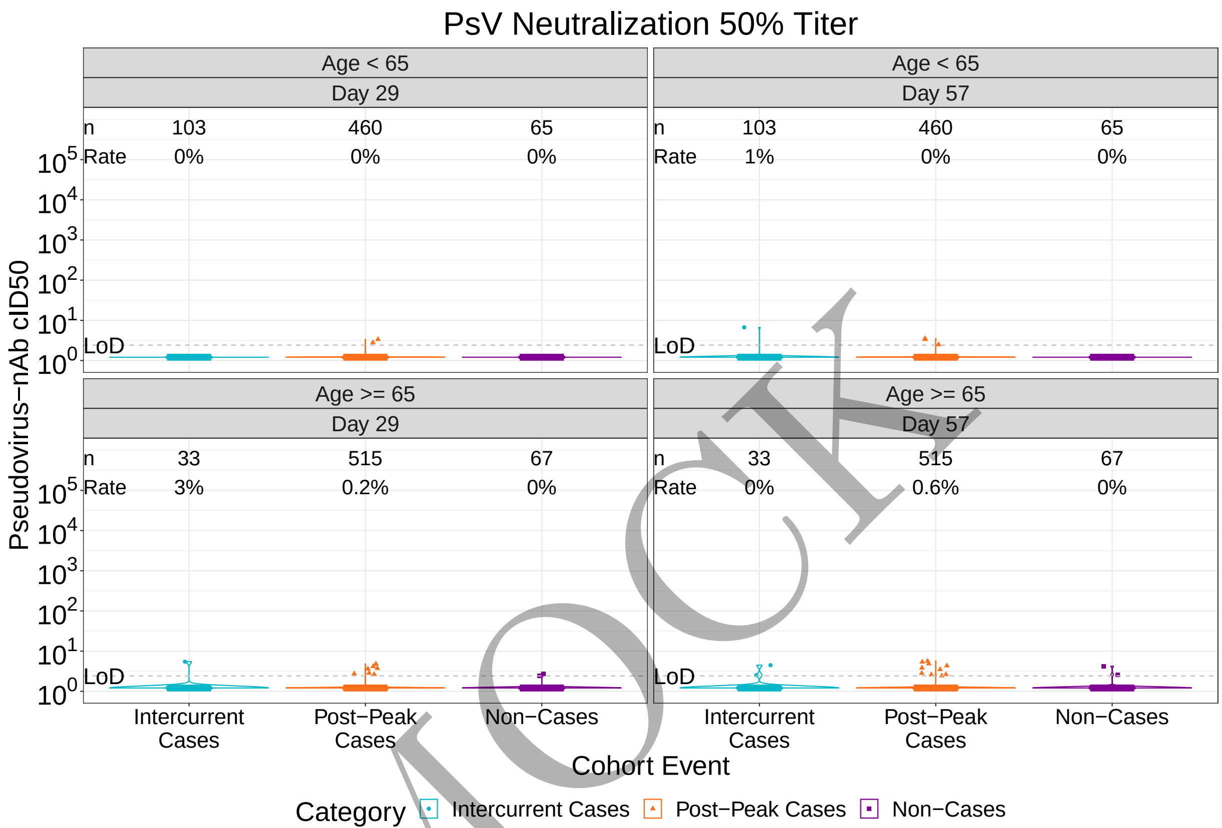

\caption{

Figure 2.5.44: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



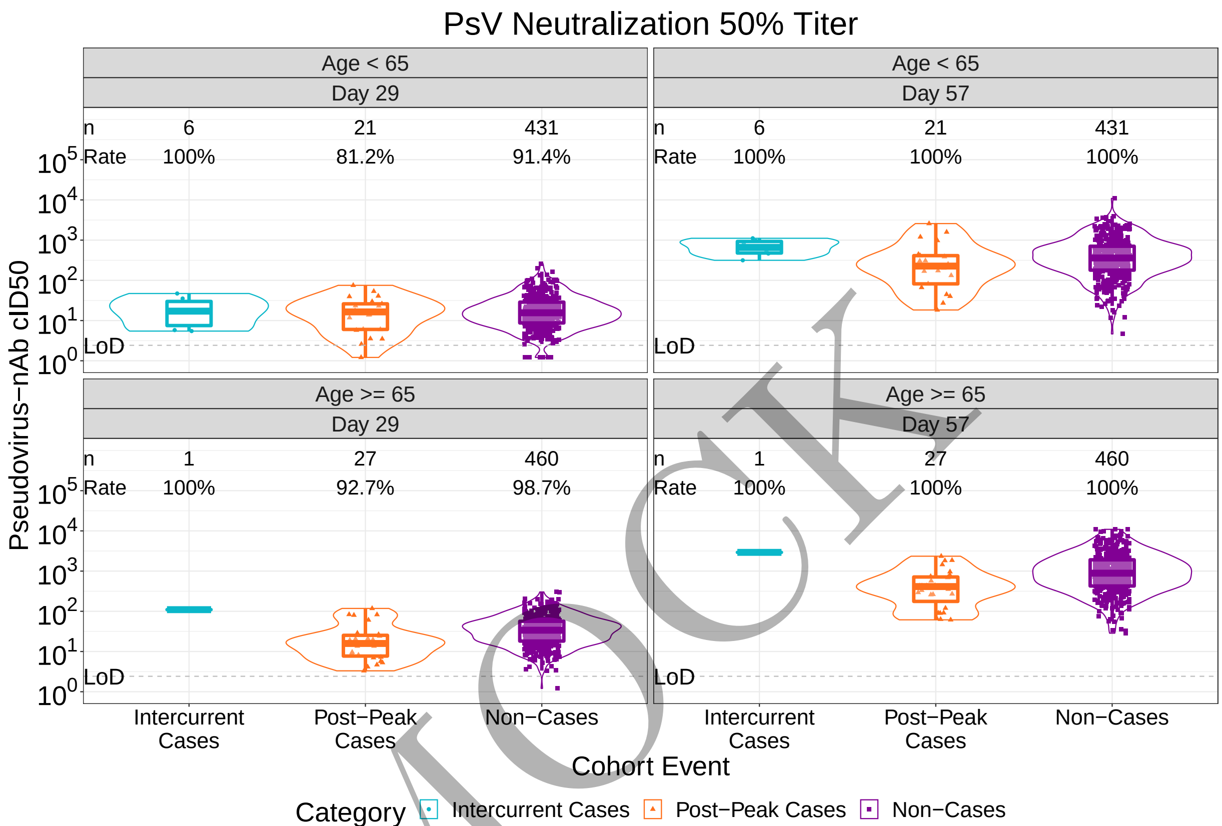

\caption{

Figure 2.5.45: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



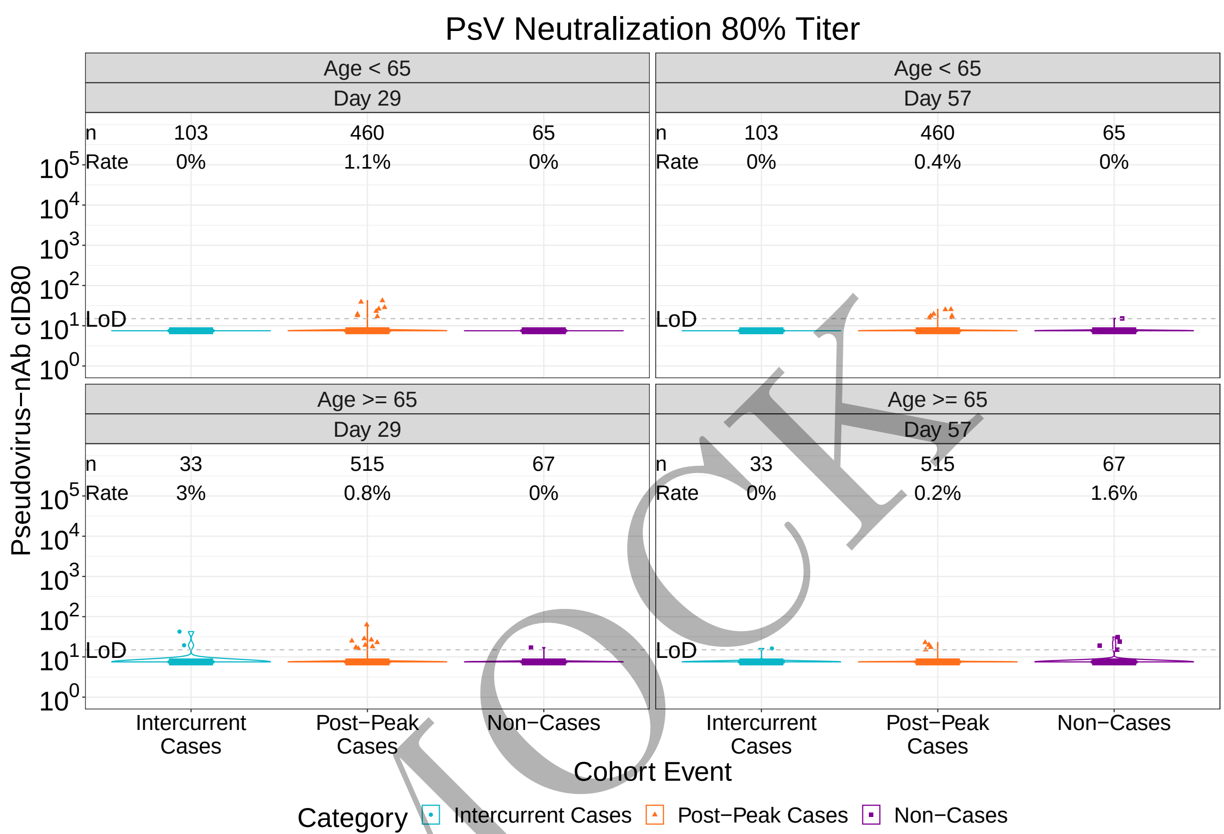

\caption{

Figure 2.5.46: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



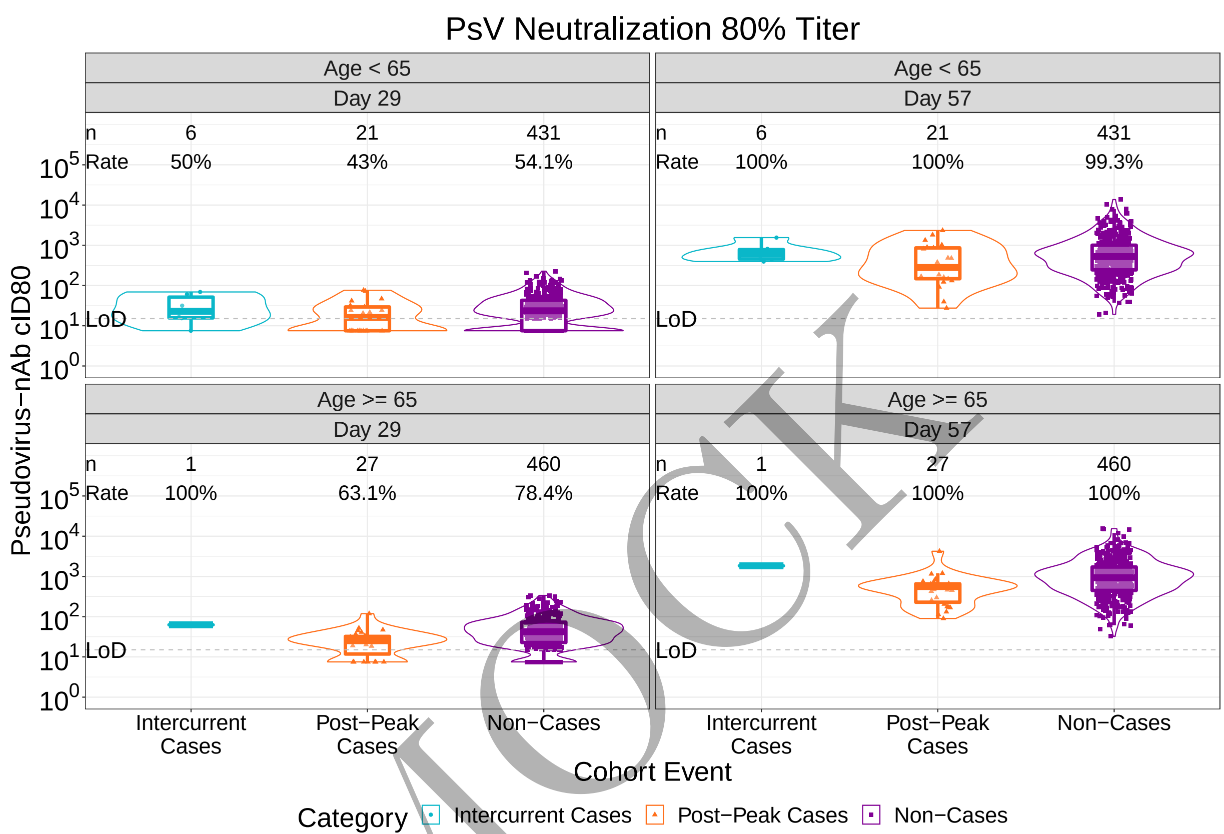

\caption{

Figure 2.5.47: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



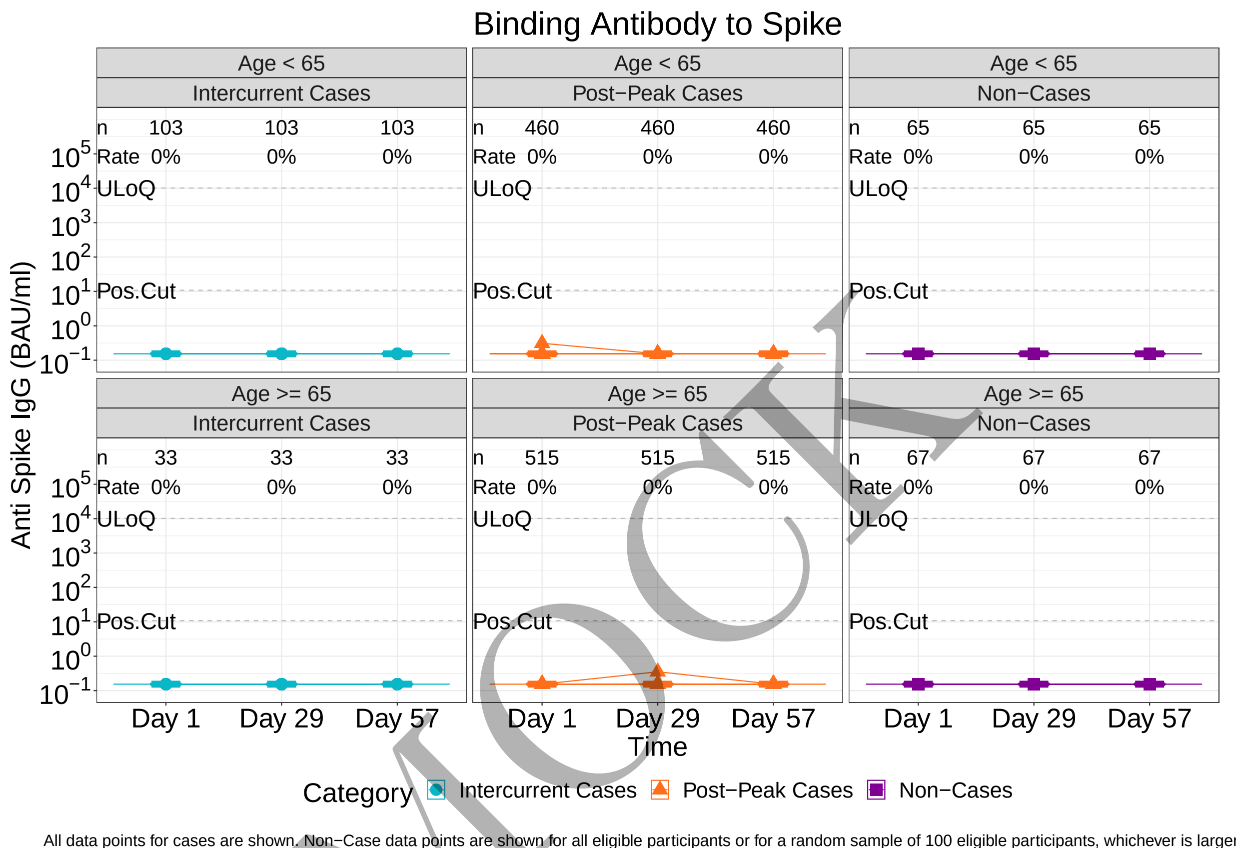

\caption{

Figure 2.5.48: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age (version 1)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}





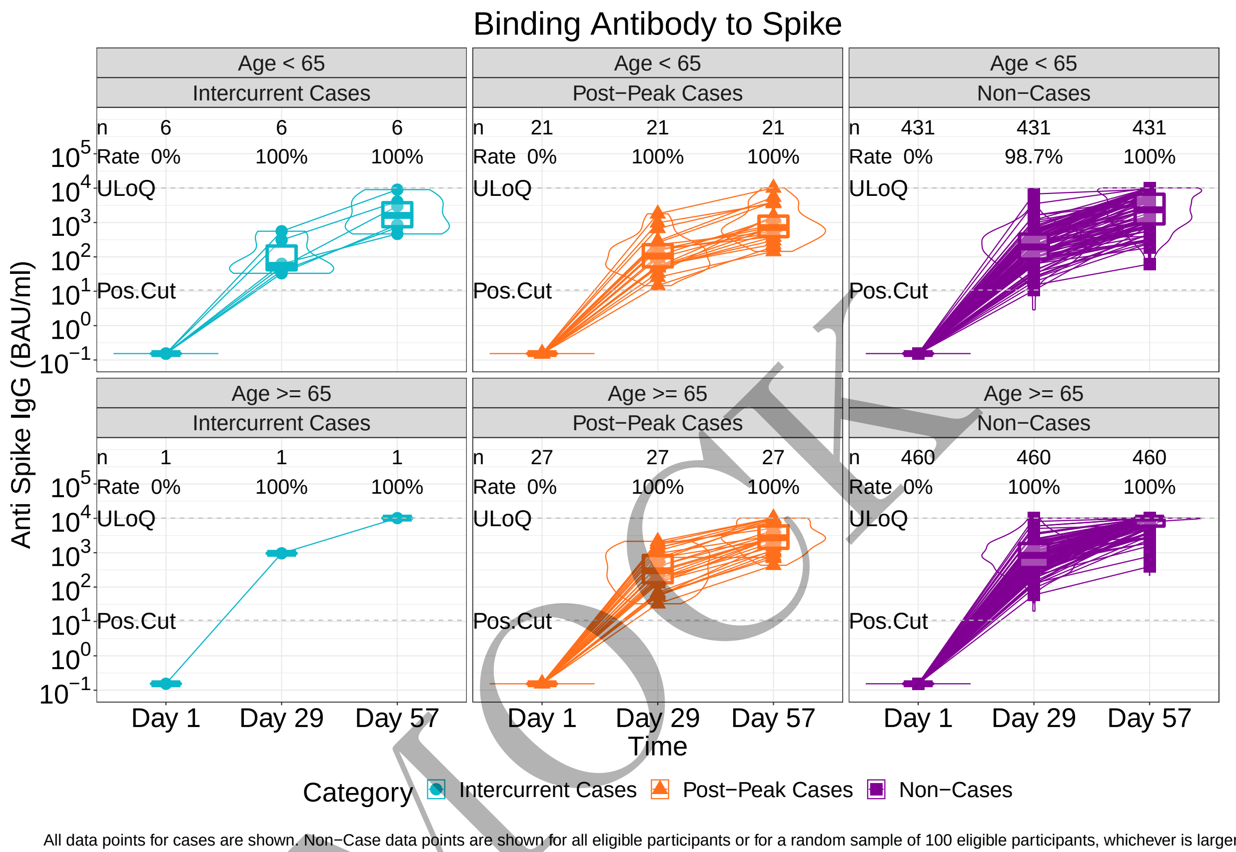

\caption{

Figure 2.5.49: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



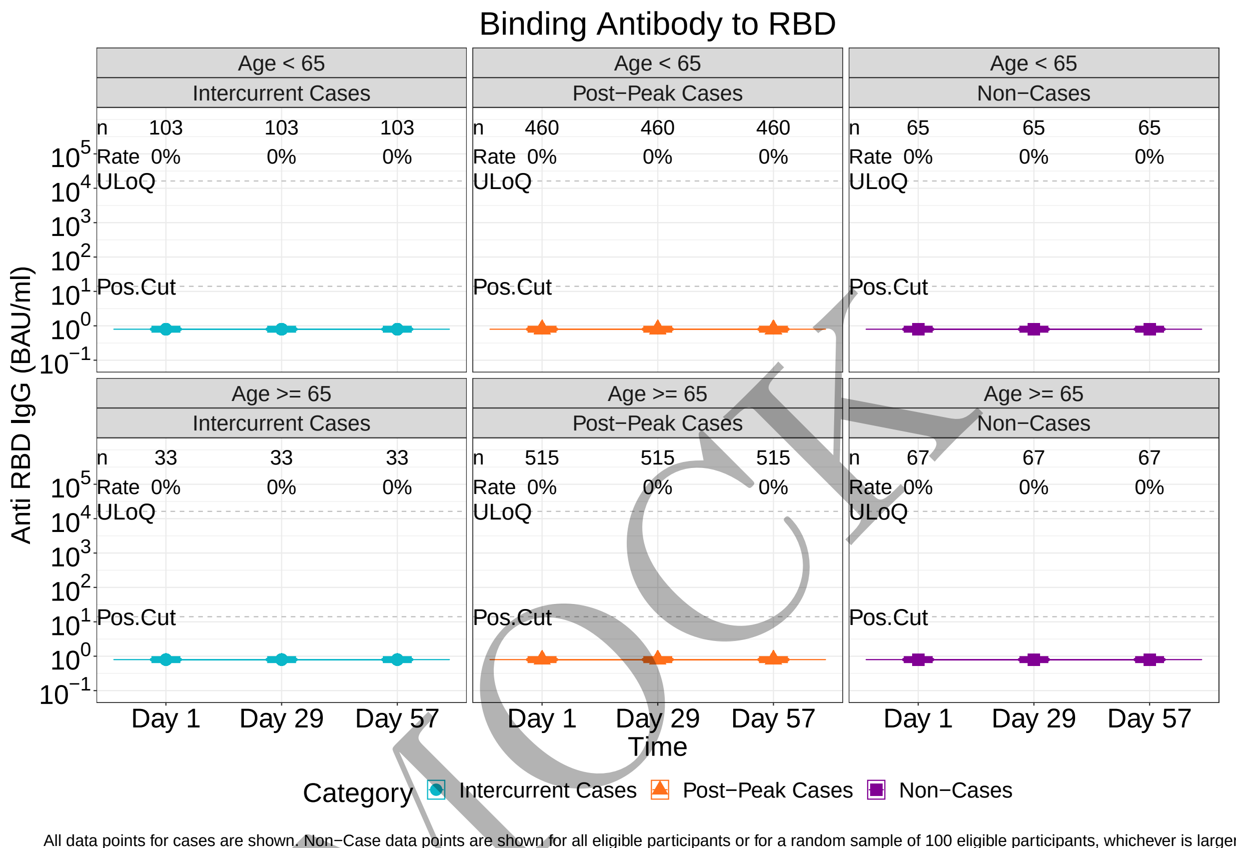

\caption{

Figure 2.5.50: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



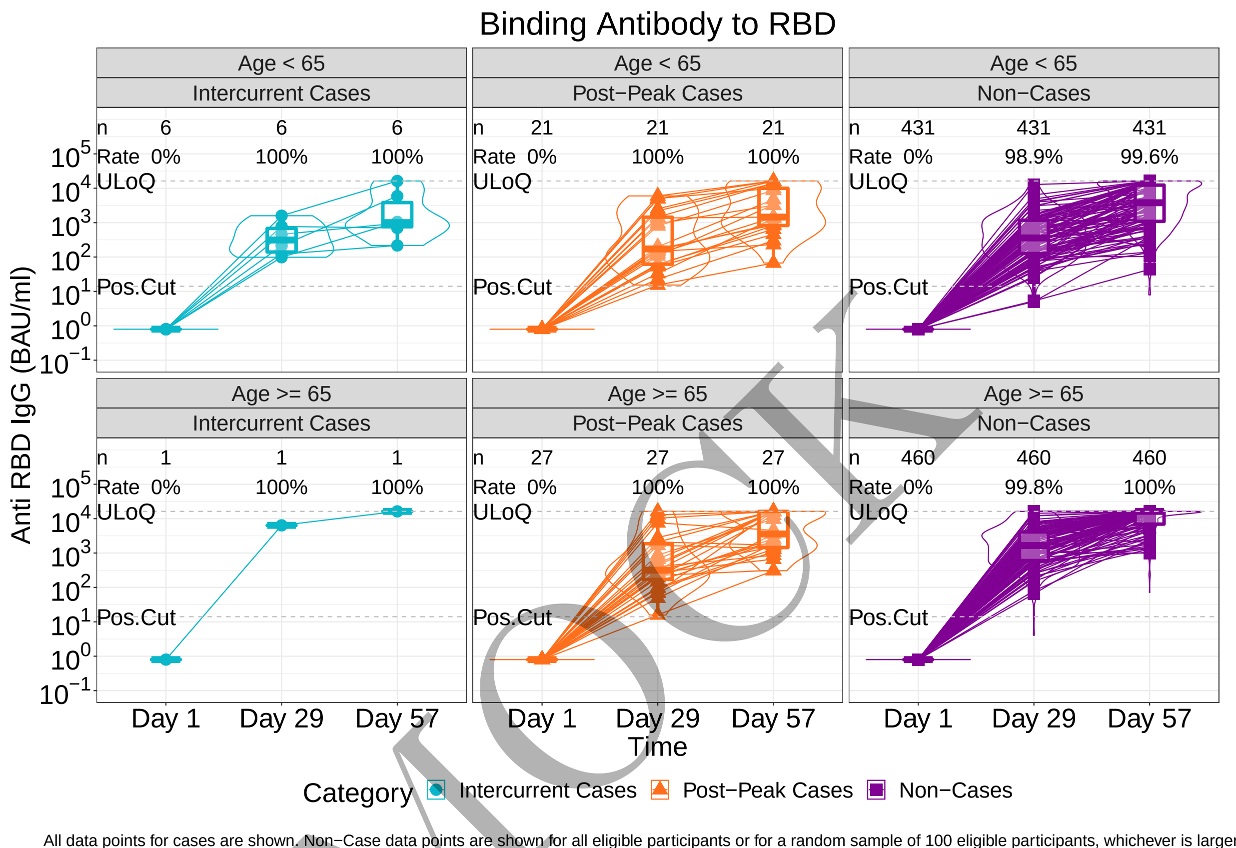

\caption{

Figure 2.5.51: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



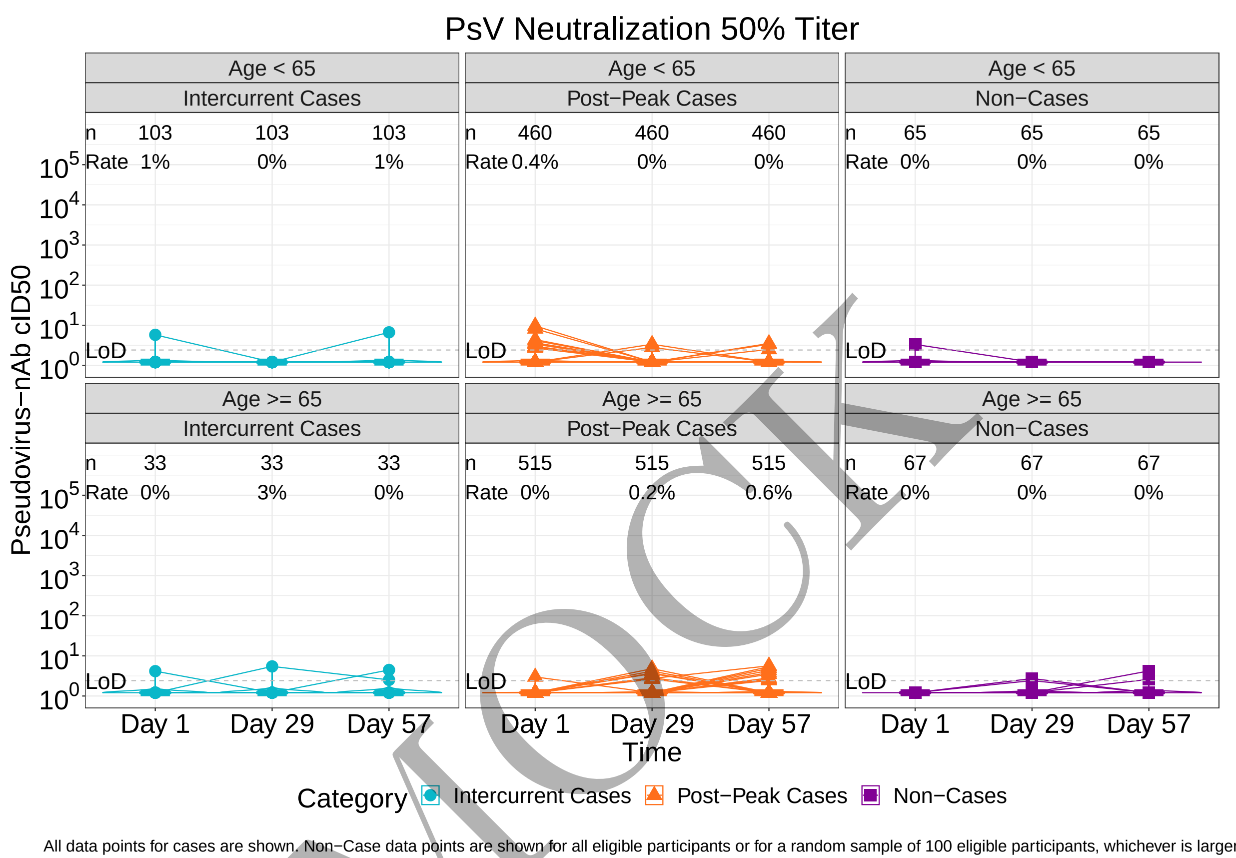

\caption{

Figure 2.5.52: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



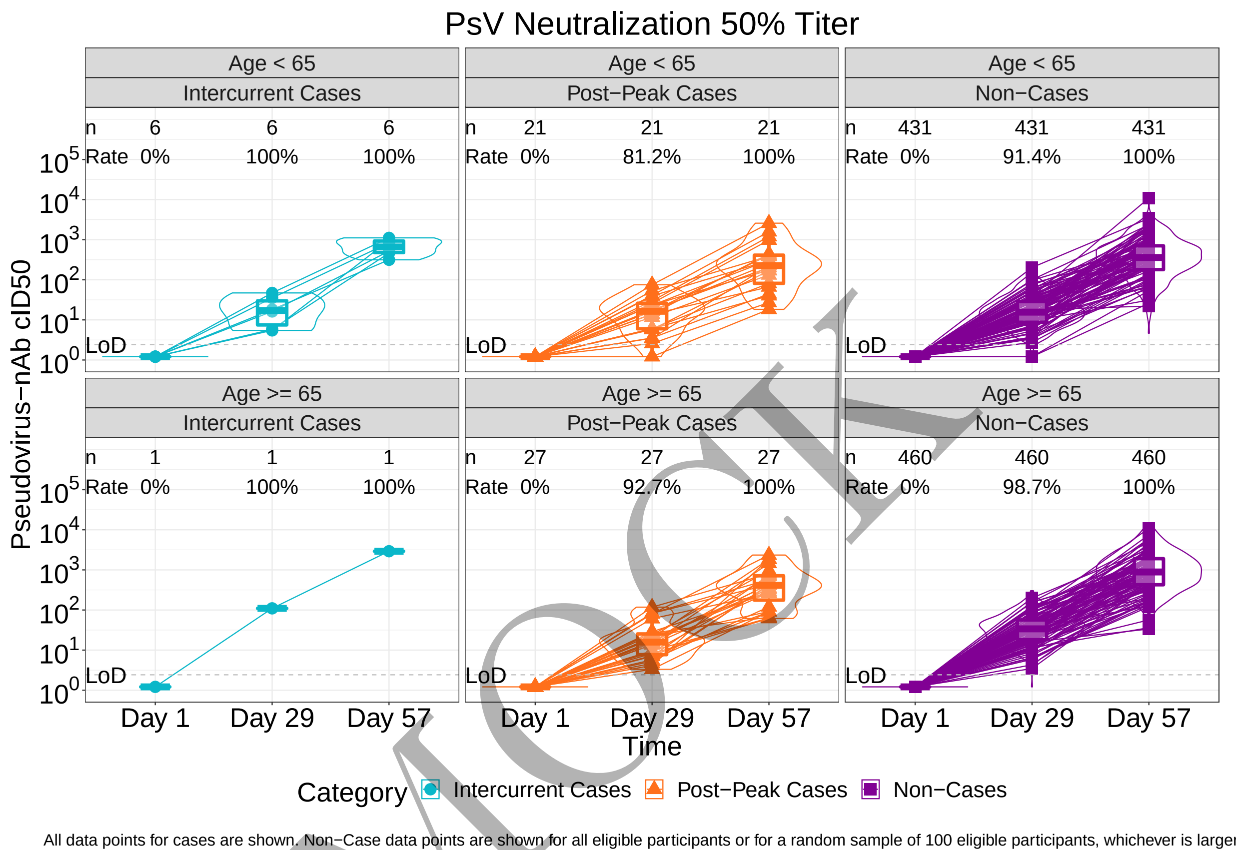

\caption{

Figure 2.5.53: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





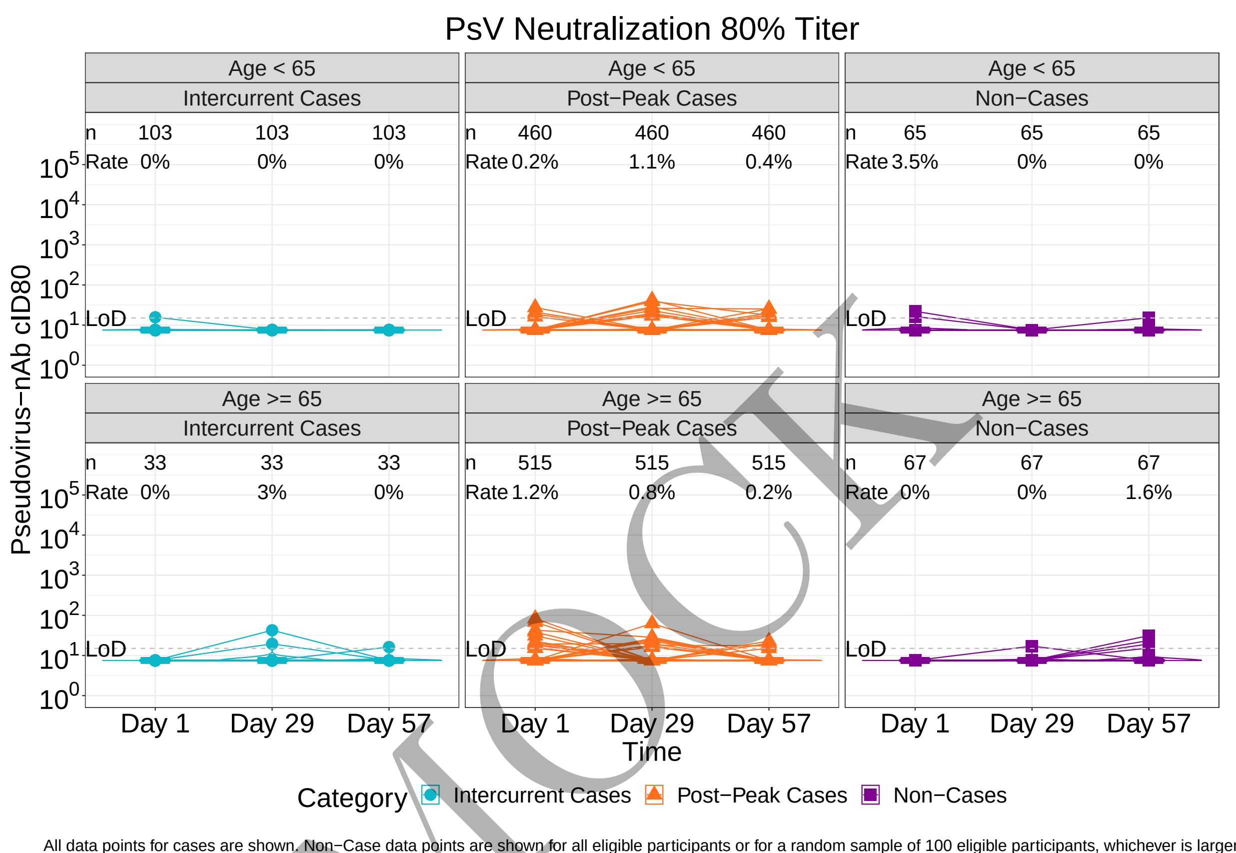

\caption{

Figure 2.5.54: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



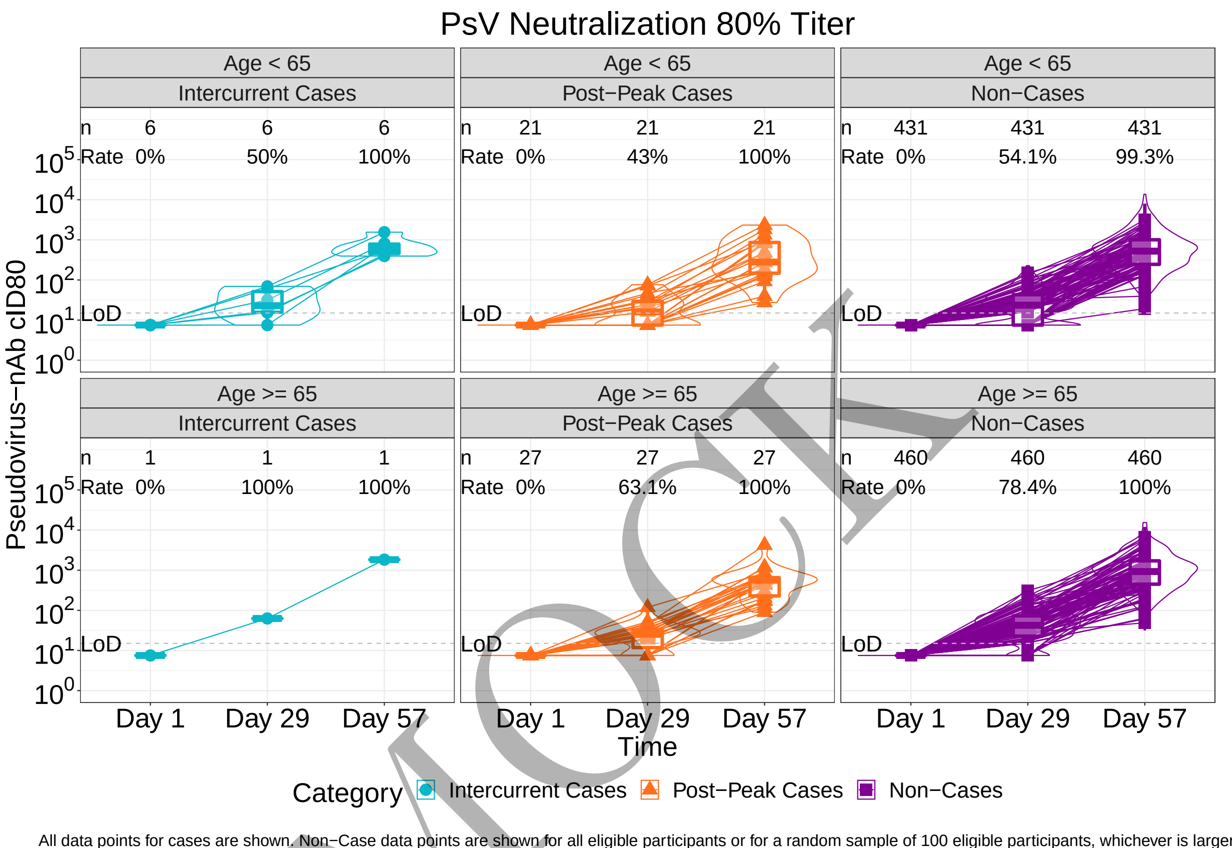

\caption{

Figure 2.5.55: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





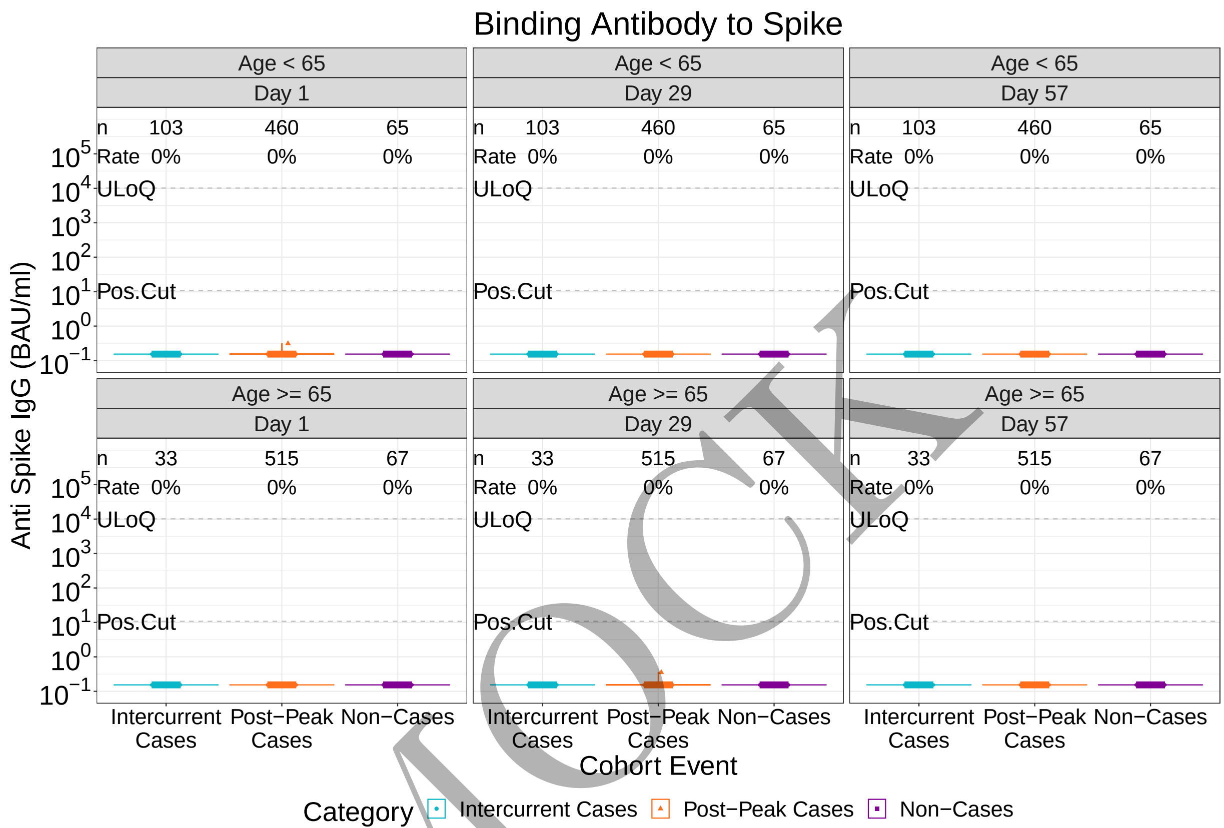

\caption{

Figure 2.5.56: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



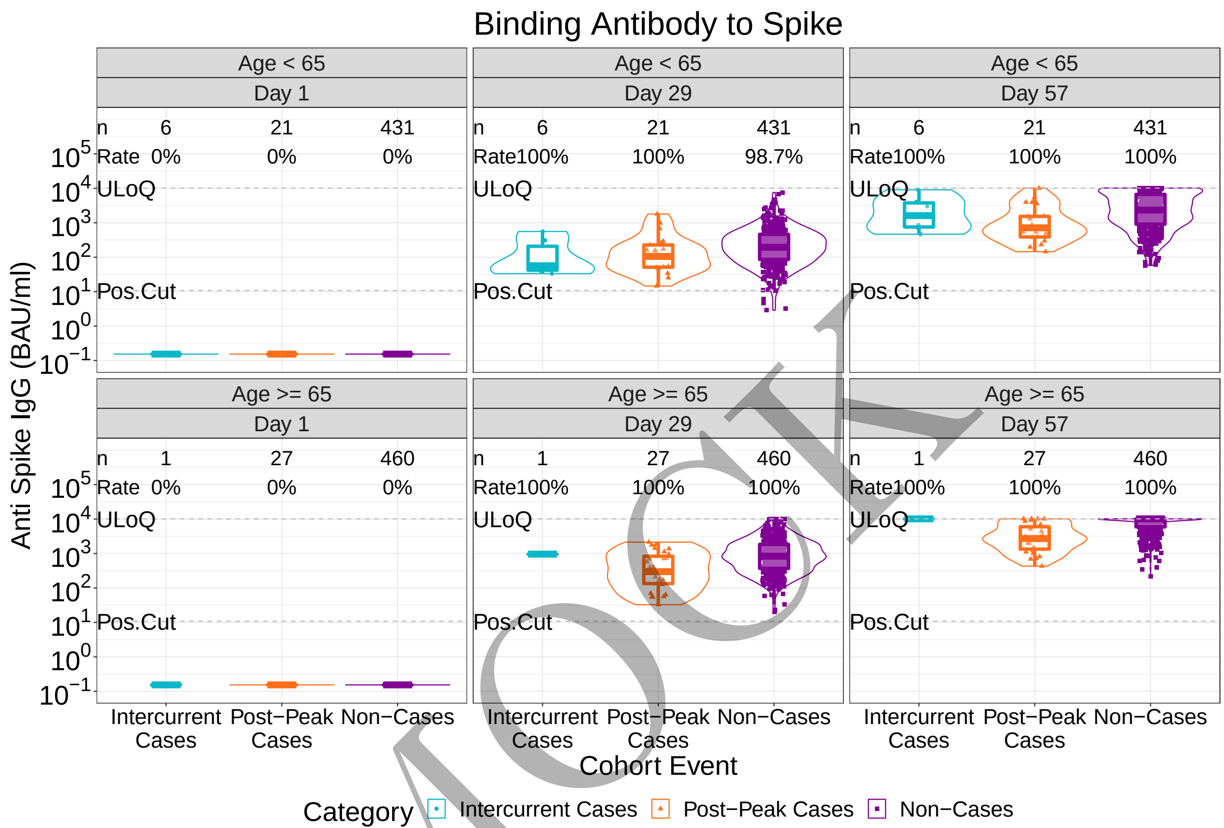

\caption{

Figure 2.5.57: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

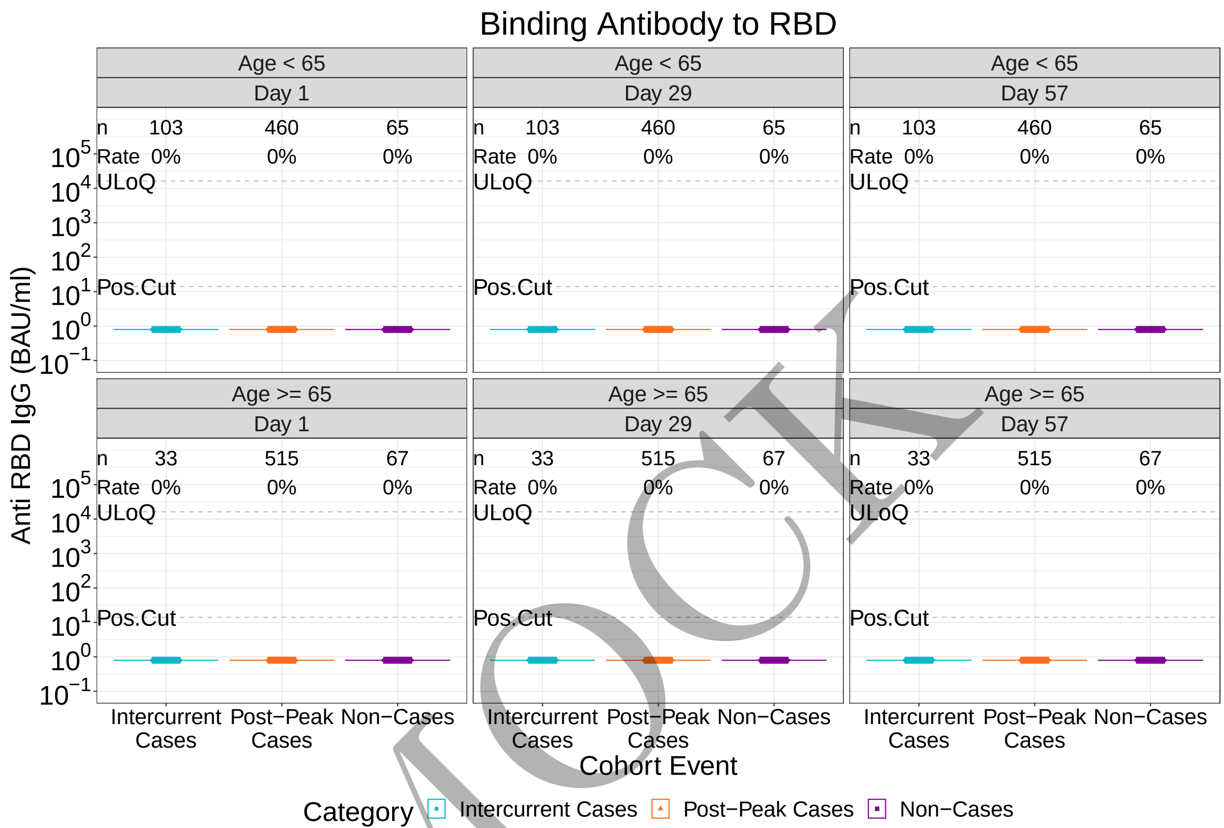
\begin{figure}




\caption{
Figure 2.5.58: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 2)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}

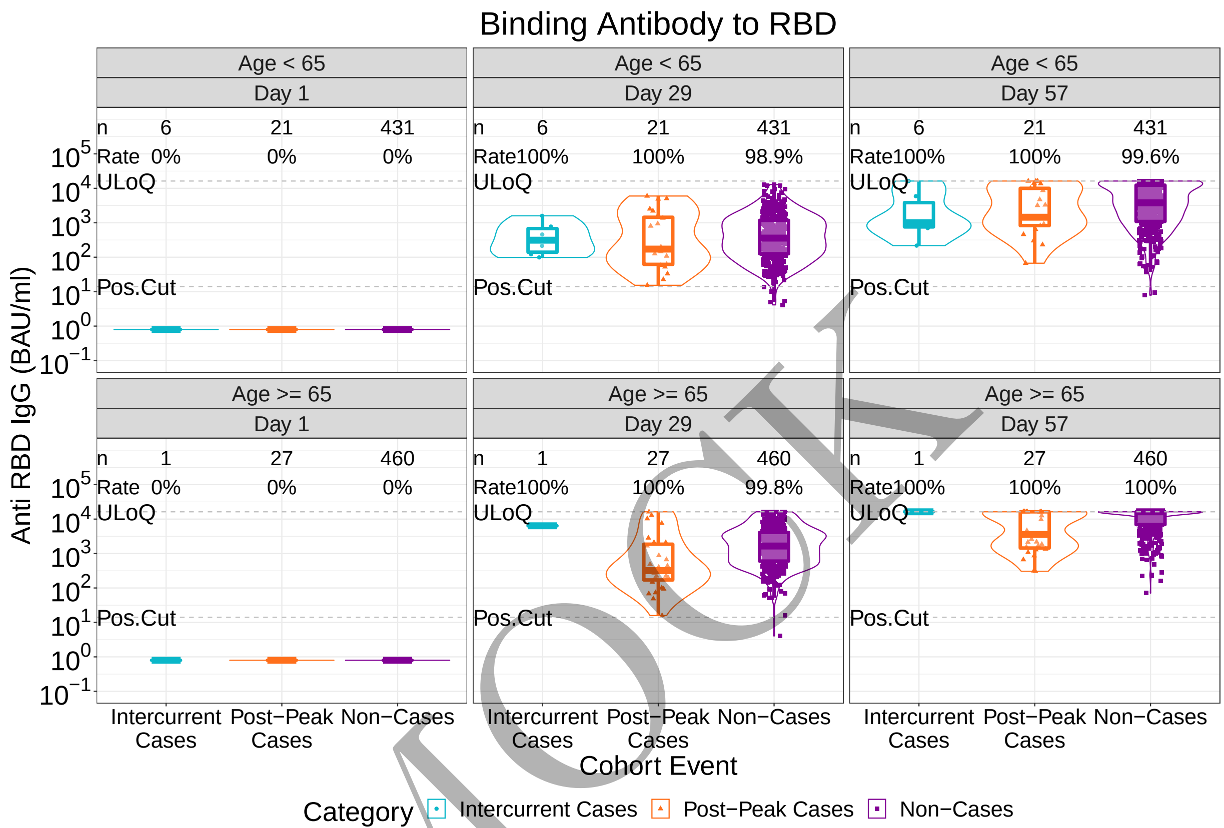





\caption{
Figure 2.5.59: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 2)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



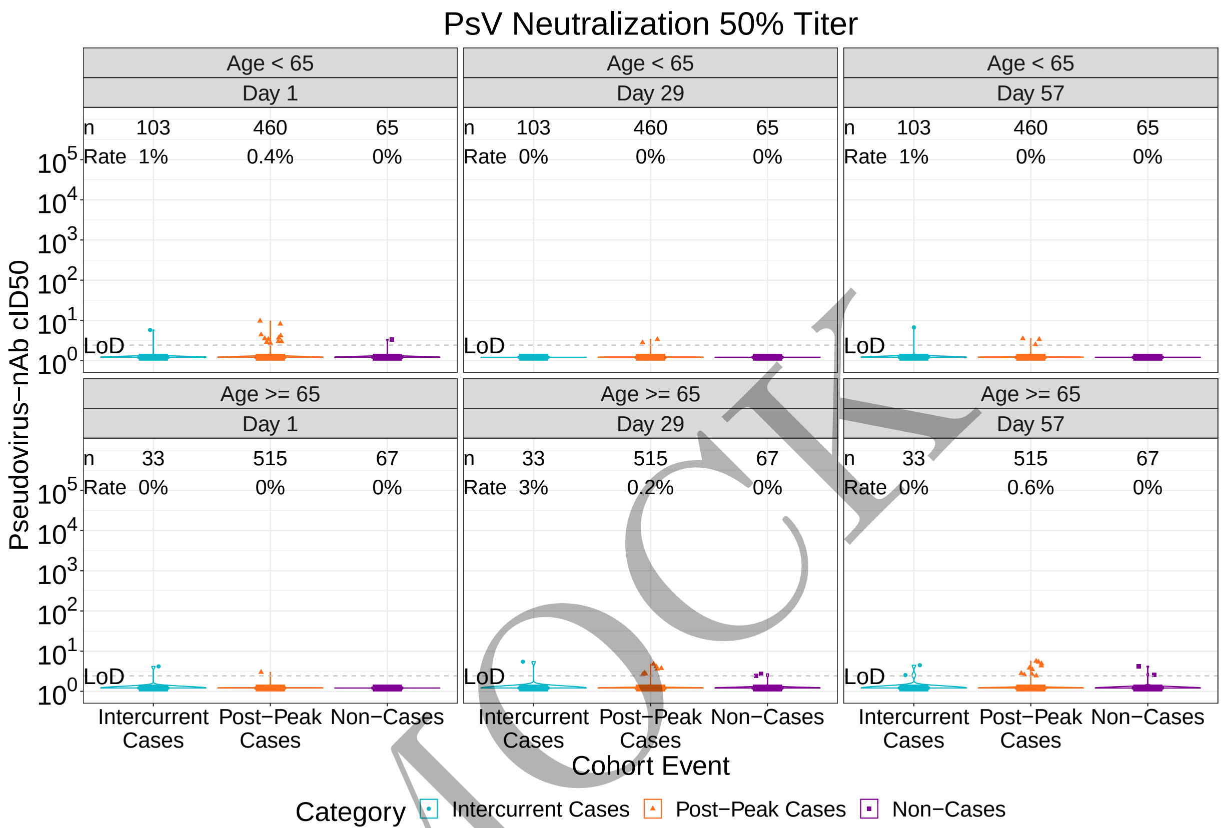

\caption{

Figure 2.5.60: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



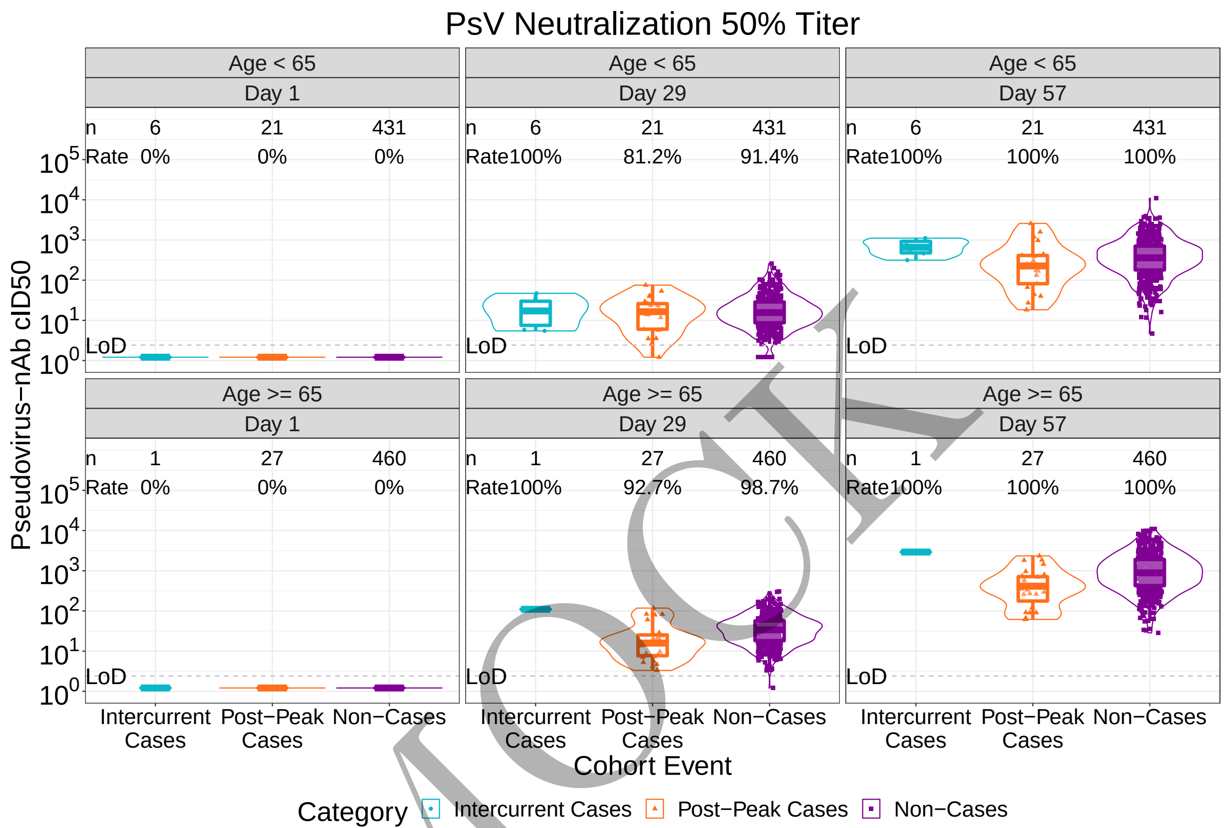

\caption{

Figure 2.5.61: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



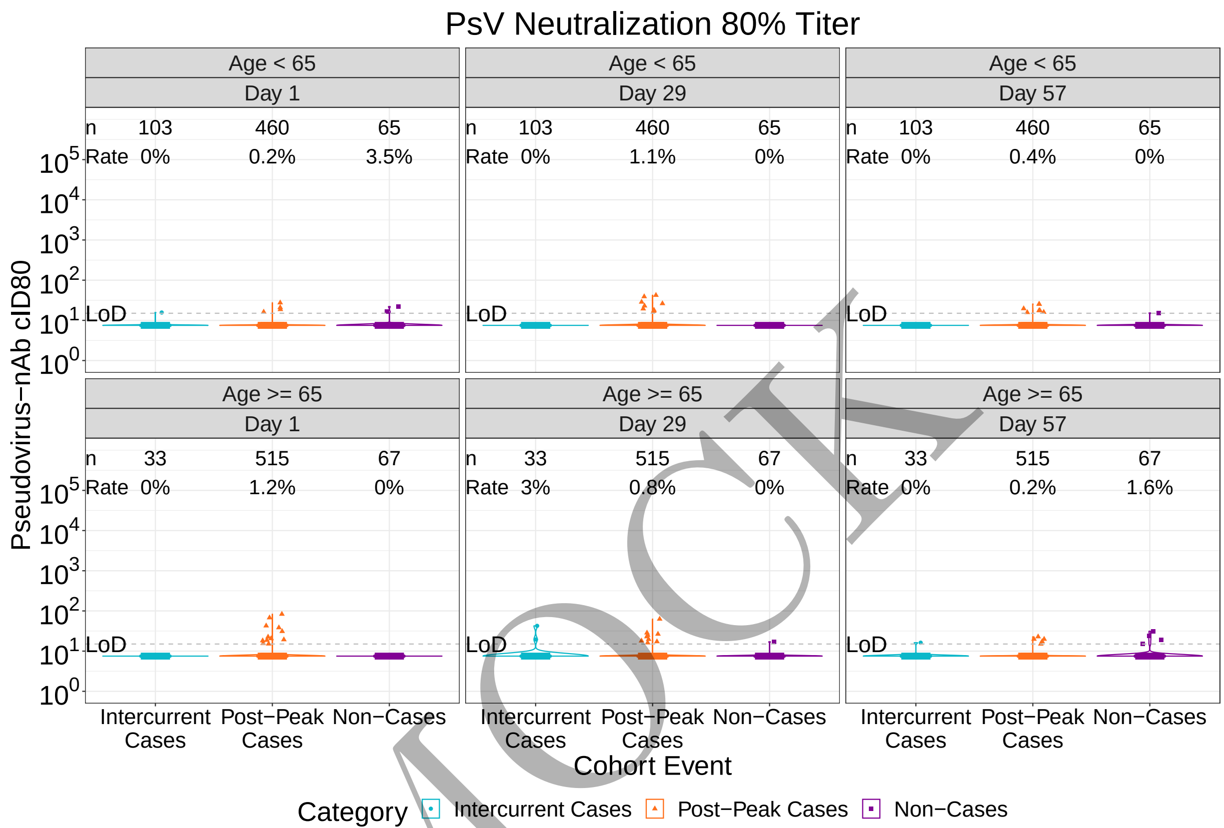

\caption{

Figure 2.5.62: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

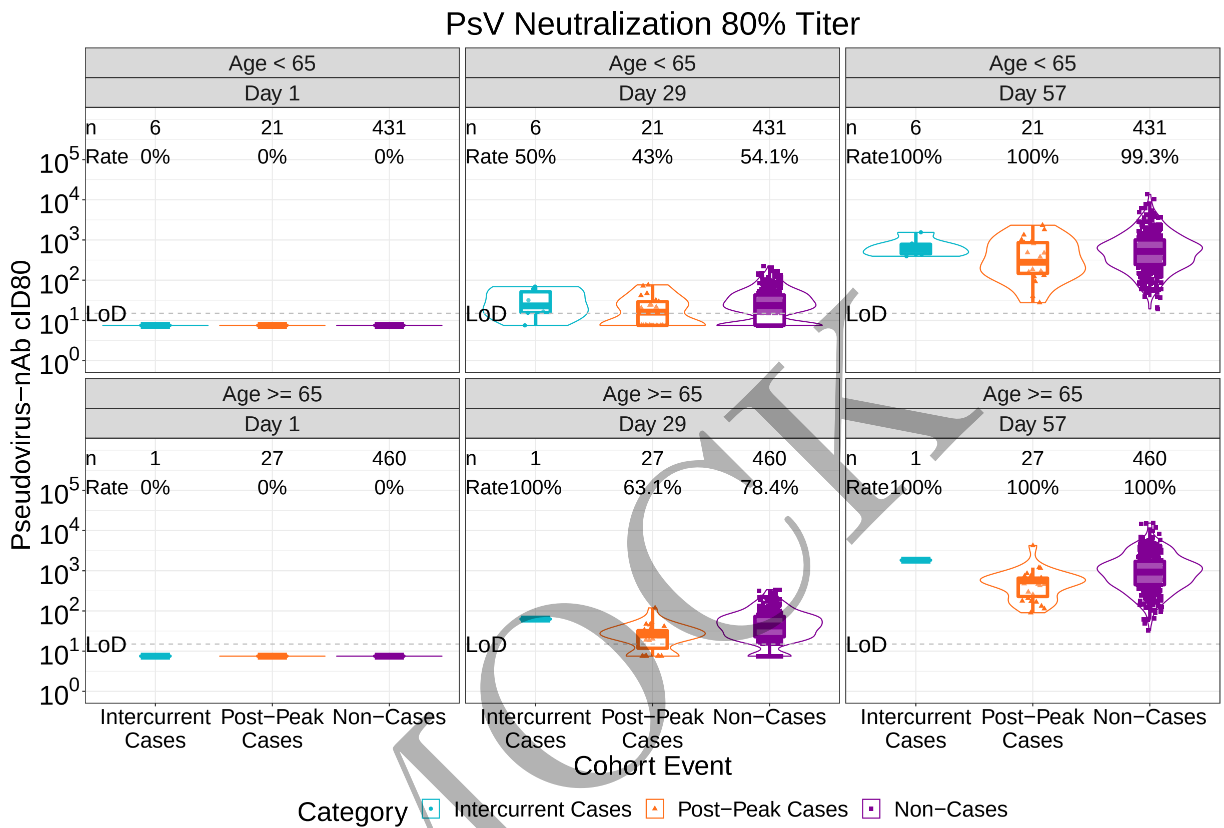
\begin{figure}




\caption{
Figure 2.5.63: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age (version 2)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

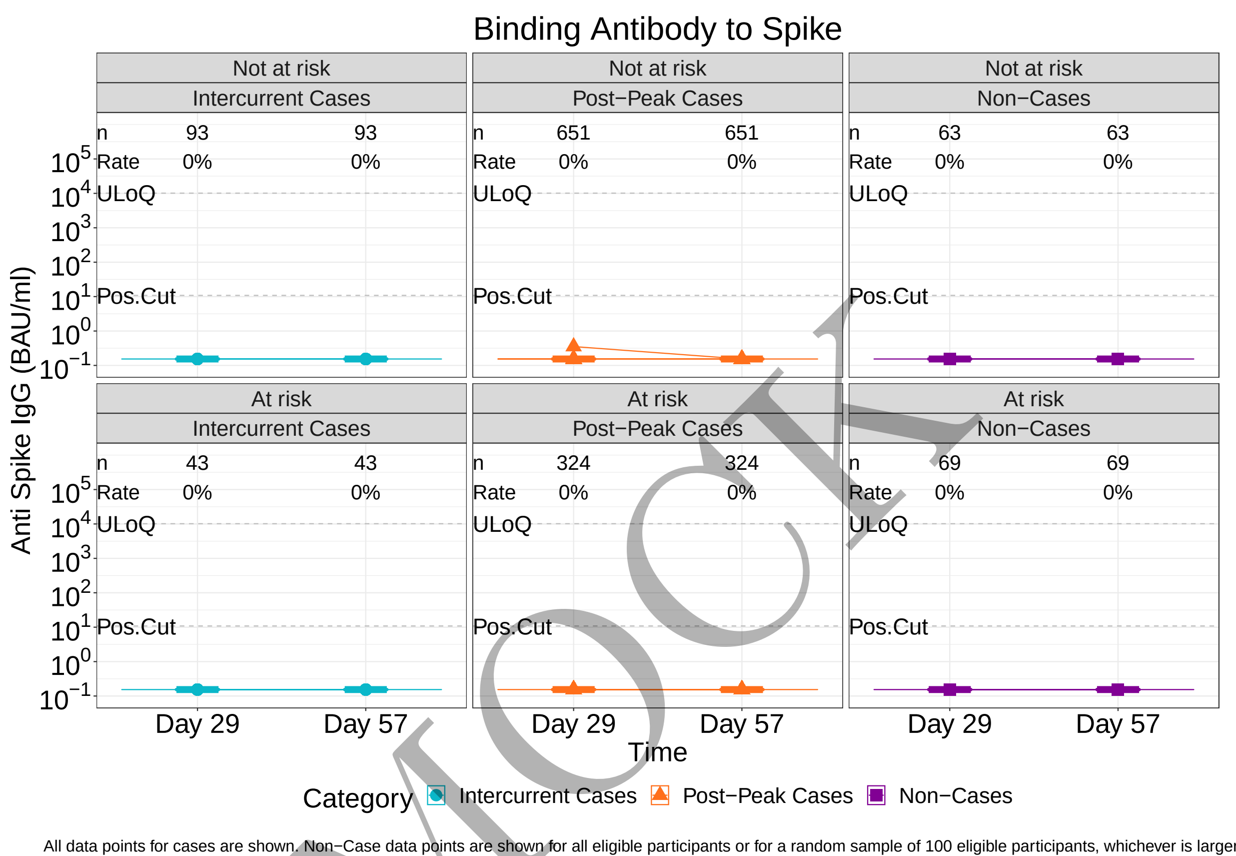
\begin{figure}




\caption{
Figure 2.5.64: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age (version 2)
} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}





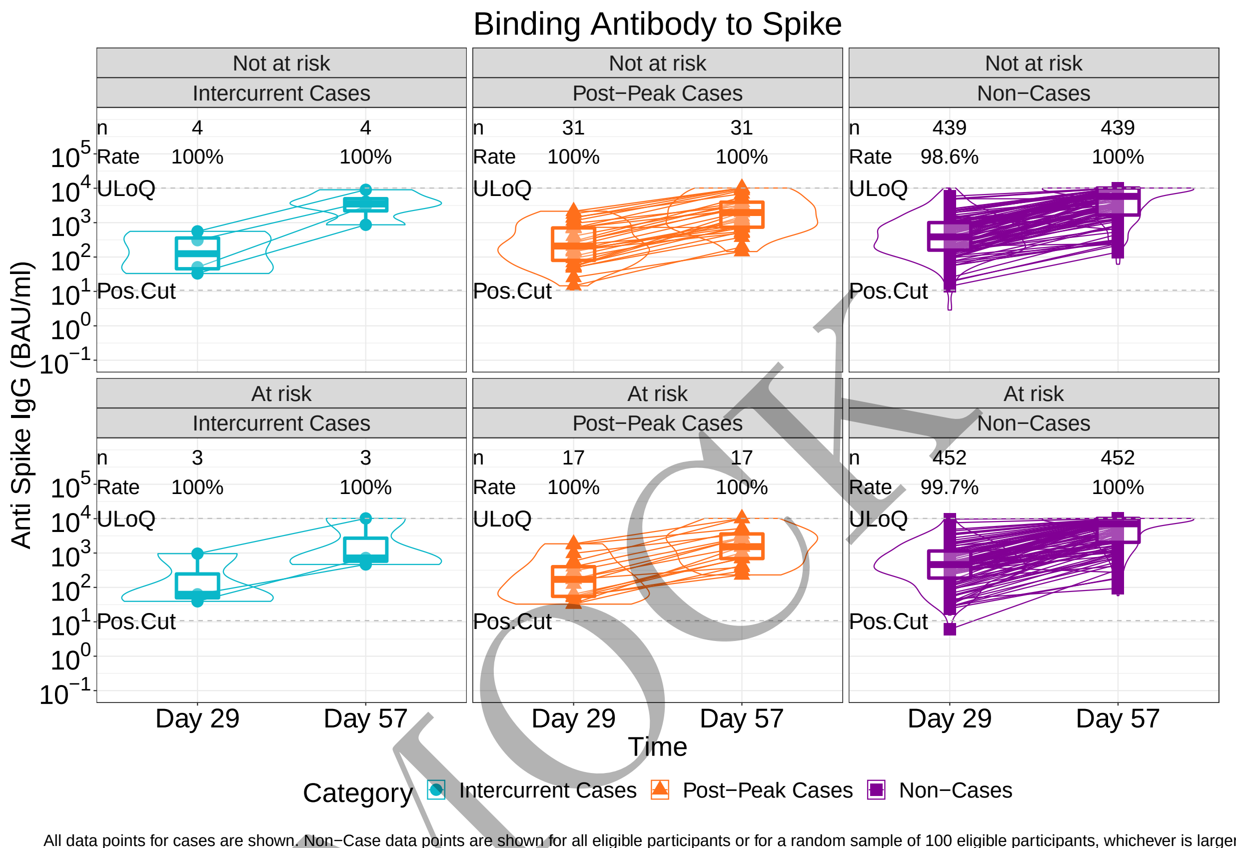
\caption{

Figure 2.5.65: lineplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



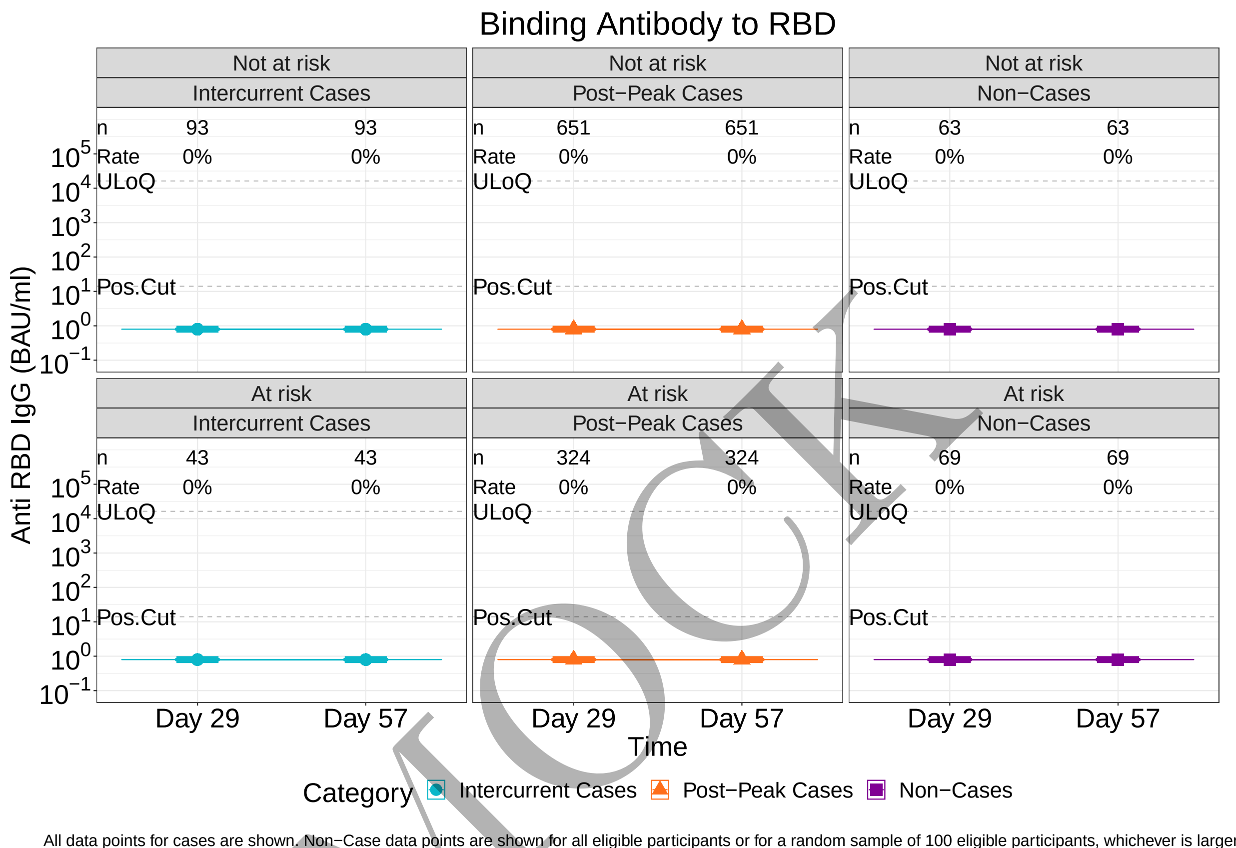

\caption{

Figure 2.5.66: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



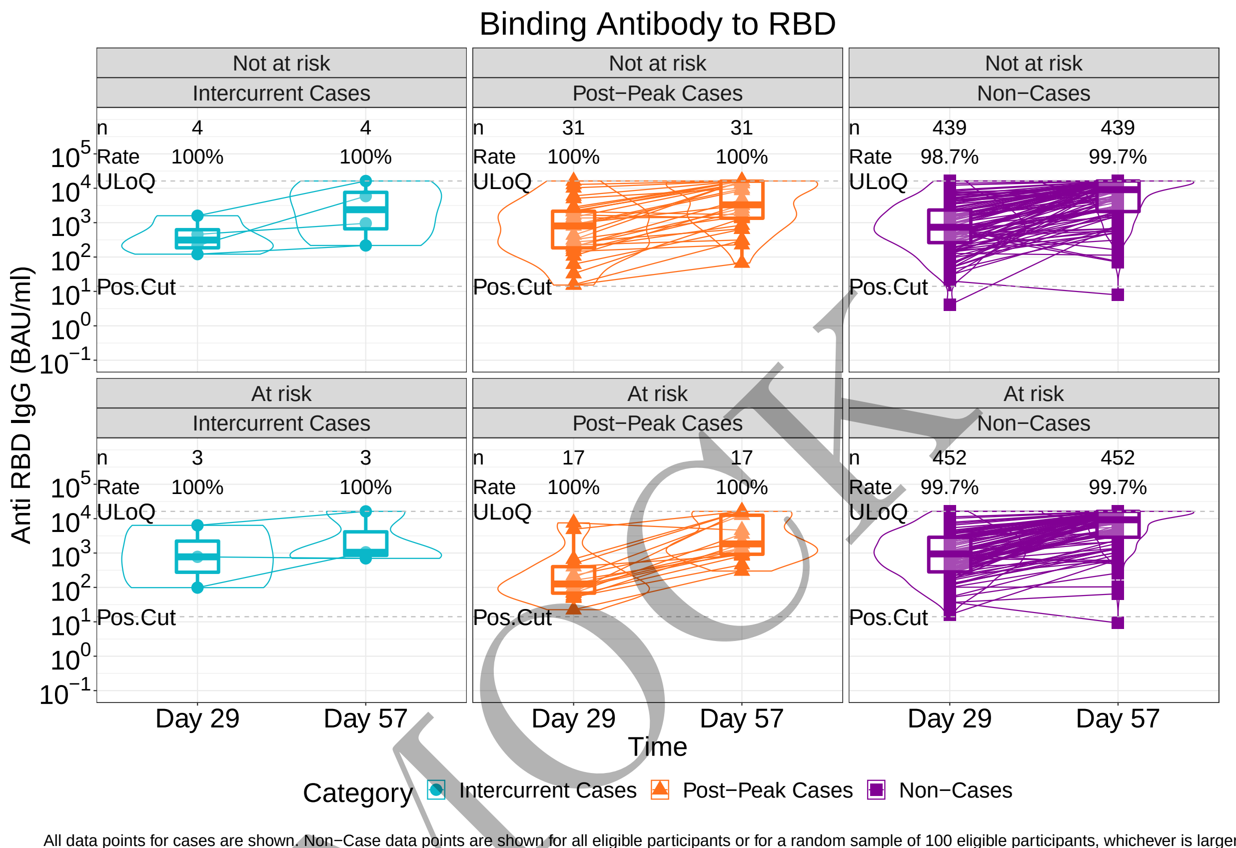

\caption{

Figure 2.5.67: lineplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



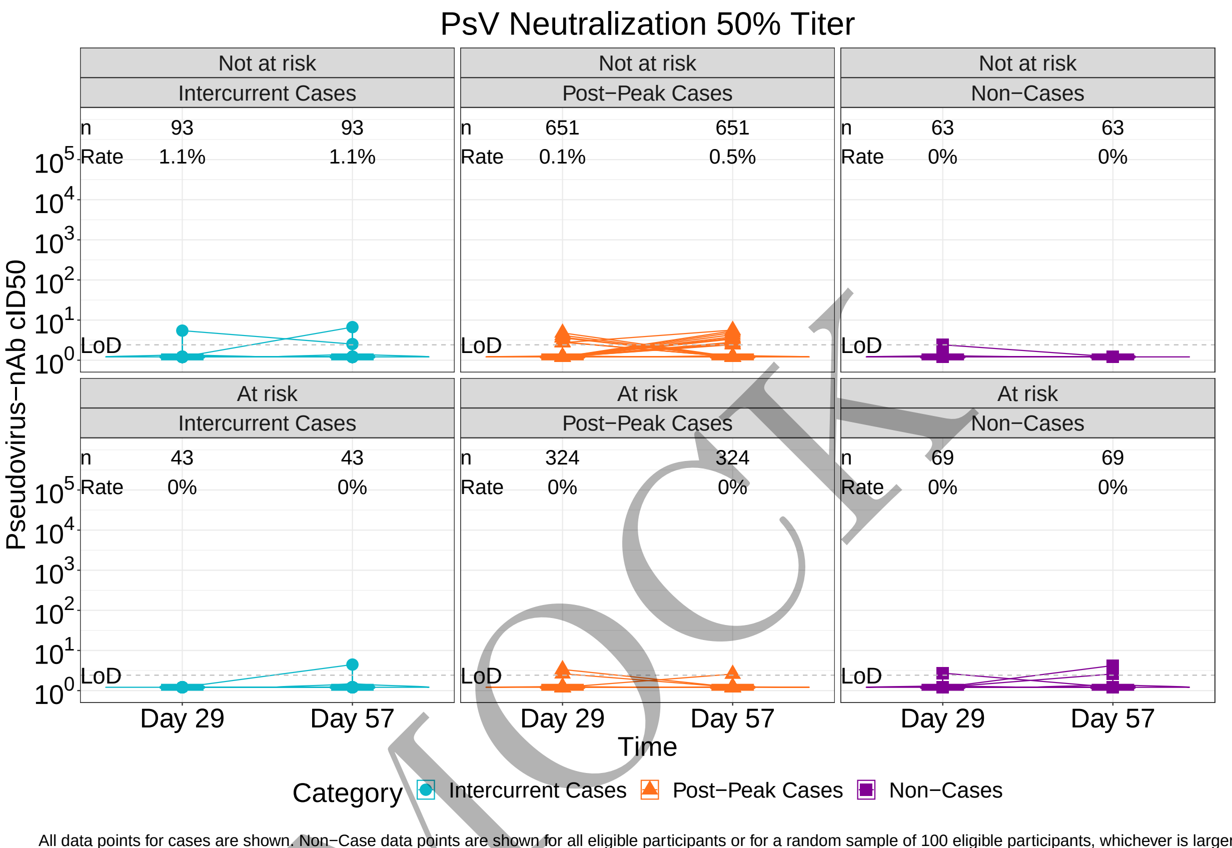

\caption{

Figure 2.5.68: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



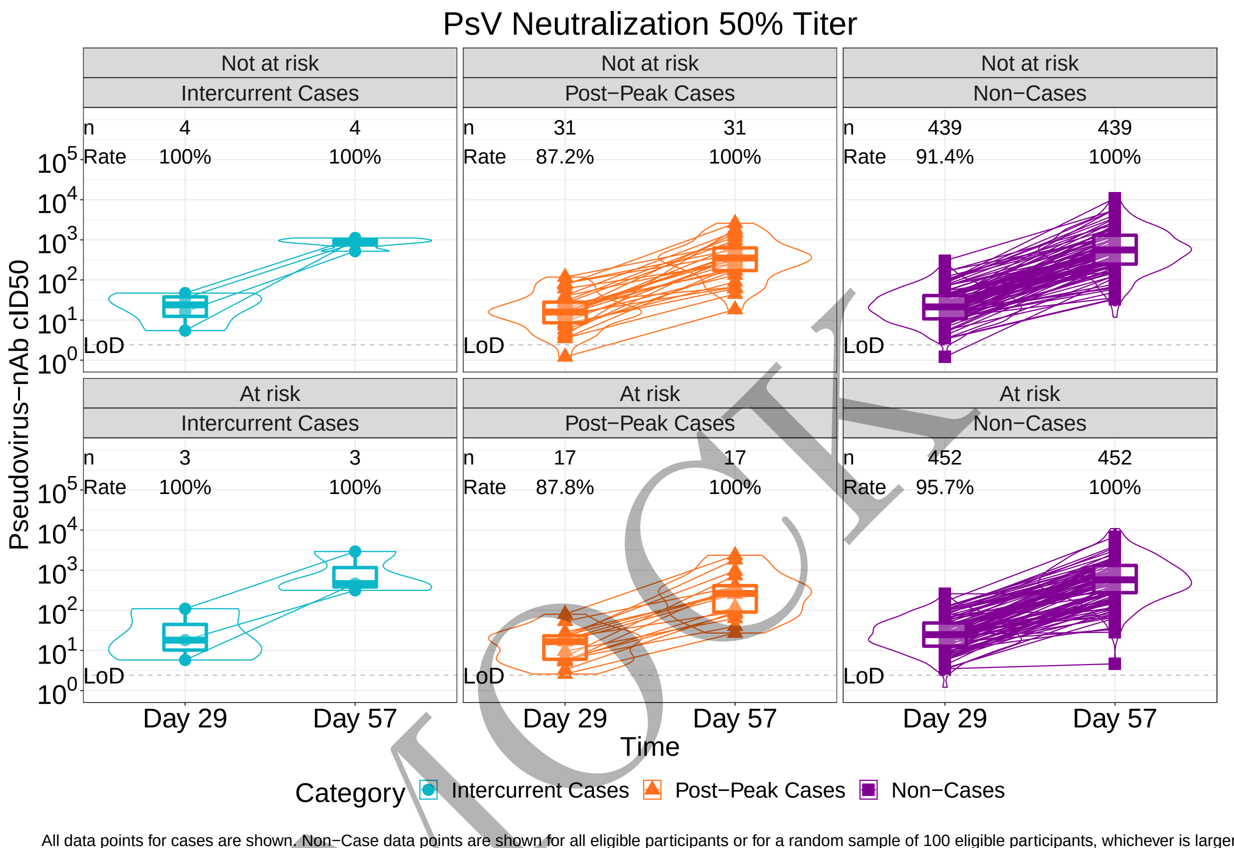

\caption{

Figure 2.5.69: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}



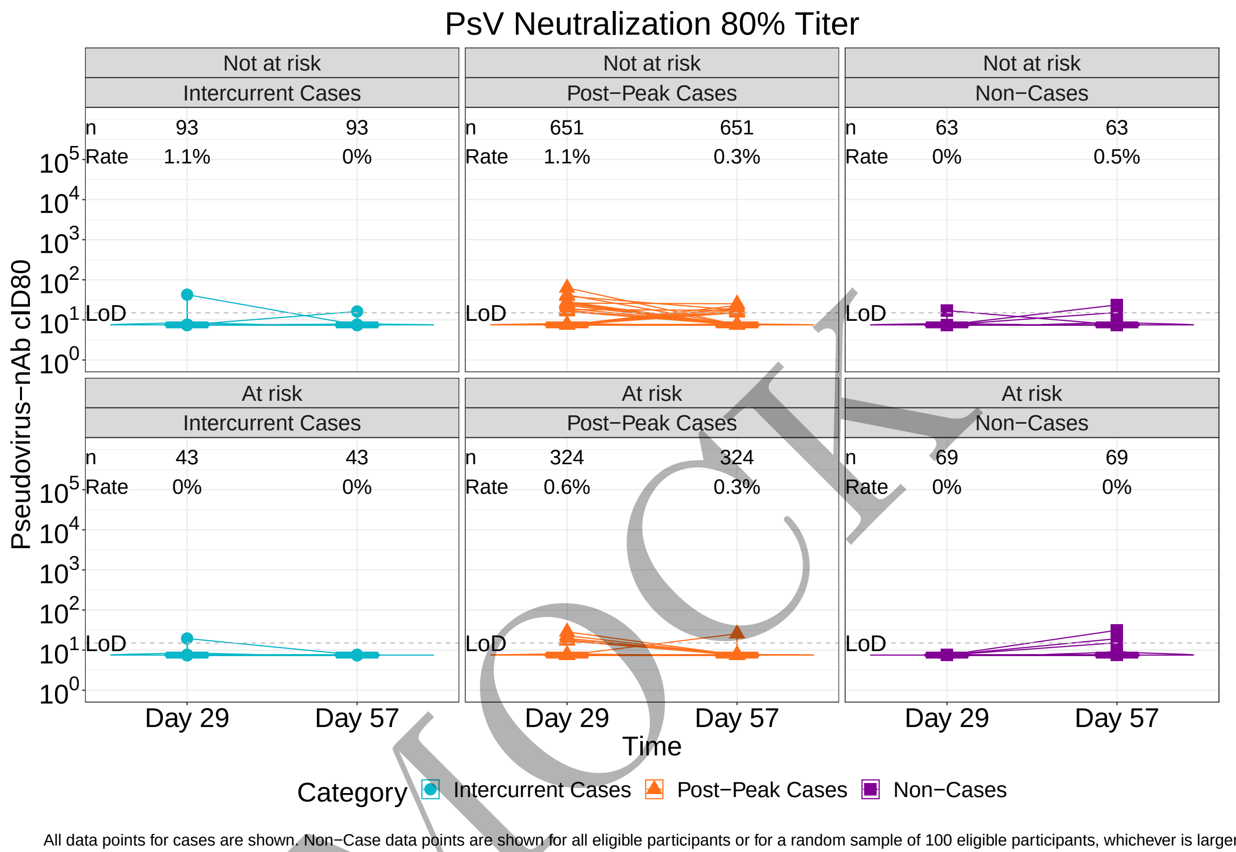

\caption{

Figure 2.5.70: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



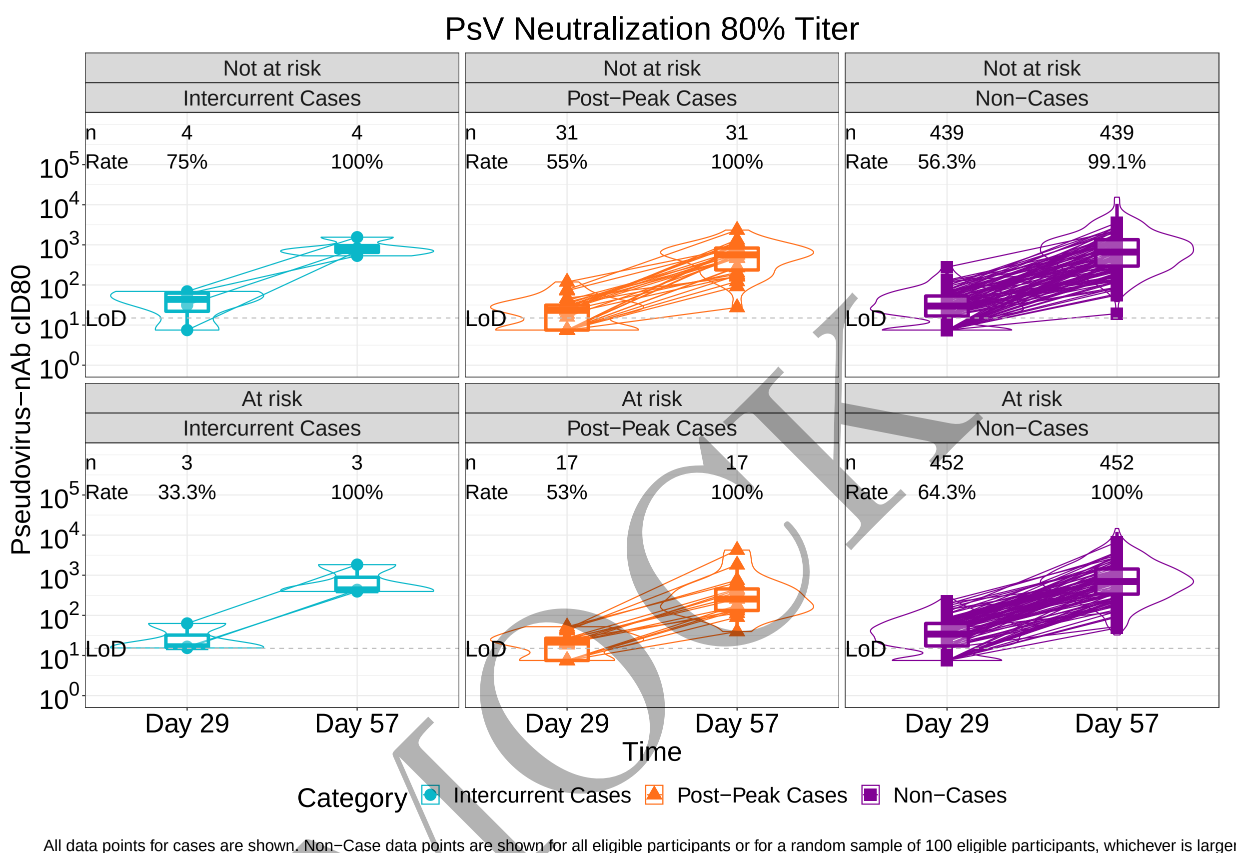

\caption{

Figure 2.5.71: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



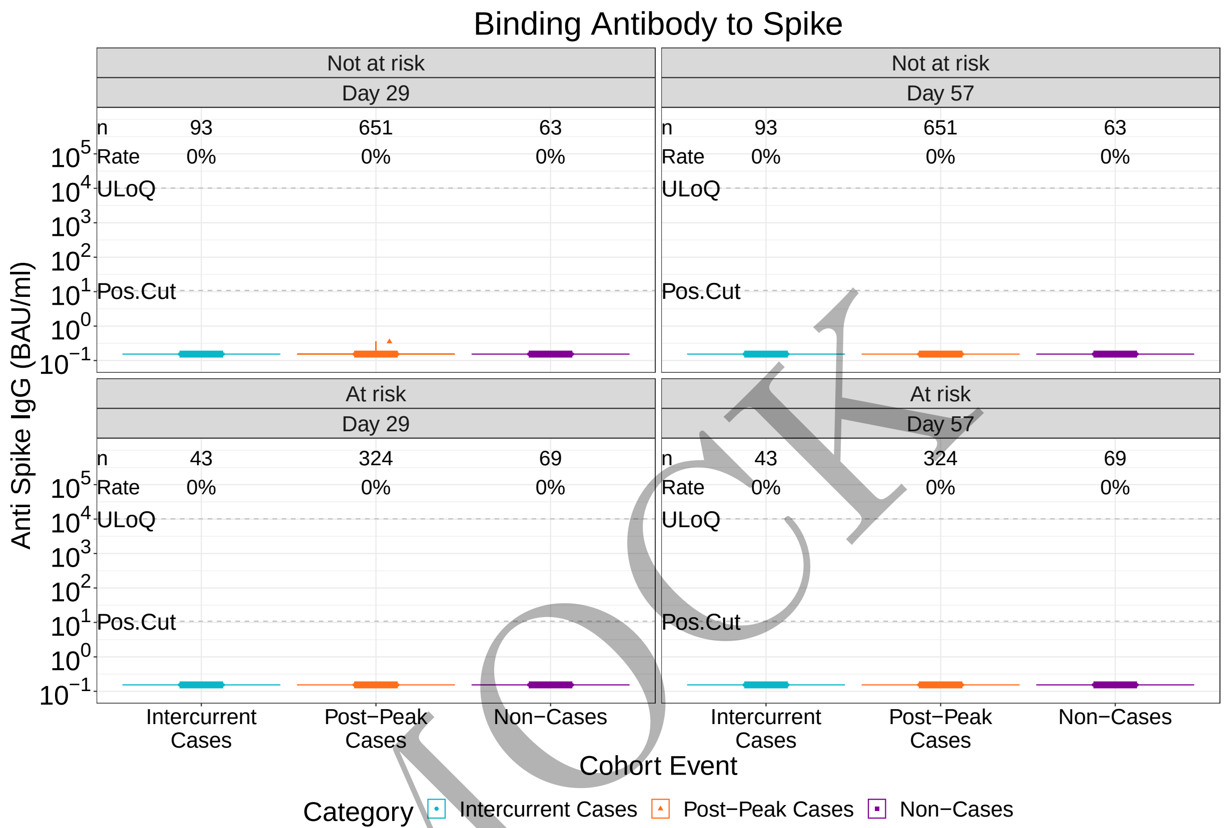

\caption{

Figure 2.5.72: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



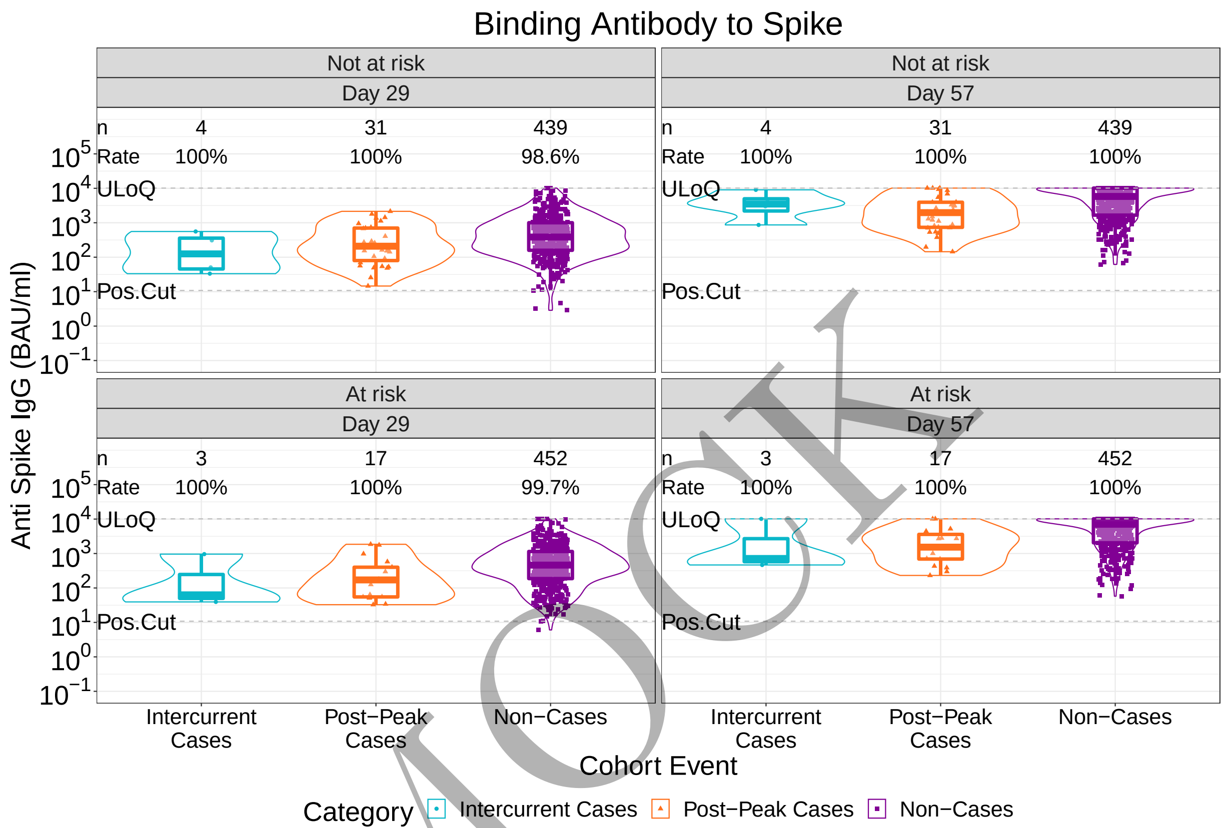

\caption{

Figure 2.5.73: violinplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}





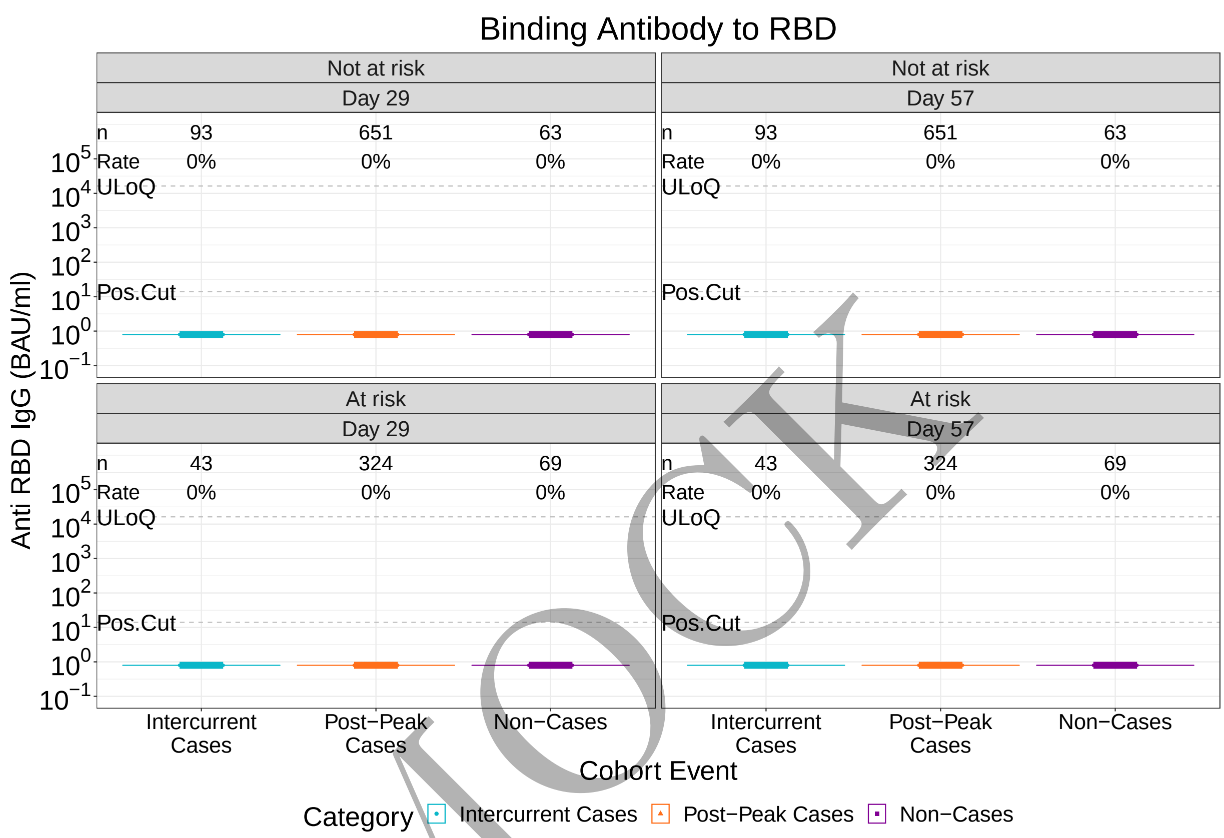

\caption{

Figure 2.5.74: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



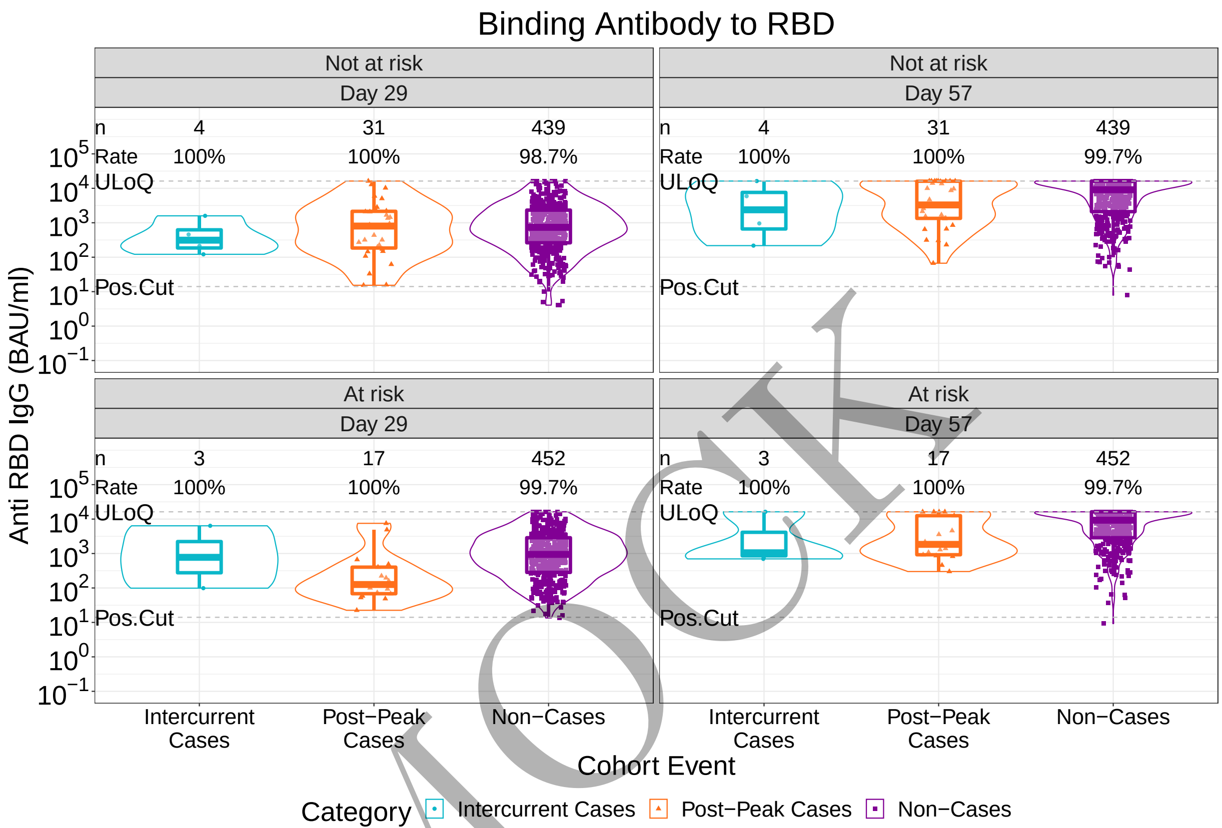

\caption{

Figure 2.5.75: violinplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



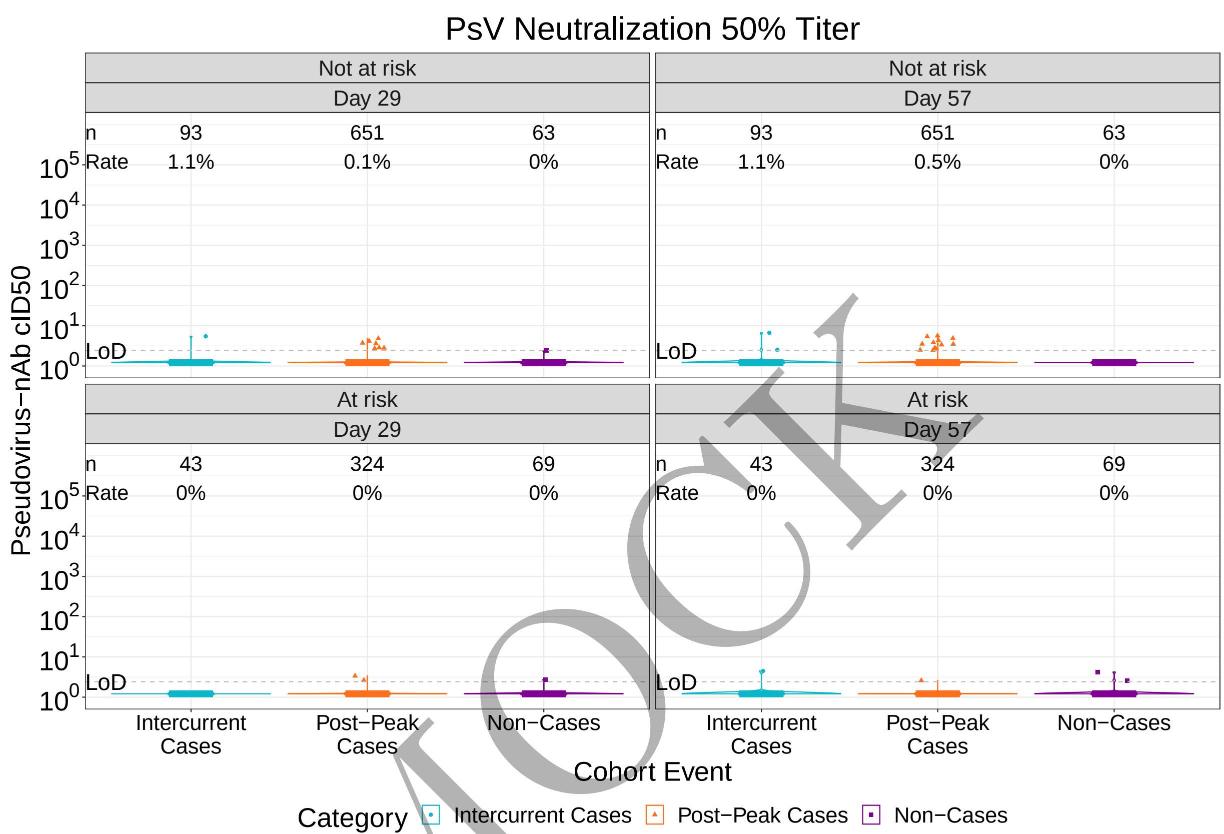

\caption{

Figure 2.5.76: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}





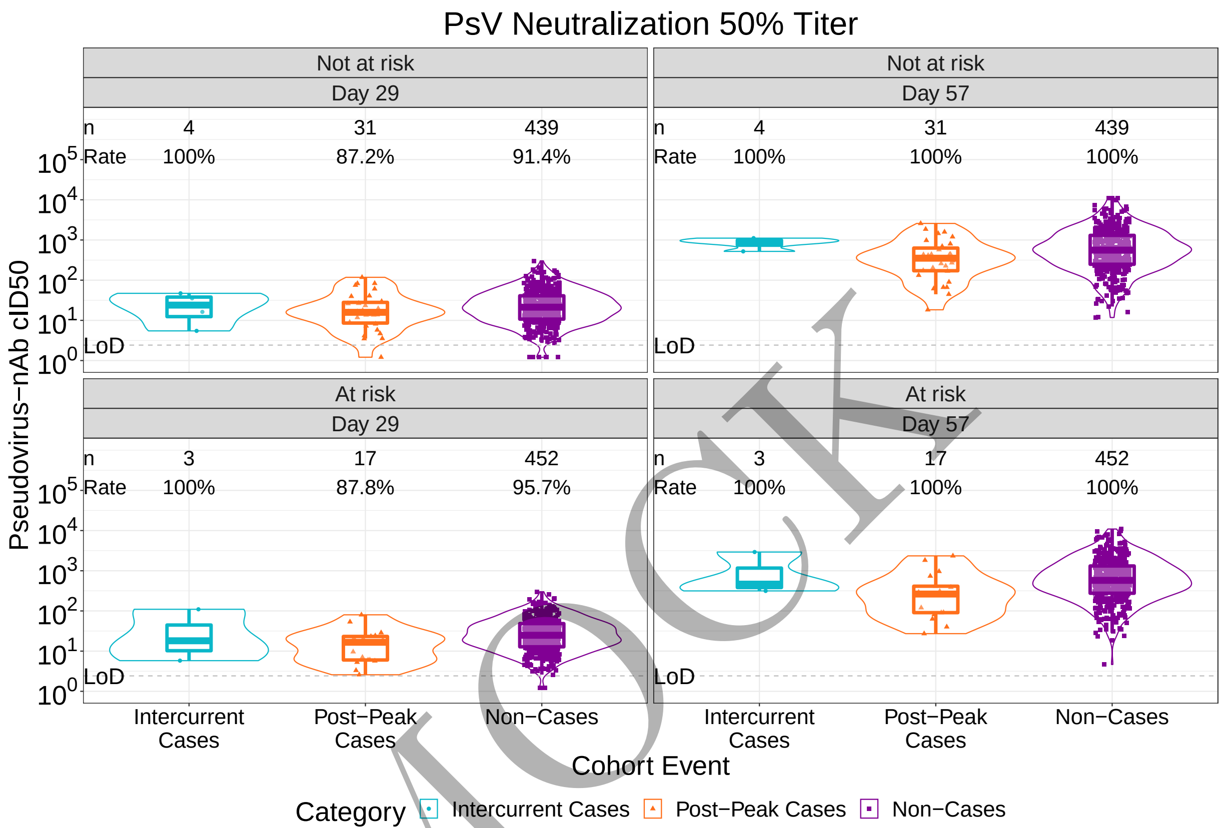

\caption{

Figure 2.5.77: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



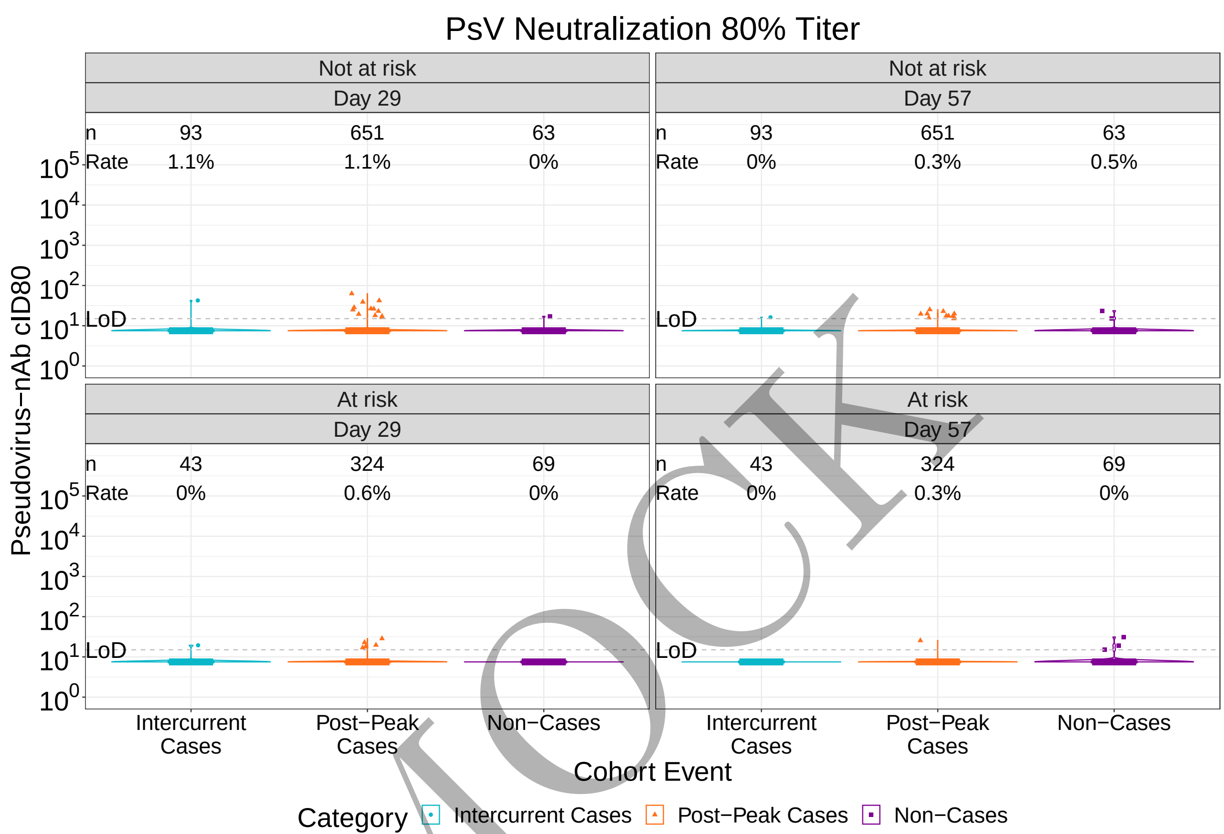

\caption{

Figure 2.5.78: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



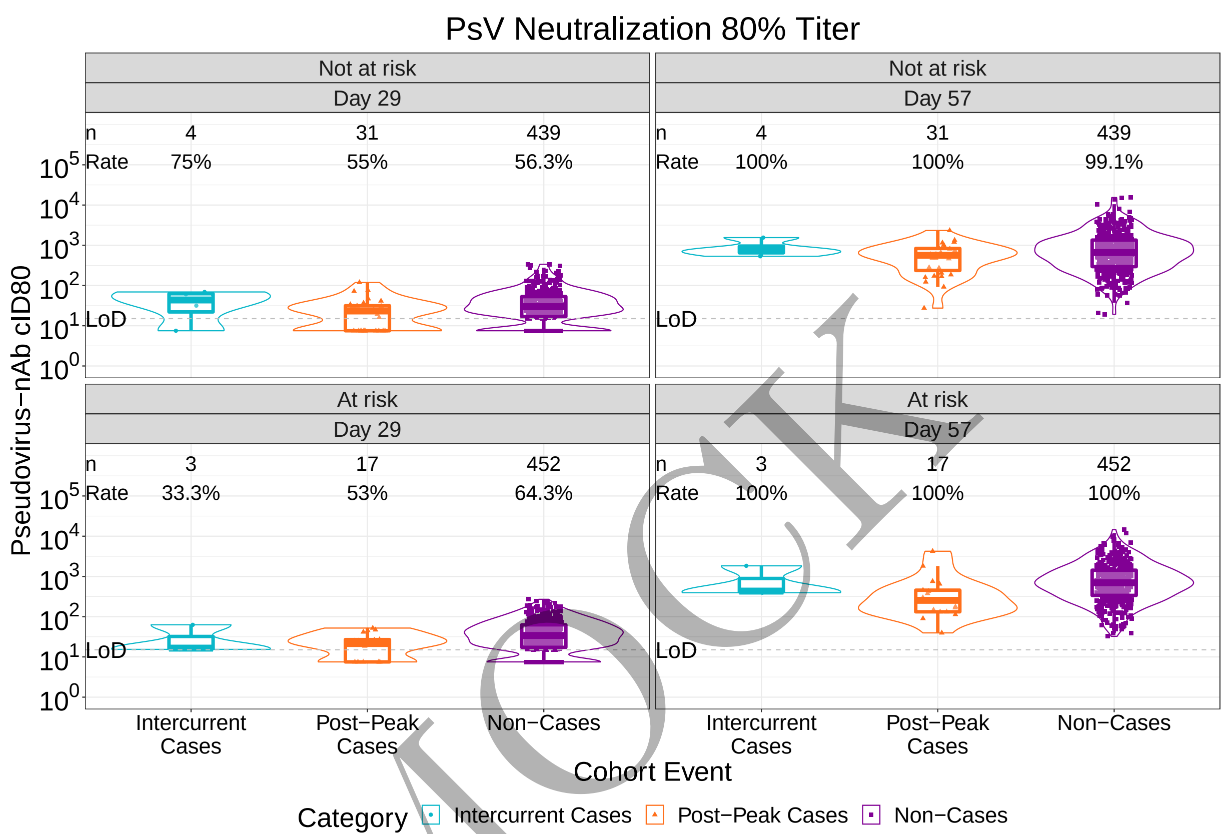

\caption{

Figure 2.5.79: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





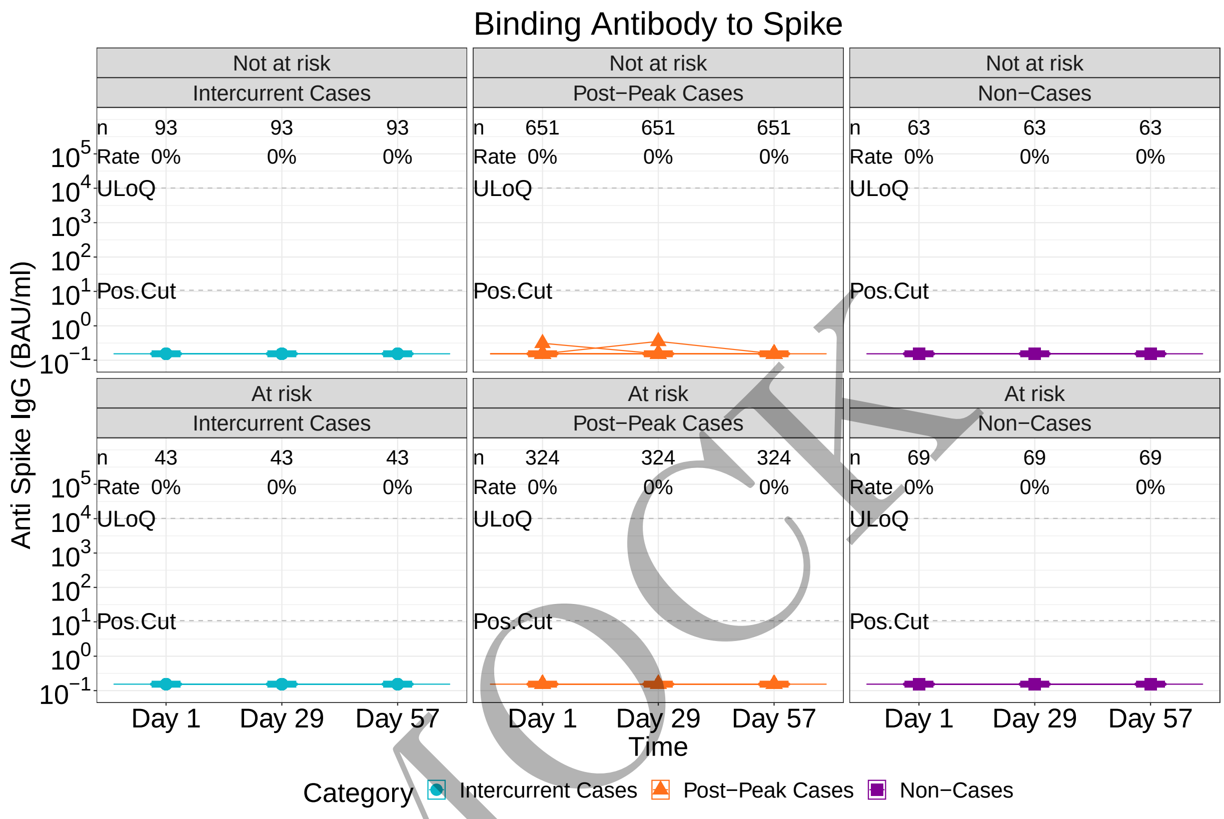
\caption{

Figure 2.5.80: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}




All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

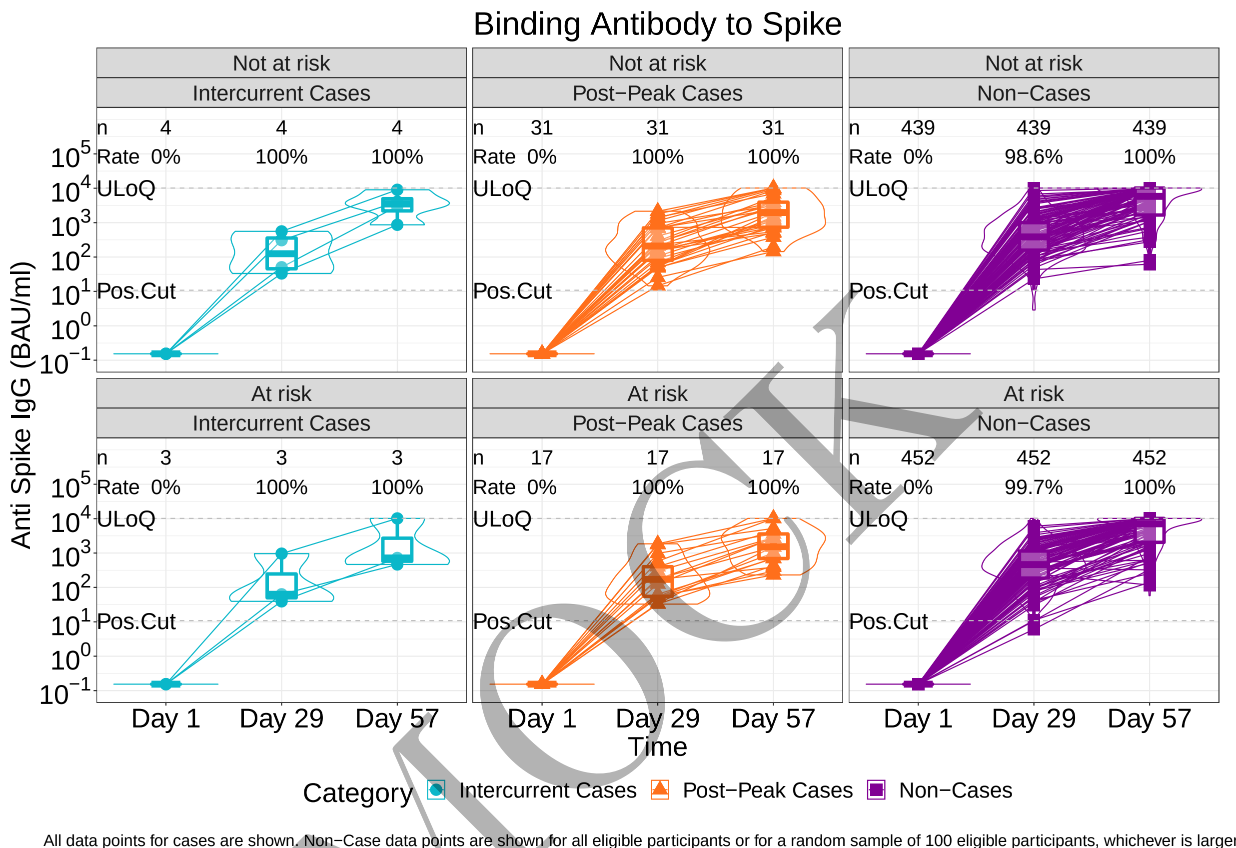
\caption{

Figure 2.5.81: lineplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



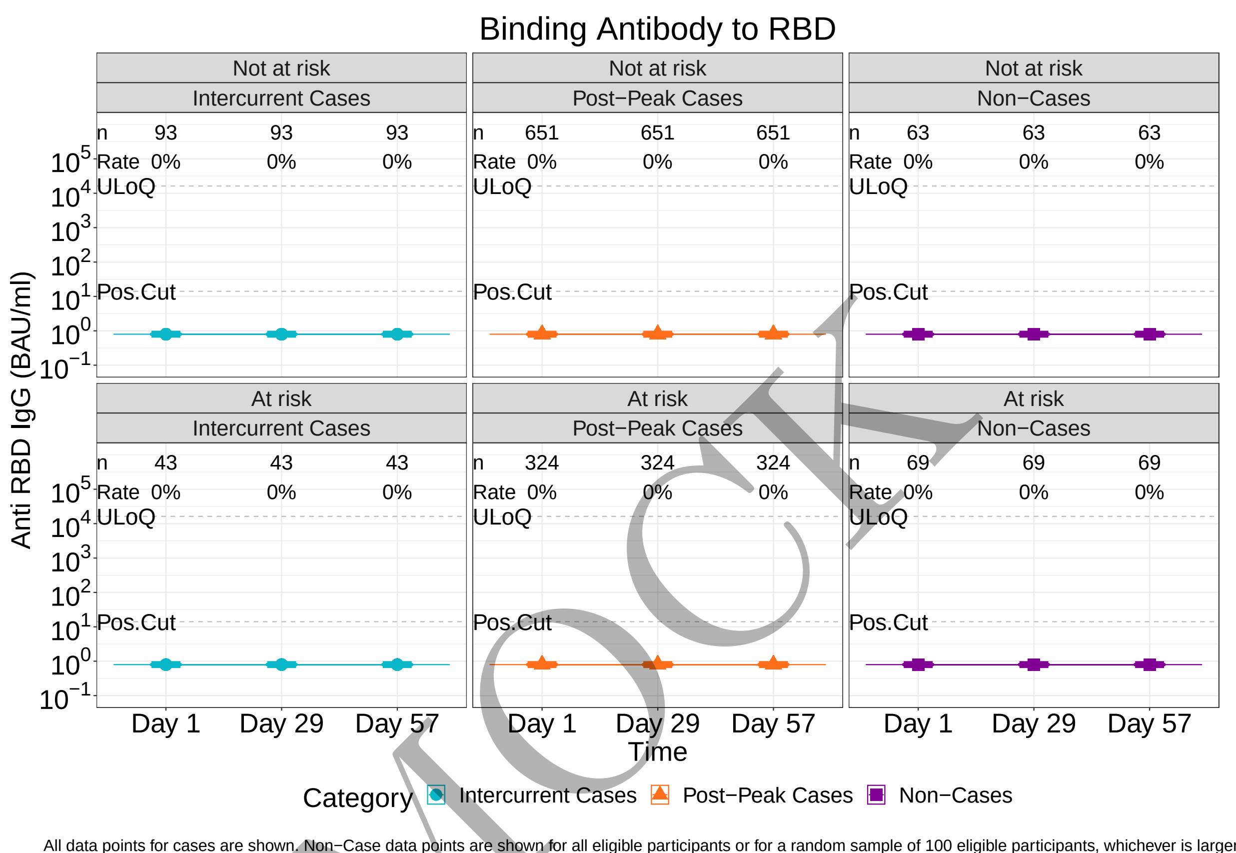

\caption{

Figure 2.5.82: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



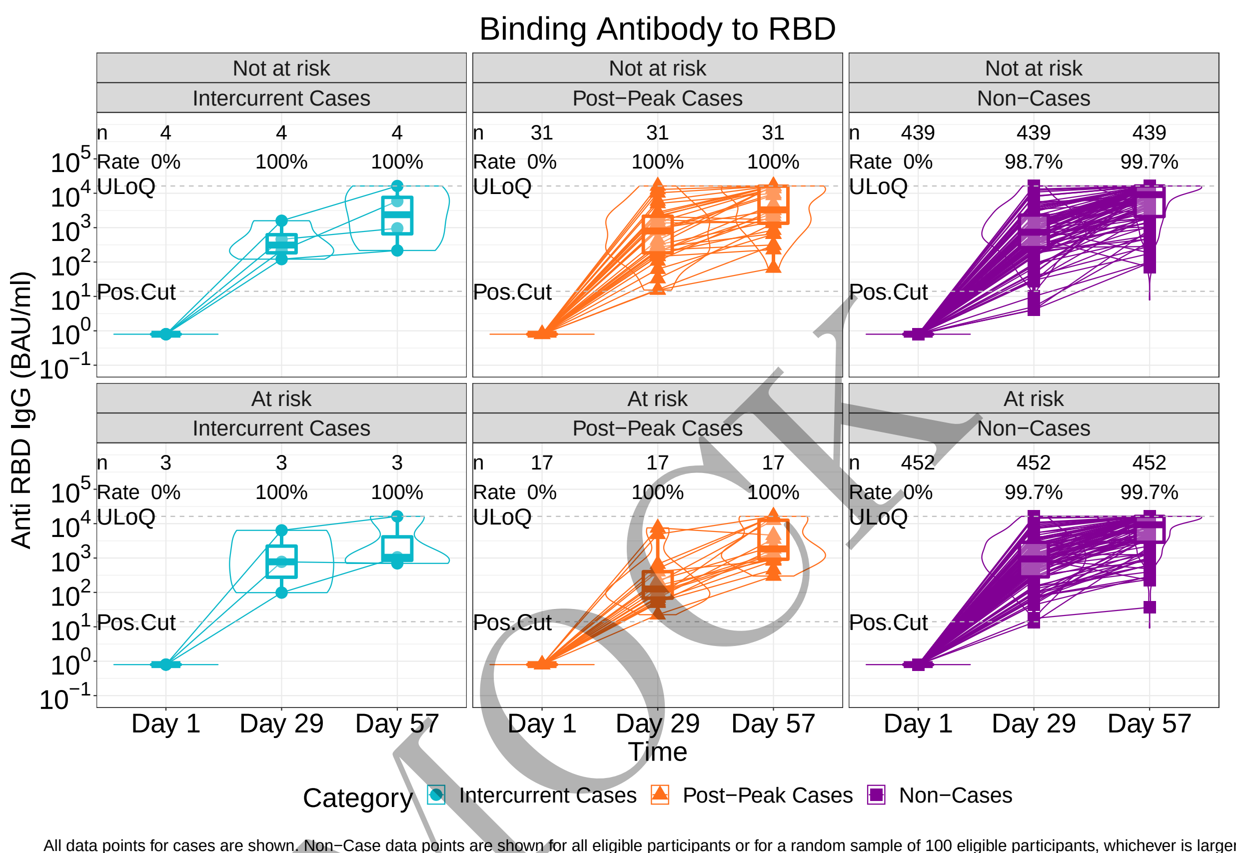

\caption{

Figure 2.5.83: lineplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



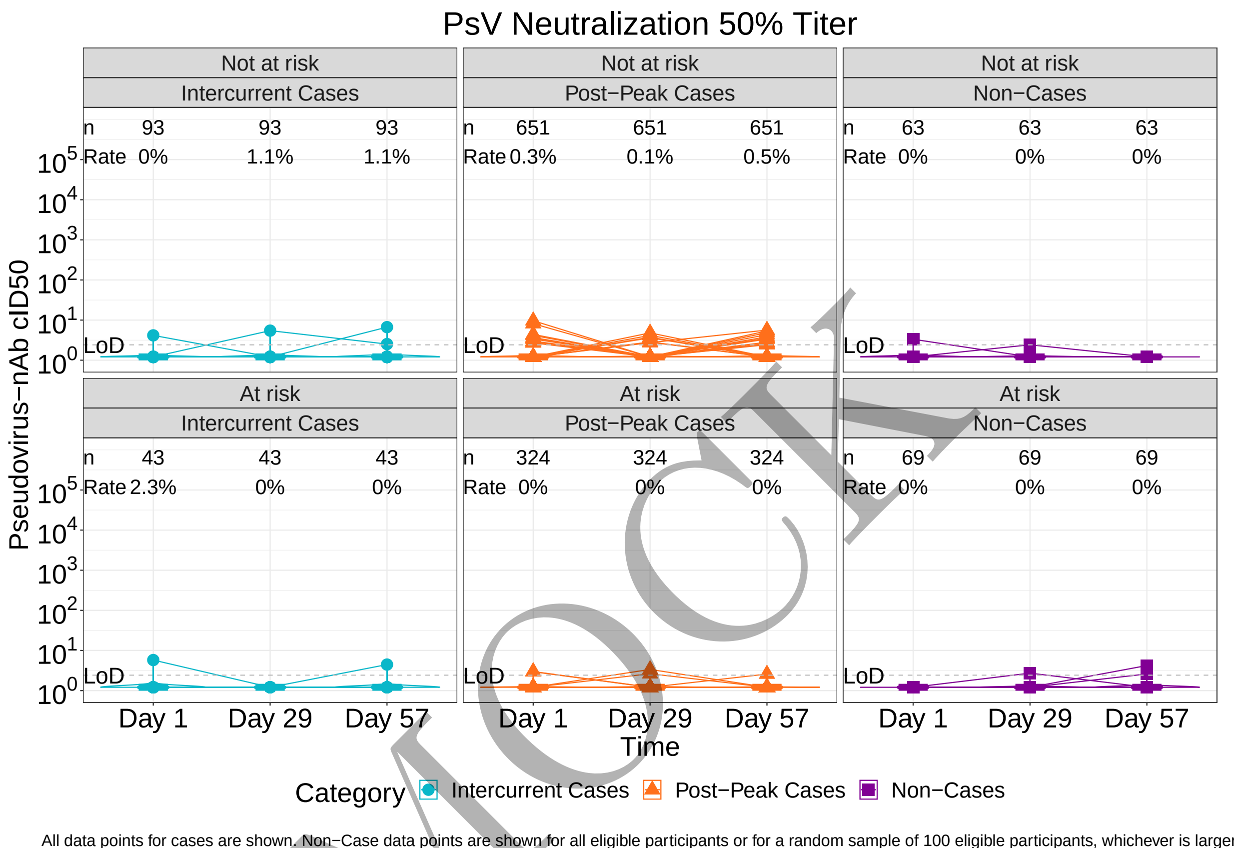

\caption{

Figure 2.5.84: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



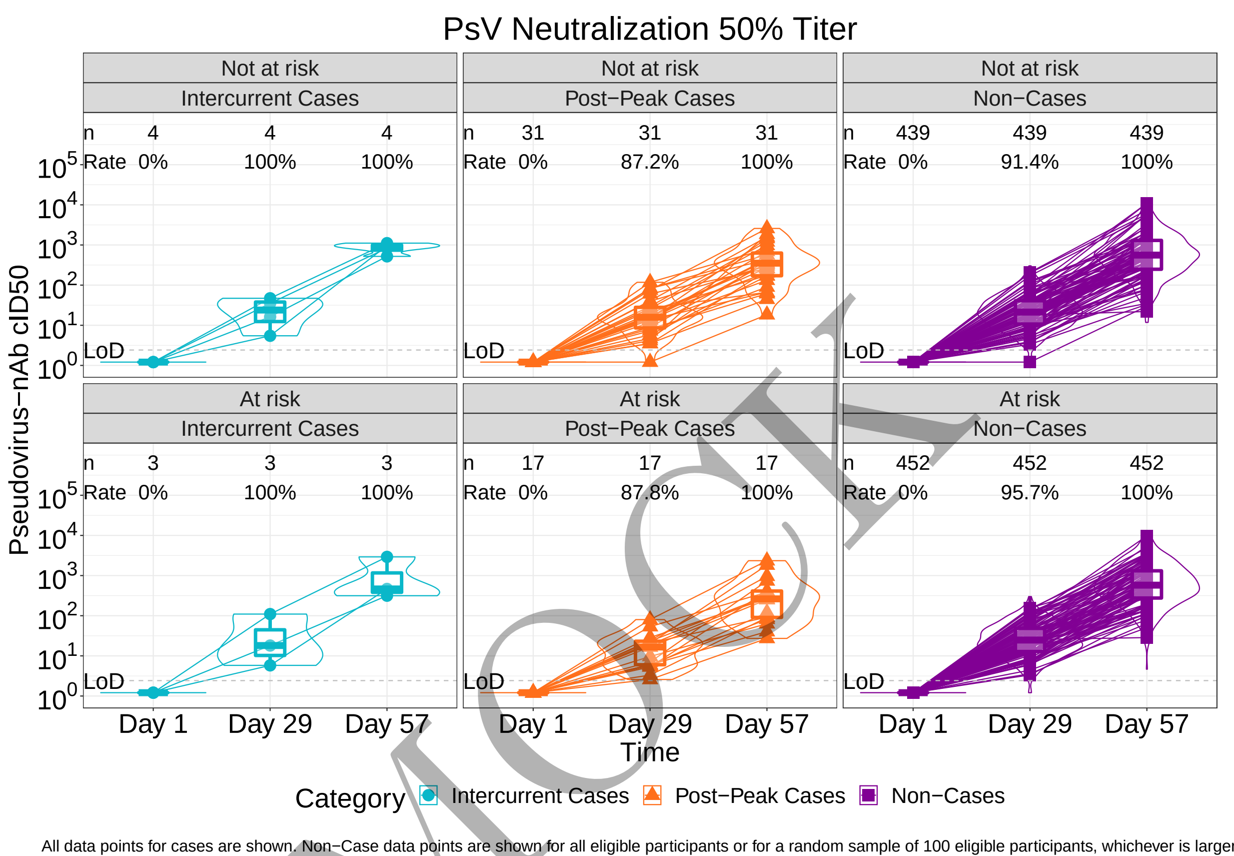

\caption{

Figure 2.5.85: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



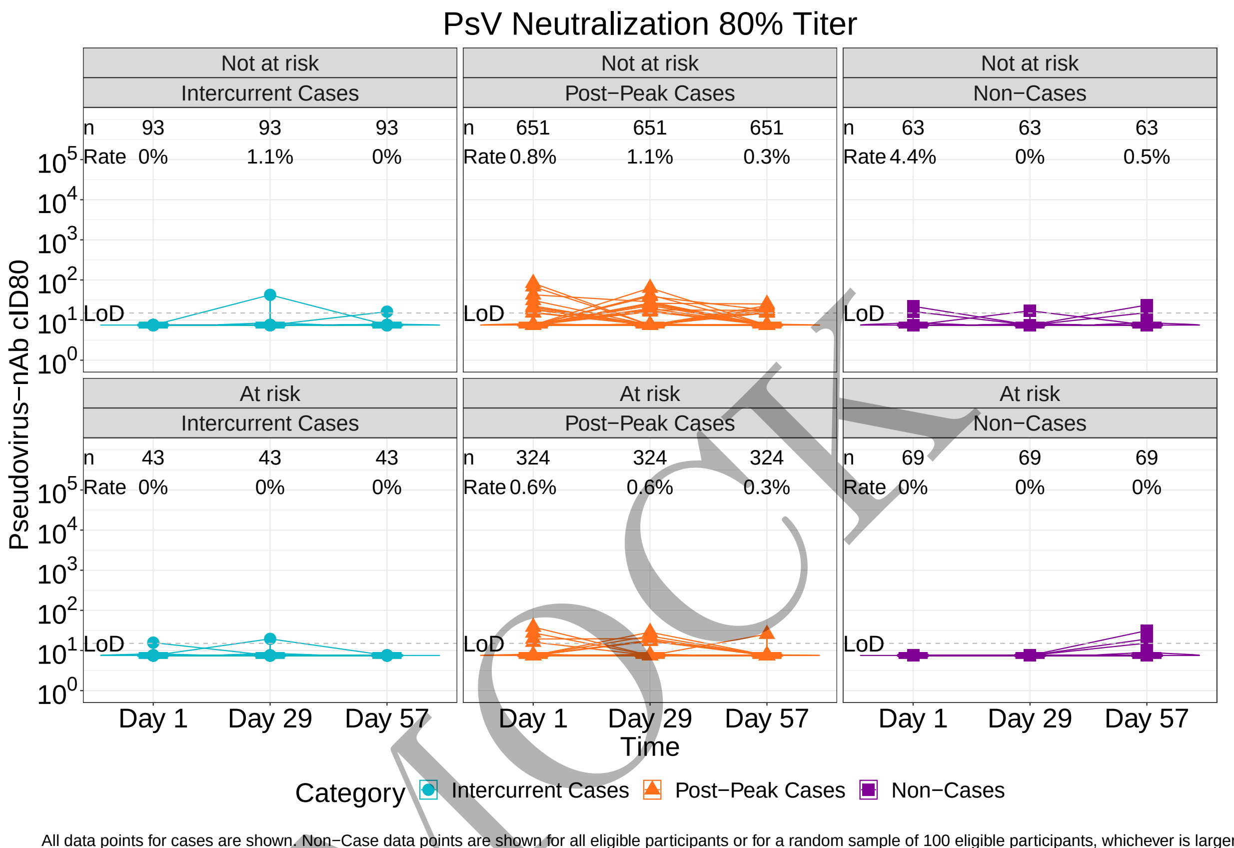

\caption{

Figure 2.5.86: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



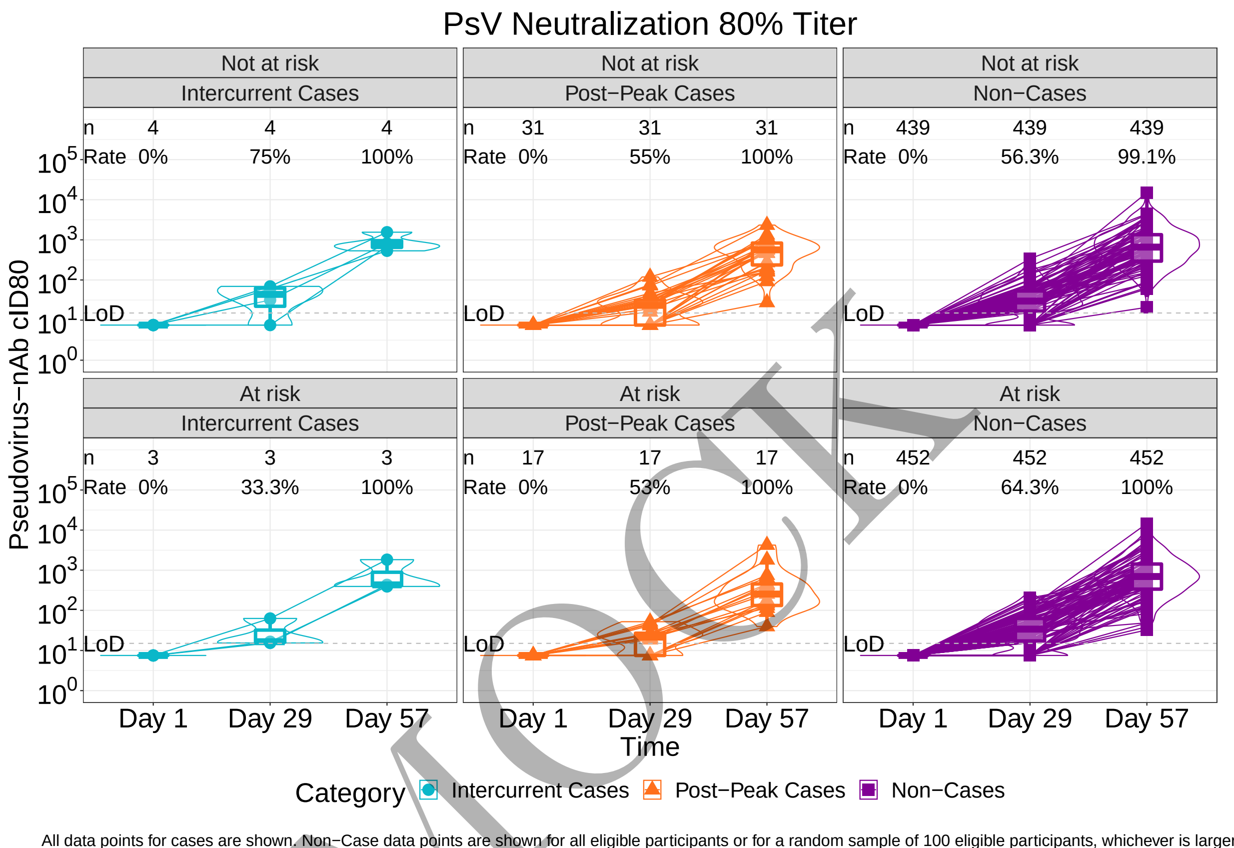

\caption{

Figure 2.5.87: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



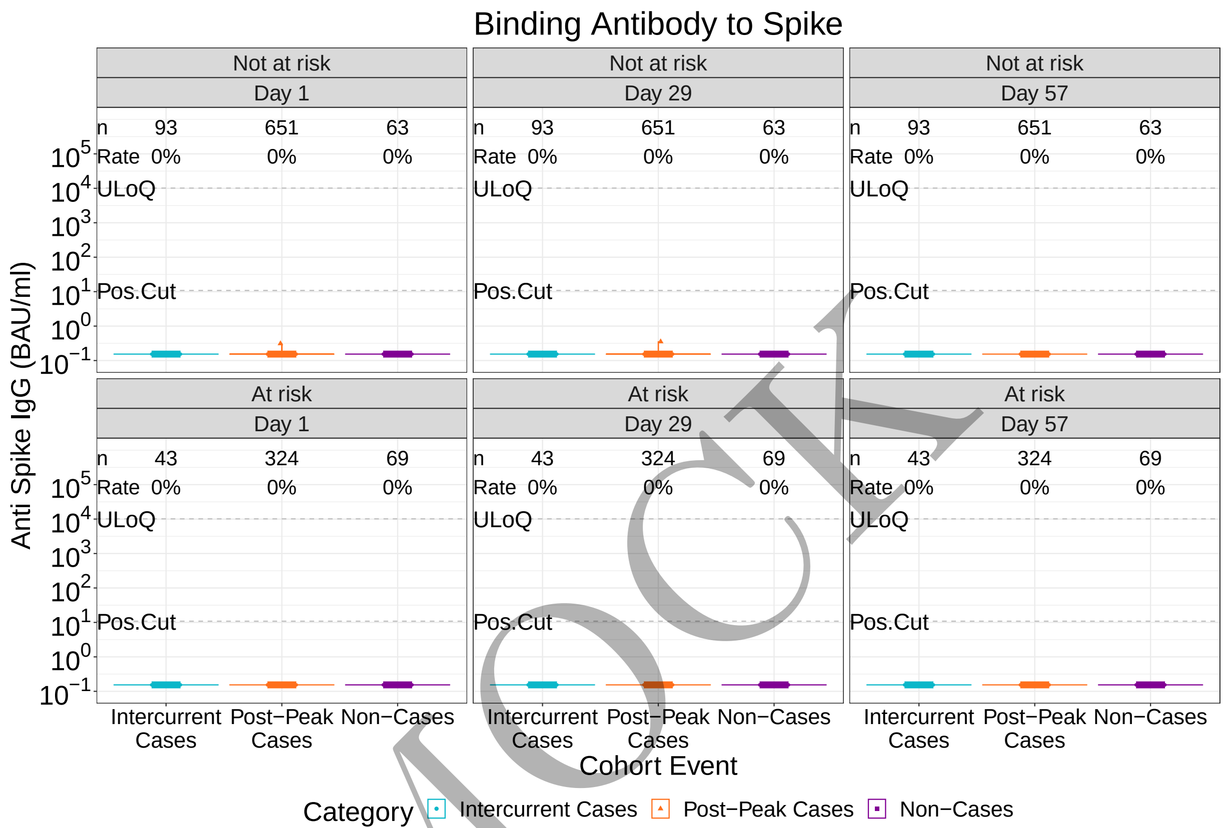

\caption{

Figure 2.5.88: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



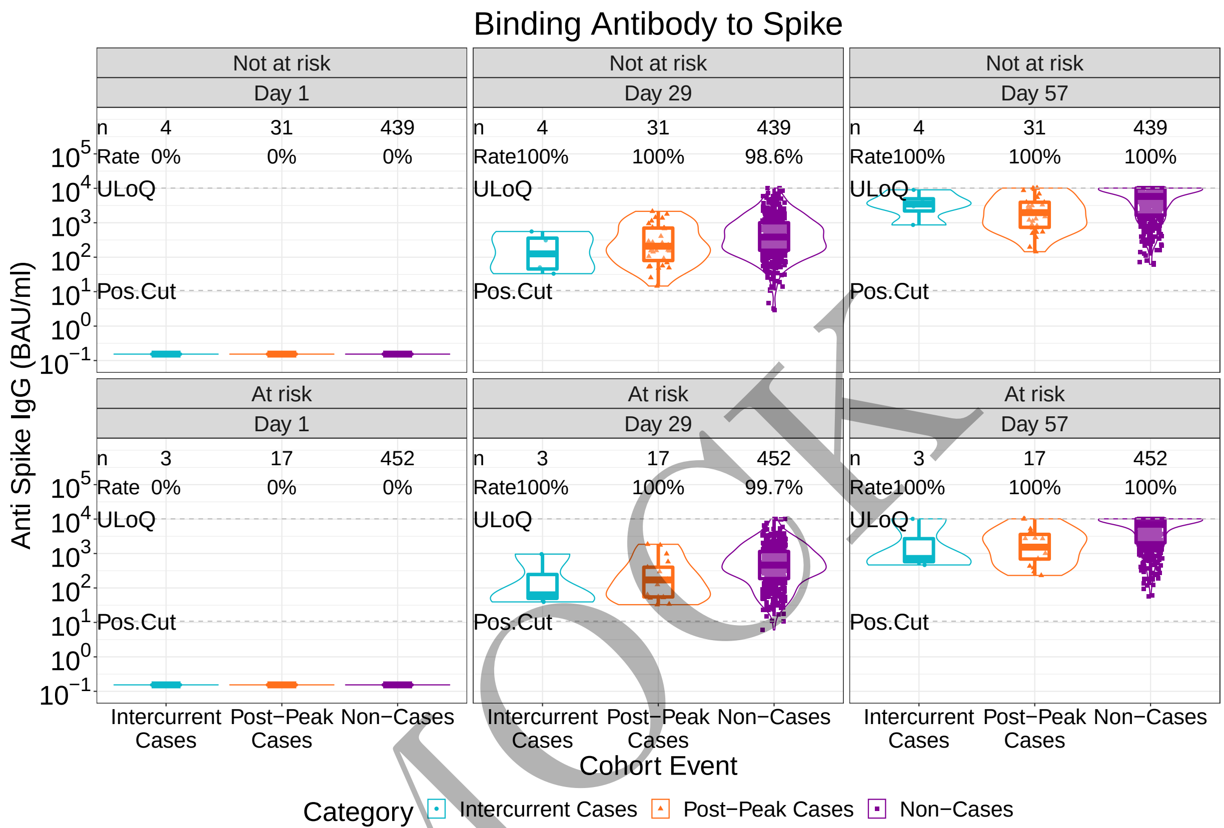

\caption{

Figure 2.5.89: violinplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



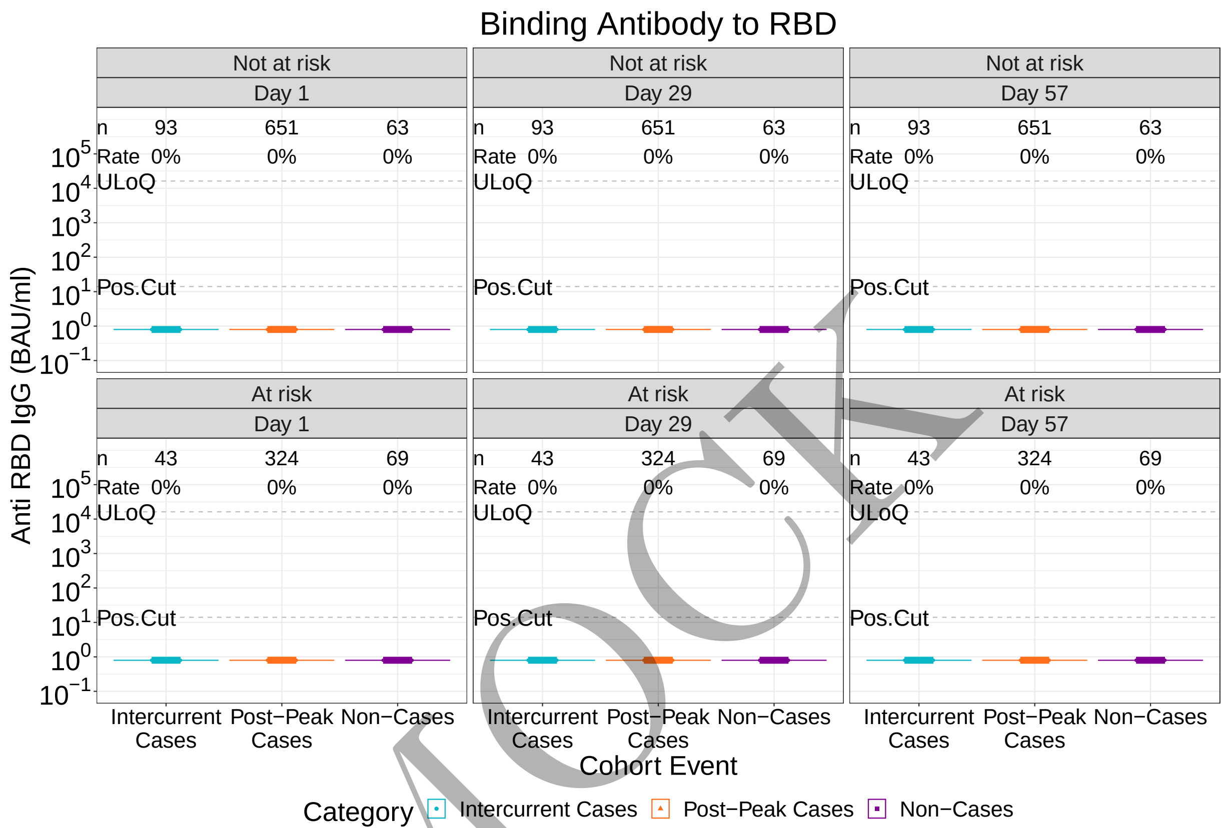

\caption{

Figure 2.5.90: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



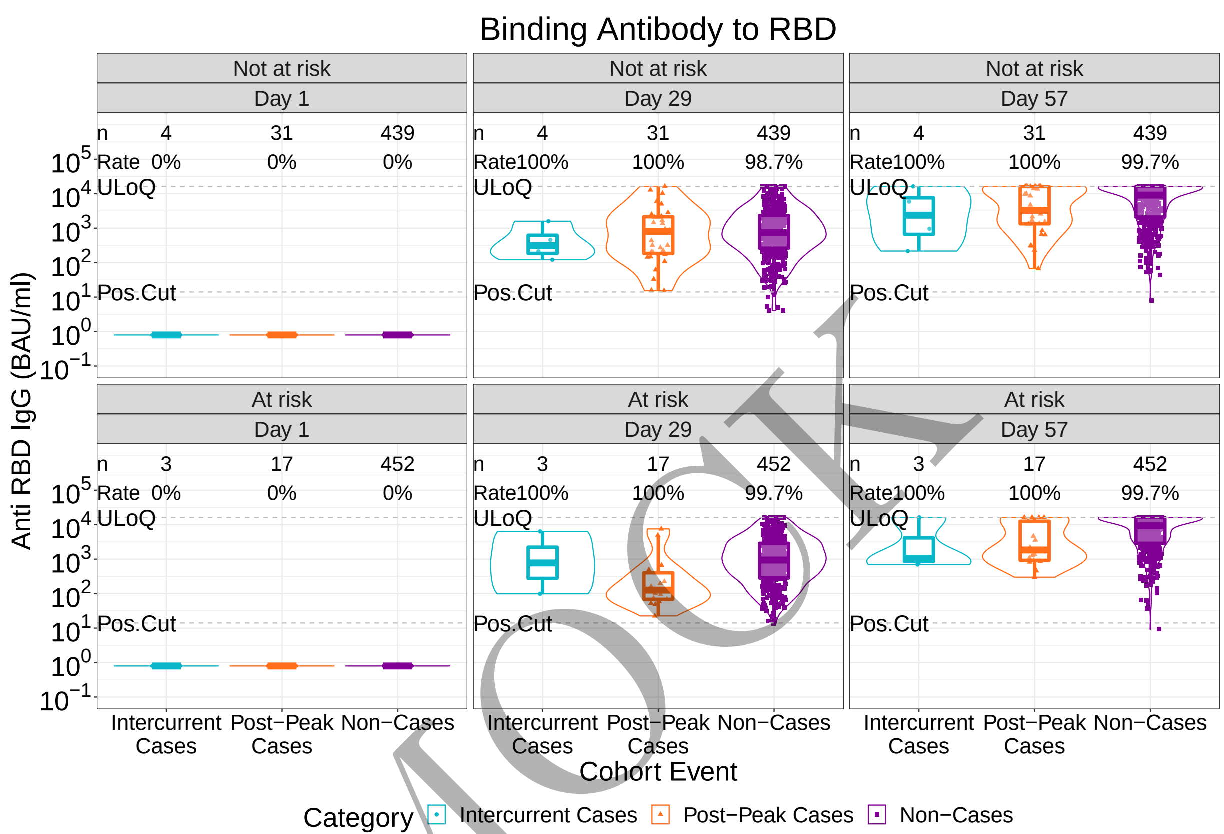

\caption{

Figure 2.5.91: violinplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



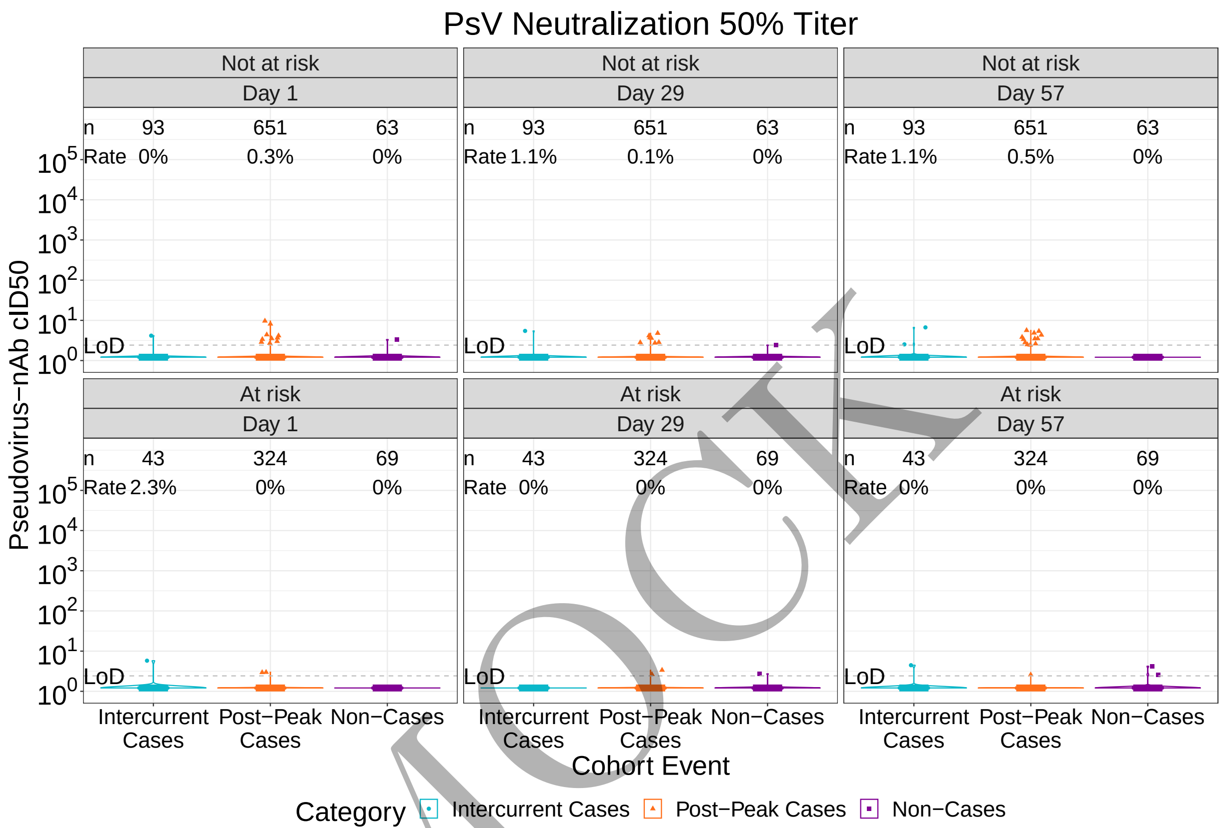

\caption{

Figure 2.5.92: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



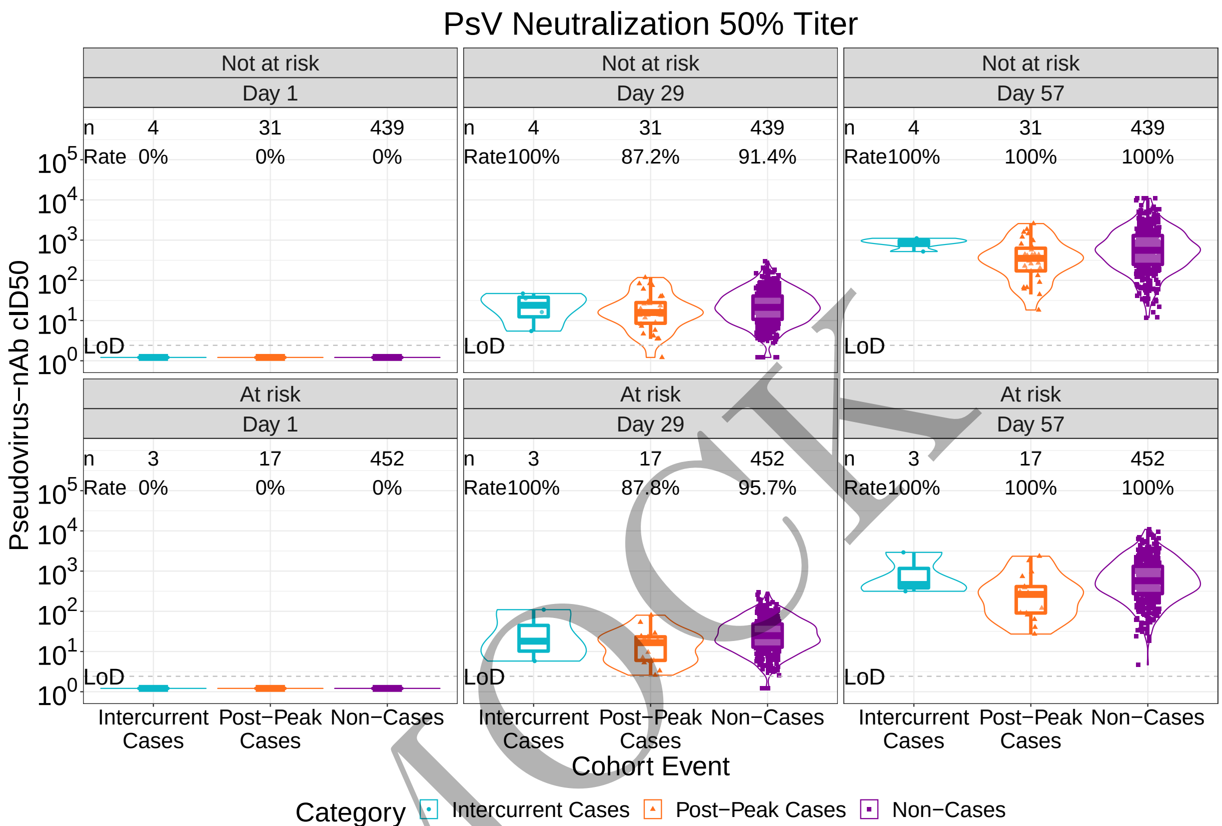

\caption{

Figure 2.5.93: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



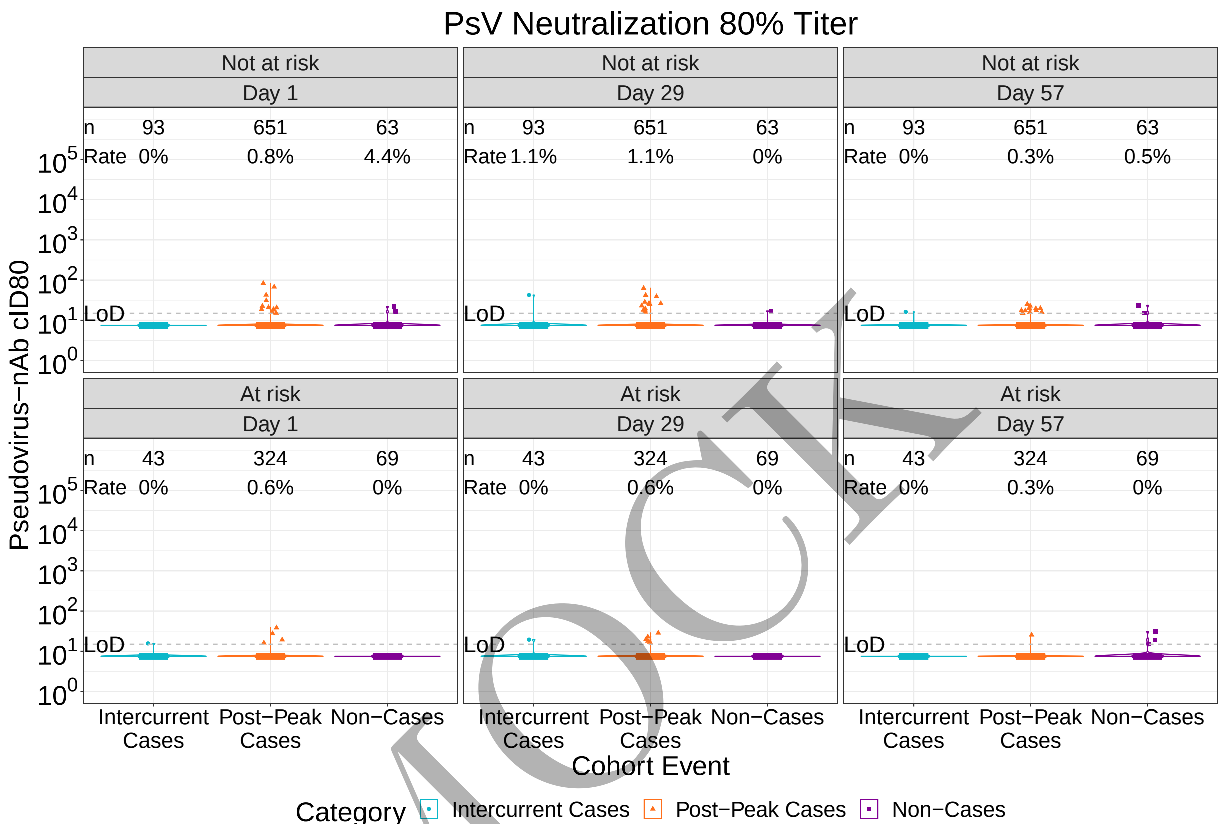

\caption{

Figure 2.5.94: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



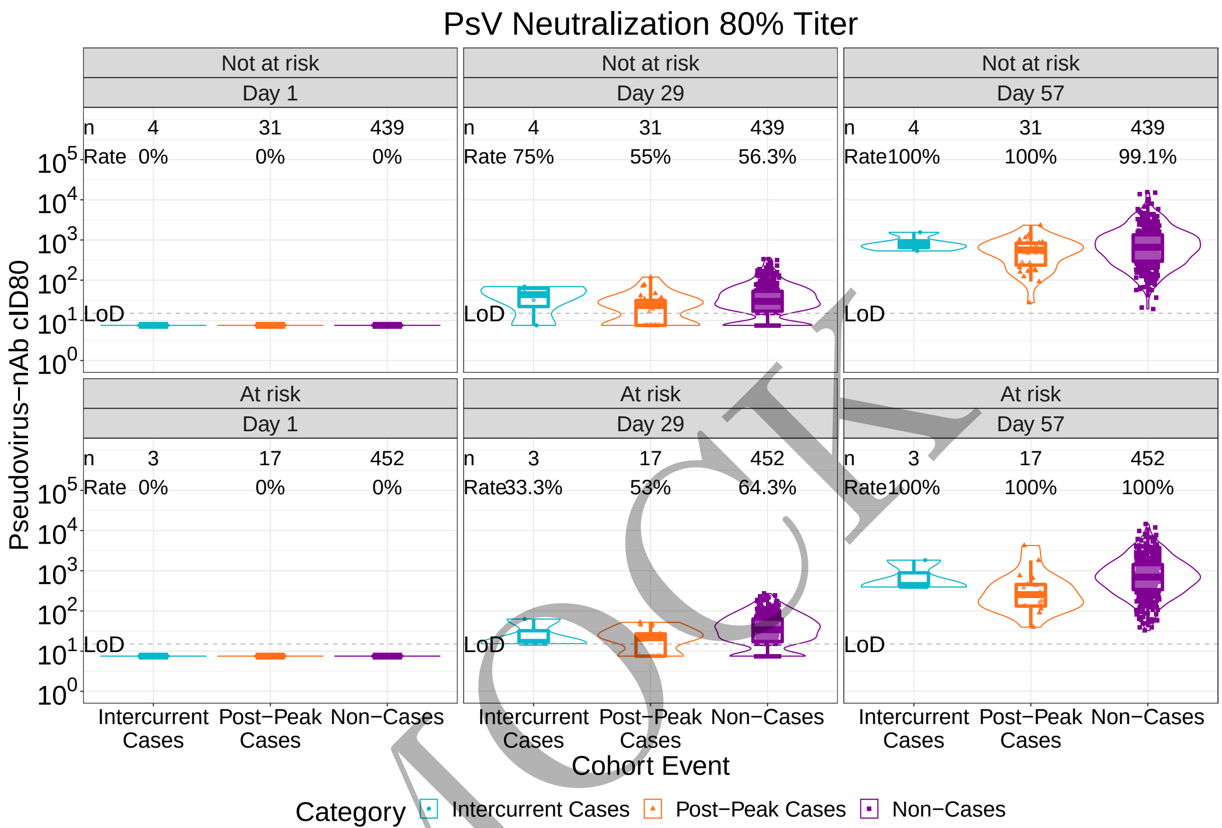

\caption{

Figure 2.5.95: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



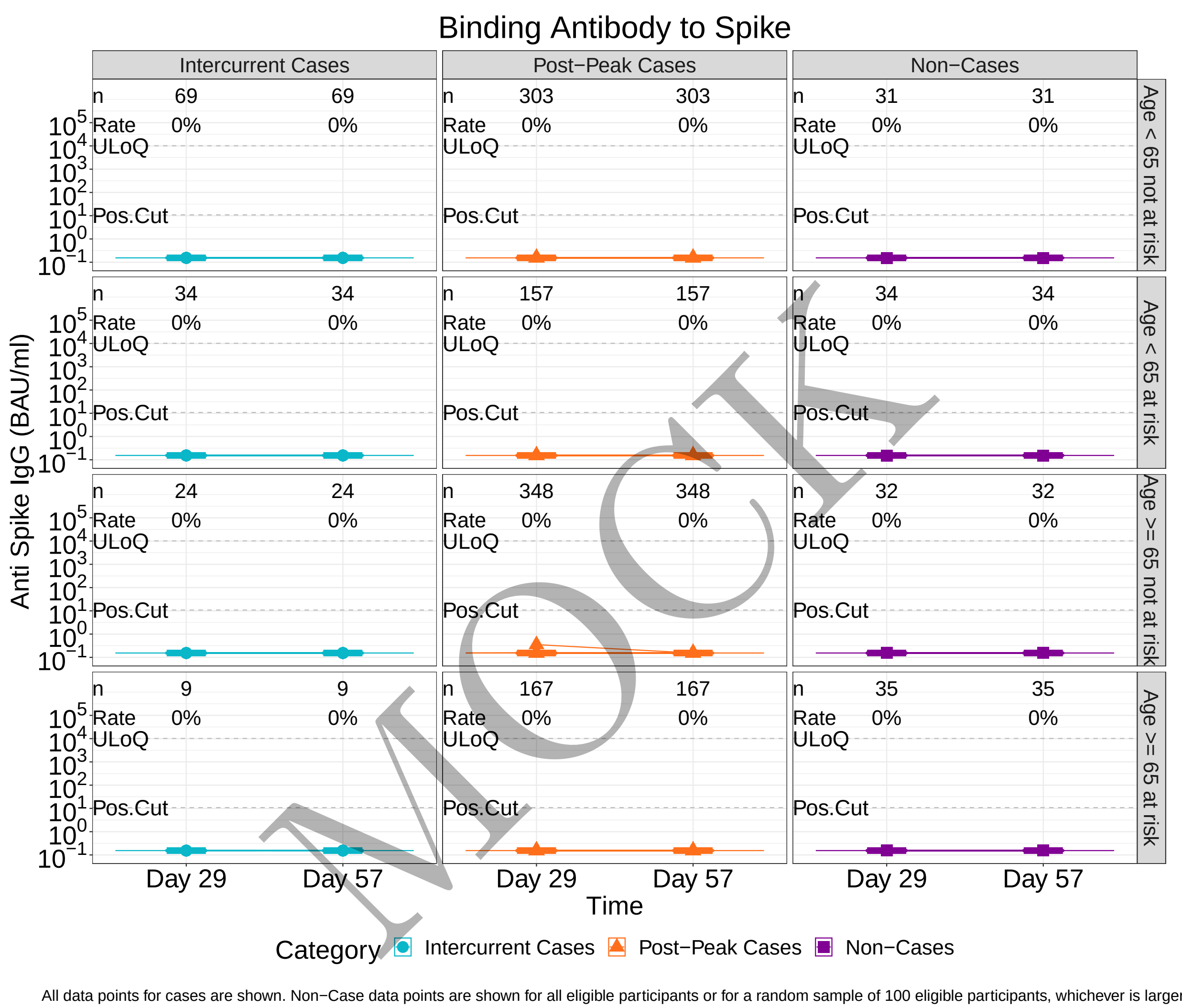

\caption{

Figure 2.5.96: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

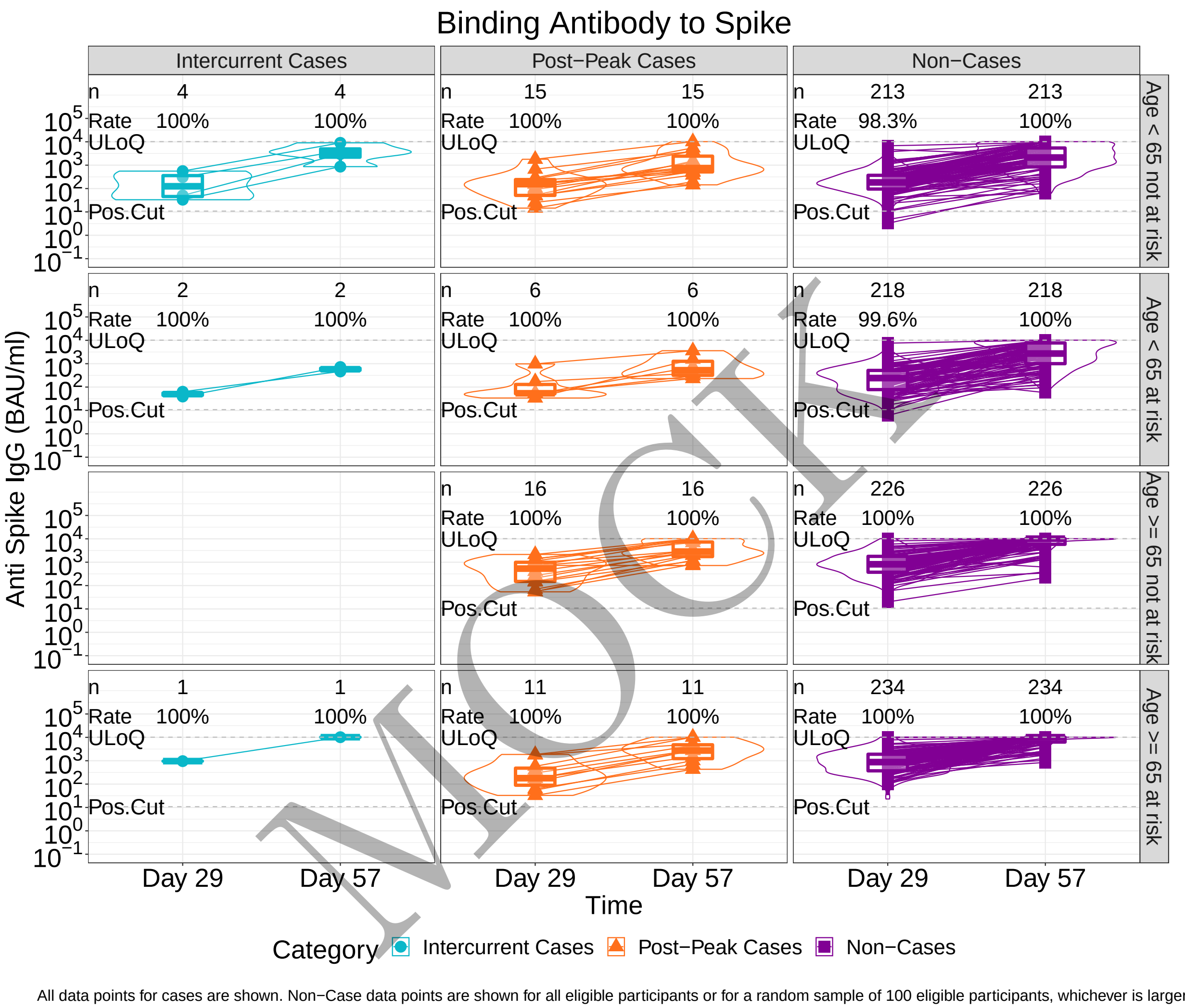
\begin{figure}




\caption{
Figure 2.5.97: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 1)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



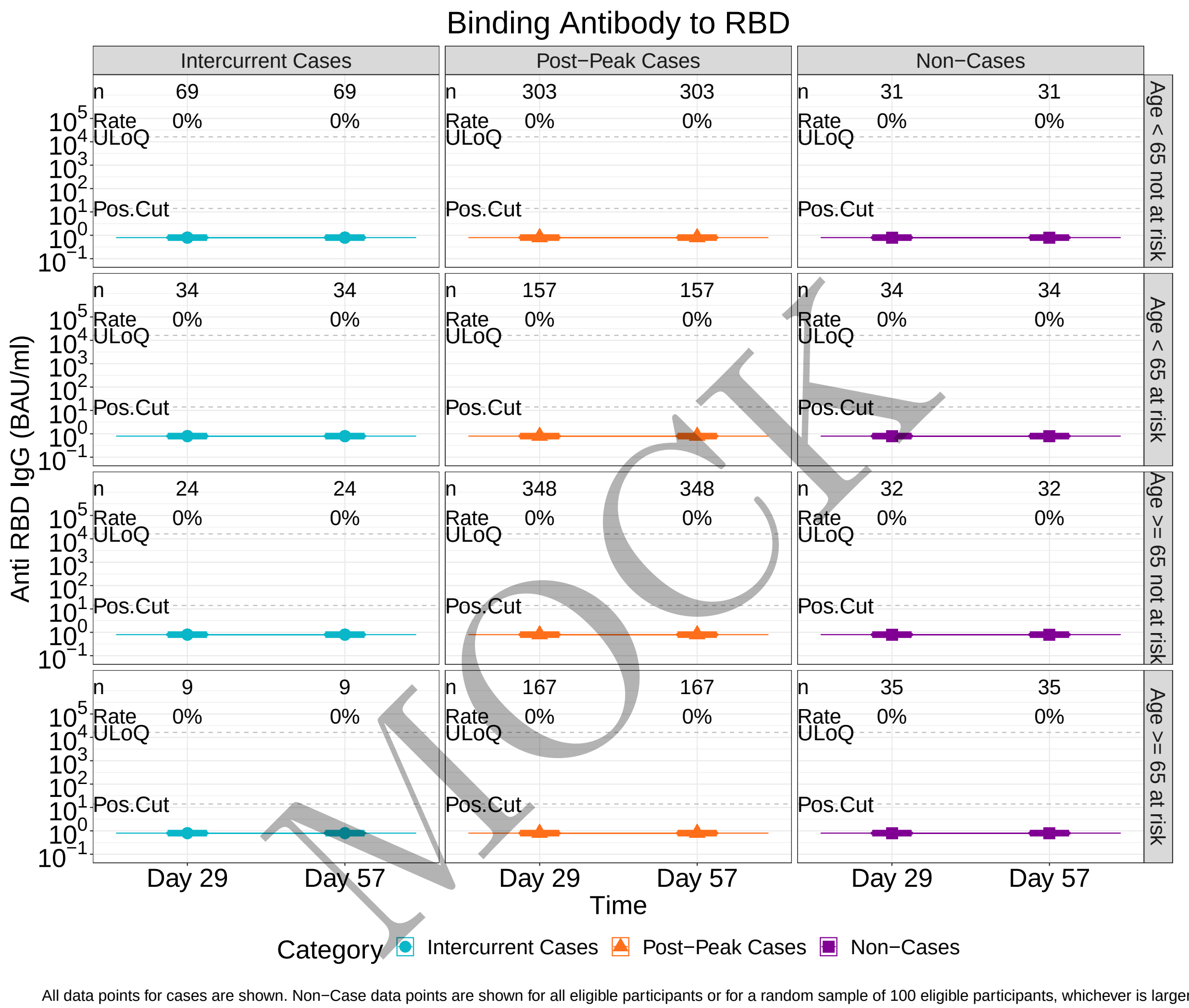

\caption{

Figure 2.5.98: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



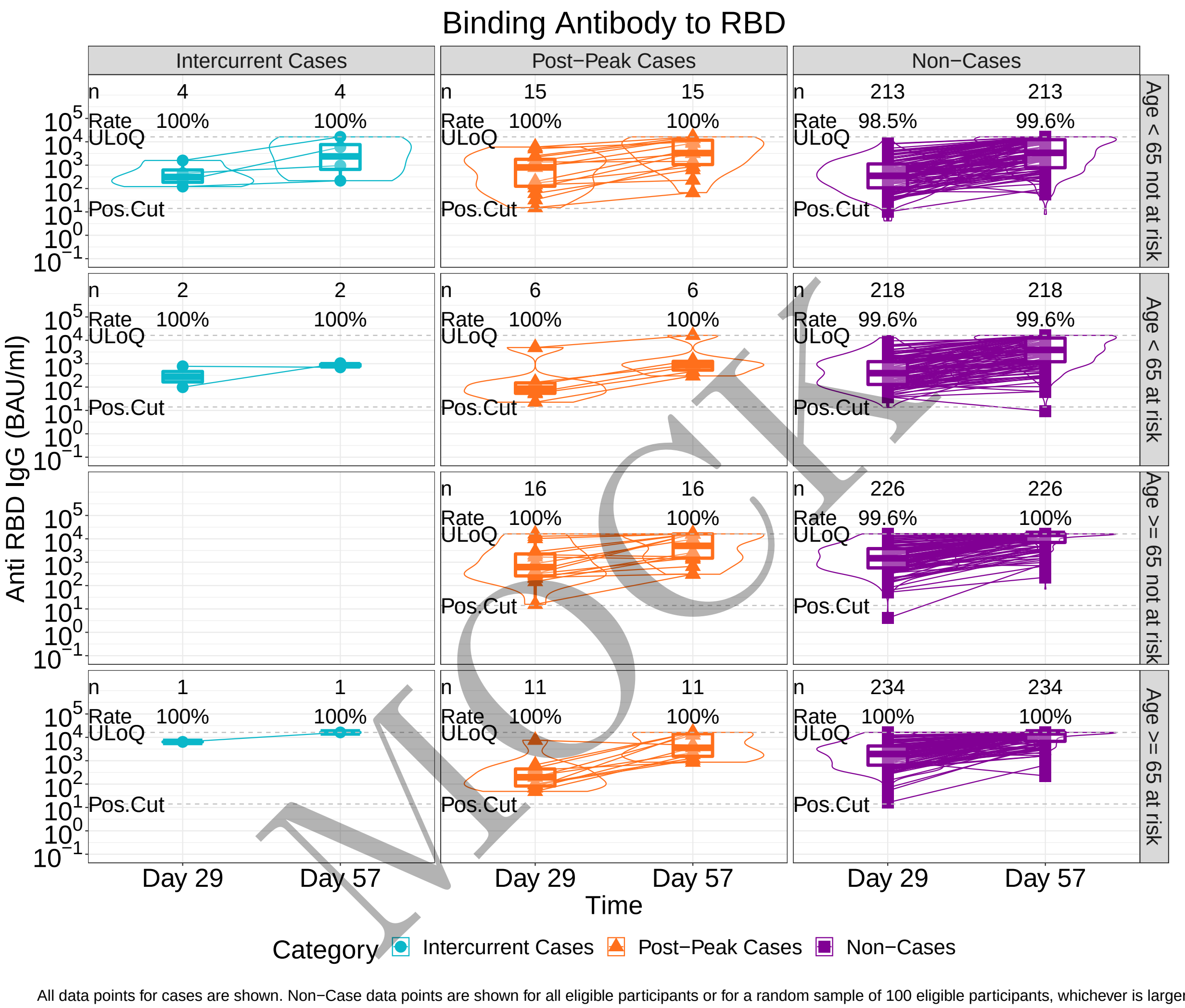

\caption{

Figure 2.5.99: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



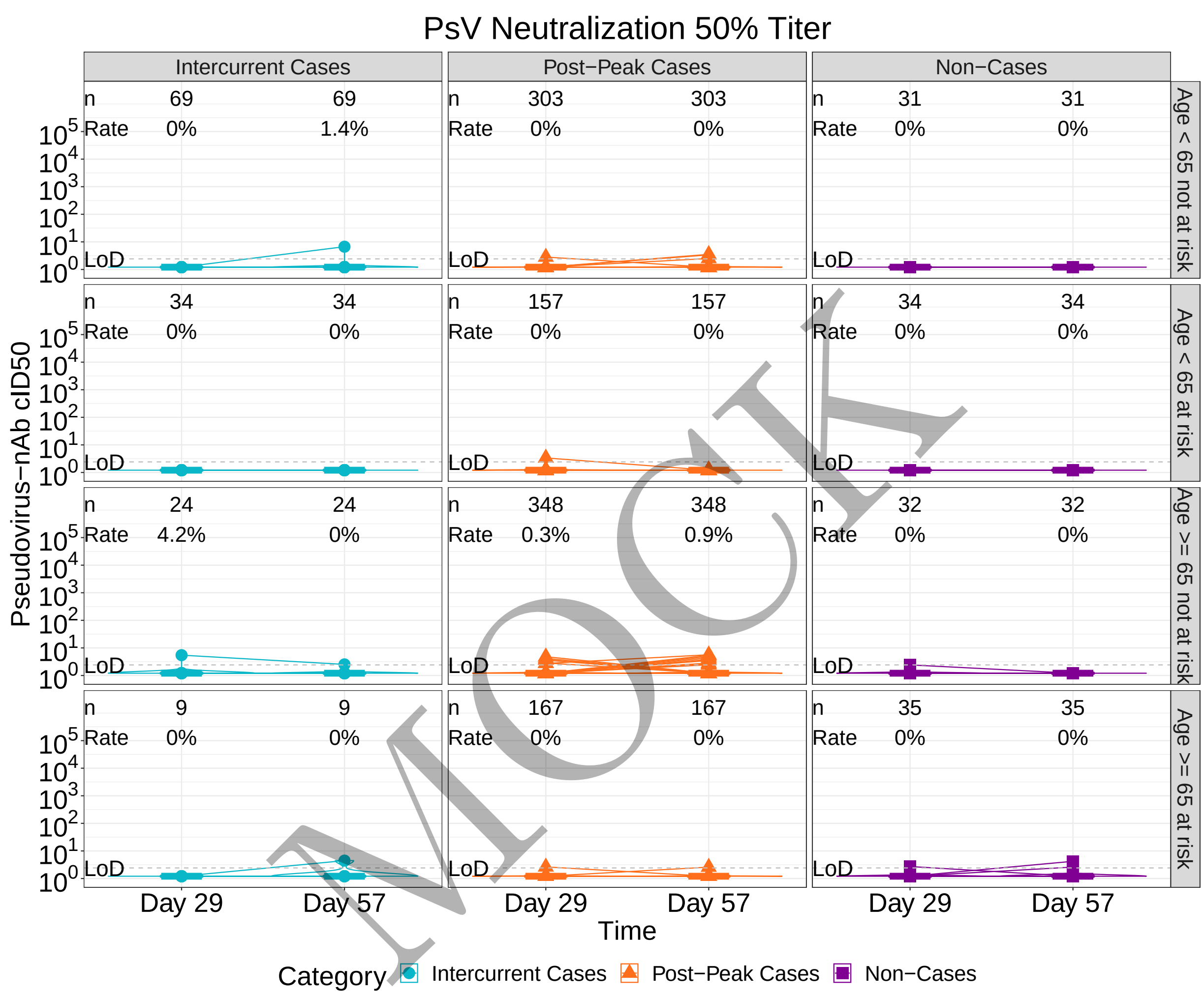

\caption{

Figure 2.5.100: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}




All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

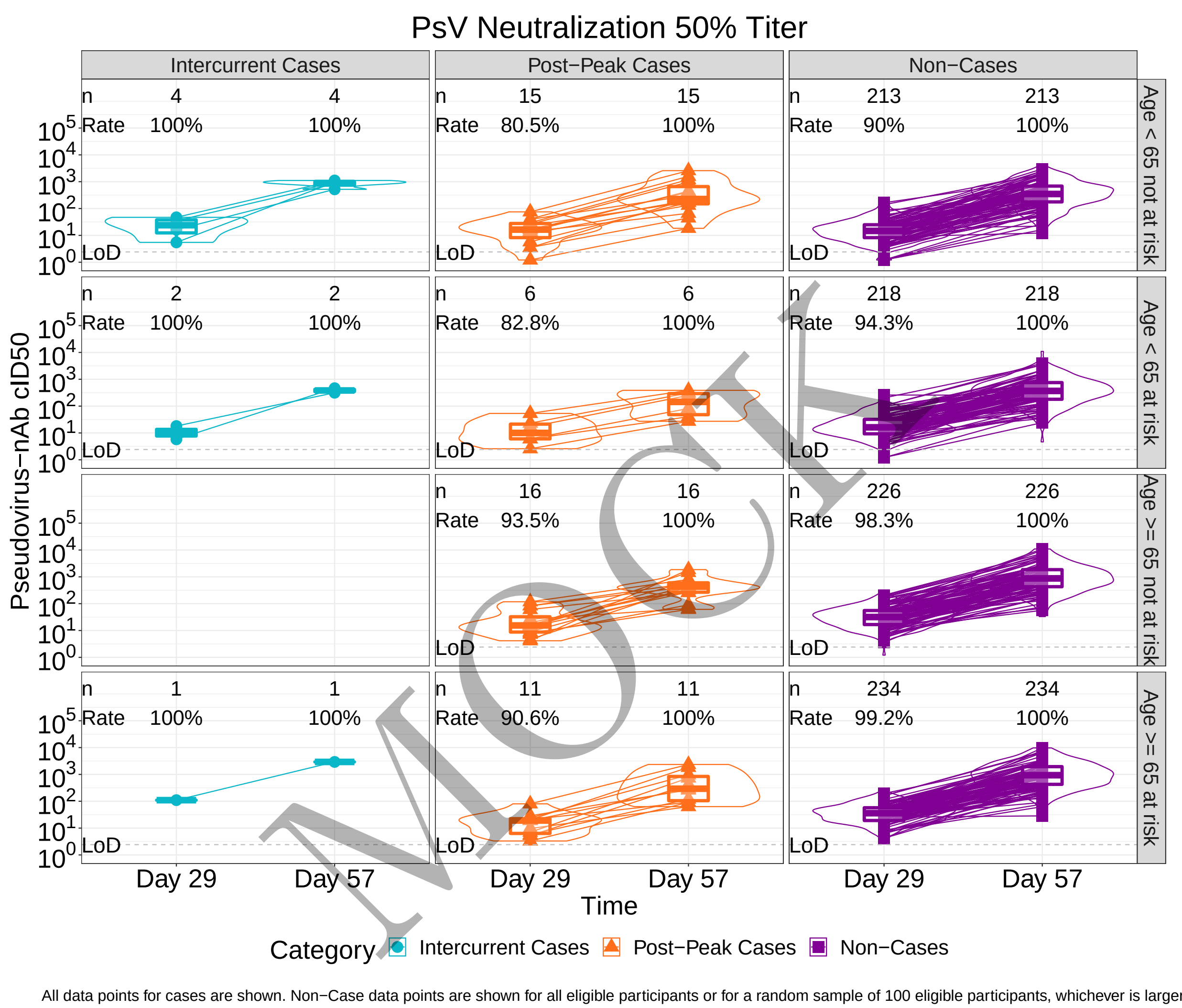
\caption{

Figure 2.5.101: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



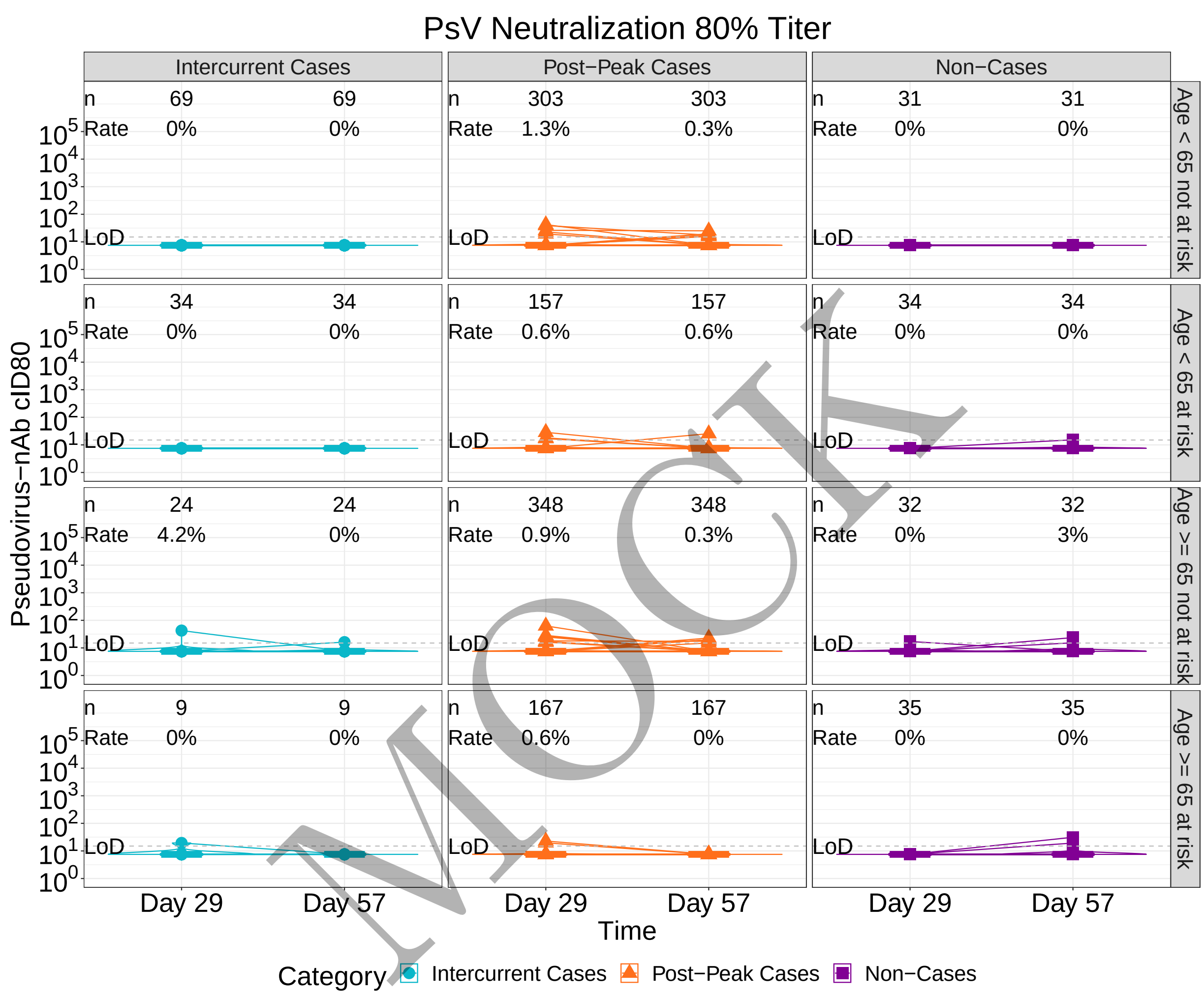

\caption{

Figure 2.5.102: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}




All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

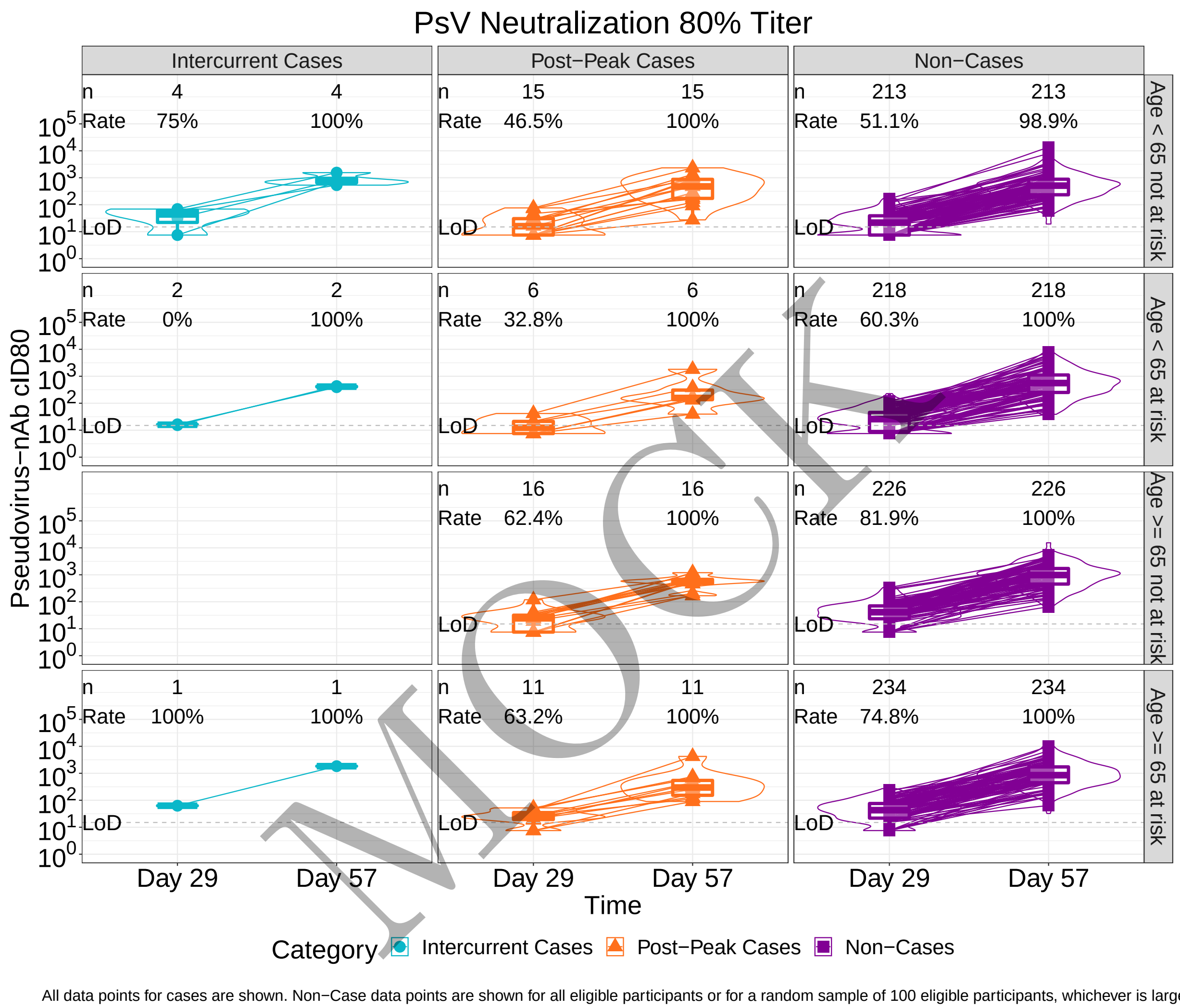
\caption{

Figure 2.5.103: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



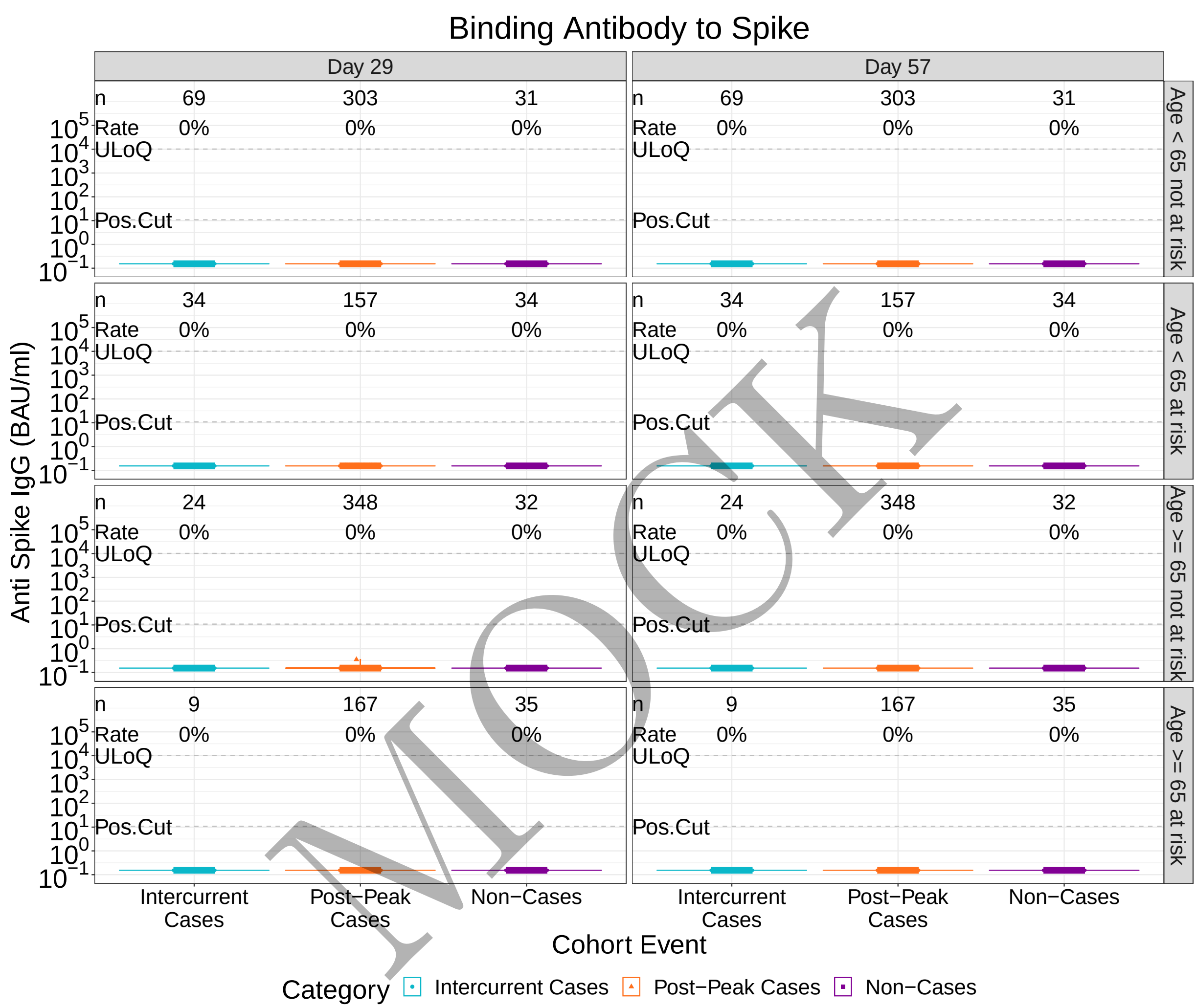

\caption{

Figure 2.5.104: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



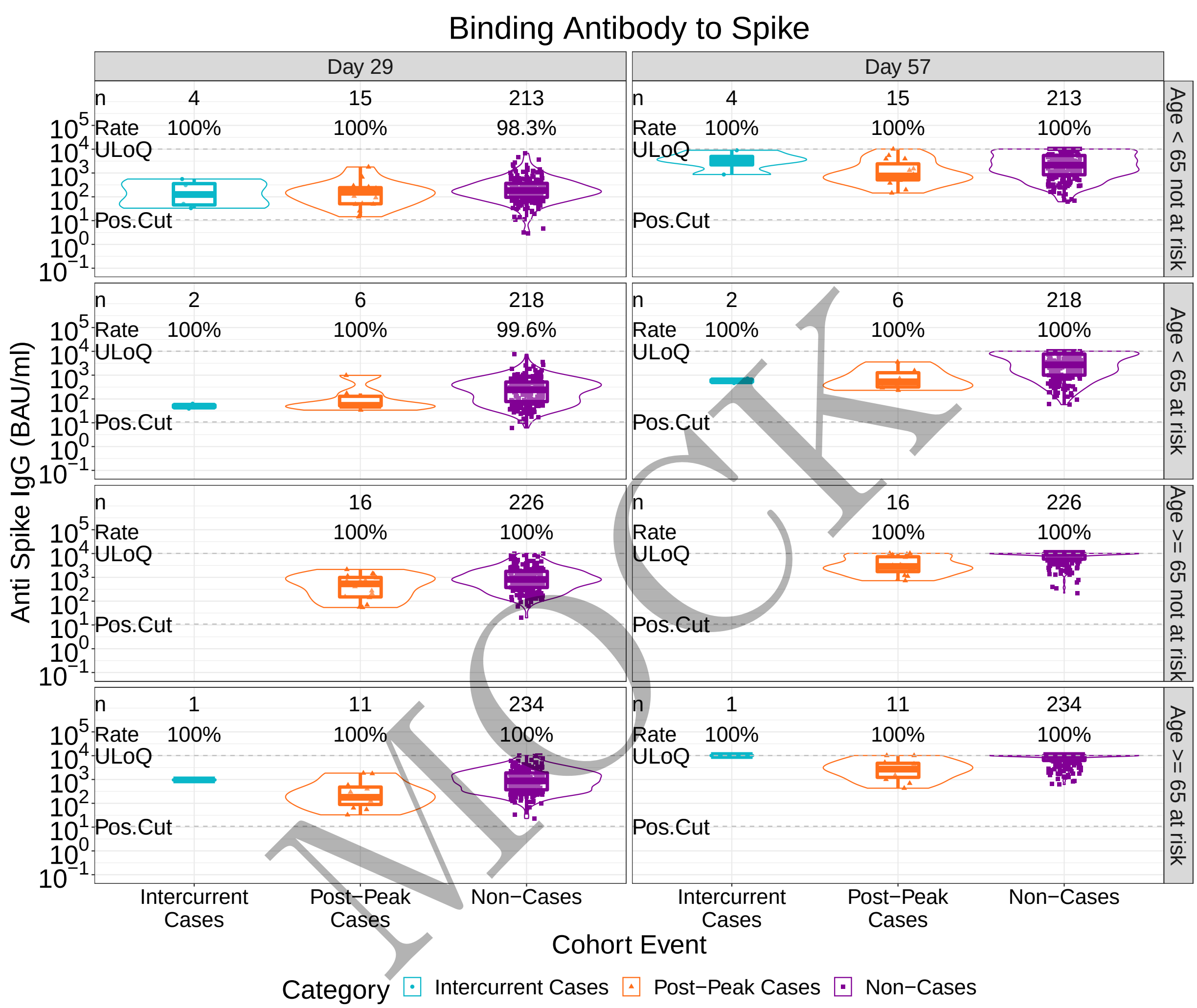

\caption{

Figure 2.5.105: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



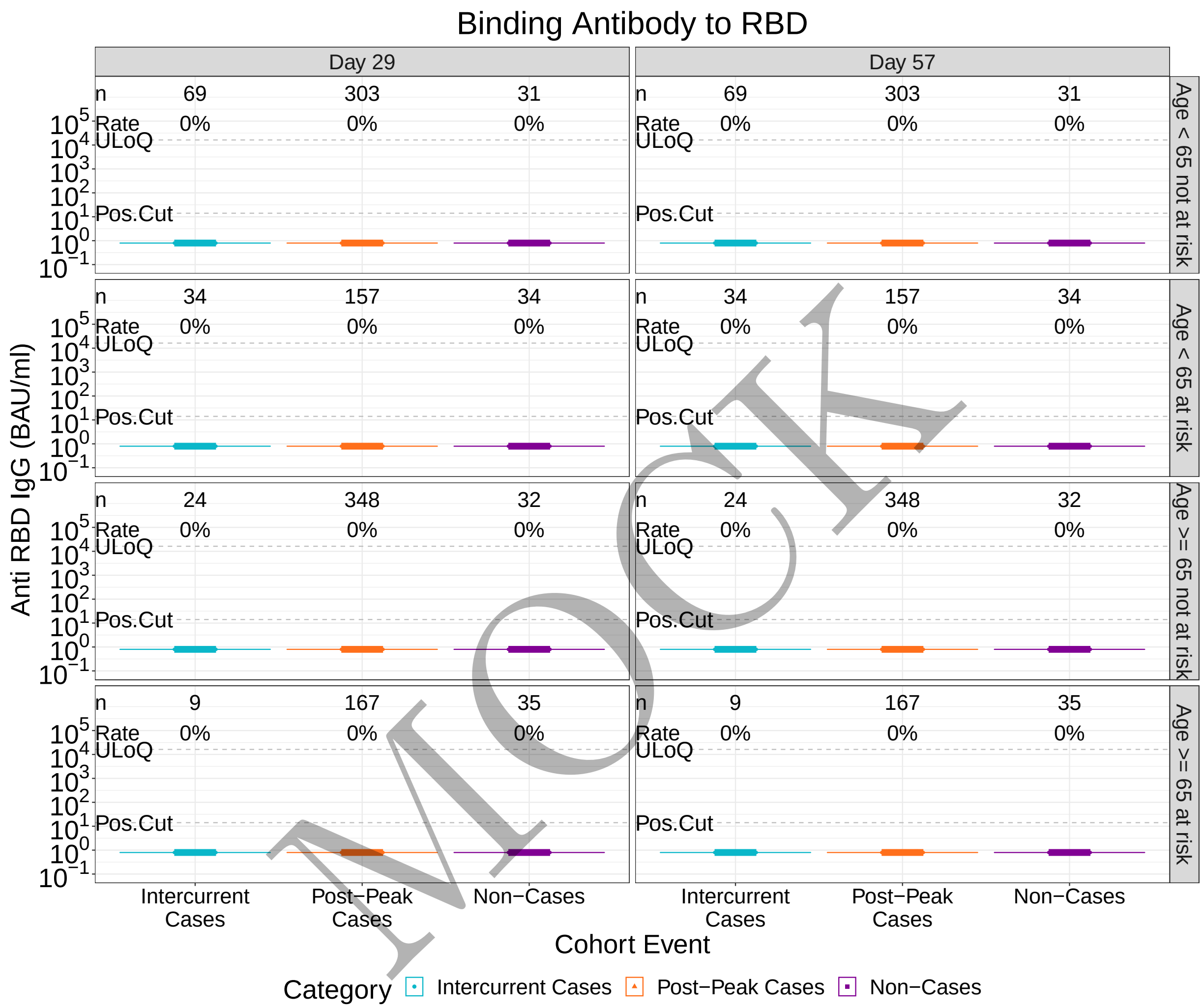

\caption{

Figure 2.5.106: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



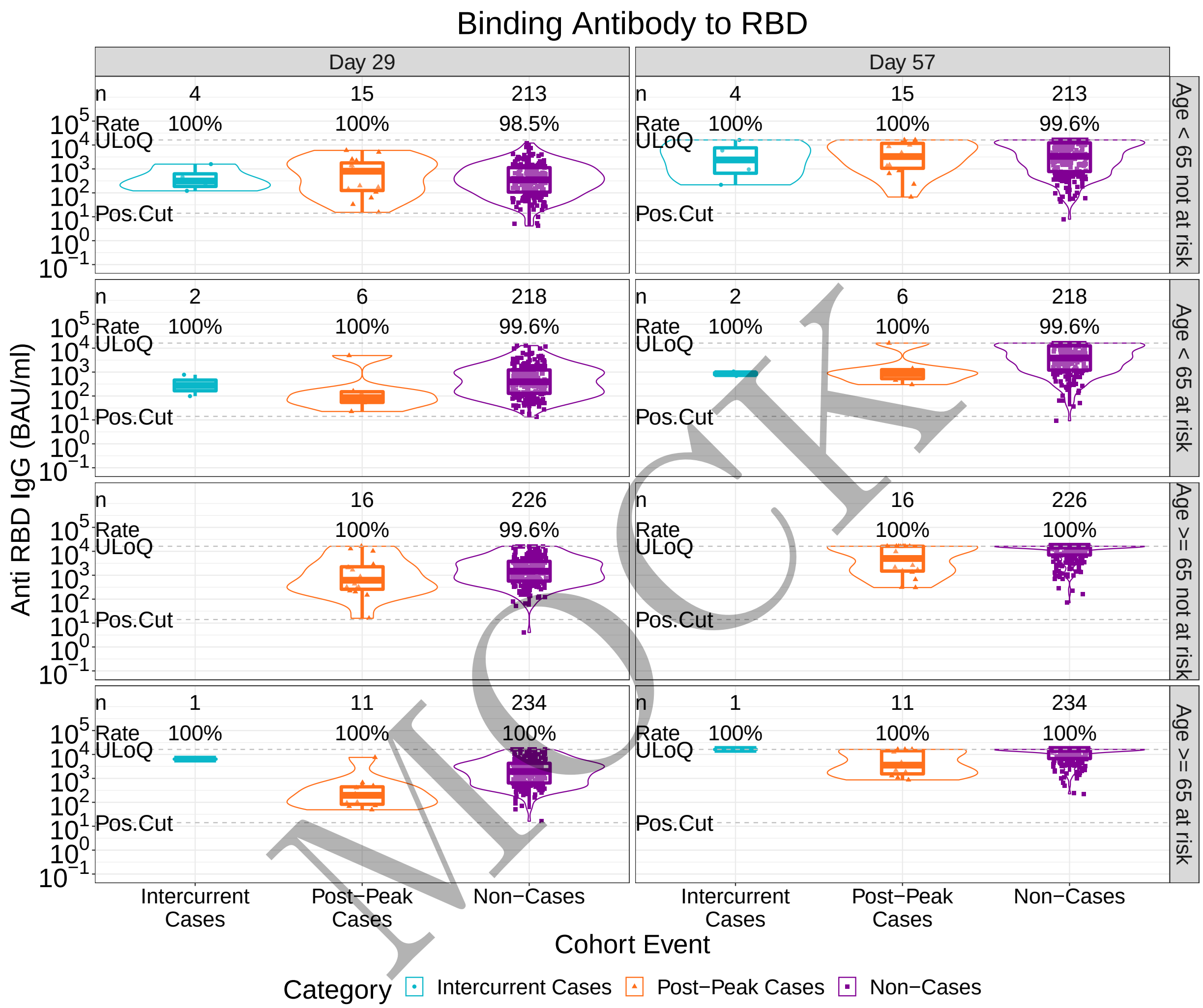

\caption{

Figure 2.5.107: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



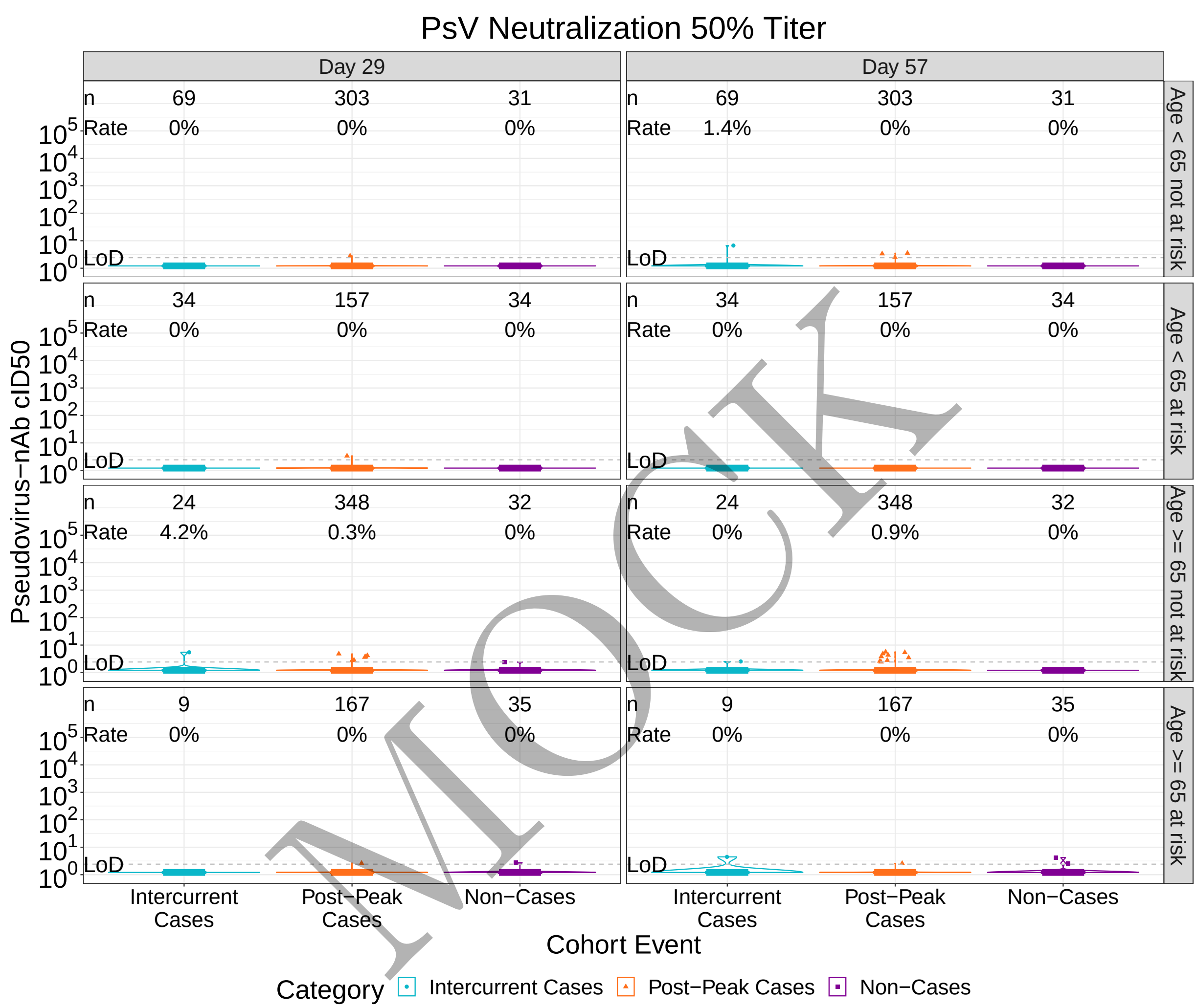

\caption{

Figure 2.5.108: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



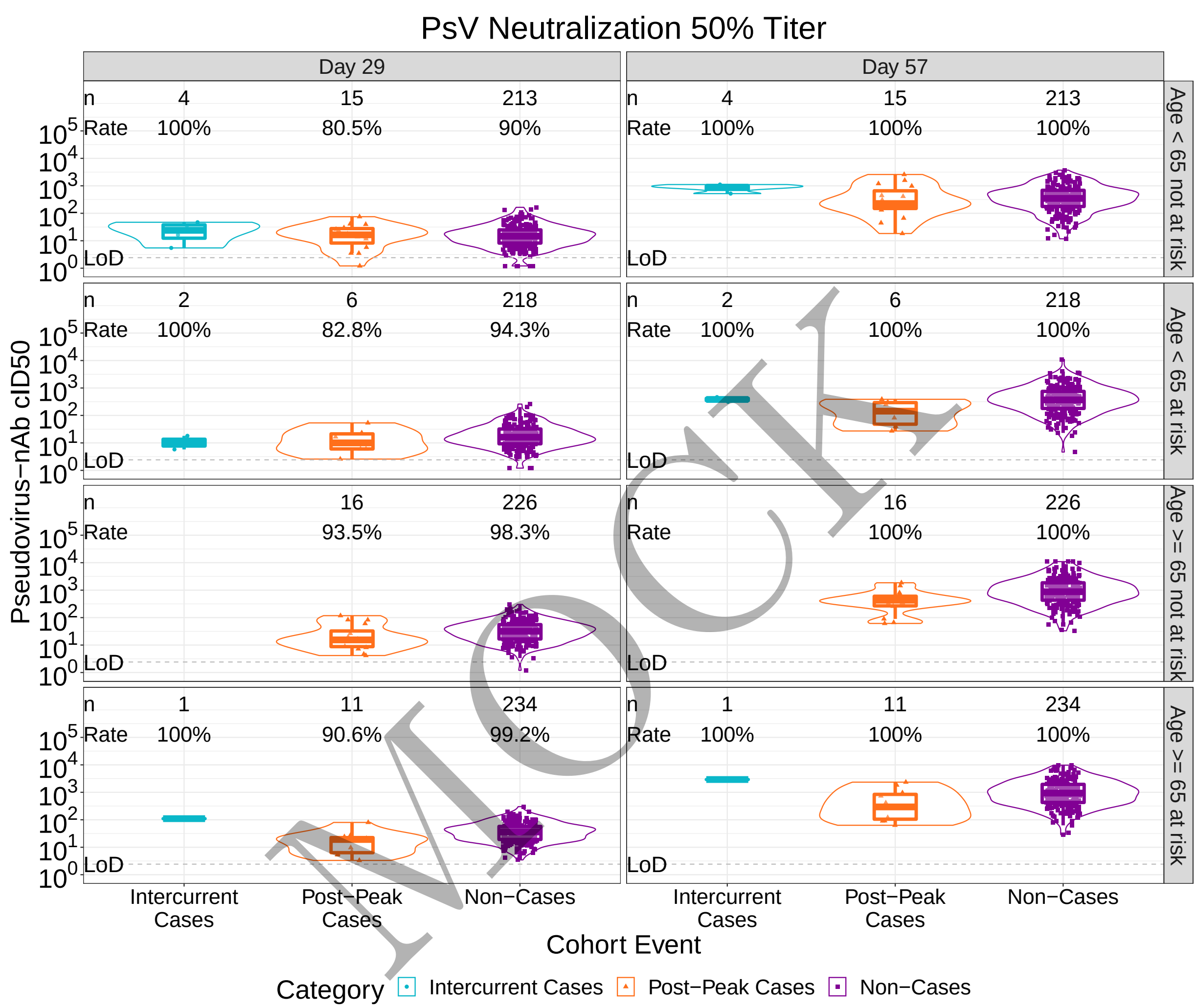

\caption{

Figure 2.5.109: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



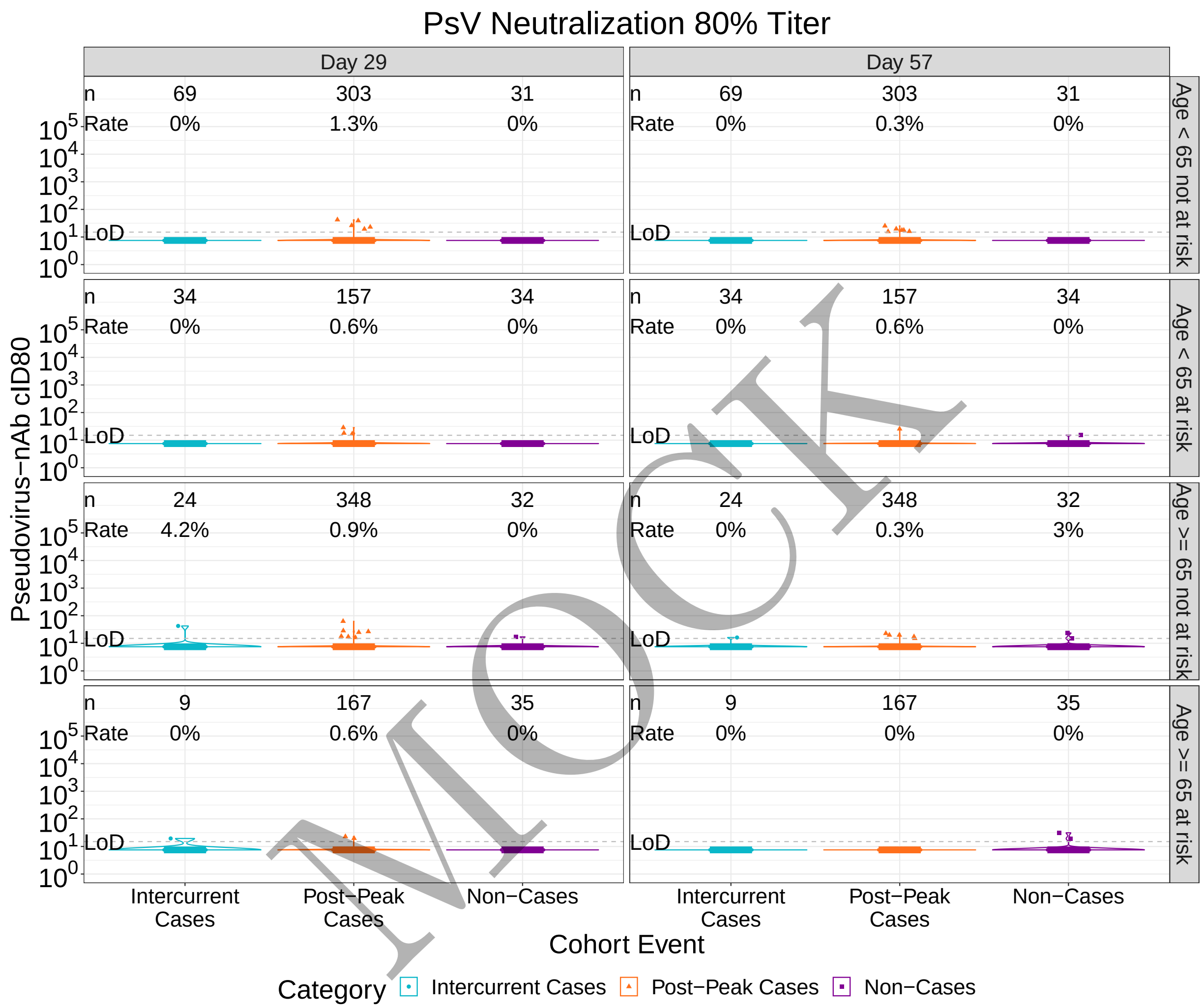

\caption{

Figure 2.5.110: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



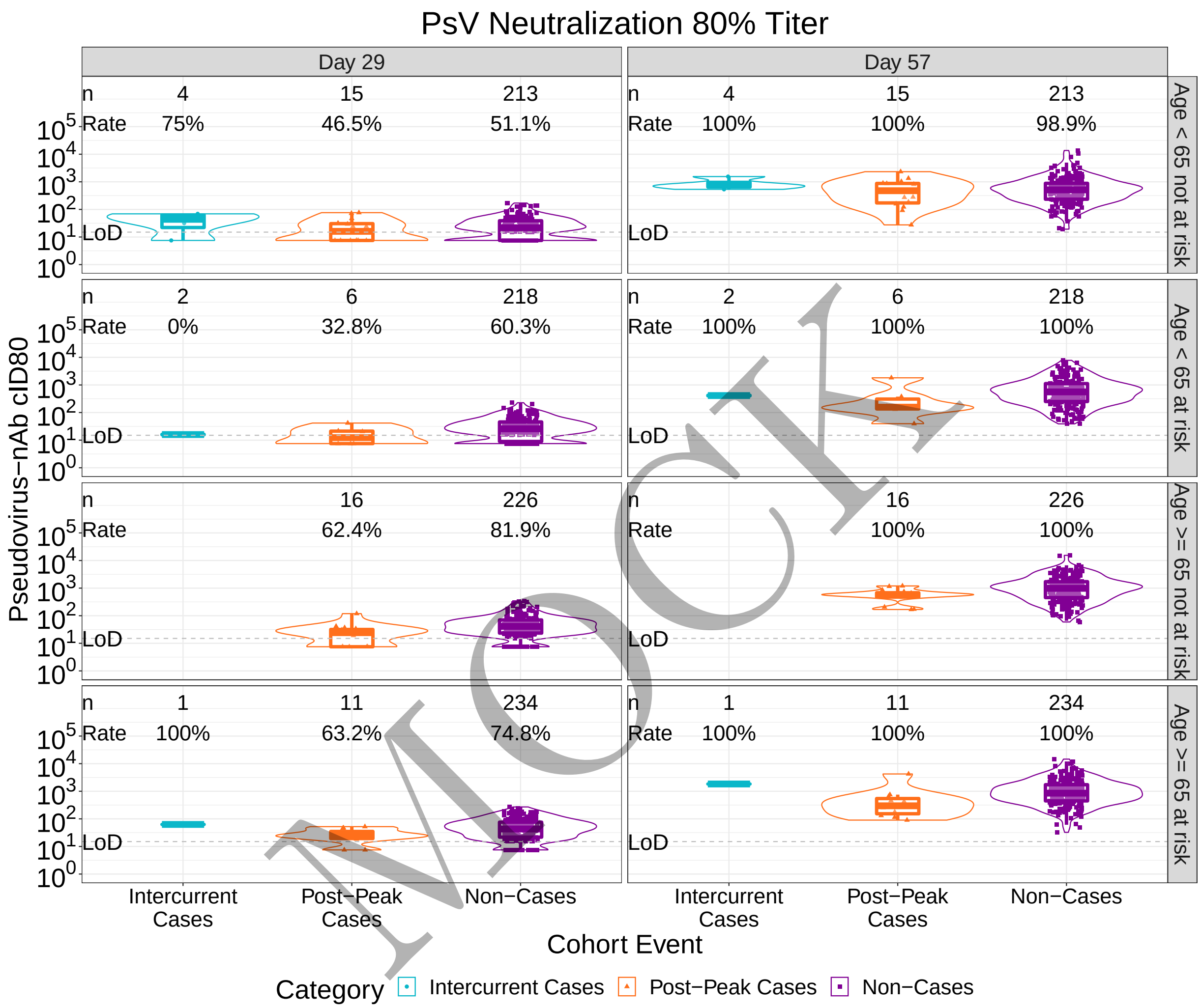

\caption{

Figure 2.5.111: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



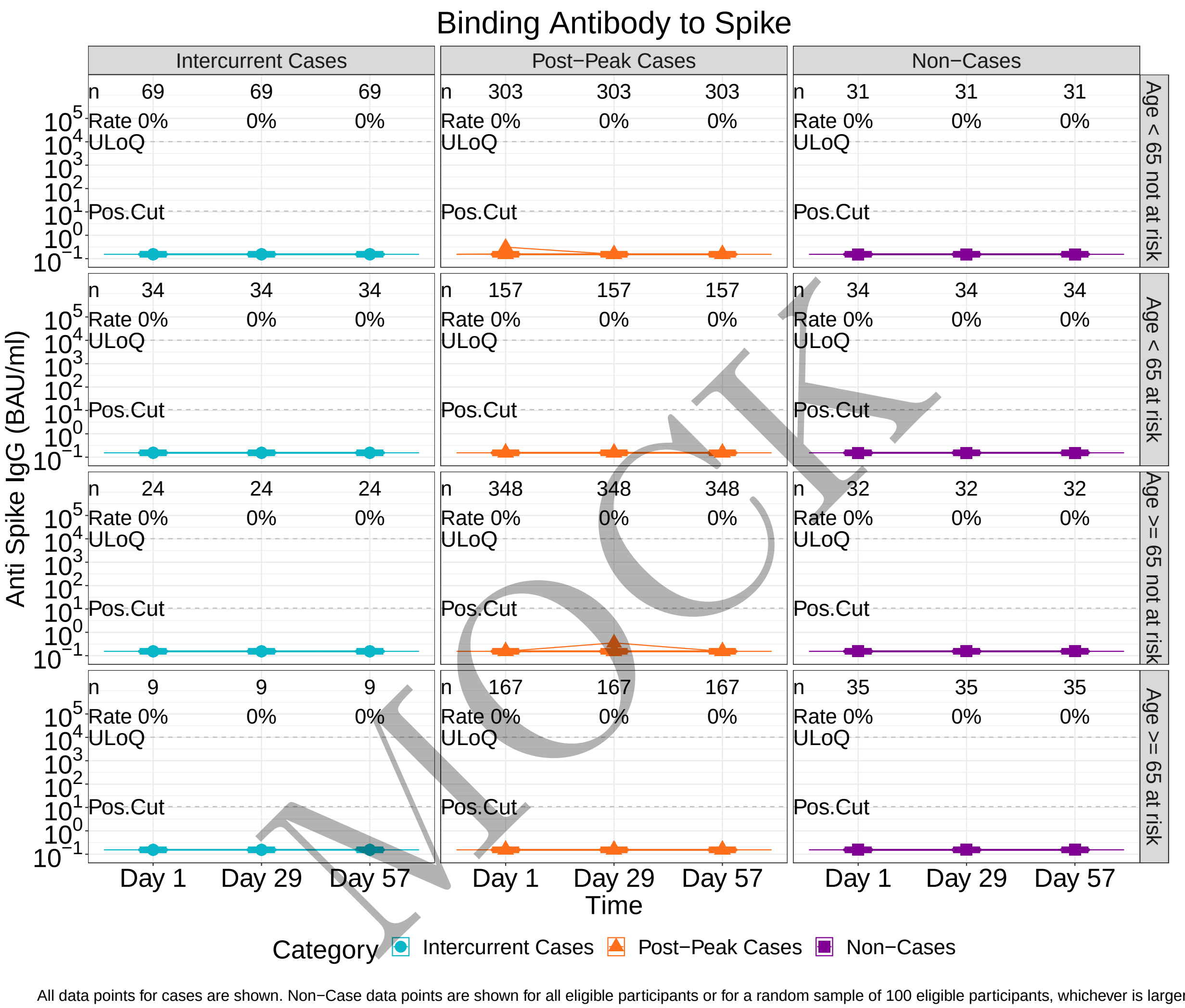

\caption{

Figure 2.5.112: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age and risk condition (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



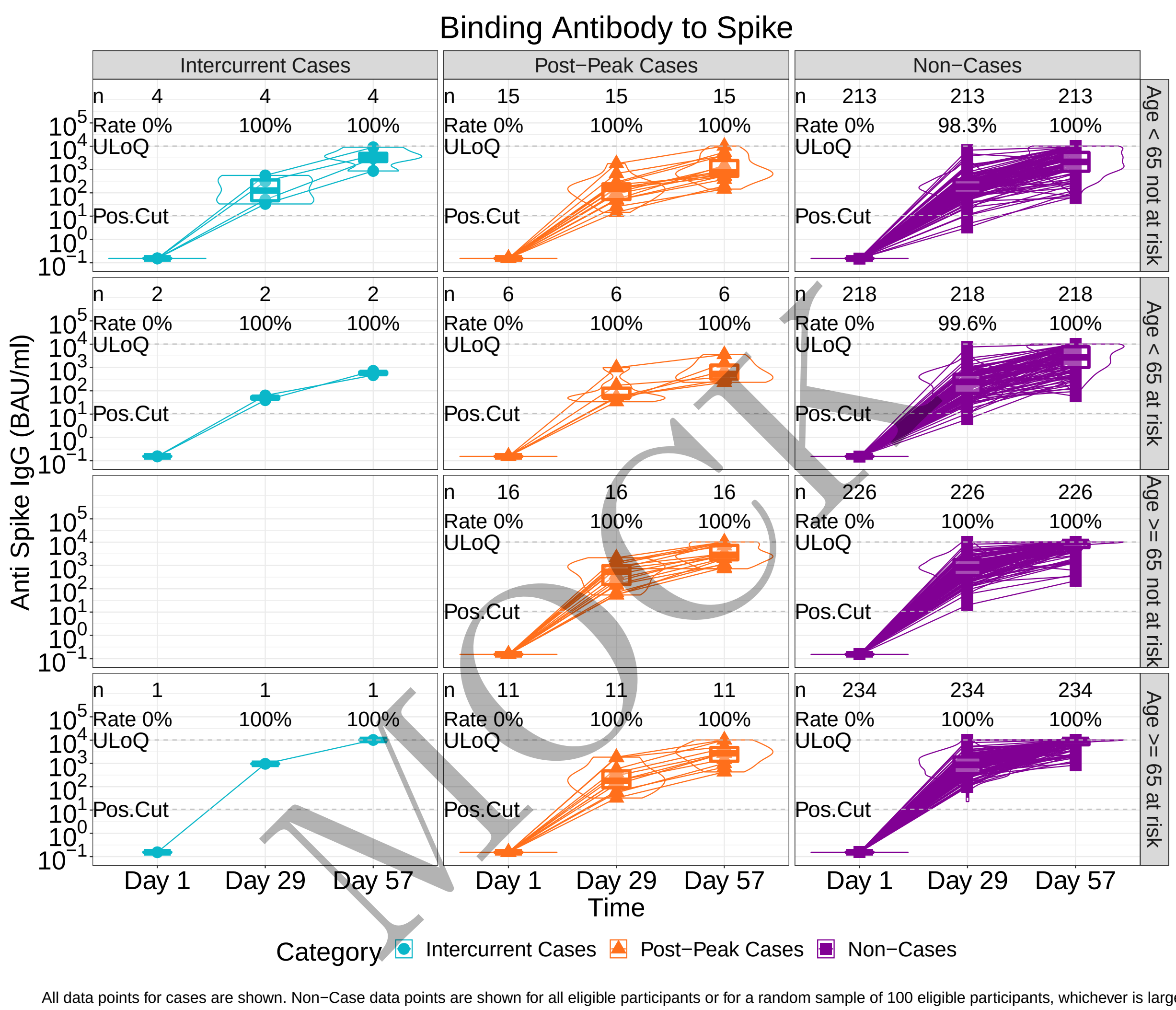

\caption{

Figure 2.5.113: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



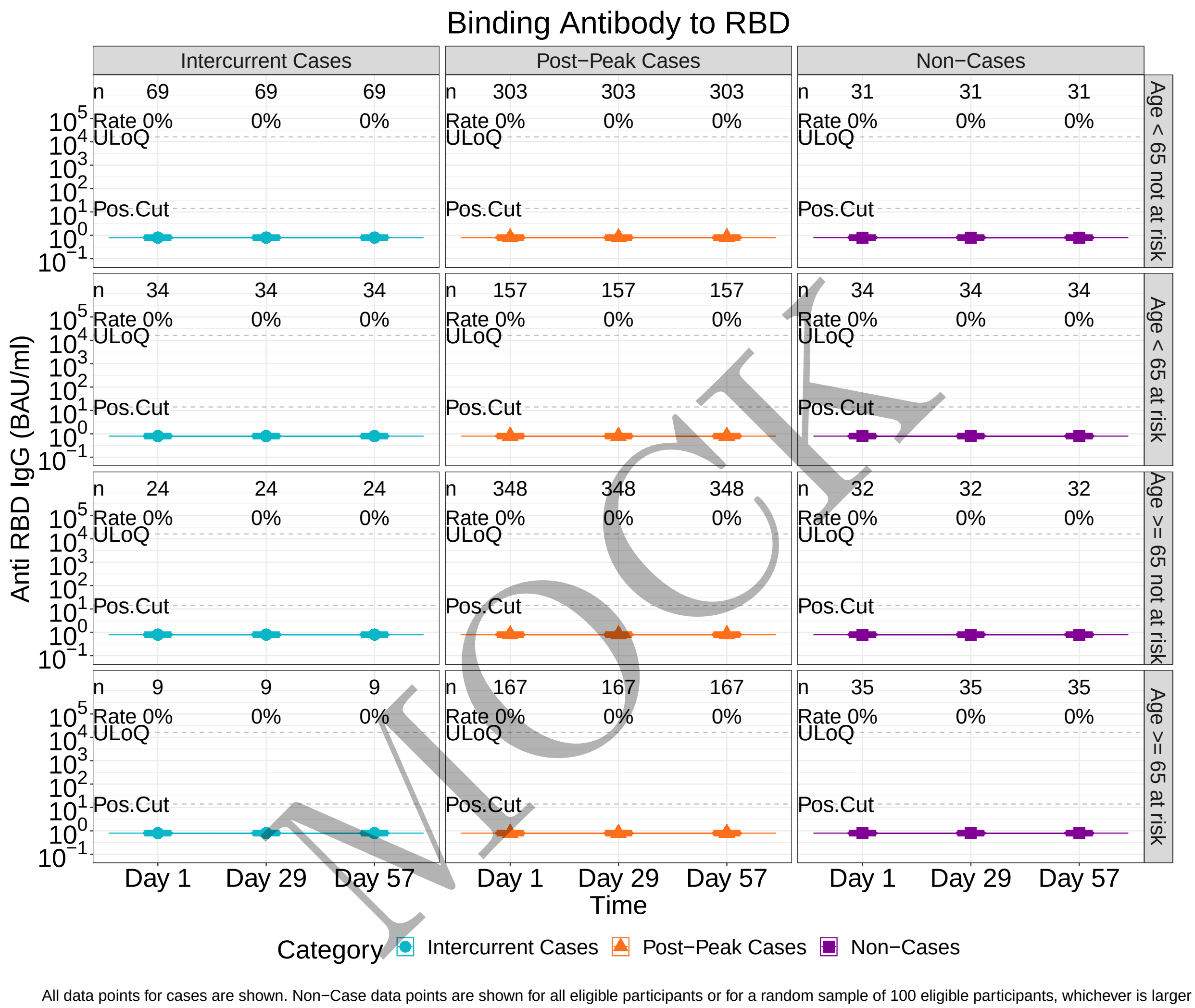

\caption{

Figure 2.5.114: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



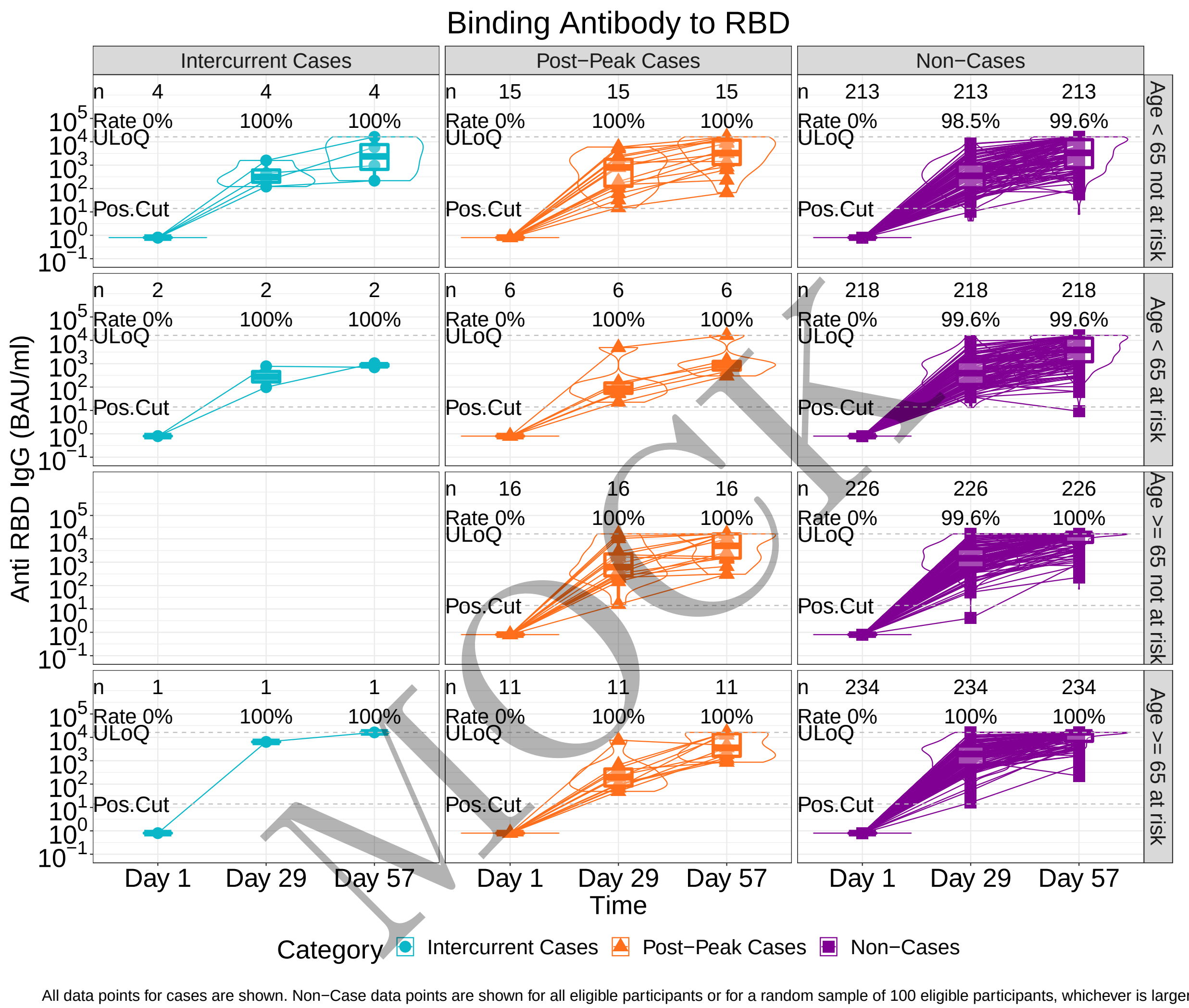

\caption{

Figure 2.5.115: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



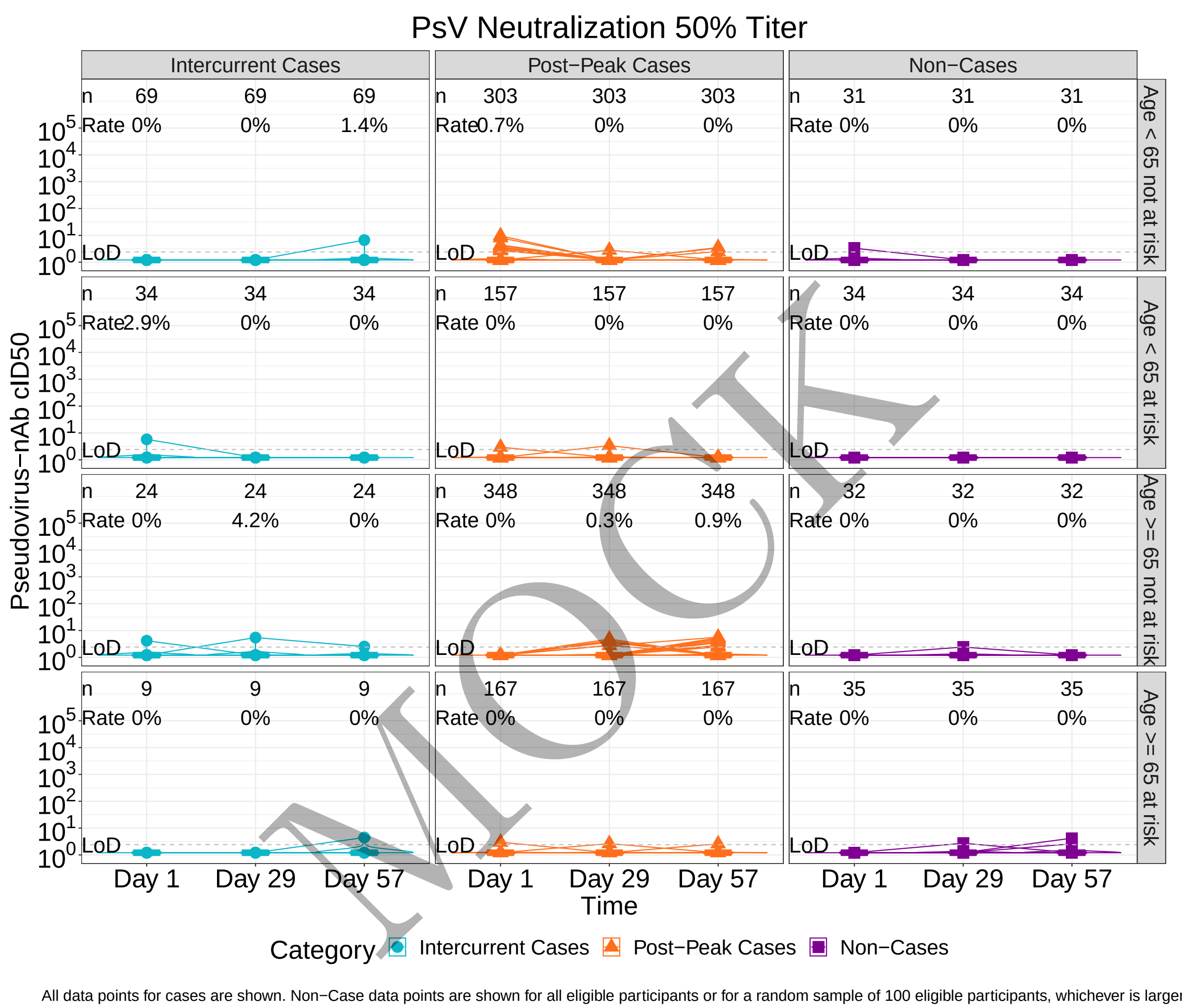

\caption{

Figure 2.5.116: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



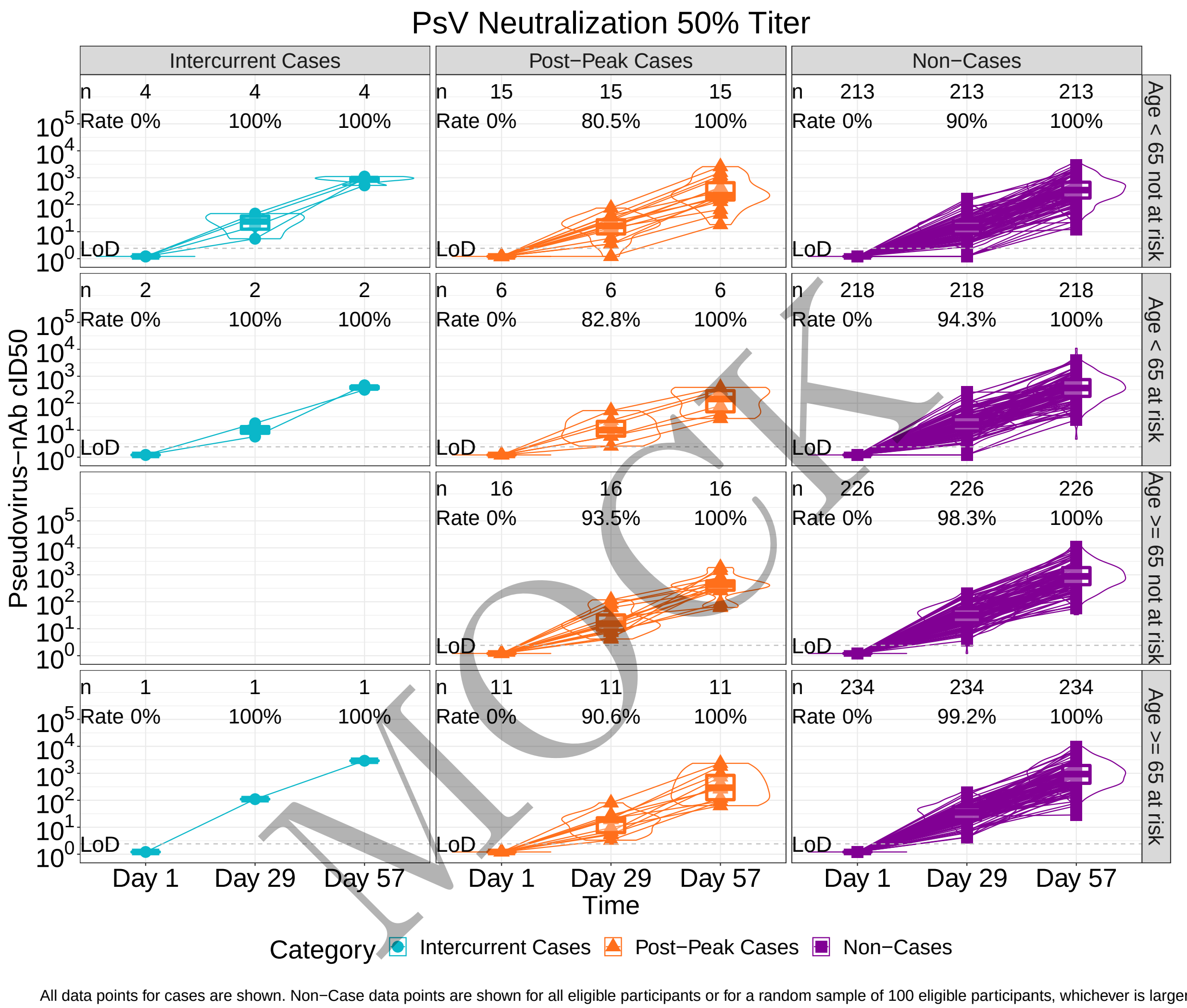

\caption{

Figure 2.5.117: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



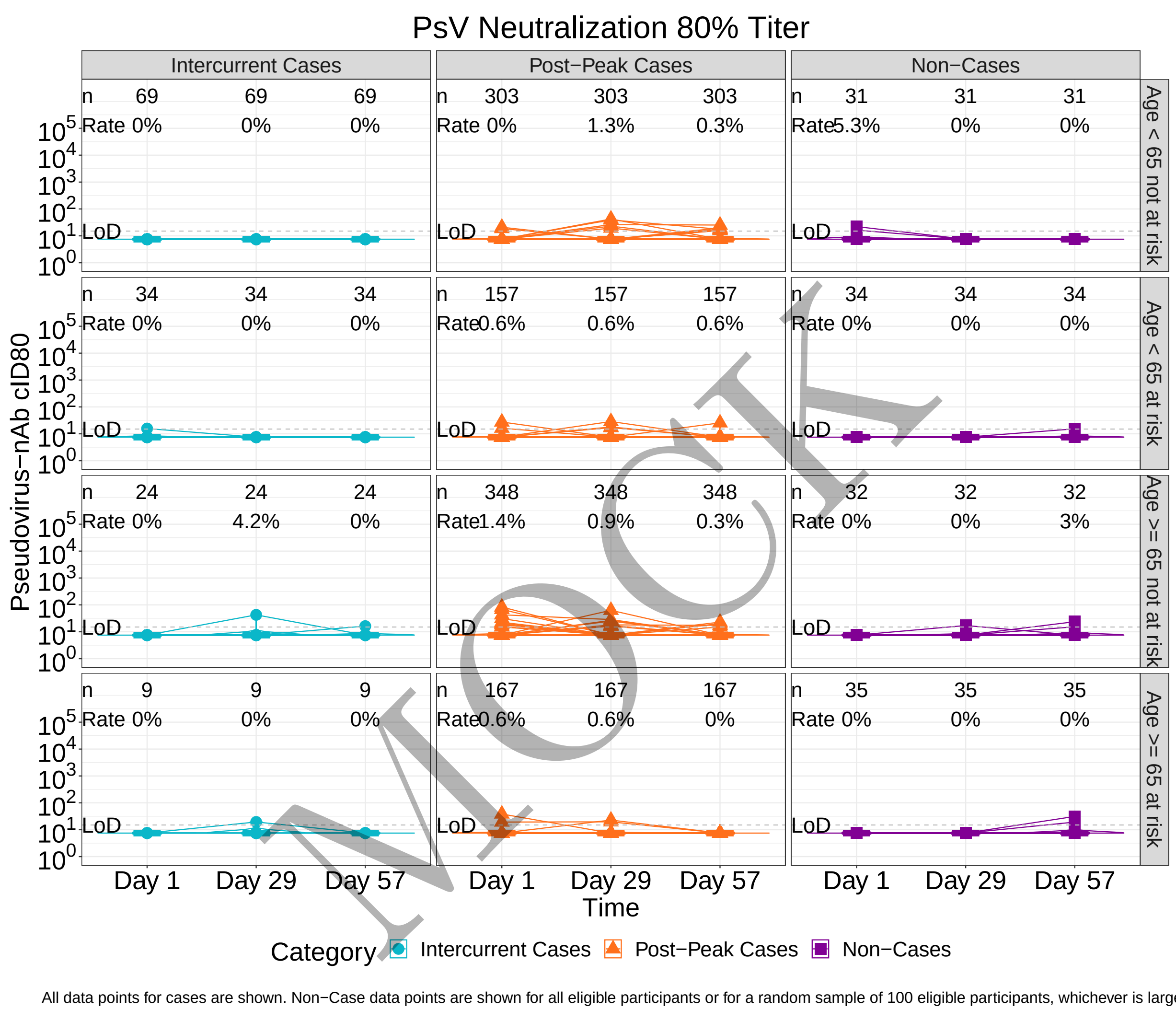

\caption{

Figure 2.5.118: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



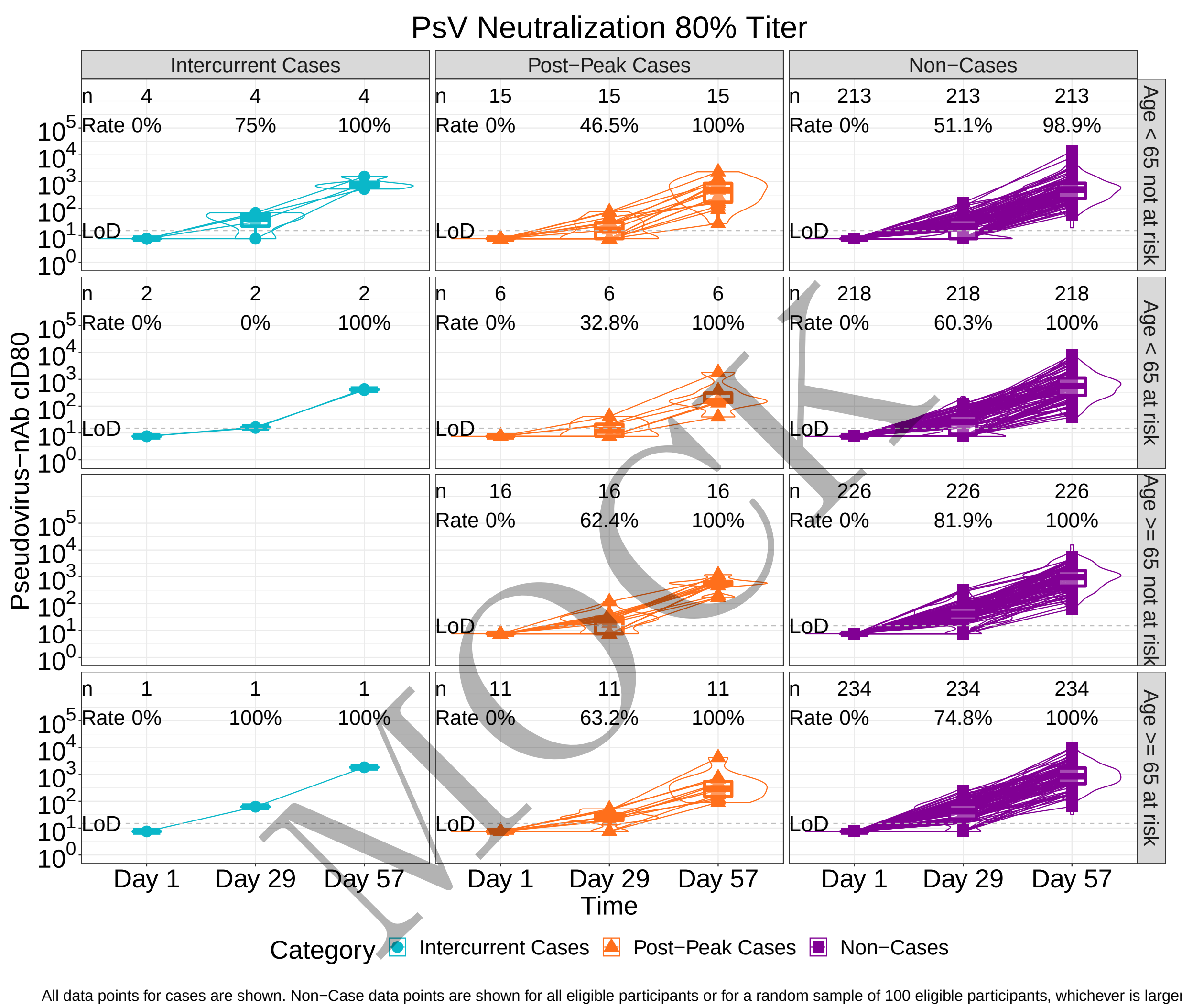

\caption{

Figure 2.5.119: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



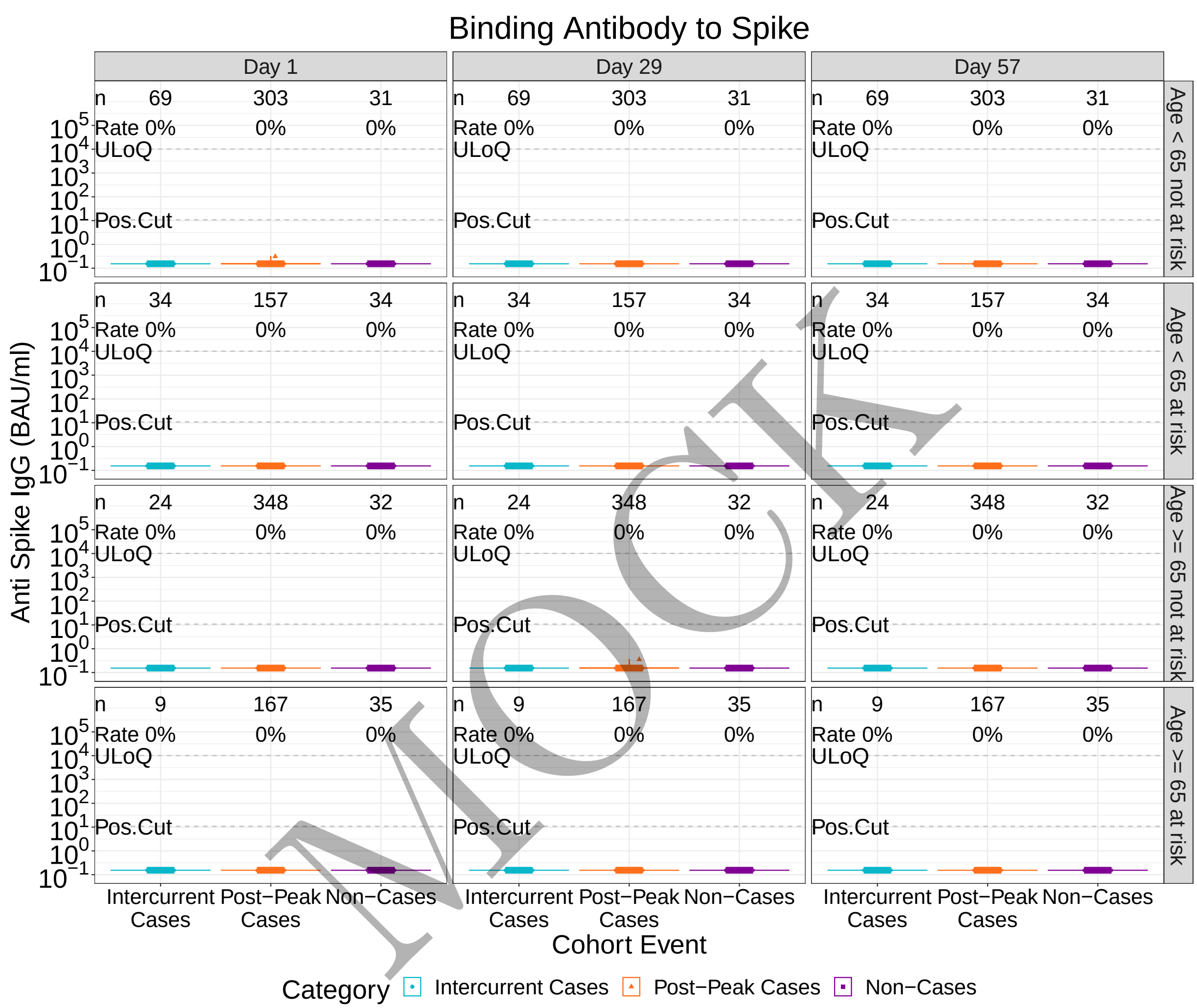

\caption{

Figure 2.5.120: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





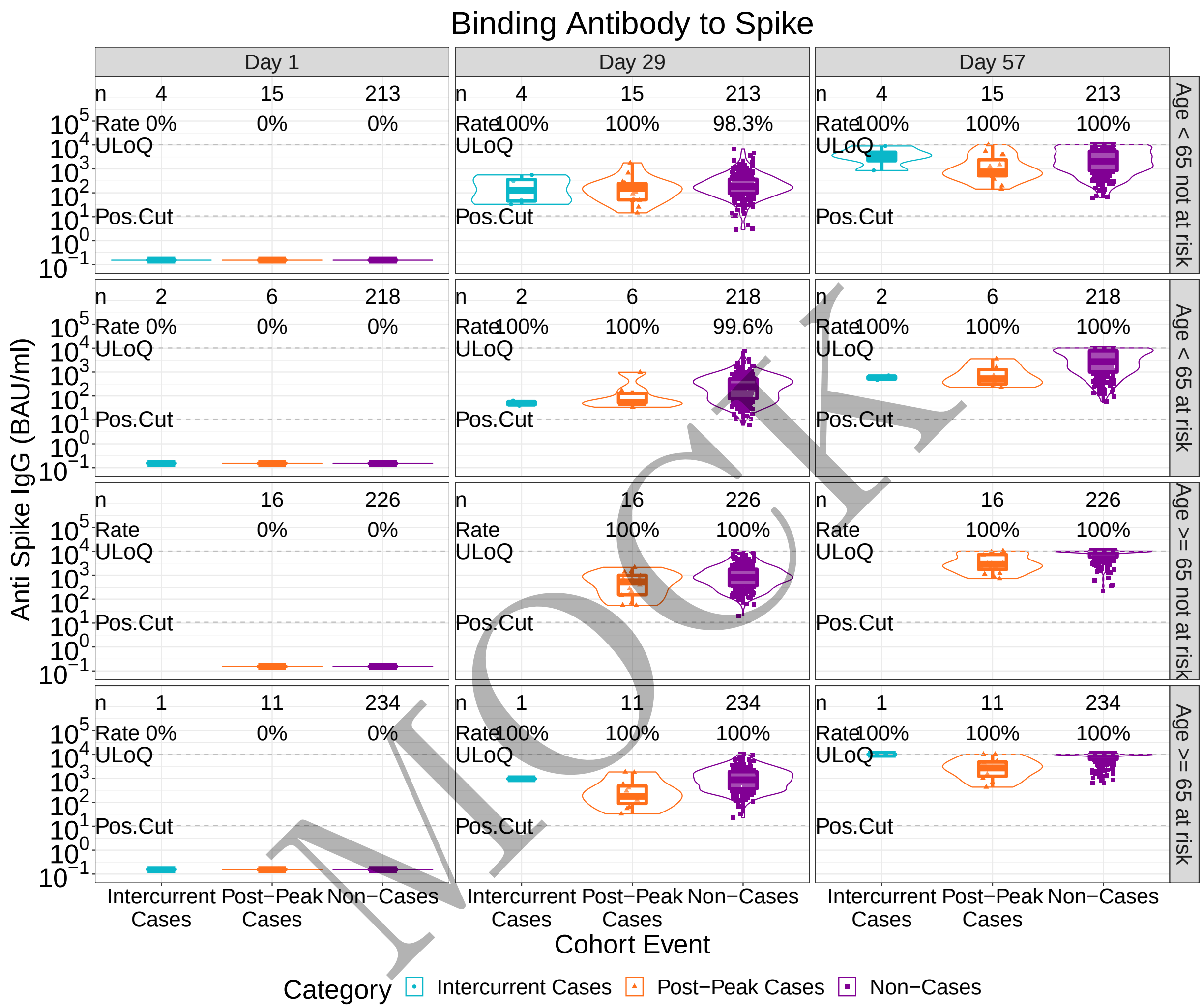

\caption{

Figure 2.5.121: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



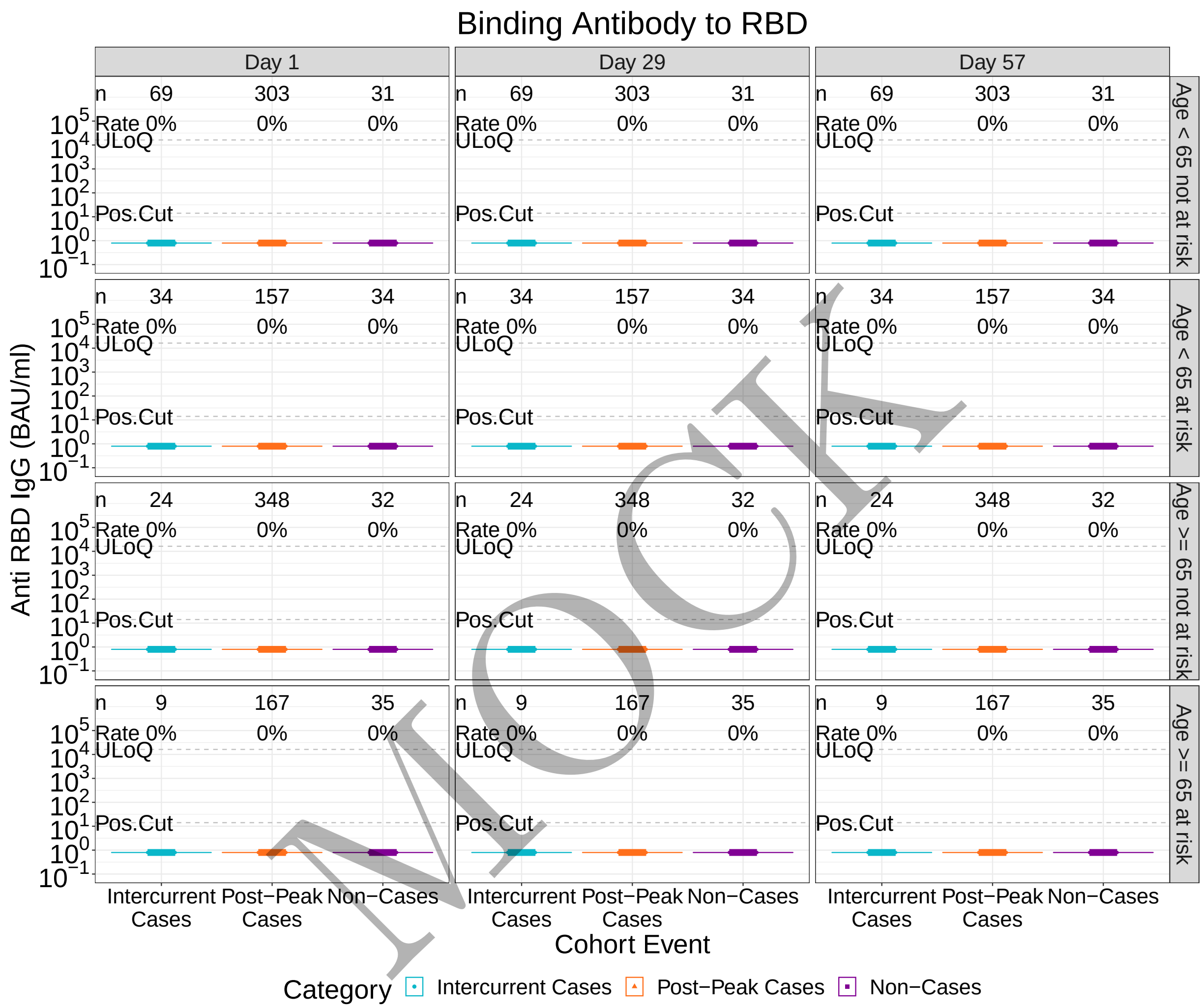

\caption{

Figure 2.5.122: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



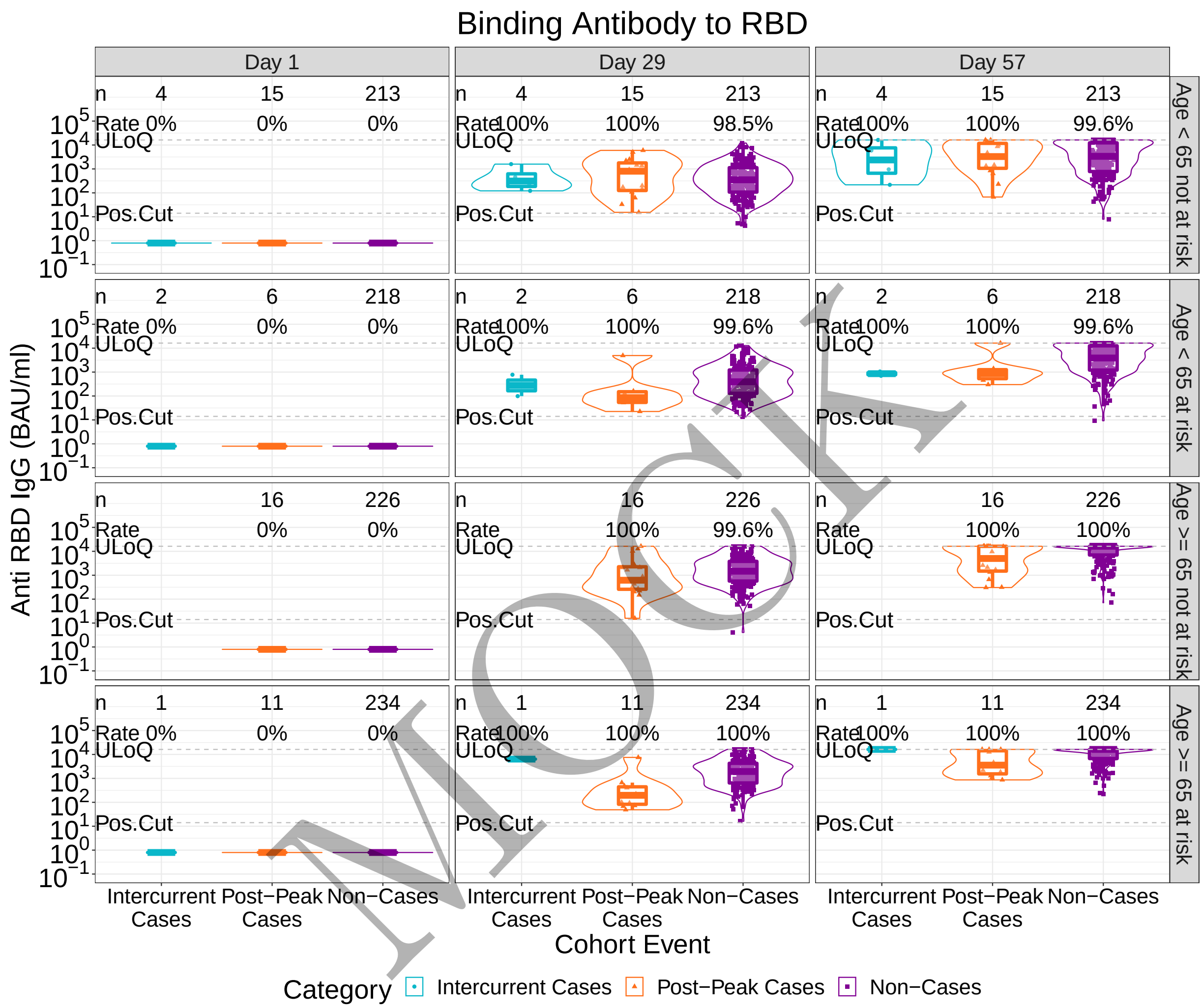

\caption{

Figure 2.5.123: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



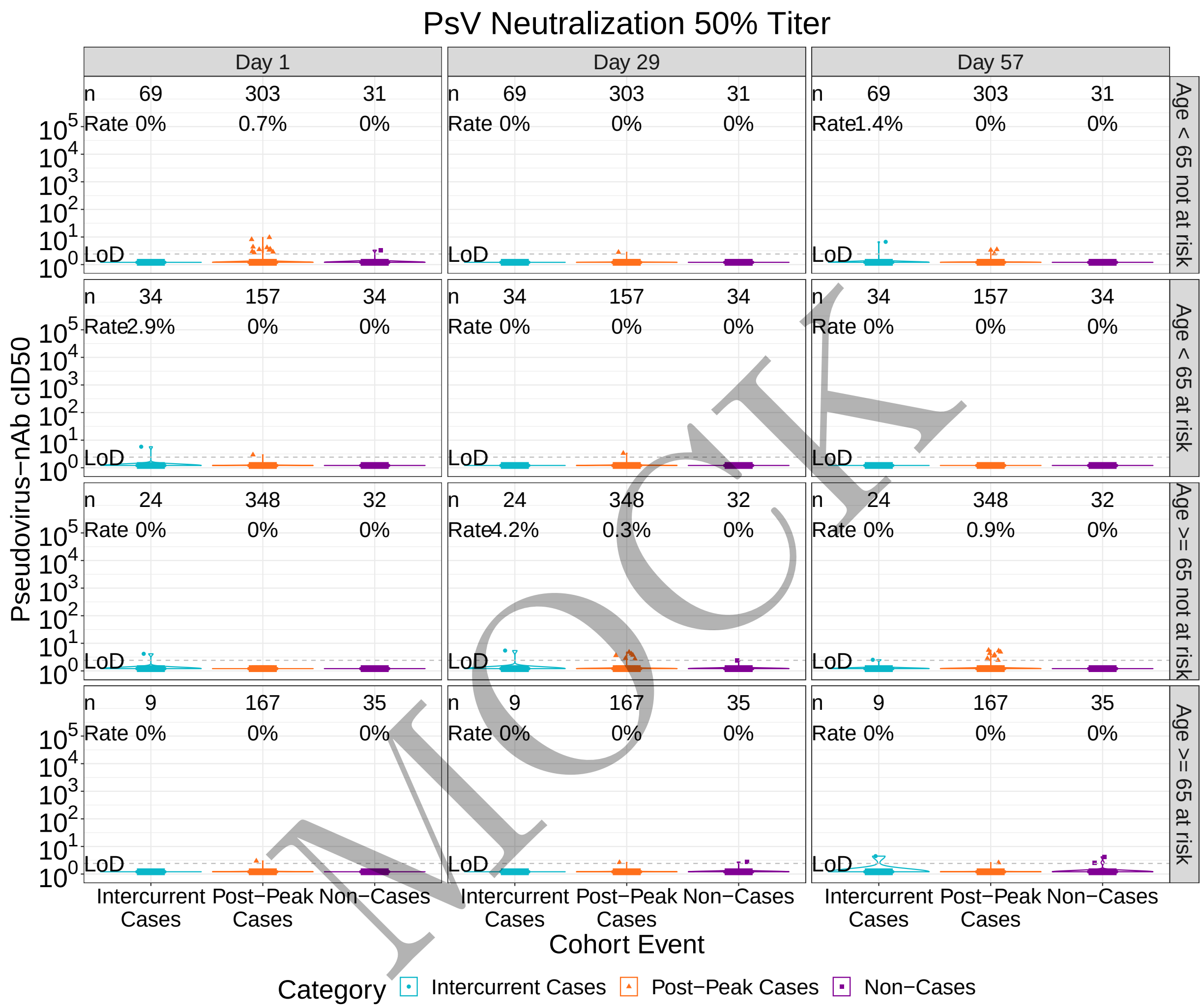

\caption{

Figure 2.5.124: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



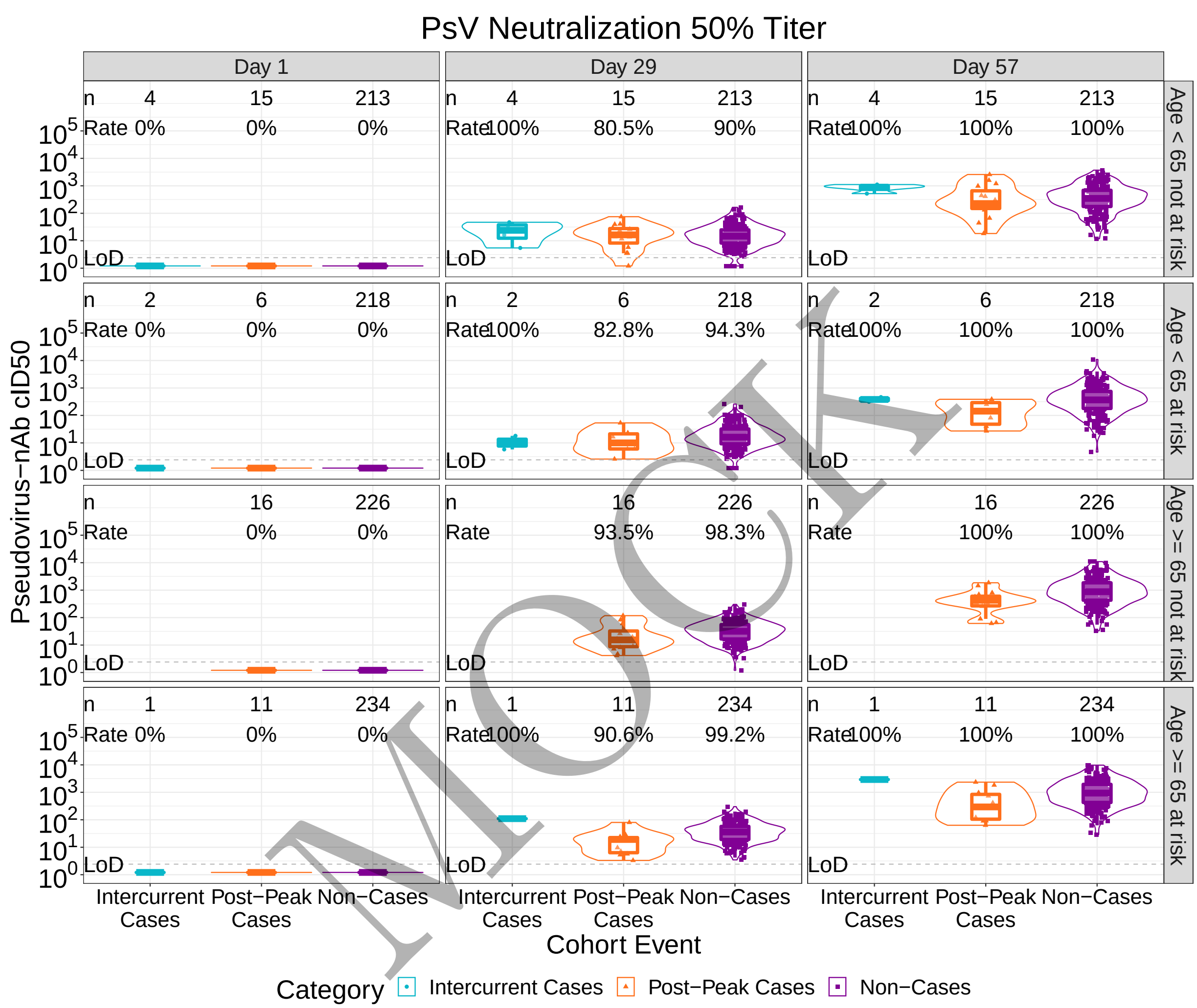

\caption{

Figure 2.5.125: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



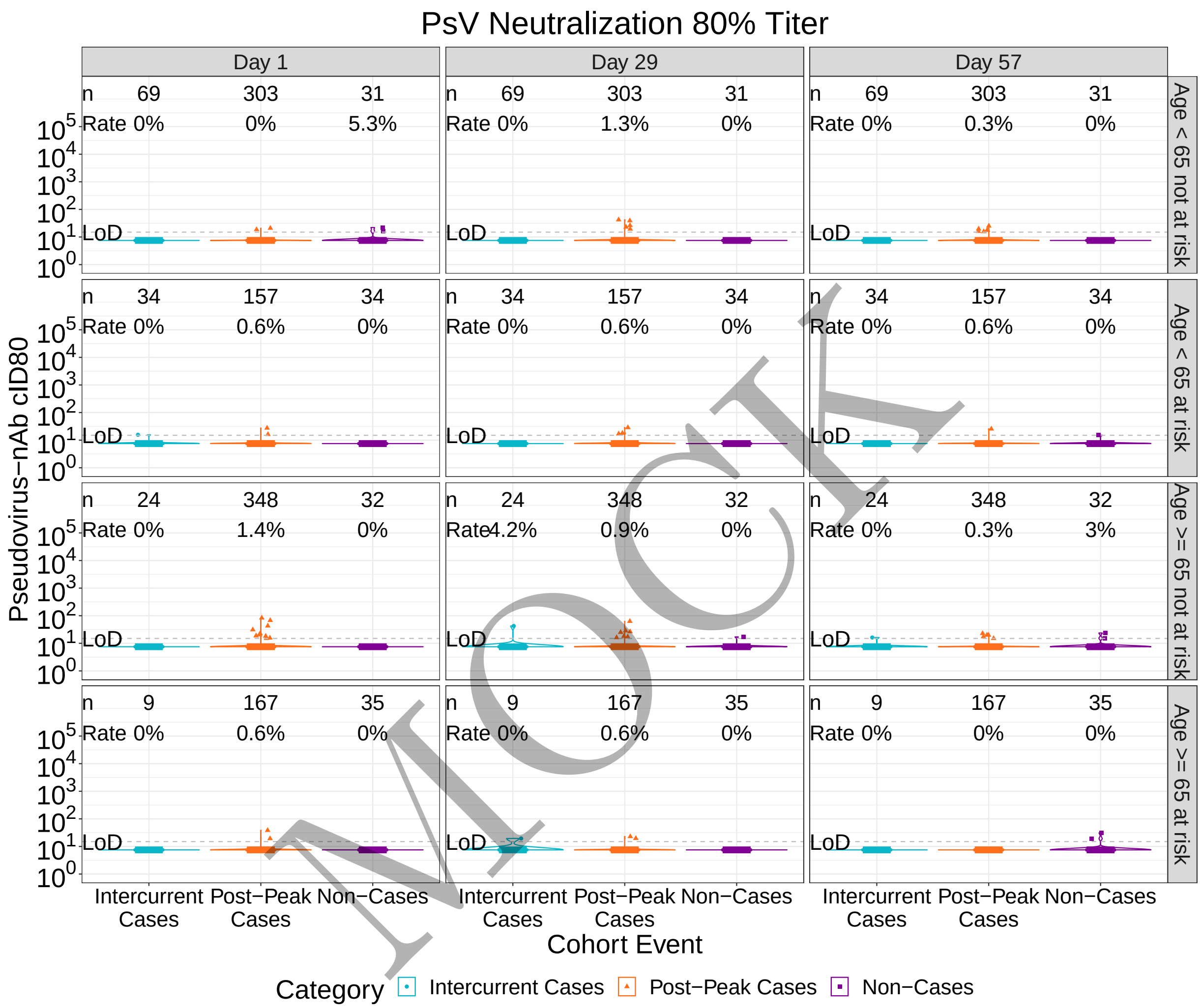

\caption{

Figure 2.5.126: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



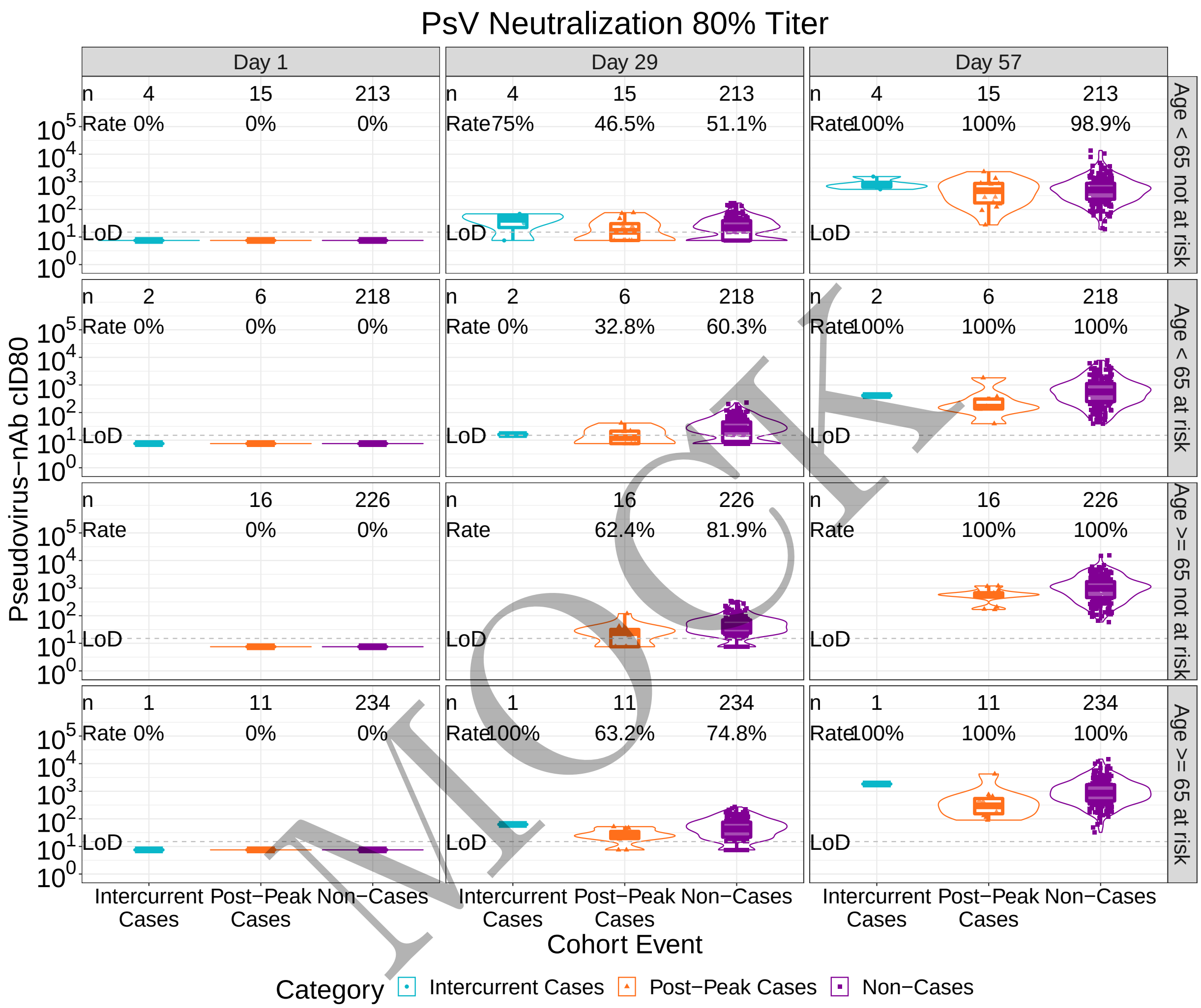

\caption{

Figure 2.5.127: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



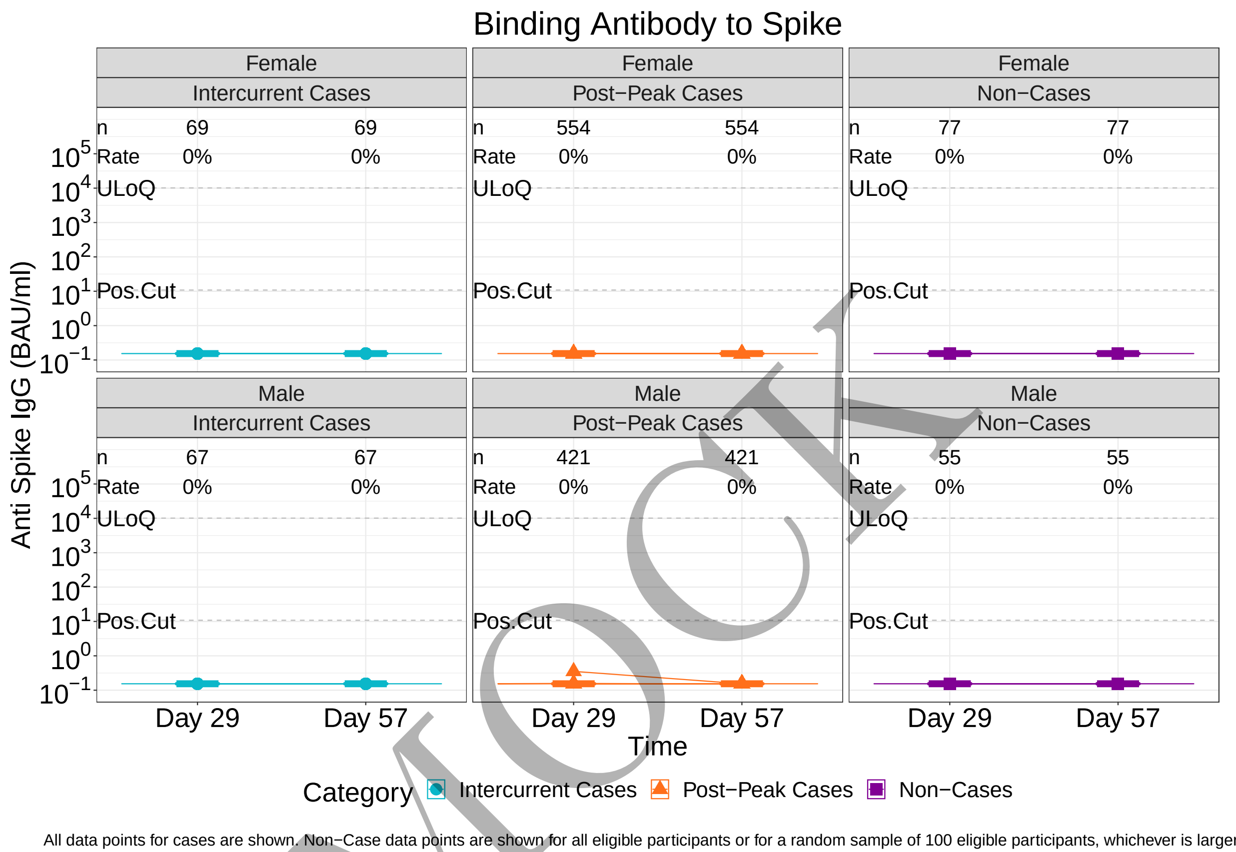

\caption{

Figure 2.5.128: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by age and risk condition (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





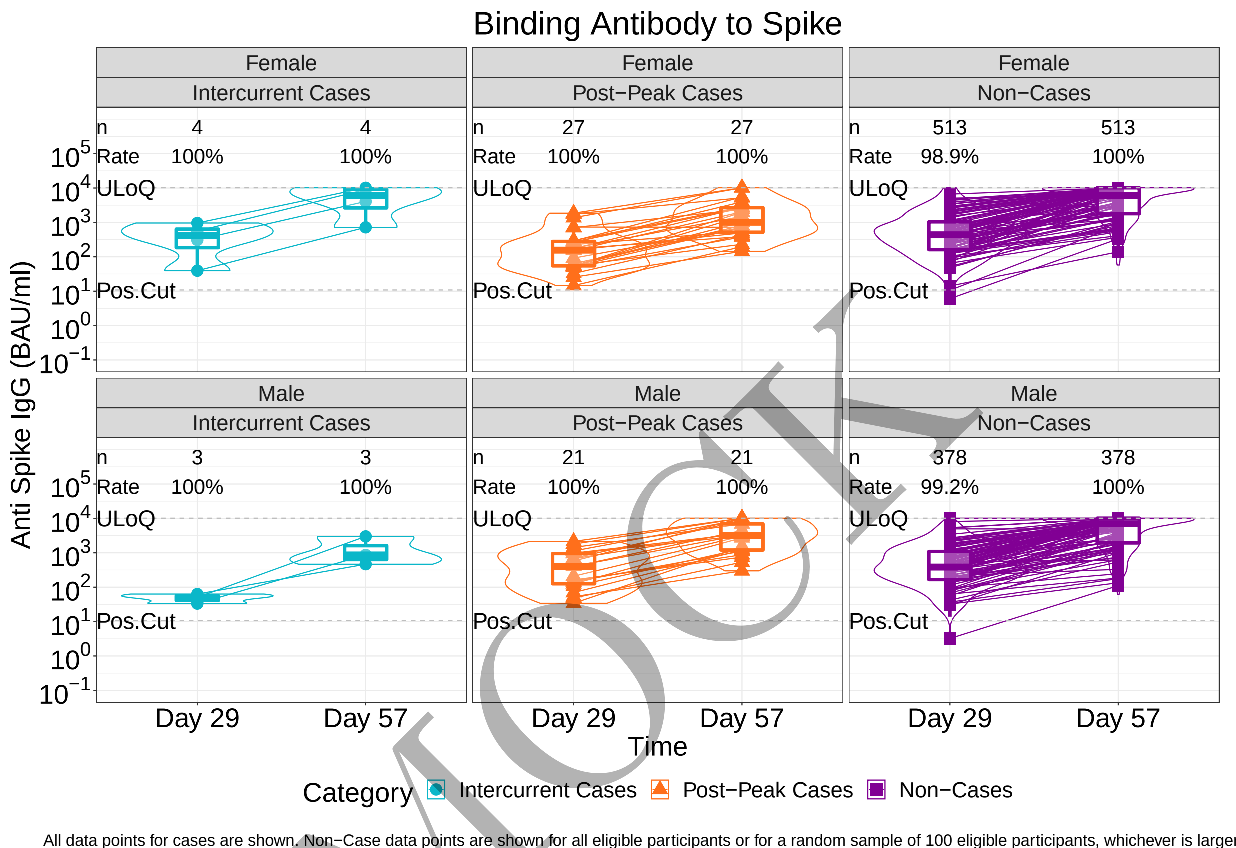

\caption{

Figure 2.5.129: lineplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





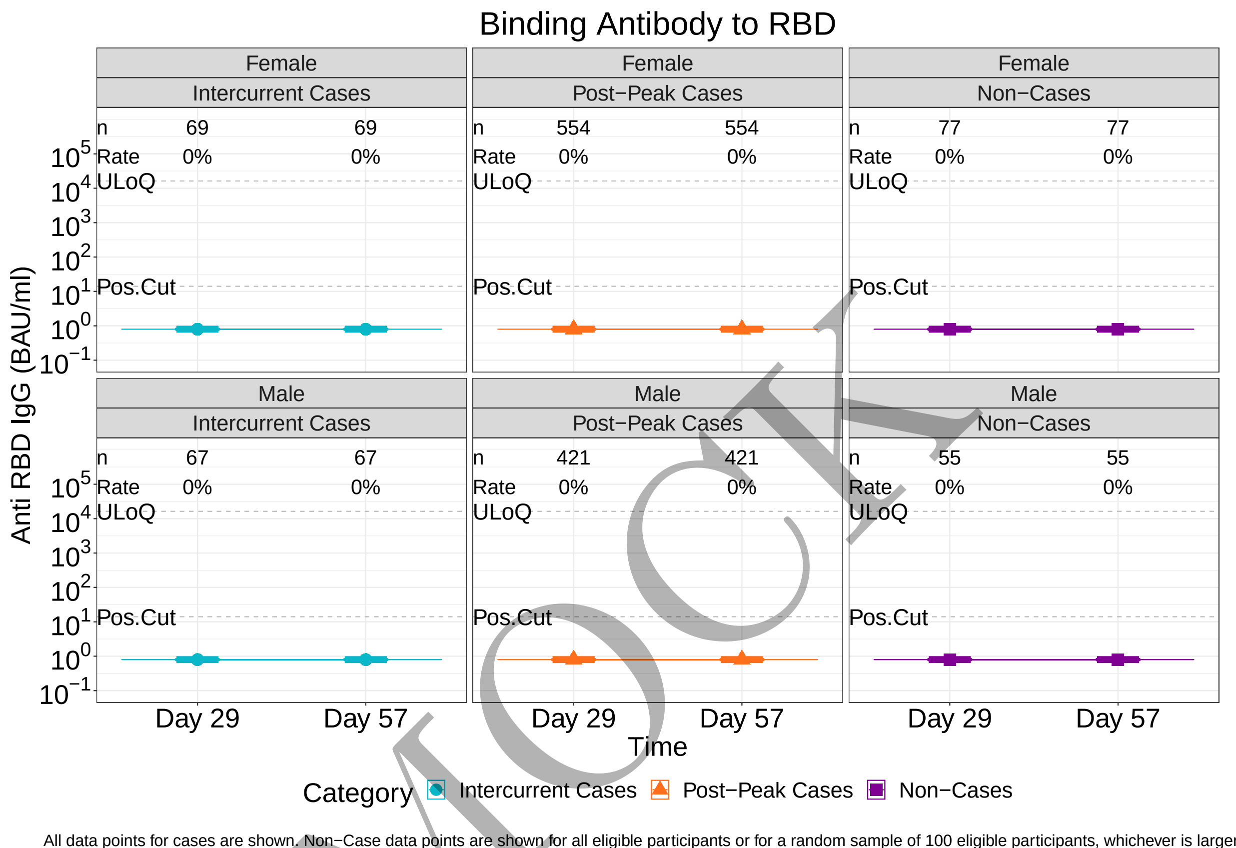

\caption{

Figure 2.5.130: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



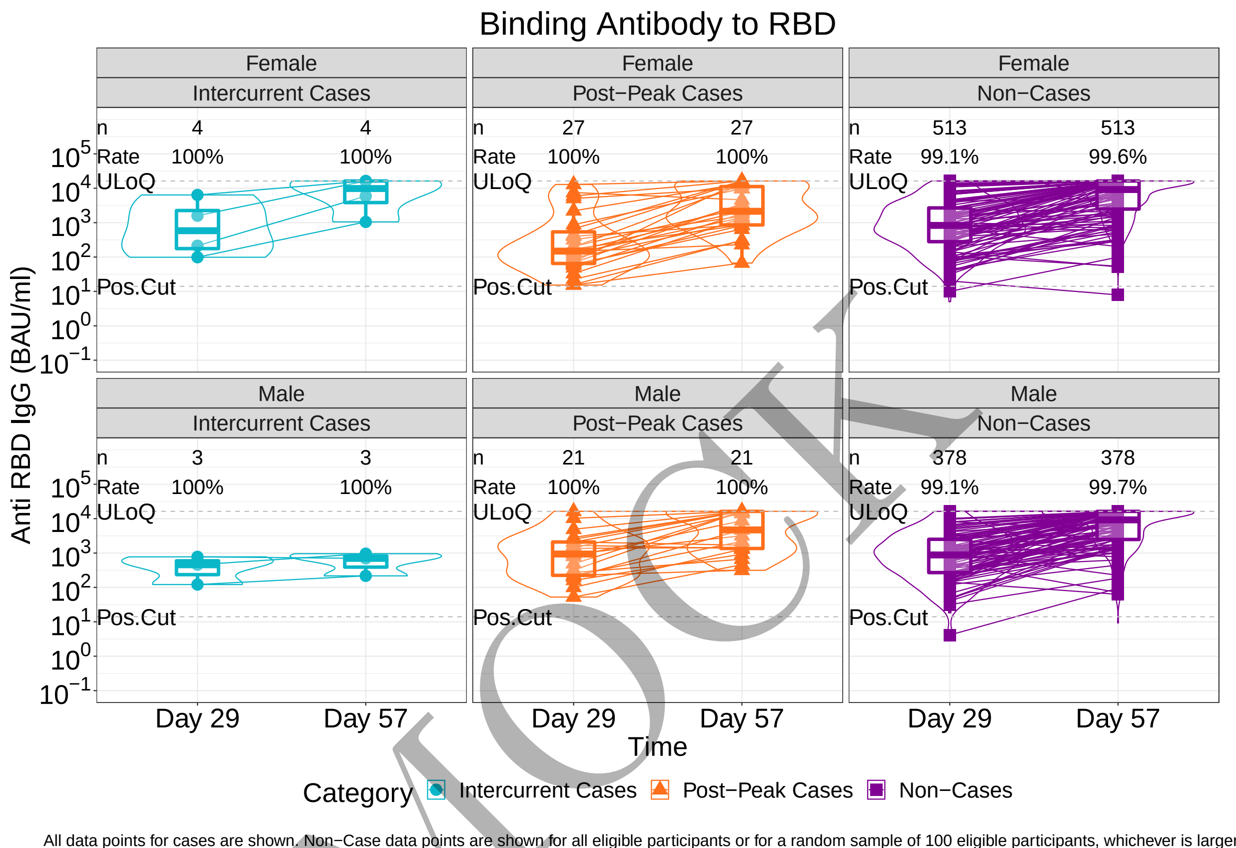

\caption{

Figure 2.5.131: lineplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



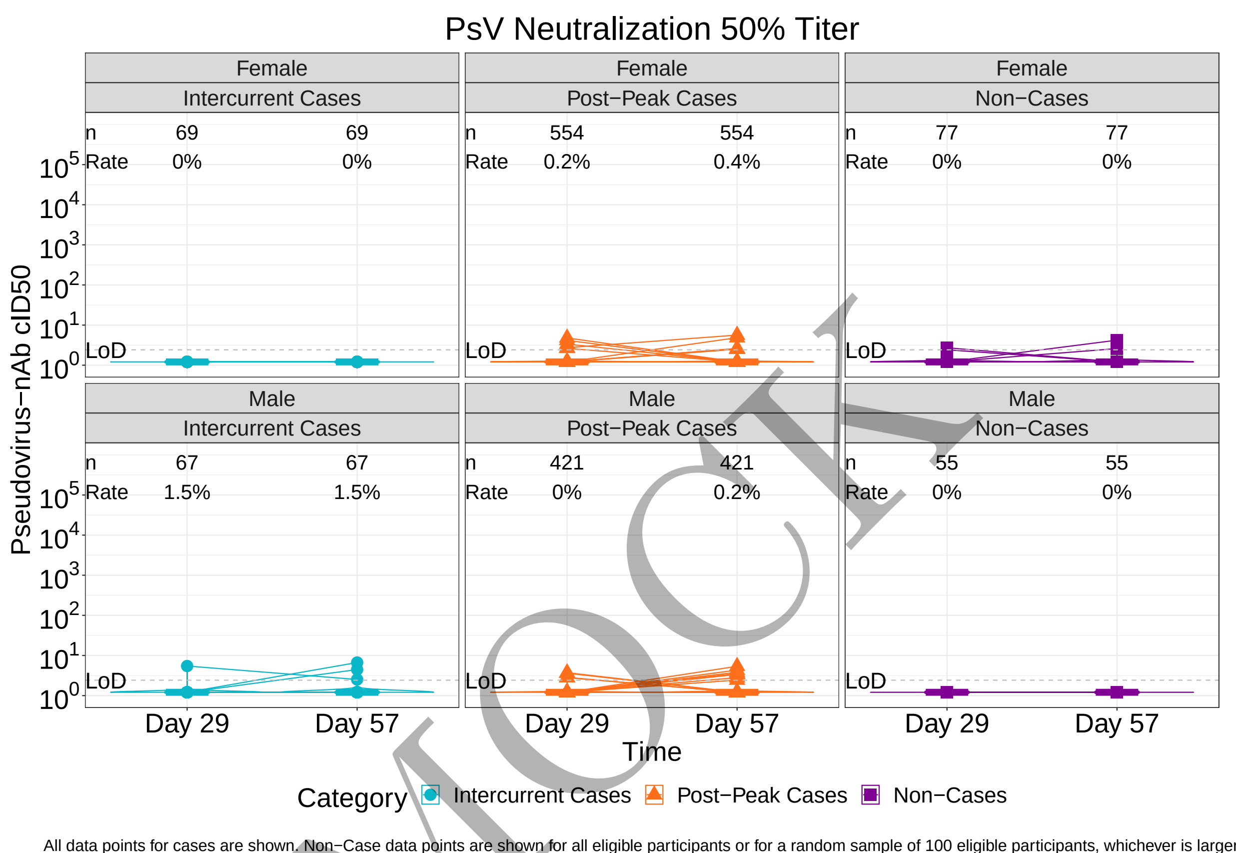

\caption{

Figure 2.5.132: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



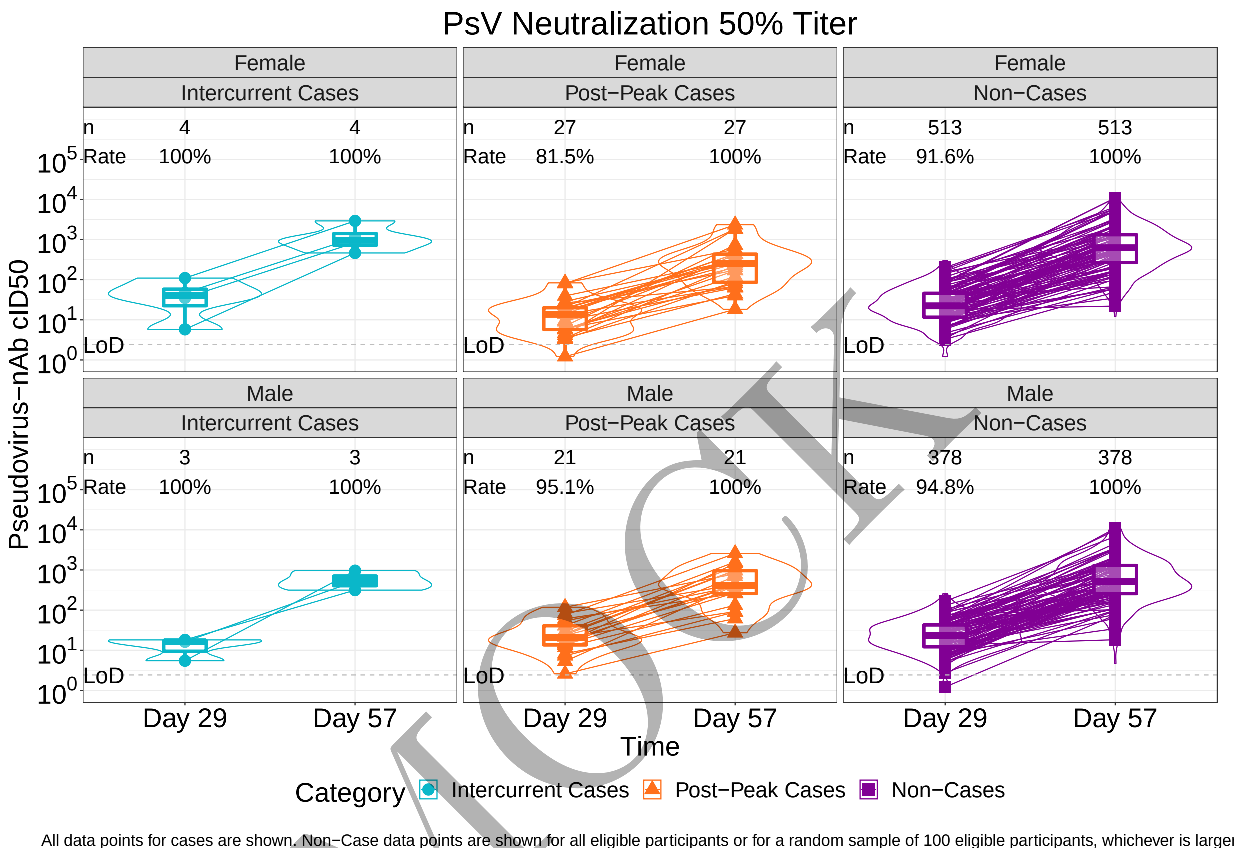

\caption{

Figure 2.5.133: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



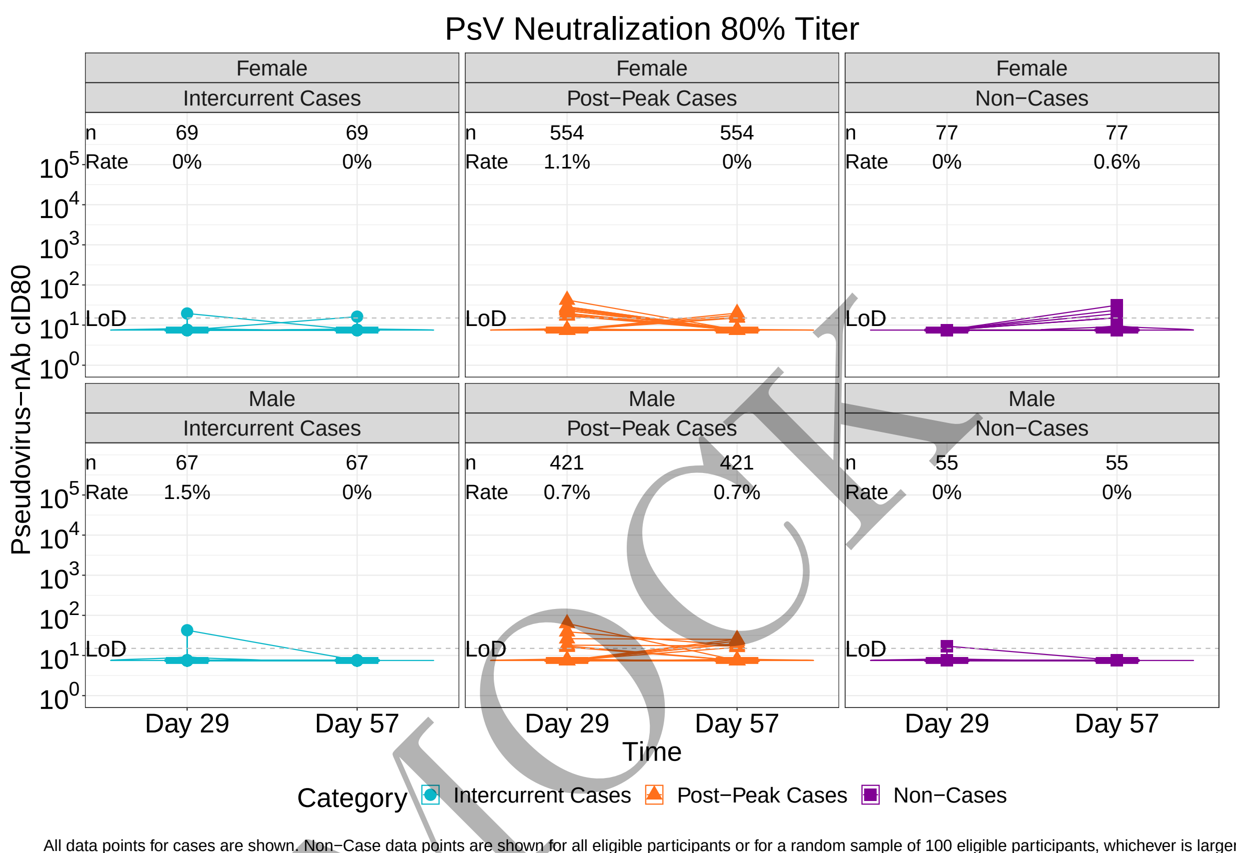

\caption{

Figure 2.5.134: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}



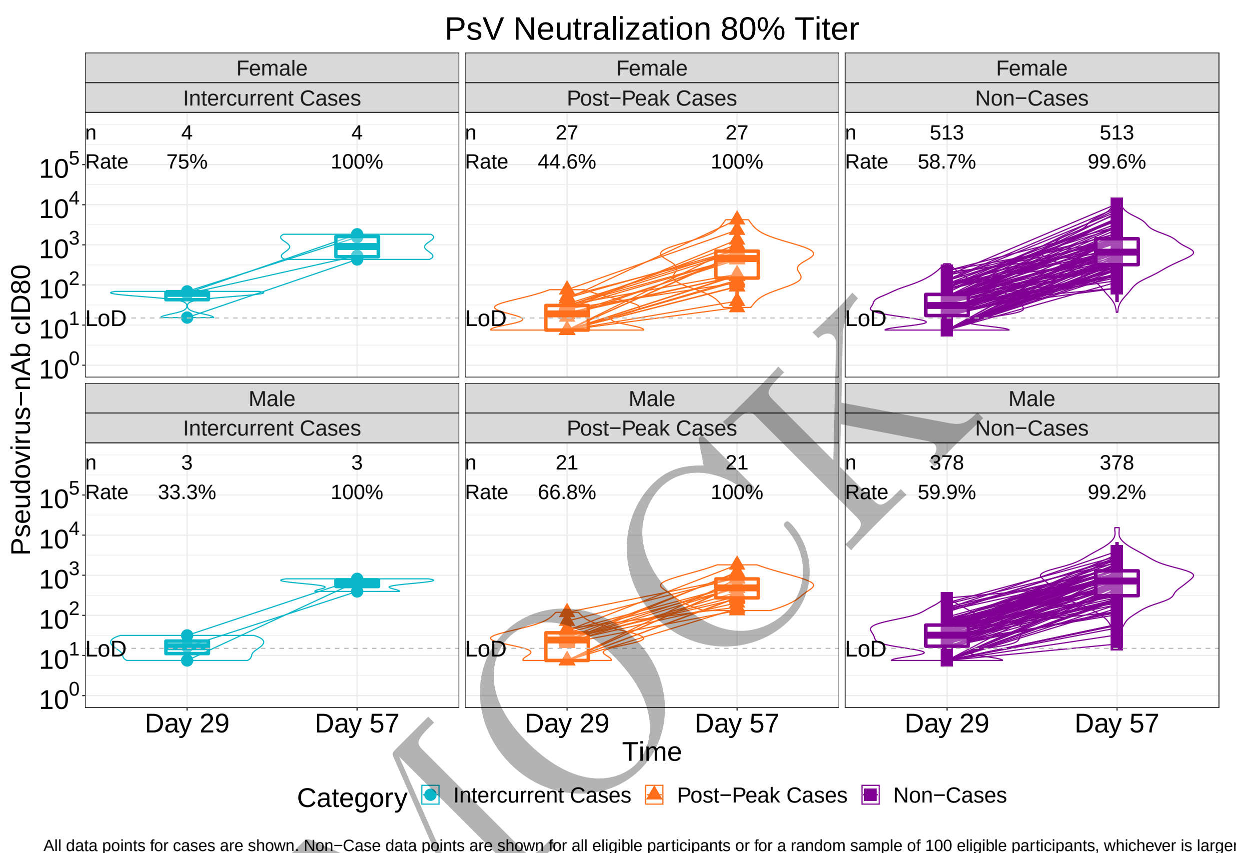

\caption{

Figure 2.5.135: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



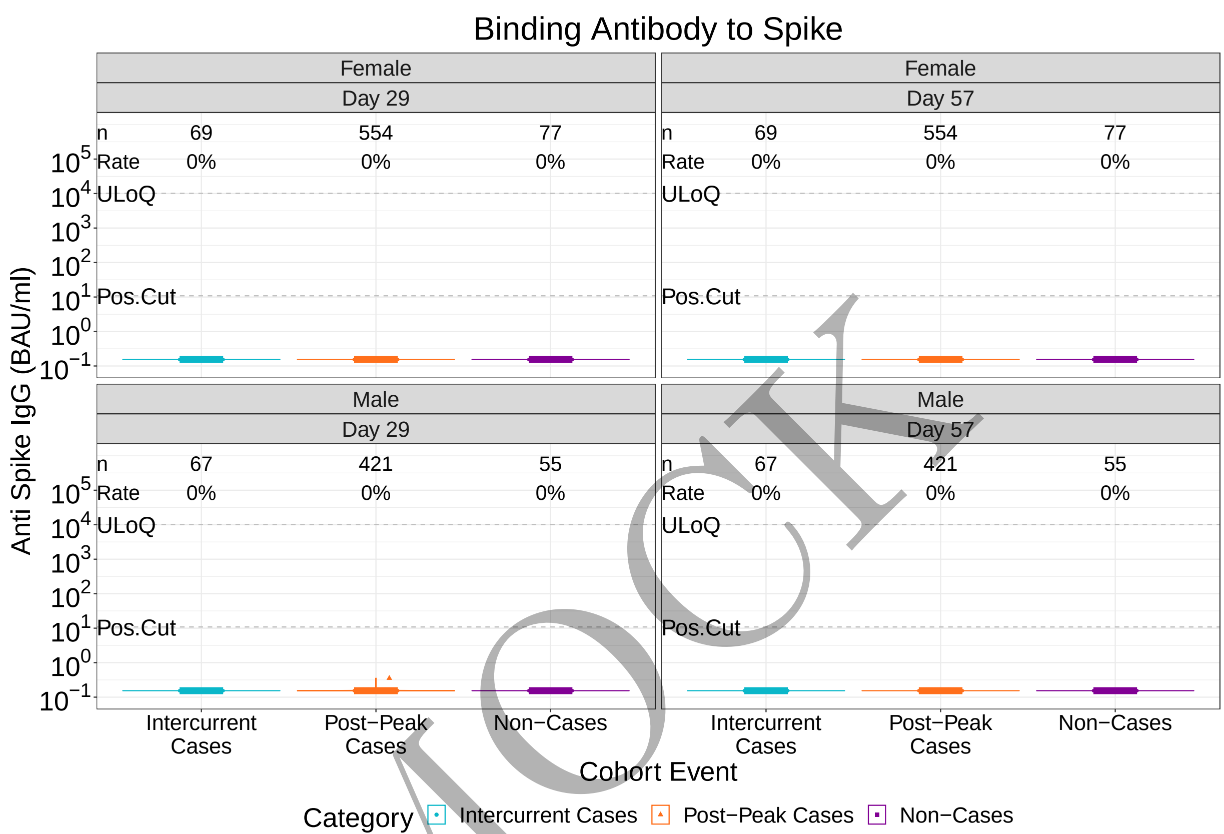

\caption{

Figure 2.5.136: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



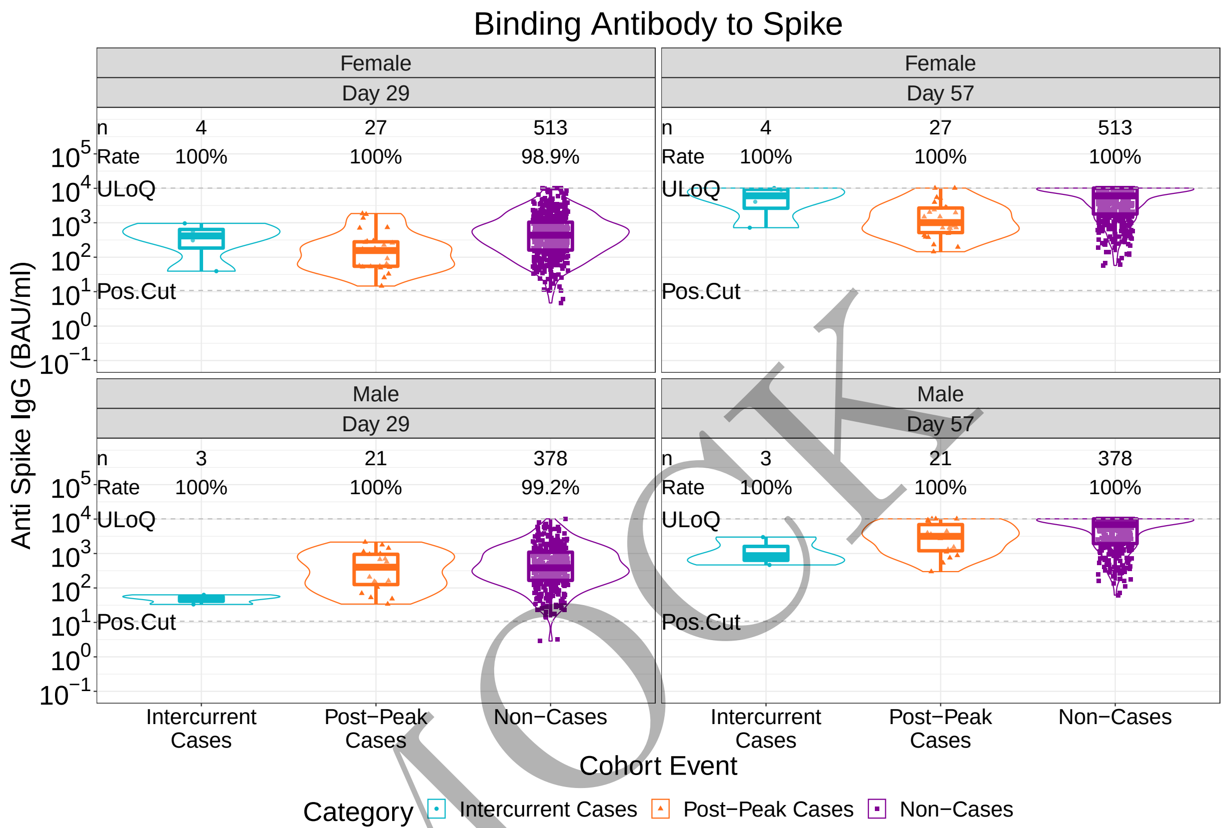

\caption{

Figure 2.5.137: violinplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



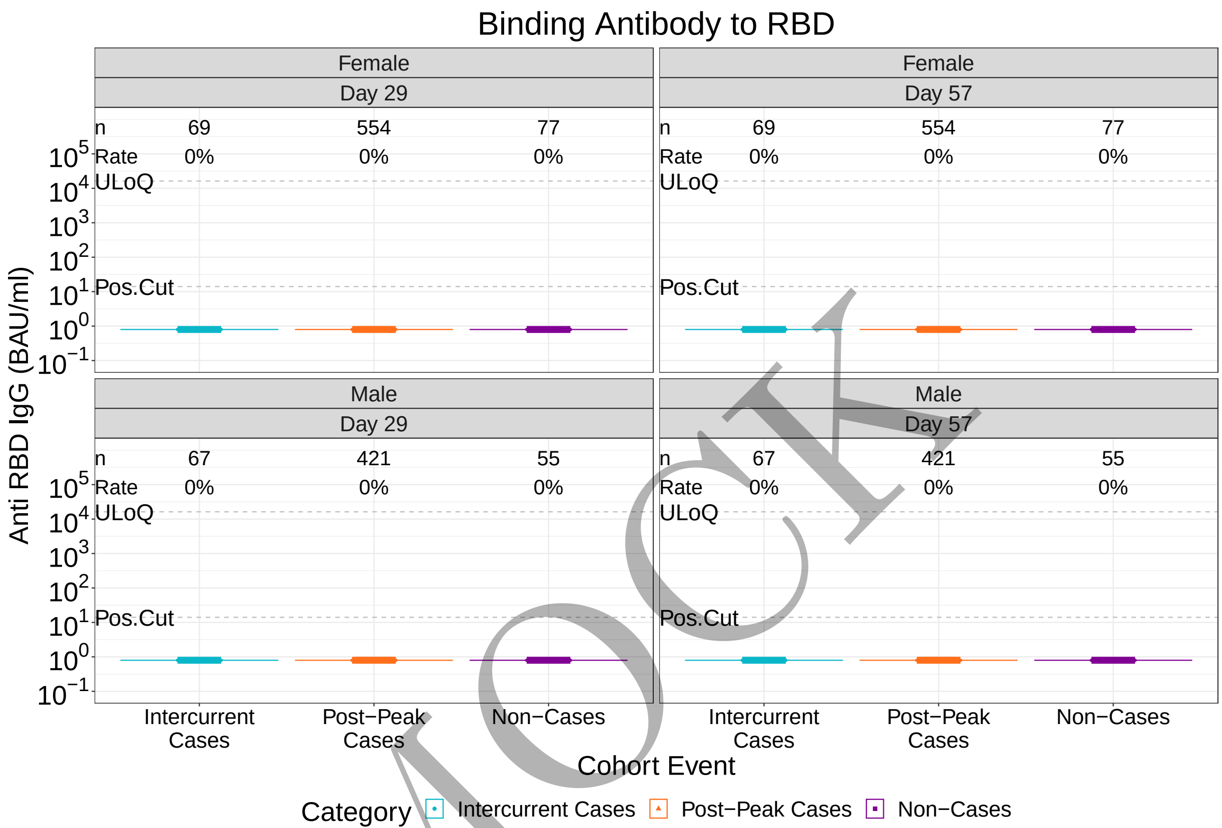

\caption{

Figure 2.5.138: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



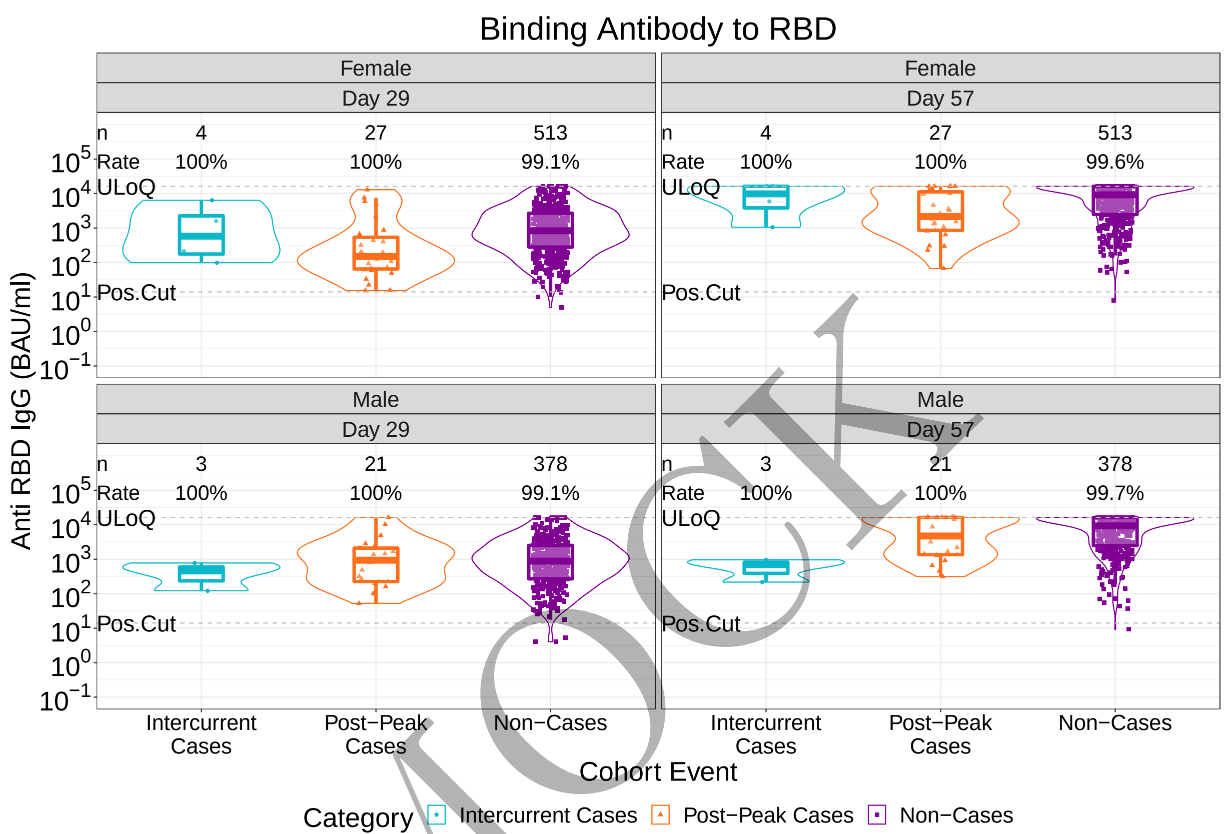

\caption{

Figure 2.5.139: violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



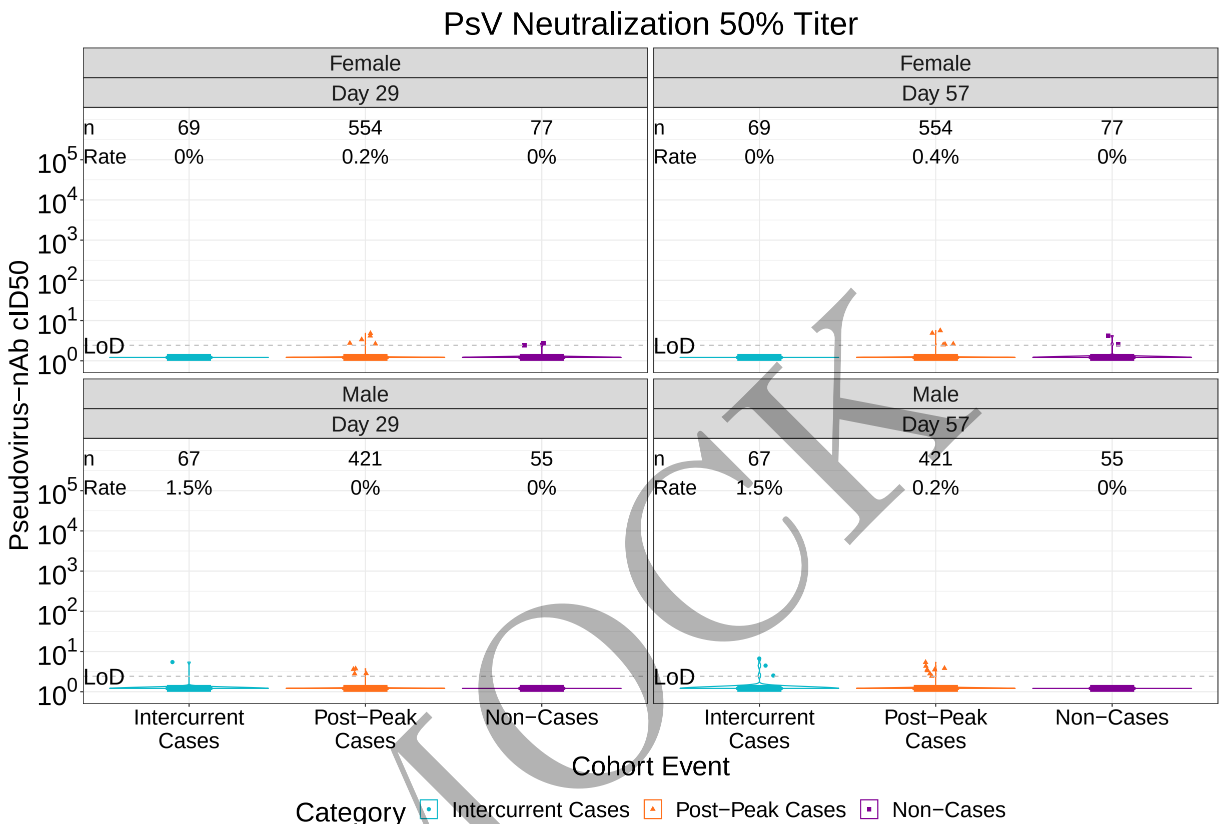

\caption{

Figure 2.5.140: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



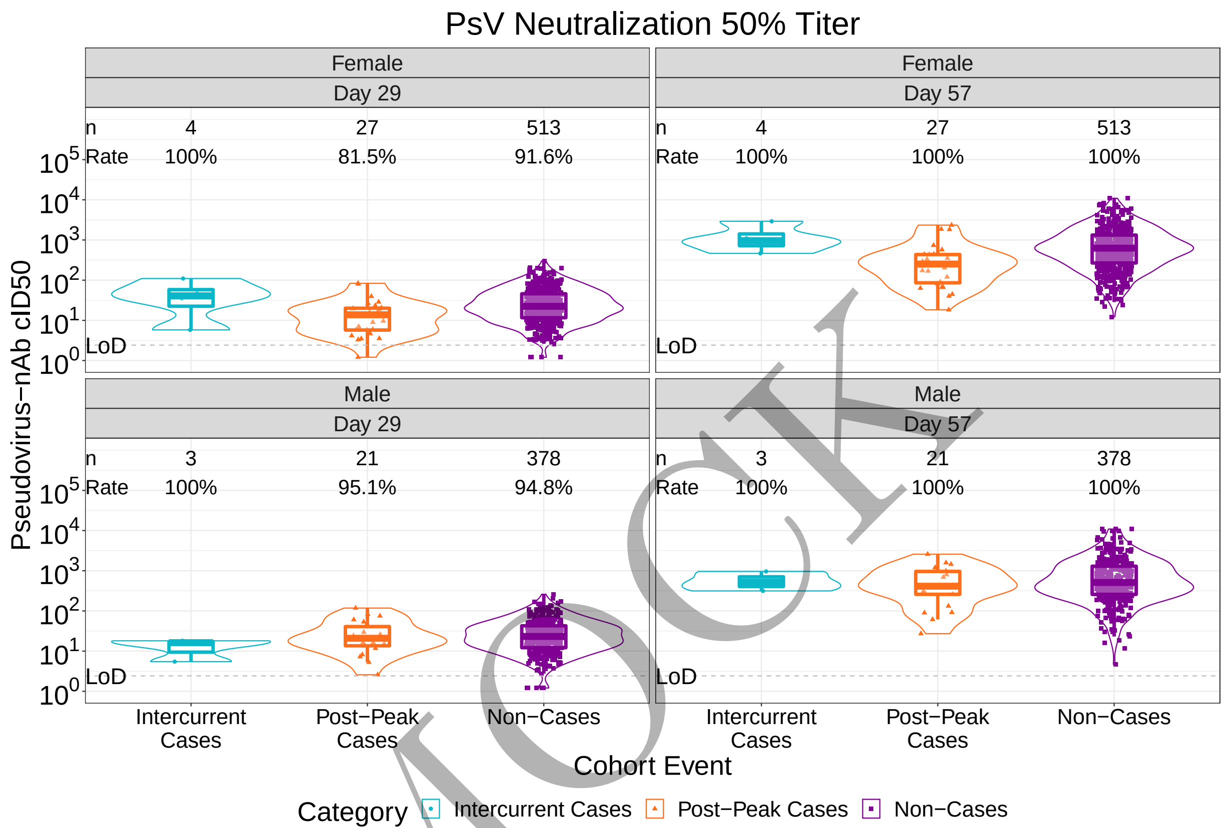

\caption{

Figure 2.5.141: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



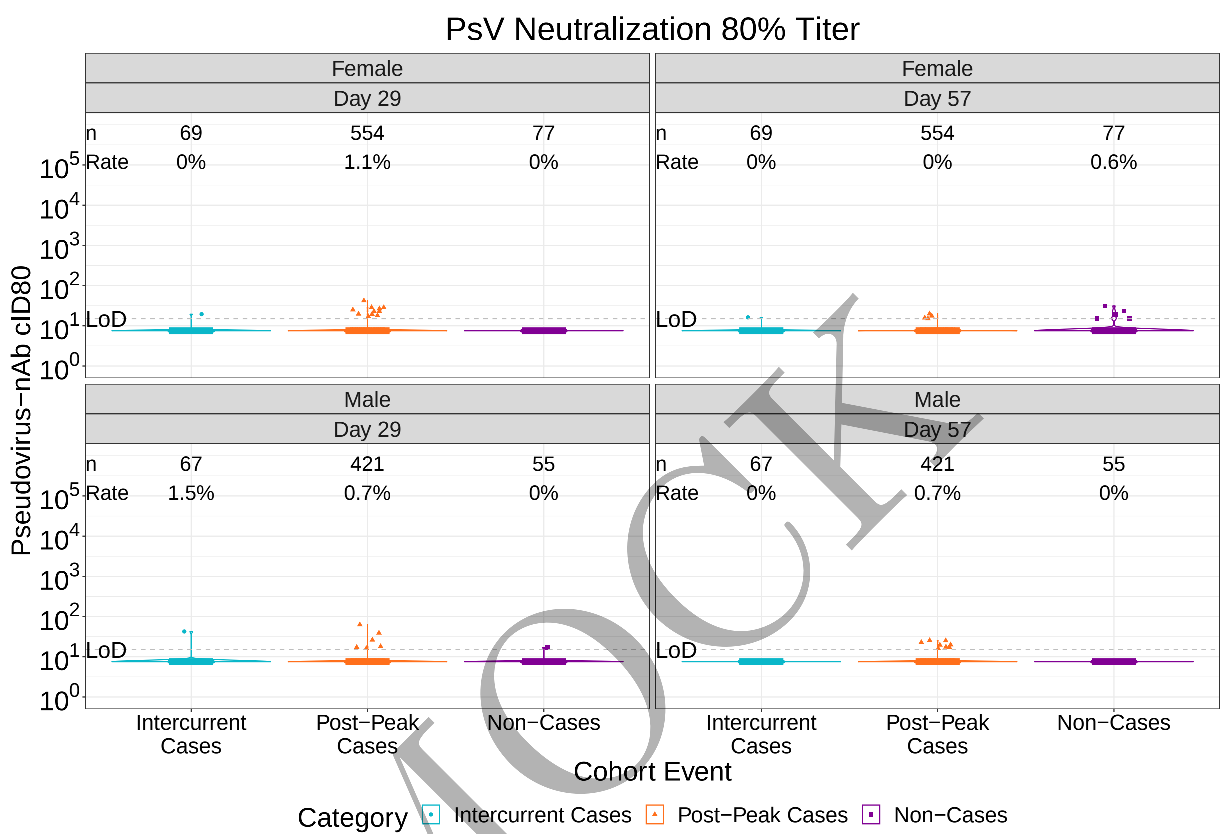

\caption{

Figure 2.5.142: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





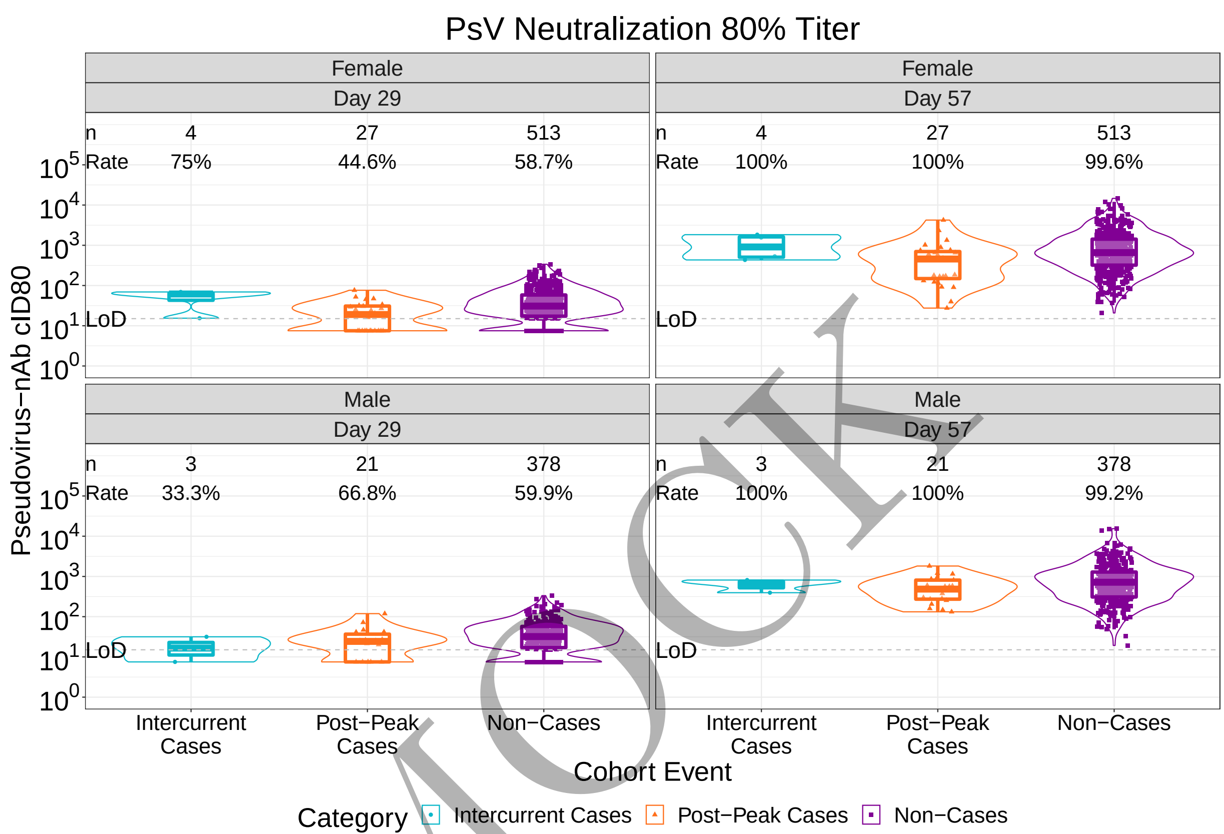

\caption{

Figure 2.5.143: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



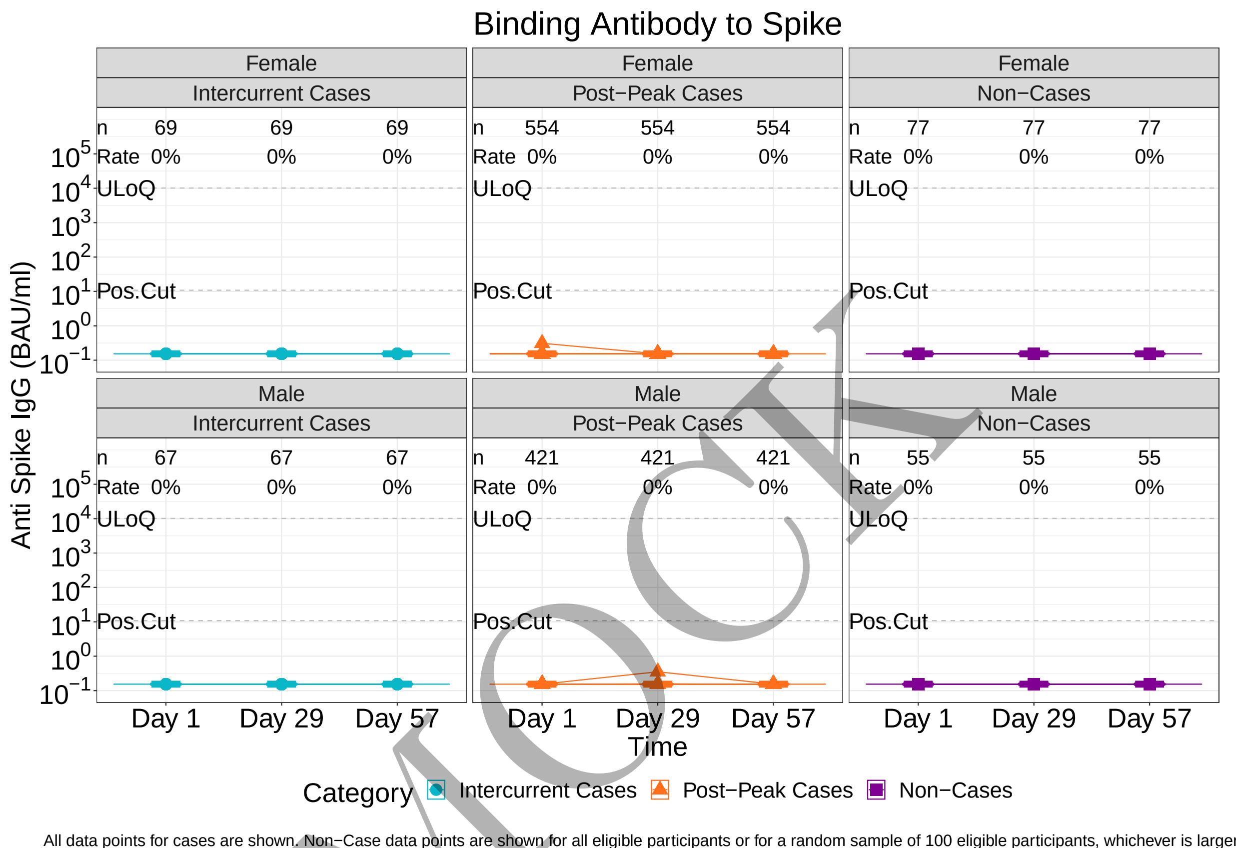

\caption{

Figure 2.5.144: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by sex assigned at birth (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





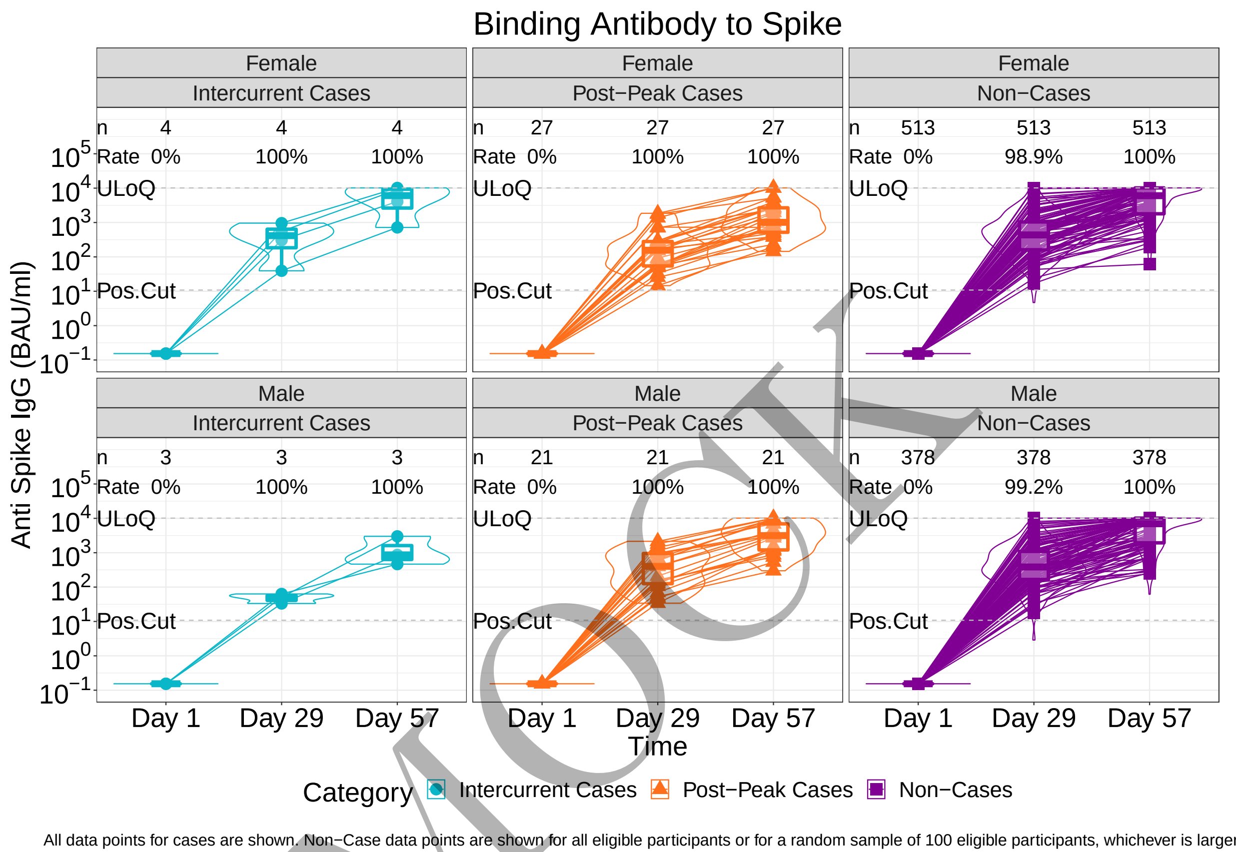

\caption{

Figure 2.5.145: lineplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



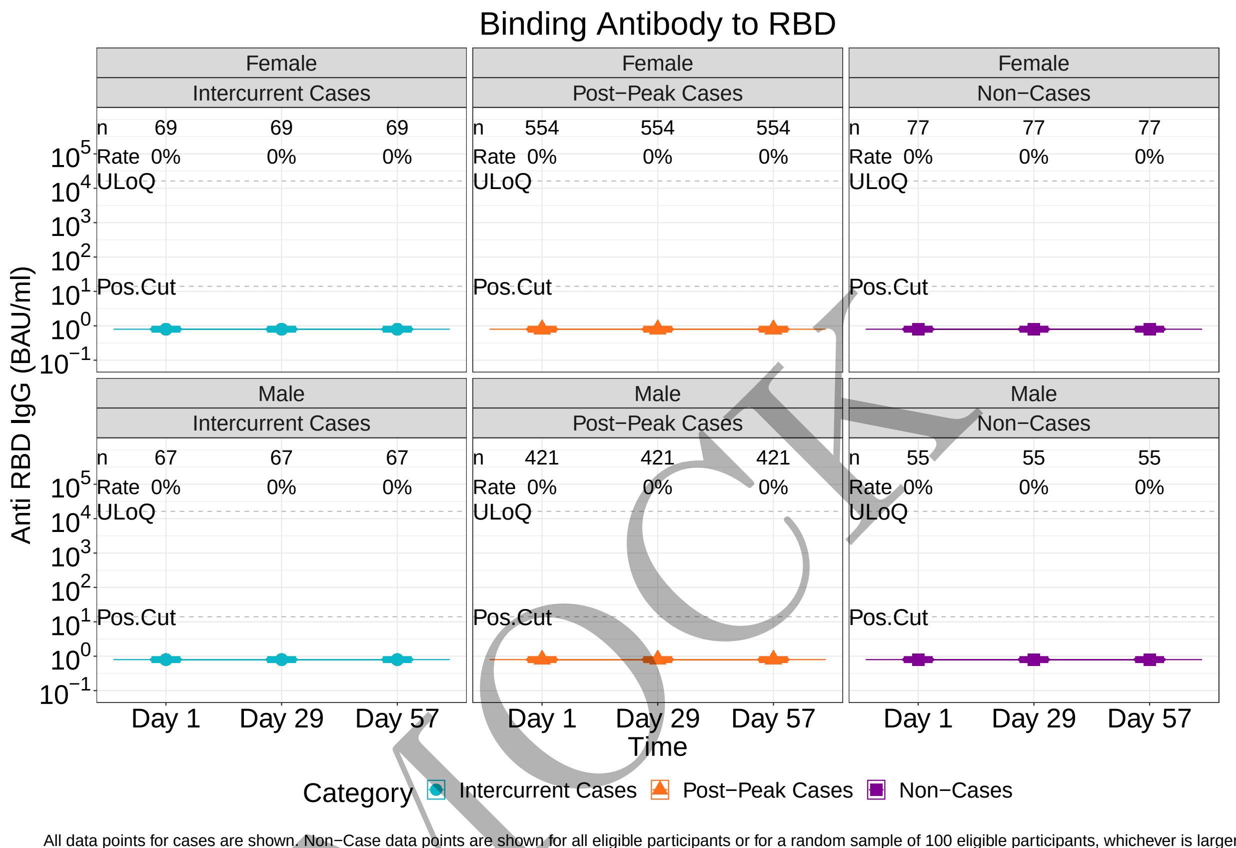

\caption{

Figure 2.5.146: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



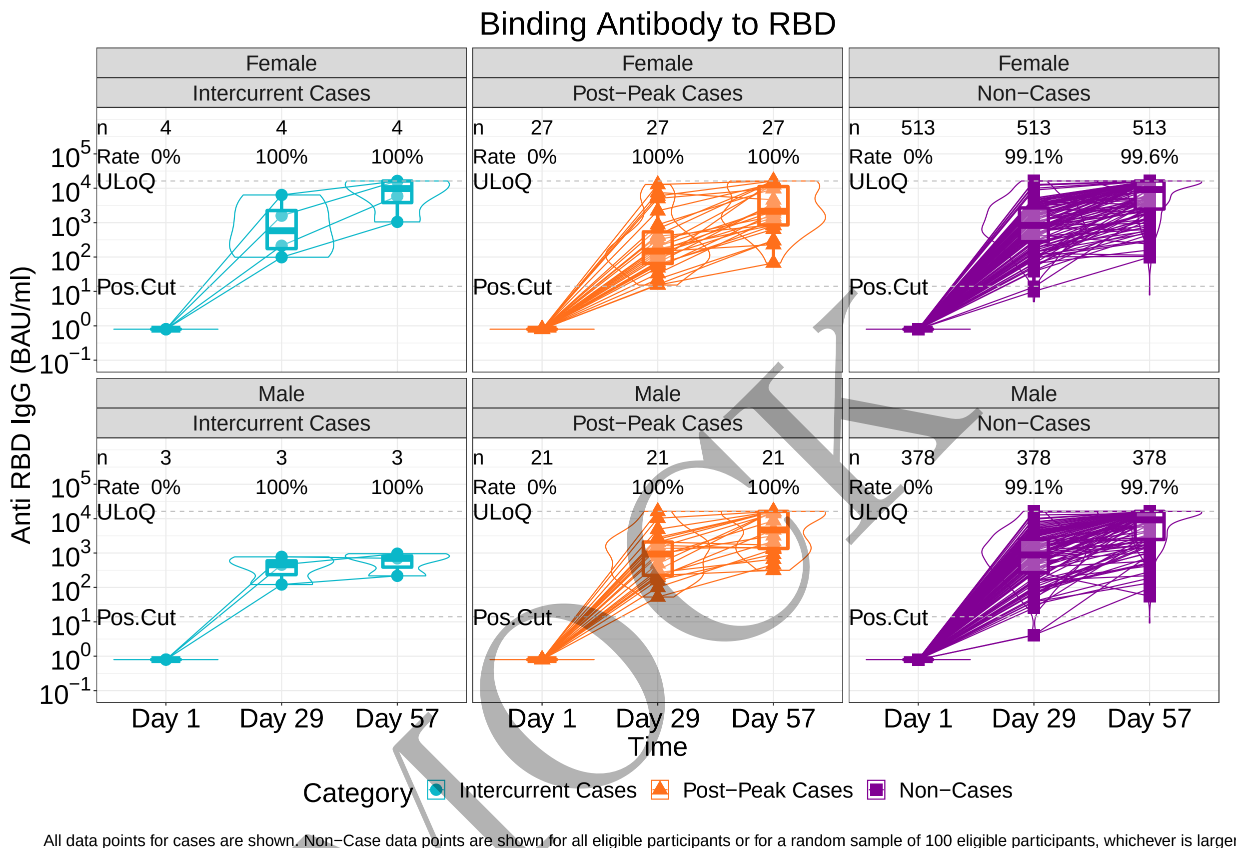

\caption{

Figure 2.5.147: lineplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



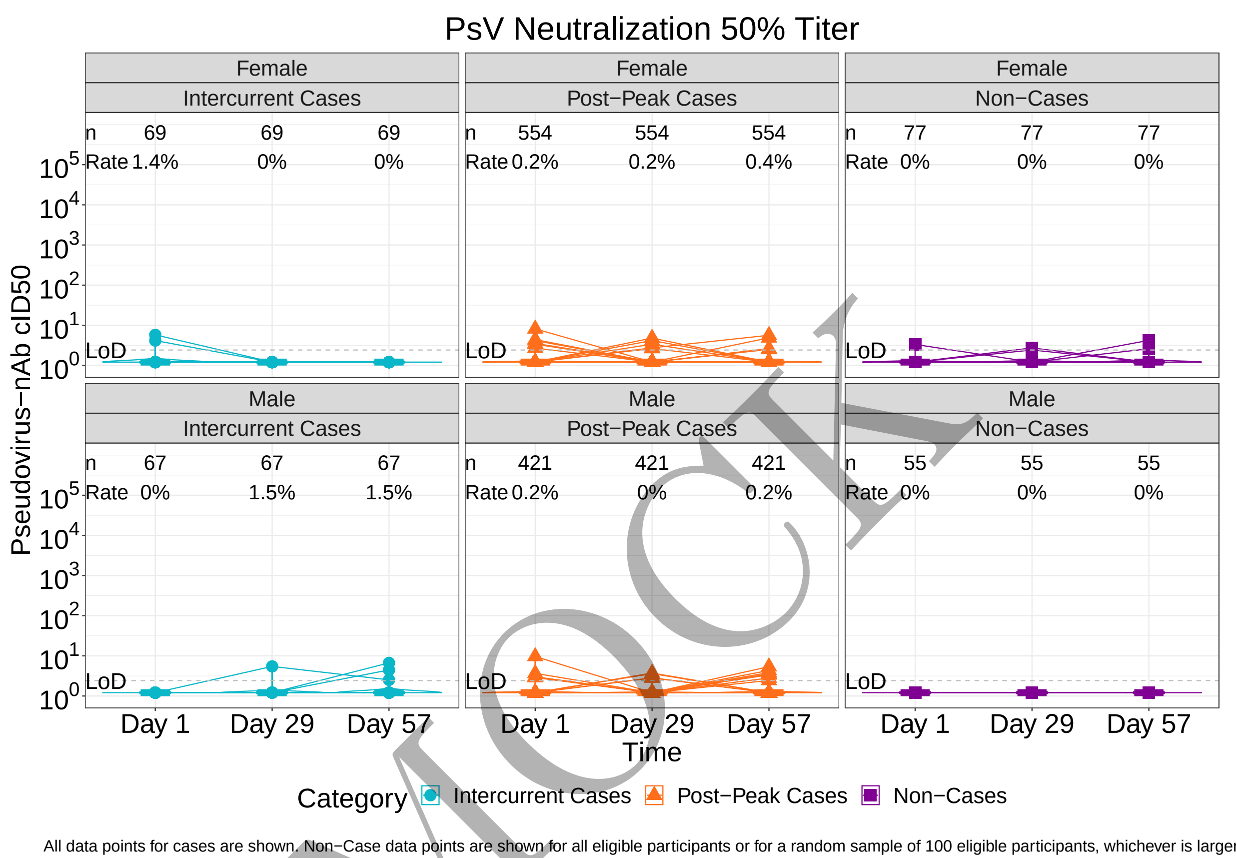

\caption{

Figure 2.5.148: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



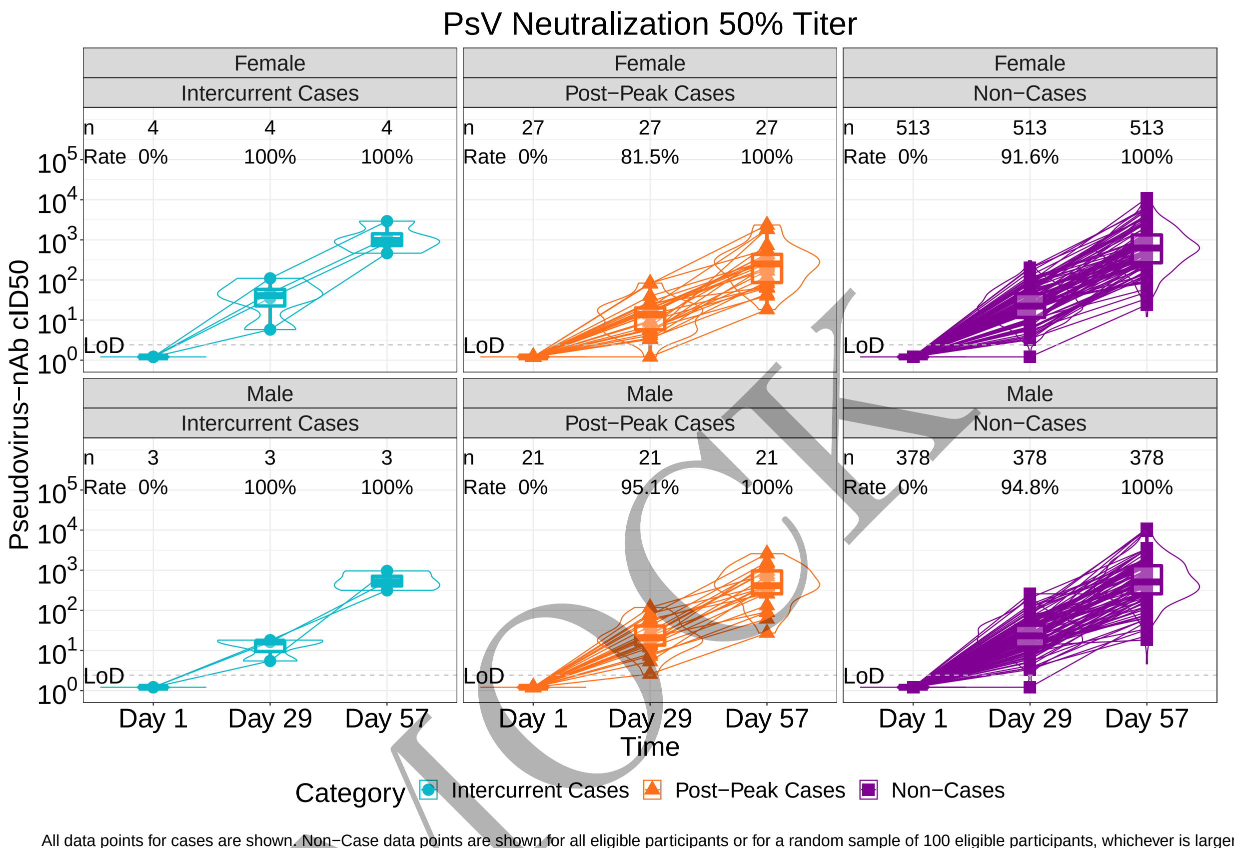

\caption{

Figure 2.5.149: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



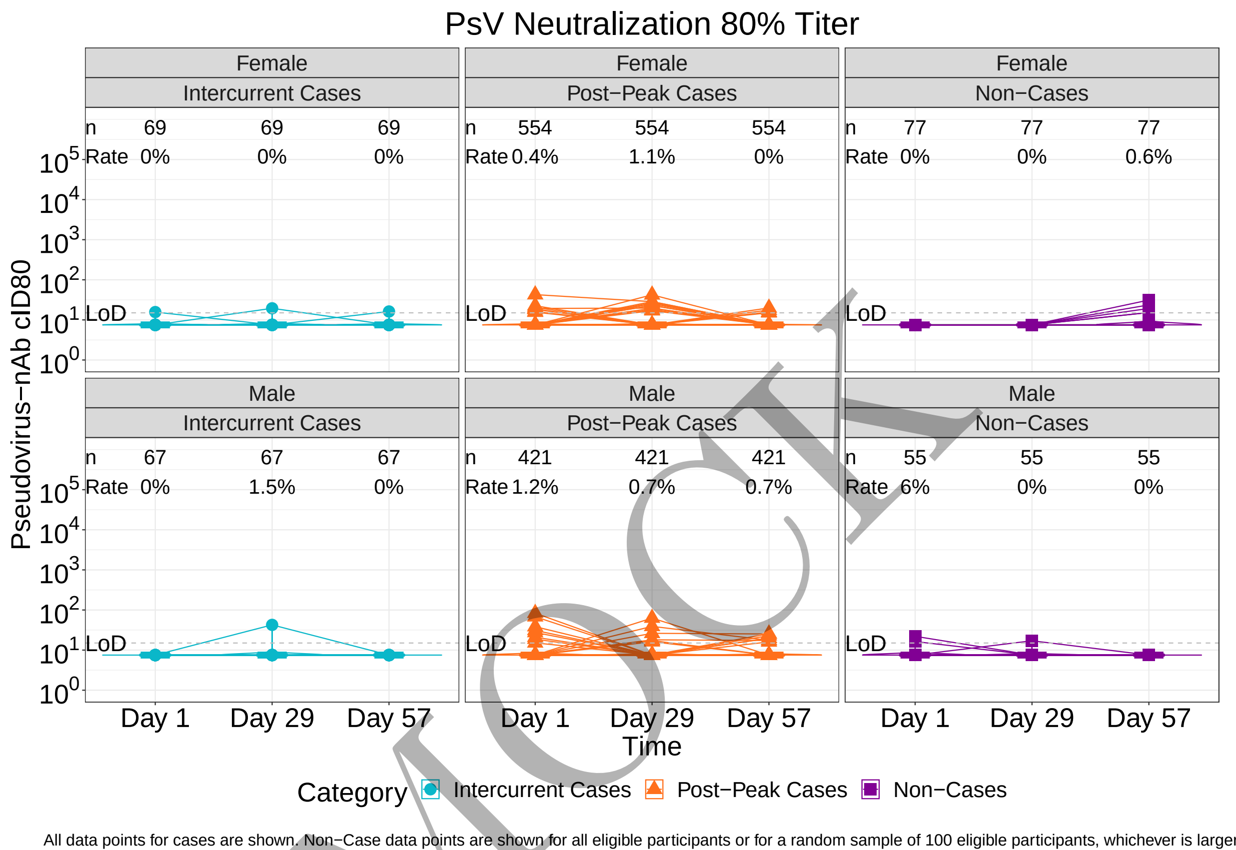

\caption{

Figure 2.5.150: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



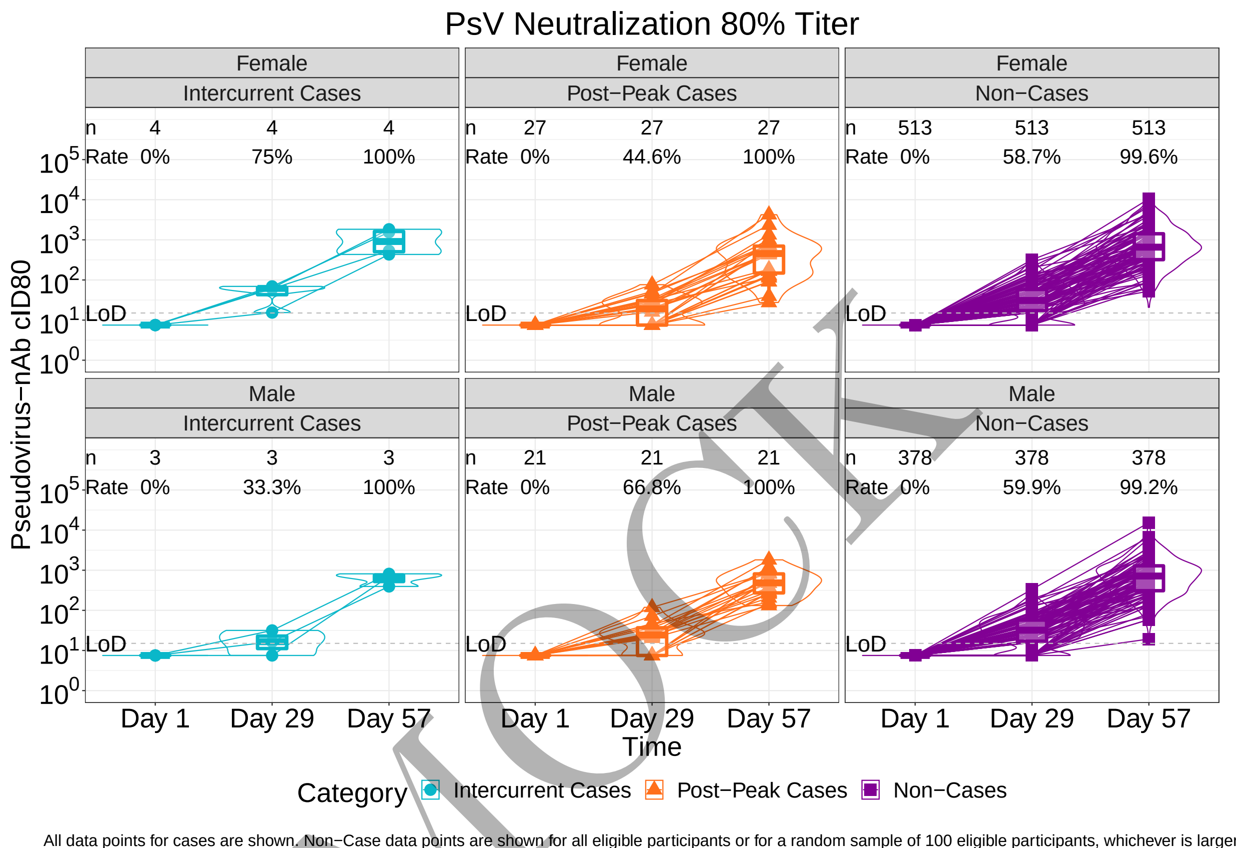

\caption{

Figure 2.5.151: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



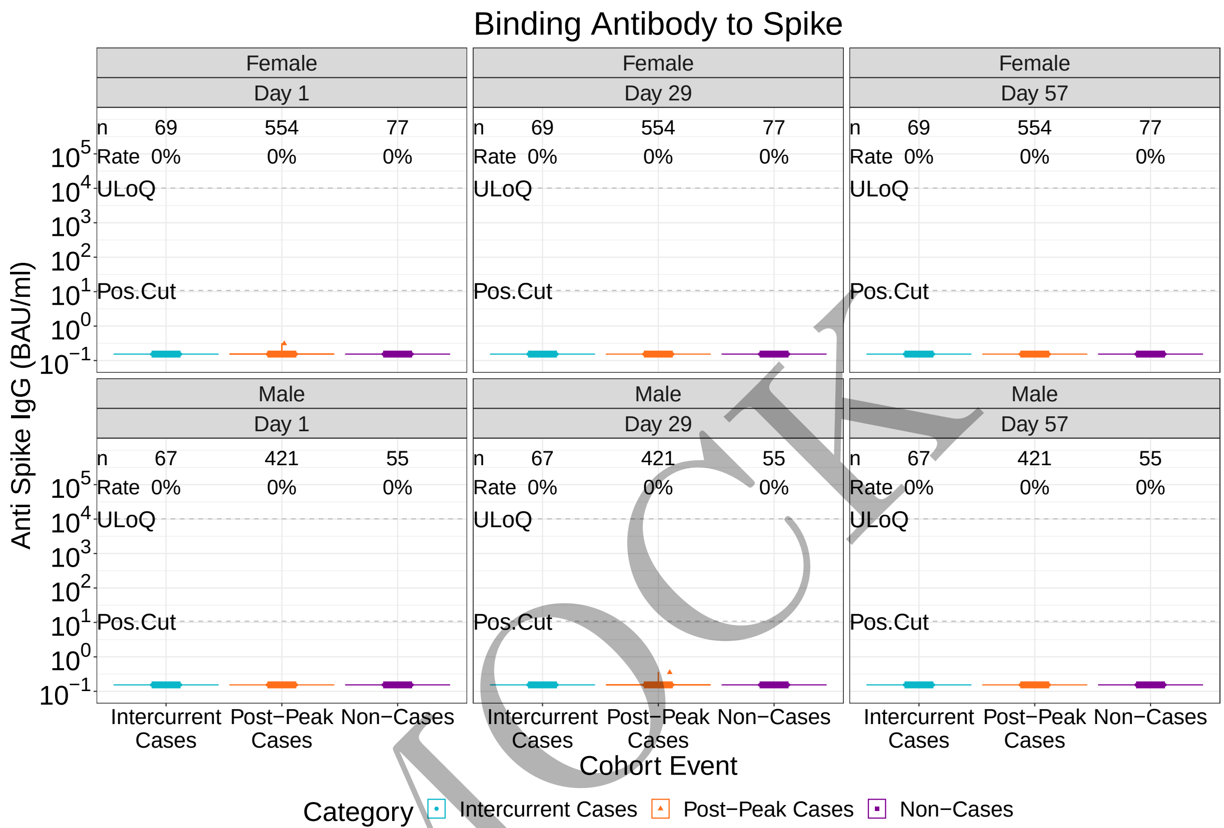

\caption{

Figure 2.5.152: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





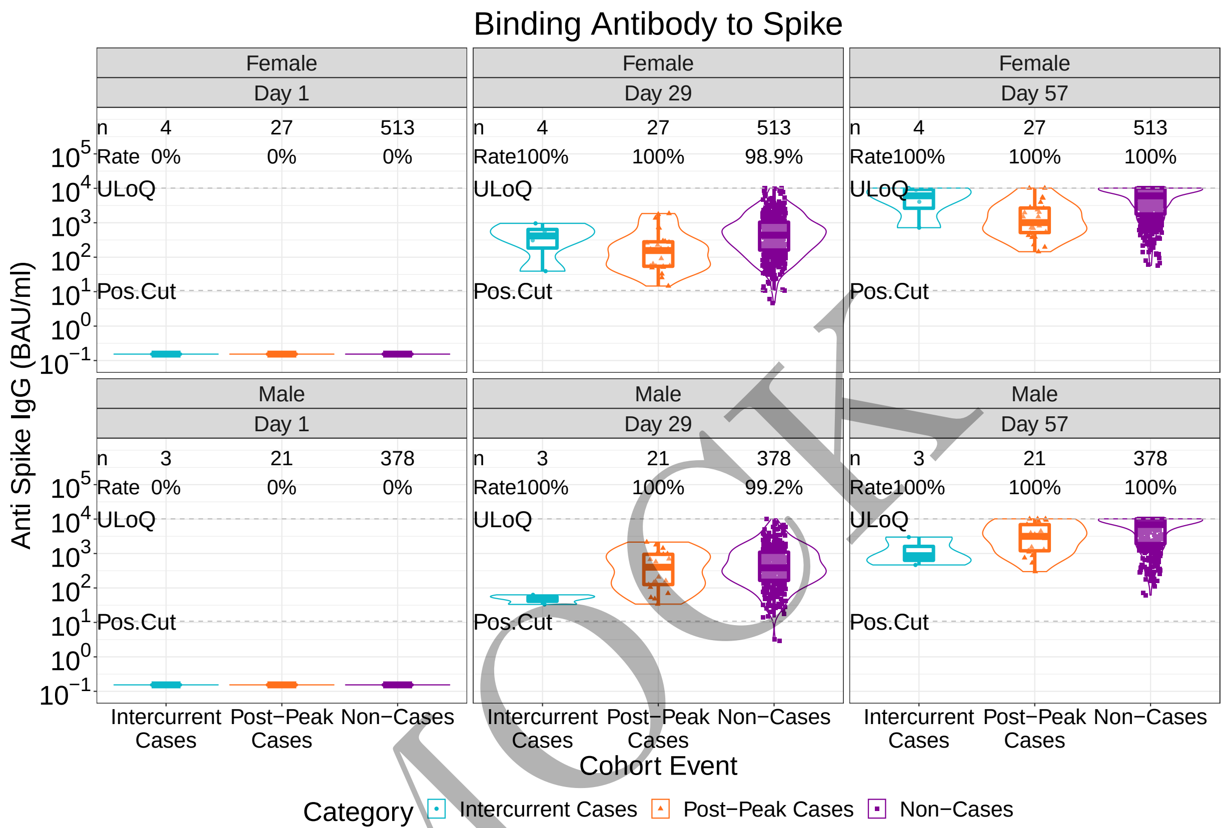

\caption{

Figure 2.5.153: violinplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



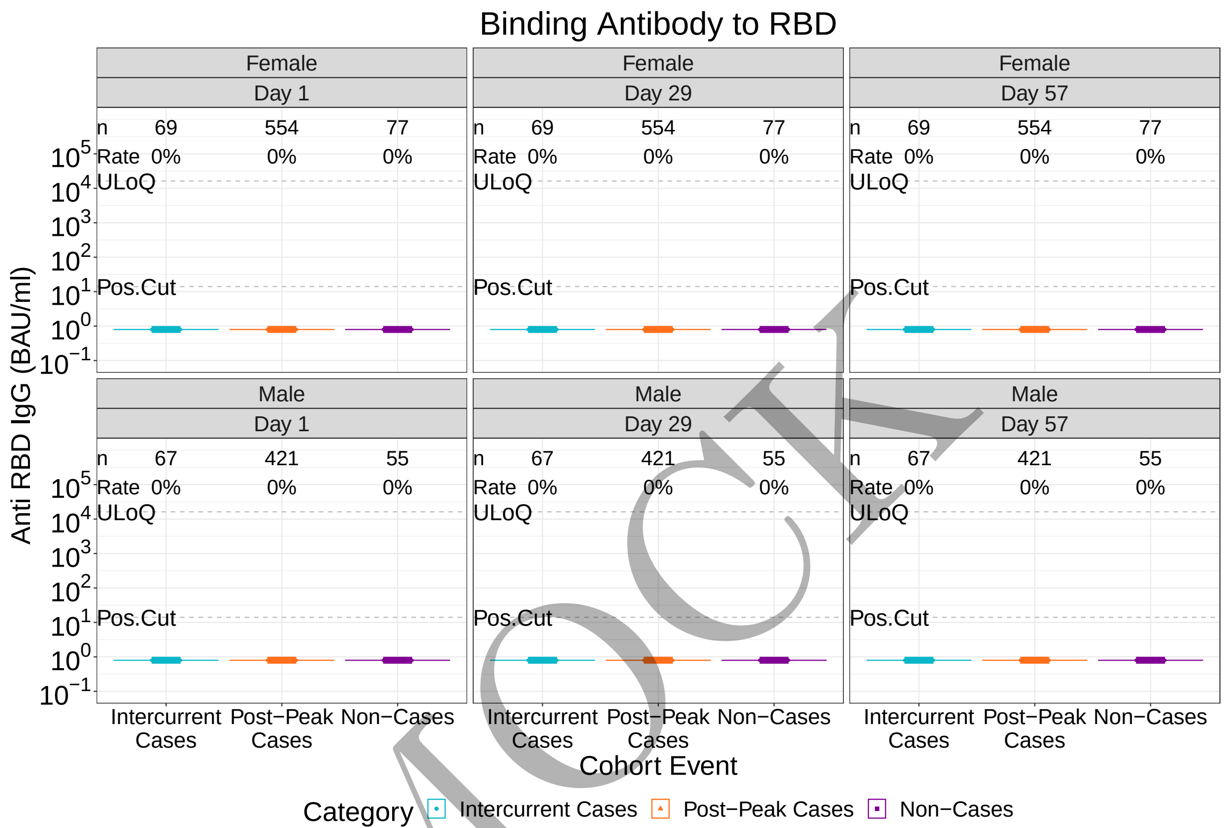

\caption{

Figure 2.5.154: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



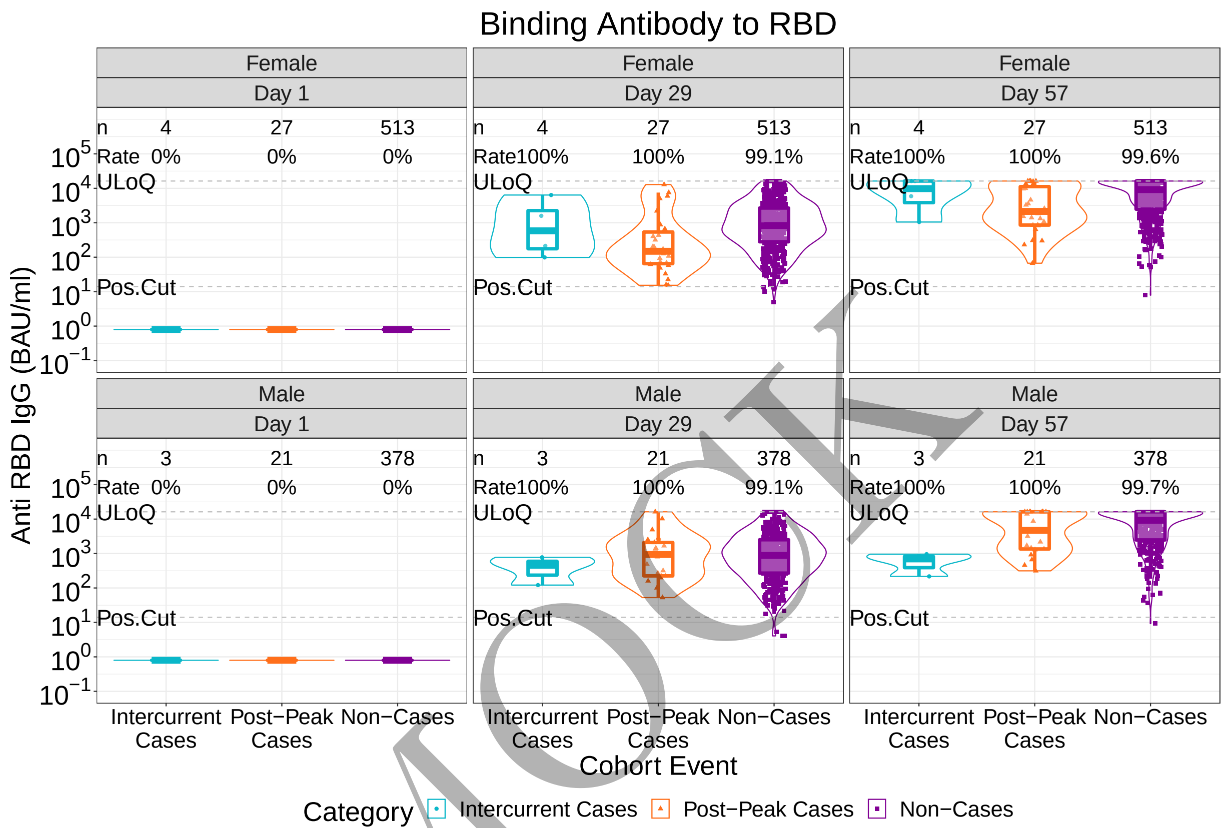

\caption{

Figure 2.5.155: violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}



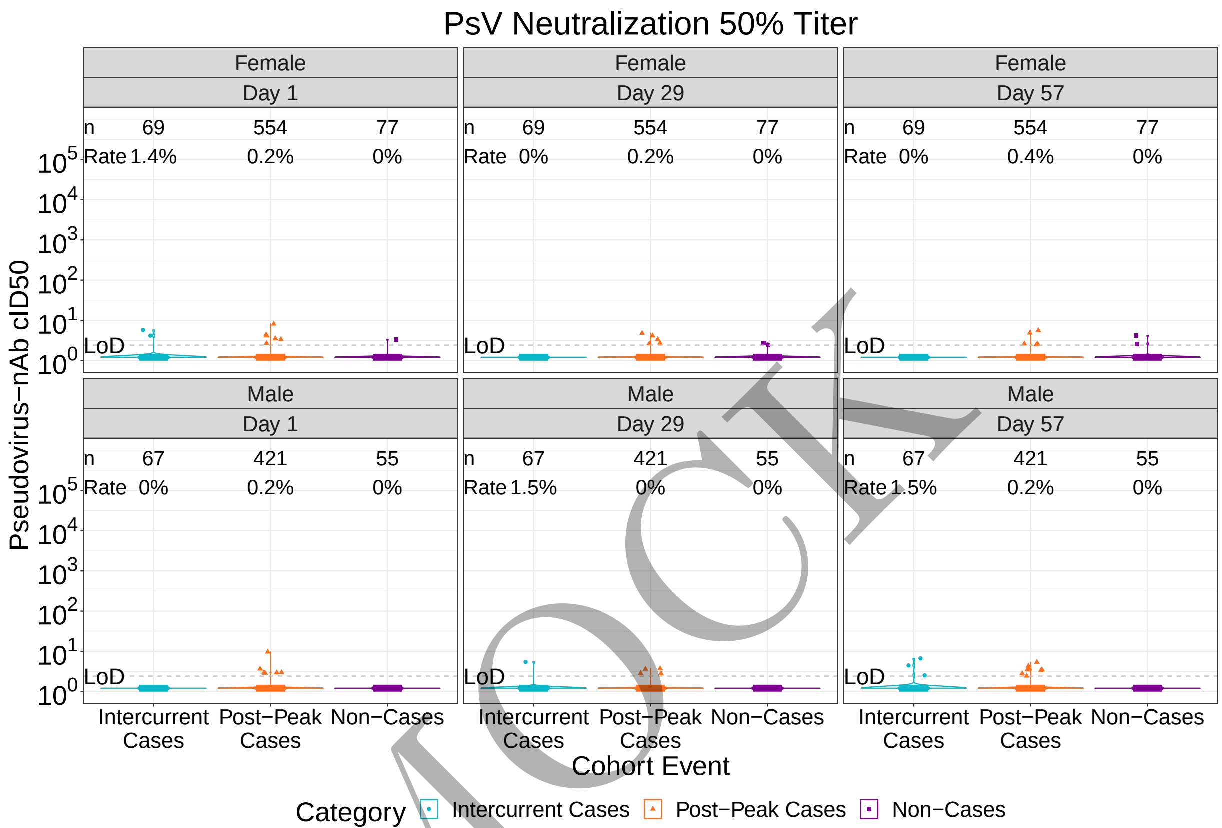

\caption{

Figure 2.5.156: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



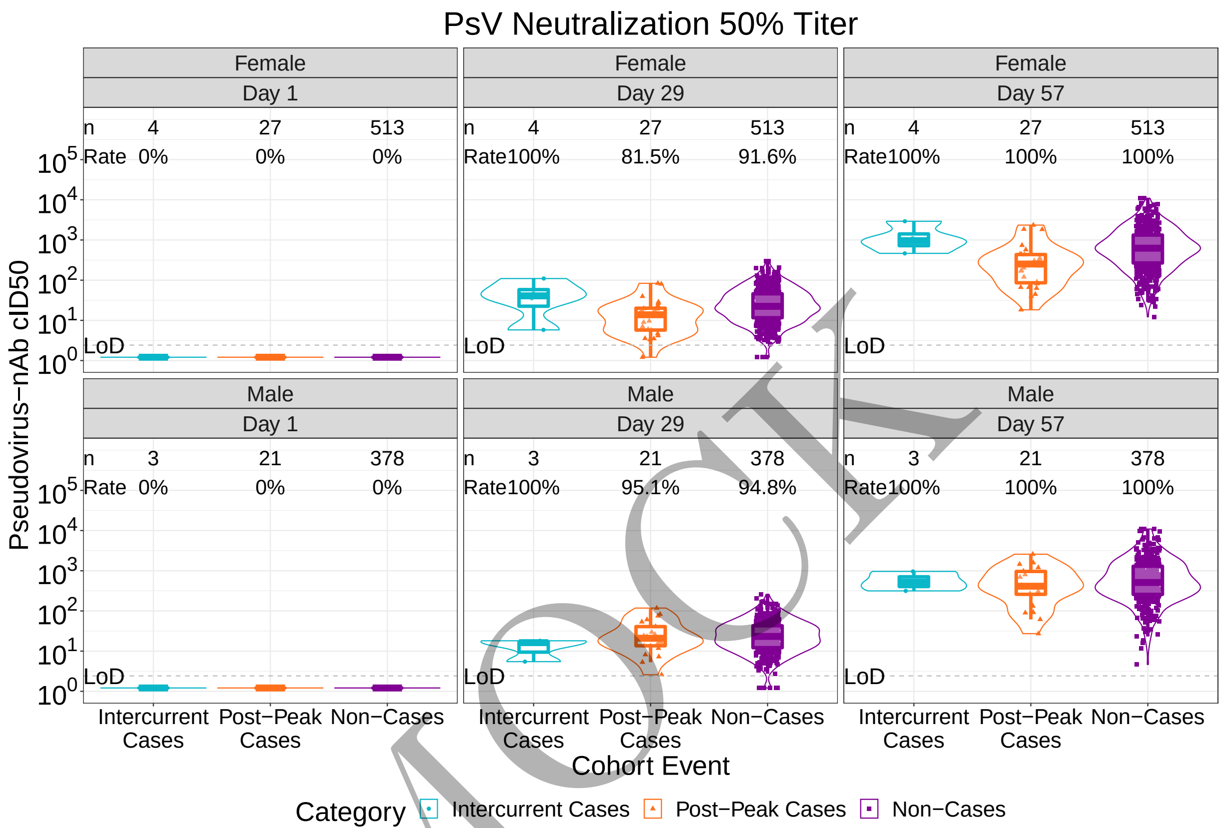

\caption{

Figure 2.5.157: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



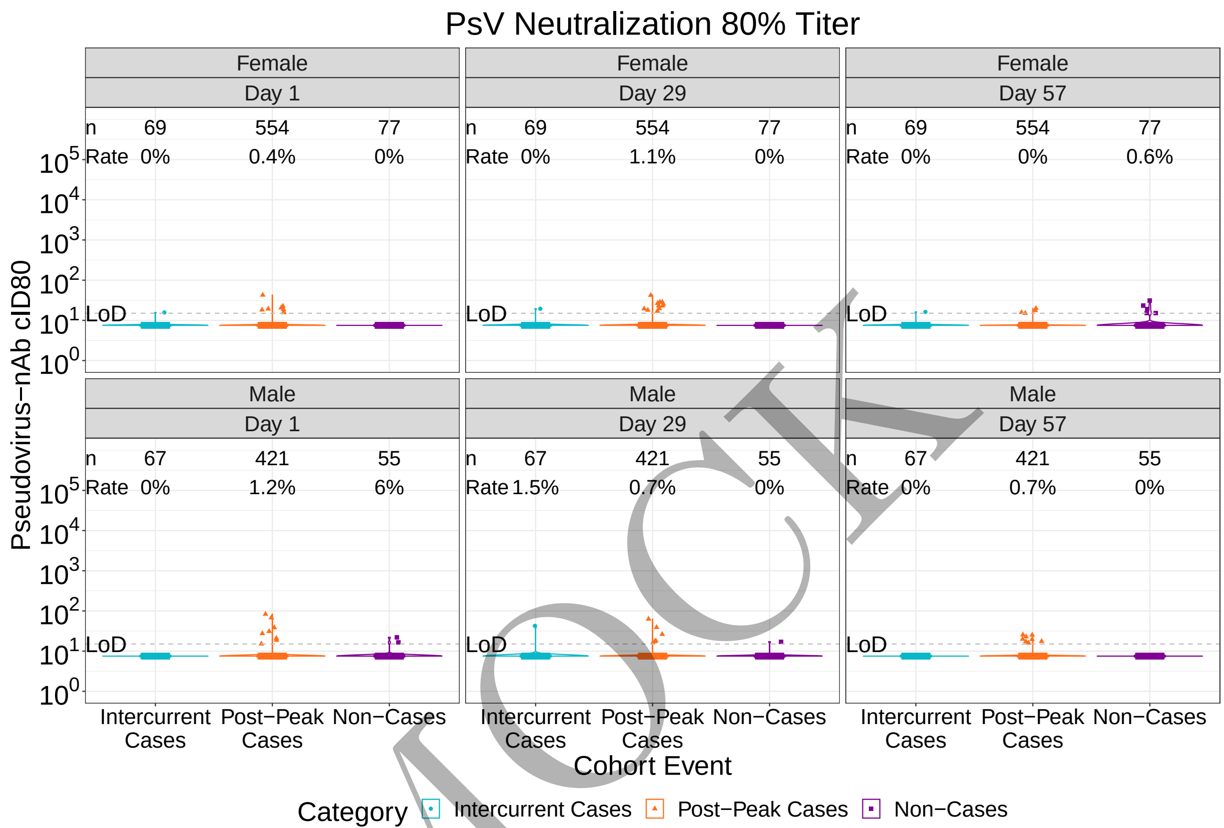

\caption{

Figure 2.5.158: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

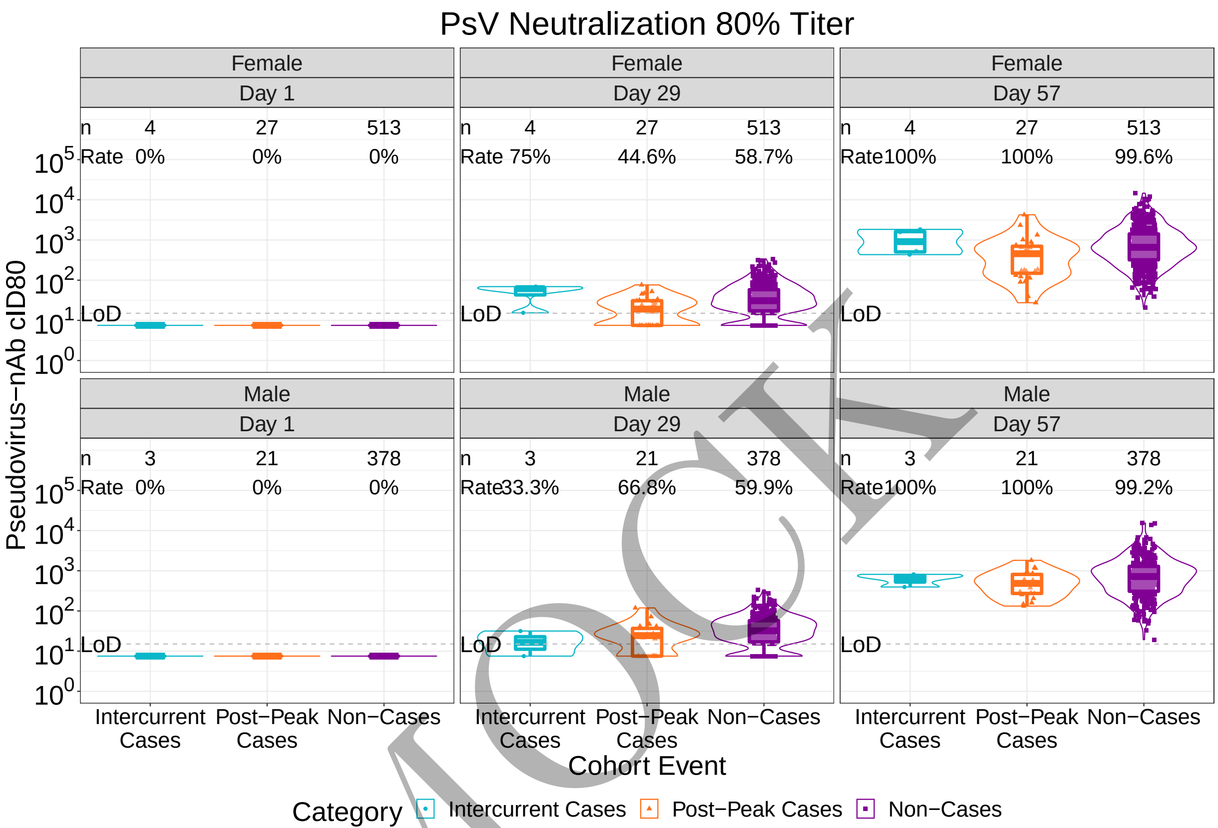
\begin{figure}




\caption{
Figure 2.5.159: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by sex assigned at birth (version 2)
} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





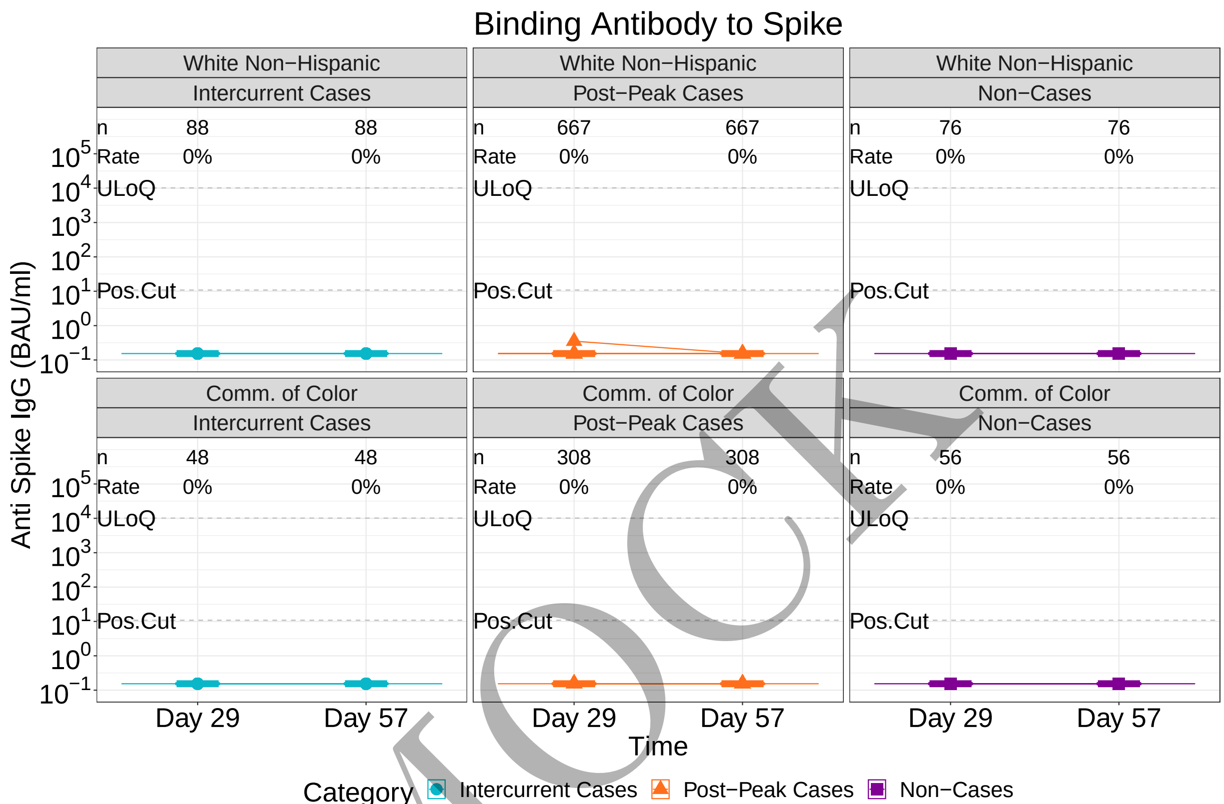

\caption{

Figure 2.5.160: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by sex assigned at birth (version 2)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}




All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

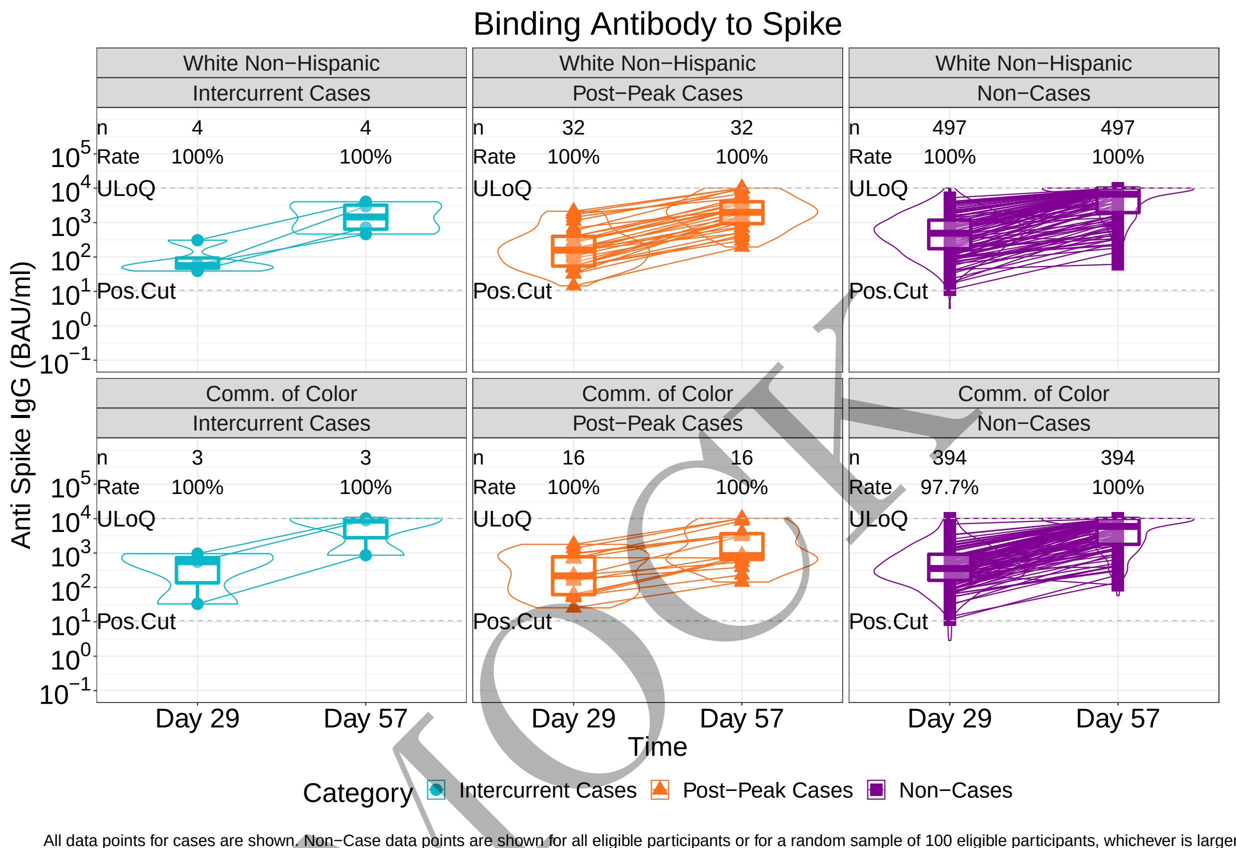
\caption{

Figure 2.5.161: lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



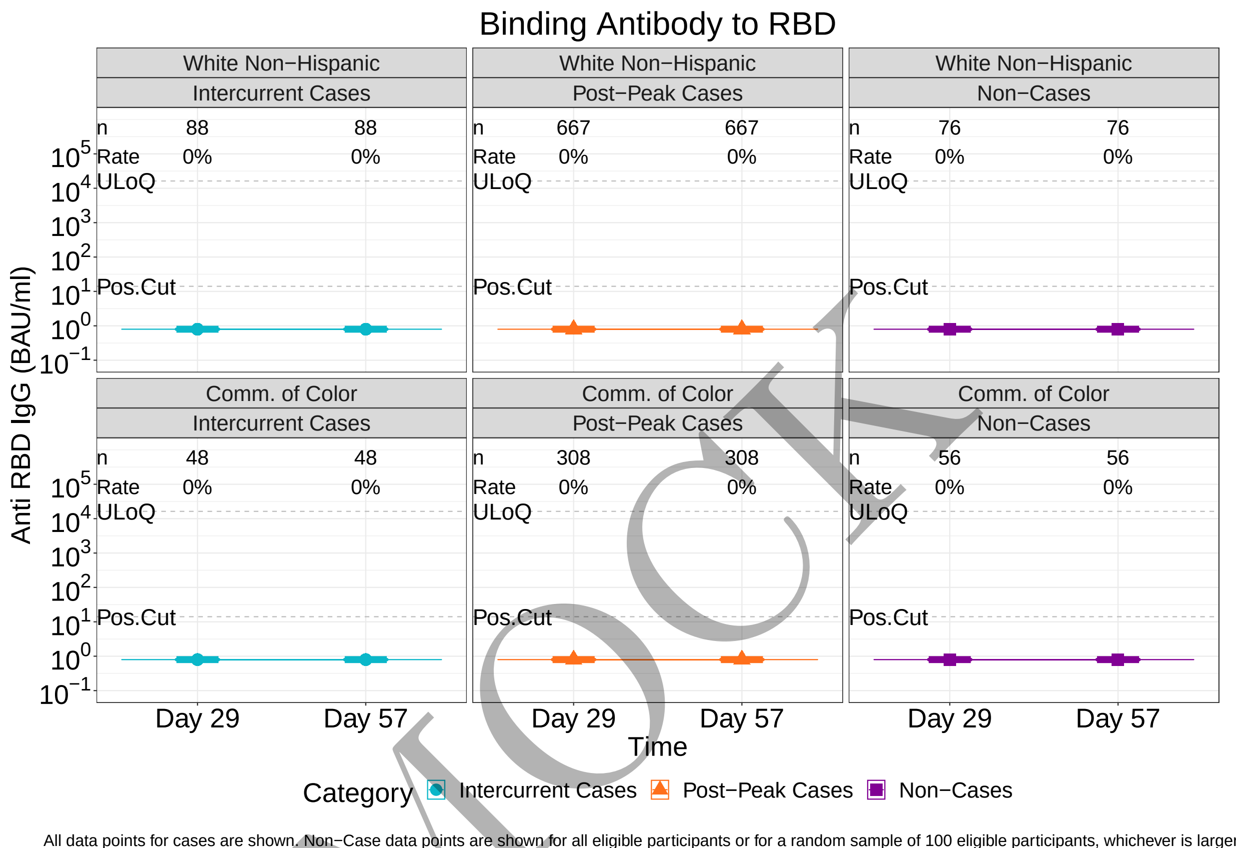

\caption{

Figure 2.5.162: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



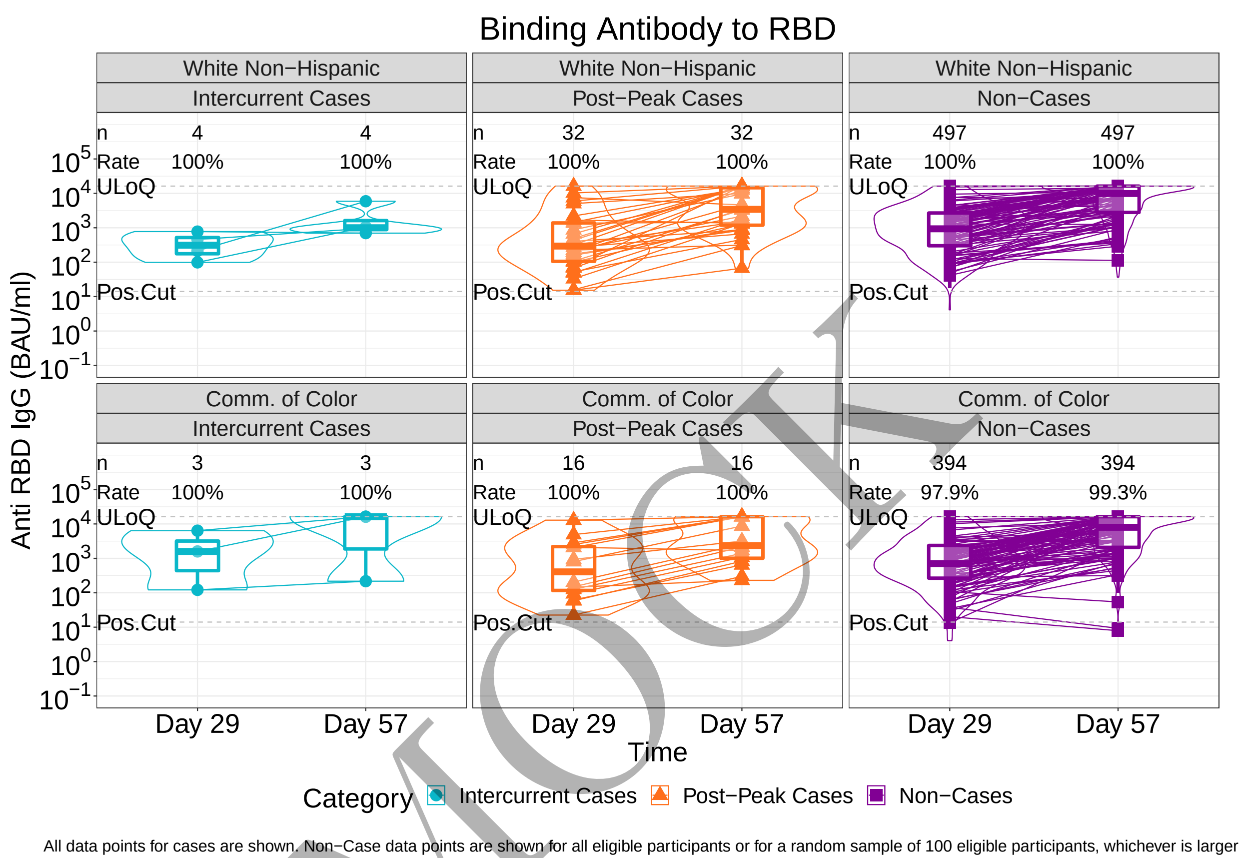

\caption{

Figure 2.5.163: lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



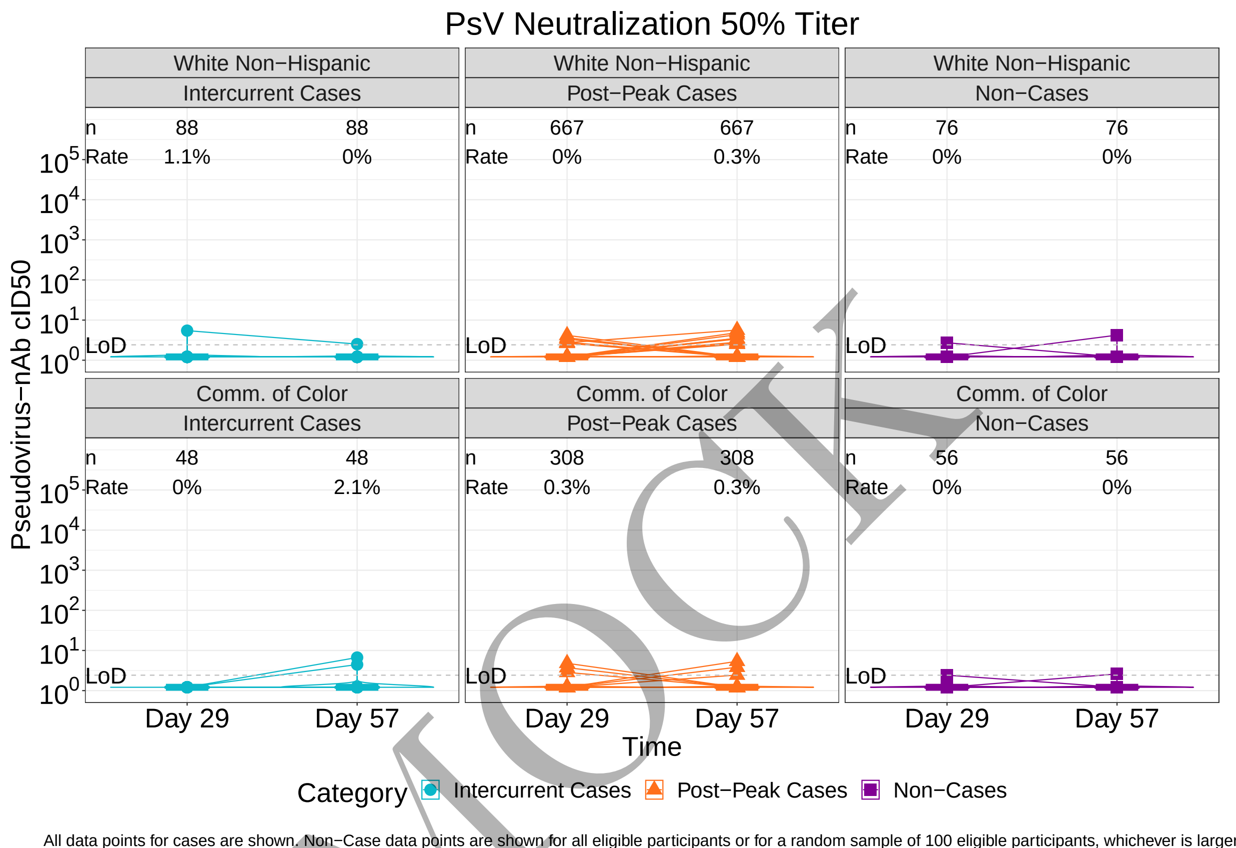

\caption{

Figure 2.5.164: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



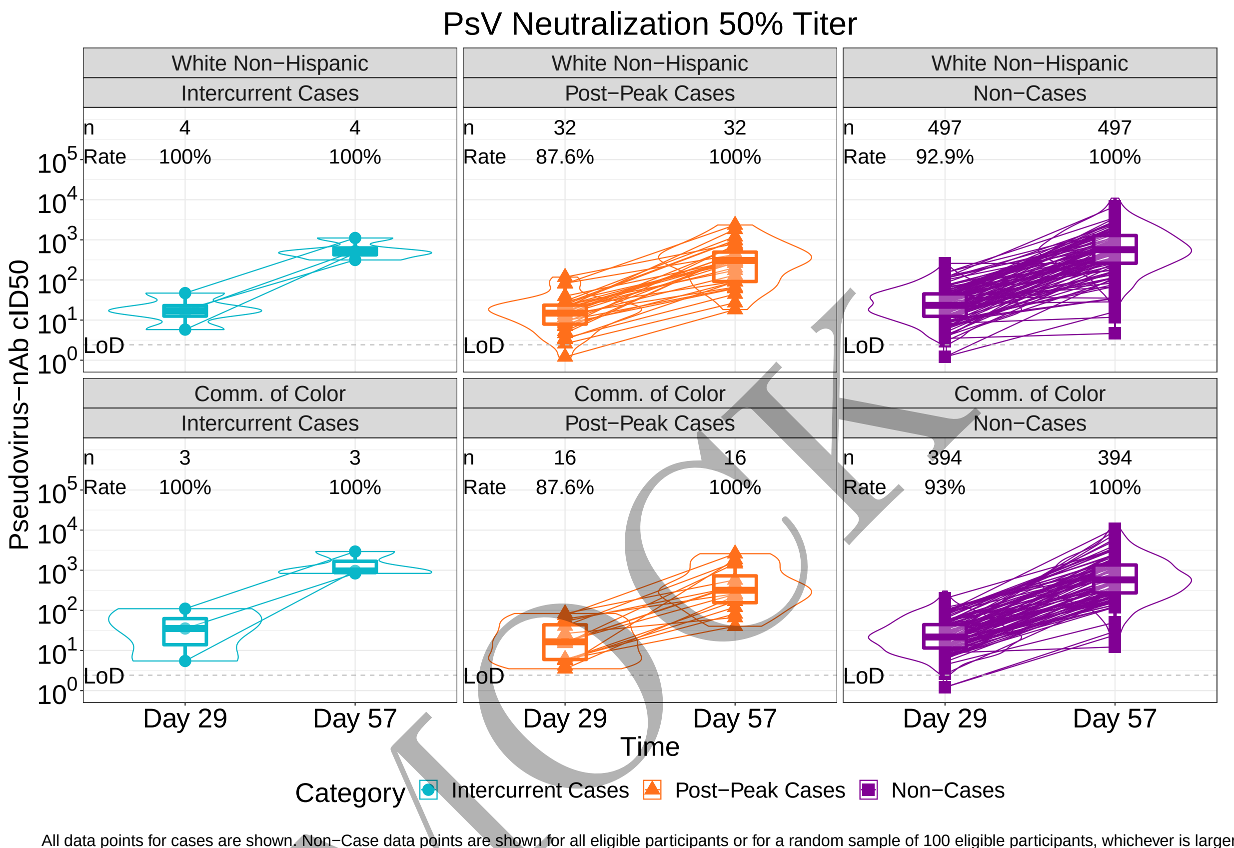

\caption{

Figure 2.5.165: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



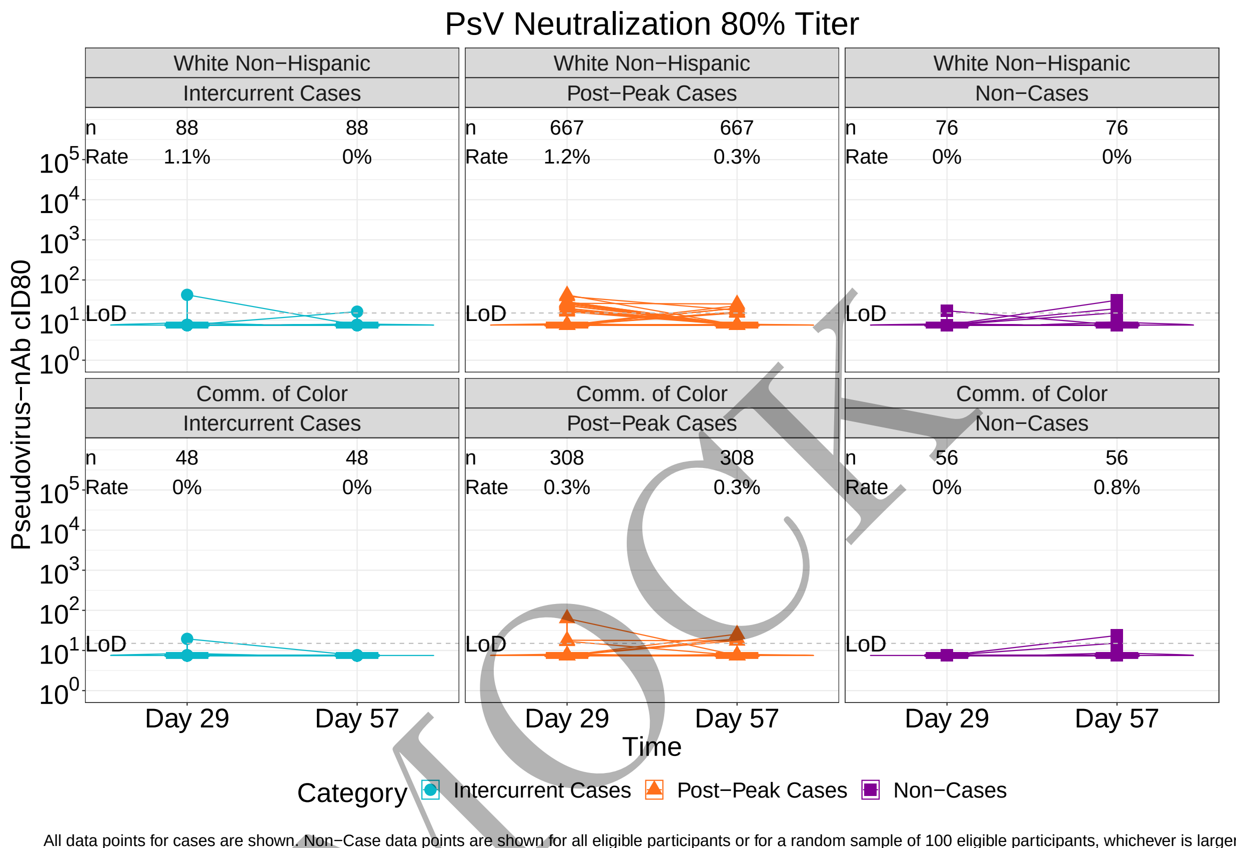

\caption{

Figure 2.5.166: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



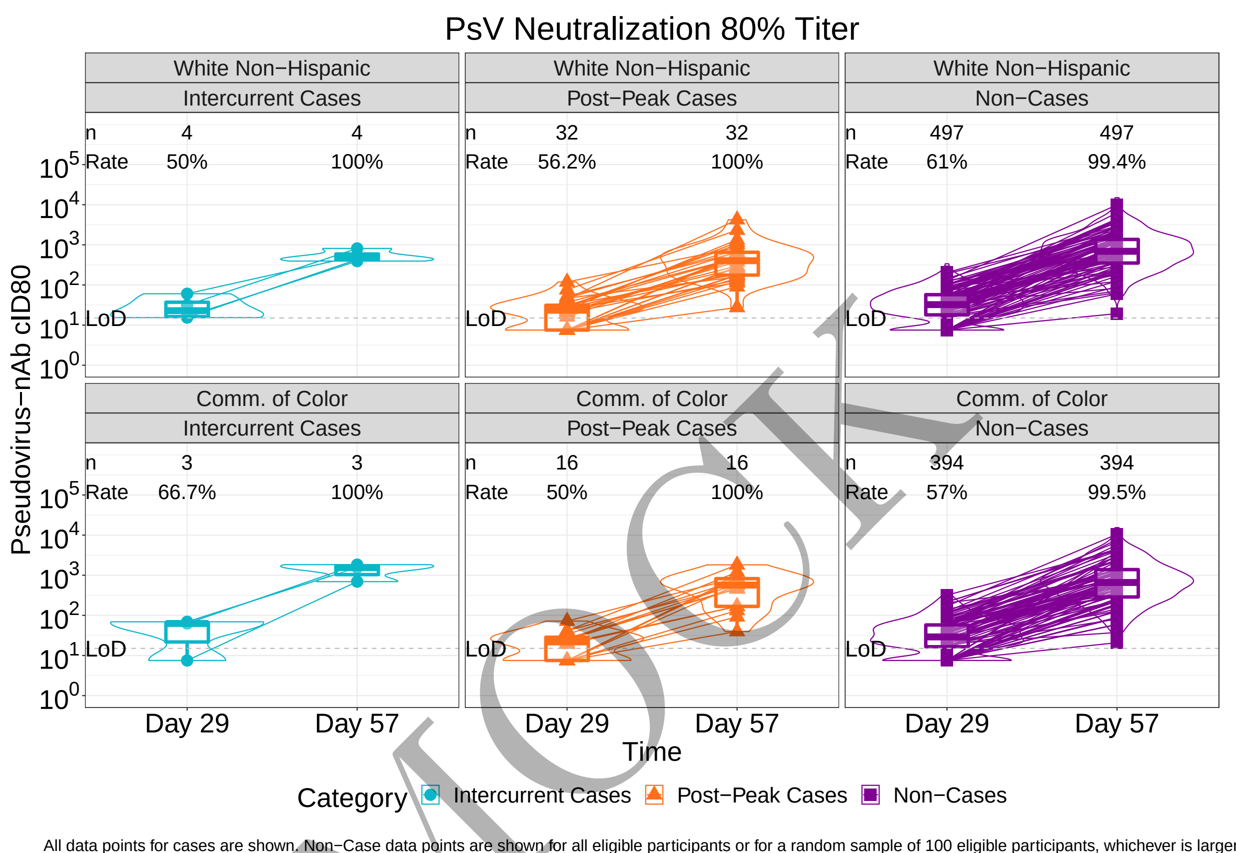

\caption{

Figure 2.5.167: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



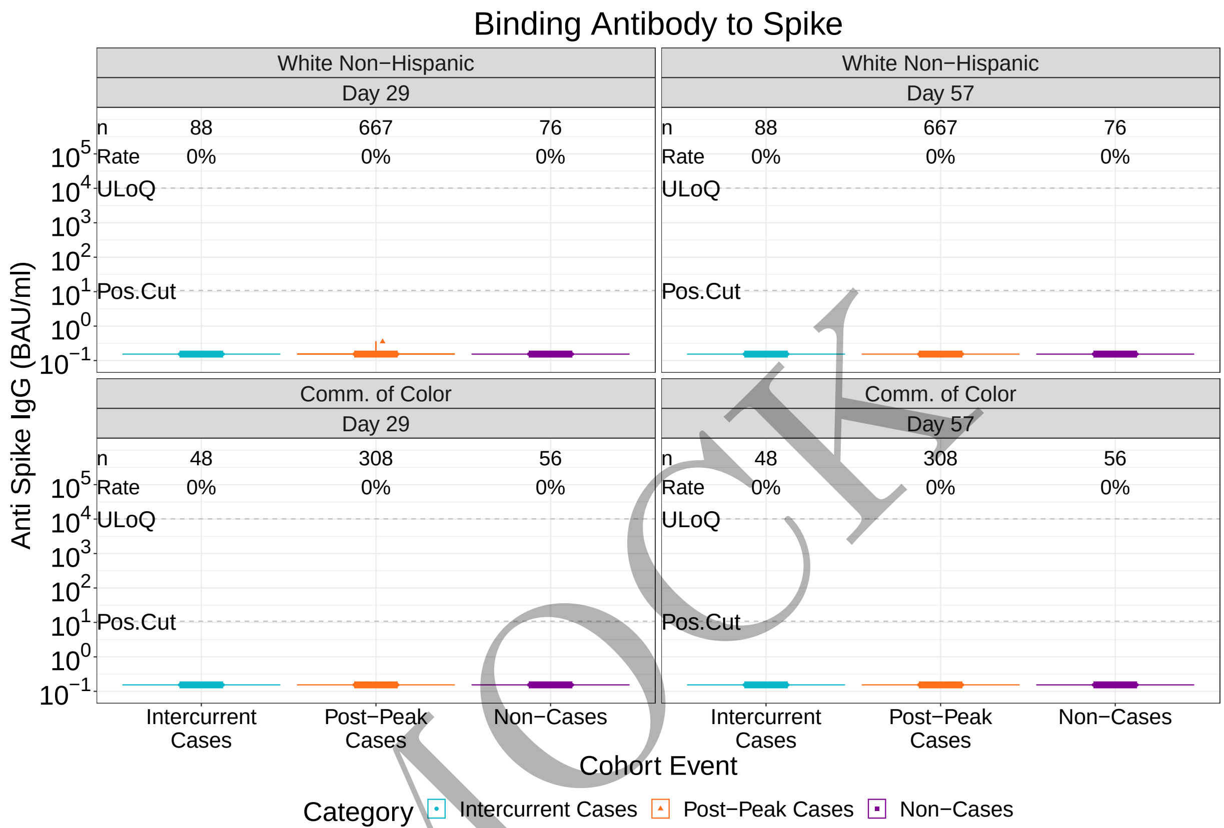

\caption{

Figure 2.5.168: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}

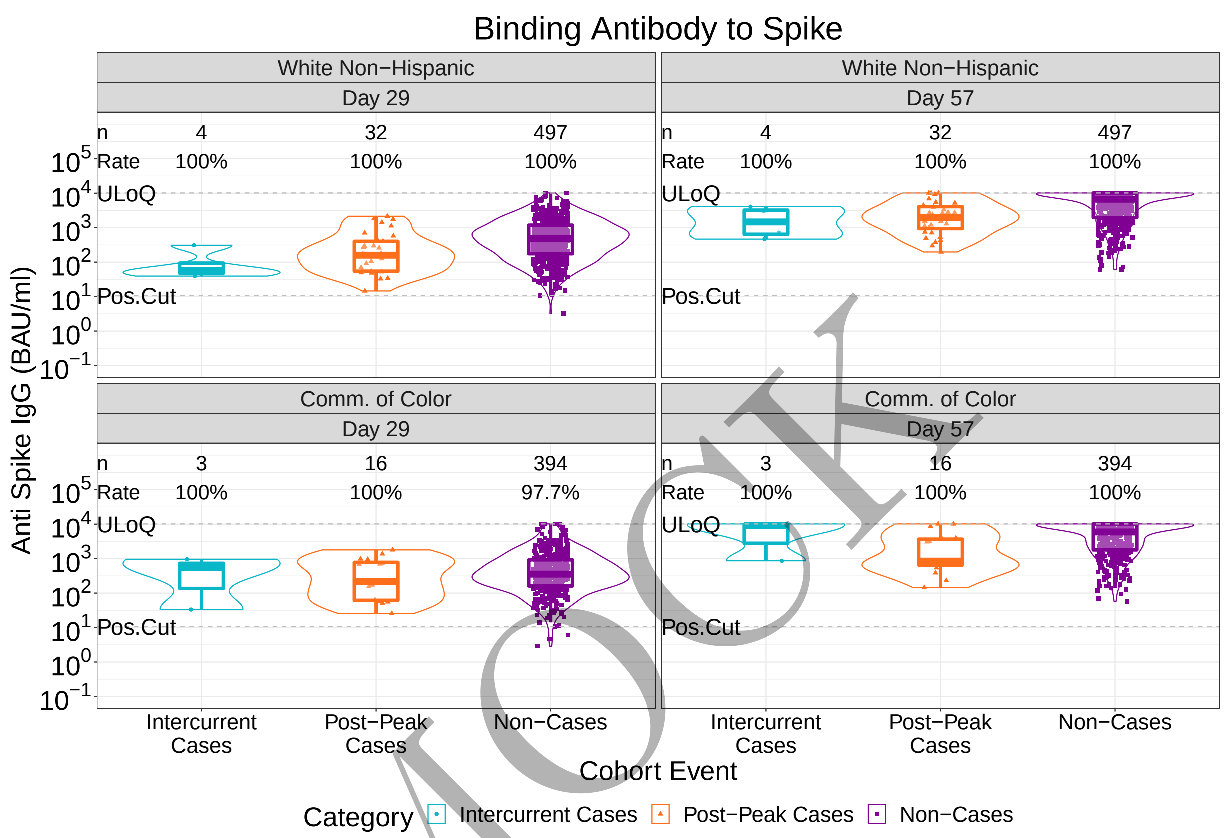



\caption{
Figure 2.5.169: violinplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



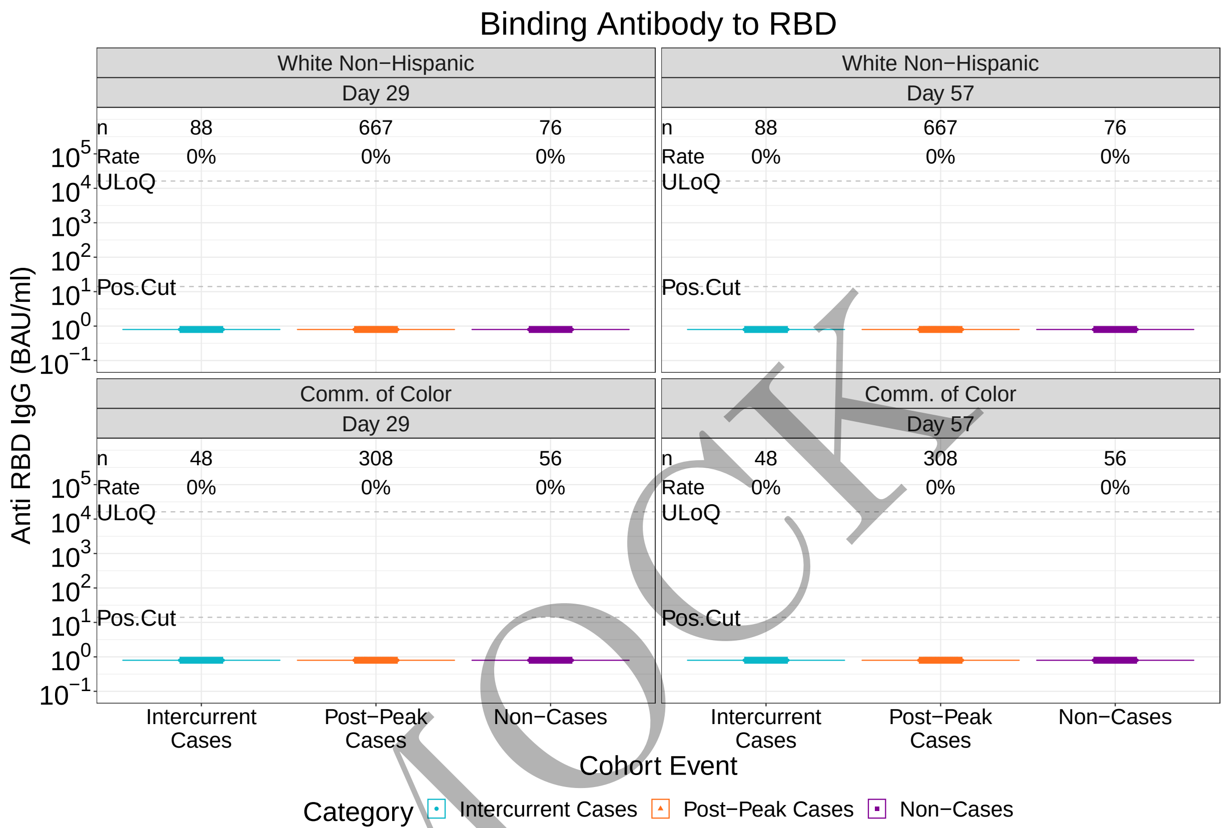

\caption{

Figure 2.5.170: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



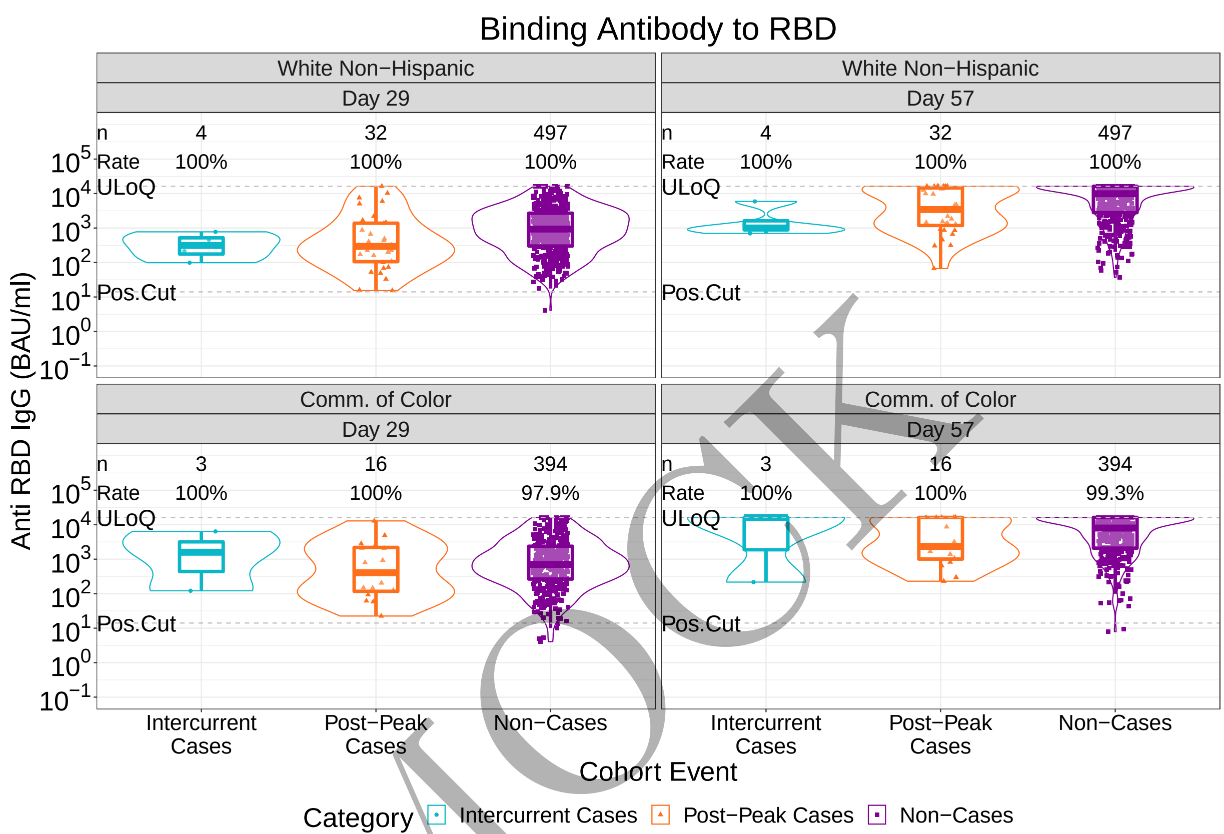

\caption{

Figure 2.5.171: violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



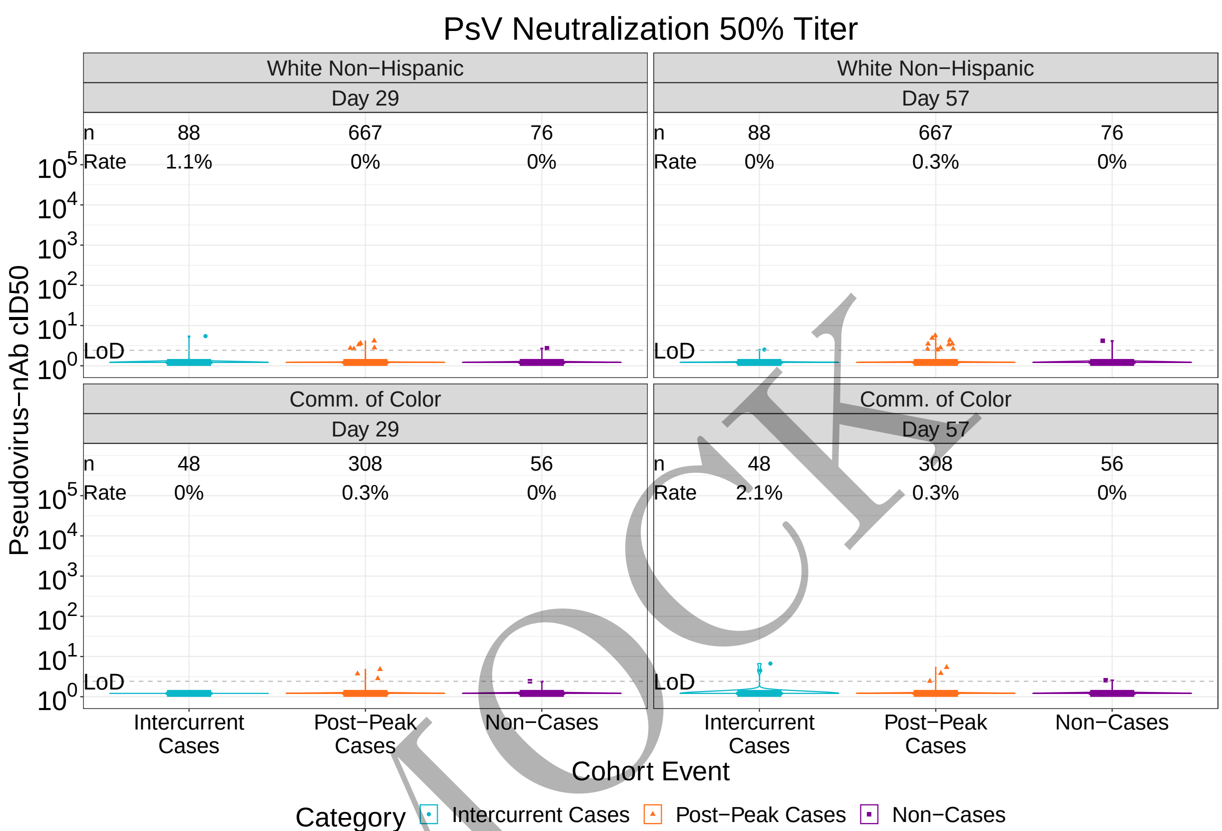

\caption{

Figure 2.5.172: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



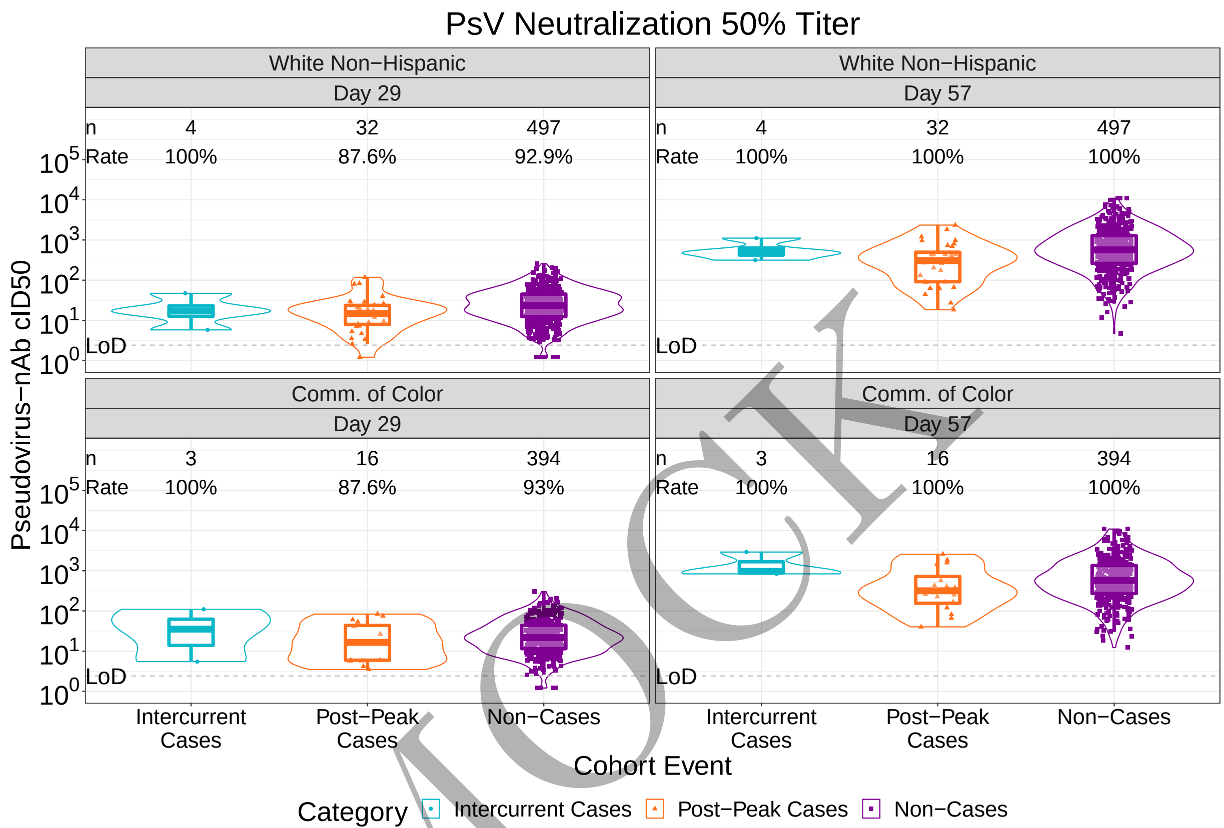

\caption{

Figure 2.5.173: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



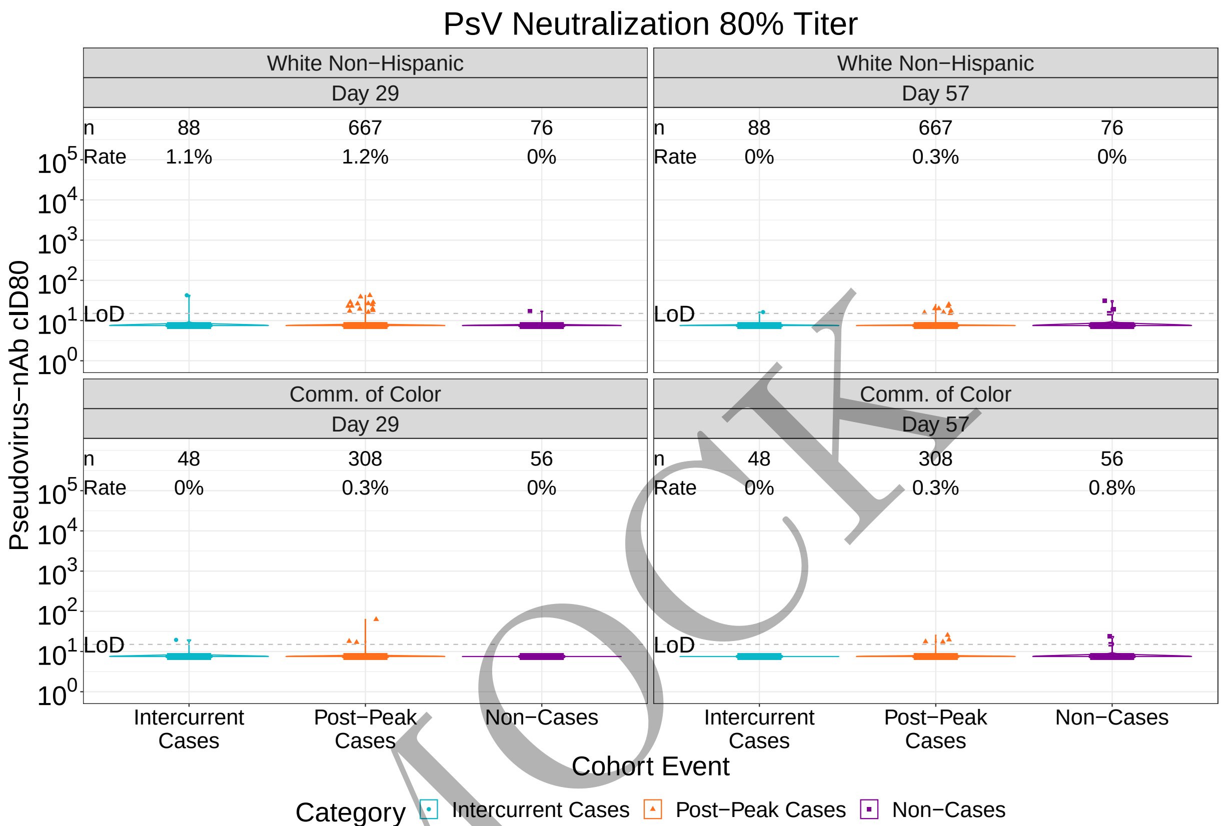

\caption{

Figure 2.5.174: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



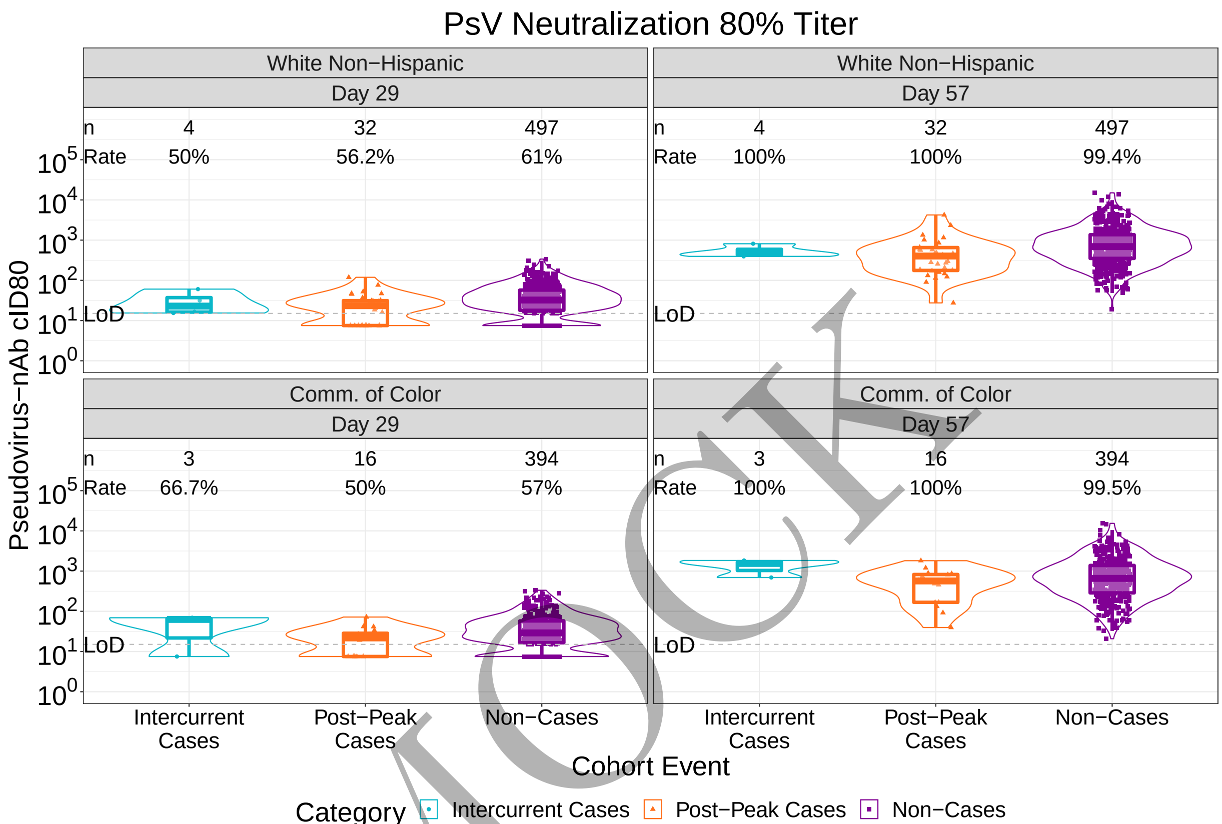

\caption{

Figure 2.5.175: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



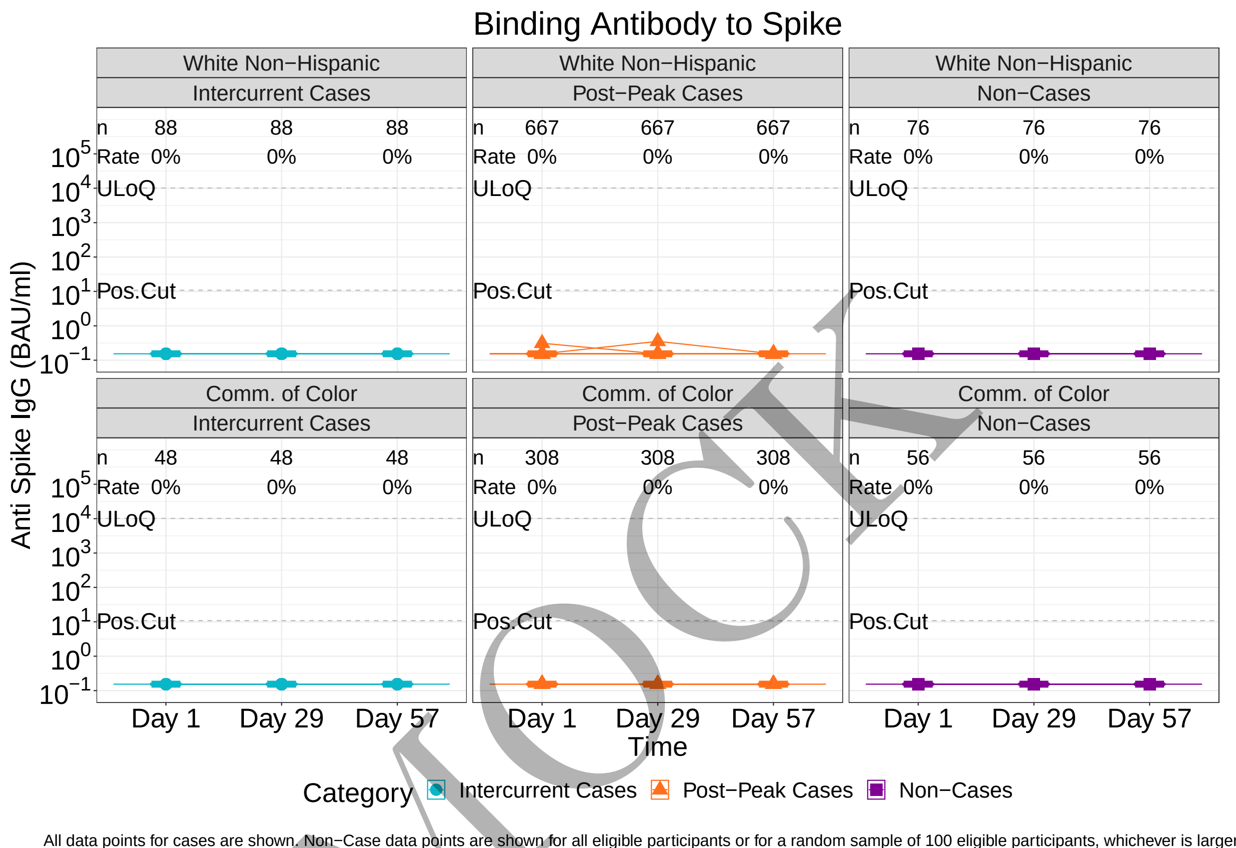

\caption{

Figure 2.5.176: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



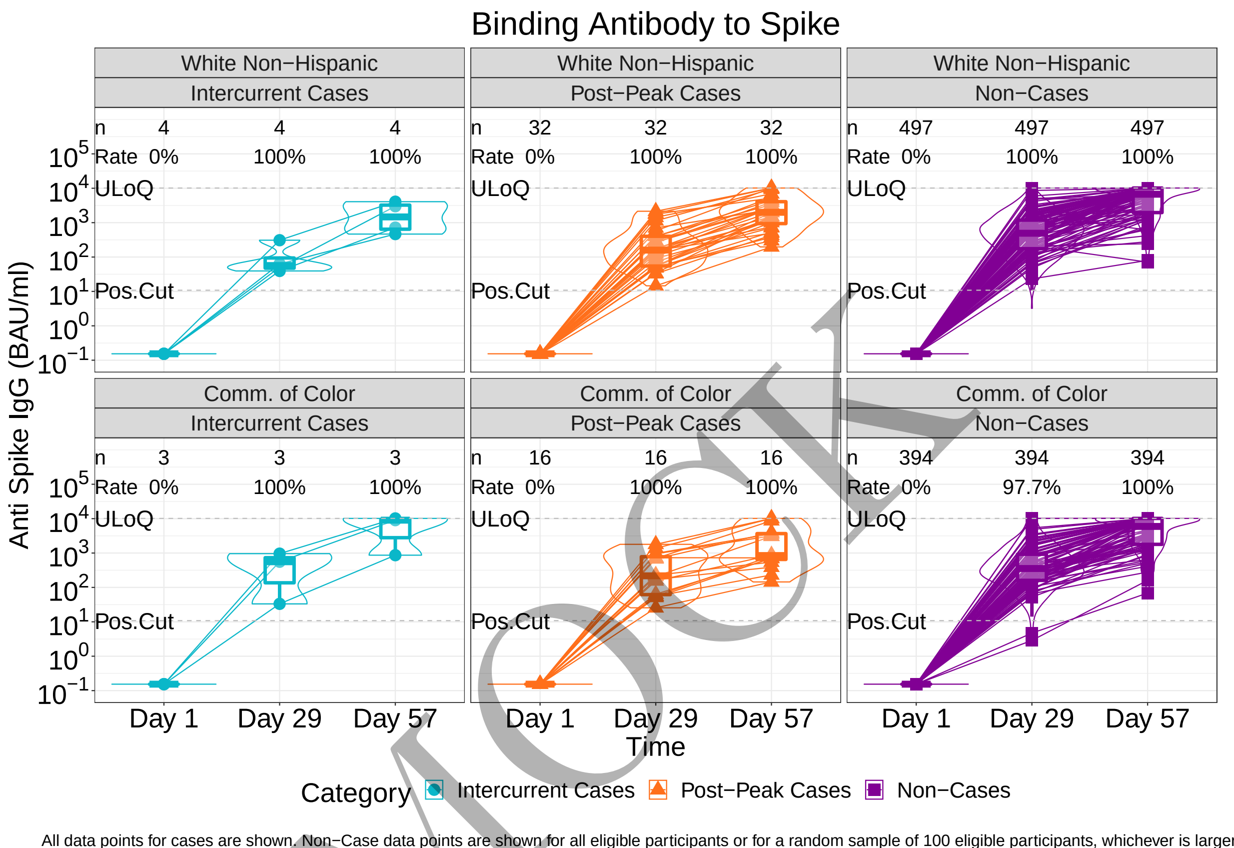

\caption{

Figure 2.5.177: lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



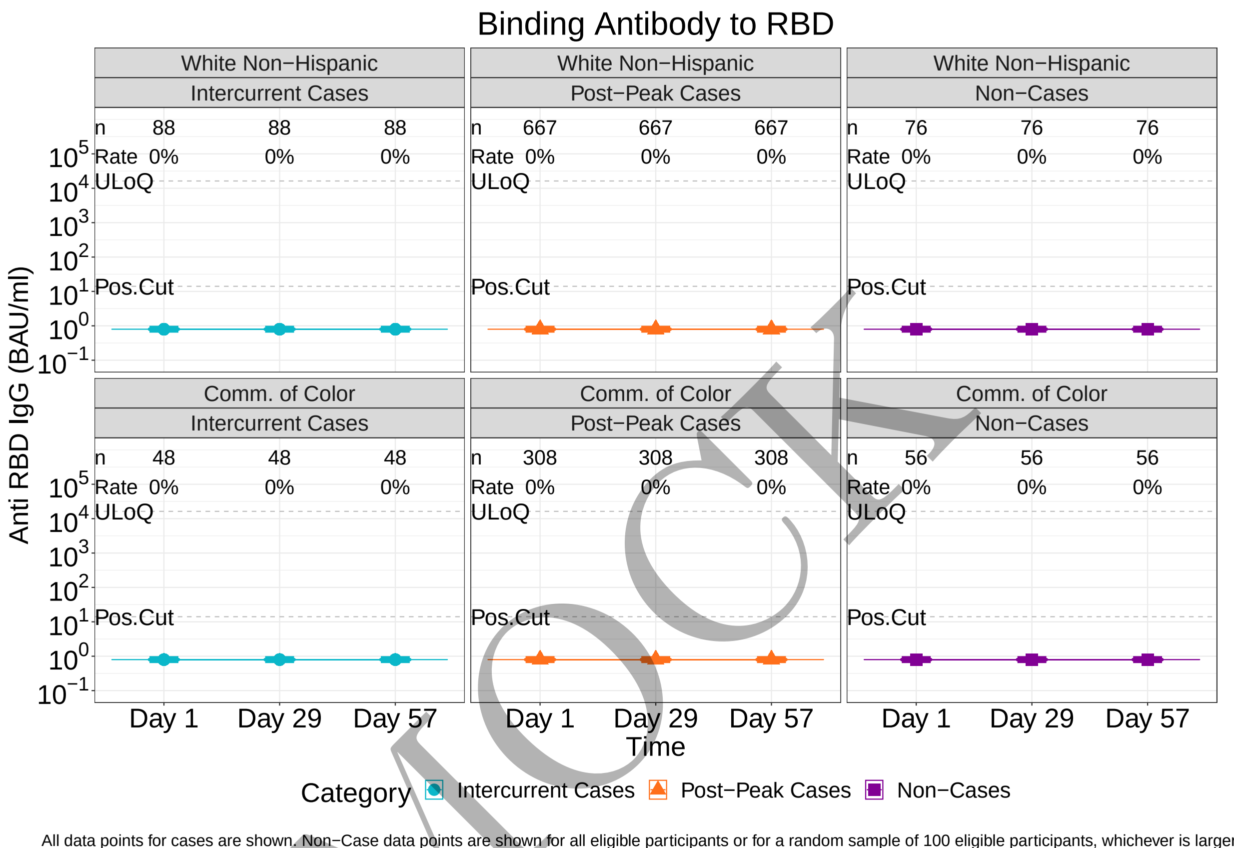

\caption{

Figure 2.5.178: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



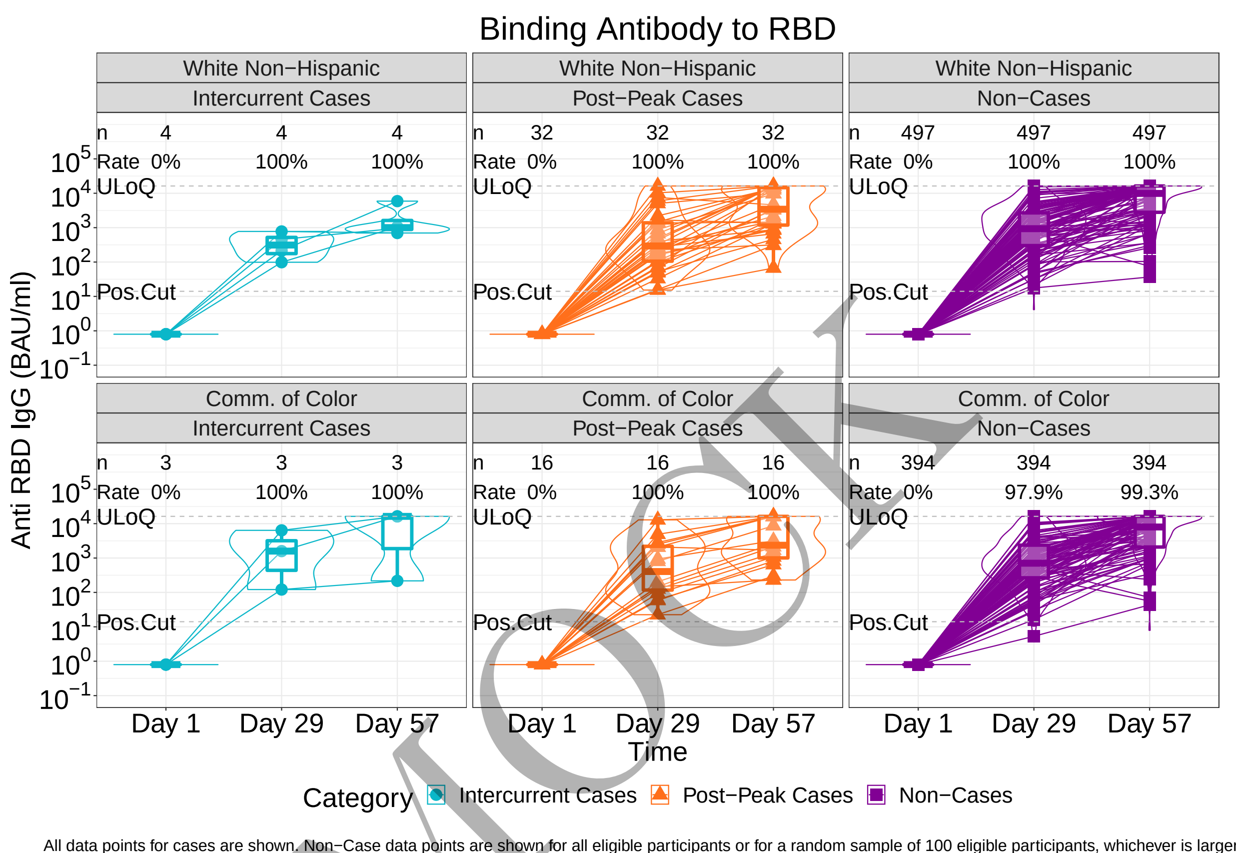

\caption{

Figure 2.5.179: lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



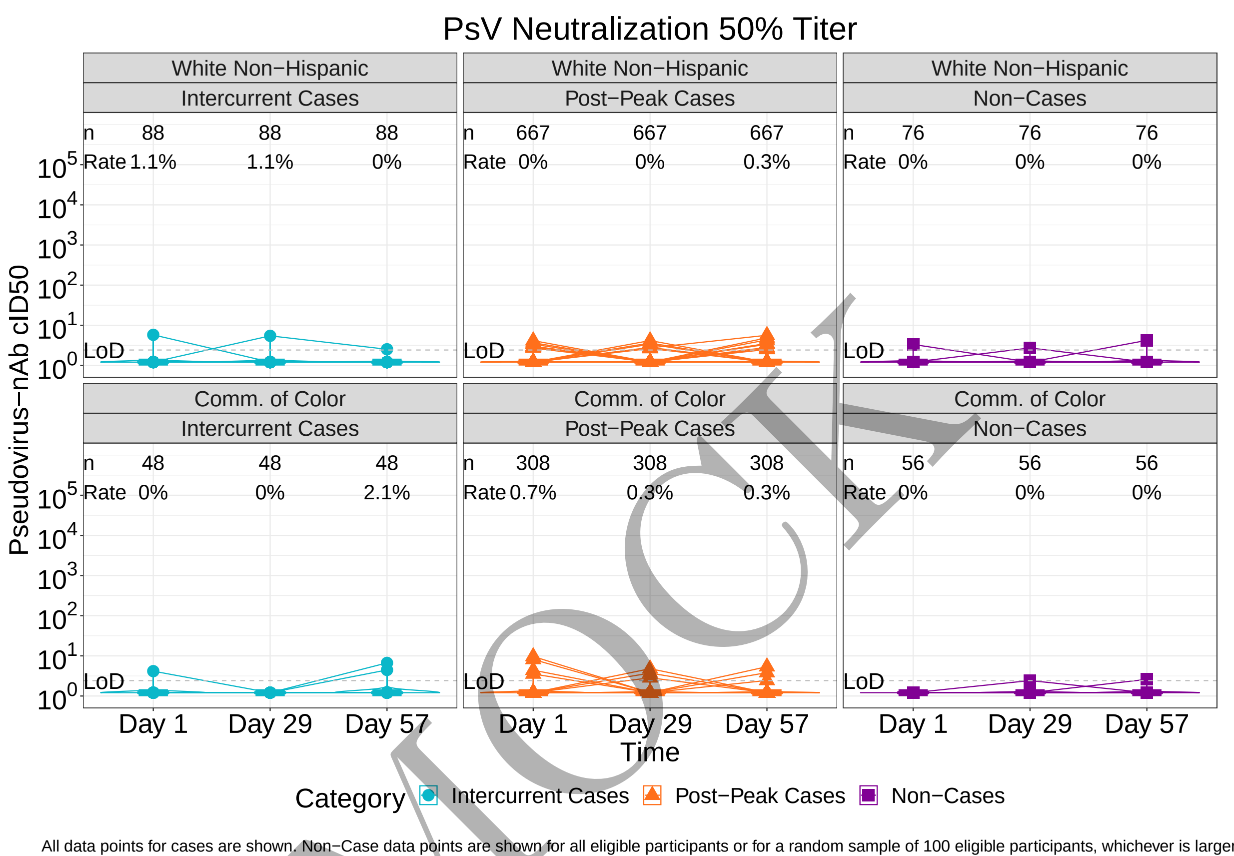

\caption{

Figure 2.5.180: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



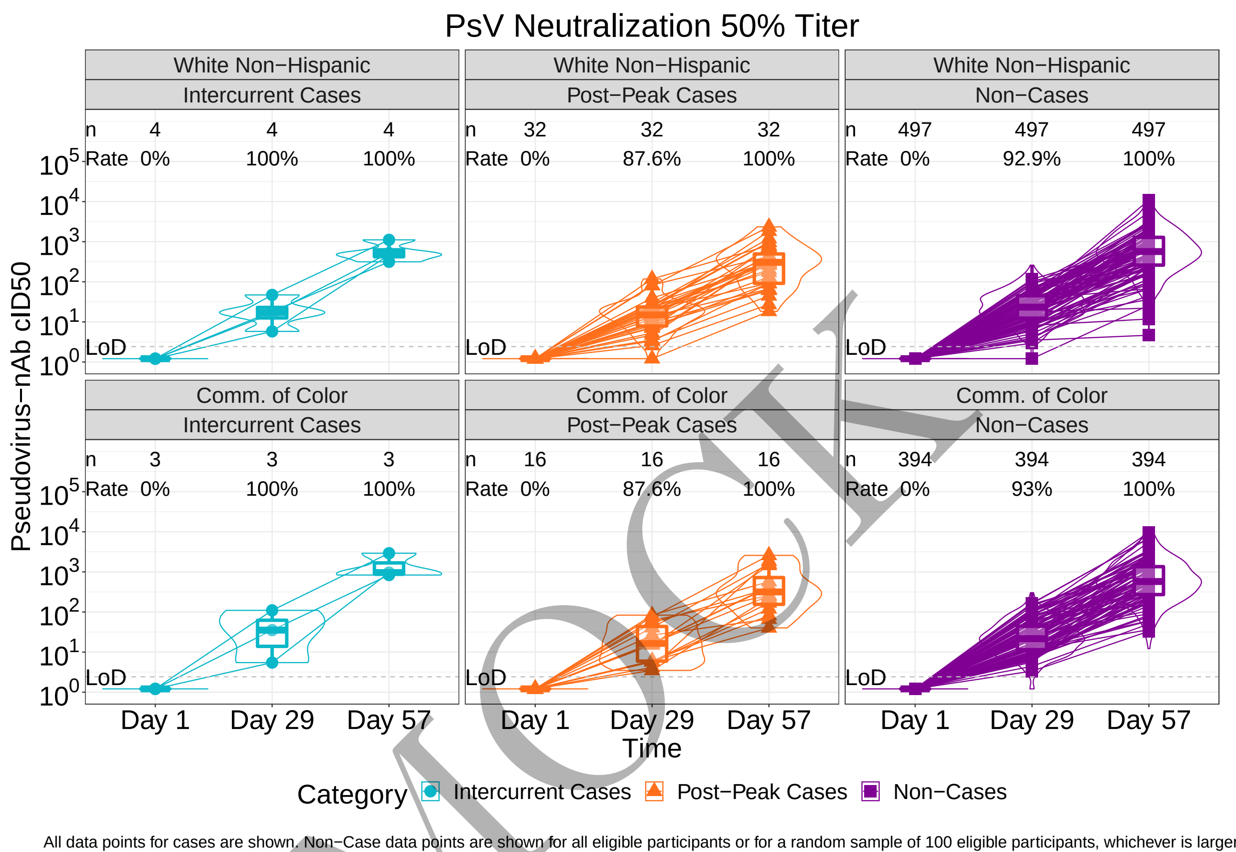

\caption{

Figure 2.5.181: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}



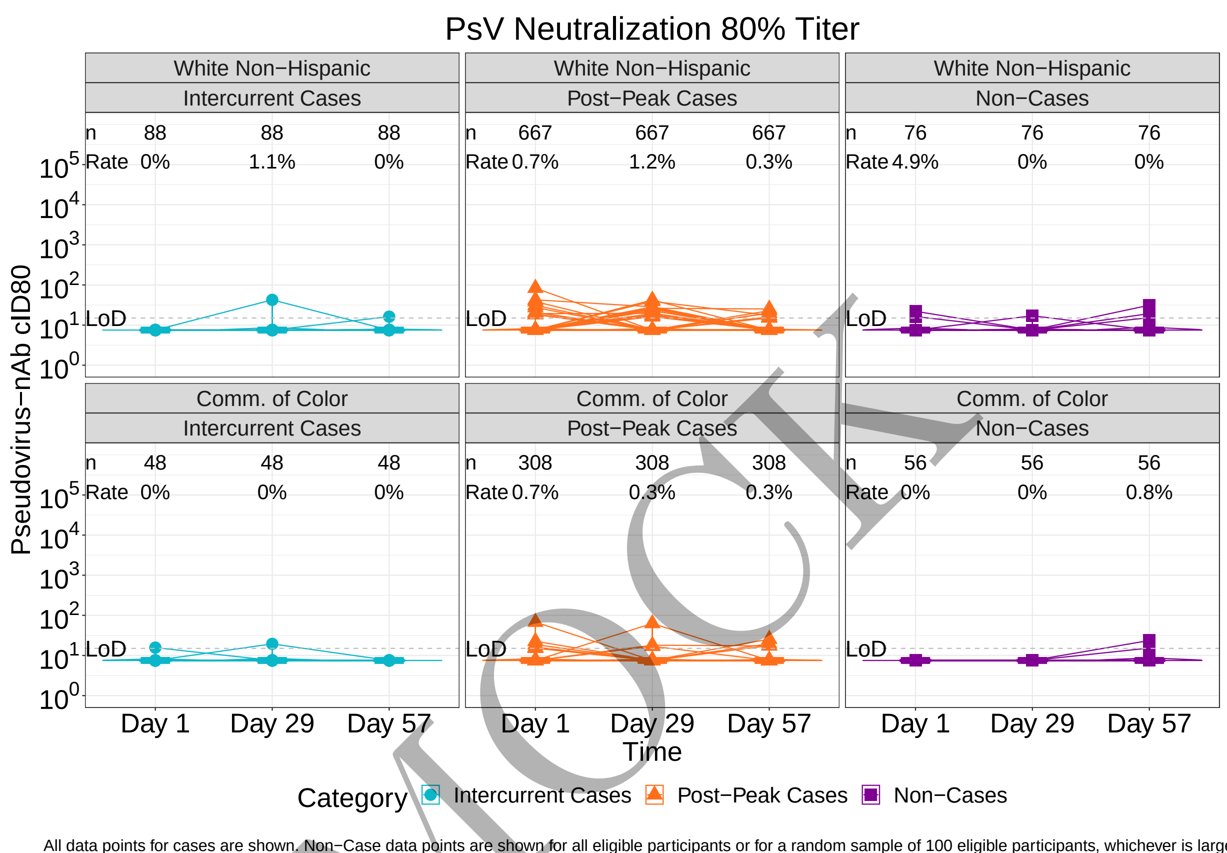

\caption{

Figure 2.5.182: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



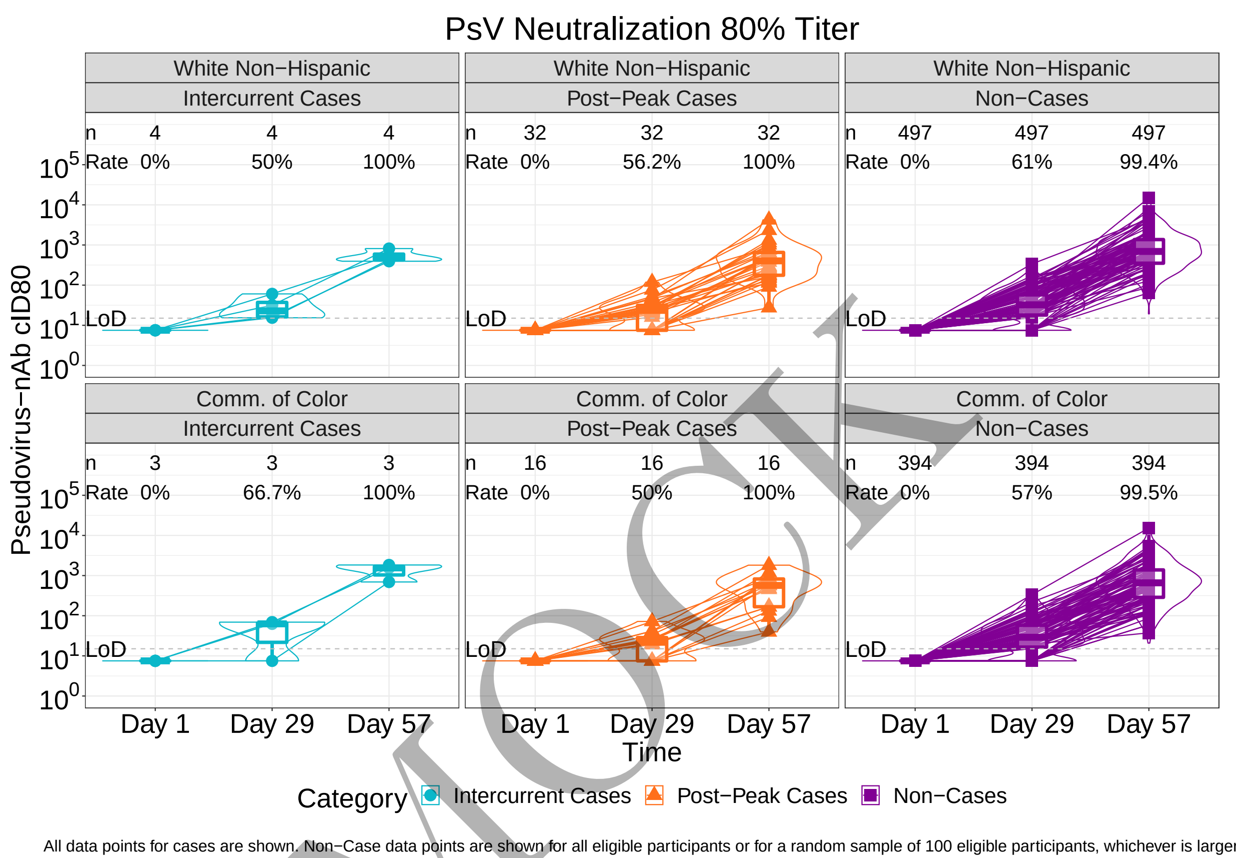

\caption{

Figure 2.5.183: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



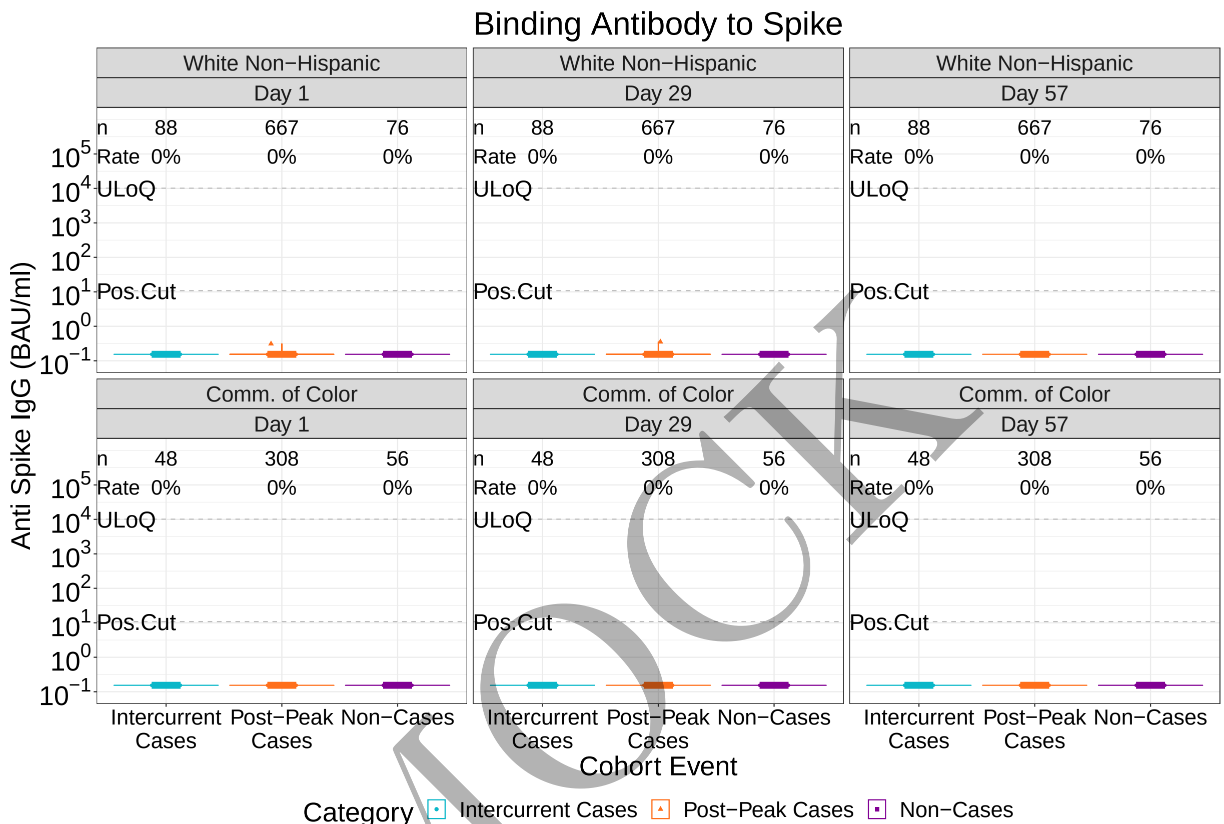

\caption{

Figure 2.5.184: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



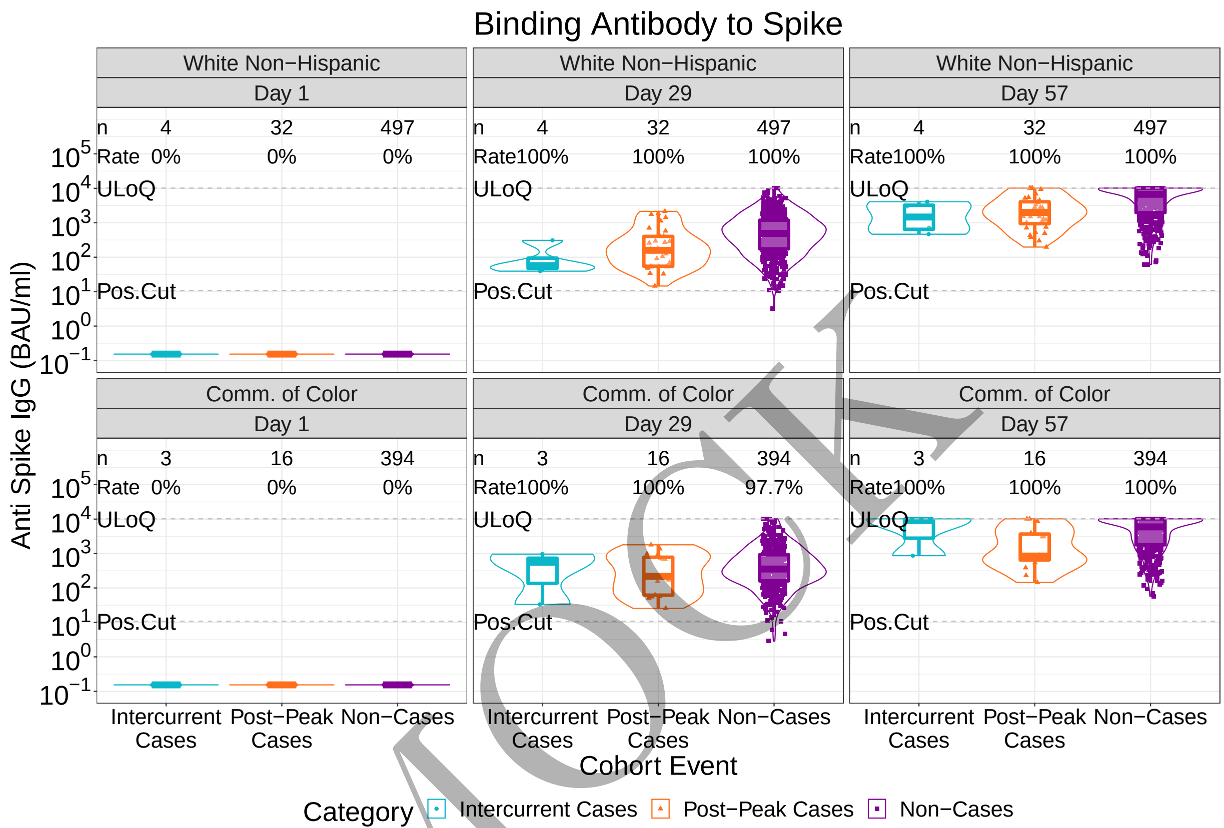

\caption{

Figure 2.5.185: violinplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



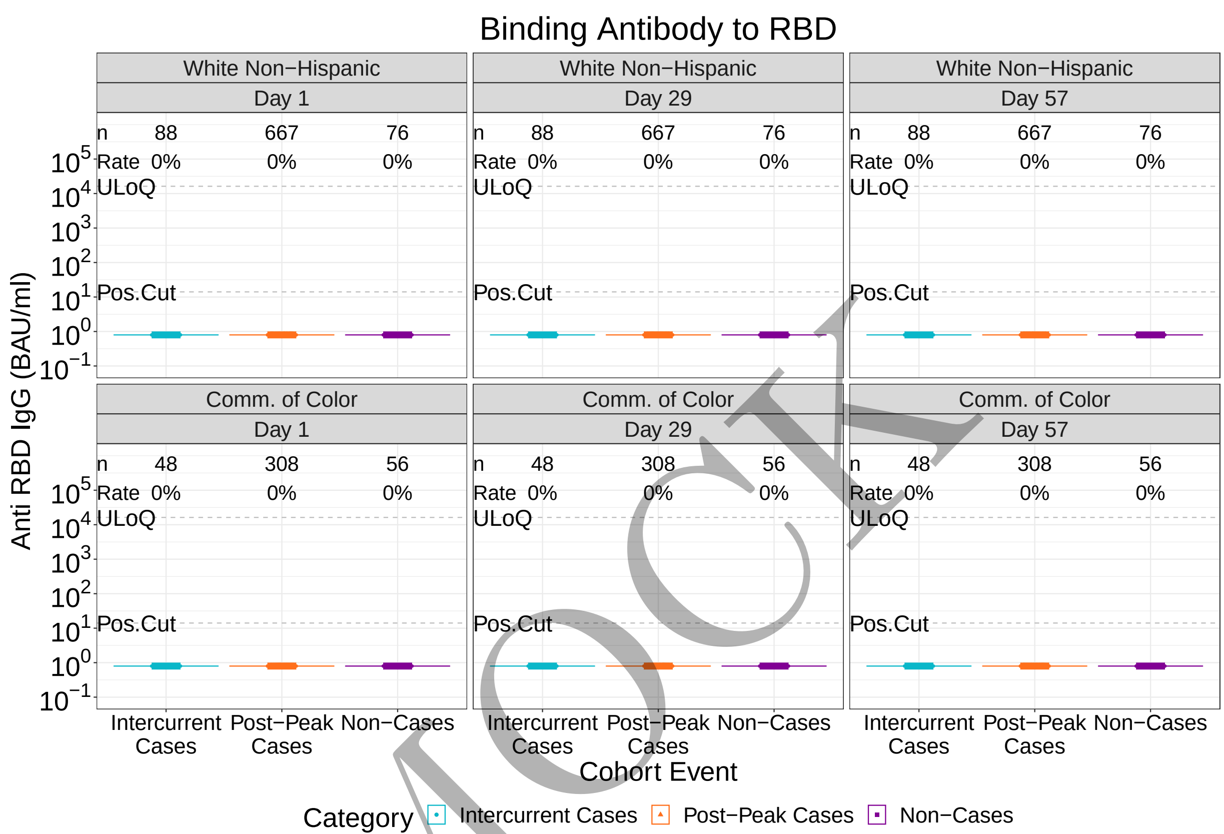

\caption{

Figure 2.5.186: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





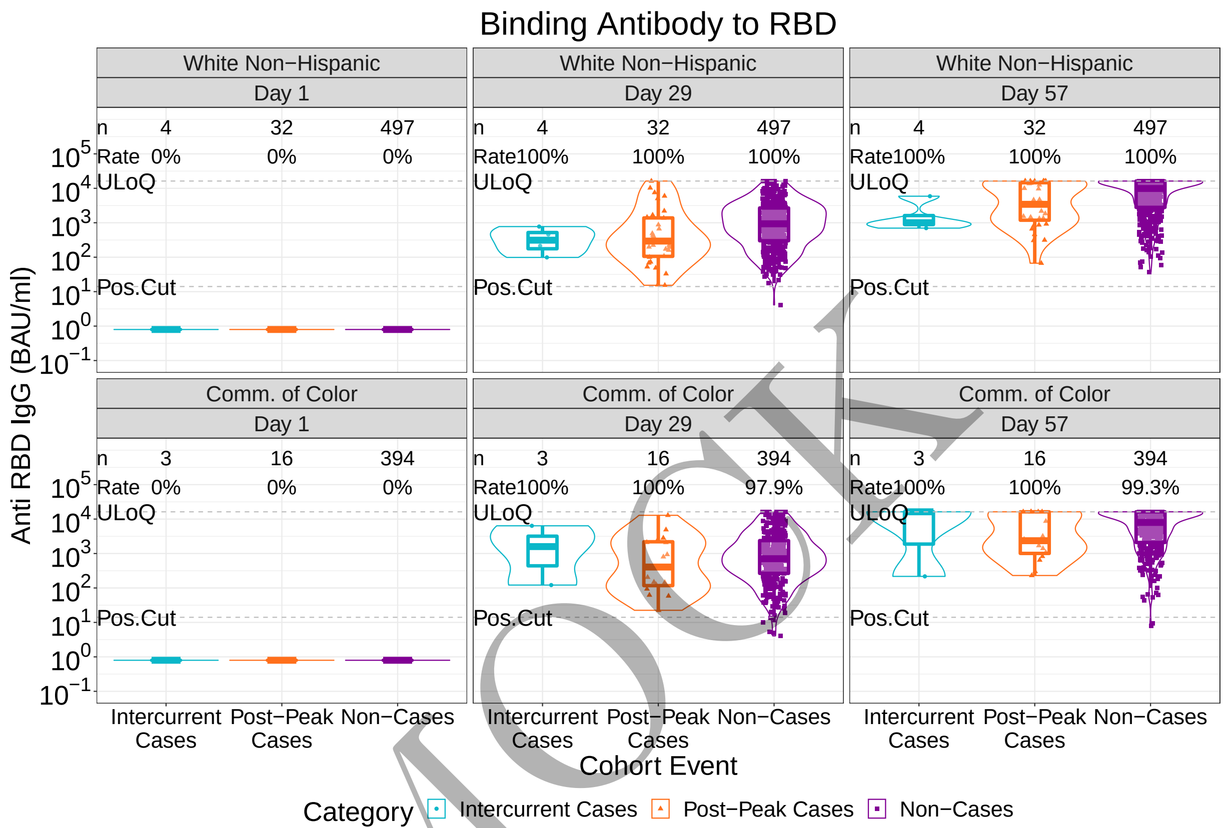

\caption{

Figure 2.5.187: violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



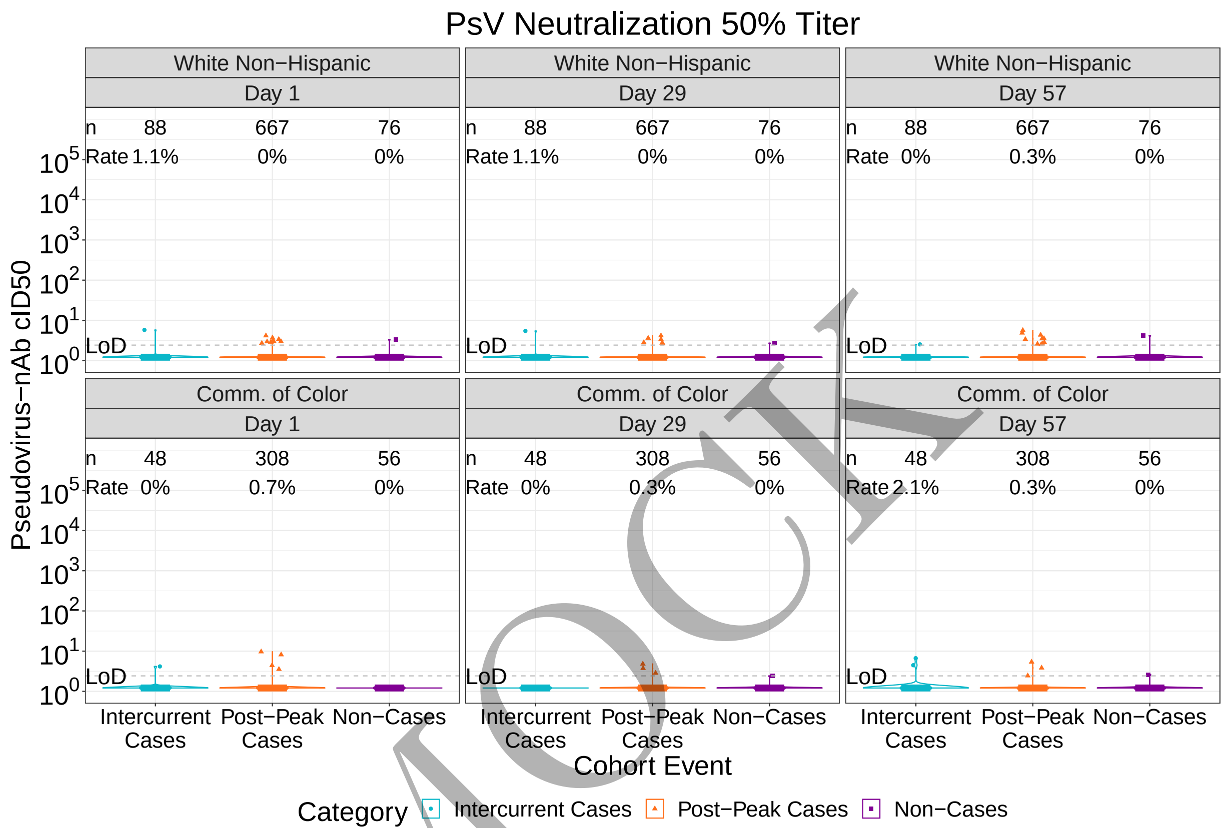

\caption{

Figure 2.5.188: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



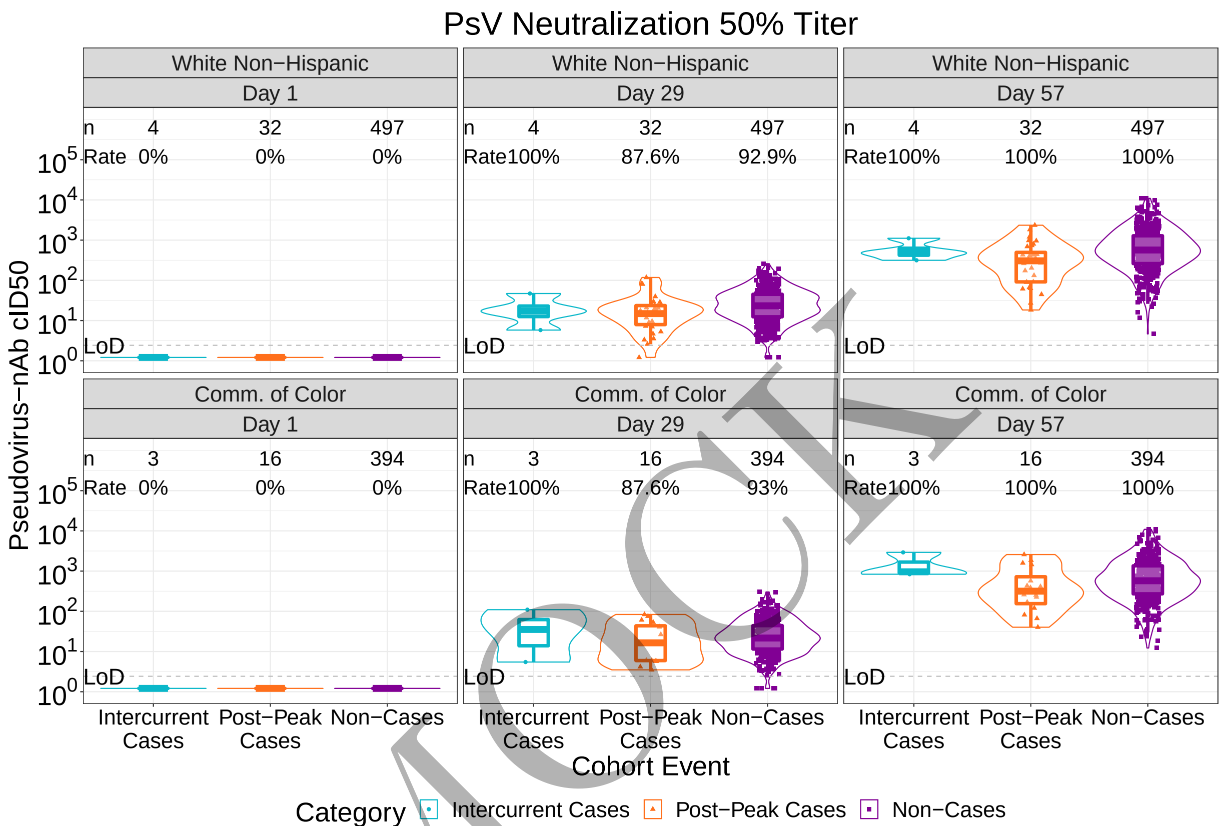

\caption{

Figure 2.5.189: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



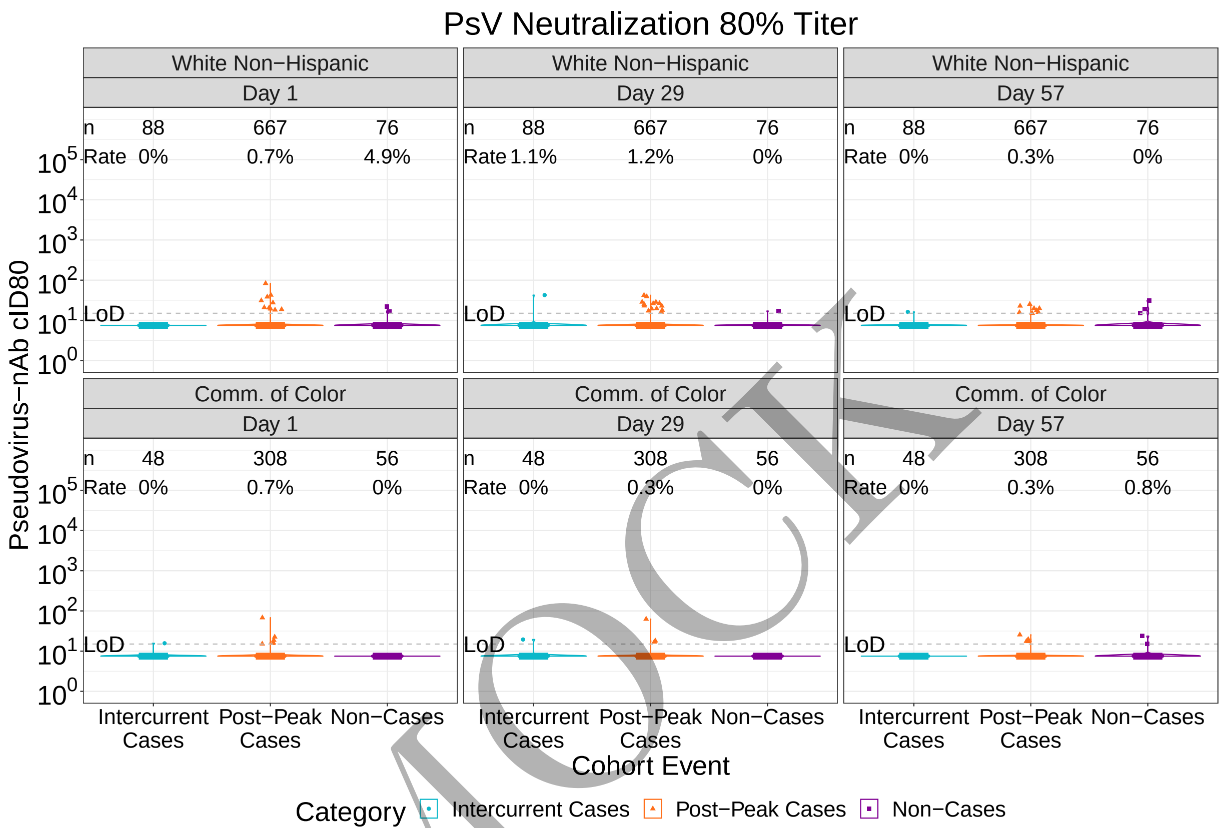

\caption{

Figure 2.5.190: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



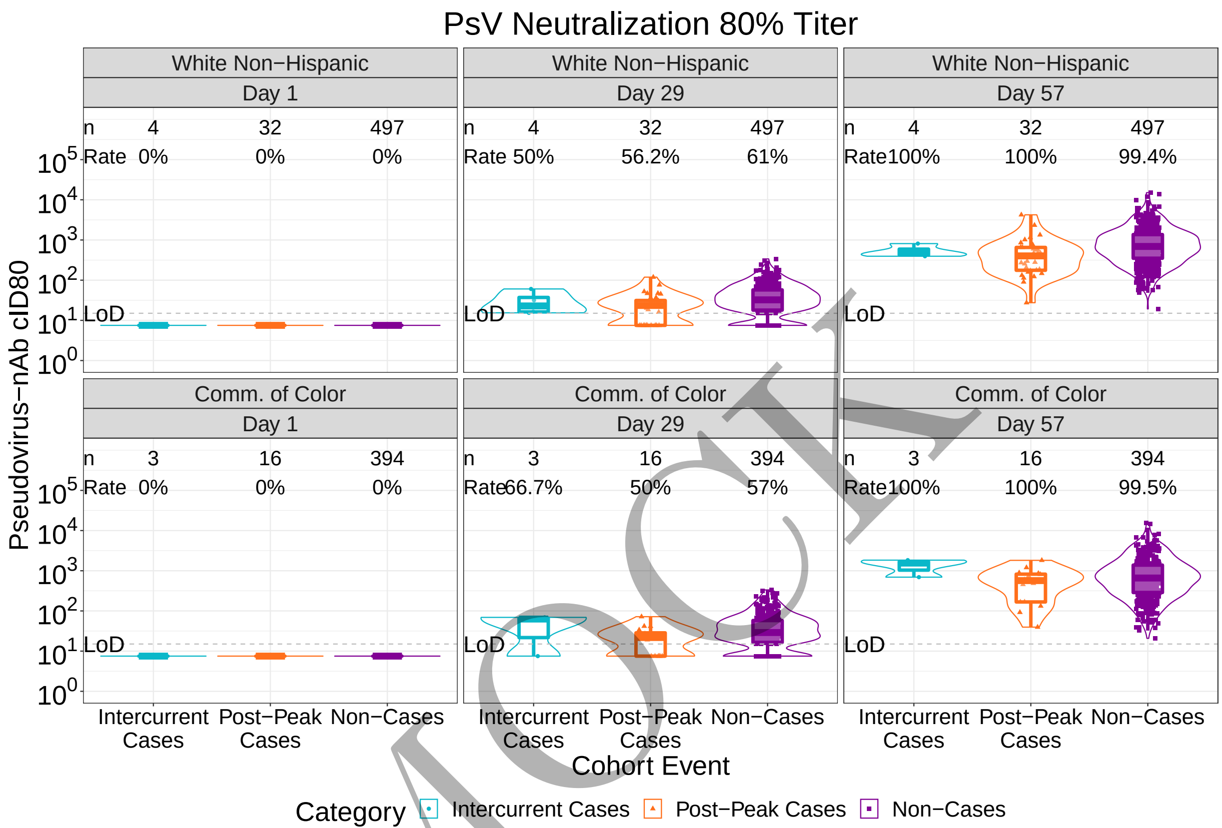

\caption{

Figure 2.5.191: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



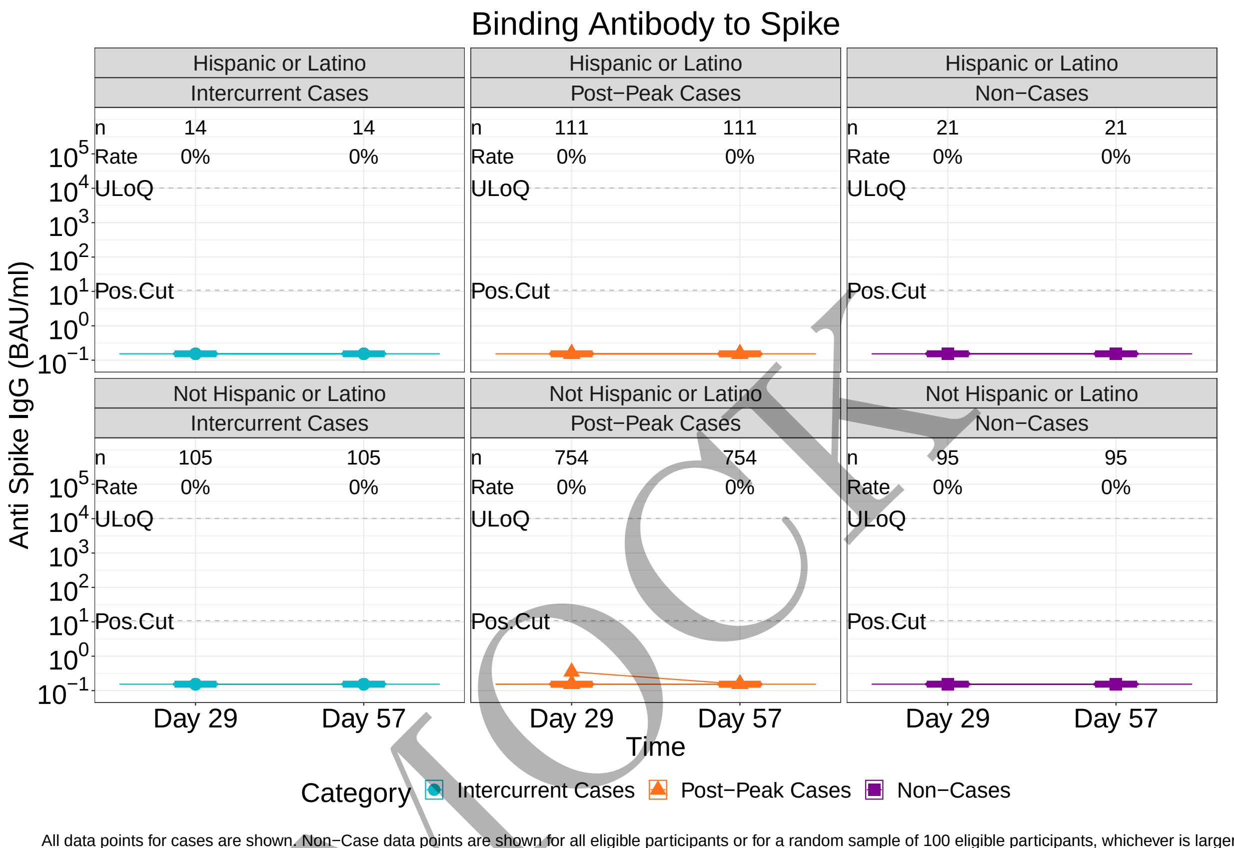

\caption{

Figure 2.5.192: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



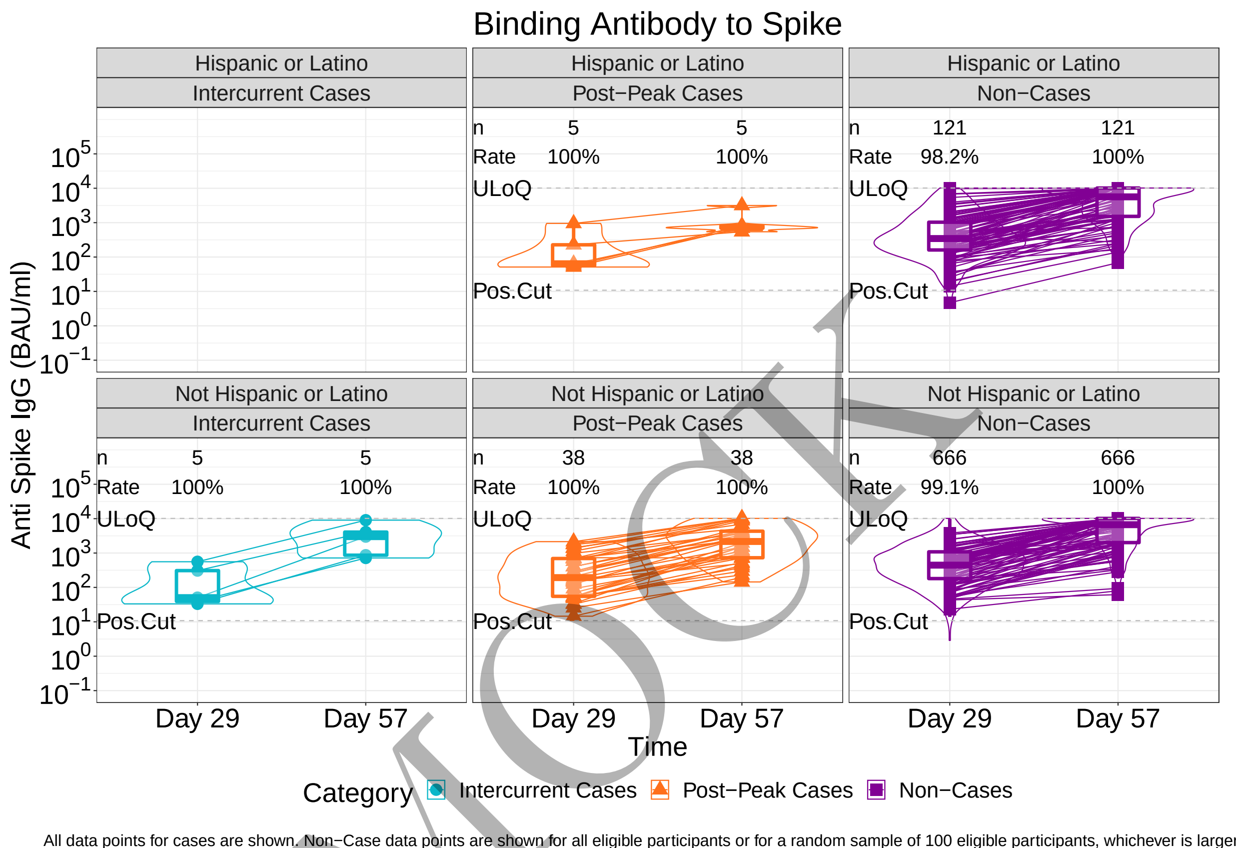

\caption{

Figure 2.5.193: lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



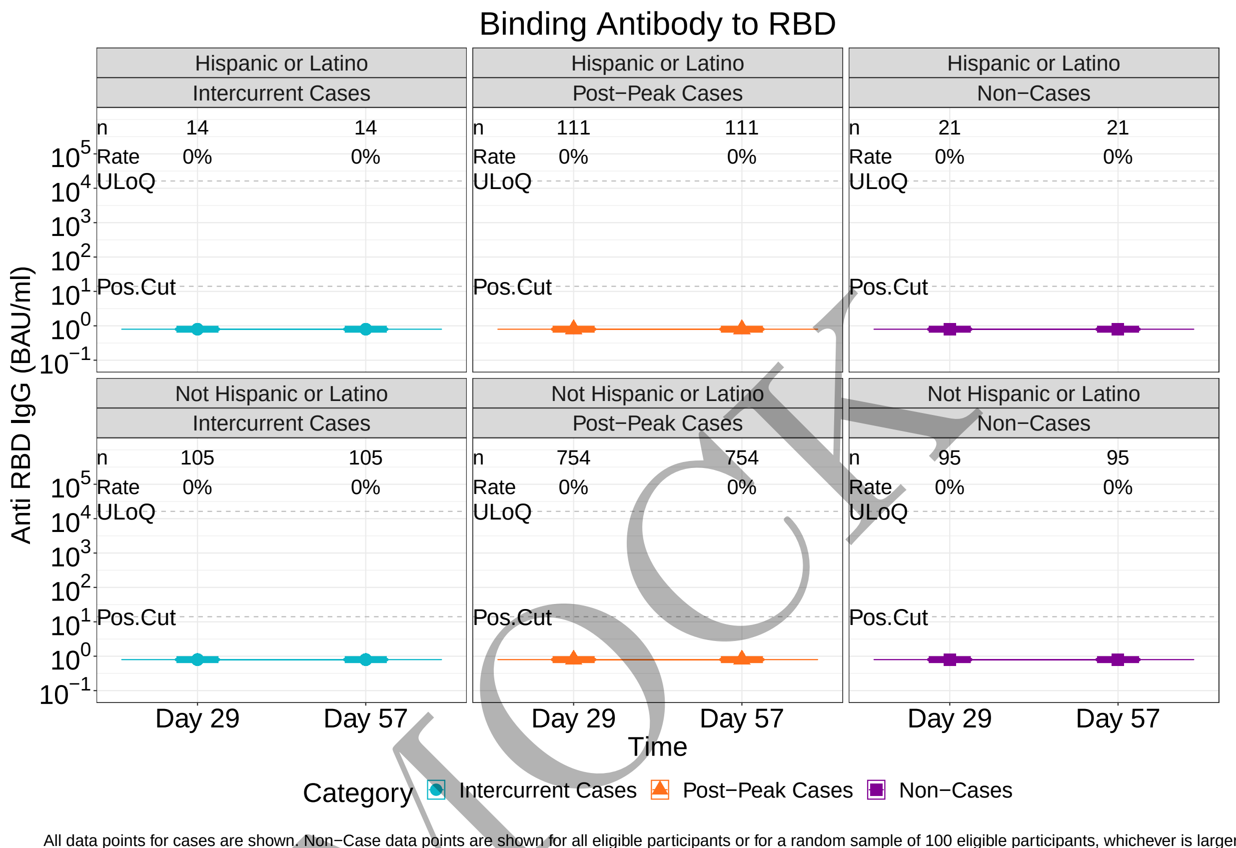

\caption{

Figure 2.5.194: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



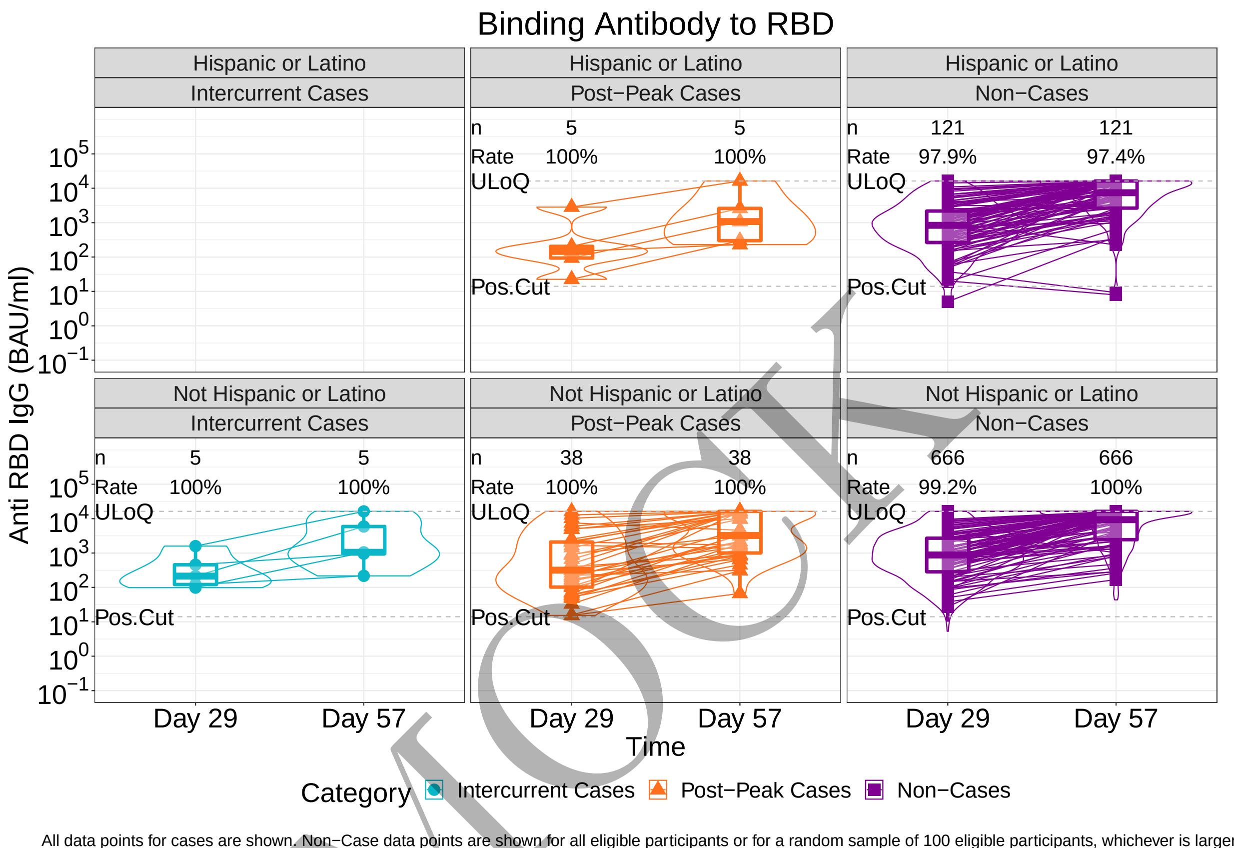

\caption{

Figure 2.5.195: lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



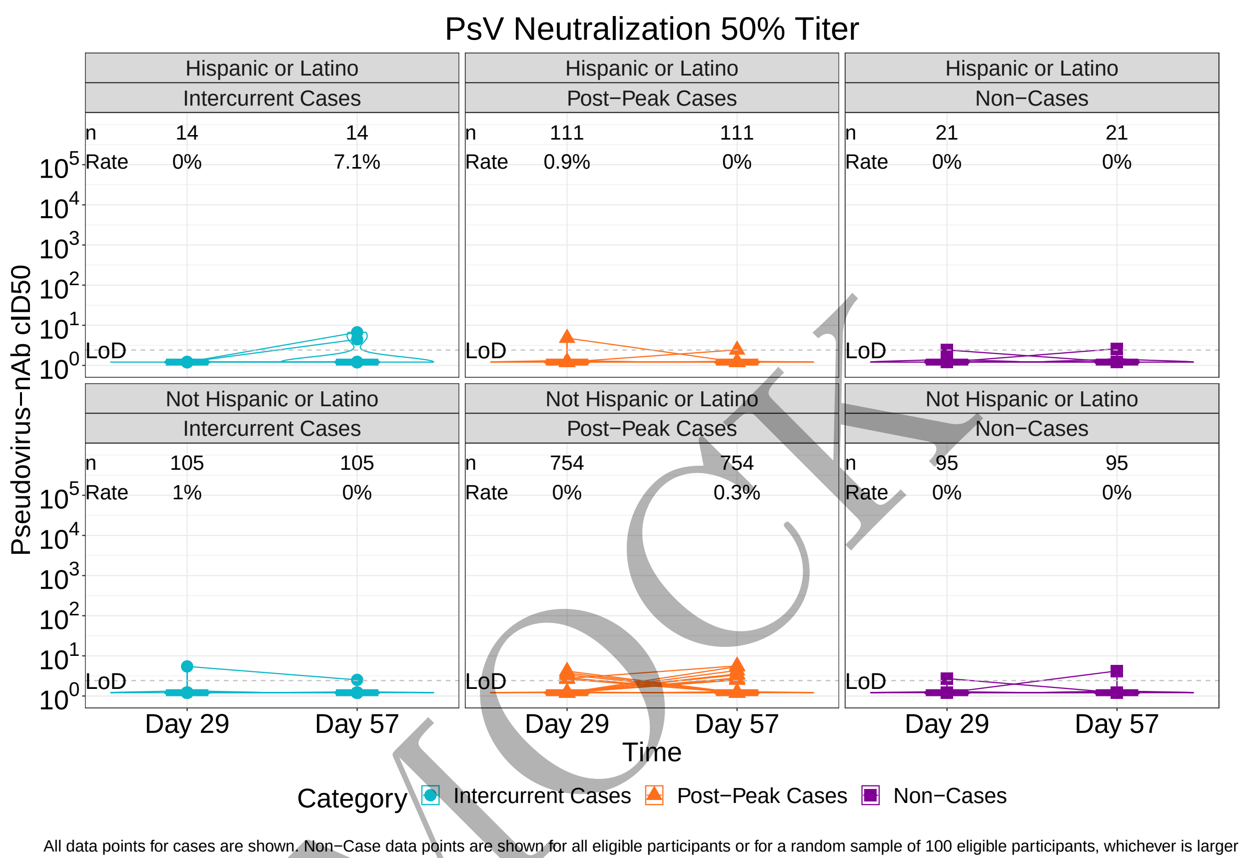

\caption{

Figure 2.5.196: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



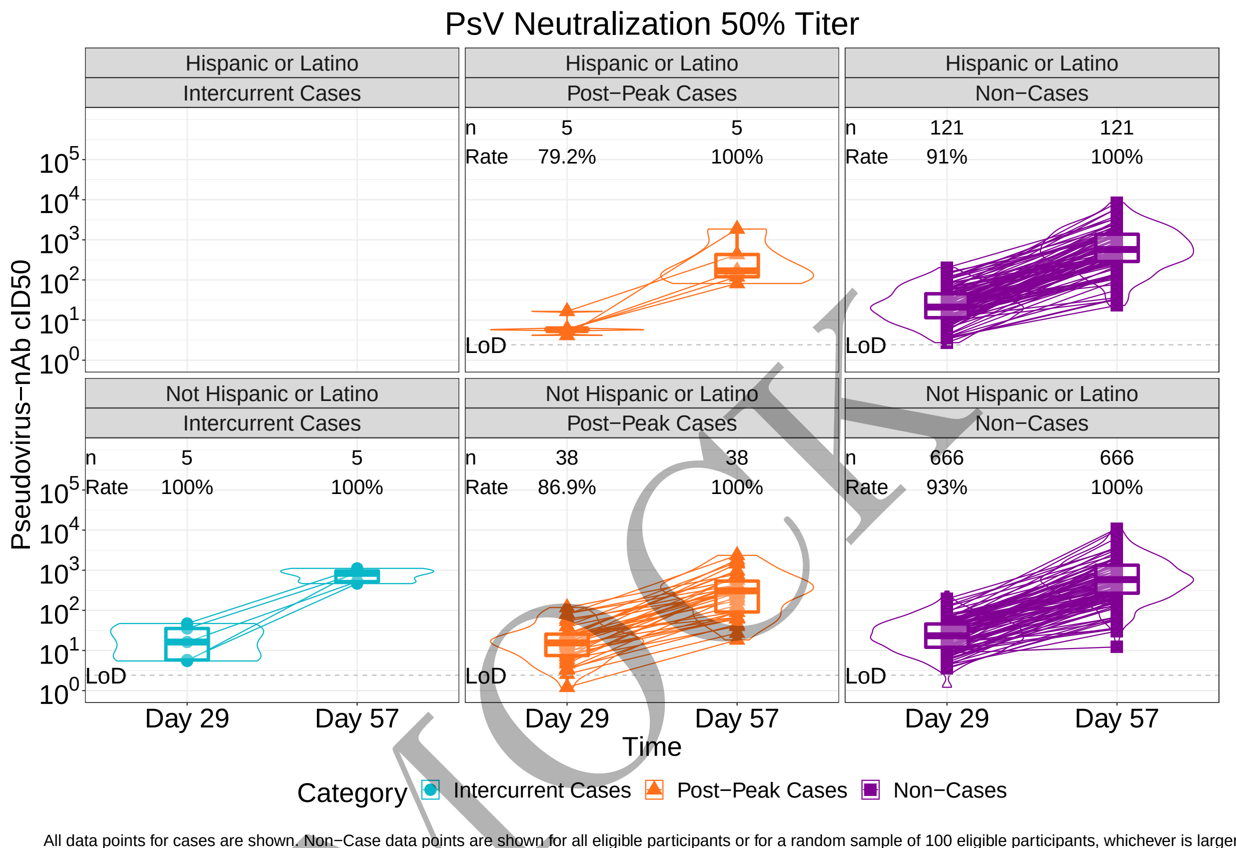

\caption{

Figure 2.5.197: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



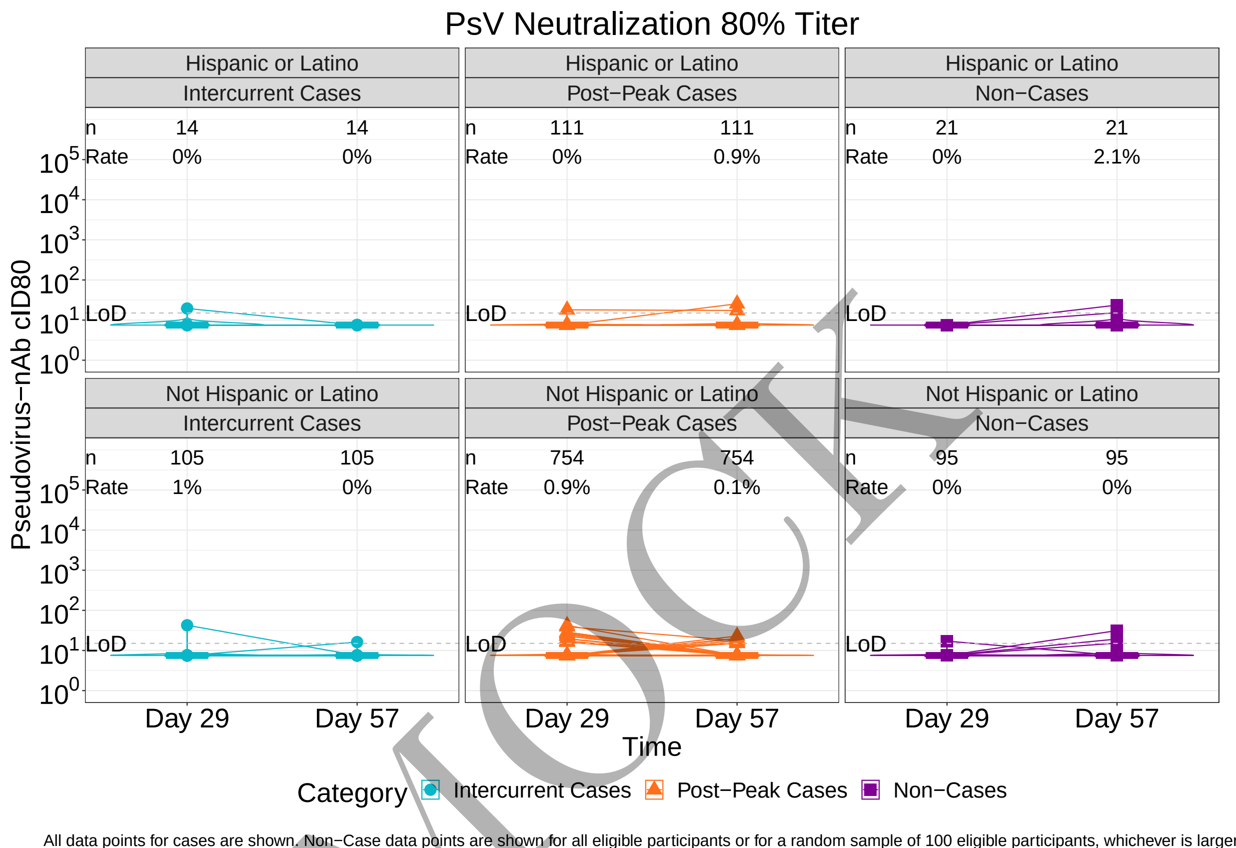

\caption{

Figure 2.5.198: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



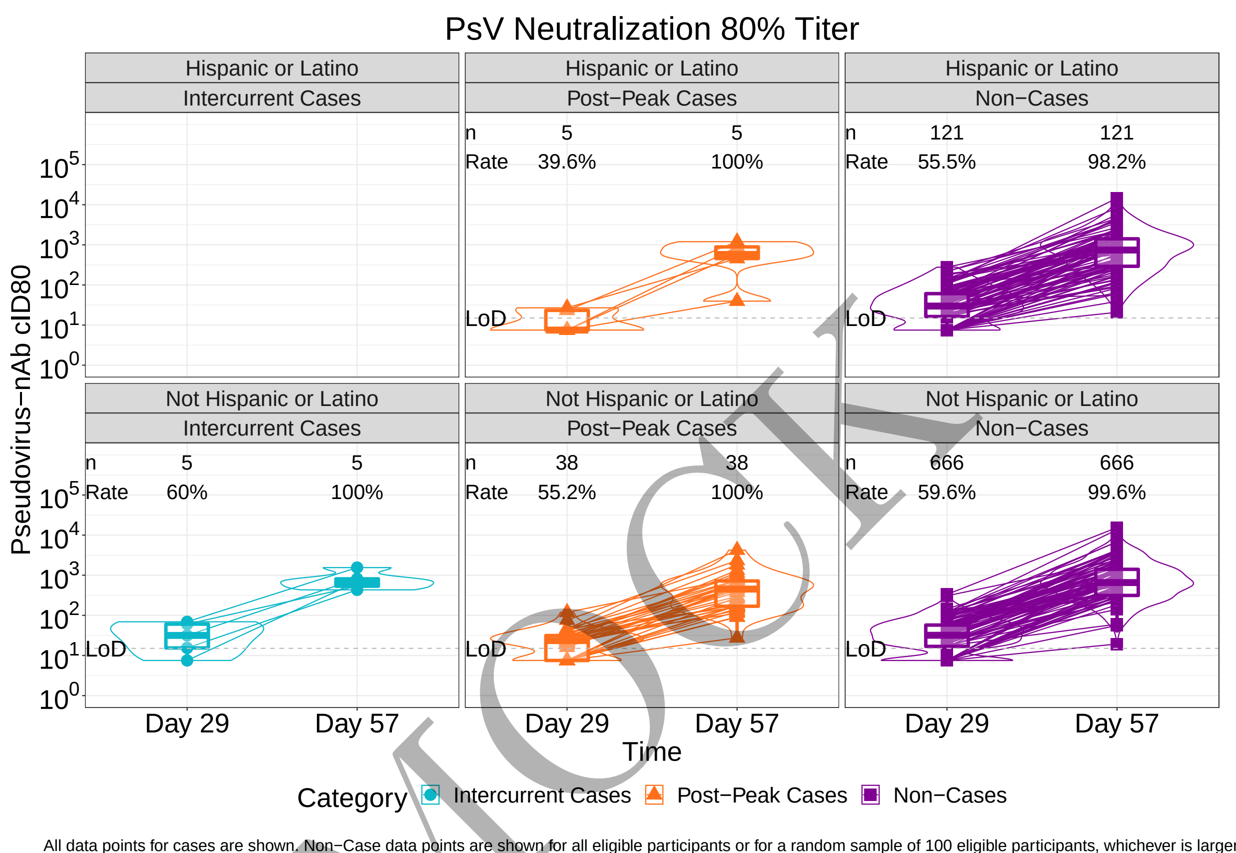

\caption{

Figure 2.5.199: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



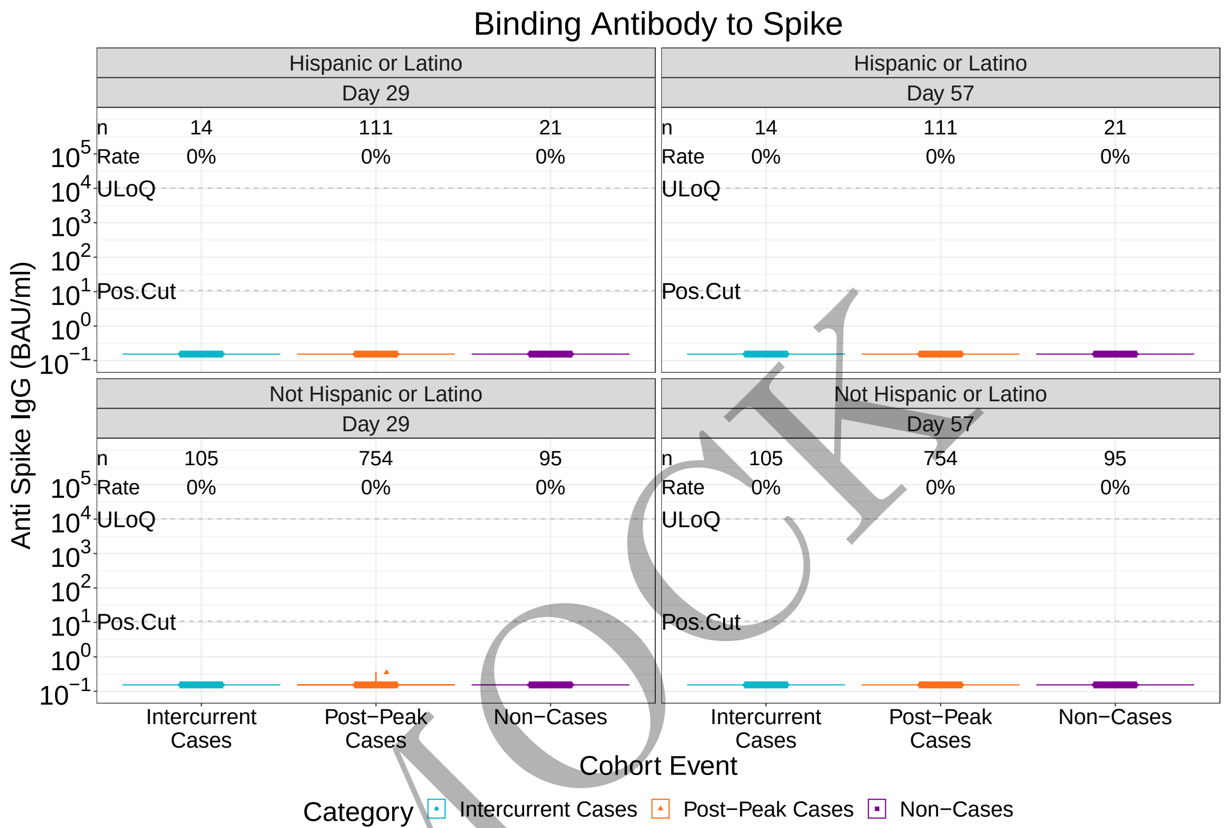

\caption{

Figure 2.5.200: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



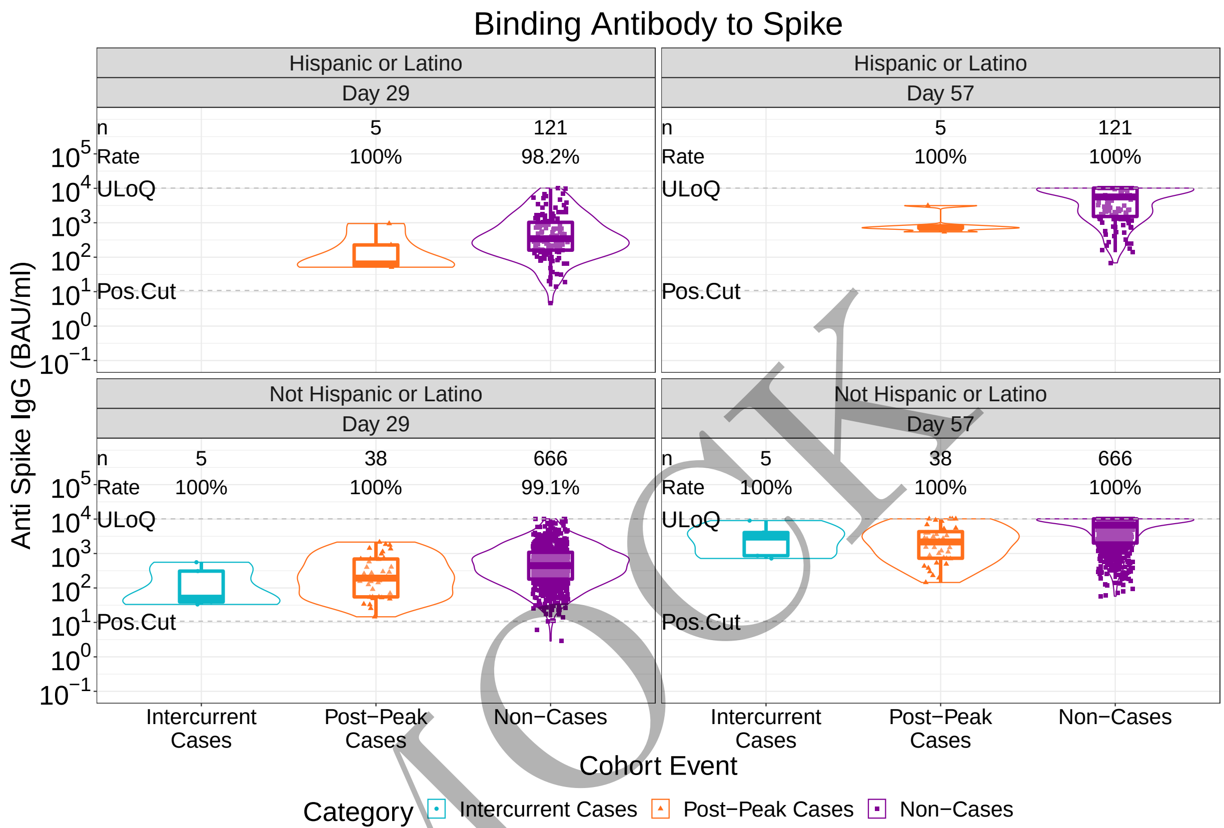

\caption{

Figure 2.5.201: violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



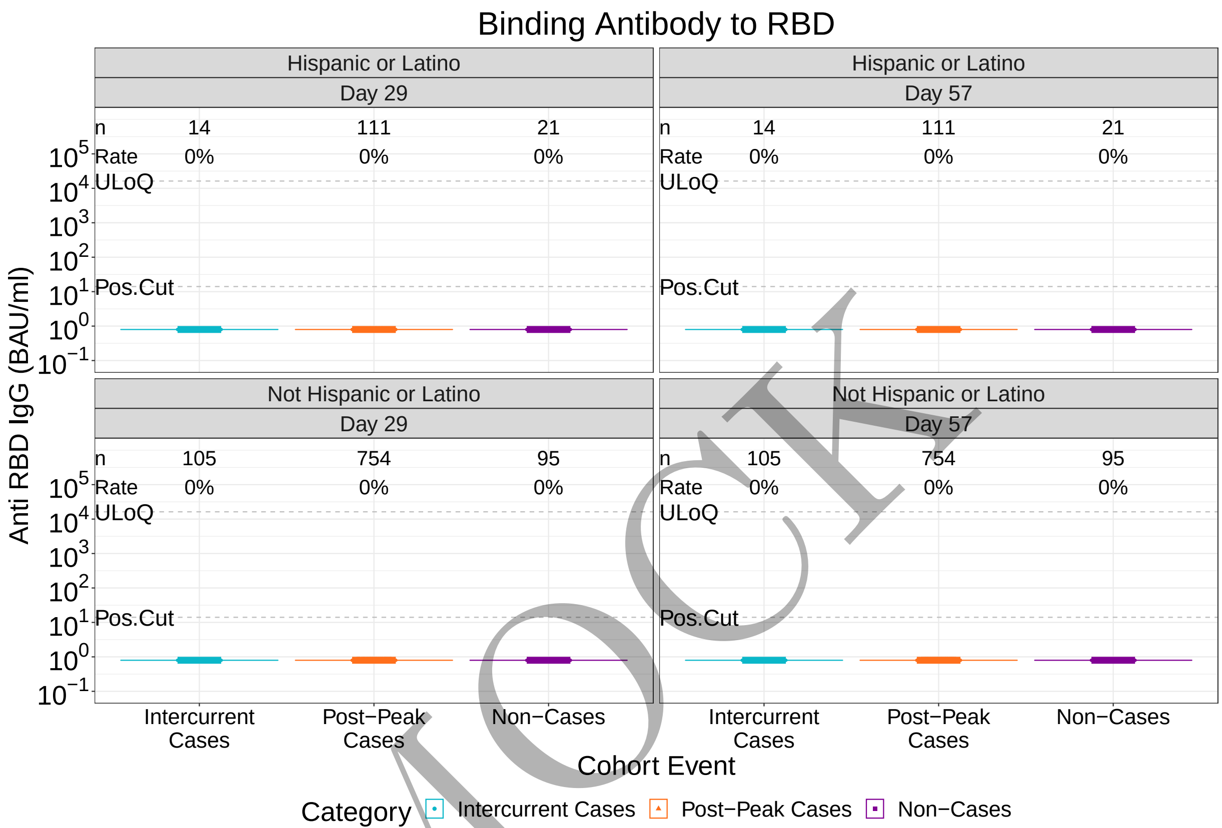

\caption{

Figure 2.5.202: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



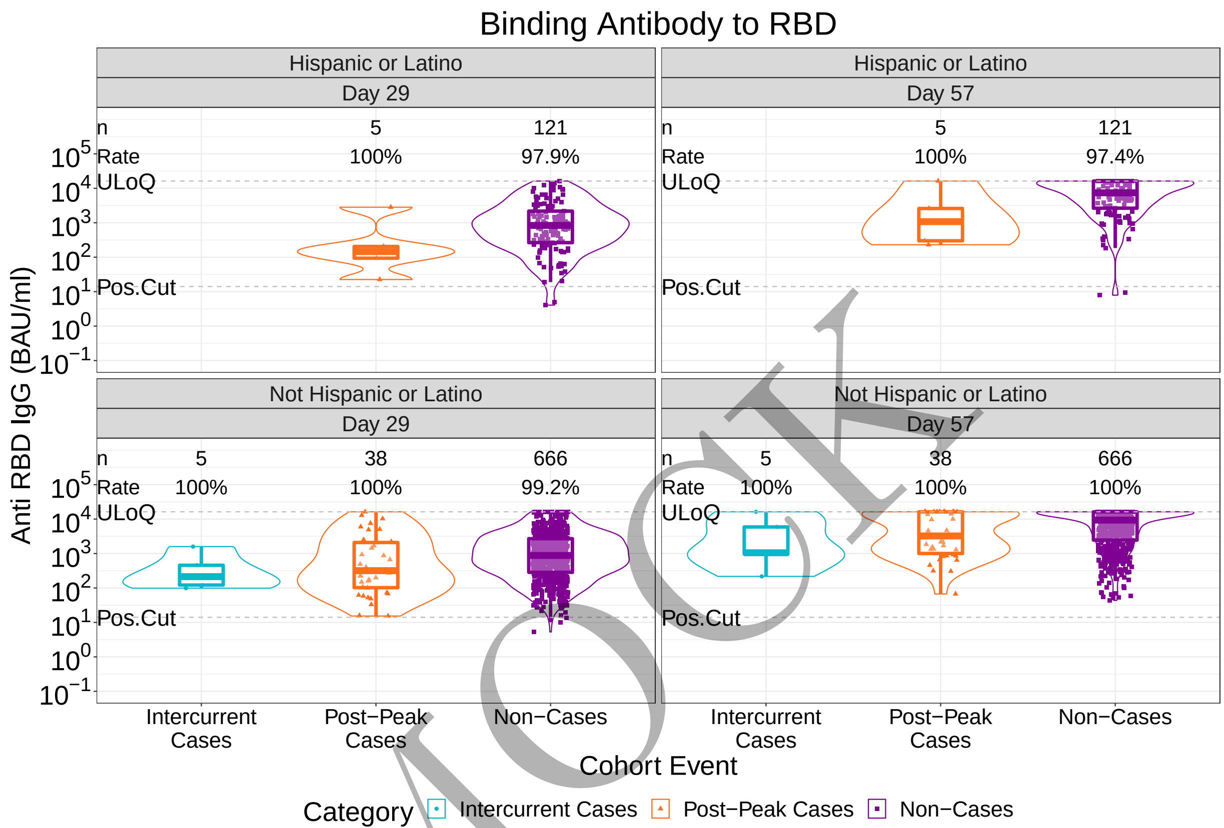

\caption{

Figure 2.5.203: violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



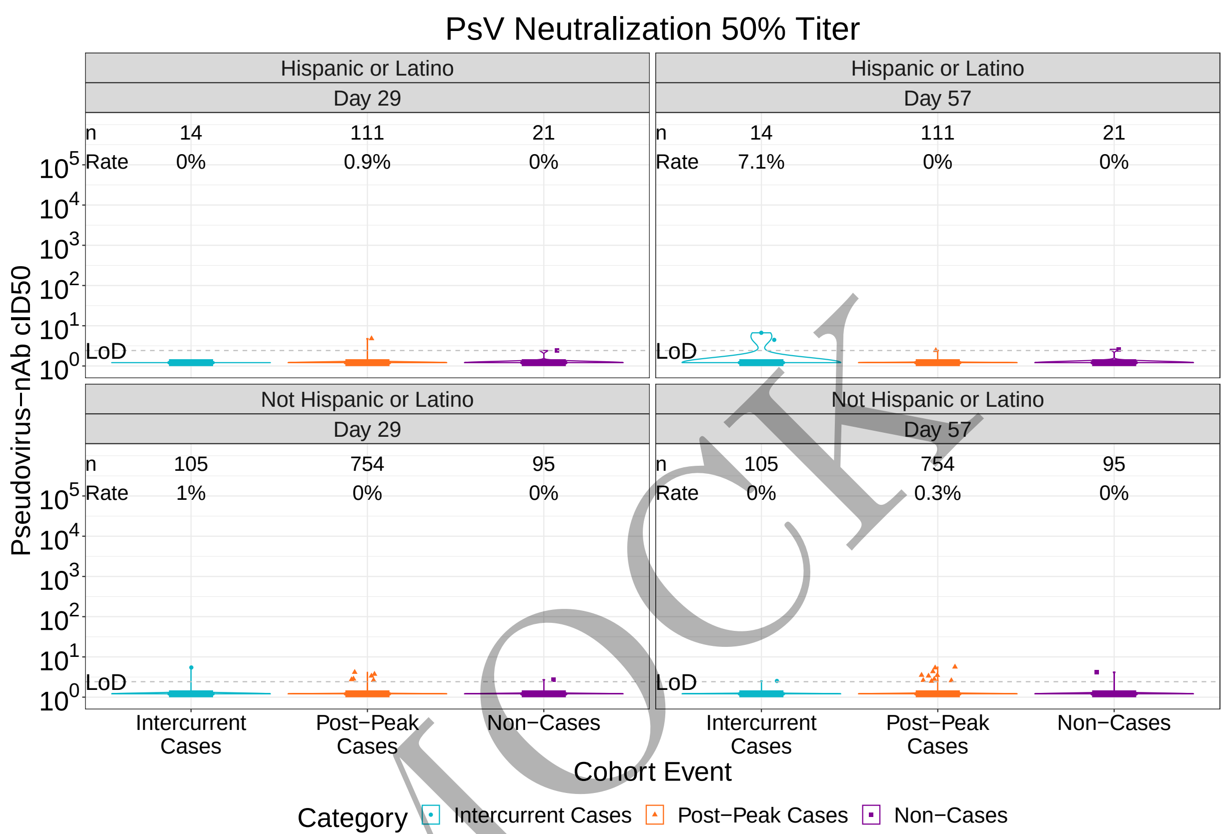

\caption{

Figure 2.5.204: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

`r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")`

\begin{figure}



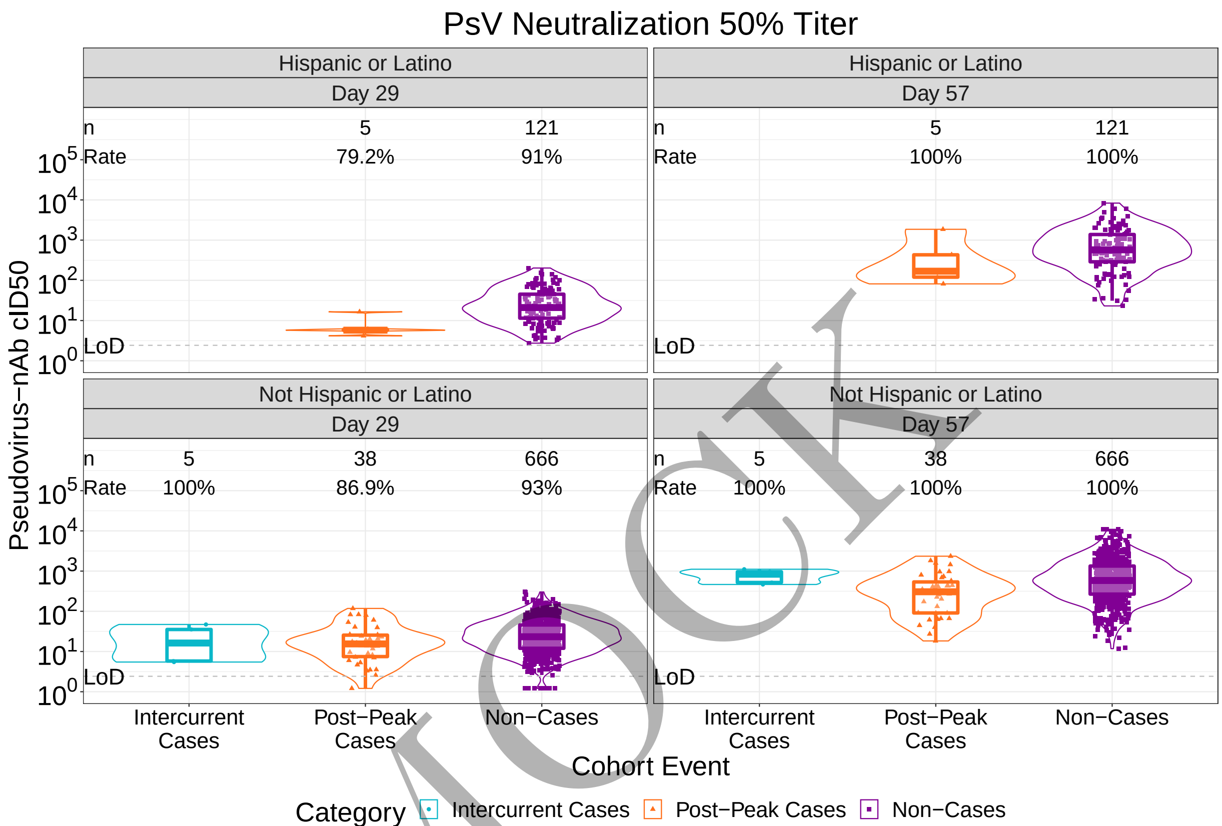

\caption{

Figure 2.5.205: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



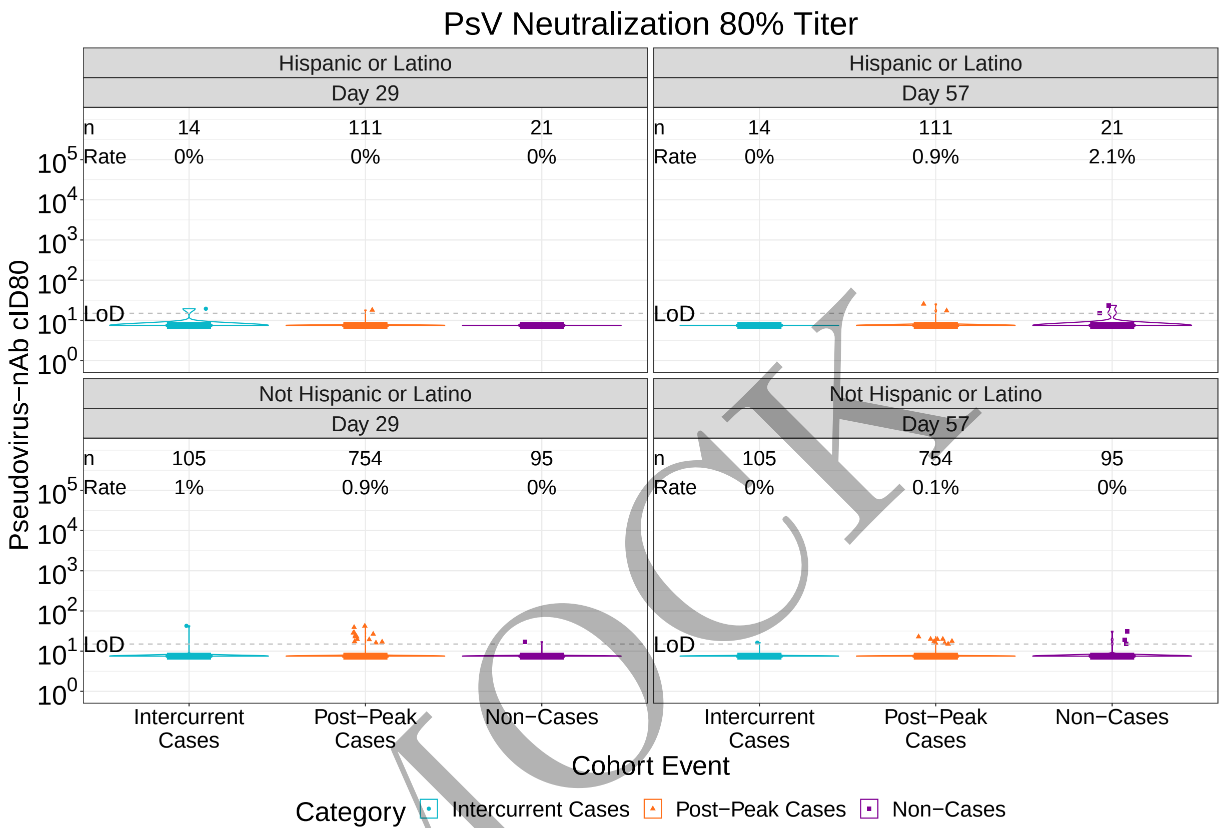

\caption{

Figure 2.5.206: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



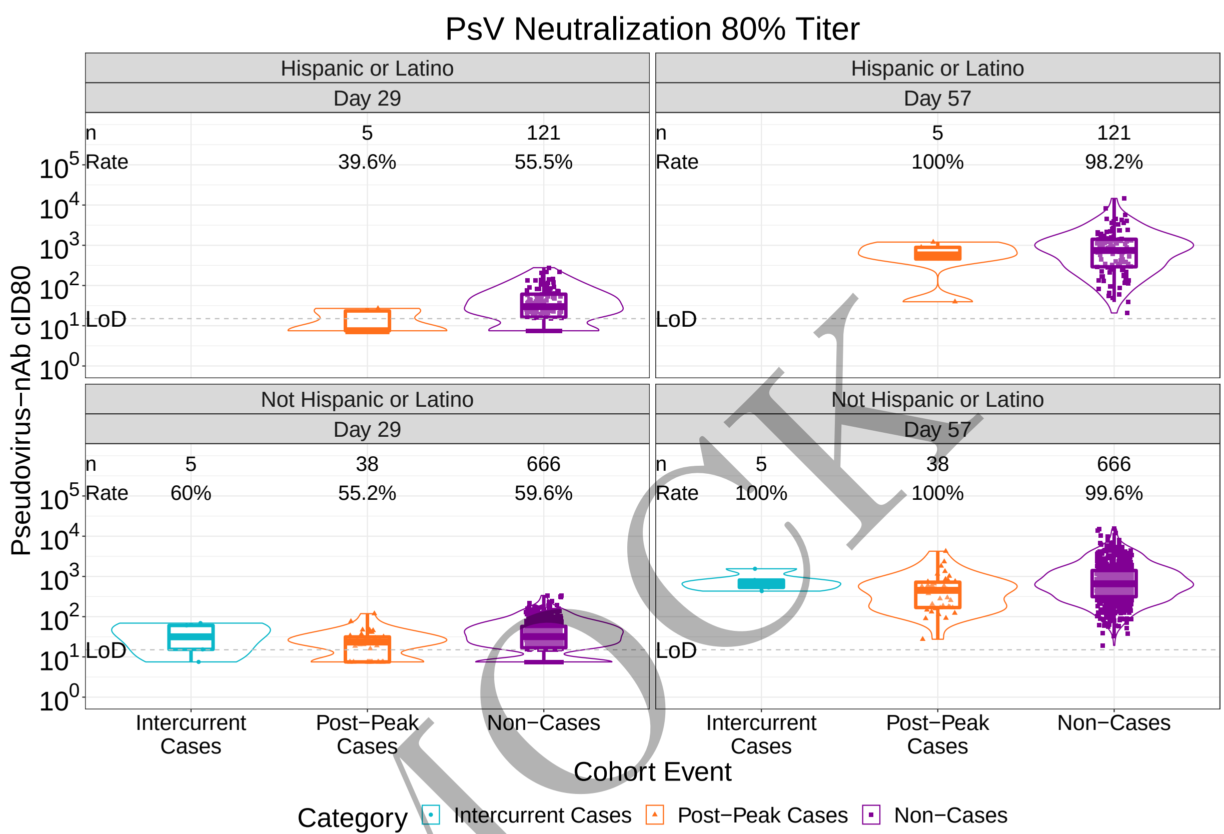

\caption{

Figure 2.5.207: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



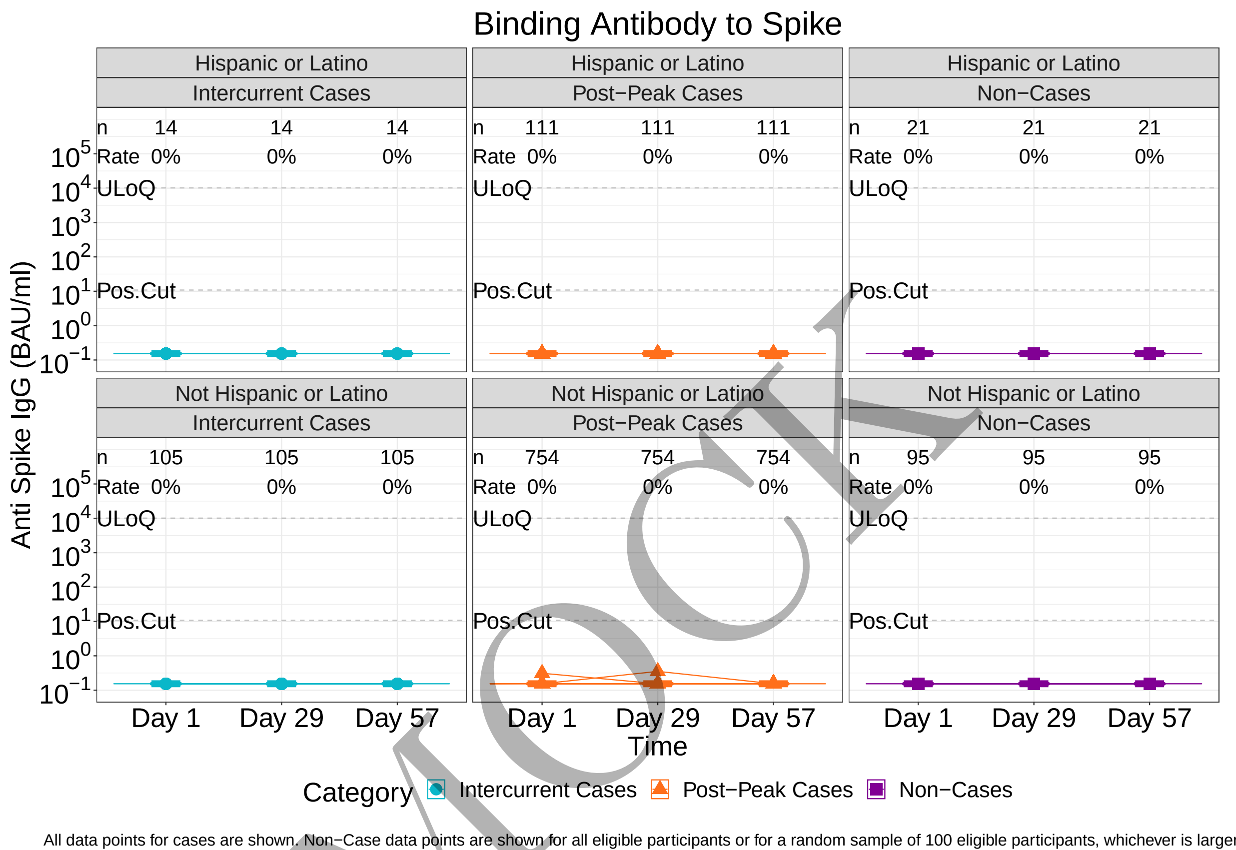

\caption{

Figure 2.5.208: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



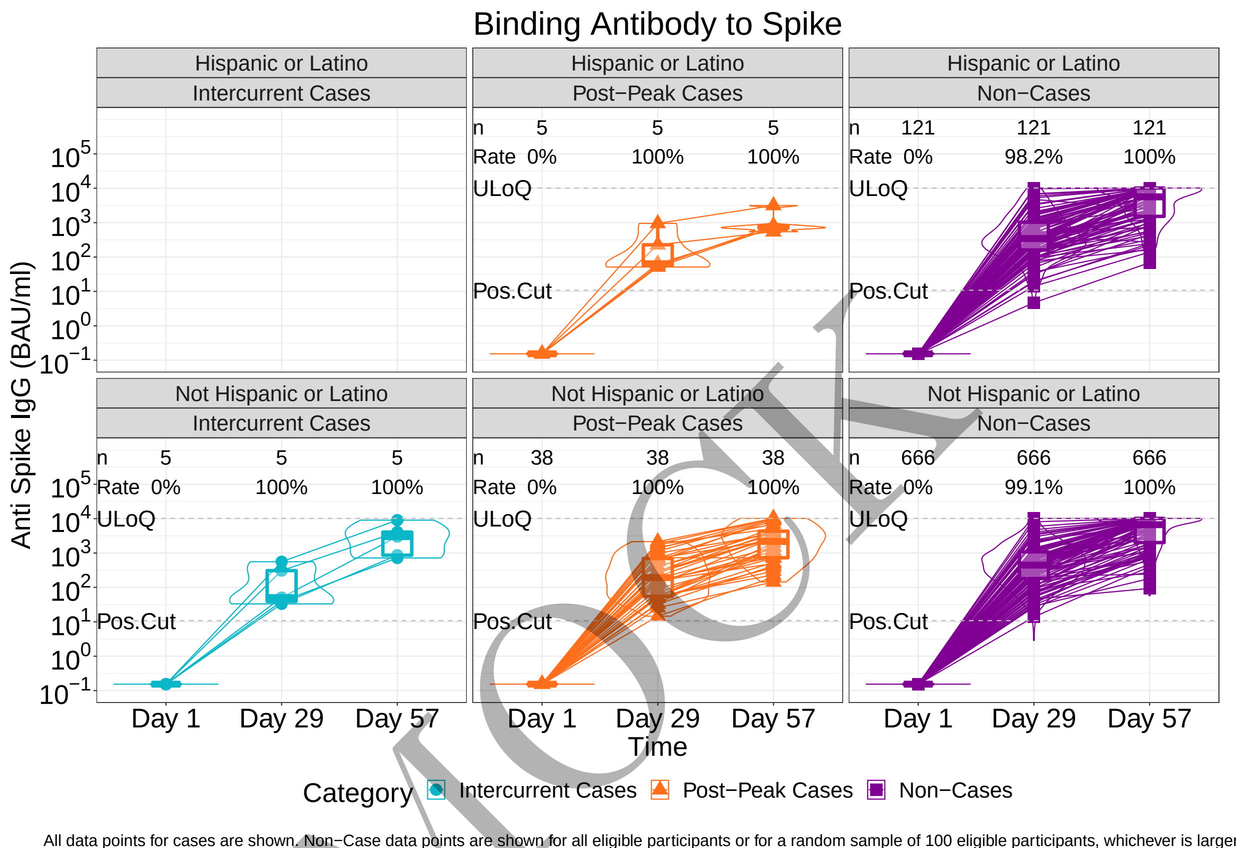

\caption{

Figure 2.5.209: lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



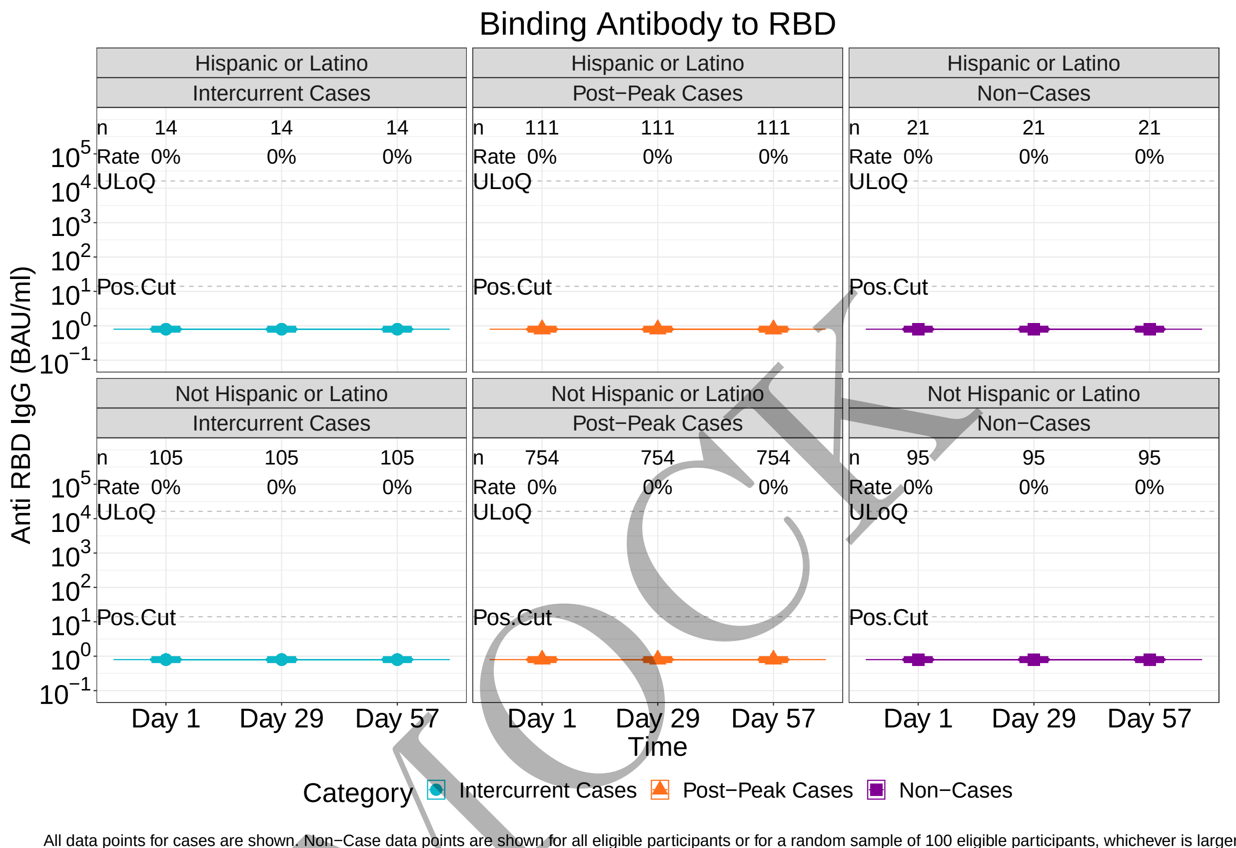

\caption{

Figure 2.5.210: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



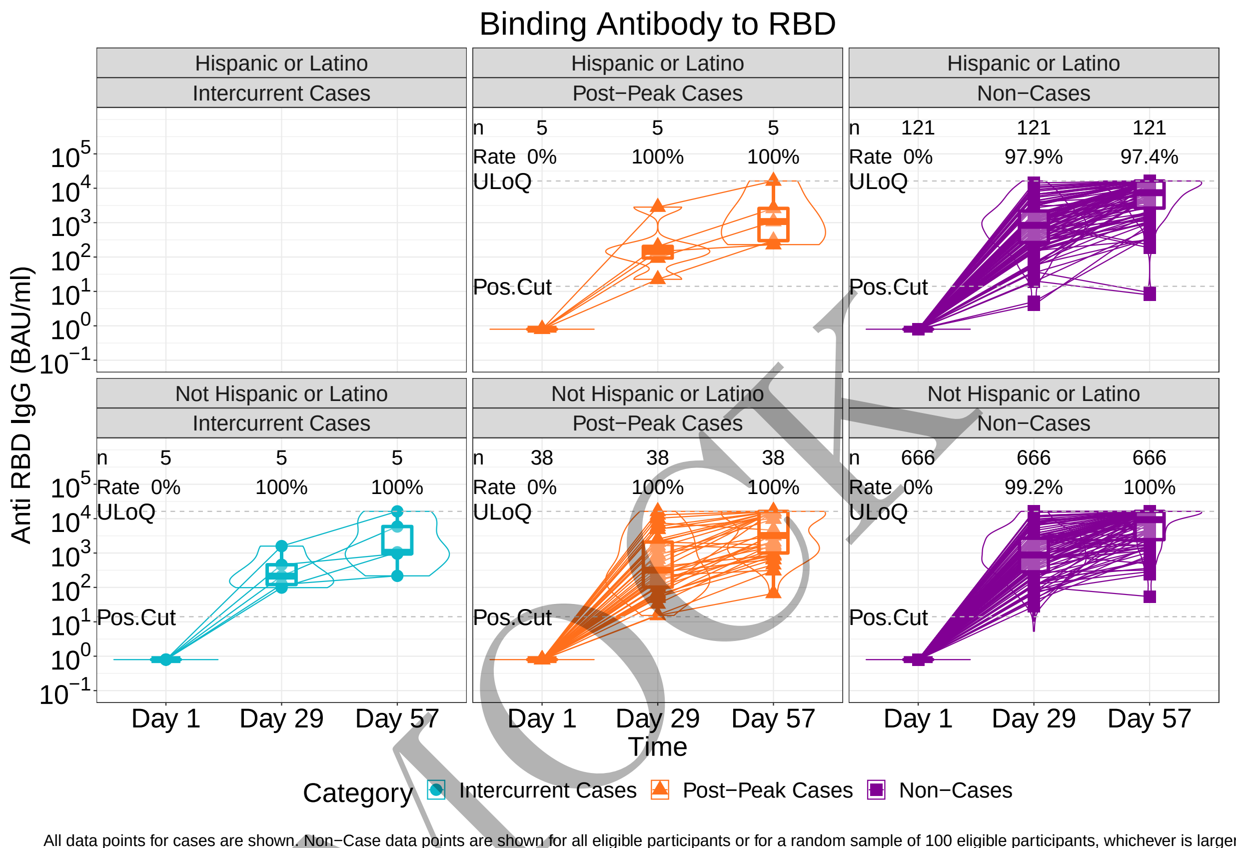

\caption{

Figure 2.5.211: lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



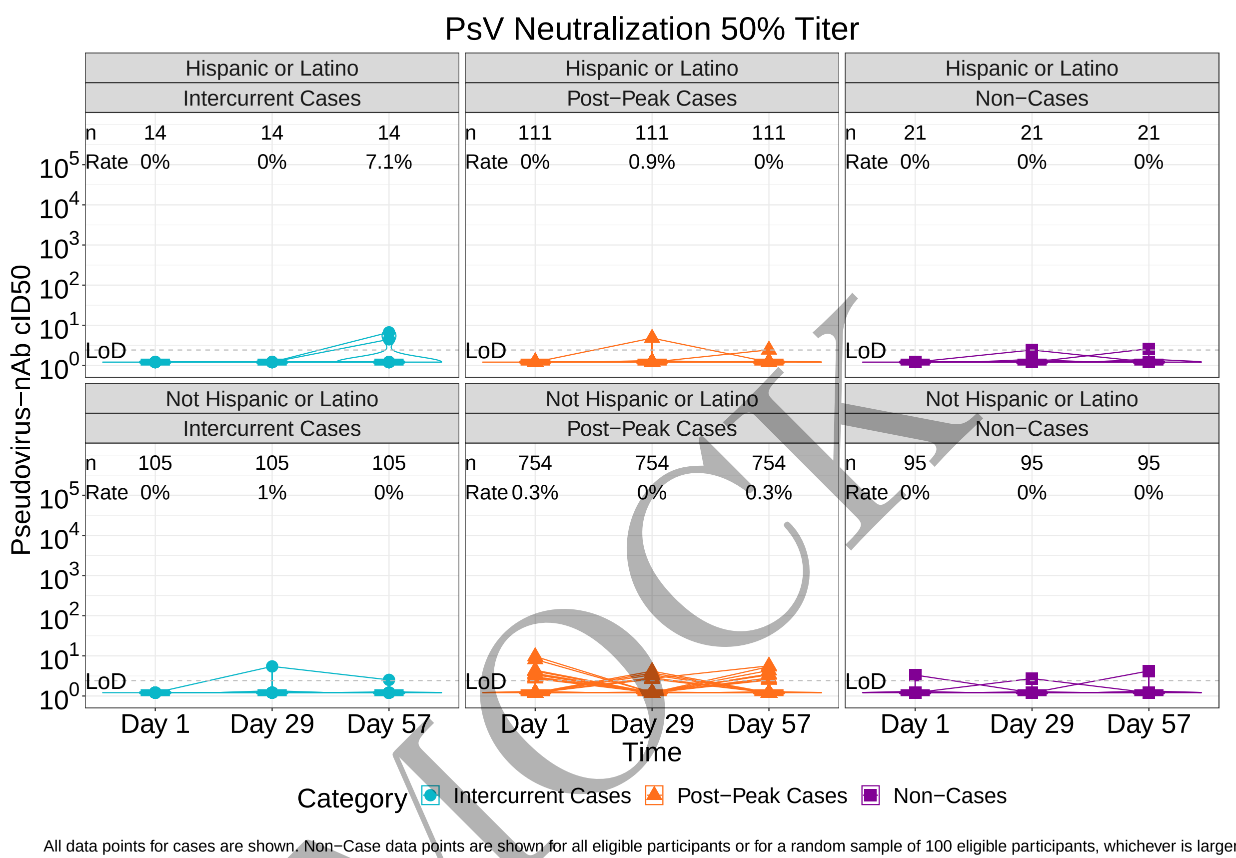

\caption{

Figure 2.5.212: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



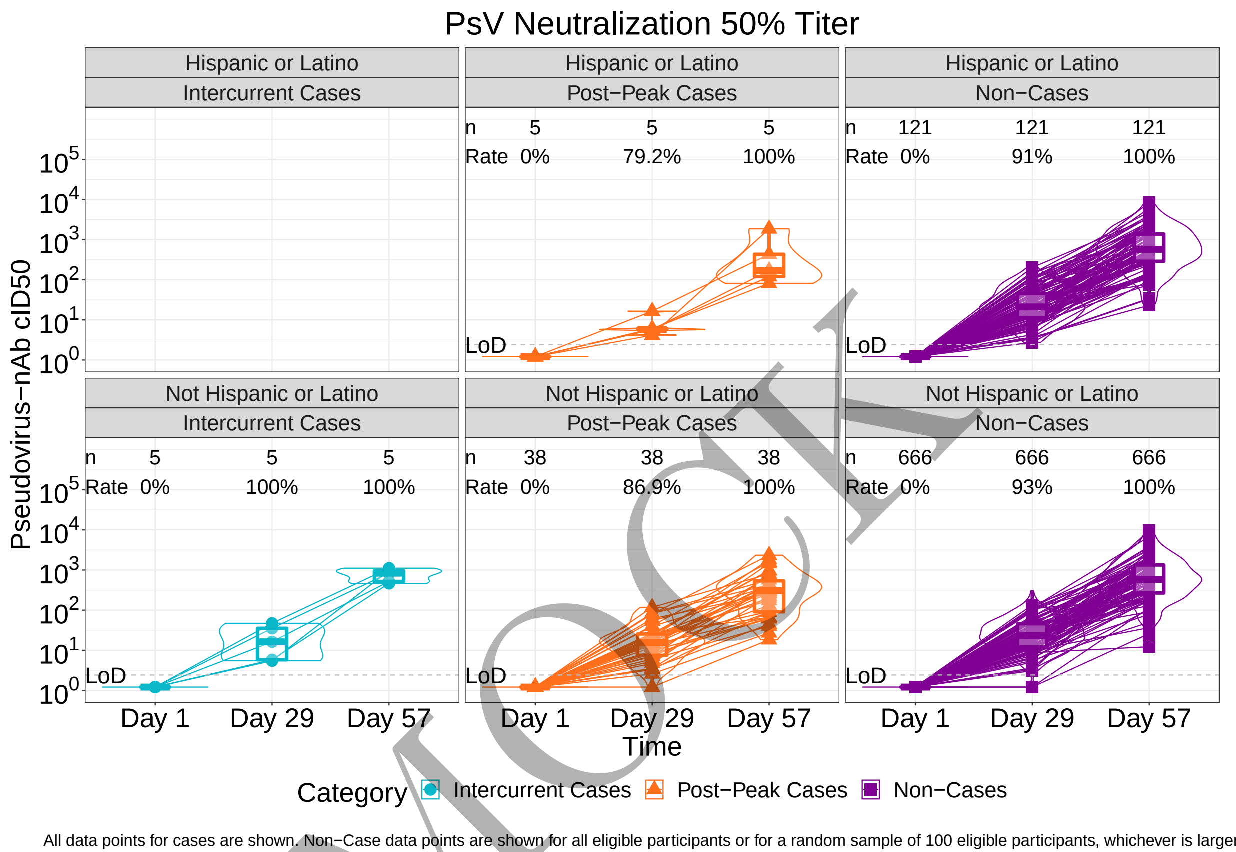

\caption{

Figure 2.5.213: lineplots of PsV Neutralization 50% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



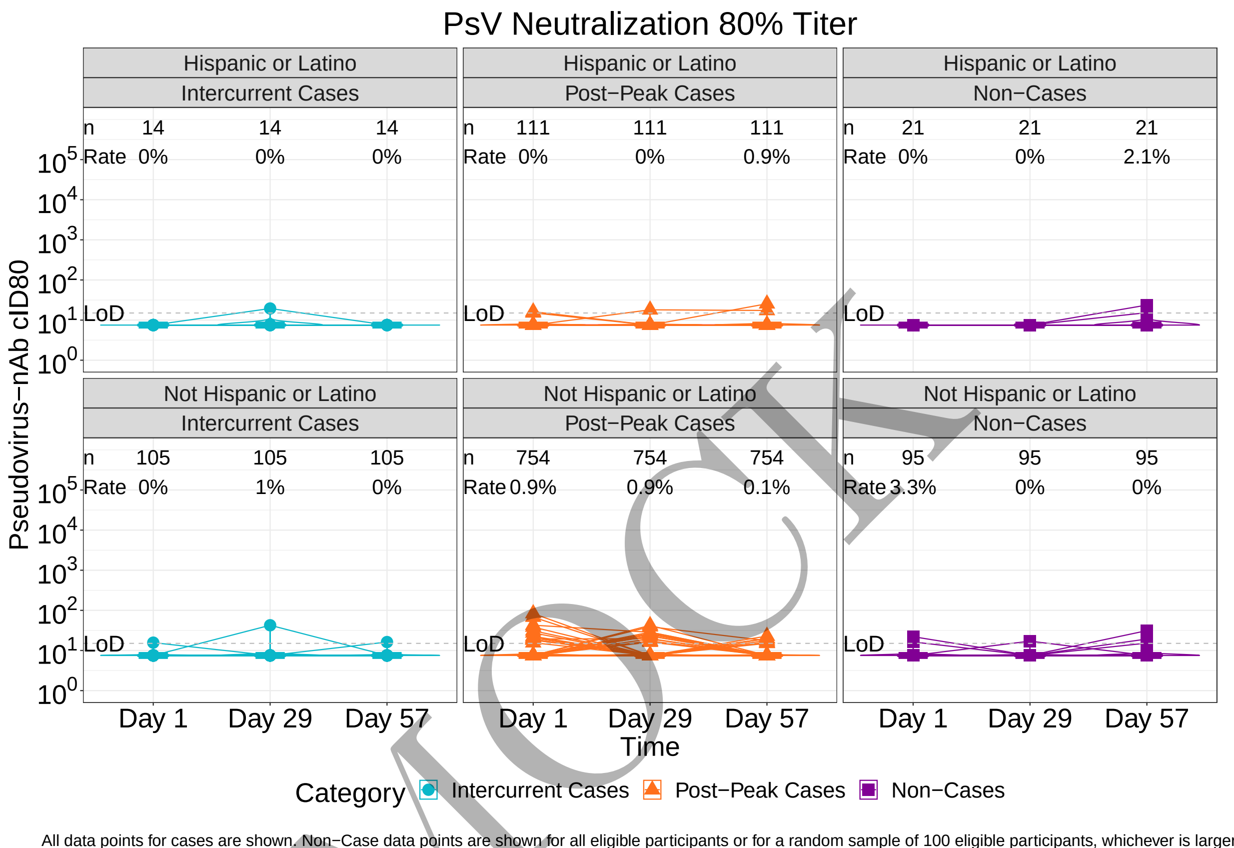

\caption{

Figure 2.5.214: lineplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



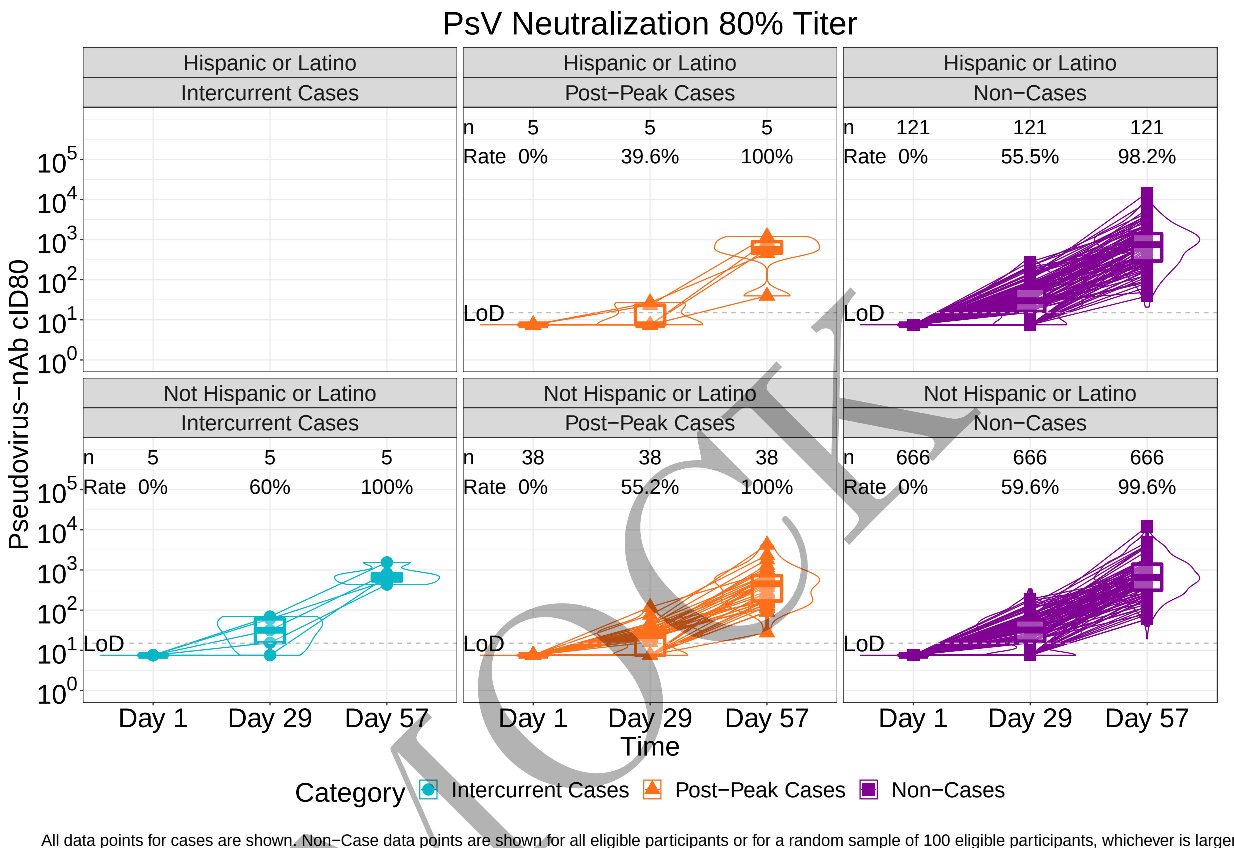

\caption{

Figure 2.5.215: lineplots of PsV Neutralization 80% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



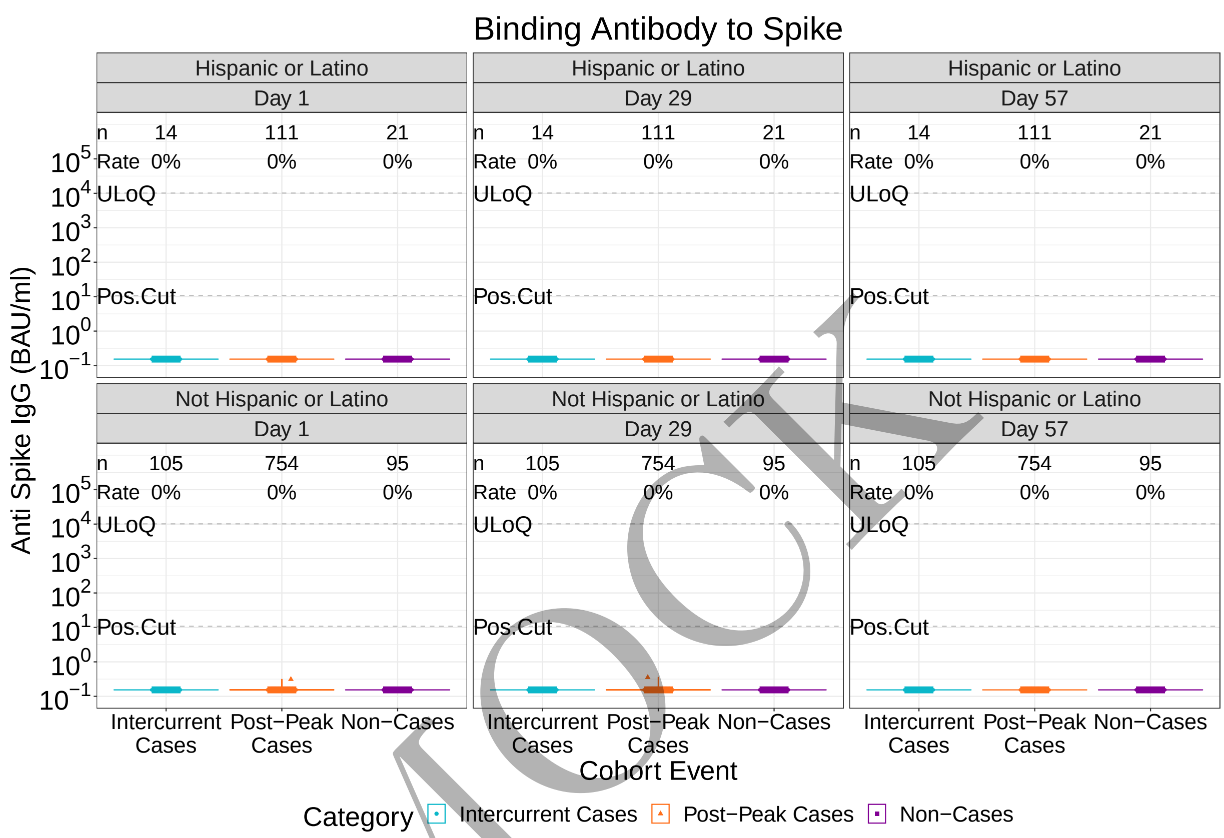

\caption{

Figure 2.5.216: lineplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



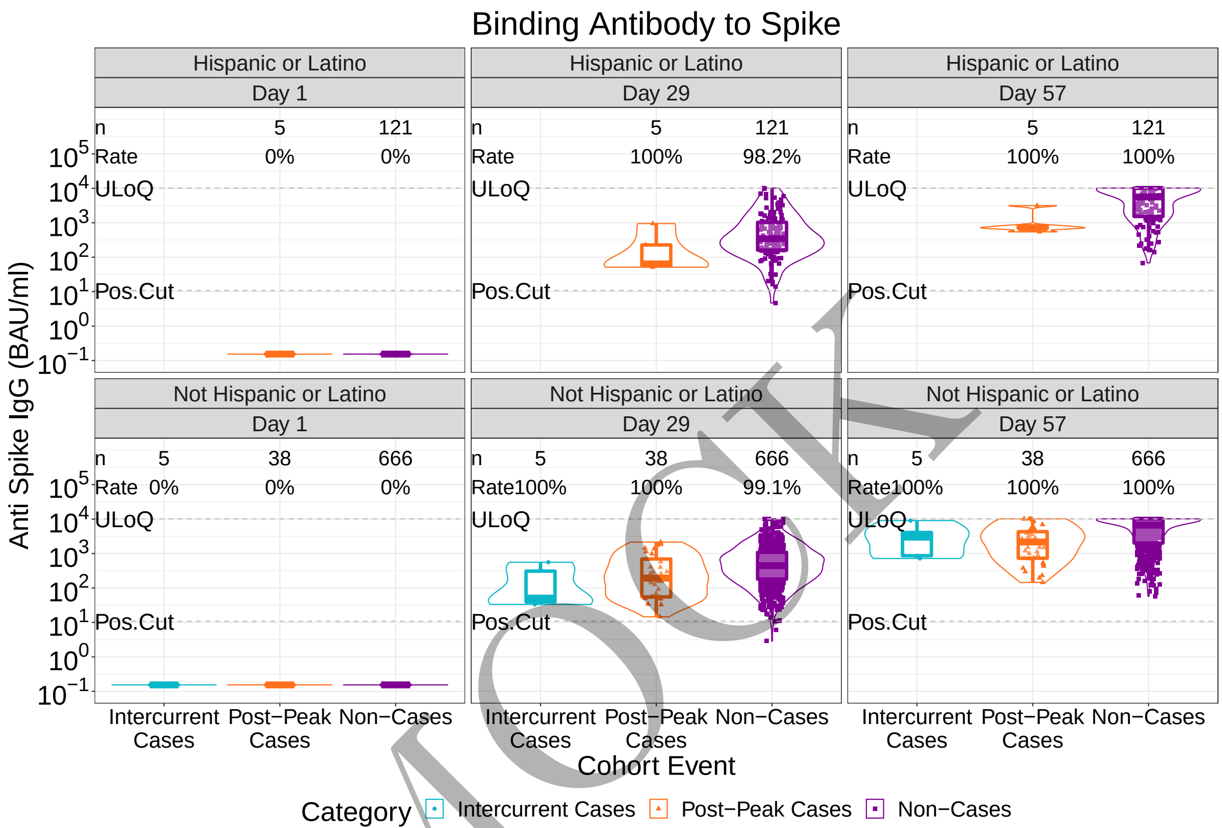

\caption{

Figure 2.5.217: violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



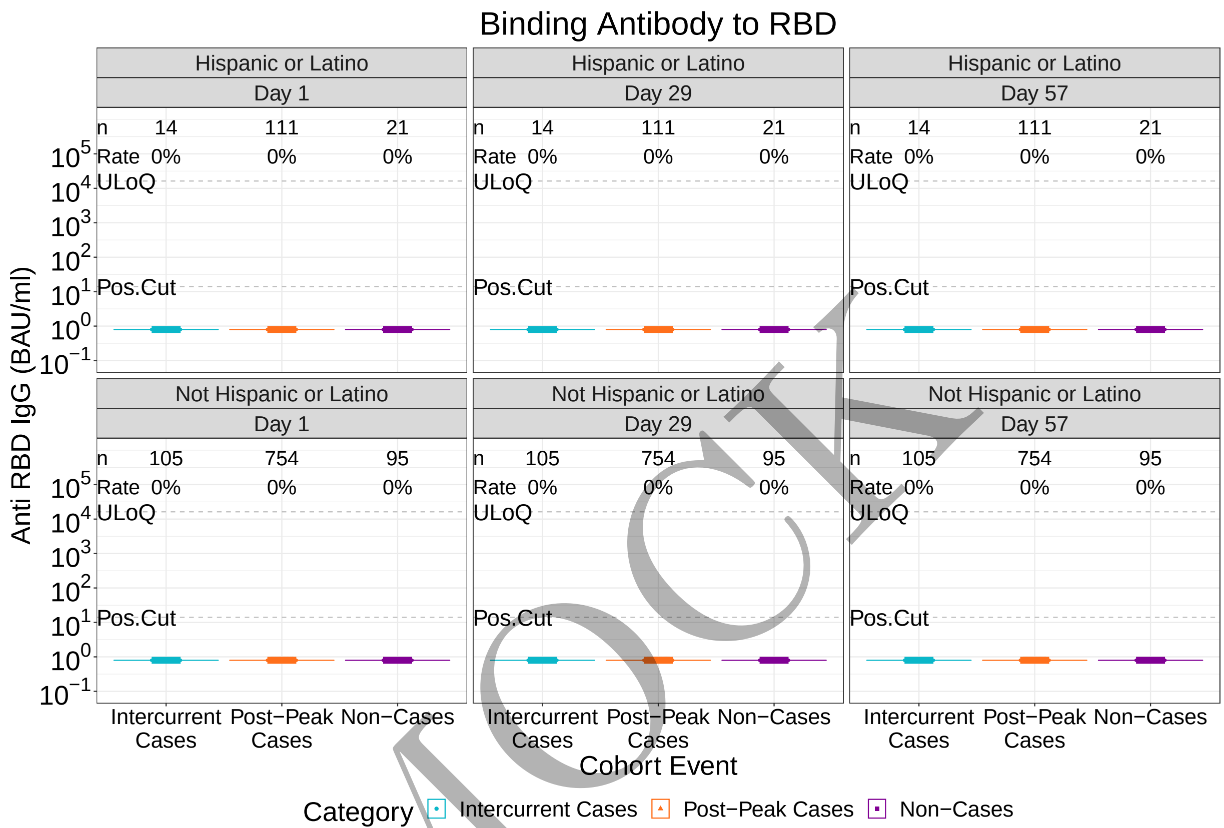

\caption{

Figure 2.5.218: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



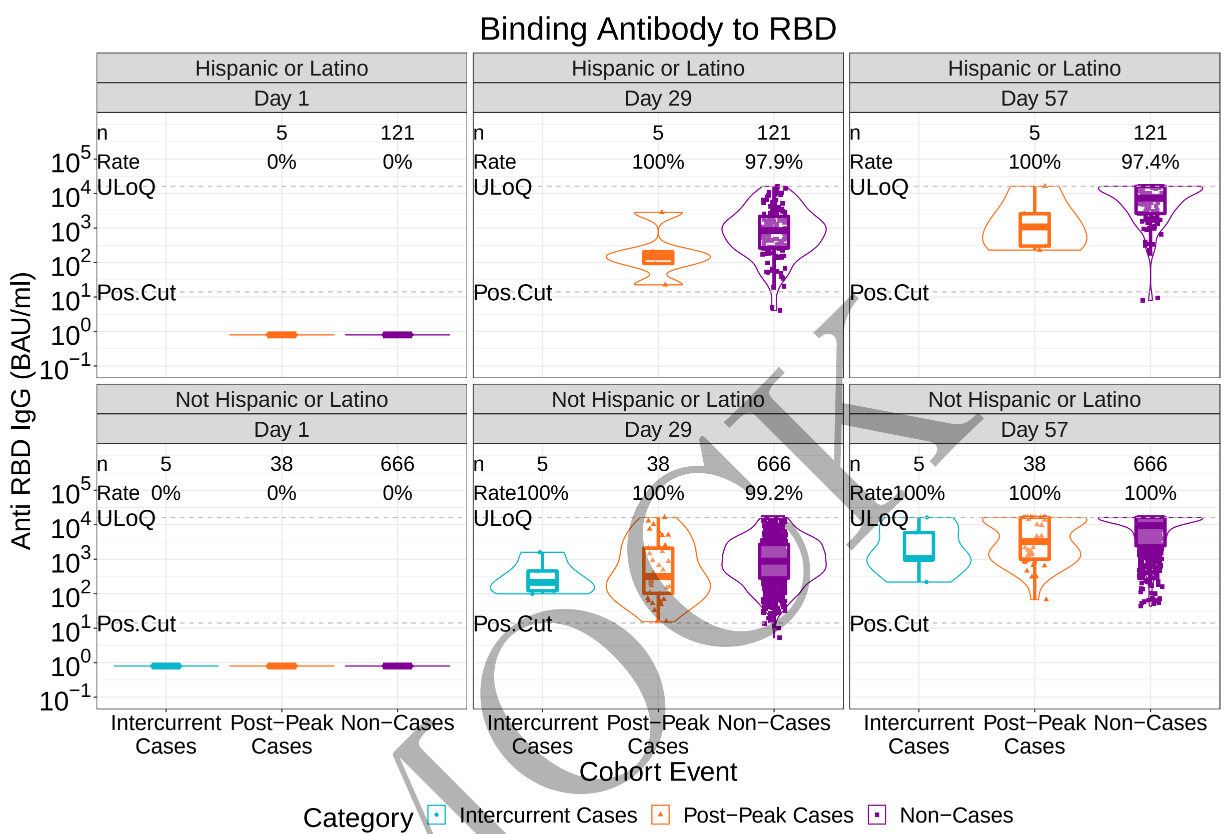

\caption{

Figure 2.5.219: violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}





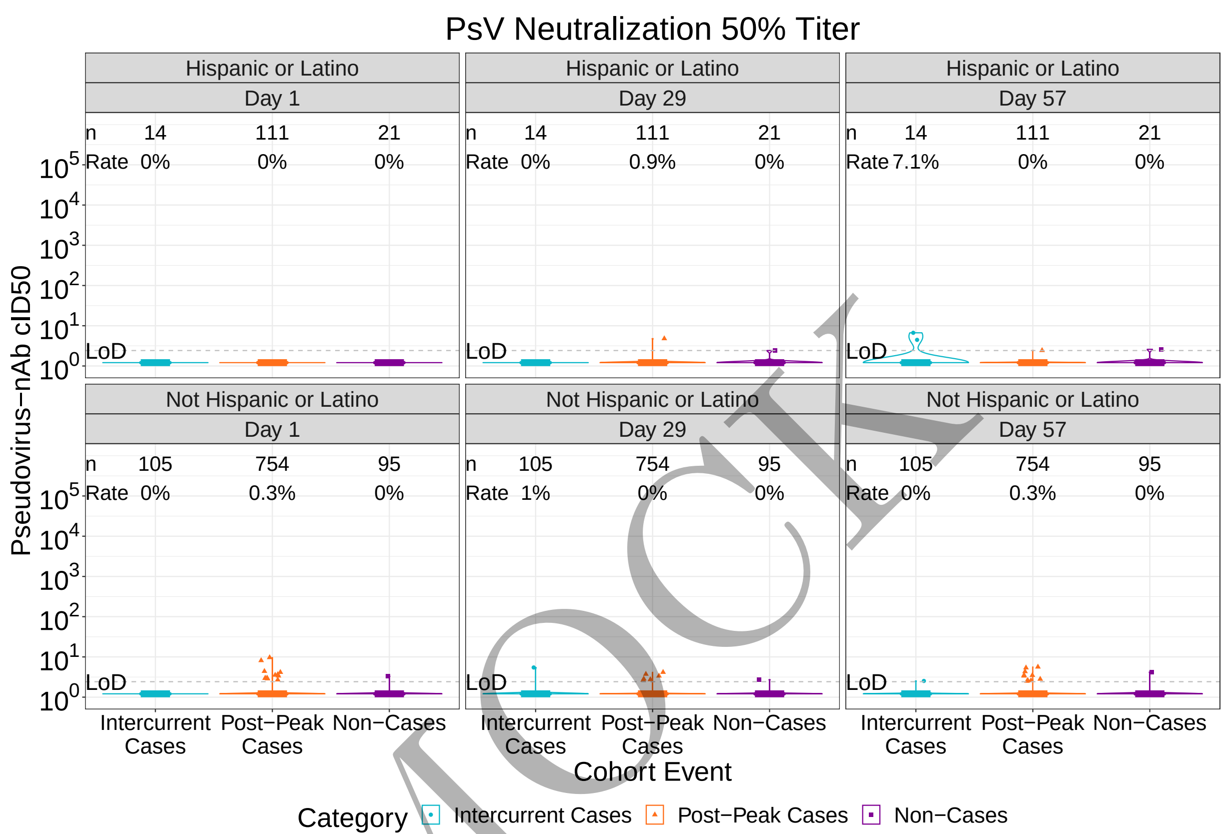

\caption{

Figure 2.5.220: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



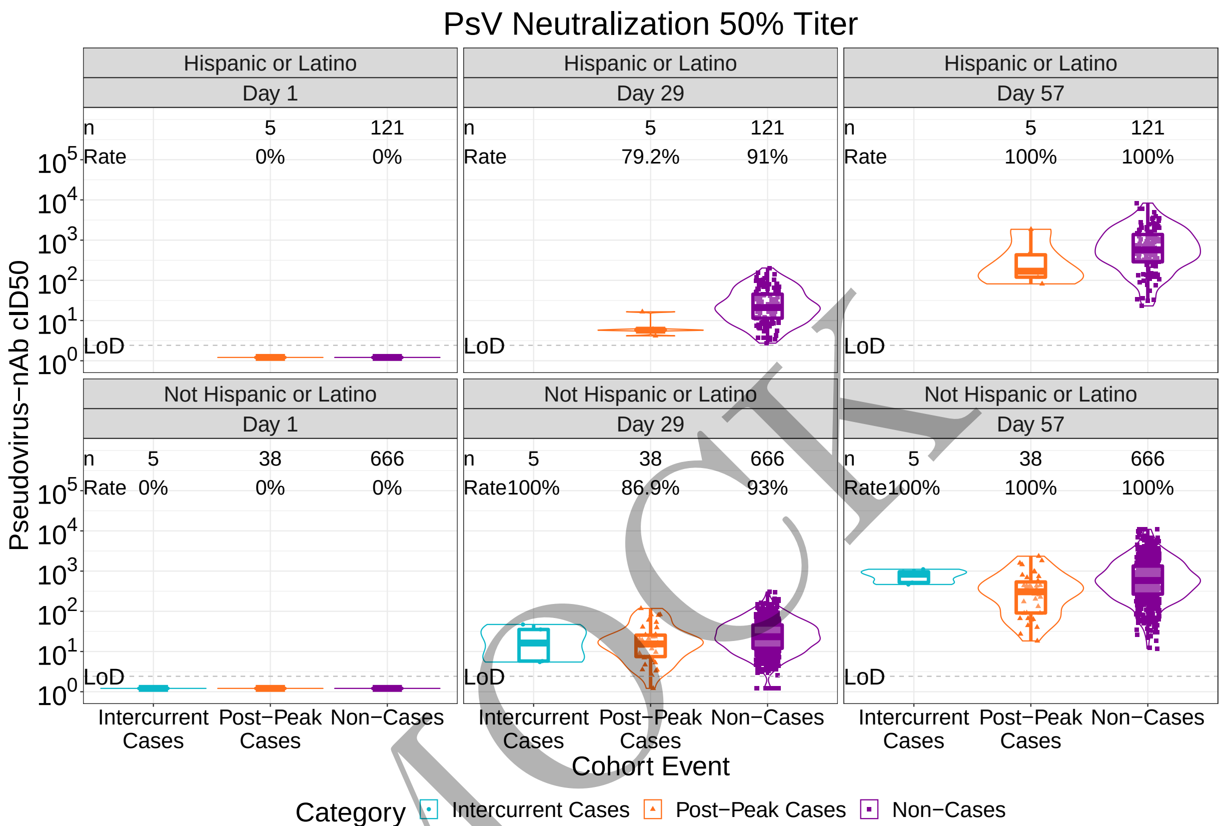

\caption{

Figure 2.5.221: violinplots of PsV Neutralization 50% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



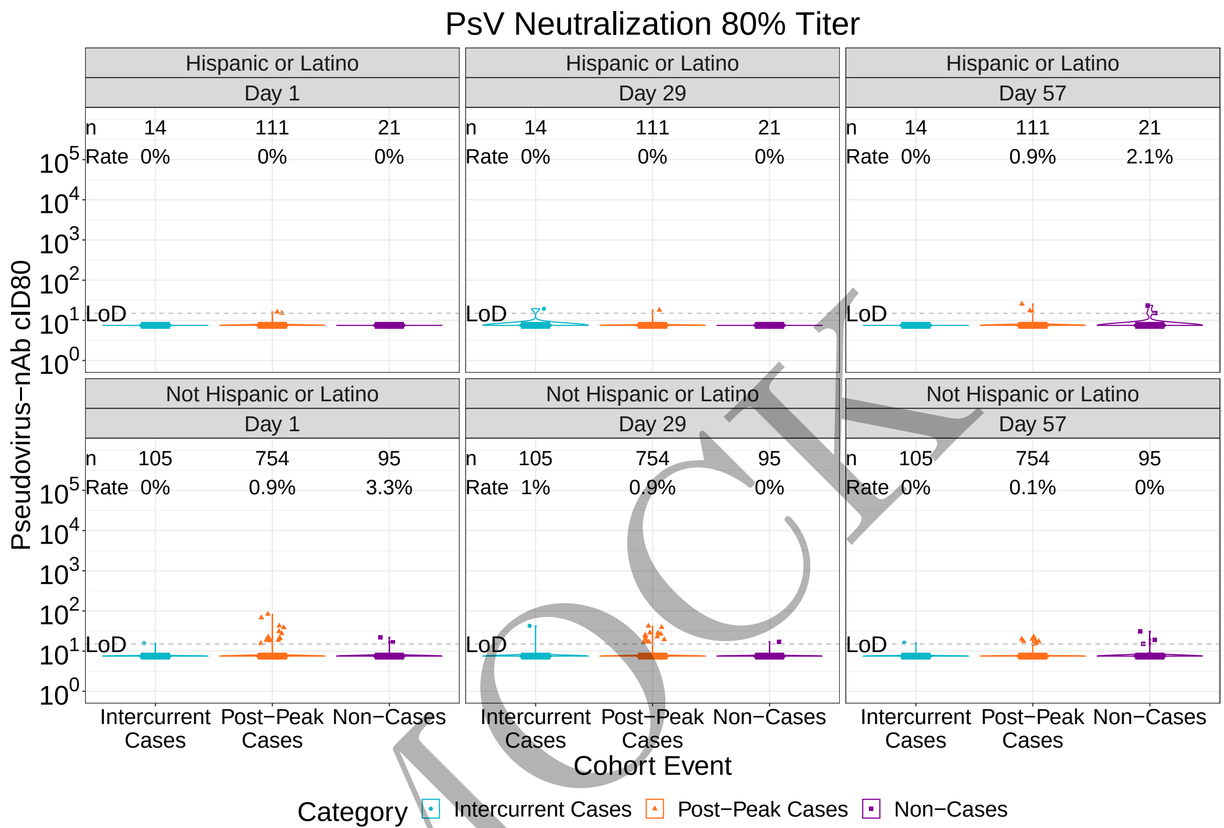

\caption{

Figure 2.5.222: violinplots of PsV Neutralization 50% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



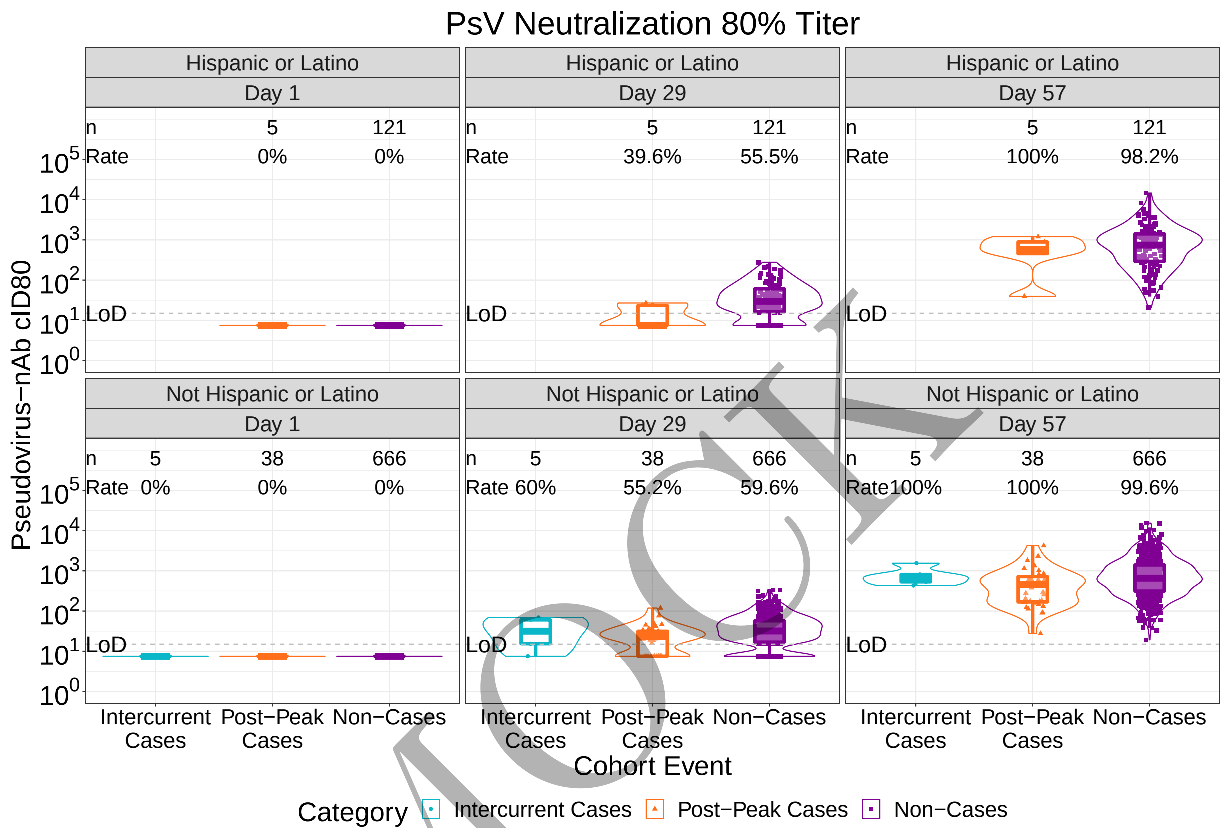

\caption{

Figure 2.5.223: violinplots of PsV Neutralization 80% Titer: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")

\begin{figure}



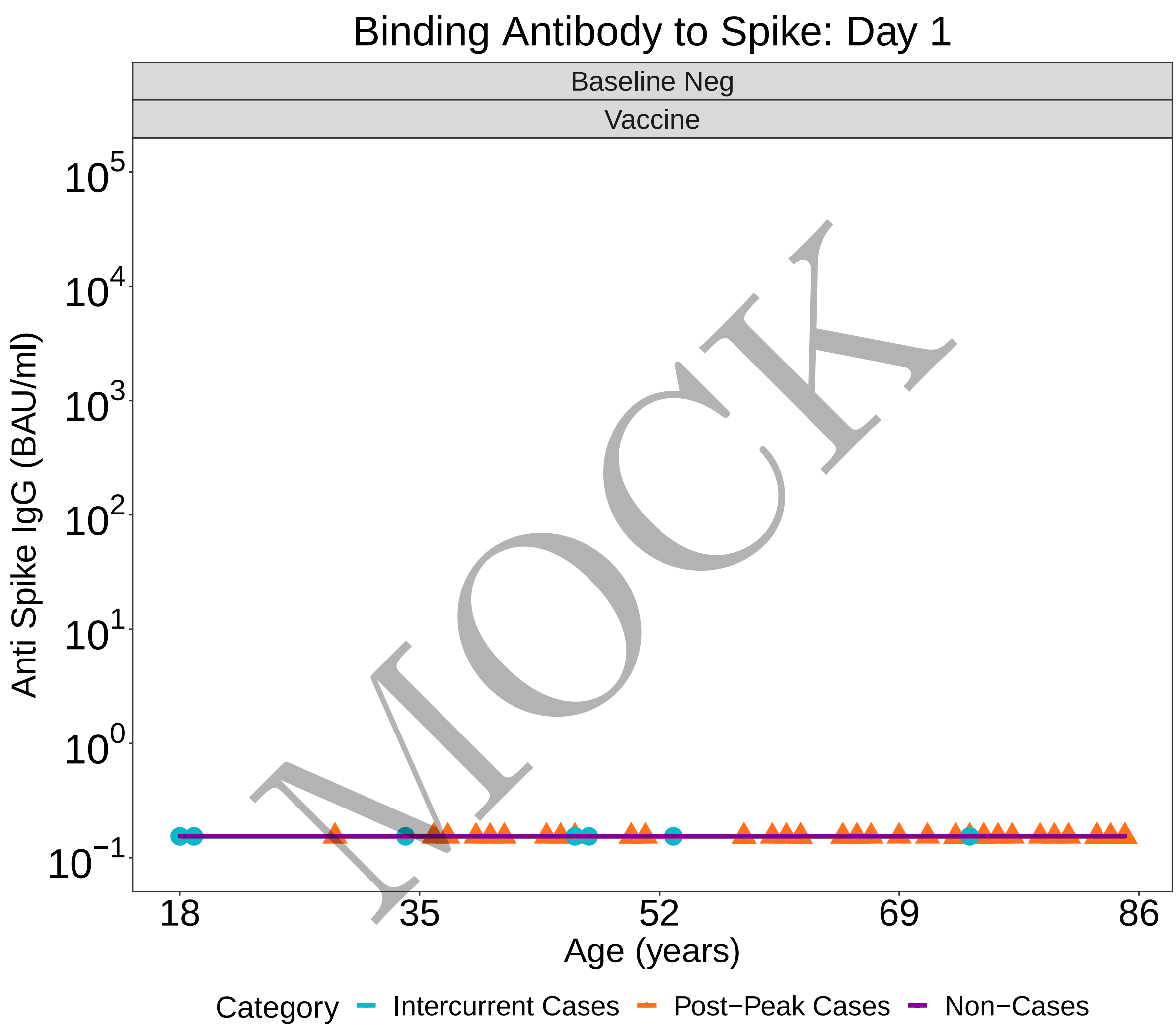

\caption{

Figure 2.5.224: violinplots of PsV Neutralization 80% Titer: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

} \end{figure}

## 3.6 Scatter plots

\begin{figure}[H]

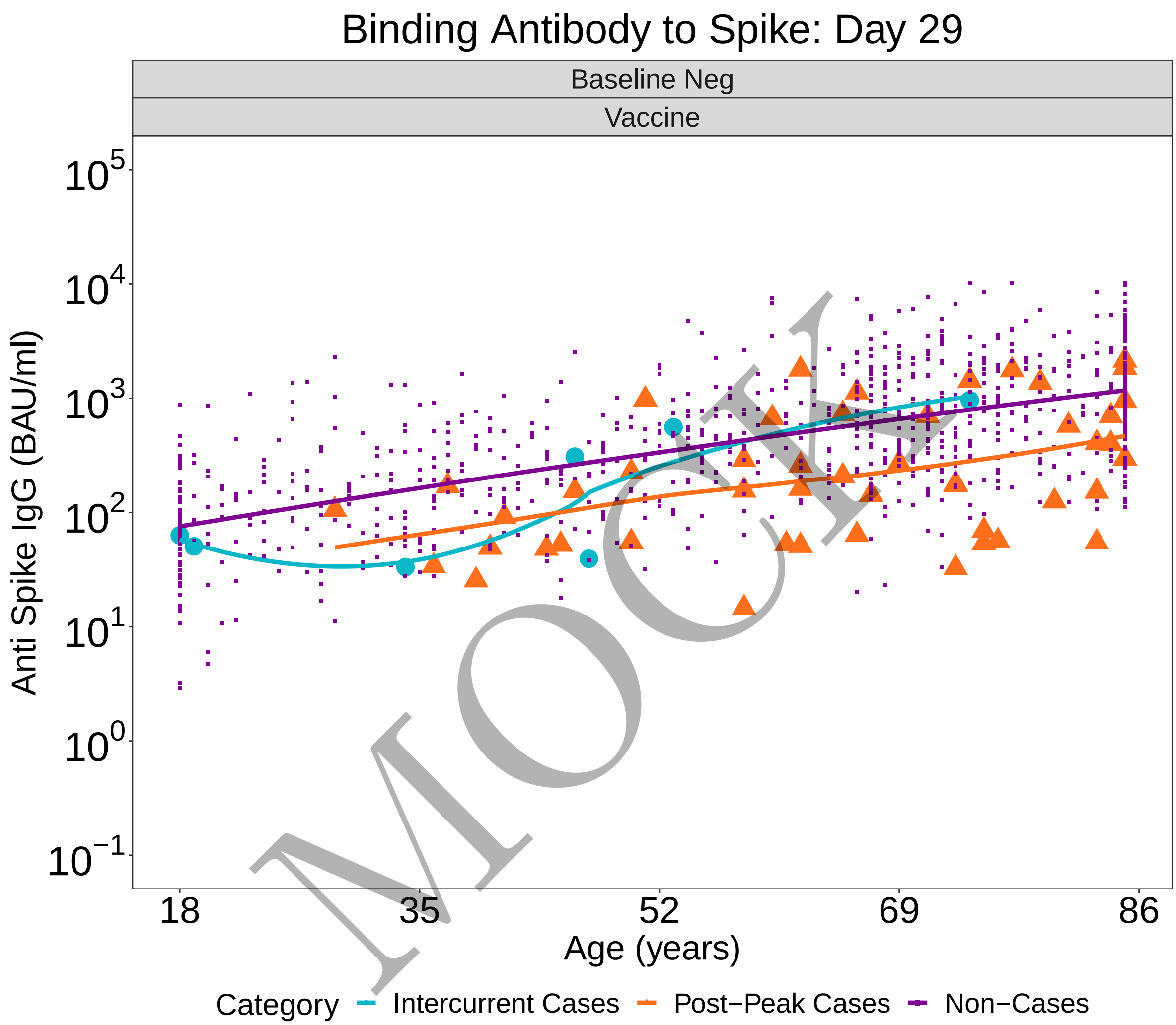



\caption{

Figure 2.6.1: scatterplots of Binding Antibody to Spike vs Age: baseline negative vaccine arm at day 1

} \end{figure}

\begin{figure}[H]

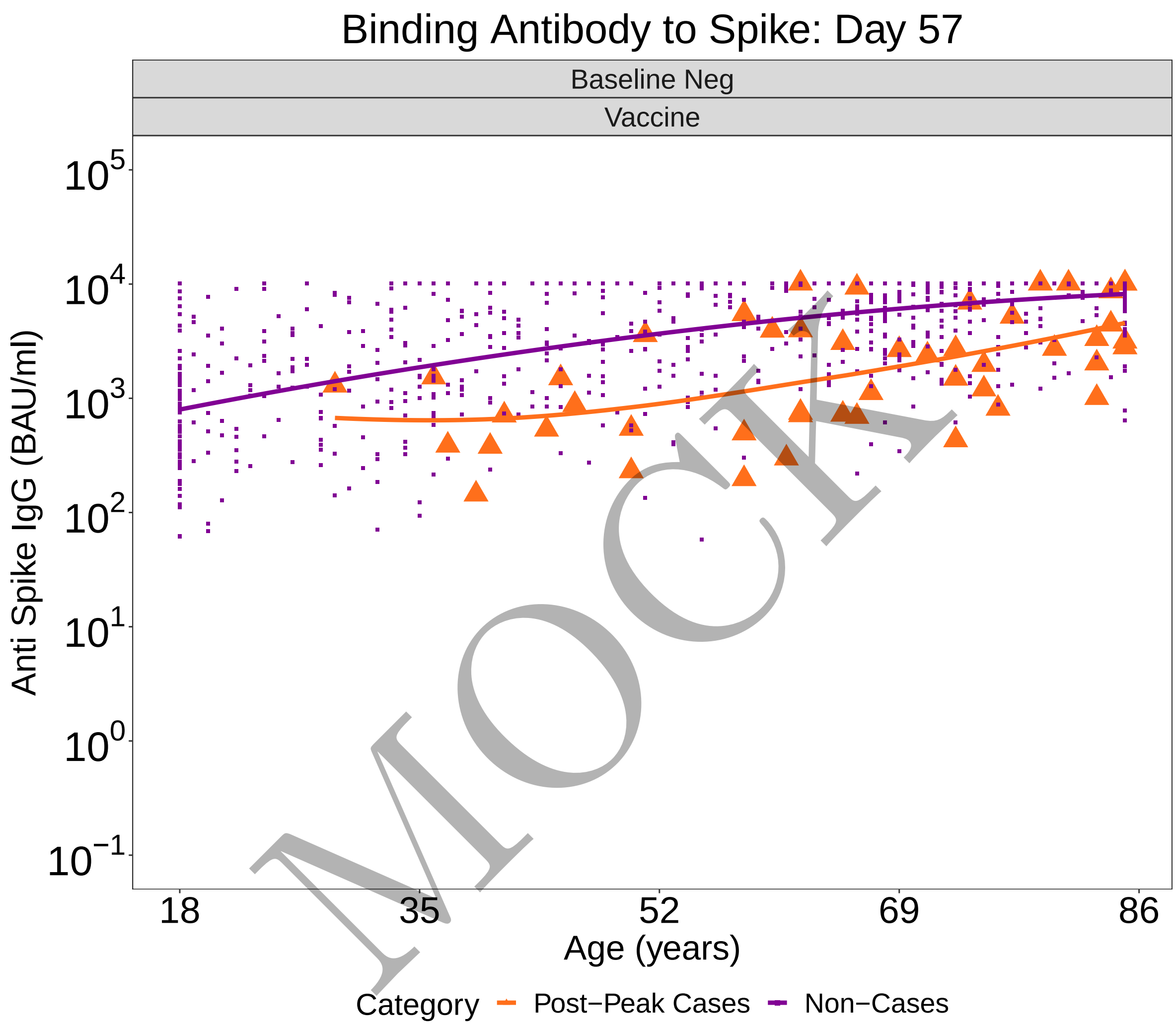



\caption{

Figure 2.6.2: scatterplots of Binding Antibody to Spike vs Age: baseline negative vaccine arm at day 29

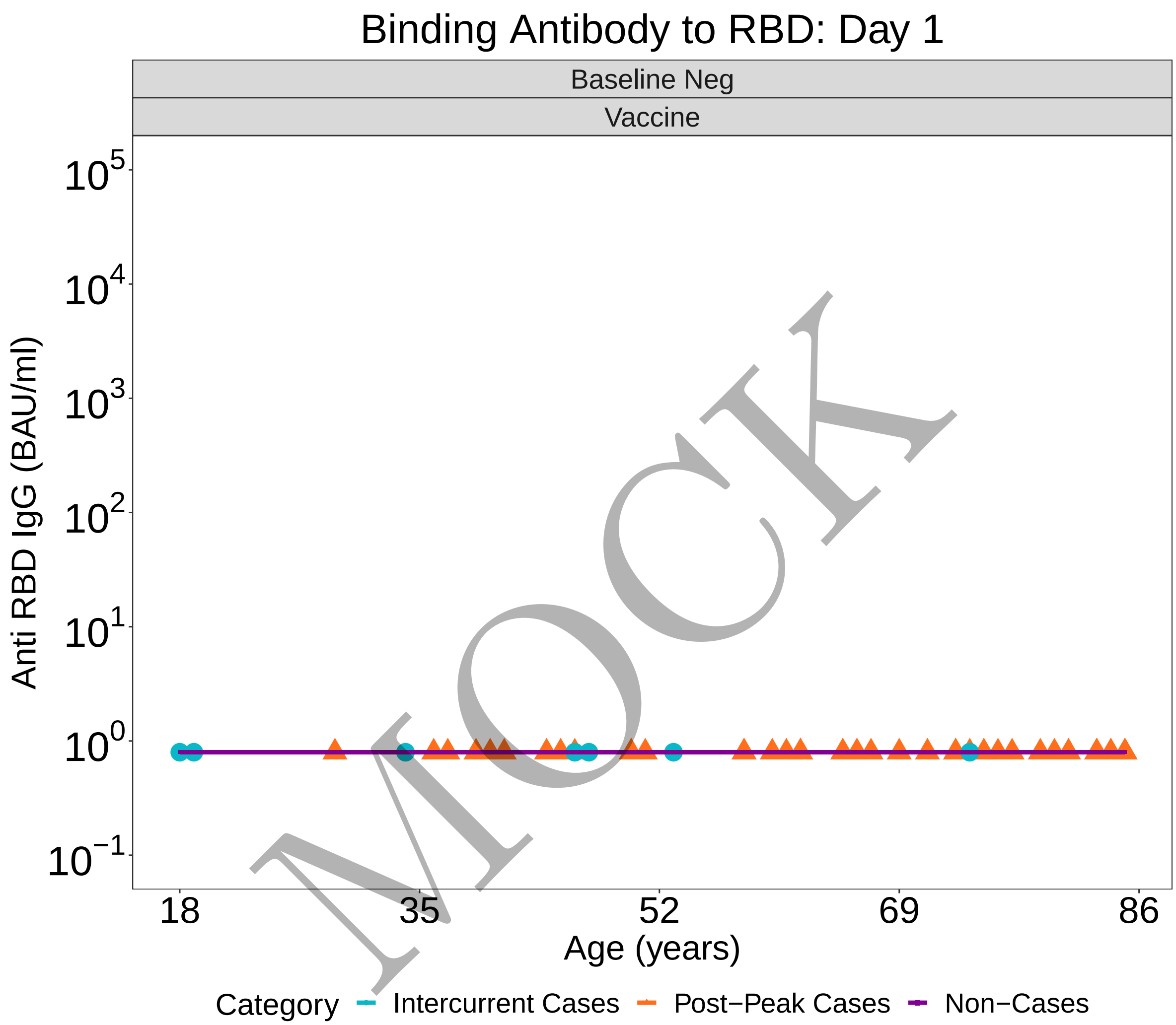
} \end{figure}

\begin{figure}[H]




\caption{
Figure 2.6.3: scatterplots of Binding Antibody to Spike vs Age: baseline negative vaccine arm at day 57
} \end{figure}

\begin{figure}[H]

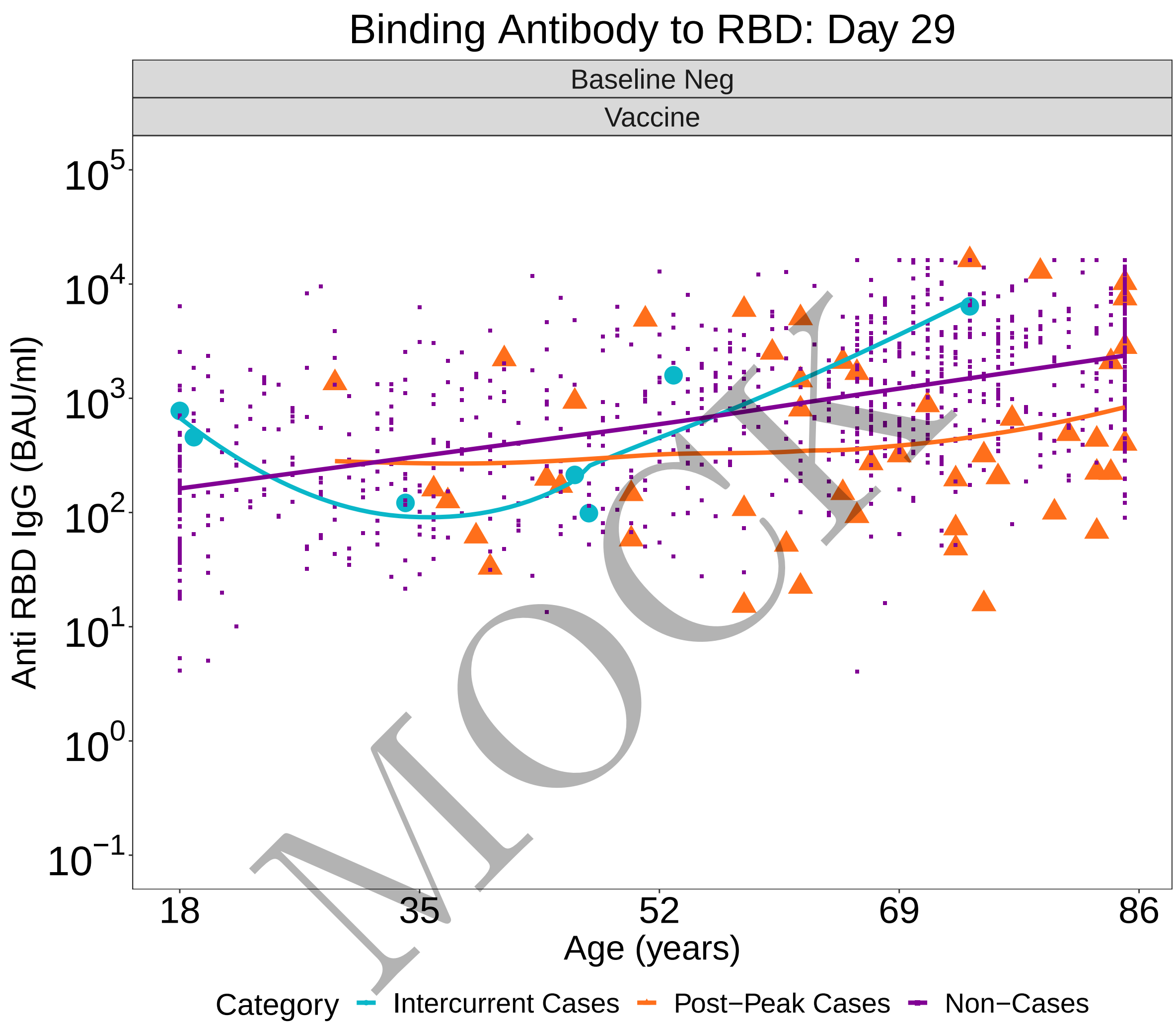



\caption{

Figure 2.6.4: scatterplots of Binding Antibody to RBD vs Age: baseline negative vaccine arm at day 1

} \end{figure}

\begin{figure}[H]

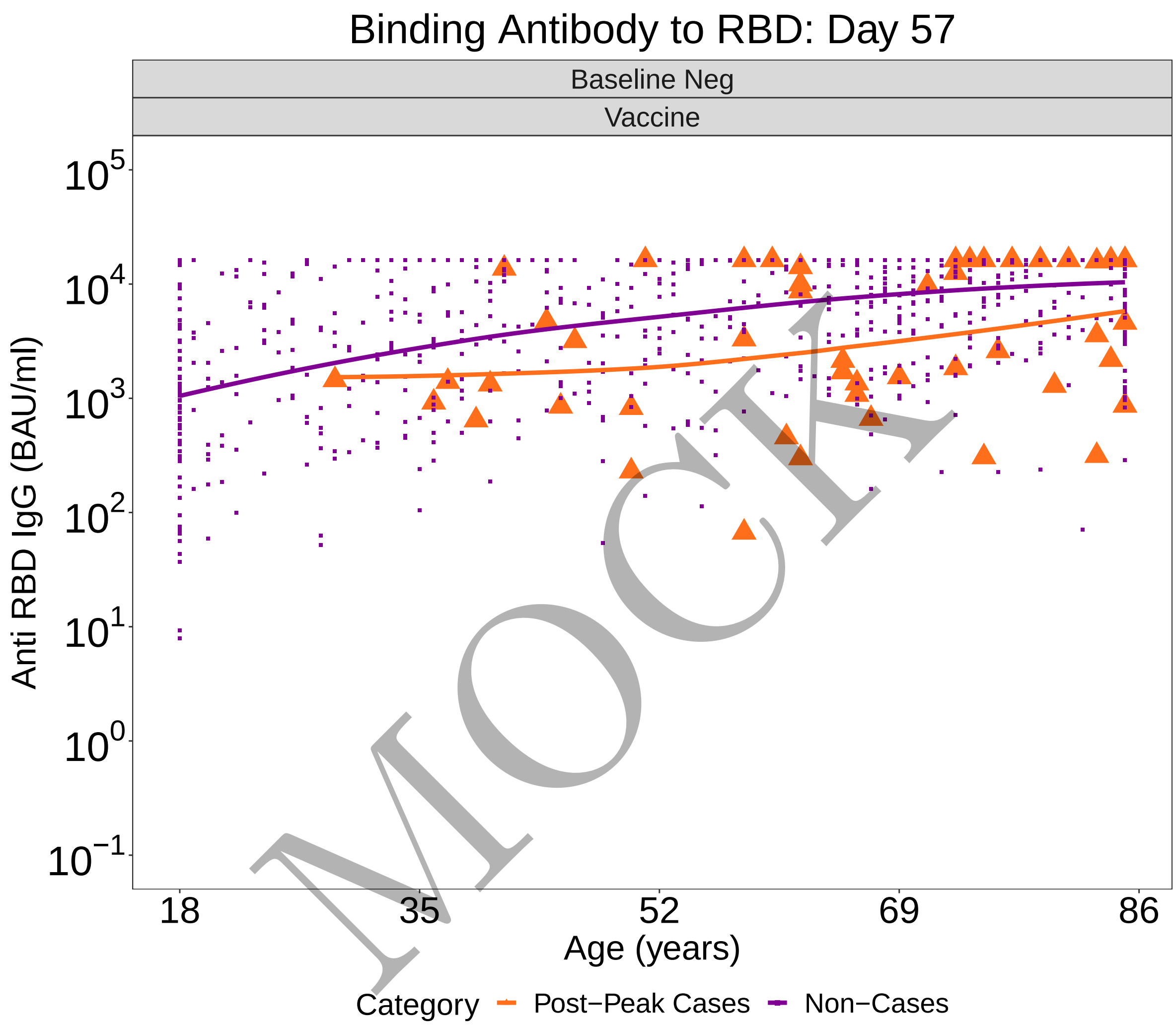



\caption{

Figure 2.6.5: scatterplots of Binding Antibody to RBD vs Age: baseline negative vaccine arm at day 29

} \end{figure}

\begin{figure}[H]

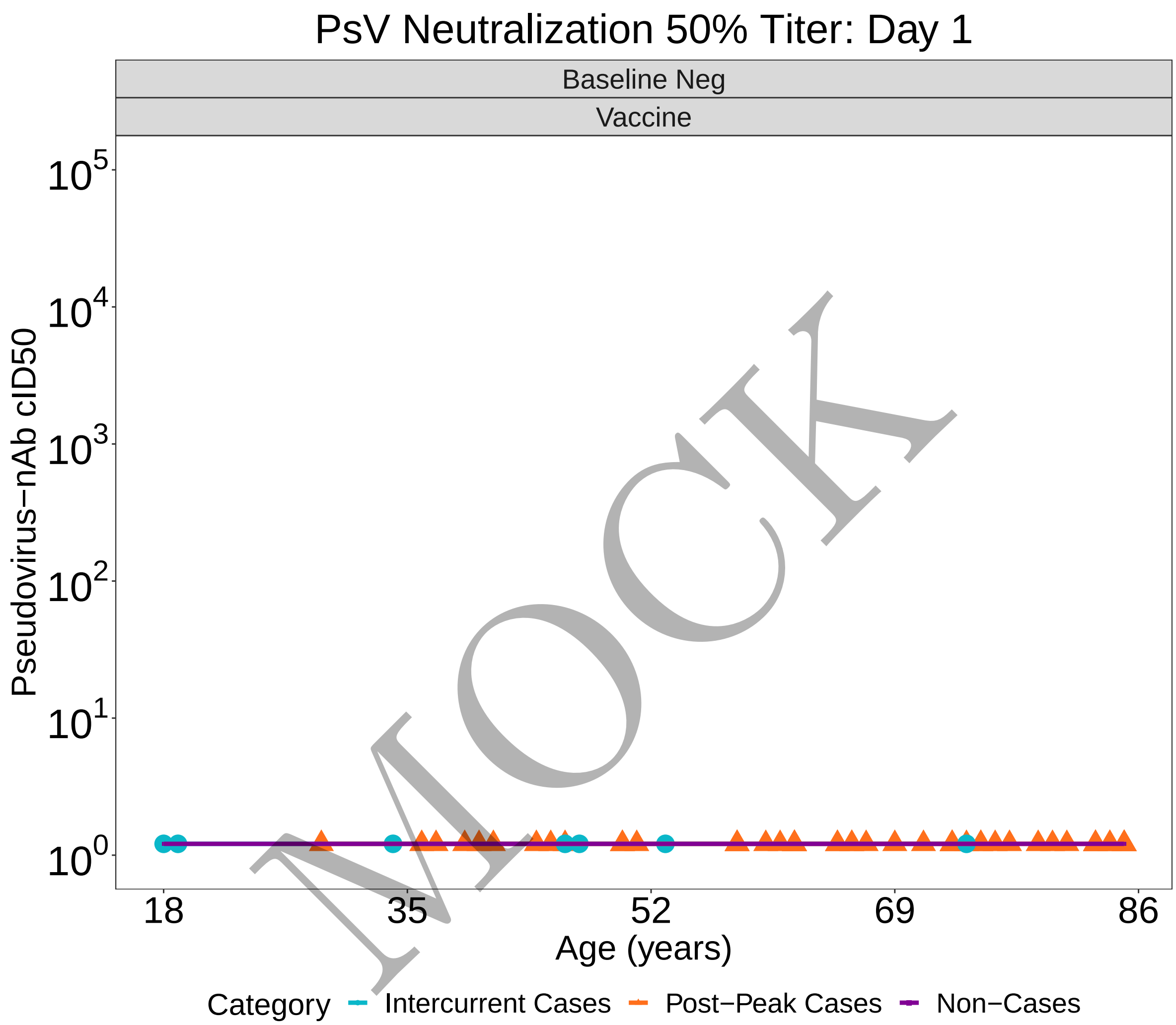



\caption{

Figure 2.6.6: scatterplots of Binding Antibody to RBD vs Age: baseline negative vaccine arm at day 57

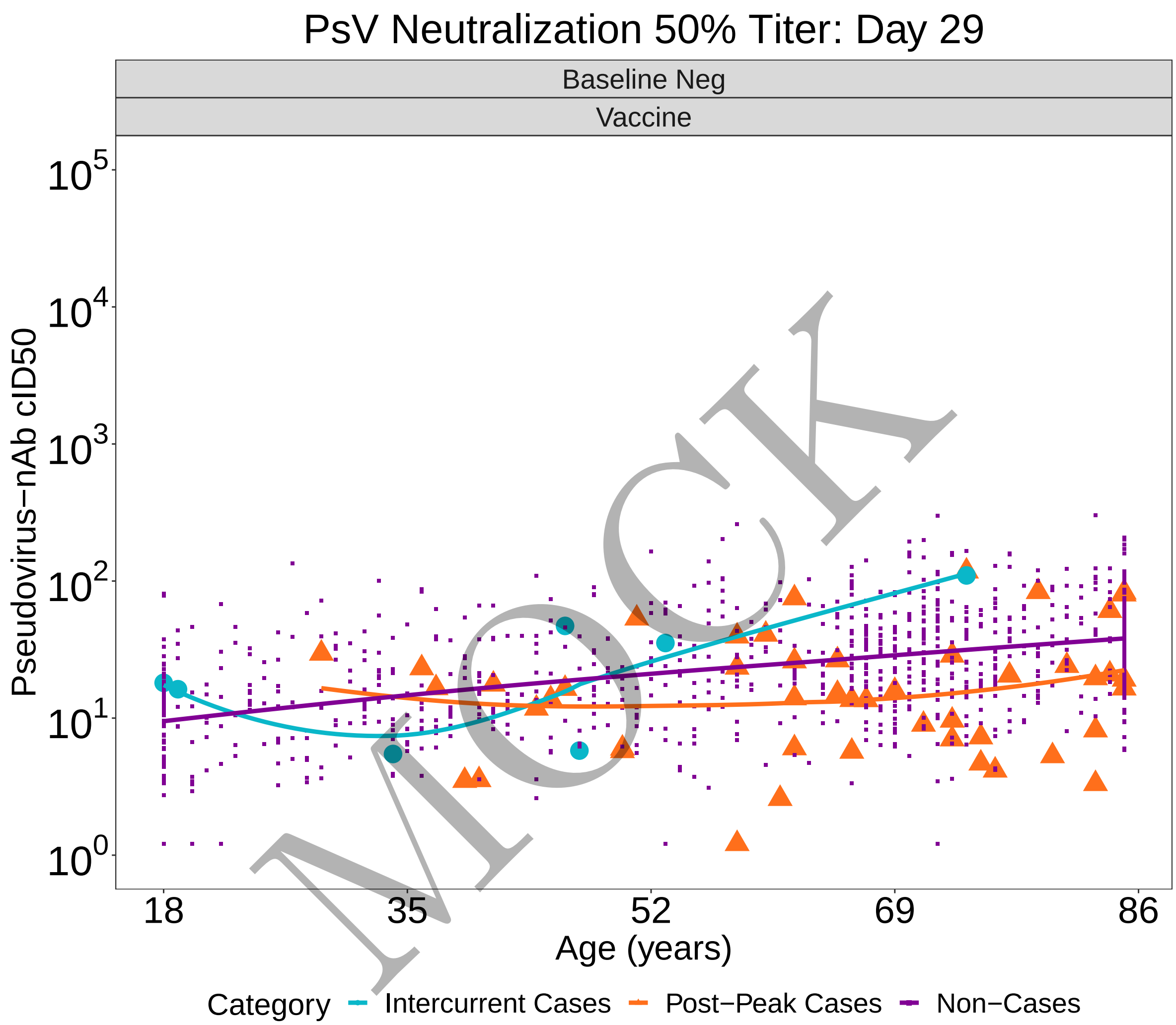
} \end{figure}

\begin{figure}[H]



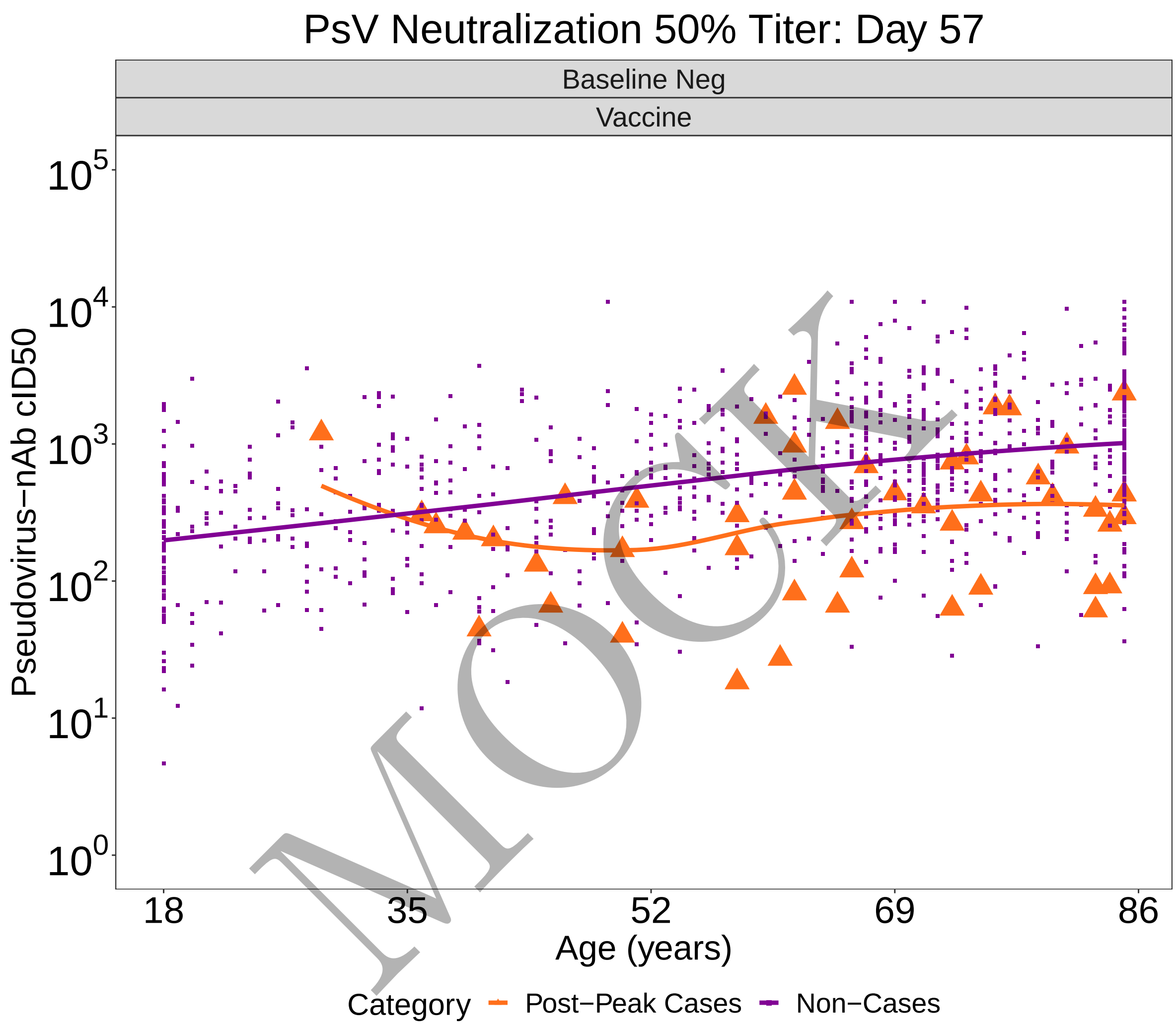

\caption{
Figure 2.6.7: scatterplots of PsV Neutralization 50% Titer vs Age: baseline negative vaccine arm at day 1
} \end{figure}

\begin{figure}[H]



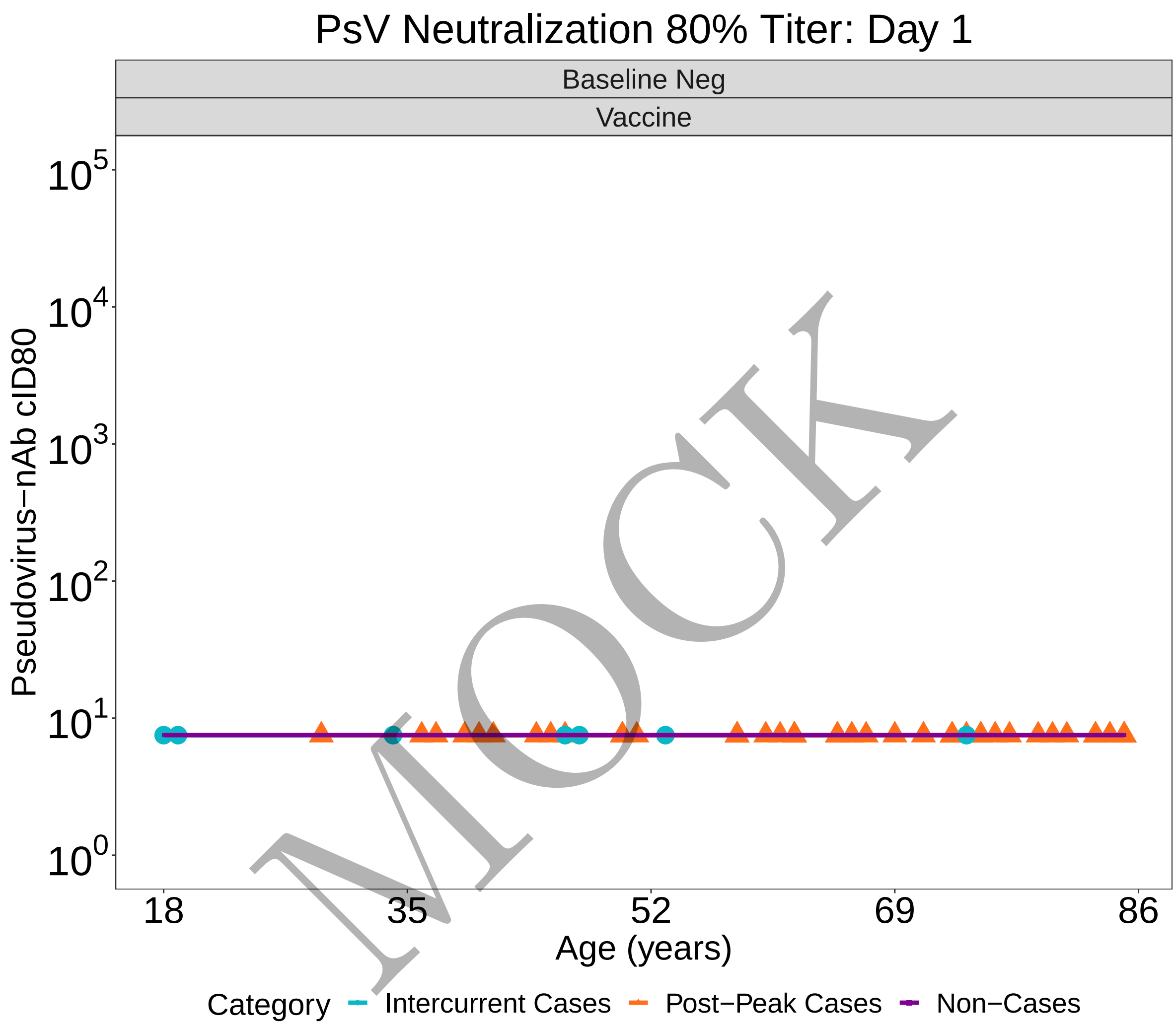

\caption{
Figure 2.6.8: scatterplots of PsV Neutralization 50% Titer vs Age: baseline negative vaccine arm at day 29
} \end{figure}

\begin{figure}[H]




\caption{
Figure 2.6.9: scatterplots of PsV Neutralization 50% Titer vs Age: baseline negative vaccine arm at day 57
} \end{figure}

\begin{figure}[H]



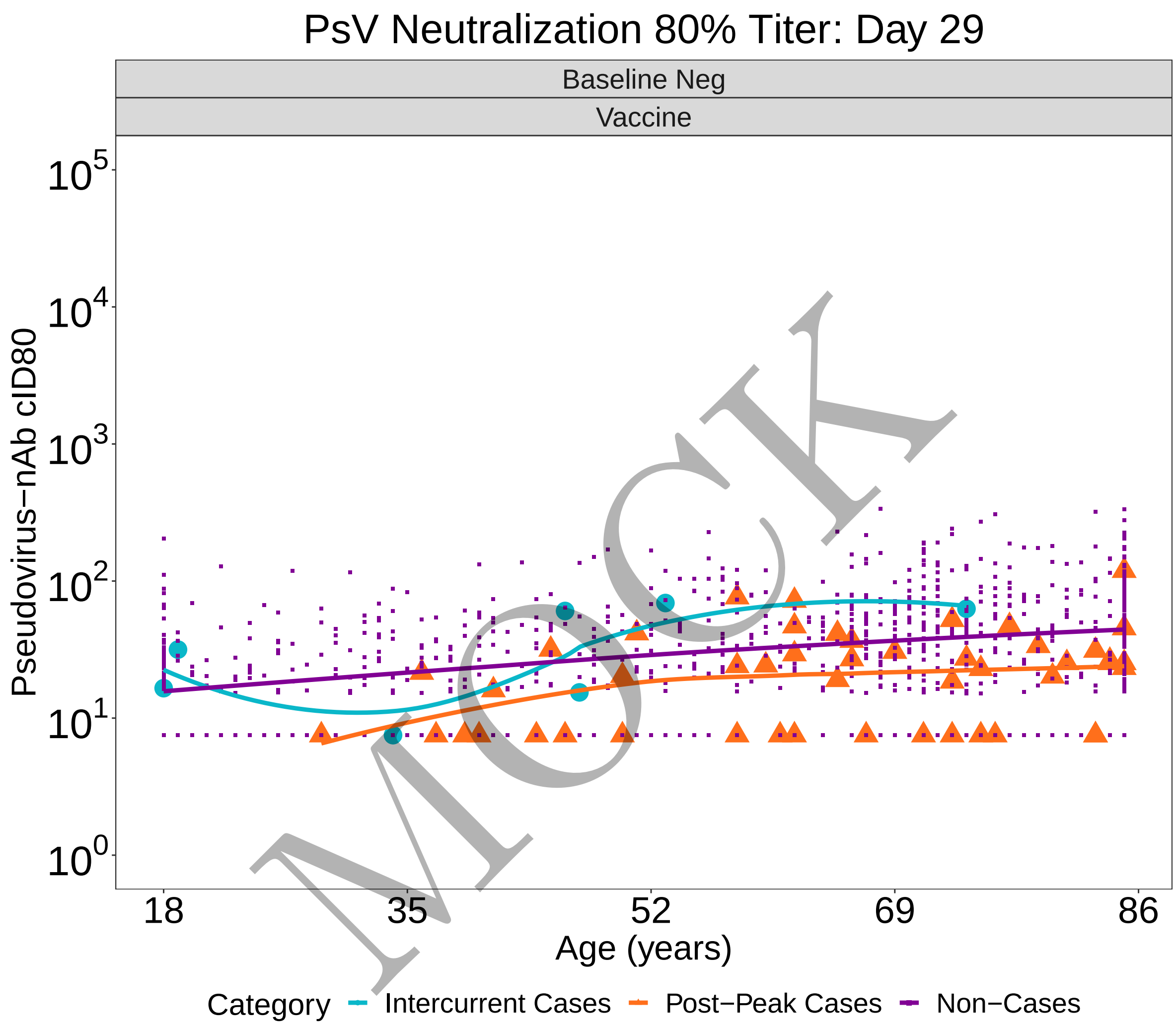


\caption{

Figure 2.6.10: scatterplots of PsV Neutralization 80% Titer vs Age: baseline negative vaccine arm at day 1

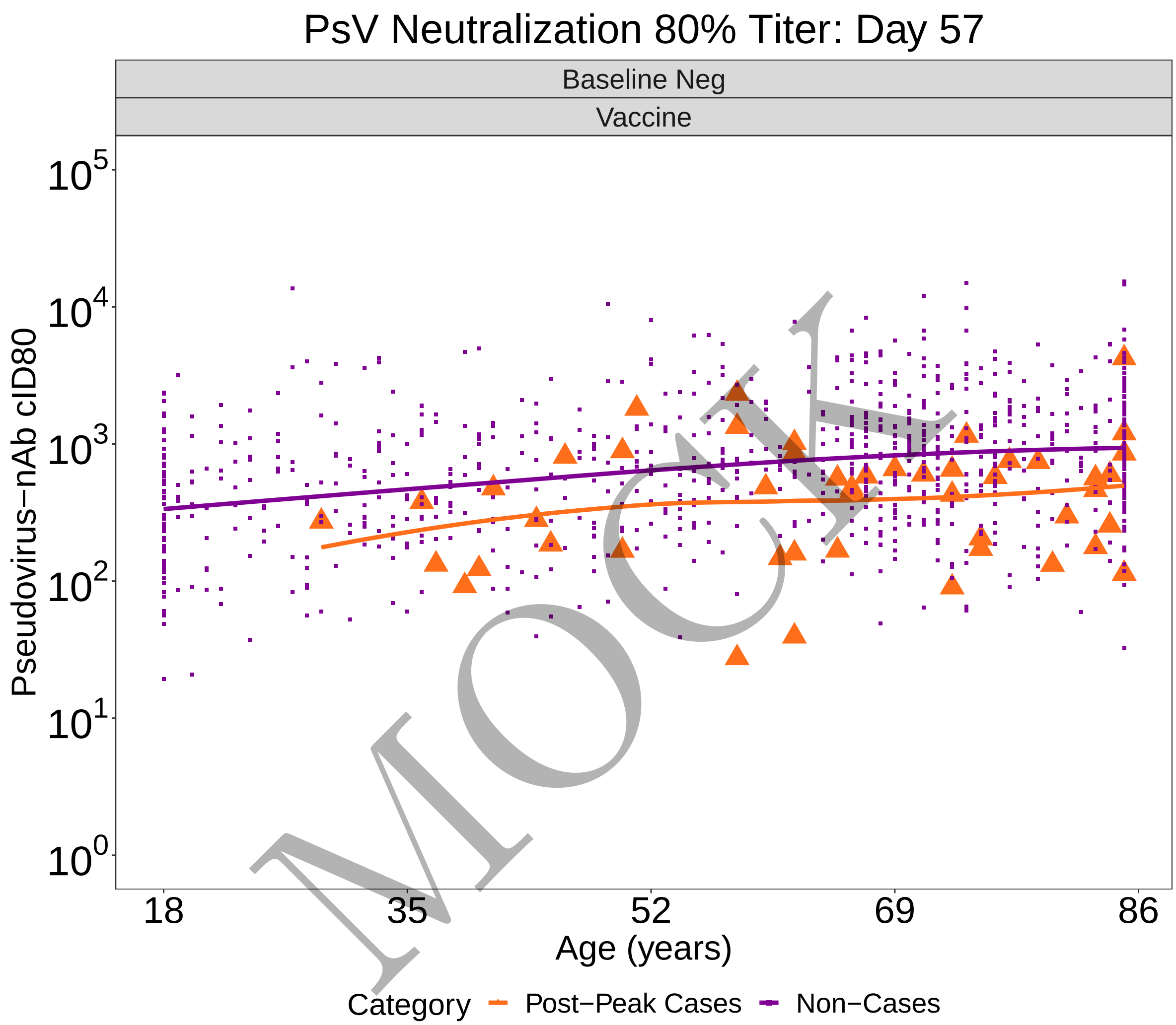
} \end{figure}

\begin{figure}[H]




\caption{
Figure 2.6.11: scatterplots of PsV Neutralization 80% Titer vs Age: baseline negative vaccine arm at day 29
} \end{figure}

\begin{figure}[H]

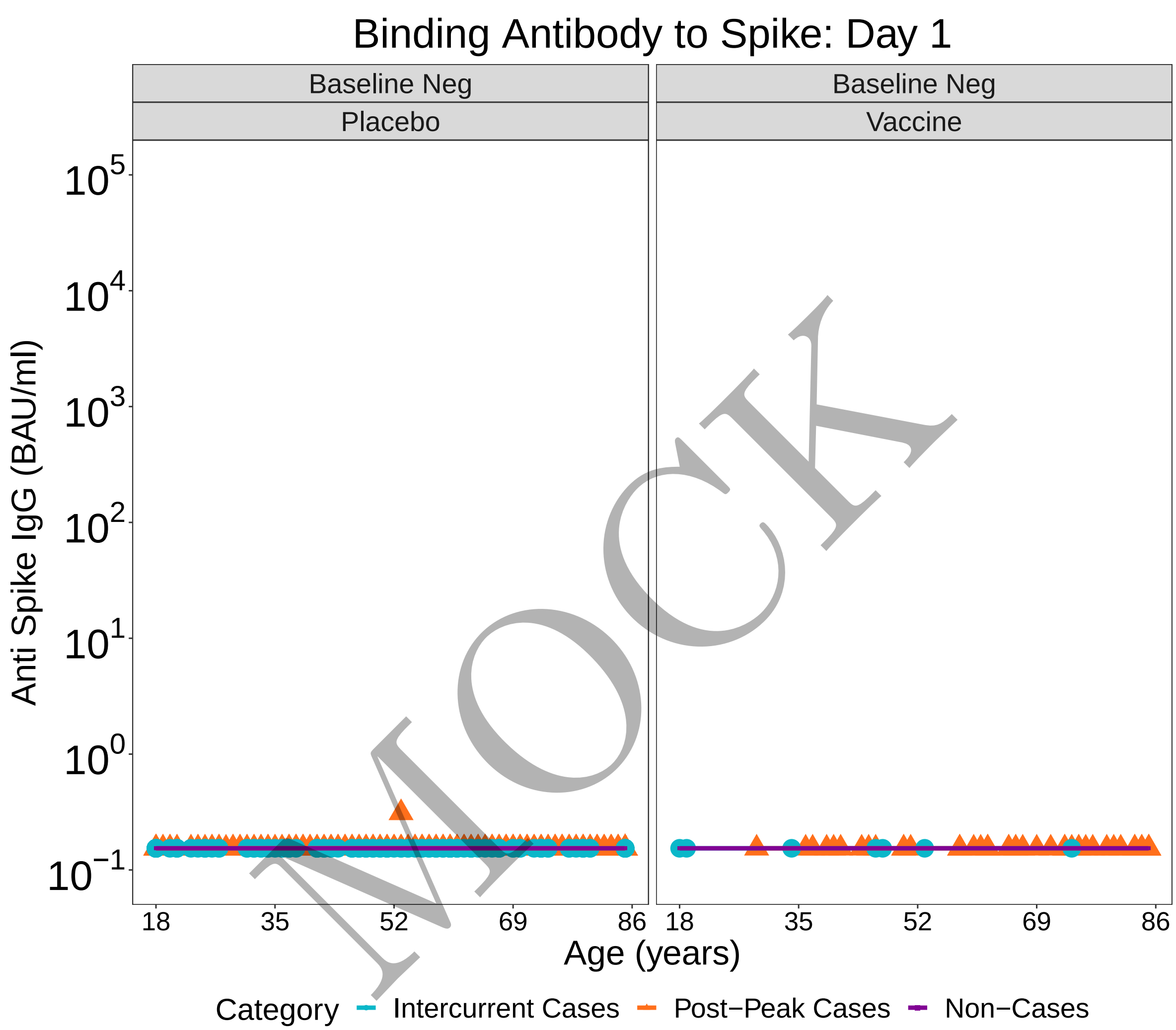



\caption{

Figure 2.6.12: scatterplots of PsV Neutralization 80% Titer vs Age: baseline negative vaccine arm at day 57

} \end{figure}

\begin{figure}[H]

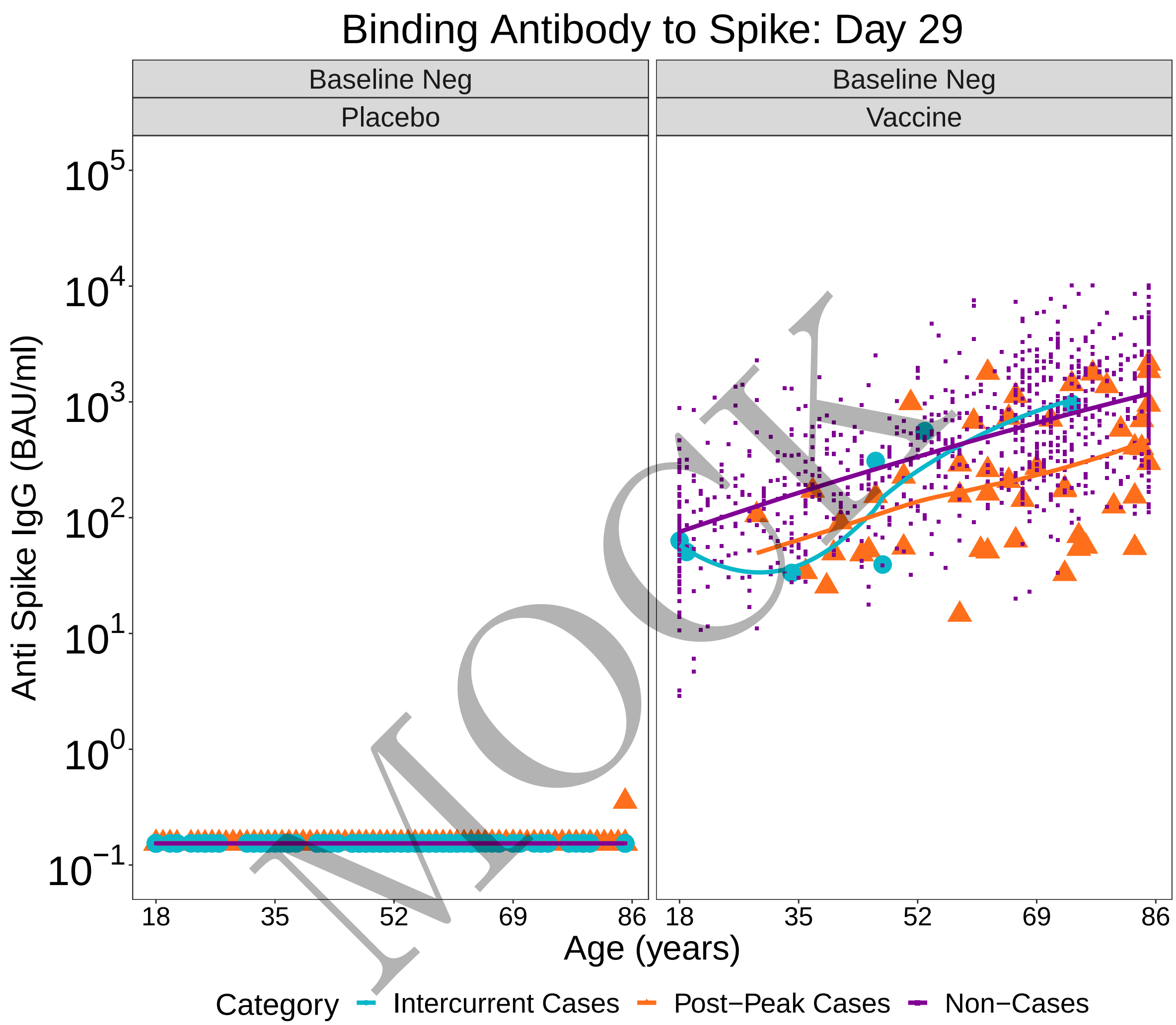



\caption{

Figure 2.6.13: scatterplots of Binding Antibody to Spike vs Age: by arm at day 1

} \end{figure}

\begin{figure}[H]

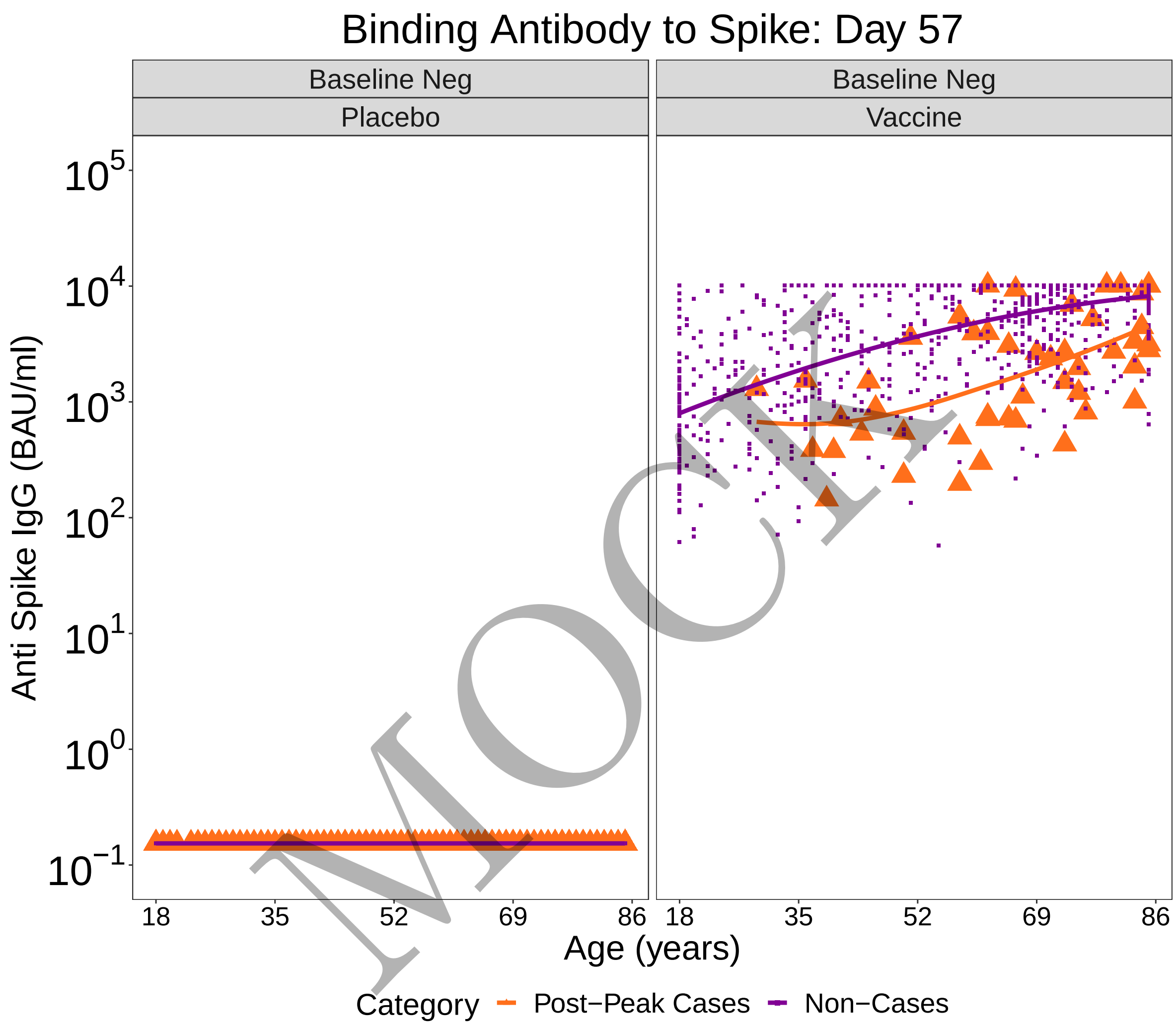



\caption{

Figure 2.6.14: scatterplots of Binding Antibody to Spike vs Age: by arm at day 29

} \end{figure}

\begin{figure}[H]

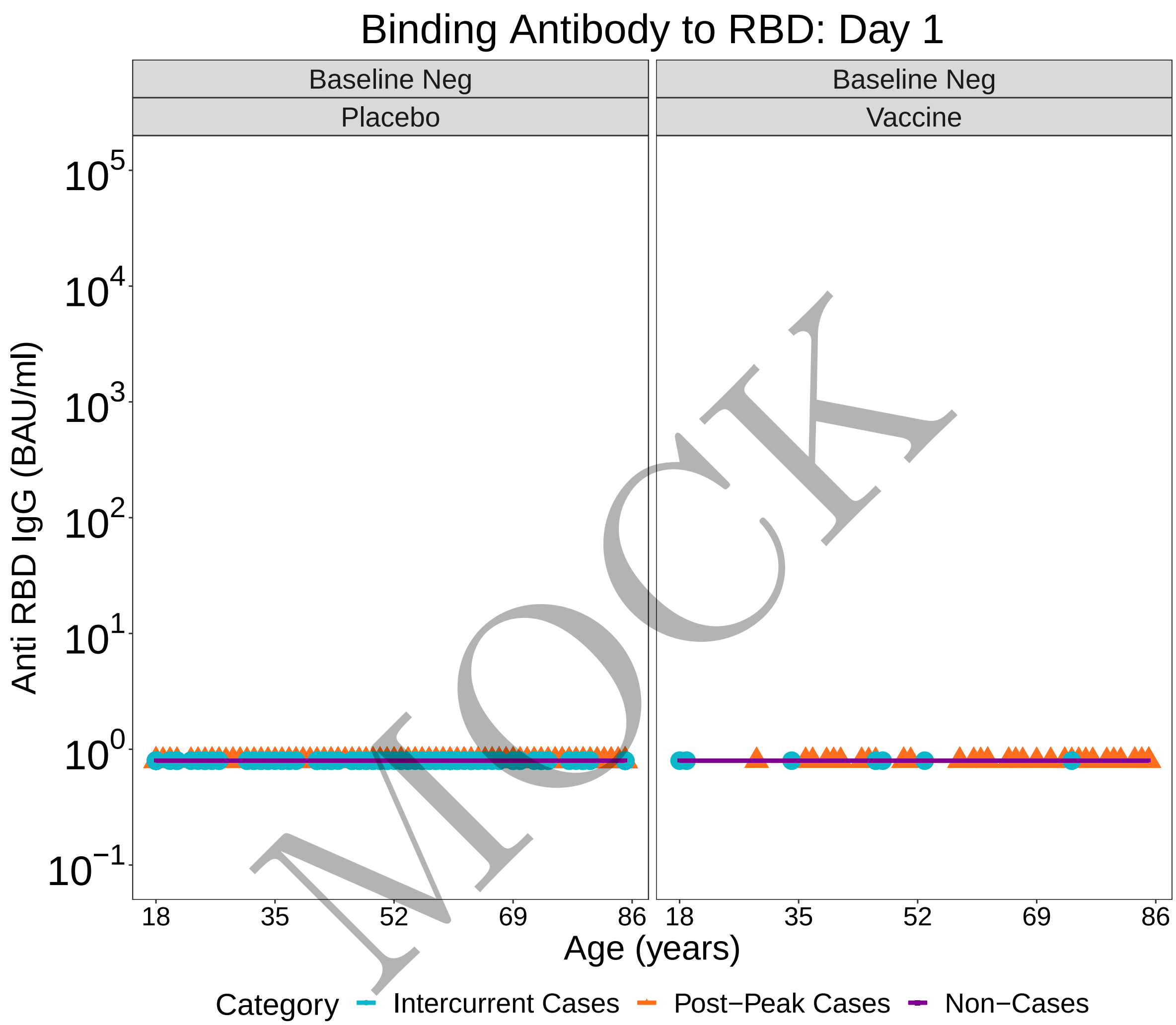



\caption{

Figure 2.6.15: scatterplots of Binding Antibody to Spike vs Age: by arm at day 57

} \end{figure}

\begin{figure}[H]

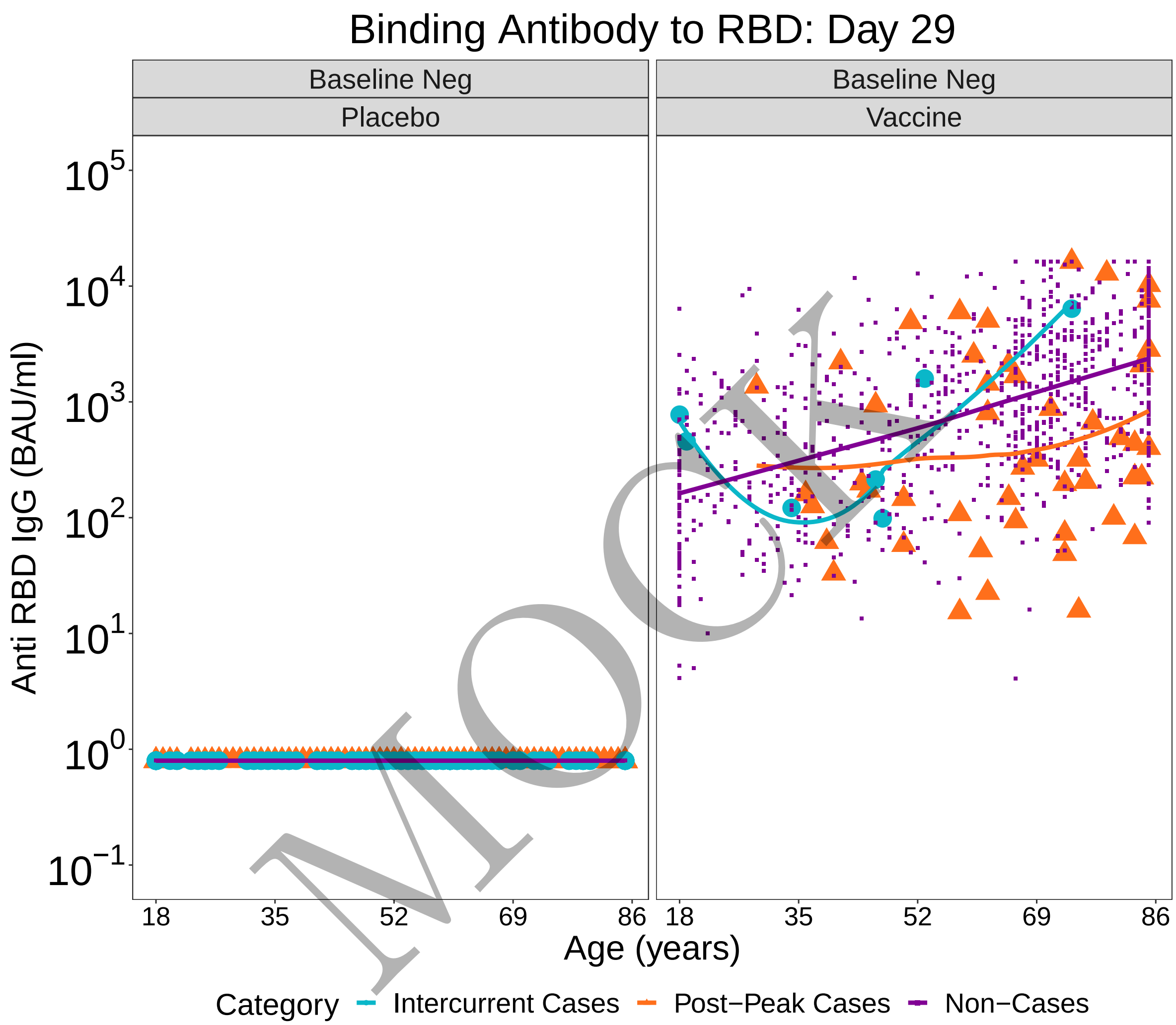



\caption{

Figure 2.6.16: scatterplots of Binding Antibody to RBD vs Age: by arm at day 1

} \end{figure}

\begin{figure}[H]

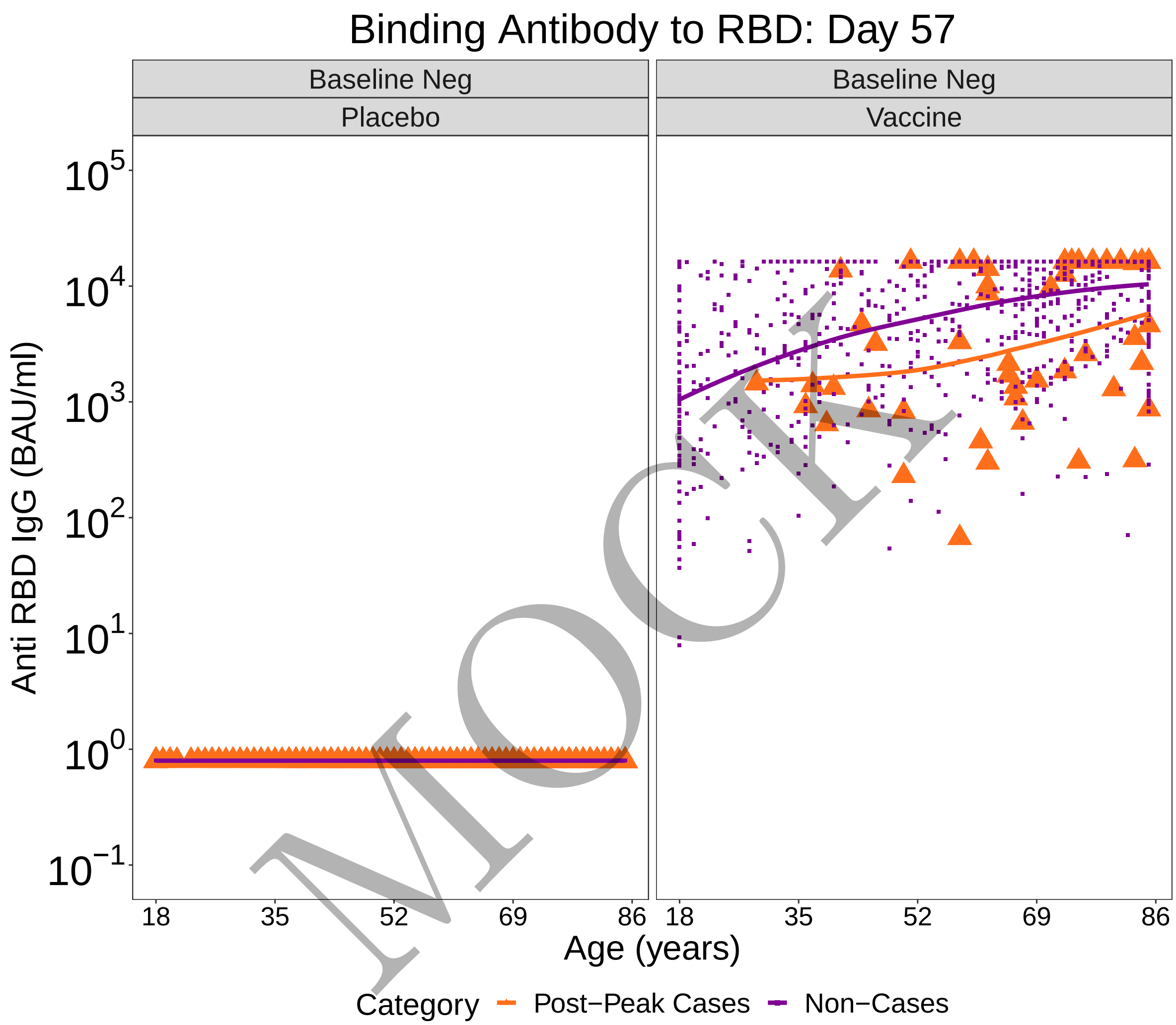



\caption{

Figure 2.6.17: scatterplots of Binding Antibody to RBD vs Age: by arm at day 29

} \end{figure}

\begin{figure}[H]

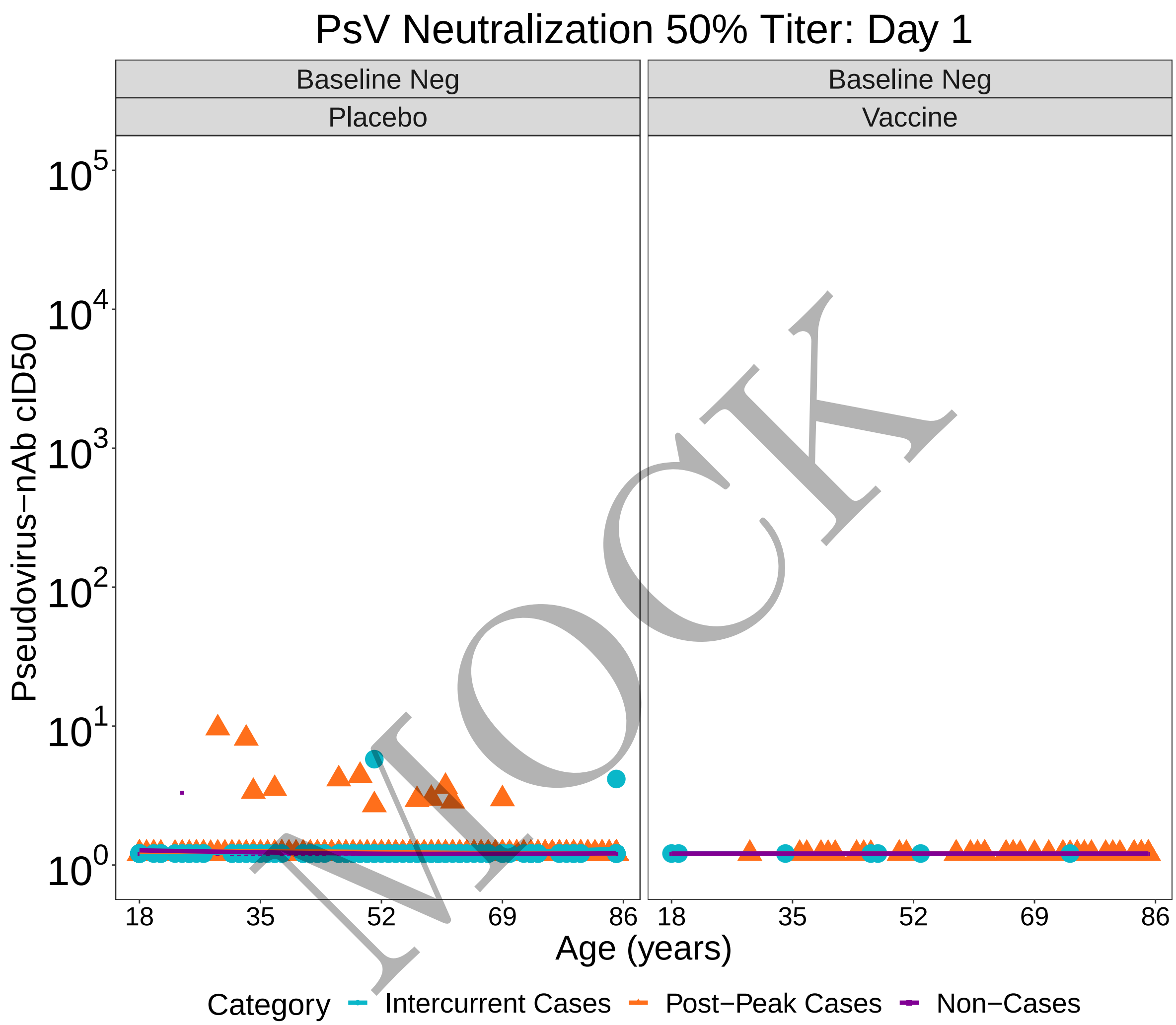



\caption{

Figure 2.6.18: scatterplots of Binding Antibody to RBD vs Age: by arm at day 57

} \end{figure}

\begin{figure}[H]

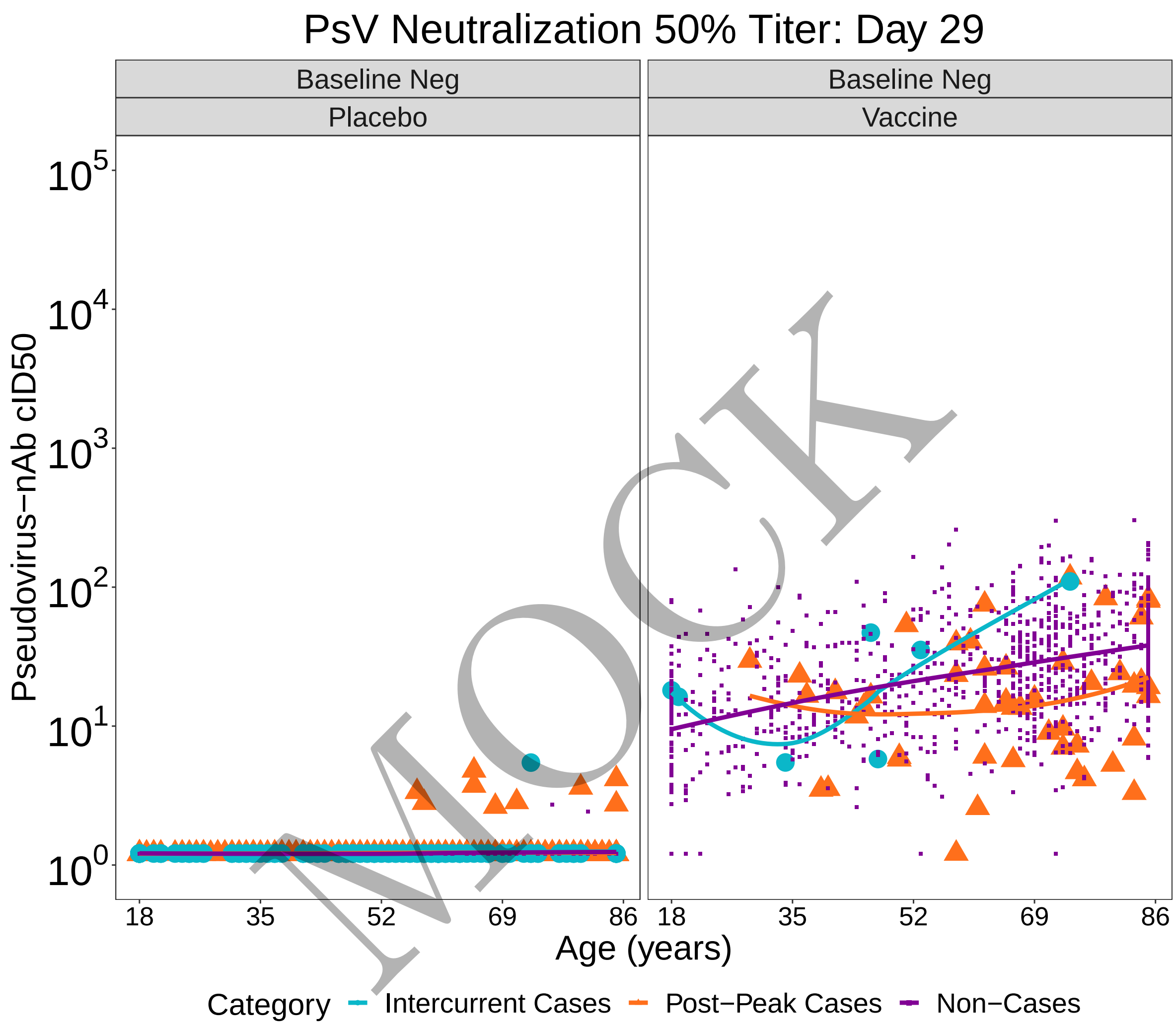



\caption{

Figure 2.6.19: scatterplots of PsV Neutralization 50% Titer vs Age: by arm at day 1

} \end{figure}

\begin{figure}[H]

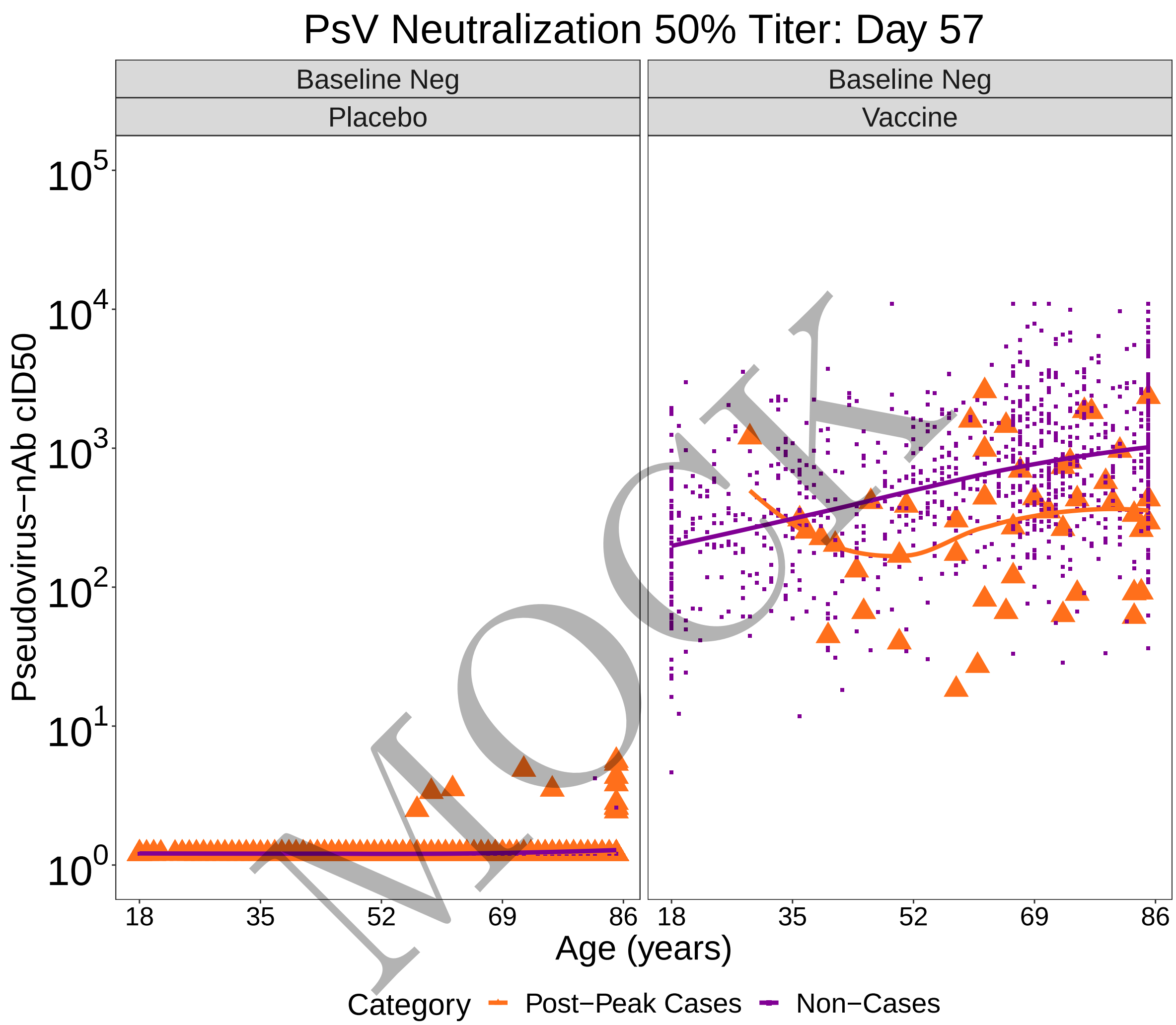



\caption{

Figure 2.6.20: scatterplots of PsV Neutralization 50% Titer vs Age: by arm at day 29

} \end{figure}

\begin{figure}[H]

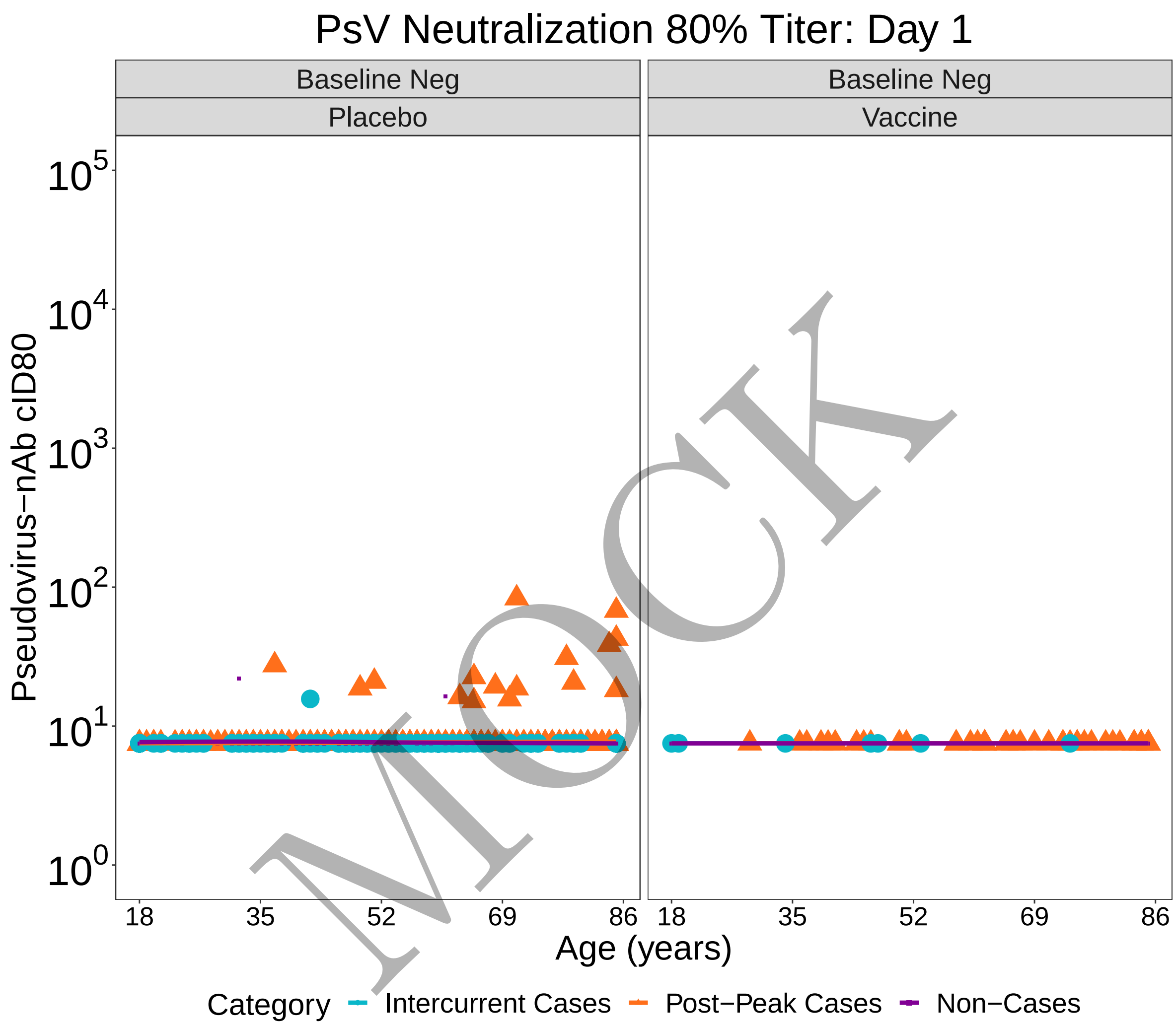



\caption{

Figure 2.6.21: scatterplots of PsV Neutralization 50% Titer vs Age: by arm at day 57

} \end{figure}

\begin{figure}[H]

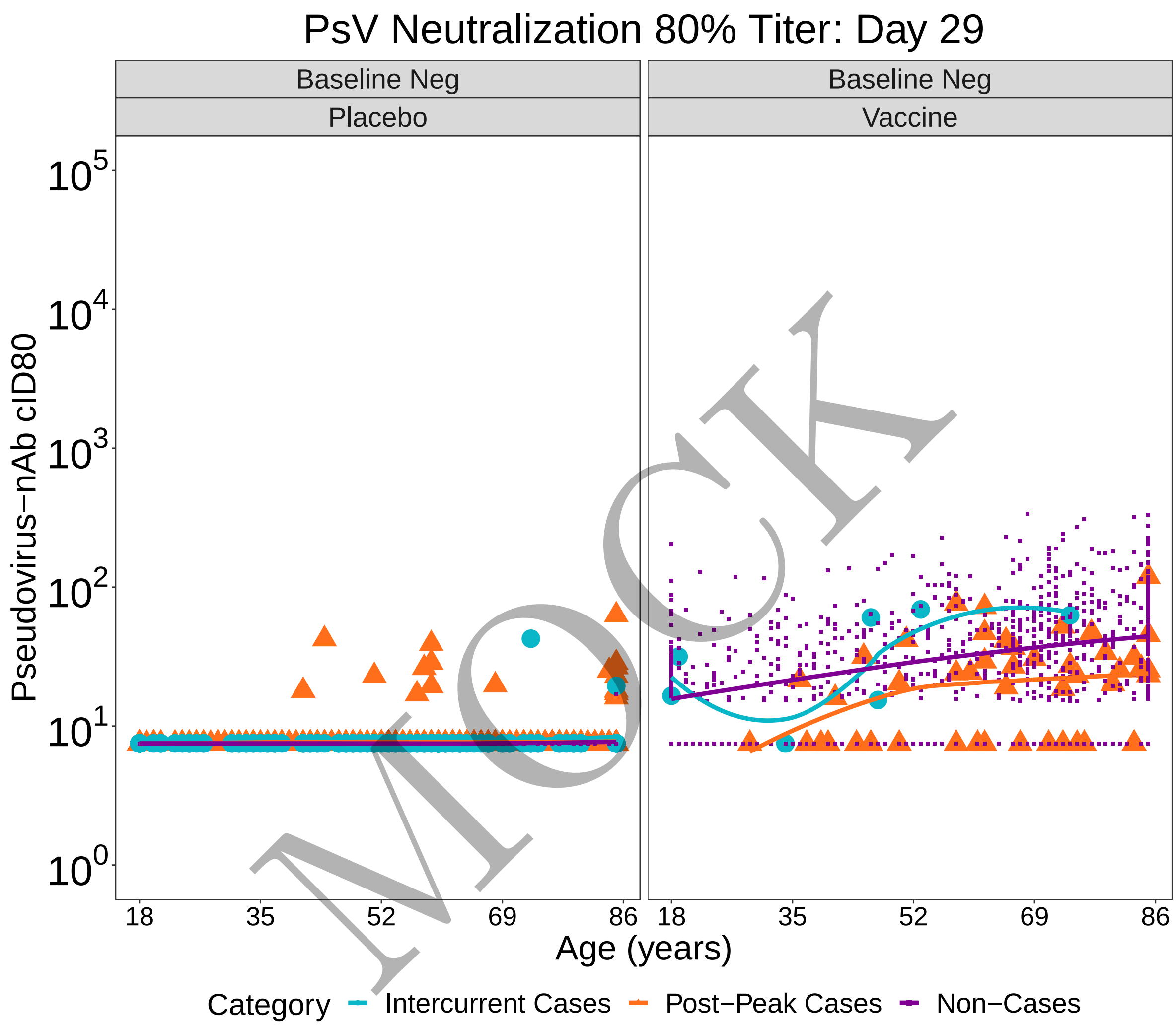



\caption{

Figure 2.6.22: scatterplots of PsV Neutralization 80% Titer vs Age: by arm at day 1

} \end{figure}

\begin{figure}[H]

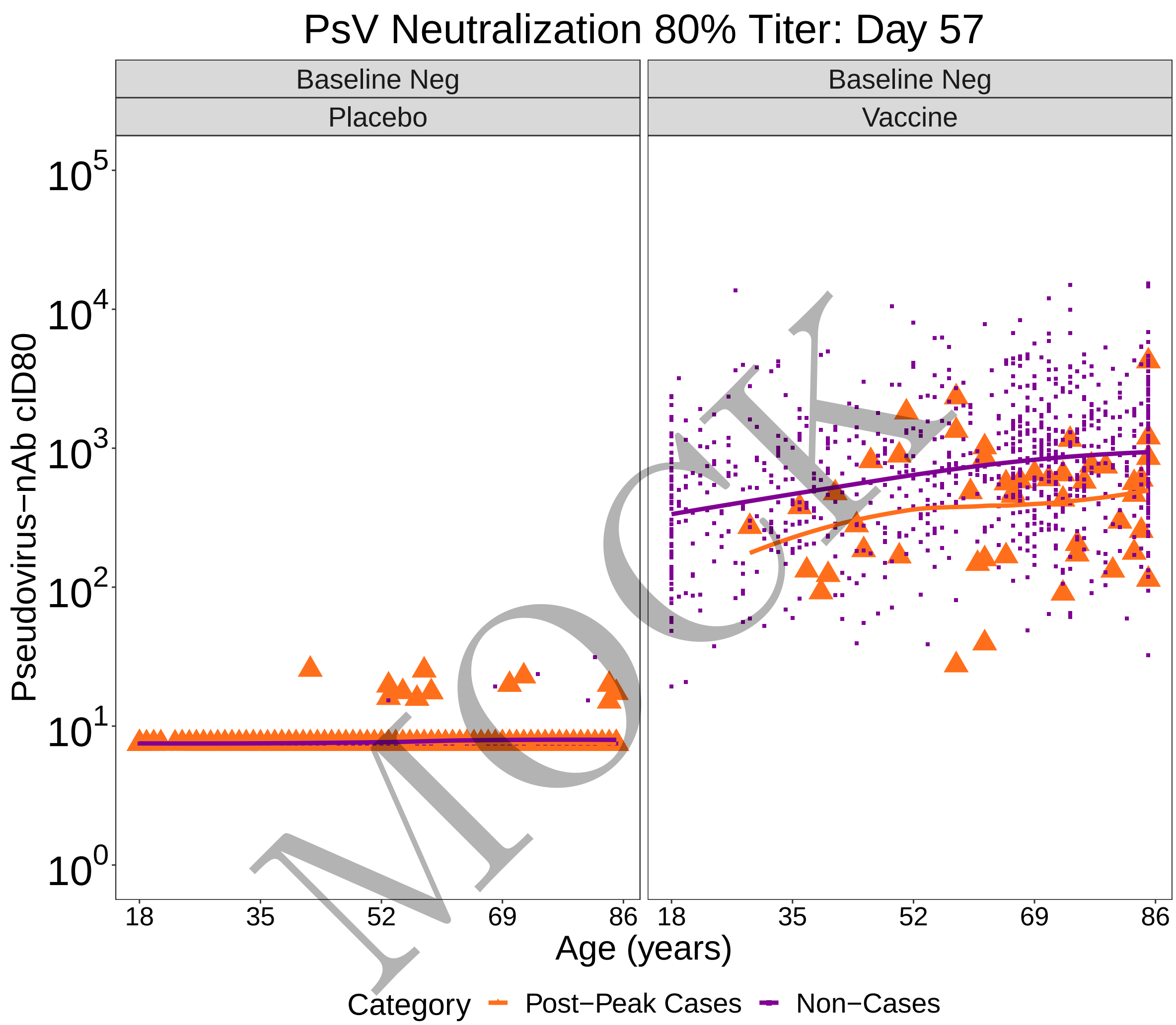



\caption{

Figure 2.6.23: scatterplots of PsV Neutralization 80% Titer vs Age: by arm at day 29

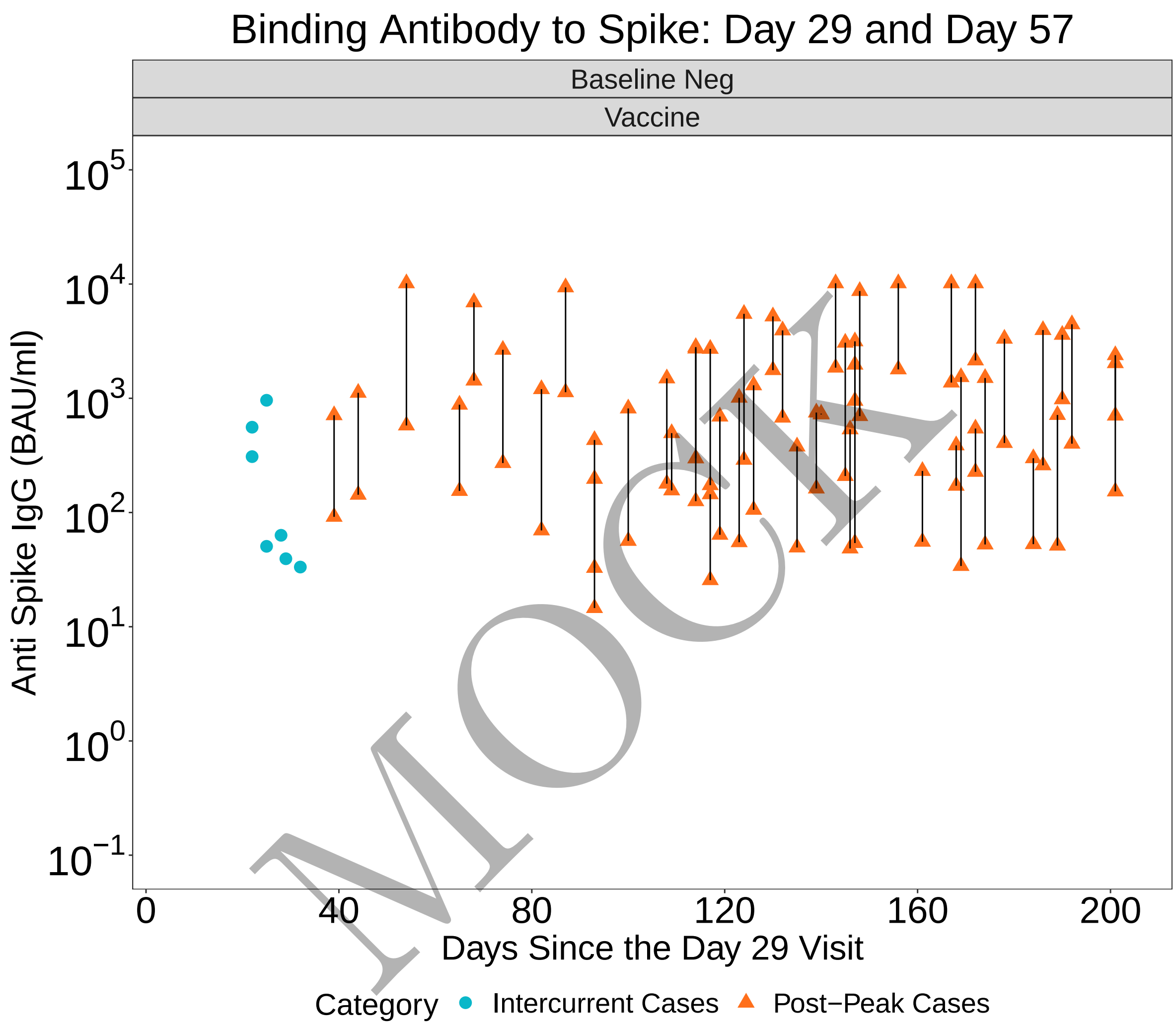
} \end{figure}

\begin{figure}[H]




\caption{
Figure 2.6.24: scatterplots of PsV Neutralization 80% Titer vs Age: by arm at day 57
} \end{figure}

\begin{figure}[H]

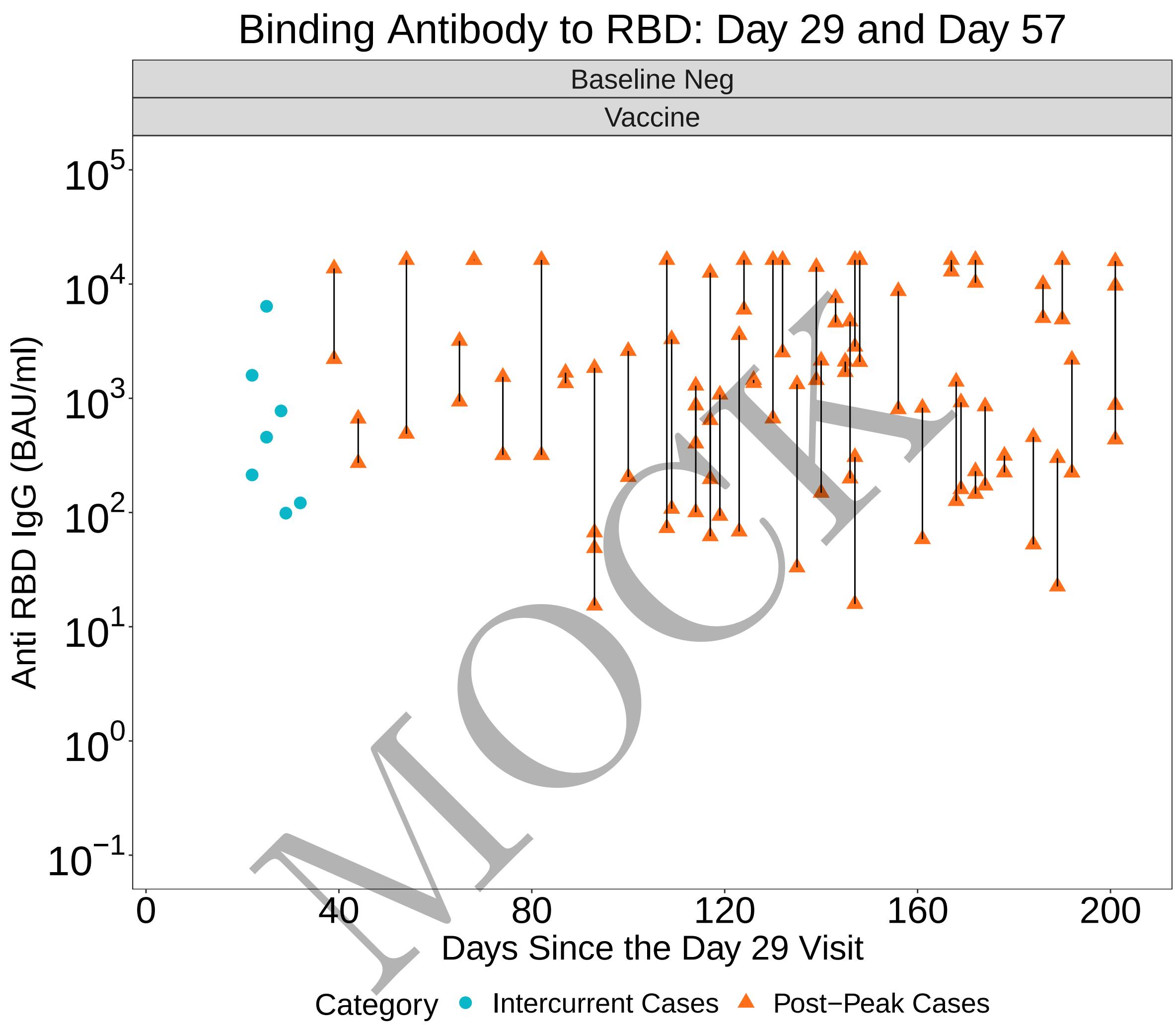



\caption{

Figure 2.6.25: scatterplots of Binding Antibody to Spike vs Days Since the Day 29 Visit: baseline negative vaccine arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]

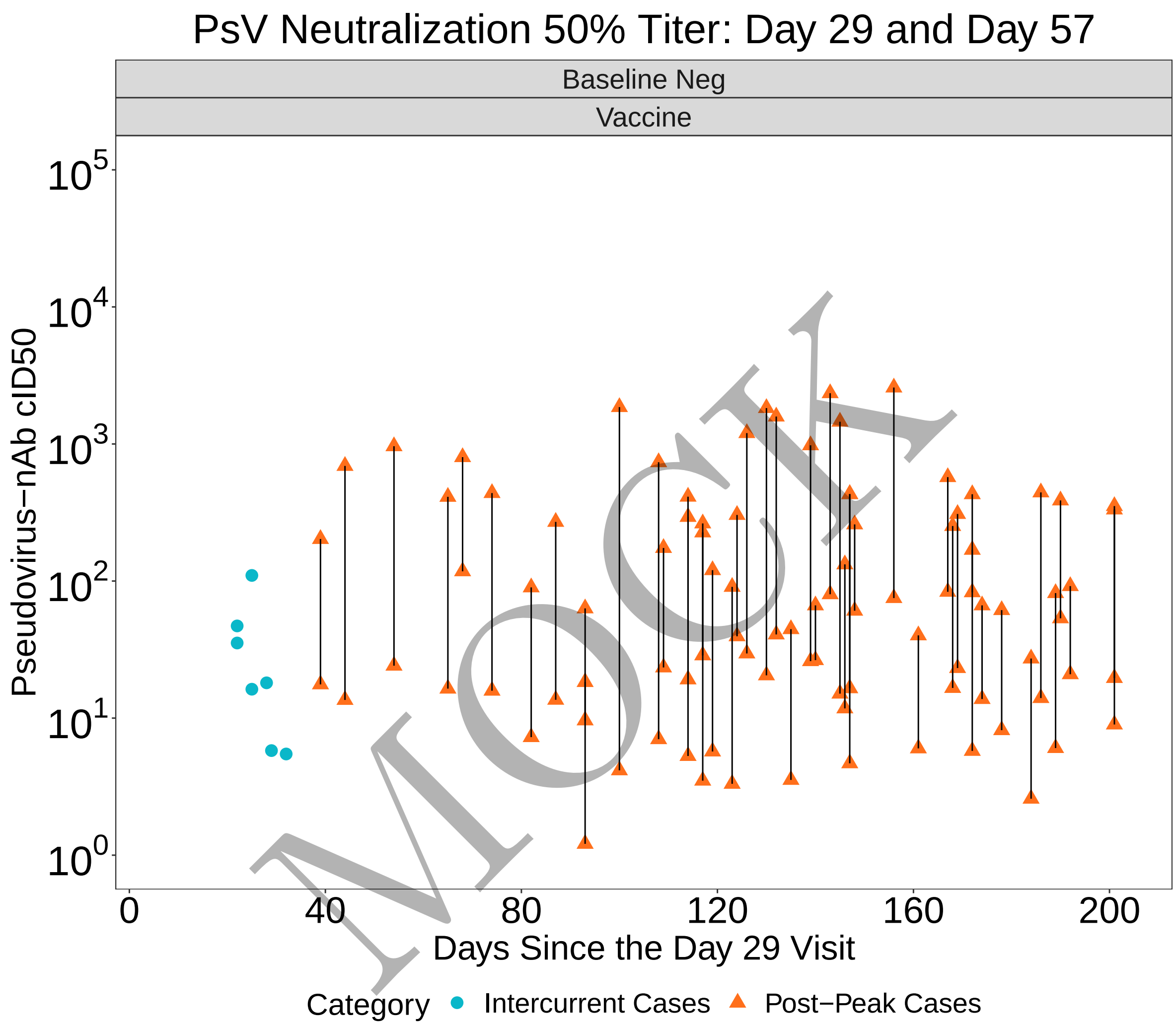



\caption{

Figure 2.6.26: scatterplots of Binding Antibody to RBD vs Days Since the Day 29 Visit: baseline negative vaccine arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]

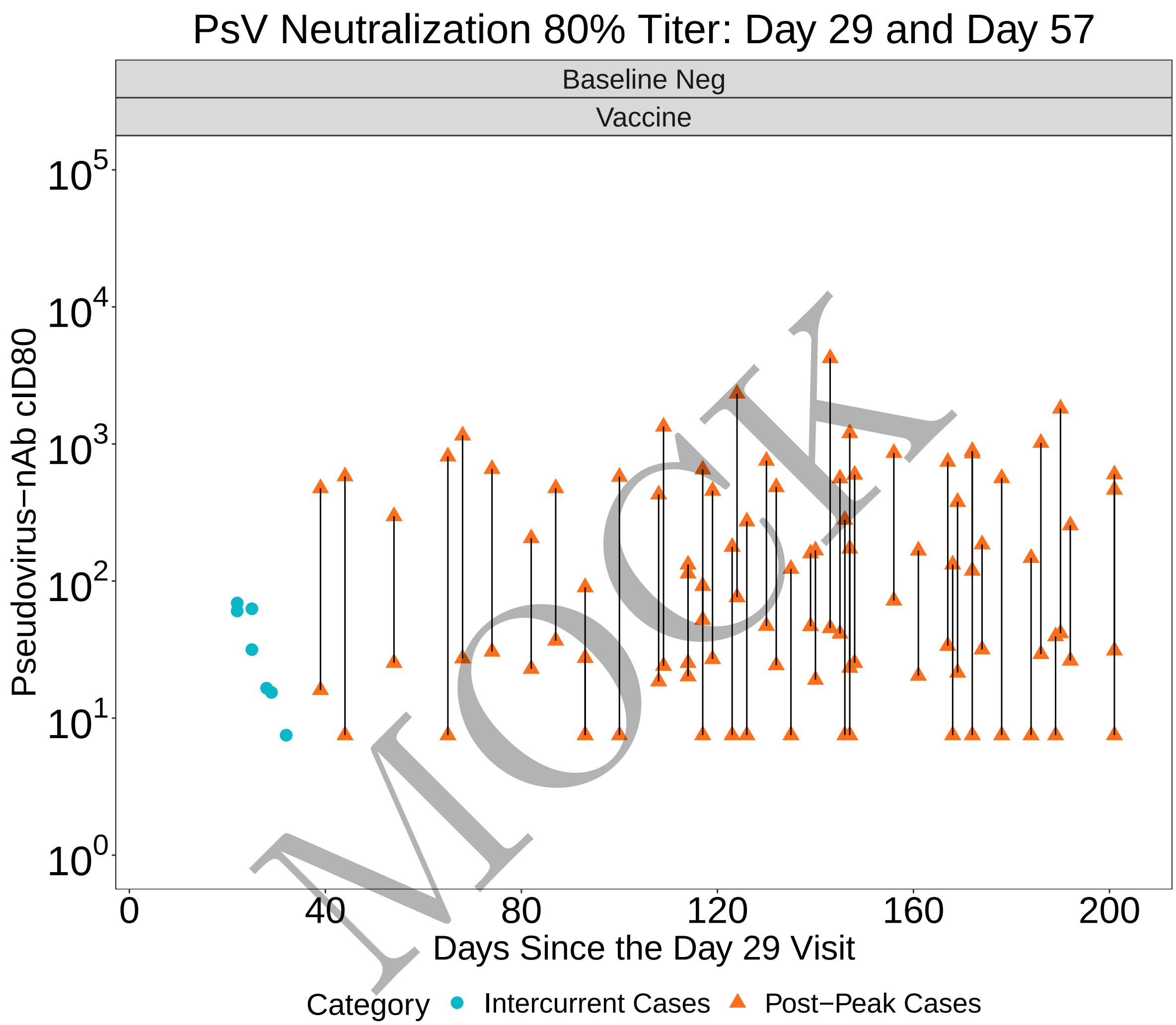



\caption{

Figure 2.6.27: scatterplots of PsV Neutralization 50% Titer vs Days Since the Day 29 Visit: baseline negative vaccine arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]



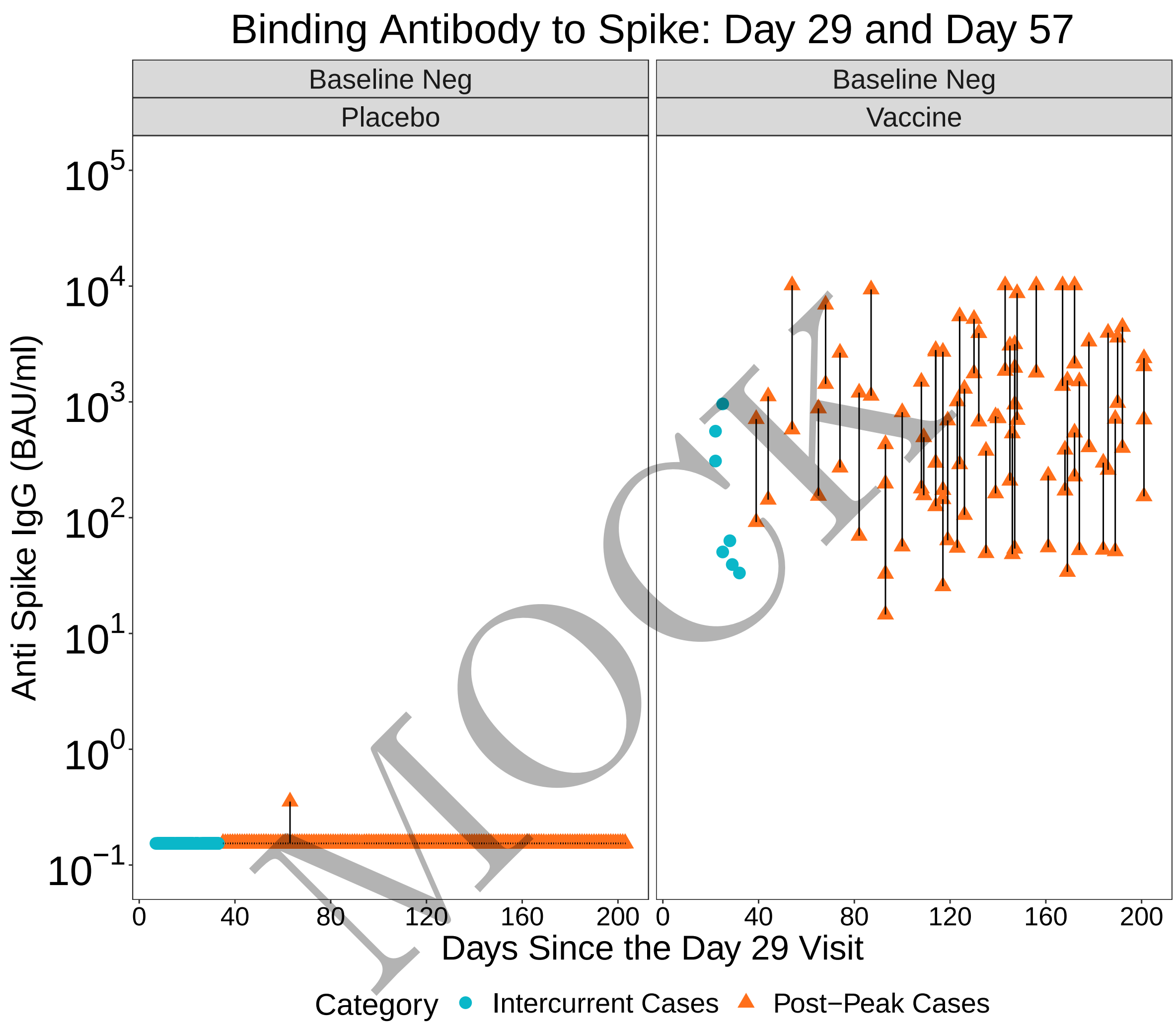



\caption{

Figure 2.6.28: scatterplots of PsV Neutralization 80% Titer vs Days Since the Day 29 Visit: baseline negative vaccine arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]

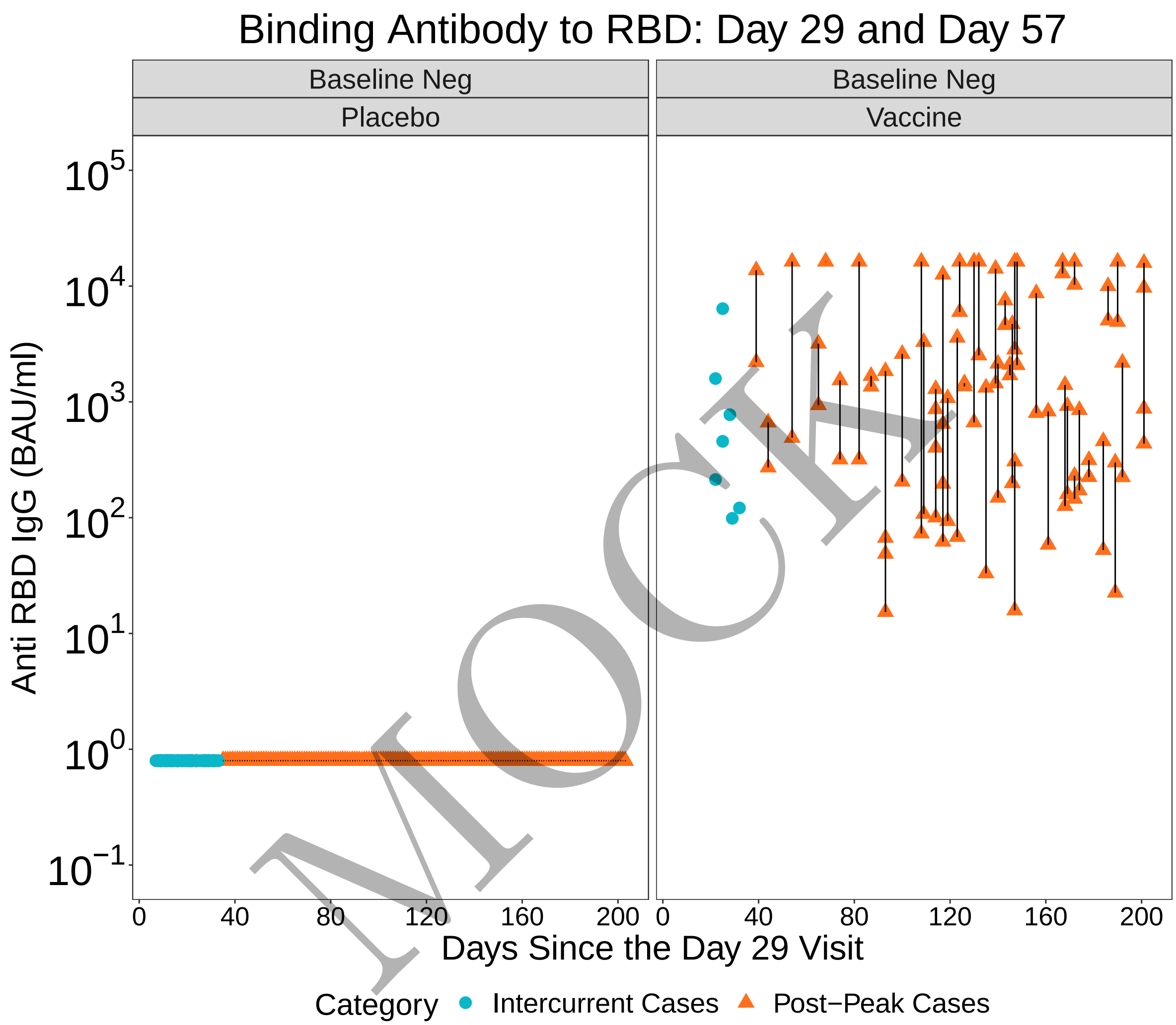



\caption{

Figure 2.6.29: scatterplots of Binding Antibody to Spike vs Days Since the Day 29 Visit: by arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]

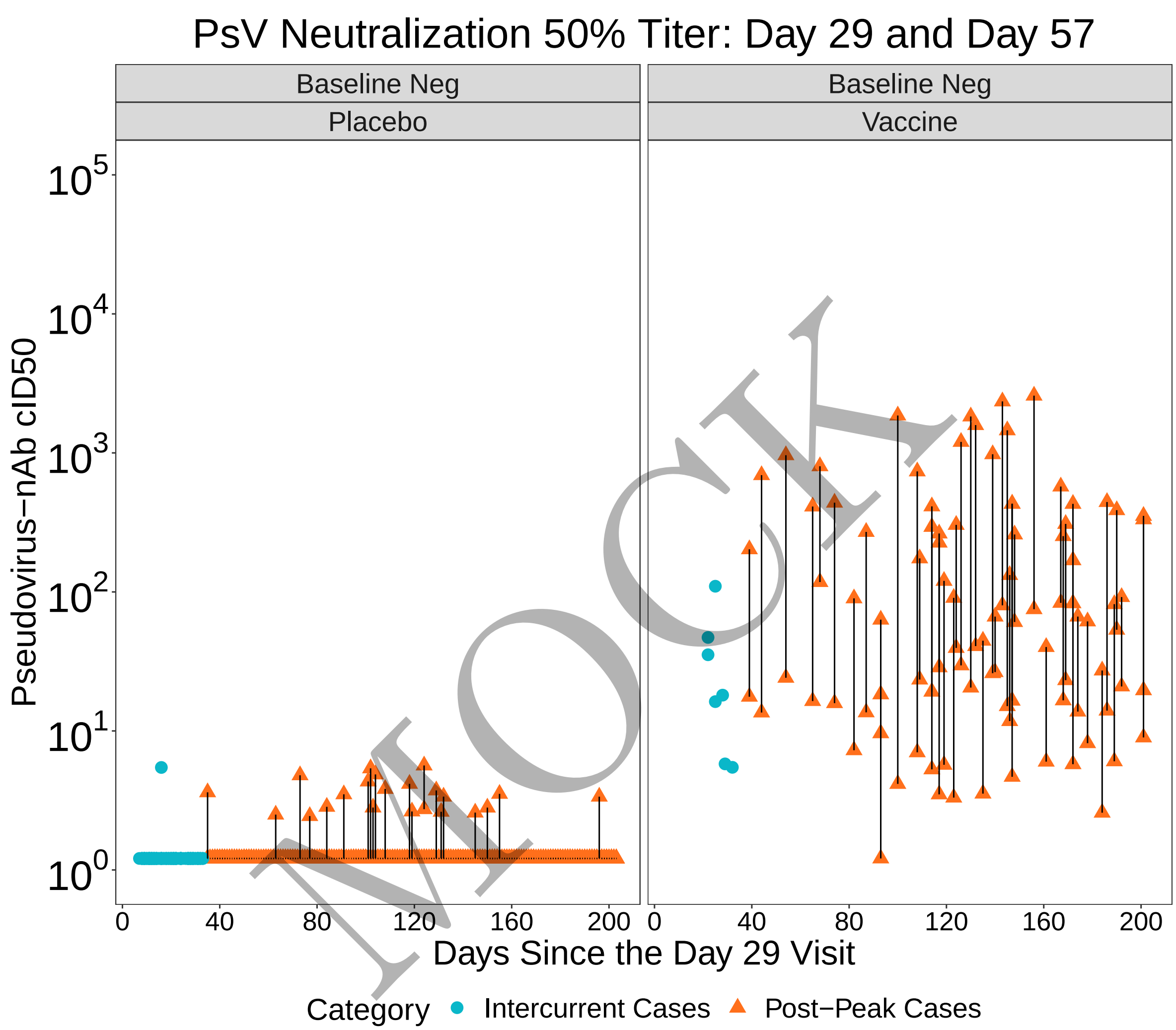



\caption{

Figure 2.6.30: scatterplots of Binding Antibody to RBD vs Days Since the Day 29 Visit: by arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]

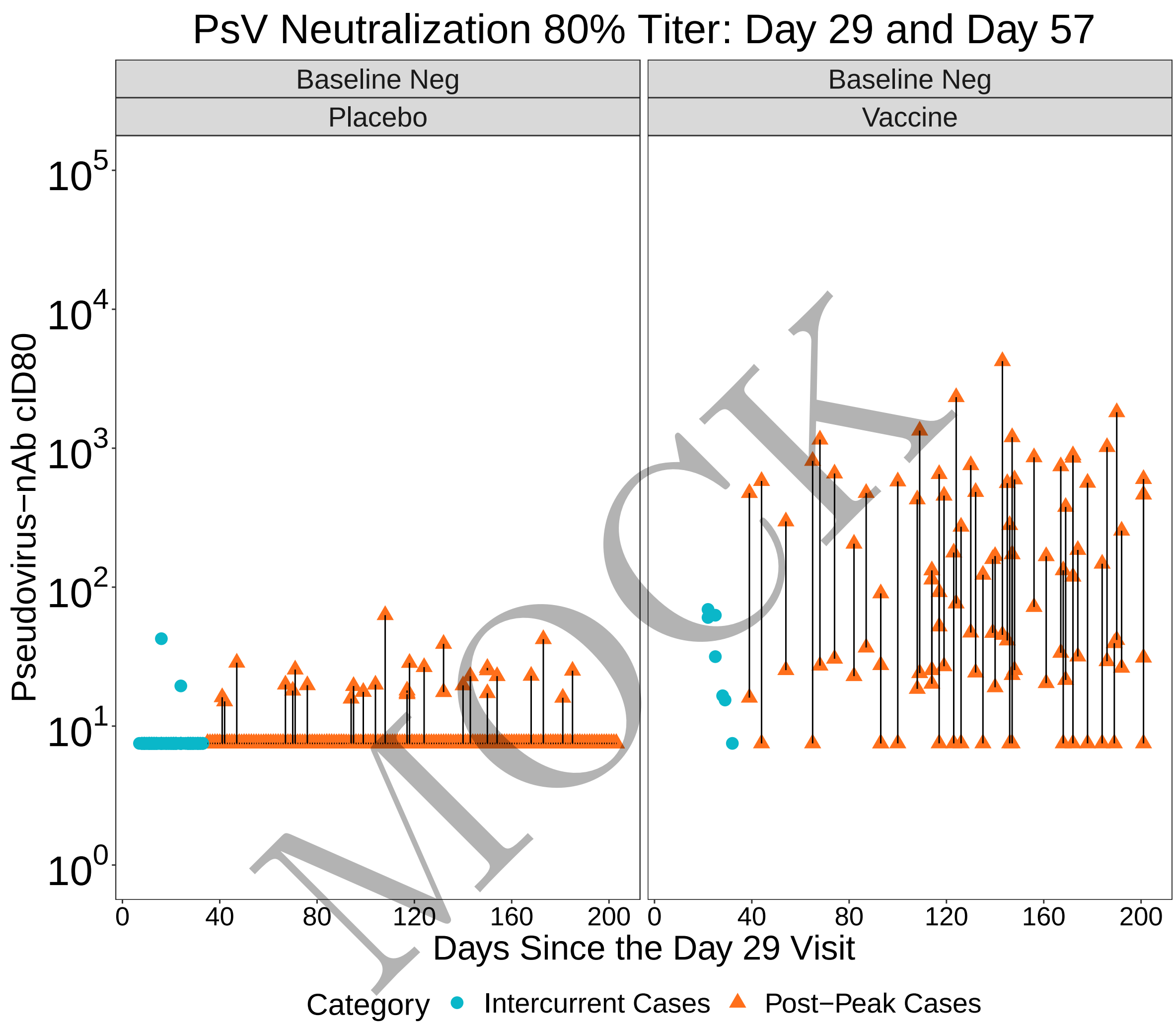



\caption{

Figure 2.6.31: scatterplots of PsV Neutralization 50% Titer vs Days Since the Day 29 Visit: by arm at Day 29 and Day 57

} \end{figure}

\begin{figure}[H]




\caption{

Figure 2.6.32: scatterplots of PsV Neutralization 80% Titer vs Days Since the Day 29 Visit: by arm at Day 29 and Day 57

} \end{figure}

# Chapter 4

# Graphical Descriptions of Time to Event Data



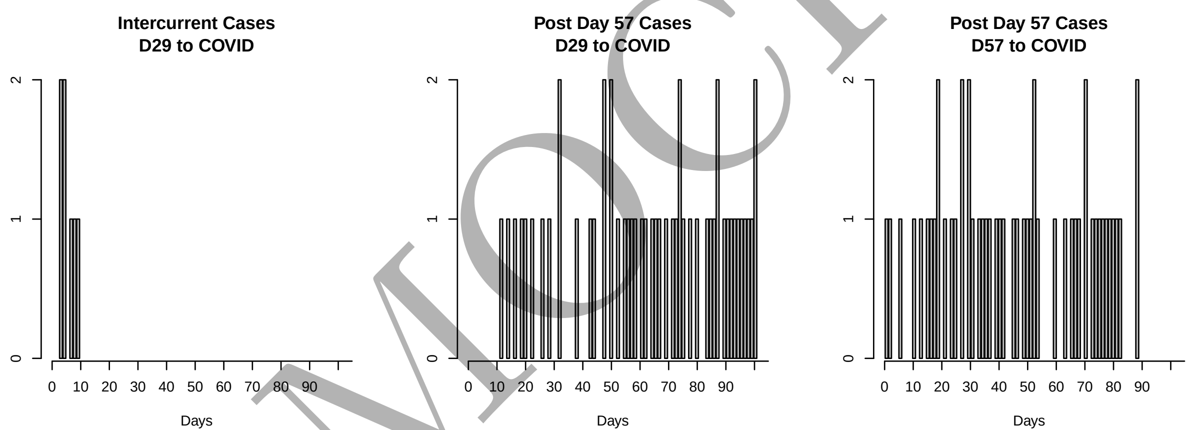



Figure 4.1: Distribution of the number of days to COVID endpoints, vaccine arm, baseline negative.

# Chapter 5

# Day D29 Univariate CoR: Cox Models of Risk



The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise.

## 5.1 Hazard ratios

Table 5.1: Inference for Day 29 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios per 10-fold increment in the marker*

| MockCOVE Immunologic Marker | No. cases / No. at-risk** | HR per 10-fold incr. Pt. Est. | 95% CI | P-value (2-sided) | q-value *** | FWER |
|---|---|---|---|---|---|---|
| Anti Spike IgG (BAU/ml) | 58/11,204 | 0.11 | (0.05-0.24) | <0.001 | <0.001 | <0.001 |
| Anti RBD IgG (BAU/ml) | 58/11,204 | 0.37 | (0.19-0.70) | 0.002 | <0.001 | <0.001 |
| Pseudovirus-nAb cID50 | 58/11,204 | 0.25 | (0.11-0.60) | 0.002 | <0.001 | <0.001 |
| Pseudovirus-nAb cID80 | 58/11,204 | 0.24 | (0.11-0.49) | <0.001 | <0.001 | <0.001 |

*Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. Maximum failure event time 201 days.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint or infected through 6 days post Day 29 visit; no. cases = number of this cohort with an observed COVID endpoint.
***q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10  replicates).

Table 5.2: Inference for Day 29 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios for Middle vs. Upper tertile vs. Lower tertile*

| MockCOVE Immunologic Marker | Tertile | No. cases / No. at-risk** | Attack rate | Haz. Ratio Pt. Est. | Haz. Ratio 95% CI | P-value (2-sided) | Overall P-value*** | Overall q-value † | Overall FWER |
|---|---|---|---|---|---|---|---|---|---|
| Anti Spike IgG (BAU/ml) | Lower | 24/3,752 | 0.0064 | 1 | N/A | N/A | <0.001 | <0.001 | <0.001 |
| | Middle | 17/3,729 | 0.0046 | 0.27 | (0.13-0.57) | <0.001 | | | |
| | Upper | 17/3,723 | 0.0046 | 0.12 | (0.05-0.29) | <0.001 | | | |
| Anti RBD IgG (BAU/ml) | Lower | 27/3,745 | 0.0072 | 1 | N/A | N/A | <0.001 | <0.001 | <0.001 |
| | Middle | 13/3,747 | 0.0035 | 0.25 | (0.11-0.56) | <0.001 | | | |
| | Upper | 18/3,712 | 0.0048 | 0.21 | (0.09-0.49) | <0.001 | | | |
| Pseudovirus-nAb cID50 | Lower | 21/3,741 | 0.0056 | 1 | N/A | N/A | 0.013 | 0.100 | 0.062 |
| | Middle | 22/3,729 | 0.0059 | 0.68 | (0.33-1.41) | 0.301 | | | |
| | Upper | 15/3,734 | 0.0040 | 0.29 | (0.12-0.68) | 0.004 | | | |
| Pseudovirus-nAb cID80 | Lower | 22/3,739 | 0.0059 | 1 | N/A | N/A | 0.007 | <0.001 | 0.043 |
| | Middle | 23/3,736 | 0.0062 | 0.78 | (0.41-1.47) | 0.442 | | | |
| | Upper | 13/3,729 | 0.0035 | 0.30 | (0.14-0.64) | 0.002 | | | |
| Placebo | | 1166/11,505 | 0.1013 | | | | | | |

*Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. Maximum failure event time 201 days. Cutpoints: Anti Spike IgG (BAU/ml) [2.18, 2.65), Anti RBD IgG (BAU/ml) [2.42, 3.06), Pseudovirus-nAb cID50 [1.08, 1.44), Pseudovirus-nAb cID80 [1.25, 1.59), all on the log10 scale.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint or infected through 6 days post Day 29 visit; no. cases = number of this cohort with an observed COVID endpoint.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.
† q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10  replicates).

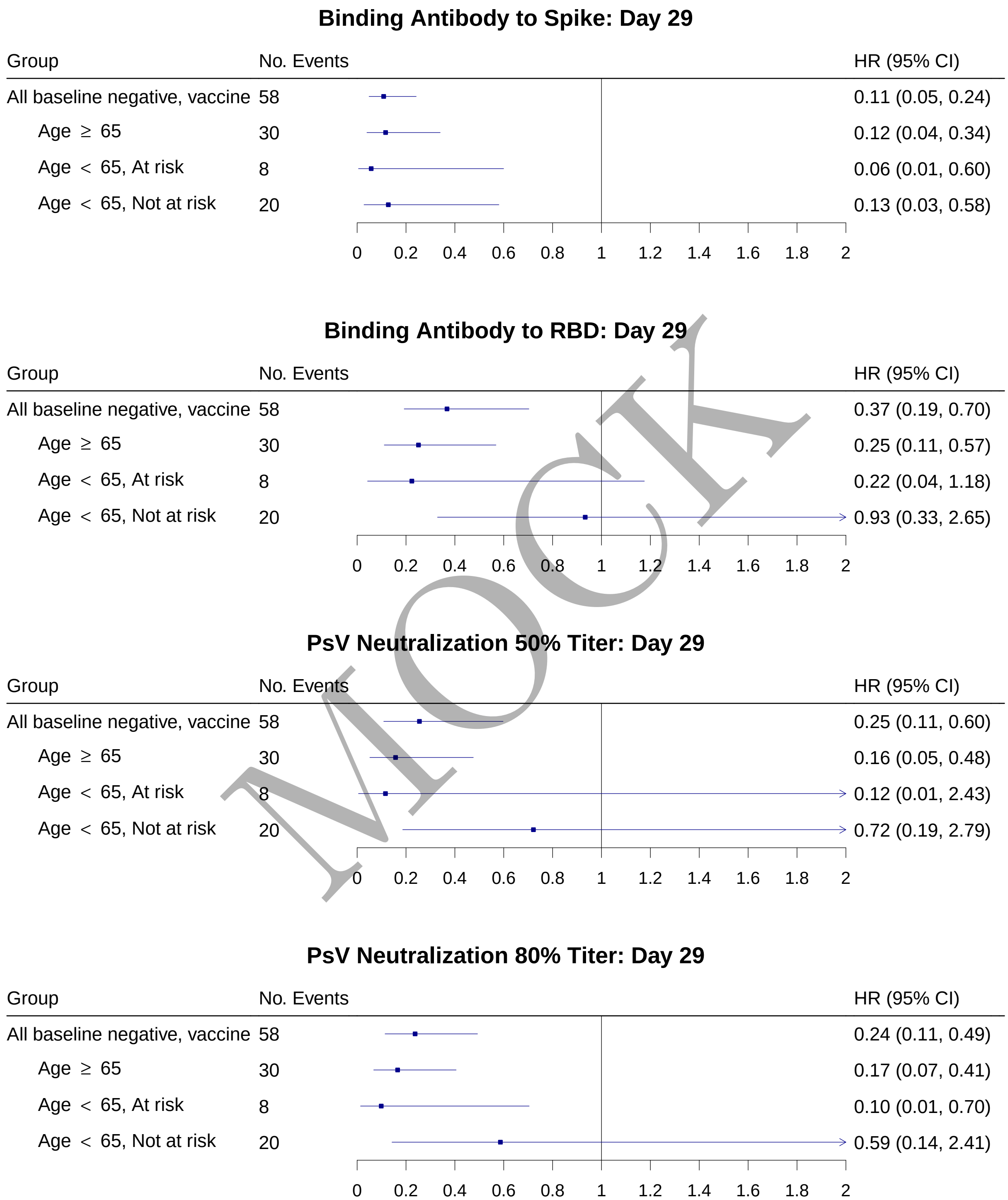




Figure 5.1: Forest plots of hazard ratios per 10-fold increase in the marker among baseline negative vaccine recipients and subgroups with 95% point-wise confidence intervals.

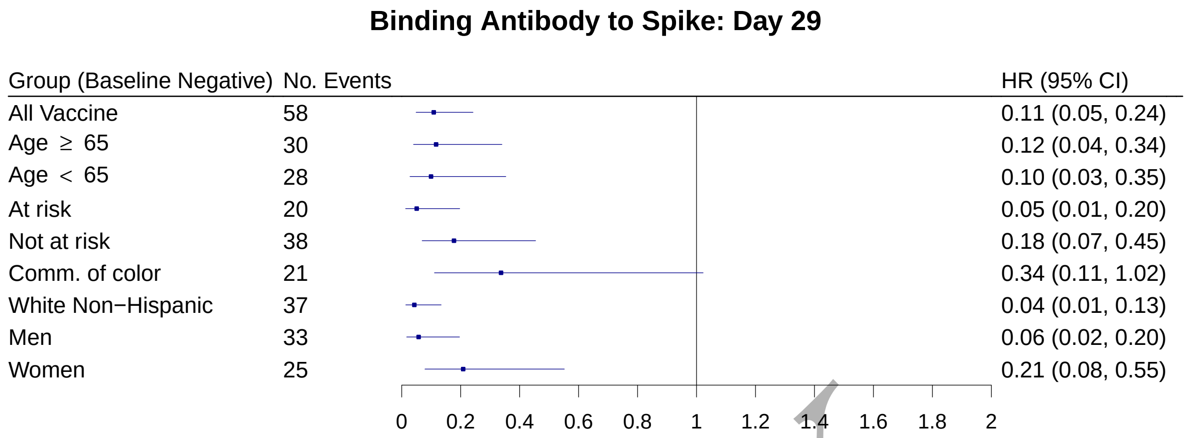



Figure 5.2: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.



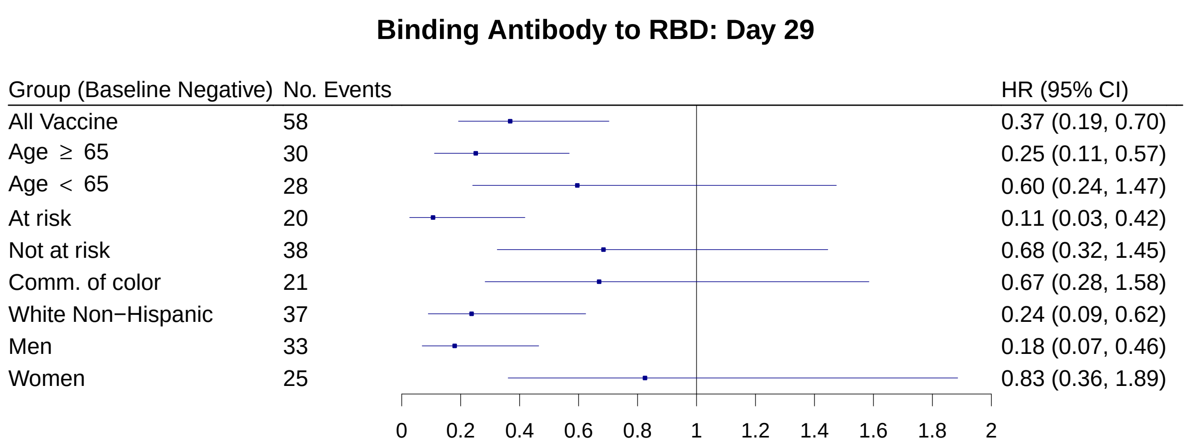



Figure 5.3: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.

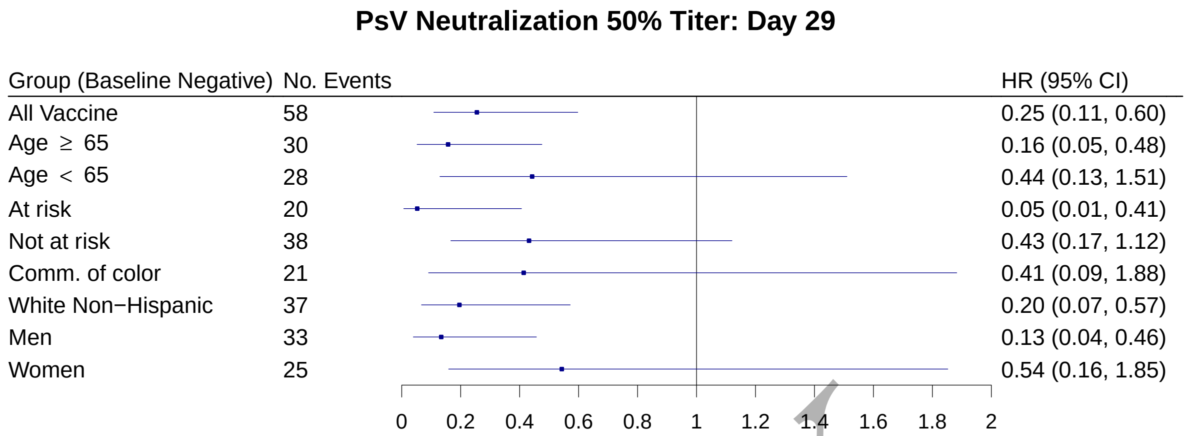



Figure 5.4: Forest plots of hazard ratios per 10-fold increase in the Day 29 pseudo neut ID50 markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.



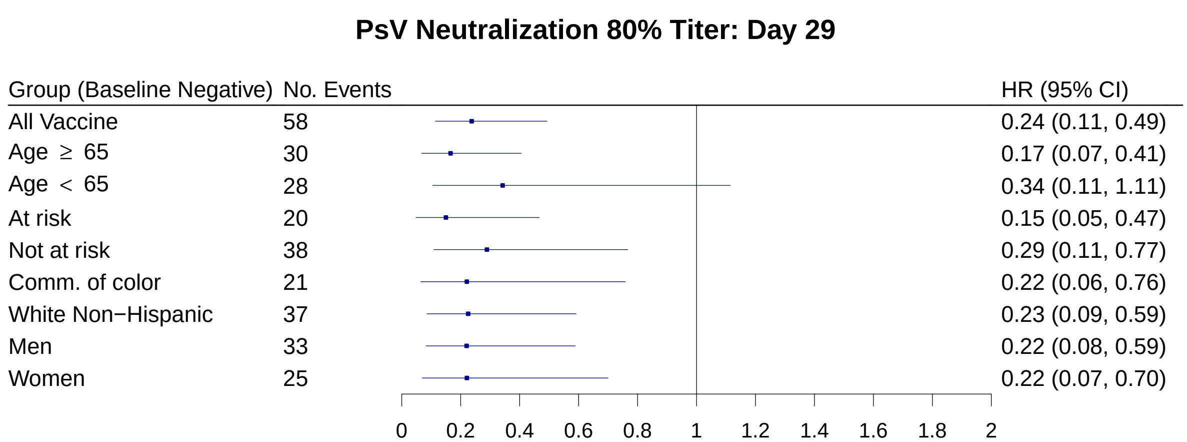


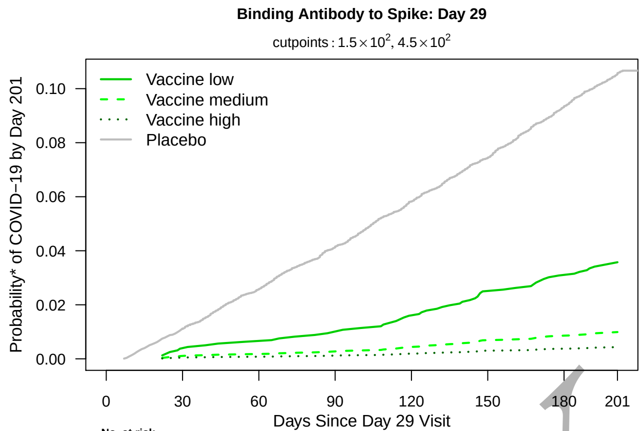

Figure 5.5: Forest plots of hazard ratios per 10-fold increase in the Day 29 pseudo neut ID80 markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.

## 5.2 Marginalized risk and controlled vaccine efficacy plots

Table 5.3: Analysis of Day 29 markers (upper vs. lower tertile) as a CoR and a controlled risk CoP.

| | marginalized risk ratio $RR_M(0,1)$ | | controlled risk ratio $RR_C(0,1)^1$ | | e(0,1)$^2$ | |
|---|---|---|---|---|---|---|
| | Point Est. | 95% CI | Point Est. | 95% CI | Point Est. | 95% CI UL |
| Anti Spike IgG (BAU/ml) | 0.12 | 0.06–0.21 | 0.16 | 0.08–0.29 | 16.1 | 8.8 |
| Anti RBD IgG (BAU/ml) | 0.21 | 0.11–0.38 | 0.28 | 0.14–0.51 | 9.0 | 4.7 |
| Pseudovirus-nAb cID50 | 0.29 | 0.24–0.37 | 0.38 | 0.32–0.50 | 6.4 | 4.8 |
| Pseudovirus-nAb cID80 | 0.30 | 0.21–0.49 | 0.40 | 0.28–0.65 | 6.1 | 3.5 |

[1]Conservative (upper bound) estimate assuming unmeasured confounding at level $RR_{UD}(0,1) = RR_{EU}(0,1) = 2$ and thus $B(0,1) = 4/3$.
[2]E-values are computed for upper tertile ($s = 1$) vs. lower tertile ($s = 0$) biomarker subgroups after controlling for MinorityInd + HighRiskInd + Age; UL = upper limit.



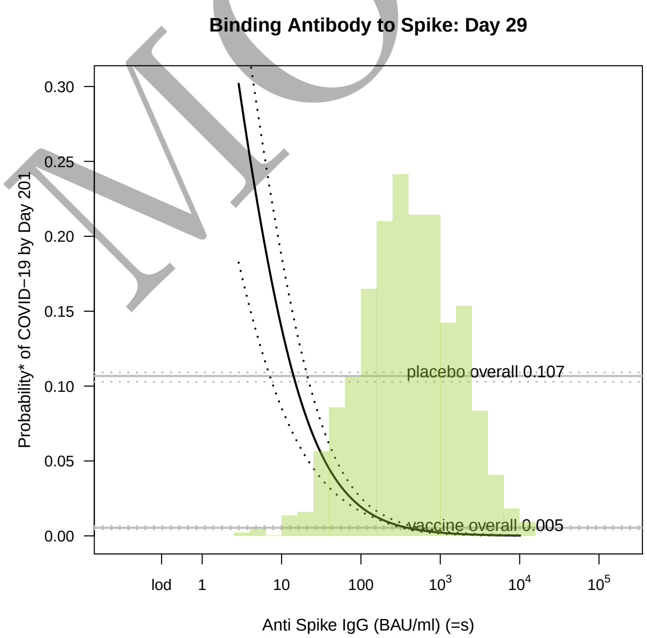

**No. at risk**

| | 0 | 30 | 60 | 90 | 120 | 150 | 180 | 201 |
|---|---|---|---|---|---|---|---|---|
| Low: | 3752 | 3749 | 3691 | 3671 | 3588 | 3583 | 3548 | 2828 |
| Med: | 3729 | 3728 | 3680 | 3650 | 3638 | 3561 | 3483 | 2688 |
| High: | 3723 | 3721 | 3690 | 3623 | 3614 | 3585 | 3518 | 2903 |
| Plac: | 11505 | 11381 | 11061 | 10703 | 10350 | 10021 | 9639 | 7830 |

**Cumulative No. of COVID−19 Endpoints**

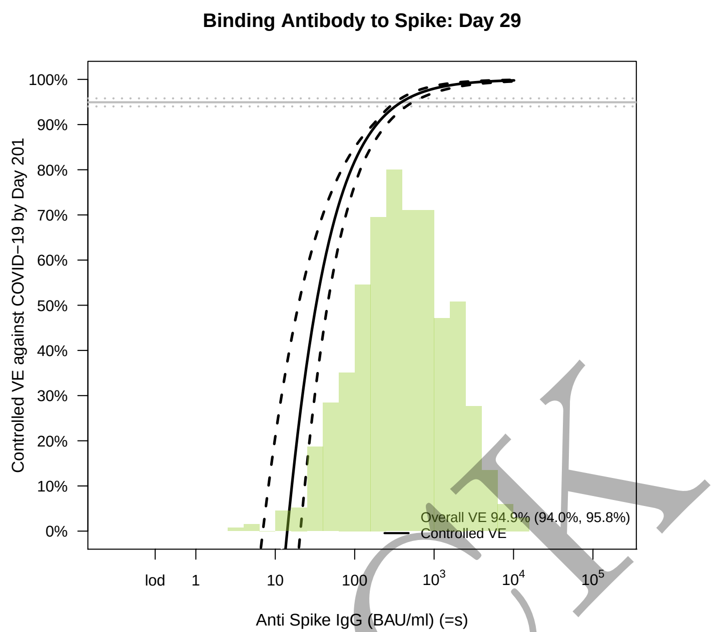
| | 0 | 30 | 60 | 90 | 120 | 150 | 180 | 201 |
|---|---|---|---|---|---|---|---|---|
| Low: | 0 | 3 | 6 | 7 | 14 | 19 | 22 | 24 |
| Med: | 0 | 1 | 1 | 3 | 7 | 11 | 14 | 17 |
| High: | 0 | 2 | 3 | 5 | 5 | 12 | 15 | 17 |
| Plac: | 0 | 129 | 296 | 473 | 658 | 835 | 1039 | 1166 |

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.



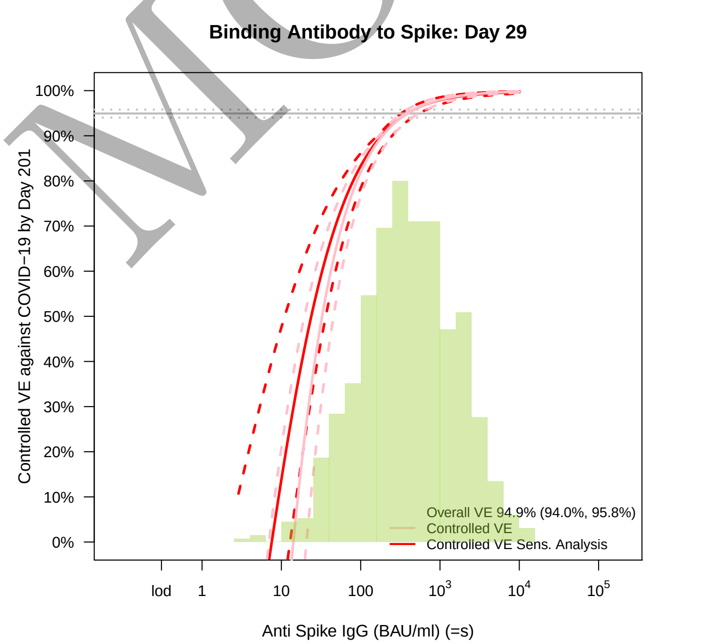

(b) Marginalized cumulative risk by Day 201 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 5.6: Marginalized cumulative risk curves (=s).



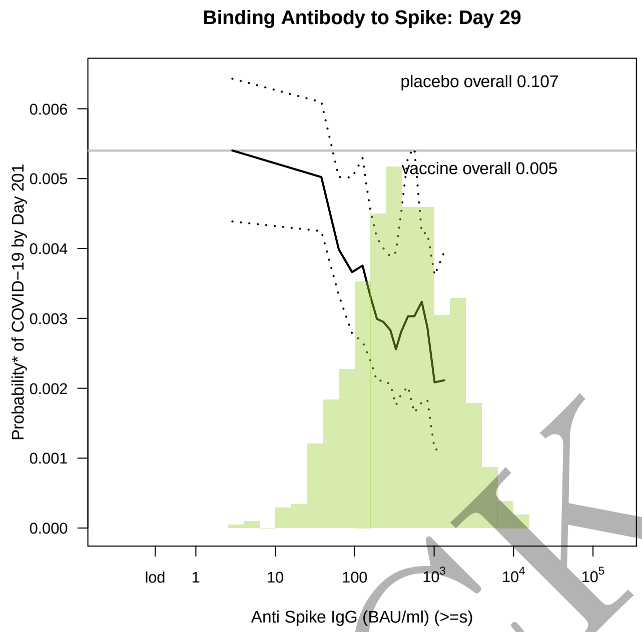

(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.



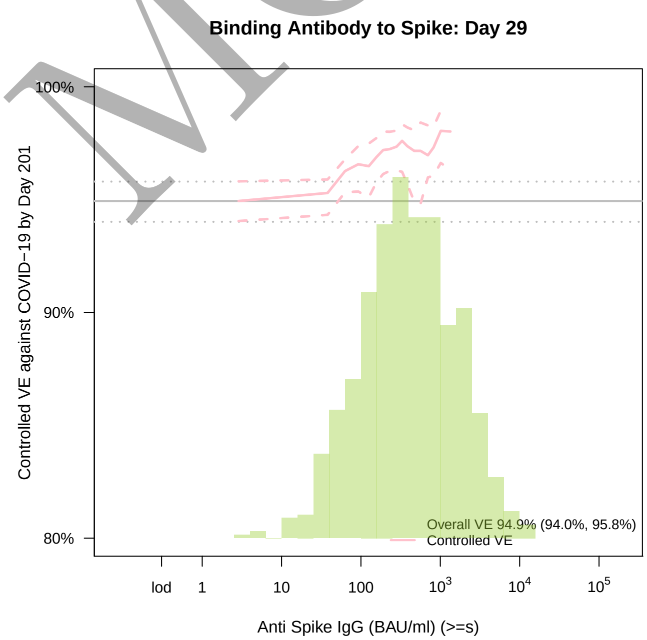



(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 5.7: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 201 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.




(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 5.8: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 5.4: Marginalized cumulative risk by Day 201 as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

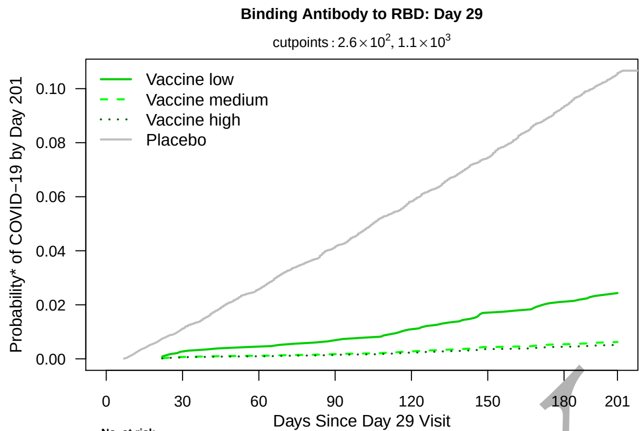
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 2.9 | .3018 (.1825,.3740) | 29 | .0590 (.0407,.0814) | 227 | .0089 (.0079,.0119) | 1294 | .0017 (.0011,.0025) |
| 3 | .2890 (.1744,.3594) | 32 | .0550 (.0383,.0756) | 228 | .0089 (.0079,.0119) | 1402 | .0016 (.0010,.0024) |
| 3 | .2764 (.1665,.3453) | 34 | .0511 (.0361,.0702) | 248 | .0082 (.0072,.0110) | 1523 | .0014 (.0009,.0022) |
| 4 | .2641 (.1589,.3314) | 37 | .0476 (.0340,.0651) | 269 | .0076 (.0066,.0102) | 1654 | .0013 (.0009,.0021) |
| 4 | .2520 (.1515,.3177) | 40 | .0442 (.0320,.0604) | 292 | .0070 (.0060,.0095) | 1779 | .0012 (.0008,.0019) |
| 4 | .2403 (.1443,.3046) | 44 | .0411 (.0301,.0559) | 318 | .0065 (.0055,.0088) | 1796 | .0012 (.0008,.0019) |
| 5 | .2288 (.1374,.2918) | 48 | .0382 (.0283,.0517) | 329 | .0063 (.0053,.0085) | 1950 | .0011 (.0007,.0018) |
| 5 | .2175 (.1307,.2792) | 52 | .0354 (.0267,.0478) | 345 | .0060 (.0050,.0081) | 2118 | .0011 (.0007,.0017) |
| 6 | .2066 (.1243,.2668) | 56 | .0329 (.0251,.0443) | 375 | .0056 (.0046,.0075) | 2238 | .0010 (.0006,.0016) |
| 6 | .1960 (.1181,.2546) | 61 | .0305 (.0236,.0410) | 407 | .0051 (.0042,.0070) | 2300 | .0010 (.0006,.0015) |
| 7 | .1858 (.1122,.2428) | 64 | .0293 (.0228,.0392) | 442 | .0047 (.0038,.0065) | 2498 | .0009 (.0005,.0014) |
| 7 | .1758 (.1064,.2311) | 66 | .0283 (.0222,.0379) | 474 | .0044 (.0035,.0061) | 2713 | .0008 (.0005,.0013) |
| 8 | .1662 (.1010,.2198) | 72 | .0262 (.0208,.0350) | 480 | .0044 (.0035,.0060) | 2946 | .0008 (.0005,.0012) |
| 8 | .1570 (.0957,.2087) | 78 | .0243 (.0196,.0323) | 500 | .0042 (.0033,.0058) | 3200 | .0007 (.0004,.0012) |
| 9 | .1480 (.0907,.1980) | 85 | .0225 (.0184,.0299) | 521 | .0041 (.0032,.0056) | 3475 | .0007 (.0004,.0011) |
| 10 | .1395 (.0859,.1875) | 92 | .0209 (.0173,.0276) | 566 | .0037 (.0029,.0052) | 3774 | .0006 (.0003,.0010) |
| 11 | .1313 (.0813,.1773) | 93 | .0208 (.0172,.0274) | 614 | .0035 (.0026,.0049) | 4098 | .0006 (.0003,.0009) |
| 12 | .1234 (.0769,.1675) | 100 | .0193 (.0163,.0254) | 667 | .0032 (.0024,.0045) | 4451 | .0005 (.0003,.0009) |
| 13 | .1159 (.0727,.1580) | 109 | .0179 (.0153,.0234) | 708 | .0030 (.0022,.0043) | 4833 | .0005 (.0003,.0008) |
| 14 | .1088 (.0687,.1488) | 118 | .0166 (.0144,.0216) | 725 | .0030 (.0022,.0042) | 5249 | .0004 (.0002,.0008) |
| 15 | .1020 (.0649,.1399) | 128 | .0153 (.0135,.0200) | 787 | .0027 (.0020,.0039) | 5700 | .0004 (.0002,.0007) |
| 16 | .0955 (.0613,.1314) | 130 | .0151 (.0133,.0197) | 855 | .0025 (.0018,.0037) | 6191 | .0004 (.0002,.0007) |
| 18 | .0893 (.0579,.1232) | 139 | .0142 (.0127,.0185) | 928 | .0023 (.0017,.0034) | 6723 | .0003 (.0002,.0006) |
| 19 | .0835 (.0546,.1154) | 151 | .0131 (.0119,.0172) | 1000 | .0022 (.0015,.0032) | 7301 | .0003 (.0002,.0006) |
| 21 | .0780 (.0515,.1079) | 164 | .0122 (.0111,.0160) | 1008 | .0022 (.0015,.0032) | 7929 | .0003 (.0001,.0006) |
| 23 | .0729 (.0486,.1007) | 178 | .0112 (.0102,.0148) | 1095 | .0020 (.0014,.0029) | 8611 | .0003 (.0001,.0005) |
| 25 | .0680 (.0458,.0939) | 194 | .0104 (.0094,.0138) | 1189 | .0018 (.0013,.0027) | 9352 | .0003 (.0001,.0005) |
| 27 | .0634 (.0432,.0875) | 210 | .0096 (.0086,.0128) | 1291 | .0017 (.0011,.0026) | 10156 | .0002 (.0001,.0005) |

Table 5.5: Controlled VE as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 201 days post Day 29 was 0.005 in vaccine recipients compared to 0.107 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 95.8%).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 2.9 | -1.8278 (-2.5181,-0.6901) | 32 | 0.4850 ( 0.3018, 0.6451) | 248 | 0.9229 ( 0.8986, 0.9320) | 1654 | 0.9875 ( 0.9809, 0.9919) |
| 3 | -1.7078 (-2.3748,-0.6151) | 34 | 0.5207 ( 0.3514, 0.6658) | 269 | 0.9287 ( 0.9059, 0.9379) | 1779 | 0.9883 ( 0.9821, 0.9925) |
| 3 | -1.5900 (-2.2335,-0.5422) | 37 | 0.5542 ( 0.3981, 0.6853) | 292 | 0.9341 ( 0.9127, 0.9433) | 1796 | 0.9884 ( 0.9822, 0.9926) |
| 4 | -1.4745 (-2.0942,-0.4715) | 40 | 0.5856 ( 0.4420, 0.7038) | 318 | 0.9391 ( 0.9191, 0.9483) | 1950 | 0.9893 ( 0.9834, 0.9932) |
| 4 | -1.3615 (-1.9572,-0.4031) | 44 | 0.6149 ( 0.4832, 0.7212) | 329 | 0.9412 ( 0.9217, 0.9504) | 2118 | 0.9901 ( 0.9846, 0.9938) |
| 4 | -1.2511 (-1.8227,-0.3368) | 48 | 0.6424 ( 0.5218, 0.7377) | 345 | 0.9437 ( 0.9250, 0.9528) | 2238 | 0.9906 ( 0.9853, 0.9942) |
| 5 | -1.1433 (-1.6927,-0.2727) | 52 | 0.6679 ( 0.5578, 0.7532) | 375 | 0.9479 ( 0.9303, 0.9570) | 2300 | 0.9909 ( 0.9857, 0.9944) |
| 5 | -1.0383 (-1.5758,-0.2109) | 56 | 0.6918 ( 0.5915, 0.7679) | 407 | 0.9519 ( 0.9353, 0.9608) | 2498 | 0.9916 ( 0.9866, 0.9949) |
| 6 | -0.9361 (-1.4615,-0.1514) | 61 | 0.7141 ( 0.6226, 0.7817) | 442 | 0.9555 ( 0.9399, 0.9642) | 2713 | 0.9922 ( 0.9876, 0.9953) |
| 6 | -0.8368 (-1.3495,-0.0940) | 64 | 0.7258 ( 0.6386, 0.7890) | 474 | 0.9584 ( 0.9435, 0.9669) | 2946 | 0.9928 ( 0.9884, 0.9957) |
| 7 | -0.7406 (-1.2398,-0.0389) | 66 | 0.7348 ( 0.6509, 0.7947) | 480 | 0.9589 ( 0.9441, 0.9674) | 3200 | 0.9934 ( 0.9892, 0.9961) |
| 7 | -0.6474 (-1.1326, 0.0141) | 72 | 0.7541 ( 0.6773, 0.8070) | 500 | 0.9605 ( 0.9461, 0.9688) | 3475 | 0.9939 ( 0.9899, 0.9965) |
| 8 | -0.5574 (-1.0279, 0.0649) | 78 | 0.7721 ( 0.7019, 0.8186) | 521 | 0.9620 ( 0.9480, 0.9702) | 3774 | 0.9943 ( 0.9906, 0.9968) |
| 8 | -0.4706 (-0.9258, 0.1136) | 85 | 0.7888 ( 0.7248, 0.8295) | 566 | 0.9649 ( 0.9516, 0.9729) | 4098 | 0.9948 ( 0.9912, 0.9971) |
| 9 | -0.3871 (-0.8264, 0.1602) | 92 | 0.8044 ( 0.7460, 0.8397) | 614 | 0.9676 ( 0.9549, 0.9753) | 4451 | 0.9952 ( 0.9917, 0.9973) |
| 10 | -0.3069 (-0.7298, 0.2048) | 93 | 0.8054 ( 0.7474, 0.8404) | 667 | 0.9700 ( 0.9580, 0.9774) | 4833 | 0.9955 ( 0.9922, 0.9976) |
| 11 | -0.2300 (-0.6360, 0.2474) | 100 | 0.8188 ( 0.7657, 0.8494) | 708 | 0.9717 ( 0.9601, 0.9789) | 5249 | 0.9959 ( 0.9927, 0.9978) |
| 12 | -0.1564 (-0.5452, 0.2880) | 109 | 0.8322 ( 0.7840, 0.8585) | 725 | 0.9723 ( 0.9609, 0.9794) | 5700 | 0.9962 ( 0.9932, 0.9980) |
| 13 | -0.0861 (-0.4573, 0.3268) | 118 | 0.8447 ( 0.8009, 0.8671) | 787 | 0.9744 ( 0.9636, 0.9812) | 6191 | 0.9965 ( 0.9936, 0.9982) |
| 14 | -0.0191 (-0.3724, 0.3637) | 128 | 0.8562 ( 0.8159, 0.8751) | 855 | 0.9764 ( 0.9661, 0.9829) | 6723 | 0.9968 ( 0.9940, 0.9983) |
| 15 | 0.0447 (-0.2906, 0.3989) | 130 | 0.8583 ( 0.8184, 0.8766) | 928 | 0.9782 ( 0.9684, 0.9844) | 7301 | 0.9970 ( 0.9944, 0.9985) |
| 16 | 0.1054 (-0.2120, 0.4323) | 139 | 0.8669 ( 0.8290, 0.8827) | 1000 | 0.9797 ( 0.9704, 0.9857) | 7929 | 0.9972 ( 0.9947, 0.9986) |
| 18 | 0.1628 (-0.1365, 0.4641) | 151 | 0.8768 ( 0.8412, 0.8898) | 1008 | 0.9798 ( 0.9706, 0.9858) | 8611 | 0.9974 ( 0.9950, 0.9987) |
| 19 | 0.2173 (-0.0642, 0.4942) | 164 | 0.8861 ( 0.8526, 0.8970) | 1095 | 0.9814 ( 0.9727, 0.9870) | 9352 | 0.9976 ( 0.9954, 0.9988) |
| 21 | 0.2688 ( 0.0048, 0.5229) | 178 | 0.8946 ( 0.8631, 0.9039) | 1189 | 0.9828 ( 0.9745, 0.9882) | 10156 | 0.9978 ( 0.9956, 0.9989) |
| 23 | 0.3174 ( 0.0707, 0.5500) | 194 | 0.9025 ( 0.8730, 0.9117) | 1291 | 0.9841 ( 0.9763, 0.9892) | 47.6 | .6424 (.5218,.7377) |
| 25 | 0.3632 ( 0.1333, 0.5758) | 210 | 0.9098 ( 0.8821, 0.9189) | 1294 | 0.9841 ( 0.9764, 0.9893) | 194 | .9025 (.8730,.9117) |
| 27 | 0.4063 ( 0.1927, 0.6002) | 227 | 0.9162 ( 0.8901, 0.9250) | 1402 | 0.9853 ( 0.9779, 0.9902) | 407 | .9519 (.9353,.9608) |
| 29 | 0.4469 ( 0.2490, 0.6233) | 228 | 0.9166 ( 0.8906, 0.9254) | 1523 | 0.9864 ( 0.9795, 0.9911) | | |

Table 5.6: Controlled VE with sensitivity analysis as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 2.9 | -0.4936 (-0.8582,.1073) | 32 | 0.5898 ( 0.4439,.7174) | 248 | 0.9238 ( 0.8998,.9328) | 1654 | 0.9864 ( 0.9793,.9912) |
| 3 | -0.4529 (-0.8108,.1334) | 34 | 0.6137 ( 0.4773,.7306) | 269 | 0.9293 ( 0.9067,.9384) | 1779 | 0.9872 ( 0.9804,.9918) |
| 3 | -0.4116 (-0.7623,.1595) | 37 | 0.6365 ( 0.5092,.7434) | 292 | 0.9345 ( 0.9132,.9437) | 1796 | 0.9873 ( 0.9805,.9919) |
| 4 | -0.3698 (-0.7128,.1854) | 40 | 0.6581 ( 0.5397,.7556) | 318 | 0.9393 ( 0.9193,.9485) | 1950 | 0.9882 ( 0.9817,.9925) |
| 4 | -0.3276 (-0.6625,.2112) | 44 | 0.6787 ( 0.5688,.7674) | 329 | 0.9413 ( 0.9219,.9505) | 2118 | 0.9890 ( 0.9828,.9931) |
| 4 | -0.2851 (-0.6114,.2369) | 48 | 0.6983 ( 0.5965,.7787) | 345 | 0.9438 ( 0.9251,.9529) | 2238 | 0.9895 ( 0.9835,.9935) |
| 5 | -0.2424 (-0.5609,.2622) | 52 | 0.7168 ( 0.6229,.7895) | 375 | 0.9480 ( 0.9303,.9570) | 2300 | 0.9897 ( 0.9839,.9937) |
| 5 | -0.1996 (-0.5160,.2873) | 56 | 0.7344 ( 0.6479,.7999) | 407 | 0.9519 ( 0.9353,.9608) | 2498 | 0.9904 ( 0.9848,.9942) |
| 6 | -0.1568 (-0.4707,.3121) | 61 | 0.7510 ( 0.6713,.8099) | 442 | 0.9555 ( 0.9399,.9642) | 2713 | 0.9911 ( 0.9857,.9946) |
| 6 | -0.1140 (-0.4249,.3365) | 64 | 0.7599 ( 0.6835,.8152) | 474 | 0.9583 ( 0.9434,.9669) | 2946 | 0.9917 ( 0.9866,.9951) |
| 7 | -0.0714 (-0.3788,.3605) | 66 | 0.7667 ( 0.6929,.8194) | 480 | 0.9588 ( 0.9441,.9673) | 3200 | 0.9922 ( 0.9874,.9955) |
| 7 | -0.0292 (-0.3323,.3841) | 72 | 0.7816 ( 0.7133,.8285) | 500 | 0.9604 ( 0.9460,.9688) | 3475 | 0.9927 ( 0.9881,.9958) |
| 8 | 0.0127 (-0.2856,.4072) | 78 | 0.7956 ( 0.7326,.8373) | 521 | 0.9619 ( 0.9478,.9701) | 3774 | 0.9932 ( 0.9887,.9961) |
| 8 | 0.0540 (-0.2387,.4299) | 85 | 0.8088 ( 0.7508,.8456) | 566 | 0.9647 ( 0.9513,.9727) | 4098 | 0.9937 ( 0.9893,.9964) |
| 9 | 0.0948 (-0.1919,.4520) | 92 | 0.8213 ( 0.7680,.8536) | 614 | 0.9673 ( 0.9545,.9750) | 4451 | 0.9941 ( 0.9899,.9967) |
| 10 | 0.1349 (-0.1451,.4736) | 93 | 0.8221 ( 0.7691,.8541) | 667 | 0.9697 ( 0.9575,.9772) | 4833 | 0.9945 ( 0.9904,.9970) |
| 11 | 0.1742 (-0.0984,.4947) | 100 | 0.8330 ( 0.7841,.8612) | 708 | 0.9713 ( 0.9595,.9786) | 5249 | 0.9948 ( 0.9909,.9972) |
| 12 | 0.2126 (-0.0521,.5152) | 109 | 0.8441 ( 0.7993,.8685) | 725 | 0.9719 ( 0.9603,.9791) | 5700 | 0.9952 ( 0.9913,.9974) |
| 13 | 0.2501 (-0.0061,.5352) | 118 | 0.8545 ( 0.8135,.8755) | 787 | 0.9739 ( 0.9628,.9809) | 6191 | 0.9955 ( 0.9918,.9976) |
| 14 | 0.2867 ( 0.0393,.5546) | 128 | 0.8643 ( 0.8263,.8822) | 855 | 0.9758 ( 0.9652,.9825) | 6723 | 0.9958 ( 0.9922,.9978) |
| 15 | 0.3222 ( 0.0842,.5734) | 130 | 0.8661 ( 0.8284,.8834) | 928 | 0.9775 ( 0.9674,.9839) | 7301 | 0.9960 ( 0.9926,.9980) |
| 16 | 0.3565 ( 0.1283,.5917) | 139 | 0.8735 ( 0.8374,.8885) | 1000 | 0.9789 ( 0.9693,.9851) | 7929 | 0.9963 ( 0.9929,.9981) |
| 18 | 0.3898 ( 0.1716,.6094) | 151 | 0.8821 ( 0.8480,.8946) | 1008 | 0.9791 ( 0.9695,.9853) | 8611 | 0.9965 ( 0.9933,.9983) |
| 19 | 0.4219 ( 0.2140,.6265) | 164 | 0.8902 ( 0.8580,.9008) | 1095 | 0.9805 ( 0.9714,.9865) | 9352 | 0.9968 ( 0.9936,.9984) |
| 21 | 0.4529 ( 0.2554,.6430) | 178 | 0.8979 ( 0.8674,.9069) | 1189 | 0.9819 ( 0.9732,.9876) | 10156 | 0.9970 ( 0.9939,.9985) |
| 23 | 0.4826 ( 0.2957,.6590) | 194 | 0.9050 ( 0.8762,.9139) | 1291 | 0.9832 ( 0.9749,.9886) | 47.6 | .6424 (.5218,.7377) |
| 25 | 0.5112 ( 0.3347,.6744) | 210 | 0.9117 ( 0.8846,.9205) | 1294 | 0.9832 ( 0.9749,.9886) | 194 | .9025 (.8730,.9117) |
| 27 | 0.5386 ( 0.3726,.6893) | 227 | 0.9175 ( 0.8919,.9262) | 1402 | 0.9843 ( 0.9764,.9895) | 407 | .9519 (.9353,.9608) |
| 29 | 0.5648 ( 0.4091,.7036) | 228 | 0.9179 ( 0.8924,.9266) | 1523 | 0.9854 ( 0.9779,.9904) | | |



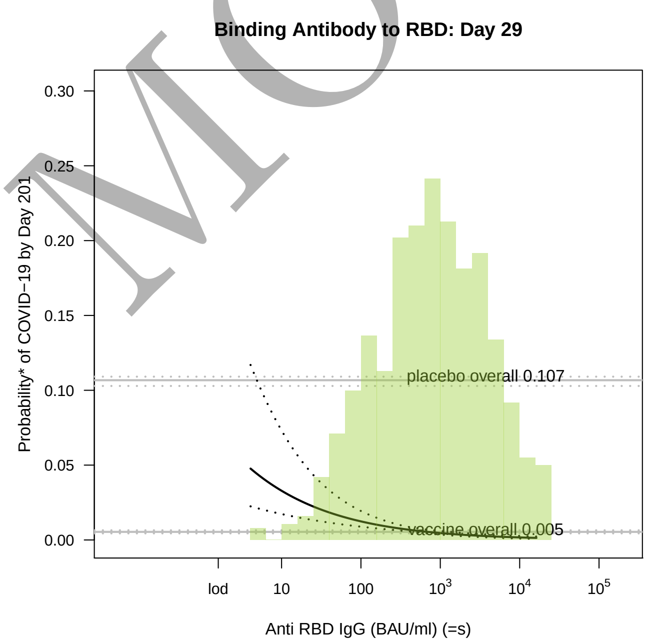

**No. at risk**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low: | 3745 | 3743 | 3730 | 3711 | 3625 | 3620 | 3550 | 2785 |
| Med: | 3747 | 3745 | 3691 | 3602 | 3596 | 3517 | 3449 | 2846 |
| High: | 3712 | 3710 | 3641 | 3631 | 3619 | 3591 | 3550 | 2788 |
| Plac: | 11505 | 11381 | 11061 | 10703 | 10350 | 10021 | 9639 | 7830 |

**Cumulative No. of COVID−19 Endpoints**

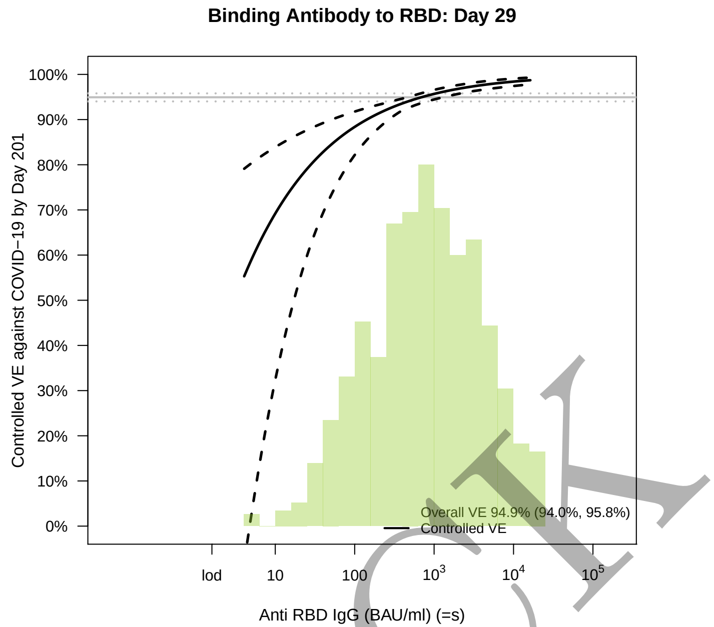
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low: | 0 | 2 | 3 | 3 | 13 | 18 | 24 | 27 |
| Med: | 0 | 2 | 4 | 7 | 8 | 9 | 11 | 13 |
| High: | 0 | 2 | 3 | 5 | 5 | 14 | 16 | 18 |
| Plac: | 0 | 129 | 296 | 473 | 658 | 835 | 1039 | 1166 |

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

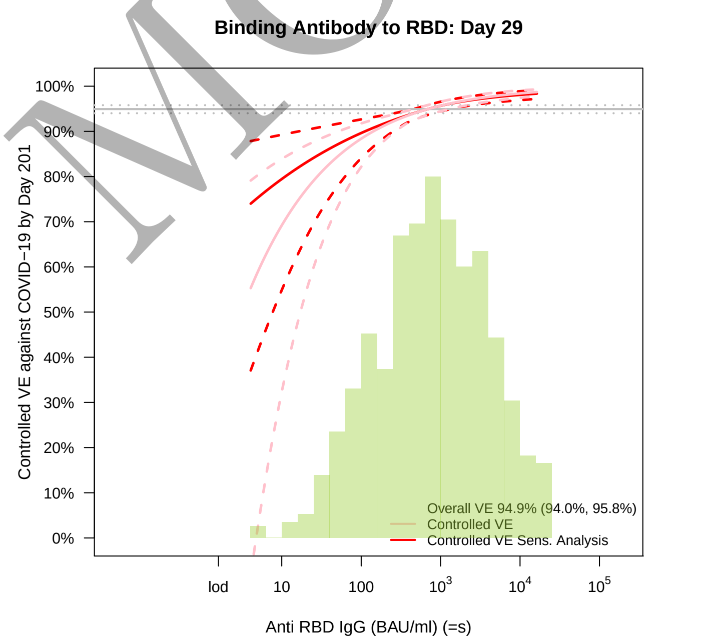



(b) Marginalized cumulative risk by Day 201 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 5.9: Marginalized cumulative risk curves (=s).

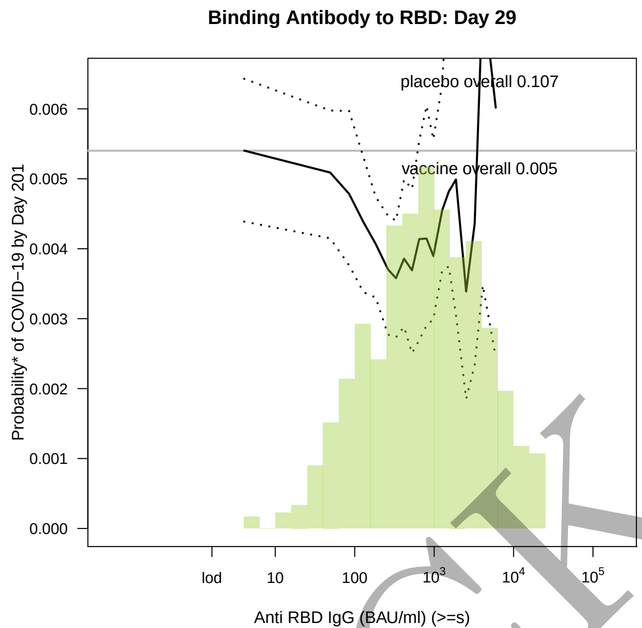



(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

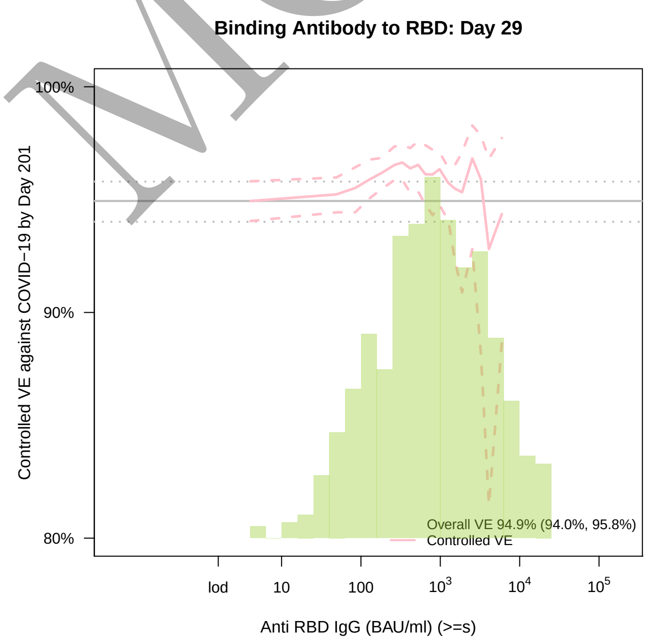



(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 5.10: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 201 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.




(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 5.11: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 5.7: Marginalized cumulative risk by Day 201 as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

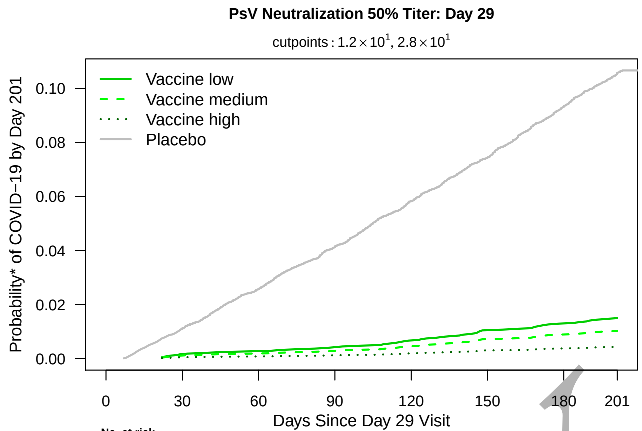
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 4.1 | .0477 (.0225,.1169) | 42 | .0179 (.0114,.0320) | 345 | .0073 (.0060,.0094) | 2178 | .0033 (.0024,.0045) |
| 4 | .0461 (.0219,.1122) | 46 | .0173 (.0111,.0305) | 375 | .0070 (.0059,.0089) | 2368 | .0032 (.0023,.0044) |
| 5 | .0445 (.0214,.1076) | 50 | .0166 (.0108,.0291) | 407 | .0068 (.0057,.0086) | 2575 | .0031 (.0022,.0042) |
| 5 | .0430 (.0209,.1031) | 55 | .0161 (.0106,.0277) | 408 | .0068 (.0057,.0086) | 2800 | .0030 (.0021,.0041) |
| 6 | .0416 (.0204,.0987) | 59 | .0155 (.0103,.0263) | 443 | .0065 (.0055,.0083) | 3045 | .0028 (.0020,.0040) |
| 6 | .0401 (.0199,.0945) | 65 | .0150 (.0101,.0251) | 482 | .0063 (.0053,.0080) | 3085 | .0028 (.0020,.0040) |
| 7 | .0388 (.0194,.0905) | 70 | .0144 (.0098,.0238) | 500 | .0062 (.0052,.0079) | 3311 | .0027 (.0019,.0039) |
| 7 | .0375 (.0190,.0866) | 76 | .0139 (.0096,.0227) | 524 | .0061 (.0051,.0077) | 3601 | .0026 (.0018,.0038) |
| 8 | .0362 (.0185,.0828) | 83 | .0134 (.0094,.0216) | 570 | .0059 (.0048,.0074) | 3915 | .0026 (.0017,.0036) |
| 9 | .0349 (.0181,.0792) | 87 | .0132 (.0092,.0210) | 620 | .0057 (.0046,.0072) | 4099 | .0025 (.0017,.0036) |
| 9 | .0337 (.0176,.0757) | 90 | .0130 (.0091,.0206) | 648 | .0056 (.0045,.0070) | 4258 | .0025 (.0016,.0035) |
| 10 | .0326 (.0172,.0723) | 98 | .0125 (.0089,.0196) | 674 | .0055 (.0044,.0069) | 4630 | .0024 (.0015,.0034) |
| 11 | .0315 (.0168,.0690) | 107 | .0121 (.0087,.0186) | 733 | .0053 (.0042,.0067) | 5034 | .0023 (.0015,.0033) |
| 12 | .0304 (.0164,.0659) | 116 | .0116 (.0085,.0177) | 797 | .0051 (.0040,.0065) | 5474 | .0022 (.0014,.0033) |
| 13 | .0293 (.0160,.0629) | 126 | .0112 (.0083,.0169) | 867 | .0049 (.0039,.0063) | 5736 | .0022 (.0014,.0032) |
| 14 | .0283 (.0156,.0600) | 129 | .0111 (.0082,.0167) | 942 | .0047 (.0037,.0061) | 5953 | .0021 (.0013,.0032) |
| 16 | .0273 (.0152,.0572) | 137 | .0108 (.0081,.0161) | 980 | .0046 (.0036,.0060) | 6473 | .0021 (.0013,.0031) |
| 17 | .0264 (.0149,.0546) | 149 | .0105 (.0079,.0153) | 1000 | .0046 (.0036,.0060) | 7039 | .0020 (.0012,.0030) |
| 18 | .0255 (.0145,.0520) | 162 | .0101 (.0077,.0146) | 1025 | .0046 (.0035,.0059) | 7654 | .0019 (.0012,.0029) |
| 20 | .0246 (.0142,.0496) | 176 | .0097 (.0075,.0139) | 1114 | .0044 (.0034,.0057) | 8323 | .0018 (.0011,.0029) |
| 22 | .0237 (.0138,.0472) | 191 | .0094 (.0073,.0133) | 1212 | .0042 (.0032,.0056) | 9050 | .0018 (.0010,.0028) |
| 24 | .0229 (.0135,.0450) | 192 | .0094 (.0073,.0132) | 1317 | .0041 (.0031,.0054) | 9841 | .0017 (.0010,.0027) |
| 26 | .0221 (.0132,.0428) | 209 | .0091 (.0071,.0126) | 1433 | .0039 (.0030,.0052) | 10701 | .0017 (.0009,.0026) |
| 28 | .0214 (.0129,.0408) | 227 | .0087 (.0070,.0120) | 1557 | .0038 (.0028,.0051) | 11636 | .0016 (.0009,.0026) |
| 30 | .0206 (.0125,.0389) | 247 | .0084 (.0068,.0114) | 1558 | .0038 (.0028,.0051) | 12653 | .0015 (.0009,.0025) |
| 33 | .0199 (.0122,.0371) | 268 | .0081 (.0066,.0109) | 1694 | .0037 (.0027,.0049) | 13759 | .0015 (.0008,.0024) |
| 36 | .0192 (.0119,.0353) | 292 | .0078 (.0064,.0103) | 1842 | .0035 (.0026,.0048) | 14962 | .0014 (.0008,.0024) |
| 39 | .0185 (.0117,.0336) | 317 | .0076 (.0062,.0098) | 2003 | .0034 (.0025,.0046) | 16269 | .0014 (.0007,.0023) |

Table 5.8: Controlled VE as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 201 days post Day 29 was 0.005 in vaccine recipients compared to 0.107 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 95.8%).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 4.1 | .5531 (-0.0817,.7912) | 46 | .8384 ( 0.7182,.8968) | 407 | .9364 ( 0.9207,.9469) | 2800 | .9724 ( 0.9617,.9805) |
| 4 | .5682 (-0.0376,.7961) | 50 | .8440 ( 0.7317,.8993) | 408 | .9364 ( 0.9208,.9469) | 3045 | .9733 ( 0.9627,.9814) |
| 5 | .5828 ( 0.0051,.8010) | 55 | .8495 ( 0.7446,.9017) | 443 | .9387 ( 0.9236,.9485) | 3085 | .9735 ( 0.9629,.9816) |
| 5 | .5969 ( 0.0466,.8058) | 59 | .8548 ( 0.7569,.9041) | 482 | .9409 ( 0.9264,.9502) | 3311 | .9743 ( 0.9637,.9823) |
| 6 | .6106 ( 0.0866,.8104) | 65 | .8599 ( 0.7686,.9064) | 500 | .9418 ( 0.9275,.9511) | 3601 | .9752 ( 0.9646,.9831) |
| 6 | .6238 ( 0.1254,.8149) | 70 | .8648 ( 0.7798,.9087) | 524 | .9430 ( 0.9290,.9522) | 3915 | .9761 ( 0.9656,.9840) |
| 7 | .6366 ( 0.1629,.8193) | 76 | .8695 ( 0.7904,.9109) | 570 | .9450 ( 0.9315,.9541) | 4099 | .9766 ( 0.9660,.9844) |
| 7 | .6490 ( 0.1991,.8237) | 83 | .8741 ( 0.8006,.9131) | 620 | .9469 ( 0.9338,.9560) | 4258 | .9769 ( 0.9665,.9847) |
| 8 | .6610 ( 0.2340,.8279) | 87 | .8767 ( 0.8062,.9143) | 648 | .9479 ( 0.9349,.9569) | 4630 | .9778 ( 0.9673,.9854) |
| 9 | .6726 ( 0.2677,.8320) | 90 | .8785 ( 0.8103,.9152) | 674 | .9488 ( 0.9359,.9578) | 5034 | .9786 ( 0.9682,.9861) |
| 9 | .6839 ( 0.3001,.8360) | 98 | .8828 ( 0.8195,.9172) | 733 | .9506 ( 0.9378,.9596) | 5474 | .9793 ( 0.9690,.9868) |
| 10 | .6947 ( 0.3314,.8400) | 107 | .8870 ( 0.8283,.9192) | 797 | .9524 ( 0.9397,.9614) | 5736 | .9797 ( 0.9694,.9871) |
| 11 | .7052 ( 0.3615,.8438) | 116 | .8909 ( 0.8365,.9212) | 867 | .9541 ( 0.9415,.9630) | 5953 | .9801 ( 0.9698,.9874) |
| 12 | .7153 ( 0.3904,.8475) | 126 | .8948 ( 0.8443,.9231) | 942 | .9557 ( 0.9432,.9647) | 6473 | .9808 ( 0.9706,.9880) |
| 13 | .7252 ( 0.4182,.8512) | 129 | .8957 ( 0.8462,.9236) | 980 | .9565 ( 0.9440,.9654) | 7039 | .9815 ( 0.9713,.9886) |
| 14 | .7346 ( 0.4449,.8548) | 137 | .8985 ( 0.8518,.9250) | 1000 | .9568 ( 0.9444,.9658) | 7654 | .9821 ( 0.9721,.9891) |
| 16 | .7438 ( 0.4706,.8583) | 149 | .9021 ( 0.8589,.9268) | 1025 | .9573 ( 0.9449,.9662) | 8323 | .9828 ( 0.9728,.9896) |
| 17 | .7527 ( 0.4952,.8617) | 162 | .9055 ( 0.8656,.9286) | 1114 | .9588 ( 0.9466,.9677) | 9050 | .9834 ( 0.9735,.9901) |
| 18 | .7612 ( 0.5188,.8650) | 176 | .9089 ( 0.8721,.9303) | 1212 | .9603 ( 0.9482,.9691) | 9841 | .9840 ( 0.9742,.9906) |
| 20 | .7695 ( 0.5414,.8683) | 191 | .9119 ( 0.8779,.9319) | 1317 | .9617 ( 0.9497,.9705) | 10701 | .9845 ( 0.9748,.9911) |
| 22 | .7775 ( 0.5631,.8714) | 192 | .9121 ( 0.8782,.9320) | 1433 | .9631 ( 0.9512,.9718) | 11636 | .9851 ( 0.9755,.9915) |
| 24 | .7853 ( 0.5839,.8745) | 209 | .9152 ( 0.8840,.9336) | 1557 | .9644 ( 0.9527,.9730) | 12653 | .9856 ( 0.9761,.9919) |
| 26 | .7927 ( 0.6037,.8775) | 227 | .9182 ( 0.8896,.9353) | 1558 | .9644 ( 0.9527,.9730) | 13759 | .9861 ( 0.9767,.9923) |
| 28 | .7999 ( 0.6227,.8805) | 247 | .9211 ( 0.8949,.9368) | 1694 | .9656 ( 0.9541,.9742) | 14962 | .9866 ( 0.9773,.9926) |
| 30 | .8069 ( 0.6407,.8834) | 268 | .9239 ( 0.8999,.9384) | 1842 | .9669 ( 0.9554,.9753) | 16269 | .9871 ( 0.9779,.9930) |
| 33 | .8136 ( 0.6576,.8862) | 292 | .9266 ( 0.9047,.9403) | 2003 | .9680 ( 0.9568,.9764) | 7.3 | .6490 (.1991,.8237) |
| 36 | .8201 ( 0.6738,.8889) | 317 | .9292 ( 0.9093,.9420) | 2178 | .9692 ( 0.9581,.9774) | 137 | .8985 (.8518,.9250) |
| 39 | .8264 ( 0.6893,.8916) | 345 | .9317 ( 0.9136,.9437) | 2368 | .9703 ( 0.9593,.9785) | 733 | .9506 (.9378,.9596) |
| 42 | .8325 ( 0.7041,.8942) | 375 | .9341 ( 0.9177,.9453) | 2575 | .9713 ( 0.9605,.9795) | | |

Table 5.9: Controlled VE with sensitivity analysis as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 4.1 | .7400 (.3708,.8785) | 46 | .8676 (.7692,.9155) | 407 | .9372 (.9217,.9476) | 2800 | .9707 (.9595,.9793) |
| 4 | .7455 (.3884,.8798) | 50 | .8710 (.7780,.9167) | 408 | .9372 (.9218,.9476) | 3045 | .9716 (.9603,.9802) |
| 5 | .7509 (.4059,.8812) | 55 | .8743 (.7866,.9179) | 443 | .9393 (.9243,.9489) | 3085 | .9717 (.9604,.9803) |
| 5 | .7562 (.4232,.8825) | 59 | .8775 (.7949,.9191) | 482 | .9413 (.9268,.9505) | 3311 | .9724 (.9611,.9810) |
| 6 | .7614 (.4403,.8838) | 65 | .8807 (.8029,.9203) | 500 | .9421 (.9279,.9513) | 3601 | .9732 (.9618,.9818) |
| 6 | .7665 (.4571,.8851) | 70 | .8838 (.8107,.9215) | 524 | .9432 (.9293,.9524) | 3915 | .9740 (.9625,.9825) |
| 7 | .7716 (.4737,.8864) | 76 | .8869 (.8182,.9227) | 570 | .9451 (.9317,.9542) | 4099 | .9744 (.9629,.9829) |
| 7 | .7765 (.4900,.8877) | 83 | .8899 (.8255,.9239) | 620 | .9470 (.9338,.9560) | 4258 | .9747 (.9632,.9832) |
| 8 | .7814 (.5061,.8890) | 87 | .8916 (.8296,.9246) | 648 | .9480 (.9349,.9570) | 4630 | .9754 (.9639,.9839) |
| 9 | .7863 (.5219,.8903) | 90 | .8928 (.8325,.9251) | 674 | .9488 (.9359,.9578) | 5034 | .9761 (.9645,.9846) |
| 9 | .7910 (.5374,.8916) | 98 | .8957 (.8393,.9263) | 733 | .9506 (.9378,.9596) | 5474 | .9768 (.9652,.9852) |
| 10 | .7957 (.5526,.8929) | 107 | .8985 (.8459,.9275) | 797 | .9524 (.9397,.9613) | 5736 | .9771 (.9655,.9855) |
| 11 | .8003 (.5674,.8942) | 116 | .9013 (.8521,.9287) | 867 | .9540 (.9414,.9630) | 5953 | .9774 (.9658,.9857) |
| 12 | .8048 (.5820,.8955) | 126 | .9041 (.8581,.9299) | 942 | .9556 (.9431,.9646) | 6473 | .9780 (.9664,.9863) |
| 13 | .8093 (.5963,.8967) | 129 | .9047 (.8595,.9302) | 980 | .9563 (.9439,.9653) | 7039 | .9786 (.9669,.9868) |
| 14 | .8136 (.6102,.8980) | 137 | .9067 (.8638,.9311) | 1000 | .9567 (.9442,.9656) | 7654 | .9792 (.9675,.9874) |
| 16 | .8180 (.6238,.8993) | 149 | .9094 (.8694,.9322) | 1025 | .9571 (.9447,.9661) | 8323 | .9797 (.9680,.9878) |
| 17 | .8222 (.6371,.9006) | 162 | .9120 (.8748,.9334) | 1114 | .9585 (.9462,.9675) | 9050 | .9803 (.9686,.9883) |
| 18 | .8263 (.6500,.9018) | 176 | .9145 (.8800,.9346) | 1212 | .9599 (.9477,.9688) | 9841 | .9808 (.9691,.9888) |
| 20 | .8304 (.6626,.9031) | 191 | .9168 (.8847,.9357) | 1317 | .9612 (.9491,.9701) | 10701 | .9813 (.9696,.9892) |
| 22 | .8345 (.6749,.9043) | 192 | .9170 (.8850,.9358) | 1433 | .9625 (.9504,.9713) | 11636 | .9818 (.9701,.9896) |
| 24 | .8384 (.6869,.9056) | 209 | .9194 (.8898,.9369) | 1557 | .9636 (.9517,.9725) | 12653 | .9823 (.9706,.9900) |
| 26 | .8423 (.6985,.9068) | 227 | .9218 (.8944,.9381) | 1558 | .9637 (.9517,.9725) | 13759 | .9827 (.9710,.9904) |
| 28 | .8461 (.7098,.9081) | 247 | .9241 (.8989,.9393) | 1694 | .9648 (.9530,.9736) | 14962 | .9832 (.9715,.9907) |
| 30 | .8498 (.7206,.9093) | 268 | .9264 (.9032,.9405) | 1842 | .9659 (.9541,.9746) | 16269 | .9836 (.9719,.9911) |
| 33 | .8535 (.7309,.9106) | 292 | .9287 (.9074,.9420) | 2003 | .9669 (.9553,.9756) | 7.3 | .6490 (.1991,.8237) |
| 36 | .8571 (.7409,.9118) | 317 | .9309 (.9114,.9434) | 2178 | .9679 (.9564,.9765) | 137 | .8985 (.8518,.9250) |
| 39 | .8607 (.7506,.9130) | 345 | .9330 (.9153,.9448) | 2368 | .9689 (.9575,.9775) | 733 | .9506 (.9378,.9596) |
| 42 | .8642 (.7600,.9142) | 375 | .9351 (.9190,.9462) | 2575 | .9698 (.9585,.9785) | | |



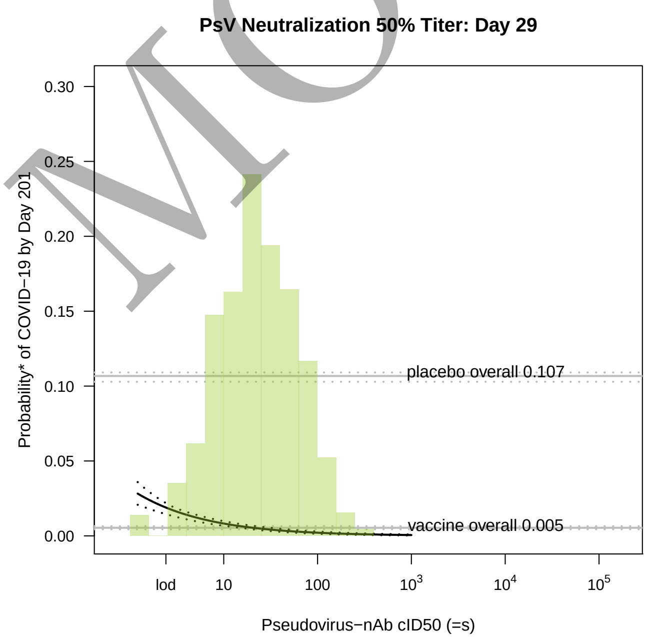

**No. at risk**

| | 0 | 30 | 60 | 90 | 120 | 150 | 180 | 201 |
|---|---|---|---|---|---|---|---|---|
| Low: | 3741 | 3740 | 3696 | 3619 | 3611 | 3583 | 3513 | 2821 |
| Med: | 3729 | 3727 | 3669 | 3637 | 3546 | 3487 | 3406 | 2734 |
| High: | 3734 | 3731 | 3697 | 3688 | 3683 | 3658 | 3631 | 2863 |
| Plac: | 11505 | 11381 | 11061 | 10703 | 10350 | 10021 | 9639 | 7830 |

**Cumulative No. of COVID−19 Endpoints**

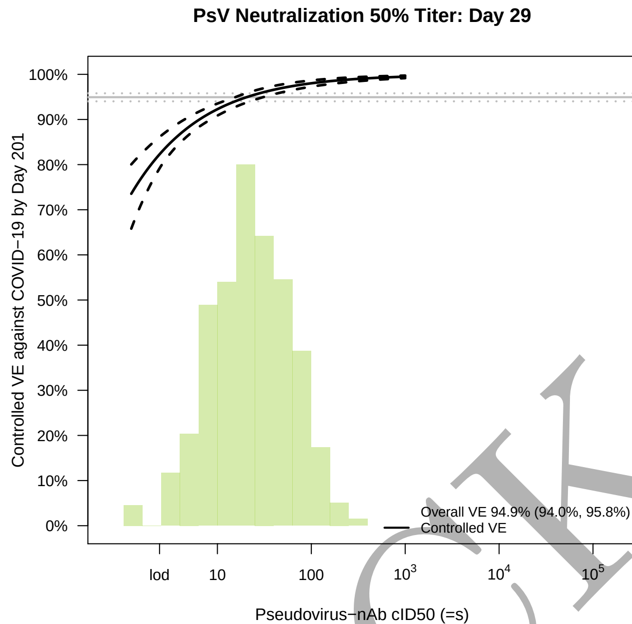
| | 0 | 30 | 60 | 90 | 120 | 150 | 180 | 201 |
|---|---|---|---|---|---|---|---|---|
| Low: | 0 | 1 | 2 | 3 | 11 | 15 | 18 | 21 |
| Med: | 0 | 2 | 5 | 8 | 11 | 16 | 19 | 22 |
| High: | 0 | 3 | 3 | 4 | 5 | 11 | 14 | 15 |
| Plac: | 0 | 129 | 296 | 473 | 658 | 835 | 1039 | 1166 |

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

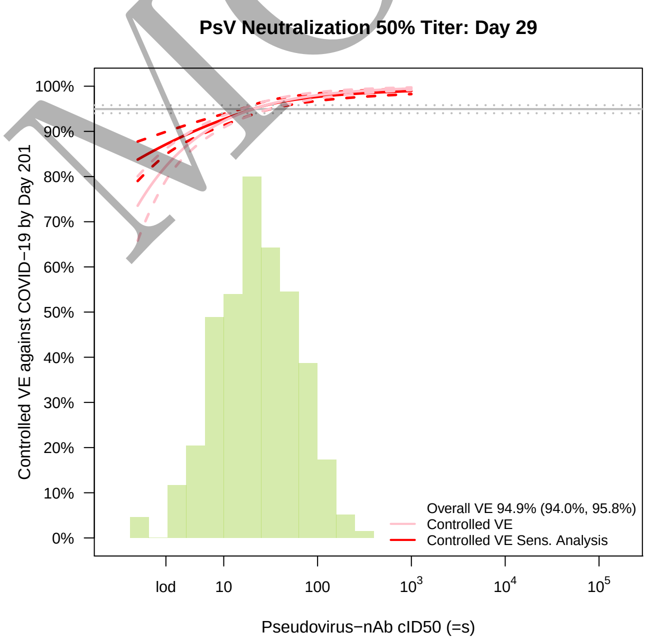



(b) Marginalized cumulative risk by Day 201 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

Figure 5.12: Marginalized cumulative risk curves (=s).

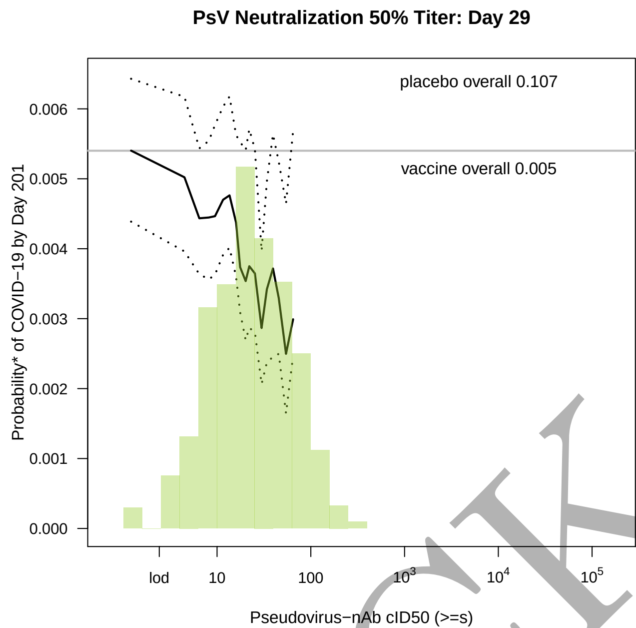



(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

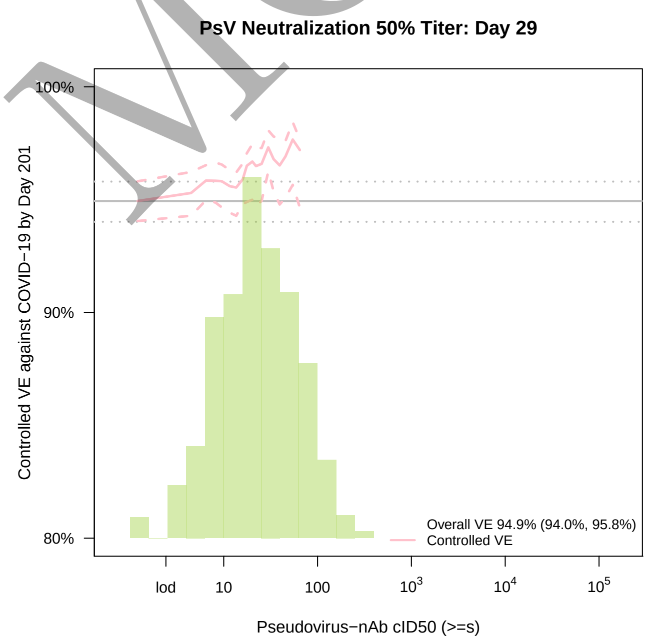



(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

Figure 5.13: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 201 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.




(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

Figure 5.14: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 5.10: Marginalized cumulative risk by Day 201 as functions of Day 29 Pseudovirus-nAb cID50 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

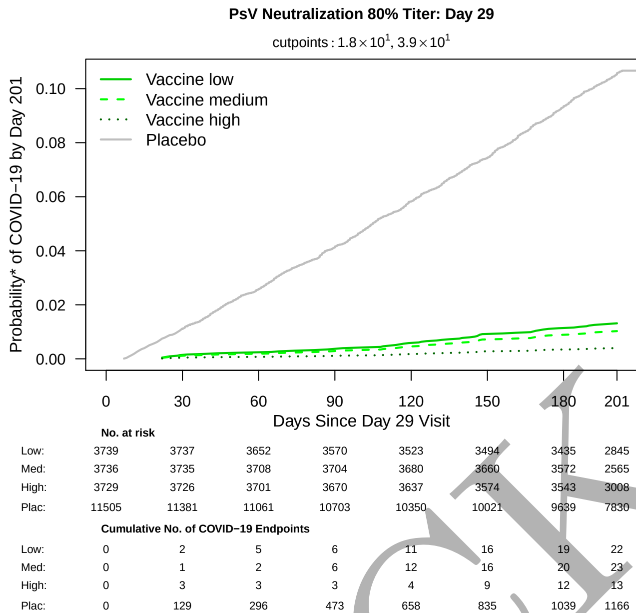
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 1.2 | .0282 (.0208,.0359) | 6 | .0114 (.0091,.0132) | 21 | .0054 (.0043,.0067) | 79 | .0024 (.0017,.0033) |
| 1 | .0273 (.0202,.0345) | 6 | .0110 (.0088,.0128) | 22 | .0052 (.0041,.0065) | 80 | .0024 (.0016,.0033) |
| 1 | .0265 (.0197,.0332) | 6 | .0107 (.0085,.0124) | 23 | .0050 (.0040,.0063) | 84 | .0023 (.0016,.0032) |
| 1 | .0256 (.0191,.0319) | 7 | .0106 (.0085,.0124) | 25 | .0048 (.0038,.0061) | 89 | .0023 (.0015,.0031) |
| 2 | .0248 (.0186,.0306) | 7 | .0103 (.0083,.0121) | 25 | .0048 (.0037,.0060) | 94 | .0022 (.0015,.0031) |
| 2 | .0240 (.0180,.0295) | 7 | .0100 (.0080,.0117) | 26 | .0047 (.0037,.0060) | 99 | .0021 (.0014,.0030) |
| 2 | .0233 (.0175,.0283) | 8 | .0097 (.0078,.0114) | 27 | .0045 (.0035,.0058) | 105 | .0021 (.0014,.0029) |
| 2 | .0225 (.0170,.0272) | 8 | .0094 (.0076,.0110) | 29 | .0044 (.0034,.0056) | 111 | .0020 (.0013,.0028) |
| 2 | .0218 (.0165,.0261) | 8 | .0093 (.0075,.0109) | 31 | .0043 (.0032,.0055) | 117 | .0019 (.0013,.0027) |
| 2 | .0211 (.0160,.0251) | 9 | .0091 (.0073,.0107) | 32 | .0041 (.0031,.0053) | 124 | .0019 (.0012,.0026) |
| 2 | .0205 (.0156,.0241) | 9 | .0088 (.0071,.0104) | 34 | .0040 (.0030,.0052) | 131 | .0018 (.0012,.0026) |
| 2 | .0198 (.0151,.0232) | 10 | .0085 (.0069,.0101) | 34 | .0040 (.0030,.0051) | 139 | .0017 (.0011,.0025) |
| 2 | .0192 (.0147,.0223) | 10 | .0084 (.0069,.0100) | 36 | .0038 (.0029,.0050) | 146 | .0017 (.0011,.0024) |
| 2 | .0186 (.0143,.0214) | 10 | .0082 (.0067,.0098) | 38 | .0037 (.0028,.0049) | 155 | .0016 (.0010,.0024) |
| 3 | .0180 (.0138,.0205) | 11 | .0079 (.0065,.0095) | 41 | .0036 (.0027,.0047) | 164 | .0016 (.0010,.0023) |
| 3 | .0174 (.0134,.0197) | 11 | .0077 (.0063,.0092) | 43 | .0035 (.0026,.0046) | 173 | .0015 (.0010,.0022) |
| 3 | .0168 (.0130,.0190) | 12 | .0074 (.0061,.0089) | 45 | .0034 (.0025,.0045) | 183 | .0015 (.0009,.0022) |
| 3 | .0163 (.0126,.0184) | 13 | .0072 (.0059,.0087) | 48 | .0033 (.0024,.0043) | 194 | .0014 (.0009,.0021) |
| 3 | .0158 (.0123,.0178) | 13 | .0070 (.0058,.0084) | 51 | .0032 (.0023,.0042) | 205 | .0014 (.0008,.0020) |
| 3 | .0153 (.0119,.0172) | 14 | .0067 (.0056,.0082) | 54 | .0031 (.0022,.0041) | 216 | .0013 (.0008,.0020) |
| 4 | .0148 (.0116,.0167) | 15 | .0065 (.0054,.0080) | 54 | .0031 (.0022,.0041) | 229 | .0013 (.0008,.0019) |
| 4 | .0143 (.0112,.0162) | 16 | .0063 (.0052,.0077) | 57 | .0030 (.0021,.0040) | 242 | .0013 (.0008,.0019) |
| 4 | .0138 (.0109,.0157) | 16 | .0063 (.0052,.0077) | 60 | .0029 (.0020,.0039) | 256 | .0012 (.0007,.0018) |
| 4 | .0134 (.0106,.0153) | 17 | .0061 (.0050,.0075) | 63 | .0028 (.0019,.0037) | 271 | .0012 (.0007,.0018) |
| 5 | .0130 (.0102,.0148) | 18 | .0059 (.0048,.0073) | 65 | .0027 (.0019,.0037) | 286 | .0011 (.0007,.0017) |
| 5 | .0126 (.0099,.0144) | 19 | .0057 (.0047,.0071) | 67 | .0027 (.0019,.0036) | 302 | .0011 (.0006,.0017) |
| 5 | .0122 (.0096,.0140) | 20 | .0055 (.0045,.0069) | 71 | .0026 (.0018,.0035) | 500 | .0008 (.0005,.0013) |
| 5 | .0118 (.0093,.0136) | 20 | .0055 (.0044,.0068) | 75 | .0025 (.0017,.0034) | 1000 | .0005 (.0003,.0009) |

Table 5.11: Controlled VE as functions of Day 29 Pseudovirus-nAb cID50 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 201 days post Day 29 was 0.005 in vaccine recipients compared to 0.107 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 95.8%).

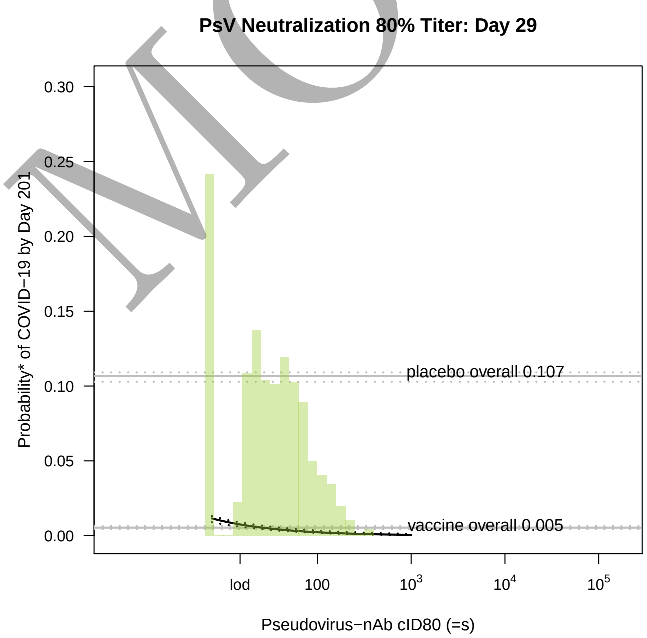
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 1.2 | .7354 (.6581,.8005) | 6 | .8968 (.8809,.9154) | 23 | .9530 (.9416,.9621) | 89 | .9787 (.9709,.9854) |
| 1 | .7438 (.6714,.8061) | 6 | .9001 (.8844,.9179) | 25 | .9546 (.9433,.9636) | 94 | .9794 (.9718,.9860) |
| 1 | .7519 (.6842,.8116) | 7 | .9006 (.8850,.9184) | 25 | .9554 (.9442,.9644) | 99 | .9801 (.9726,.9865) |
| 1 | .7597 (.6965,.8170) | 7 | .9033 (.8878,.9204) | 26 | .9560 (.9449,.9650) | 105 | .9807 (.9734,.9870) |
| 2 | .7674 (.7083,.8222) | 7 | .9064 (.8911,.9227) | 27 | .9575 (.9464,.9664) | 111 | .9814 (.9741,.9875) |
| 2 | .7747 (.7197,.8272) | 8 | .9094 (.8943,.9250) | 29 | .9588 (.9480,.9677) | 117 | .9820 (.9749,.9880) |
| 2 | .7819 (.7306,.8322) | 8 | .9123 (.8974,.9272) | 31 | .9602 (.9495,.9690) | 124 | .9825 (.9756,.9885) |
| 2 | .7888 (.7411,.8370) | 8 | .9130 (.8981,.9277) | 32 | .9615 (.9509,.9702) | 131 | .9831 (.9763,.9889) |
| 2 | .7955 (.7513,.8417) | 9 | .9152 (.9004,.9294) | 34 | .9627 (.9523,.9714) | 139 | .9837 (.9769,.9893) |
| 2 | .8020 (.7610,.8464) | 9 | .9179 (.9033,.9315) | 34 | .9628 (.9524,.9714) | 146 | .9842 (.9776,.9897) |
| 2 | .8083 (.7704,.8509) | 10 | .9206 (.9062,.9335) | 36 | .9639 (.9537,.9725) | 155 | .9847 (.9782,.9901) |
| 2 | .8144 (.7794,.8552) | 10 | .9212 (.9068,.9340) | 38 | .9651 (.9550,.9736) | 164 | .9852 (.9788,.9905) |
| 2 | .8204 (.7881,.8595) | 10 | .9231 (.9089,.9355) | 41 | .9662 (.9563,.9746) | 173 | .9857 (.9794,.9909) |
| 2 | .8261 (.7964,.8636) | 11 | .9256 (.9116,.9374) | 43 | .9673 (.9575,.9756) | 183 | .9862 (.9800,.9912) |
| 3 | .8317 (.8040,.8676) | 11 | .9280 (.9142,.9393) | 45 | .9684 (.9588,.9765) | 194 | .9866 (.9806,.9916) |
| 3 | .8370 (.8108,.8715) | 12 | .9303 (.9167,.9411) | 48 | .9694 (.9599,.9774) | 205 | .9870 (.9811,.9919) |
| 3 | .8422 (.8173,.8753) | 13 | .9326 (.9192,.9428) | 51 | .9704 (.9611,.9783) | 216 | .9875 (.9817,.9922) |
| 3 | .8473 (.8237,.8789) | 13 | .9348 (.9216,.9446) | 54 | .9714 (.9622,.9791) | 229 | .9879 (.9822,.9925) |
| 3 | .8522 (.8298,.8825) | 14 | .9369 (.9239,.9462) | 54 | .9714 (.9622,.9792) | 242 | .9883 (.9827,.9928) |
| 3 | .8569 (.8356,.8860) | 15 | .9389 (.9261,.9479) | 57 | .9723 (.9633,.9800) | 256 | .9886 (.9832,.9930) |
| 4 | .8615 (.8409,.8893) | 16 | .9409 (.9283,.9499) | 60 | .9732 (.9643,.9807) | 271 | .9890 (.9837,.9933) |
| 4 | .8659 (.8459,.8926) | 16 | .9411 (.9285,.9501) | 63 | .9741 (.9654,.9815) | 286 | .9894 (.9841,.9936) |
| 4 | .8702 (.8509,.8957) | 17 | .9428 (.9304,.9519) | 65 | .9744 (.9657,.9817) | 302 | .9897 (.9846,.9938) |
| 4 | .8744 (.8556,.8988) | 18 | .9447 (.9325,.9537) | 67 | .9749 (.9664,.9822) | 500 | .9924 (.9881,.9956) |
| 5 | .8784 (.8602,.9018) | 19 | .9464 (.9344,.9556) | 71 | .9757 (.9673,.9829) | 1000 | .9949 (.9917,.9973) |
| 5 | .8823 (.8647,.9047) | 20 | .9482 (.9363,.9573) | 75 | .9765 (.9683,.9836) | | ( , ) |
| 5 | .8861 (.8690,.9075) | 20 | .9489 (.9370,.9580) | 79 | .9773 (.9692,.9842) | 6 | .9001 (.8844,.9179) |
| 5 | .8898 (.8732,.9102) | 21 | .9499 (.9381,.9590) | 80 | .9774 (.9694,.9843) | 21 | .9499 (.9381,.9590) |
| 6 | .8933 (.8773,.9129) | 22 | .9515 (.9399,.9606) | 84 | .9780 (.9701,.9848) | | |

Table 5.12: Controlled VE with sensitivity analysis as functions of Day 29 Pseudovirus-nAb cID50 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 1.2 | .8376 (.7901,.8775) | 6 | .9093 (.8954,.9258) | 23 | .9530 (.9416,.9621) | 89 | .9753 (.9662,.9830) |
| 1 | .8404 (.7954,.8793) | 6 | .9114 (.8975,.9273) | 25 | .9545 (.9432,.9636) | 94 | .9758 (.9668,.9835) |
| 1 | .8433 (.8005,.8810) | 7 | .9118 (.8979,.9275) | 25 | .9553 (.9440,.9643) | 99 | .9764 (.9675,.9840) |
| 1 | .8461 (.8056,.8828) | 7 | .9135 (.8996,.9288) | 26 | .9559 (.9447,.9649) | 105 | .9769 (.9681,.9844) |
| 2 | .8489 (.8105,.8845) | 7 | .9155 (.9016,.9302) | 27 | .9572 (.9462,.9662) | 111 | .9774 (.9686,.9849) |
| 2 | .8516 (.8154,.8862) | 8 | .9175 (.9037,.9317) | 29 | .9585 (.9476,.9675) | 117 | .9779 (.9692,.9853) |
| 2 | .8544 (.8201,.8879) | 8 | .9195 (.9057,.9332) | 31 | .9597 (.9489,.9686) | 124 | .9784 (.9697,.9857) |
| 2 | .8571 (.8248,.8897) | 8 | .9200 (.9062,.9335) | 32 | .9609 (.9502,.9697) | 131 | .9788 (.9703,.9861) |
| 2 | .8597 (.8294,.8914) | 9 | .9215 (.9078,.9346) | 34 | .9620 (.9514,.9708) | 139 | .9793 (.9708,.9865) |
| 2 | .8624 (.8338,.8932) | 9 | .9234 (.9098,.9360) | 34 | .9620 (.9514,.9709) | 146 | .9797 (.9712,.9868) |
| 2 | .8650 (.8382,.8949) | 10 | .9253 (.9118,.9375) | 36 | .9630 (.9525,.9718) | 155 | .9801 (.9717,.9872) |
| 2 | .8676 (.8425,.8967) | 10 | .9258 (.9122,.9378) | 38 | .9641 (.9537,.9728) | 164 | .9805 (.9722,.9875) |
| 2 | .8701 (.8467,.8984) | 10 | .9272 (.9137,.9389) | 41 | .9650 (.9547,.9737) | 173 | .9809 (.9726,.9878) |
| 2 | .8726 (.8509,.9001) | 11 | .9291 (.9157,.9403) | 43 | .9660 (.9558,.9745) | 183 | .9813 (.9731,.9882) |
| 3 | .8751 (.8546,.9018) | 11 | .9309 (.9177,.9417) | 45 | .9668 (.9568,.9754) | 194 | .9817 (.9735,.9885) |
| 3 | .8776 (.8579,.9035) | 12 | .9327 (.9196,.9431) | 48 | .9677 (.9577,.9762) | 205 | .9821 (.9739,.9888) |
| 3 | .8800 (.8611,.9052) | 13 | .9345 (.9215,.9445) | 51 | .9685 (.9586,.9769) | 216 | .9824 (.9743,.9891) |
| 3 | .8824 (.8643,.9068) | 13 | .9363 (.9234,.9459) | 54 | .9693 (.9595,.9777) | 229 | .9828 (.9747,.9893) |
| 3 | .8848 (.8674,.9085) | 14 | .9381 (.9253,.9473) | 54 | .9693 (.9595,.9777) | 242 | .9831 (.9751,.9896) |
| 3 | .8872 (.8704,.9101) | 15 | .9398 (.9272,.9486) | 57 | .9701 (.9604,.9784) | 256 | .9834 (.9755,.9899) |
| 4 | .8895 (.8731,.9117) | 16 | .9416 (.9291,.9504) | 60 | .9708 (.9612,.9790) | 271 | .9838 (.9758,.9901) |
| 4 | .8918 (.8757,.9133) | 16 | .9417 (.9293,.9506) | 63 | .9715 (.9620,.9797) | 286 | .9841 (.9762,.9904) |
| 4 | .8941 (.8783,.9149) | 17 | .9433 (.9310,.9522) | 65 | .9718 (.9622,.9799) | 302 | .9844 (.9766,.9906) |
| 4 | .8964 (.8809,.9165) | 18 | .9449 (.9328,.9540) | 67 | .9722 (.9627,.9803) | 500 | .9868 (.9794,.9924) |
| 5 | .8986 (.8834,.9181) | 19 | .9466 (.9346,.9557) | 71 | .9729 (.9635,.9809) | 1000 | .9894 (.9826,.9943) |
| 5 | .9008 (.8859,.9196) | 20 | .9482 (.9364,.9574) | 75 | .9735 (.9642,.9815) | | ( , ) |
| 5 | .9030 (.8884,.9212) | 20 | .9489 (.9371,.9580) | 79 | .9741 (.9649,.9820) | 6 | .9001 (.8844,.9179) |
| 5 | .9051 (.8909,.9227) | 21 | .9499 (.9381,.9590) | 80 | .9742 (.9650,.9821) | 21 | .9499 (.9381,.9590) |
| 6 | .9072 (.8933,.9242) | 22 | .9515 (.9399,.9606) | 84 | .9747 (.9656,.9825) | | |

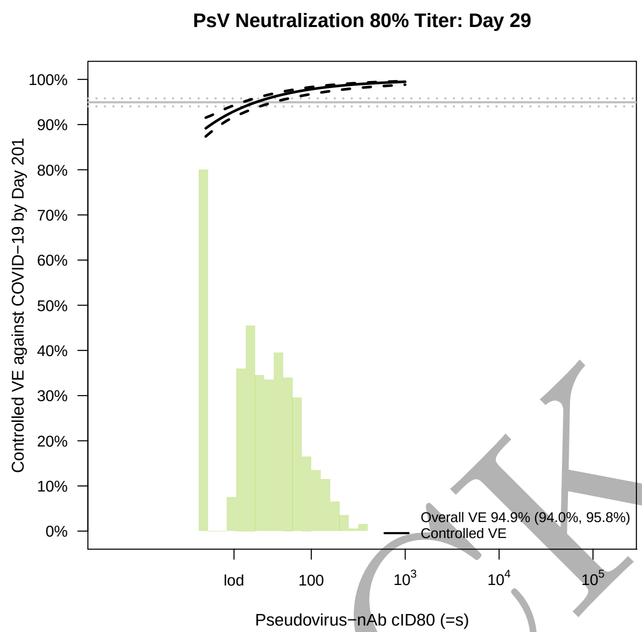



(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

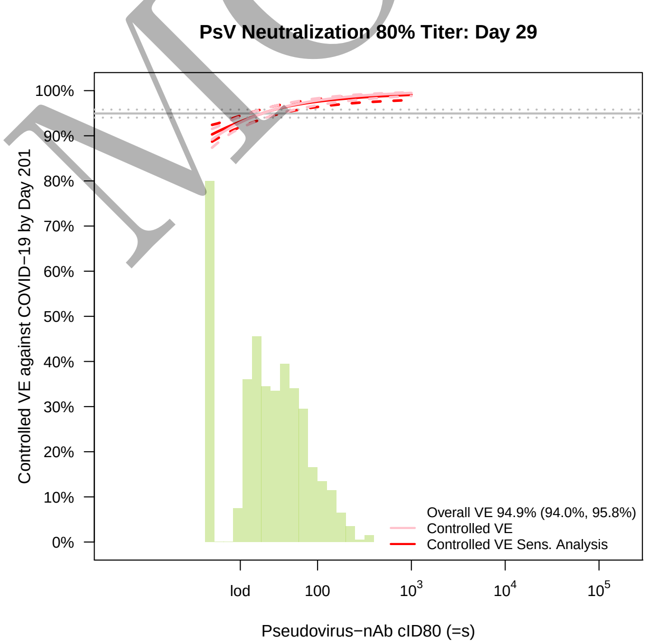



(b) Marginalized cumulative risk by Day 201 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

Figure 5.15: Marginalized cumulative risk curves (=s).

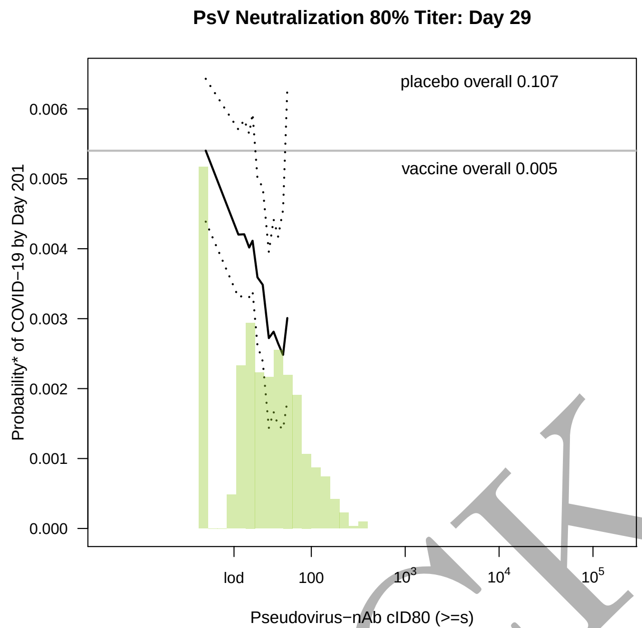



(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

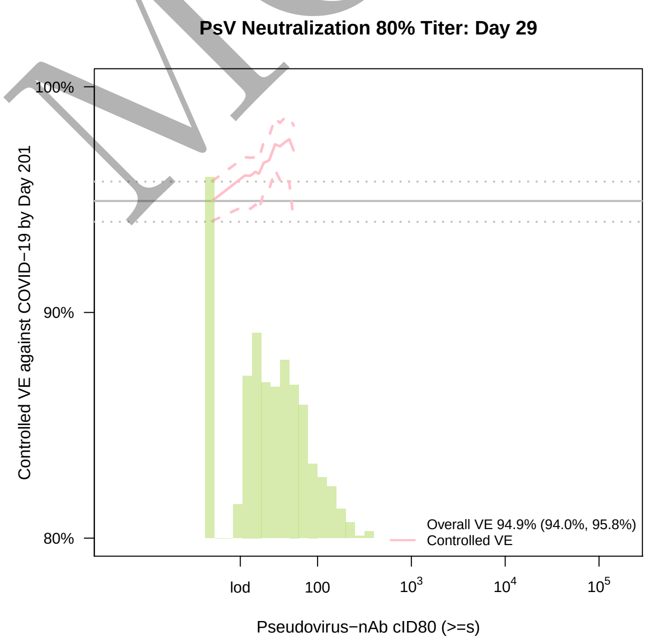



(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

Figure 5.16: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 201 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.




(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

Figure 5.17: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 5.13: Marginalized cumulative risk by Day 201 as functions of Day 29 Pseudovirus-nAb cID80 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 7.5 | .0116 (.0090,.0132) | 20 | .0064 (.0051,.0078) | 49 | .0036 (.0029,.0049) | 129 | .0020 (.0015,.0031) |
| 8 | .0116 (.0090,.0132) | 20 | .0062 (.0050,.0076) | 51 | .0035 (.0028,.0048) | 134 | .0019 (.0015,.0030) |
| 8 | .0116 (.0090,.0132) | 21 | .0061 (.0049,.0075) | 53 | .0034 (.0028,.0047) | 139 | .0019 (.0015,.0030) |
| 8 | .0113 (.0088,.0129) | 22 | .0060 (.0048,.0074) | 55 | .0033 (.0027,.0046) | 145 | .0018 (.0014,.0029) |
| 8 | .0110 (.0086,.0126) | 22 | .0059 (.0047,.0073) | 58 | .0033 (.0026,.0045) | 151 | .0018 (.0014,.0029) |
| 8 | .0108 (.0084,.0123) | 23 | .0058 (.0046,.0072) | 60 | .0032 (.0026,.0045) | 157 | .0018 (.0014,.0028) |
| 9 | .0105 (.0083,.0120) | 24 | .0057 (.0045,.0071) | 62 | .0031 (.0025,.0044) | 163 | .0017 (.0013,.0028) |
| 9 | .0103 (.0081,.0117) | 25 | .0055 (.0044,.0069) | 64 | .0031 (.0025,.0043) | 169 | .0017 (.0013,.0027) |
| 9 | .0100 (.0079,.0115) | 26 | .0054 (.0043,.0068) | 65 | .0030 (.0024,.0043) | 176 | .0016 (.0013,.0027) |
| 10 | .0098 (.0077,.0112) | 27 | .0053 (.0042,.0067) | 67 | .0030 (.0024,.0042) | 183 | .0016 (.0012,.0026) |
| 10 | .0096 (.0075,.0110) | 27 | .0053 (.0042,.0067) | 70 | .0029 (.0023,.0042) | 190 | .0016 (.0012,.0026) |
| 11 | .0093 (.0074,.0107) | 28 | .0051 (.0041,.0065) | 73 | .0028 (.0023,.0041) | 197 | .0015 (.0012,.0025) |
| 11 | .0091 (.0072,.0105) | 29 | .0050 (.0040,.0064) | 75 | .0028 (.0022,.0040) | 205 | .0015 (.0011,.0025) |
| 11 | .0089 (.0071,.0103) | 30 | .0049 (.0039,.0063) | 75 | .0028 (.0022,.0040) | 213 | .0014 (.0011,.0024) |
| 12 | .0087 (.0069,.0101) | 31 | .0048 (.0038,.0062) | 78 | .0027 (.0021,.0039) | 221 | .0014 (.0011,.0024) |
| 12 | .0085 (.0067,.0099) | 32 | .0047 (.0038,.0060) | 81 | .0026 (.0021,.0039) | 230 | .0014 (.0010,.0024) |
| 13 | .0083 (.0066,.0097) | 34 | .0046 (.0037,.0059) | 85 | .0026 (.0020,.0038) | 239 | .0013 (.0010,.0023) |
| 13 | .0081 (.0064,.0095) | 35 | .0045 (.0036,.0058) | 88 | .0025 (.0020,.0037) | 248 | .0013 (.0010,.0023) |
| 14 | .0079 (.0063,.0093) | 35 | .0044 (.0036,.0058) | 91 | .0024 (.0019,.0037) | 258 | .0013 (.0010,.0022) |
| 14 | .0077 (.0061,.0091) | 36 | .0044 (.0035,.0057) | 92 | .0024 (.0019,.0037) | 268 | .0013 (.0009,.0022) |
| 15 | .0075 (.0060,.0090) | 38 | .0042 (.0034,.0056) | 95 | .0024 (.0019,.0036) | 279 | .0012 (.0009,.0022) |
| 15 | .0074 (.0059,.0089) | 39 | .0041 (.0033,.0055) | 99 | .0023 (.0018,.0035) | 290 | .0012 (.0009,.0021) |
| 16 | .0074 (.0059,.0088) | 41 | .0040 (.0033,.0054) | 103 | .0023 (.0018,.0035) | 301 | .0012 (.0009,.0021) |
| 16 | .0072 (.0057,.0086) | 42 | .0040 (.0032,.0053) | 107 | .0022 (.0017,.0034) | 313 | .0011 (.0009,.0020) |
| 17 | .0070 (.0056,.0084) | 44 | .0039 (.0031,.0052) | 111 | .0022 (.0017,.0033) | 325 | .0011 (.0008,.0020) |
| 17 | .0069 (.0055,.0083) | 45 | .0038 (.0031,.0051) | 115 | .0021 (.0017,.0033) | 338 | .0011 (.0008,.0020) |
| 18 | .0067 (.0053,.0081) | 46 | .0038 (.0030,.0051) | 120 | .0021 (.0016,.0032) | 500 | .0008 (.0006,.0017) |
| 19 | .0065 (.0052,.0079) | 48 | .0037 (.0030,.0050) | 124 | .0020 (.0016,.0032) | 1000 | .0006 (.0004,.0012) |

Table 5.14: Controlled VE as functions of Day 29 Pseudovirus-nAb cID80 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 201 days post Day 29 was 0.005 in vaccine recipients compared to 0.107 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 95.8%).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 7.5 | .8916 (.8737,.9152) | 20 | .9417 (.9291,.9525) | 53 | .9679 (.9564,.9741) | 145 | .9828 (.9728,.9867) |
| 8 | .8916 (.8737,.9152) | 21 | .9430 (.9305,.9536) | 55 | .9687 (.9572,.9748) | 151 | .9832 (.9733,.9871) |
| 8 | .8916 (.8737,.9152) | 22 | .9436 (.9312,.9541) | 58 | .9694 (.9579,.9754) | 157 | .9836 (.9738,.9874) |
| 8 | .8942 (.8767,.9167) | 22 | .9444 (.9319,.9547) | 60 | .9701 (.9587,.9760) | 163 | .9840 (.9742,.9877) |
| 8 | .8967 (.8796,.9181) | 23 | .9457 (.9333,.9557) | 62 | .9708 (.9594,.9766) | 169 | .9844 (.9747,.9880) |
| 8 | .8991 (.8825,.9195) | 24 | .9470 (.9346,.9567) | 64 | .9713 (.9599,.9771) | 176 | .9847 (.9752,.9883) |
| 9 | .9015 (.8853,.9210) | 25 | .9482 (.9360,.9578) | 65 | .9715 (.9602,.9772) | 183 | .9851 (.9756,.9886) |
| 9 | .9038 (.8880,.9227) | 26 | .9494 (.9372,.9588) | 67 | .9722 (.9609,.9778) | 190 | .9854 (.9760,.9889) |
| 9 | .9060 (.8907,.9243) | 27 | .9505 (.9383,.9597) | 70 | .9729 (.9616,.9784) | 197 | .9858 (.9765,.9892) |
| 10 | .9082 (.8933,.9261) | 27 | .9506 (.9384,.9598) | 73 | .9735 (.9623,.9789) | 205 | .9861 (.9769,.9895) |
| 10 | .9104 (.8958,.9278) | 28 | .9518 (.9396,.9607) | 75 | .9741 (.9629,.9794) | 213 | .9865 (.9773,.9897) |
| 11 | .9125 (.8983,.9294) | 29 | .9529 (.9407,.9617) | 75 | .9741 (.9630,.9795) | 221 | .9868 (.9777,.9900) |
| 11 | .9146 (.9007,.9311) | 30 | .9541 (.9419,.9626) | 78 | .9747 (.9636,.9800) | 230 | .9871 (.9781,.9902) |
| 11 | .9166 (.9031,.9326) | 31 | .9551 (.9430,.9635) | 81 | .9753 (.9643,.9805) | 239 | .9874 (.9785,.9905) |
| 12 | .9185 (.9054,.9342) | 32 | .9562 (.9441,.9644) | 85 | .9759 (.9649,.9810) | 248 | .9877 (.9789,.9907) |
| 12 | .9205 (.9077,.9357) | 34 | .9572 (.9451,.9652) | 88 | .9765 (.9655,.9815) | 258 | .9880 (.9793,.9910) |
| 13 | .9223 (.9096,.9372) | 35 | .9582 (.9462,.9660) | 91 | .9770 (.9662,.9819) | 268 | .9883 (.9797,.9912) |
| 13 | .9242 (.9114,.9386) | 35 | .9585 (.9465,.9663) | 92 | .9771 (.9662,.9820) | 279 | .9885 (.9800,.9914) |
| 14 | .9259 (.9132,.9400) | 36 | .9592 (.9472,.9669) | 95 | .9776 (.9668,.9824) | 290 | .9888 (.9804,.9916) |
| 14 | .9277 (.9149,.9414) | 38 | .9602 (.9482,.9676) | 99 | .9781 (.9674,.9828) | 301 | .9891 (.9807,.9919) |
| 15 | .9294 (.9167,.9428) | 39 | .9611 (.9492,.9684) | 103 | .9786 (.9680,.9833) | 313 | .9893 (.9810,.9921) |
| 15 | .9303 (.9176,.9435) | 41 | .9621 (.9502,.9692) | 107 | .9791 (.9685,.9837) | 325 | .9896 (.9813,.9923) |
| 16 | .9311 (.9183,.9441) | 42 | .9630 (.9512,.9699) | 111 | .9796 (.9691,.9841) | 338 | .9898 (.9816,.9925) |
| 16 | .9327 (.9200,.9454) | 44 | .9638 (.9521,.9706) | 115 | .9801 (.9697,.9845) | 500 | .9921 (.9844,.9942) |
| 17 | .9343 (.9216,.9466) | 45 | .9643 (.9526,.9710) | 120 | .9806 (.9702,.9849) | 1000 | .9948 (.9883,.9963) |
| 17 | .9358 (.9231,.9479) | 46 | .9647 (.9530,.9713) | 124 | .9811 (.9707,.9853) | | ( , ) |
| 18 | .9373 (.9247,.9491) | 48 | .9655 (.9539,.9721) | 129 | .9815 (.9713,.9857) | 8 | .8991 (.8825,.9195) |
| 19 | .9388 (.9262,.9502) | 49 | .9663 (.9547,.9728) | 134 | .9819 (.9718,.9860) | 27 | .9505 (.9383,.9597) |
| 20 | .9402 (.9277,.9514) | 51 | .9671 (.9556,.9735) | 139 | .9824 (.9723,.9864) | | |

Table 5.15: Controlled VE with sensitivity analysis as functions of Day 29 Pseudovirus-nAb cID80 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 7.5 | .9031 (.8870,.9242) | 20 | .9421 (.9297,.9529) | 53 | .9669 (.9549,.9733) | 145 | .9797 (.9679,.9843) |
| 8 | .9031 (.8870,.9242) | 21 | .9434 (.9310,.9539) | 55 | .9675 (.9556,.9739) | 151 | .9800 (.9682,.9846) |
| 8 | .9031 (.8870,.9242) | 22 | .9439 (.9315,.9543) | 58 | .9682 (.9562,.9744) | 157 | .9804 (.9686,.9849) |
| 8 | .9048 (.8891,.9250) | 22 | .9446 (.9322,.9549) | 60 | .9688 (.9568,.9750) | 163 | .9807 (.9690,.9852) |
| 8 | .9065 (.8911,.9259) | 23 | .9459 (.9335,.9558) | 62 | .9694 (.9574,.9755) | 169 | .9810 (.9693,.9855) |
| 8 | .9082 (.8932,.9268) | 24 | .9471 (.9348,.9568) | 64 | .9698 (.9579,.9759) | 176 | .9813 (.9697,.9857) |
| 9 | .9099 (.8951,.9278) | 25 | .9483 (.9360,.9578) | 65 | .9700 (.9580,.9760) | 183 | .9817 (.9700,.9860) |
| 9 | .9116 (.8971,.9290) | 26 | .9495 (.9372,.9588) | 67 | .9706 (.9586,.9765) | 190 | .9820 (.9703,.9863) |
| 9 | .9132 (.8991,.9301) | 27 | .9505 (.9383,.9597) | 70 | .9712 (.9592,.9770) | 197 | .9823 (.9707,.9865) |
| 10 | .9148 (.9010,.9314) | 27 | .9506 (.9384,.9598) | 73 | .9717 (.9597,.9775) | 205 | .9826 (.9710,.9868) |
| 10 | .9164 (.9029,.9326) | 28 | .9518 (.9396,.9607) | 75 | .9722 (.9602,.9780) | 213 | .9829 (.9713,.9870) |
| 11 | .9180 (.9047,.9339) | 29 | .9529 (.9407,.9617) | 75 | .9723 (.9603,.9780) | 221 | .9831 (.9716,.9872) |
| 11 | .9196 (.9066,.9351) | 30 | .9540 (.9418,.9626) | 78 | .9728 (.9608,.9784) | 230 | .9834 (.9719,.9875) |
| 11 | .9211 (.9084,.9363) | 31 | .9551 (.9429,.9634) | 81 | .9733 (.9613,.9789) | 239 | .9837 (.9722,.9877) |
| 12 | .9226 (.9102,.9375) | 32 | .9561 (.9440,.9643) | 85 | .9738 (.9618,.9793) | 248 | .9840 (.9725,.9879) |
| 12 | .9242 (.9120,.9387) | 34 | .9571 (.9450,.9651) | 88 | .9743 (.9623,.9797) | 258 | .9842 (.9728,.9881) |
| 13 | .9256 (.9135,.9399) | 35 | .9581 (.9460,.9659) | 91 | .9748 (.9628,.9801) | 268 | .9845 (.9731,.9884) |
| 13 | .9271 (.9149,.9410) | 35 | .9583 (.9462,.9661) | 92 | .9748 (.9628,.9802) | 279 | .9847 (.9734,.9886) |
| 14 | .9286 (.9163,.9422) | 36 | .9590 (.9469,.9667) | 95 | .9752 (.9633,.9805) | 290 | .9850 (.9736,.9888) |
| 14 | .9300 (.9177,.9433) | 38 | .9599 (.9478,.9674) | 99 | .9757 (.9637,.9809) | 301 | .9852 (.9738,.9890) |
| 15 | .9314 (.9190,.9444) | 39 | .9608 (.9487,.9681) | 103 | .9761 (.9642,.9813) | 313 | .9855 (.9740,.9892) |
| 15 | .9322 (.9198,.9450) | 41 | .9616 (.9496,.9688) | 107 | .9765 (.9646,.9817) | 325 | .9857 (.9743,.9893) |
| 16 | .9328 (.9204,.9455) | 42 | .9624 (.9504,.9695) | 111 | .9770 (.9651,.9820) | 338 | .9859 (.9745,.9895) |
| 16 | .9342 (.9218,.9466) | 44 | .9632 (.9513,.9701) | 115 | .9774 (.9655,.9824) | 500 | .9880 (.9765,.9912) |
| 17 | .9355 (.9231,.9477) | 45 | .9636 (.9517,.9705) | 120 | .9778 (.9659,.9827) | 1000 | .9909 (.9794,.9935) |
| 17 | .9369 (.9244,.9487) | 46 | .9640 (.9521,.9708) | 124 | .9782 (.9663,.9831) | | ( , ) |
| 18 | .9382 (.9258,.9498) | 48 | .9647 (.9529,.9714) | 129 | .9786 (.9667,.9834) | 8 | .8991 (.8825,.9195) |
| 19 | .9395 (.9271,.9508) | 49 | .9655 (.9536,.9721) | 134 | .9789 (.9671,.9837) | 27 | .9505 (.9383,.9597) |
| 20 | .9408 (.9284,.9518) | 51 | .9662 (.9543,.9727) | 139 | .9793 (.9675,.9840) | | |

# Chapter 6

# Day D57 Univariate CoR: Cox Models of Risk



The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise.

## 6.1 Hazard ratios

Table 6.1: Inference for Day 57 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios per 10-fold increment in the marker*

| MockCOVE Immunologic Marker | No. cases / No. at-risk** | HR per 10-fold incr. Pt. Est. | 95% CI | P-value (2-sided) | q-value *** | FWER |
|---|---|---|---|---|---|---|
| Anti Spike IgG (BAU/ml) | 51/11,163 | 0.07 | (0.04-0.14) | <0.001 | <0.001 | <0.001 |
| Anti RBD IgG (BAU/ml) | 51/11,163 | 0.35 | (0.21-0.58) | <0.001 | <0.001 | <0.001 |
| Pseudovirus-nAb cID50 | 51/11,163 | 0.19 | (0.10-0.38) | <0.001 | <0.001 | <0.001 |
| Pseudovirus-nAb cID80 | 51/11,163 | 0.21 | (0.10-0.41) | <0.001 | <0.001 | <0.001 |

*Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. Maximum failure event time 173 days.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint or infected through 6 days post Day 57 visit; no. cases = number of this cohort with an observed COVID endpoint.
***q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10  replicates).

Table 6.2: Inference for Day 57 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios for Middle vs. Upper tertile vs. Lower tertile*

| MockCOVE Immunologic Marker | Tertile | No. cases / No. at-risk** | Attack rate | Haz. Ratio Pt. Est. | Haz. Ratio 95% CI | P-value (2-sided) | Overall P-value*** | Overall q-value † | Overall FWER |
|---|---|---|---|---|---|---|---|---|---|
| Anti Spike IgG (BAU/ml) | Lower | 28/4,218 | 0.0066 | 1 | N/A | N/A | <0.001 | <0.001 | <0.001 |
| | Middle | 18/4,193 | 0.0043 | 0.20 | (0.10-0.41) | <0.001 | | | |
| | Upper | 5/2,752 | 0.0018 | 0.04 | (0.01-0.11) | <0.001 | | | |
| Anti RBD IgG (BAU/ml) | Lower | 26/4,145 | 0.0063 | 1 | N/A | N/A | <0.001 | <0.001 | <0.001 |
| | Middle | 13/4,137 | 0.0031 | 0.27 | (0.12-0.59) | 0.001 | | | |
| | Upper | 13/2,881 | 0.0045 | 0.18 | (0.08-0.42) | <0.001 | | | |
| Pseudovirus-nAb cID50 | Lower | 23/3,724 | 0.0062 | 1 | N/A | N/A | <0.001 | <0.001 | <0.001 |
| | Middle | 16/3,726 | 0.0043 | 0.40 | (0.20-0.82) | 0.013 | | | |
| | Upper | 12/3,712 | 0.0032 | 0.18 | (0.08-0.41) | <0.001 | | | |
| Pseudovirus-nAb cID80 | Lower | 21/3,722 | 0.0056 | 1 | N/A | N/A | 0.003 | <0.001 | 0.013 |
| | Middle | 19/3,720 | 0.0051 | 0.58 | (0.29-1.17) | 0.128 | | | |
| | Upper | 11/3,721 | 0.0030 | 0.24 | (0.10-0.54) | <0.001 | | | |
| Placebo | | 1010/11,301 | 0.0894 | | | | | | |

*Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. Maximum failure event time 173 days. Cutpoints: Anti Spike IgG (BAU/ml) [3.31, 4.01), Anti RBD IgG (BAU/ml) [3.44, 4.21), Pseudovirus-nAb cID50 [2.43, 2.85), Pseudovirus-nAb cID80 [2.55, 2.93), all on the log10 scale.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint or infected through 6 days post Day 57 visit; no. cases = number of this cohort with an observed COVID endpoint.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.
† q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10 replicates).

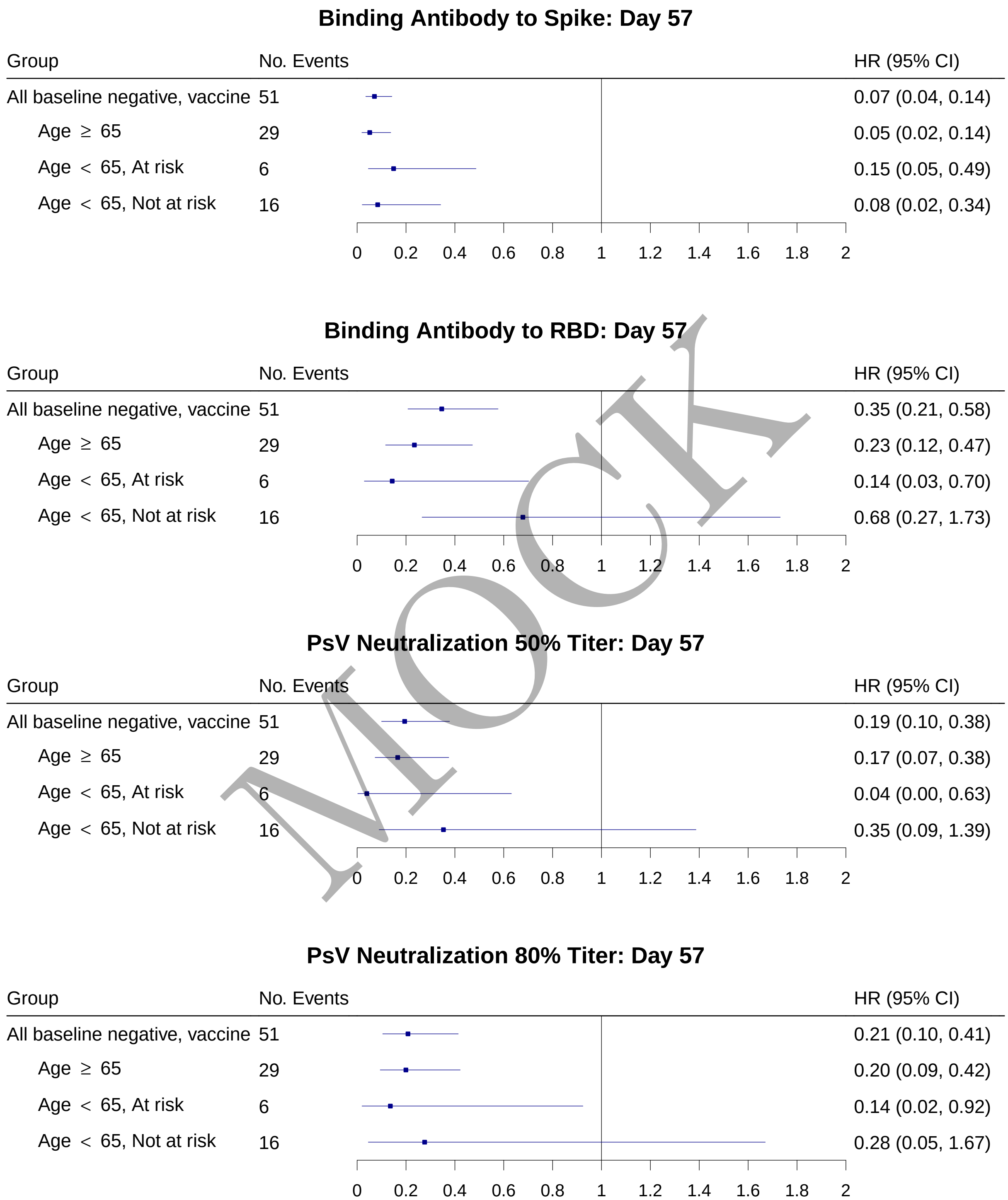



Figure 6.1: Forest plots of hazard ratios per 10-fold increase in the marker among baseline negative vaccine recipients and subgroups with 95% point-wise confidence intervals.

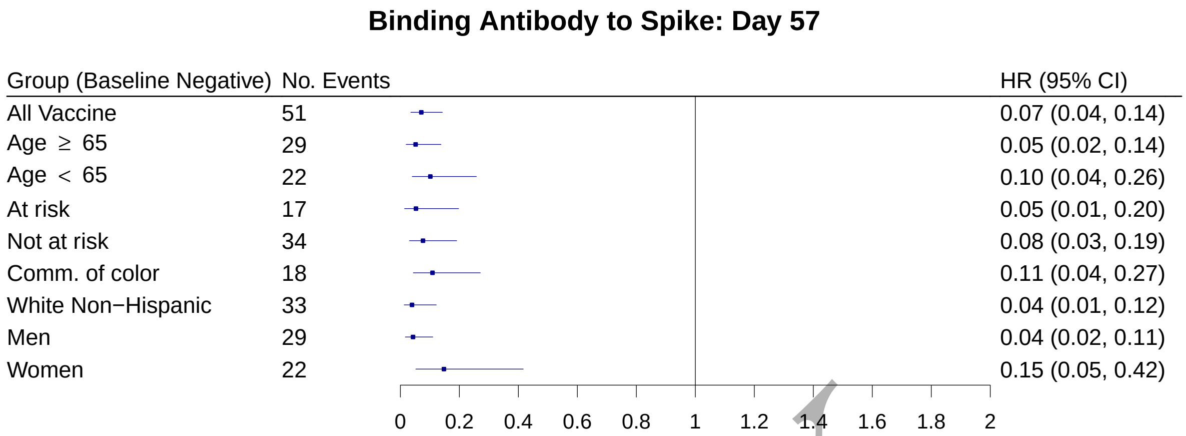



Figure 6.2: Forest plots of hazard ratios per 10-fold increase in the Day 57 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.



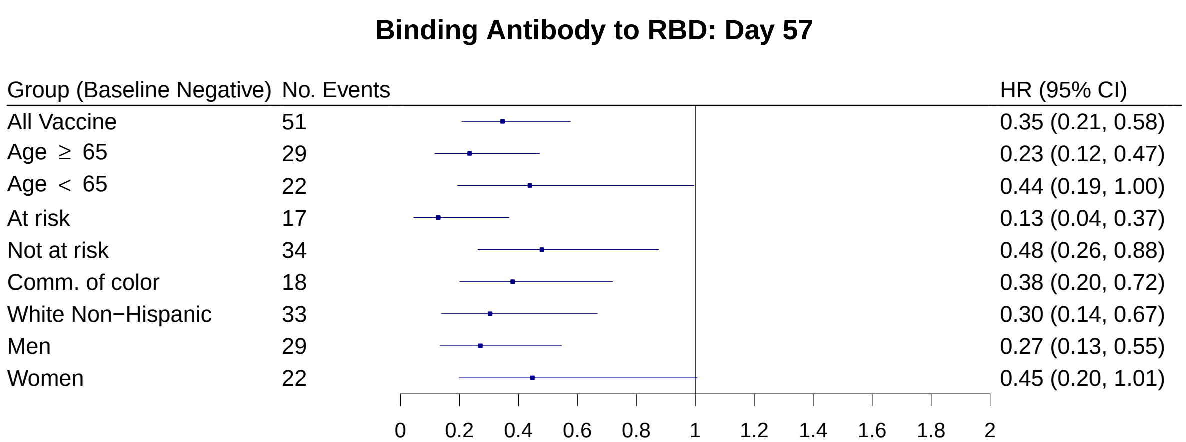



Figure 6.3: Forest plots of hazard ratios per 10-fold increase in the Day 57 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.

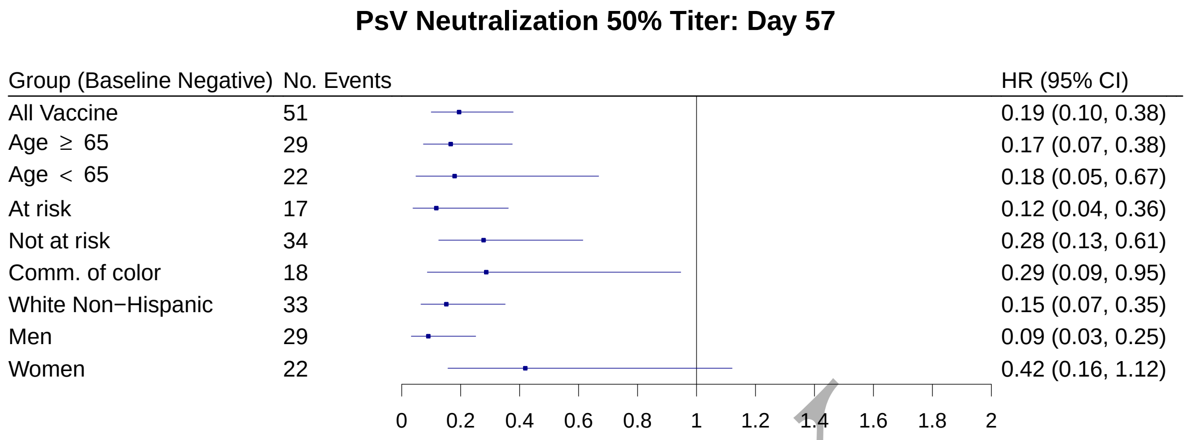



Figure 6.4: Forest plots of hazard ratios per 10-fold increase in the Day 57 pseudo neut ID50 markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.



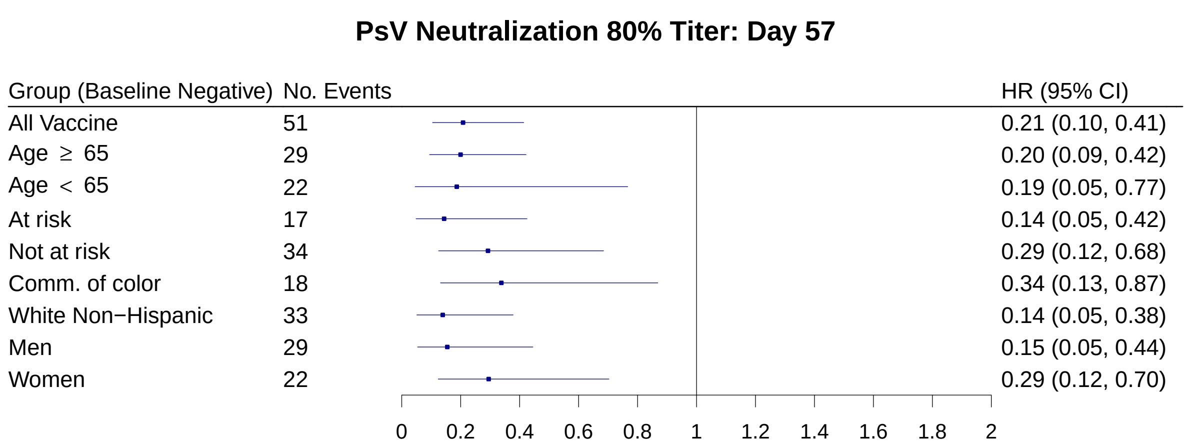


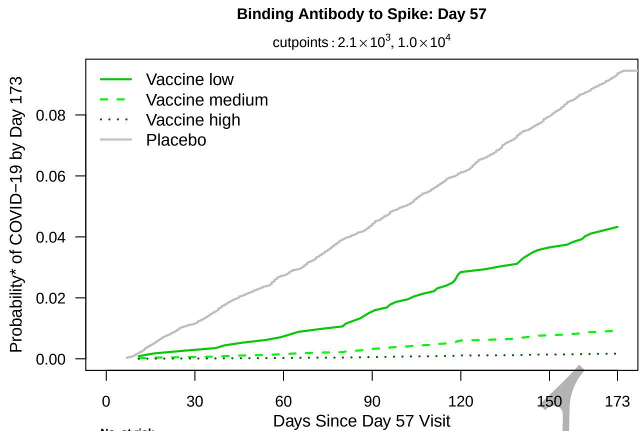

Figure 6.5: Forest plots of hazard ratios per 10-fold increase in the Day 57 pseudo neut ID80 markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals.

## 6.2 Marginalized risk and controlled vaccine efficacy plots

Table 6.3: Analysis of Day 57 markers (upper vs. lower tertile) as a CoR and a controlled risk CoP.

| | marginalized risk ratio $RR_M(0,1)$ | | controlled risk ratio $RR_C(0,1)$[1] | | e(0,1)[2] | |
|---|---|---|---|---|---|---|
| | Point Est. | 95% CI | Point Est. | 95% CI | Point Est. | 95% CI UL |
| Anti Spike IgG (BAU/ml) | 0.04 | 0.03–0.06 | 0.05 | 0.03–0.08 | 50.9 | 34.9 |
| Anti RBD IgG (BAU/ml) | 0.18 | 0.08–0.38 | 0.25 | 0.11–0.50 | 10.3 | 4.8 |
| Pseudovirus-nAb cID50 | 0.18 | 0.12–0.31 | 0.24 | 0.16–0.41 | 10.5 | 6.0 |
| Pseudovirus-nAb cID80 | 0.24 | 0.10–0.46 | 0.32 | 0.14–0.62 | 7.9 | 3.7 |

[1]Conservative (upper bound) estimate assuming unmeasured confounding at level $RR_{UD}(0,1) = RR_{EU}(0,1) = 2$ and thus $B(0,1) = 4/3$.
[2]E-values are computed for upper tertile ($s = 1$) vs. lower tertile ($s = 0$) biomarker subgroups after controlling for MinorityInd + HighRiskInd + Age; UL = upper limit.



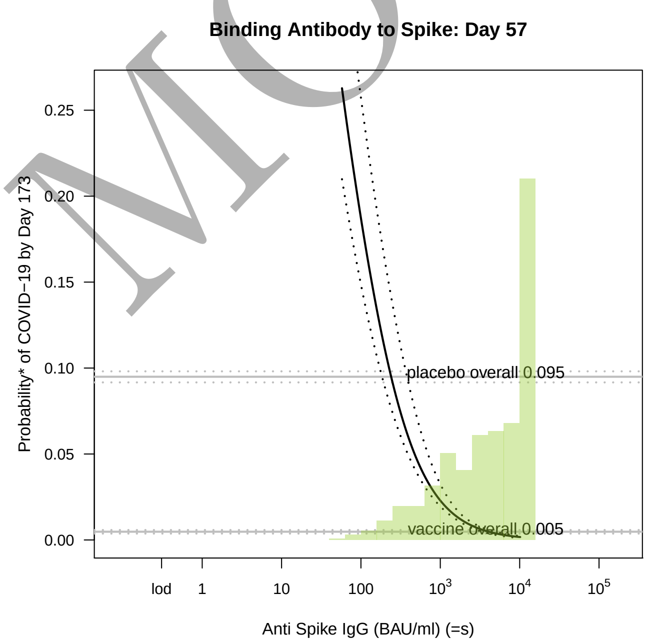

**No. at risk**

| | 0 | 30 | 60 | 90 | 120 | 150 | 173 |
|---|---|---|---|---|---|---|---|
| Low: | 4218 | 4123 | 4059 | 3991 | 3950 | 3856 | 3071 |
| Med: | 4193 | 4176 | 4130 | 4107 | 4064 | 4013 | 3151 |
| High: | 2752 | 2739 | 2731 | 2719 | 2691 | 2656 | 2170 |
| Plac: | 11301 | 11054 | 10708 | 10369 | 10023 | 9635 | 7815 |

**Cumulative No. of COVID−19 Endpoints**

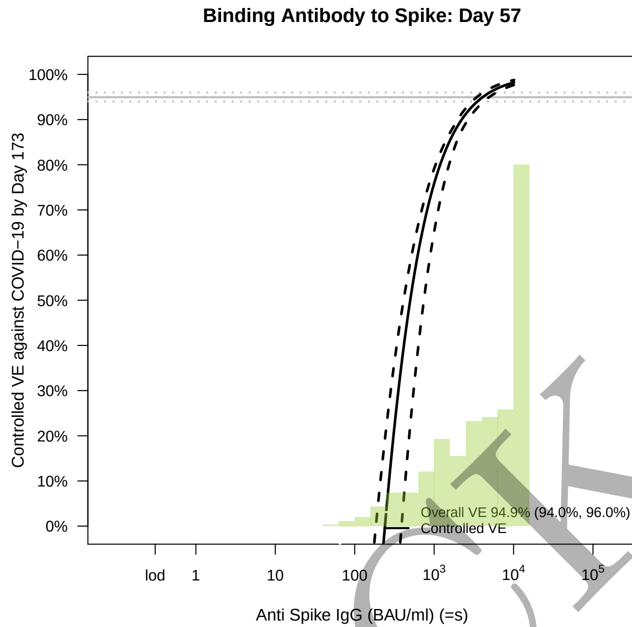
| | 0 | 30 | 60 | 90 | 120 | 150 | 173 |
|---|---|---|---|---|---|---|---|
| Low: | 0 | 2 | 4 | 11 | 19 | 24 | 28 |
| Med: | 0 | 0 | 3 | 6 | 13 | 14 | 18 |
| High: | 0 | 1 | 1 | 1 | 2 | 5 | 5 |
| Plac: | 0 | 131 | 305 | 489 | 672 | 869 | 1010 |

(a) Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

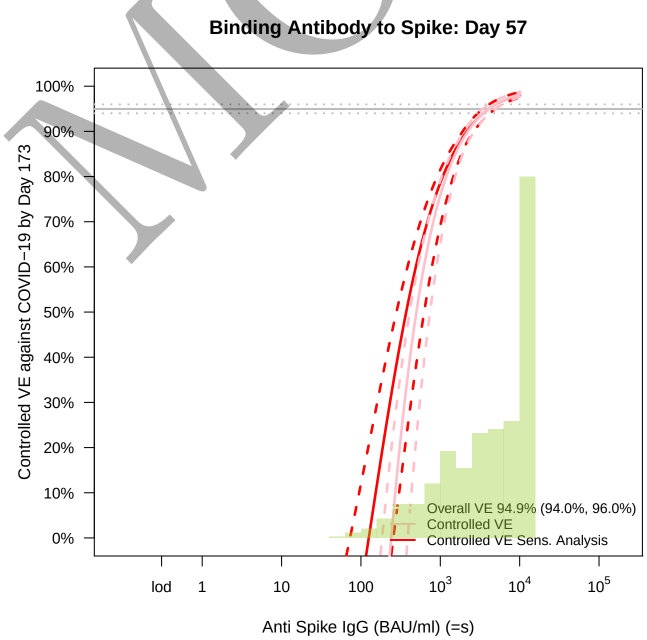



(b) Marginalized cumulative risk by Day 173 as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 6.6: Marginalized cumulative risk curves (=s).

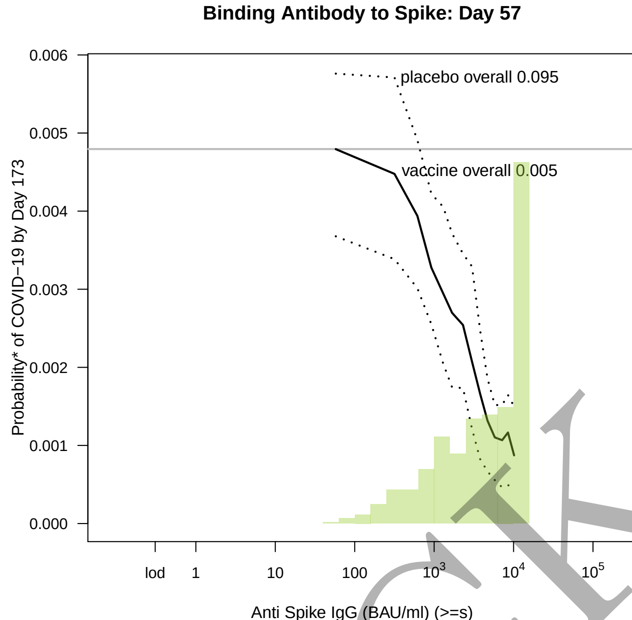



(a) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

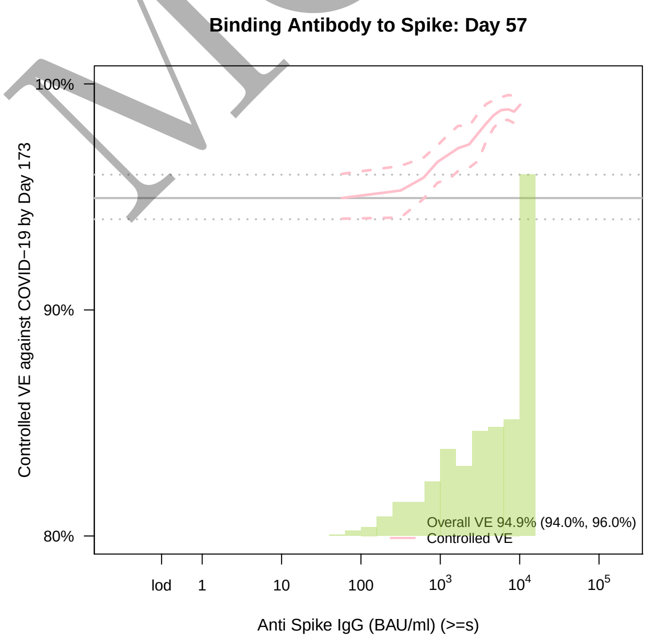



(b) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 6.7: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 173 post Day 57 visit as functions of Day 57 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.




(b) Controlled VE as functions of Day 57 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 6.8: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 6.4: Marginalized cumulative risk by Day 173 as functions of Day 57 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

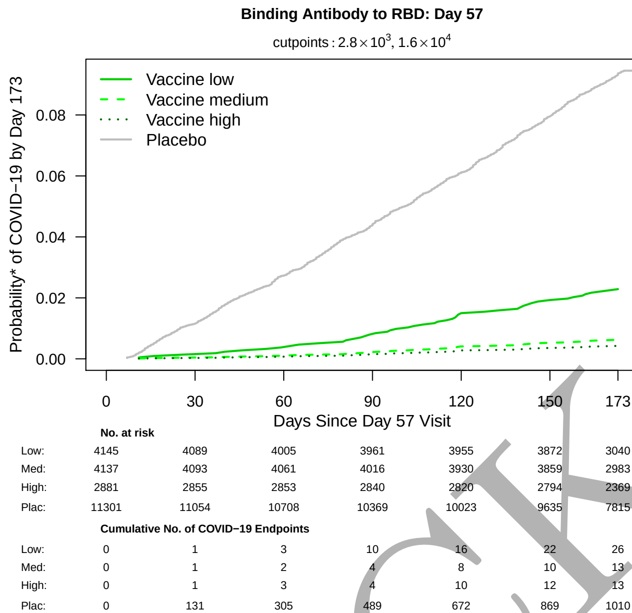
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 57.7 | .2628 (.2099,.3457) | 249 | .0920 (.0743,.1374) | 922 | .0250 (.0212,.0359) | 3392 | .0059 (.0047,.0072) |
| 61 | .2551 (.2035,.3369) | 262 | .0878 (.0710,.1318) | 968 | .0237 (.0202,.0338) | 3573 | .0056 (.0044,.0067) |
| 64 | .2475 (.1973,.3281) | 276 | .0838 (.0679,.1262) | 1000 | .0229 (.0195,.0325) | 3765 | .0052 (.0042,.0064) |
| 67 | .2400 (.1912,.3194) | 291 | .0799 (.0649,.1208) | 1020 | .0224 (.0191,.0317) | 3967 | .0049 (.0039,.0060) |
| 71 | .2326 (.1852,.3109) | 307 | .0761 (.0620,.1155) | 1075 | .0212 (.0181,.0297) | 4180 | .0047 (.0036,.0057) |
| 75 | .2253 (.1793,.3024) | 323 | .0725 (.0592,.1103) | 1133 | .0200 (.0171,.0278) | 4404 | .0044 (.0034,.0054) |
| 79 | .2182 (.1735,.2940) | 341 | .0690 (.0565,.1052) | 1193 | .0189 (.0162,.0260) | 4640 | .0041 (.0032,.0051) |
| 83 | .2111 (.1678,.2857) | 359 | .0657 (.0539,.1003) | 1257 | .0179 (.0153,.0243) | 4685 | .0041 (.0032,.0051) |
| 88 | .2042 (.1622,.2775) | 378 | .0625 (.0513,.0955) | 1325 | .0169 (.0145,.0227) | 4889 | .0039 (.0030,.0048) |
| 92 | .1974 (.1567,.2694) | 399 | .0594 (.0489,.0909) | 1359 | .0164 (.0141,.0220) | 5151 | .0037 (.0028,.0046) |
| 97 | .1907 (.1514,.2614) | 420 | .0564 (.0466,.0864) | 1396 | .0159 (.0137,.0212) | 5427 | .0035 (.0026,.0043) |
| 103 | .1841 (.1461,.2535) | 442 | .0536 (.0444,.0820) | 1471 | .0150 (.0130,.0198) | 5718 | .0033 (.0025,.0041) |
| 108 | .1776 (.1410,.2458) | 466 | .0509 (.0422,.0778) | 1549 | .0142 (.0122,.0185) | 6024 | .0031 (.0023,.0039) |
| 114 | .1713 (.1360,.2381) | 491 | .0483 (.0401,.0737) | 1633 | .0134 (.0115,.0173) | 6347 | .0029 (.0022,.0037) |
| 120 | .1651 (.1311,.2305) | 500 | .0474 (.0395,.0723) | 1720 | .0126 (.0109,.0161) | 6688 | .0027 (.0020,.0035) |
| 126 | .1590 (.1263,.2231) | 517 | .0458 (.0381,.0698) | 1812 | .0119 (.0102,.0150) | 7046 | .0026 (.0019,.0033) |
| 133 | .1530 (.1216,.2157) | 545 | .0434 (.0362,.0660) | 1909 | .0113 (.0097,.0141) | 7245 | .0025 (.0018,.0032) |
| 140 | .1472 (.1171,.2085) | 574 | .0412 (.0344,.0623) | 2012 | .0106 (.0091,.0132) | 7424 | .0024 (.0017,.0031) |
| 148 | .1415 (.1126,.2014) | 605 | .0390 (.0327,.0588) | 2120 | .0100 (.0085,.0124) | 7822 | .0023 (.0016,.0030) |
| 156 | .1359 (.1083,.1944) | 638 | .0370 (.0310,.0555) | 2233 | .0094 (.0080,.0117) | 8241 | .0021 (.0015,.0028) |
| 164 | .1305 (.1040,.1875) | 643 | .0366 (.0307,.0550) | 2353 | .0089 (.0075,.0110) | 8683 | .0020 (.0014,.0027) |
| 173 | .1252 (.0999,.1808) | 672 | .0350 (.0294,.0523) | 2479 | .0084 (.0070,.0103) | 9149 | .0019 (.0013,.0025) |
| 182 | .1200 (.0959,.1741) | 708 | .0332 (.0279,.0492) | 2612 | .0079 (.0066,.0097) | 9639 | .0018 (.0012,.0024) |
| 192 | .1150 (.0920,.1676) | 746 | .0314 (.0264,.0463) | 2752 | .0075 (.0061,.0091) | 10156 | .0017 (.0011,.0022) |
| 202 | .1101 (.0883,.1613) | 786 | .0297 (.0251,.0436) | 2876 | .0071 (.0058,.0087) | 10156 | .0017 (.0011,.0022) |
| 213 | .1054 (.0846,.1552) | 828 | .0281 (.0237,.0409) | 2900 | .0070 (.0058,.0086) | 10156 | .0017 (.0011,.0022) |
| 224 | .1008 (.0811,.1491) | 872 | .0266 (.0225,.0384) | 3055 | .0066 (.0054,.0081) | 10156 | .0017 (.0011,.0022) |
| 236 | .0963 (.0776,.1432) | 919 | .0251 (.0213,.0360) | 3219 | .0063 (.0051,.0076) | 10156 | .0017 (.0011,.0022) |

Table 6.5: Controlled VE as functions of Day 57 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 173 days post Day 57 was 0.005 in vaccine recipients compared to 0.095 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 96.0%).

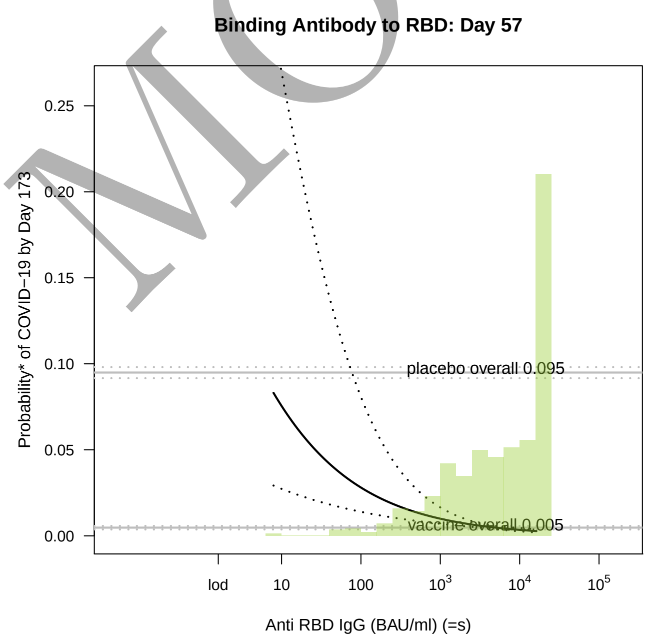
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 57.7 | -1.7677 (-2.6860,-1.1863) | 262 | 0.0752 (-0.4148, 0.2511) | 1000 | 0.7585 ( 0.6516, 0.7914) | 3967 | 0.9480 ( 0.9359, 0.9579) |
| 61 | -1.6866 (-2.5917,-1.1219) | 276 | 0.1177 (-0.3552, 0.2840) | 1020 | 0.7636 ( 0.6602, 0.7957) | 4180 | 0.9510 ( 0.9396, 0.9606) |
| 64 | -1.6066 (-2.4984,-1.0584) | 291 | 0.1587 (-0.2969, 0.3159) | 1075 | 0.7767 ( 0.6818, 0.8064) | 4404 | 0.9538 ( 0.9431, 0.9631) |
| 67 | -1.5276 (-2.4061,-0.9959) | 307 | 0.1982 (-0.2399, 0.3466) | 1133 | 0.7890 ( 0.7021, 0.8166) | 4640 | 0.9564 ( 0.9462, 0.9654) |
| 71 | -1.4499 (-2.3147,-0.9344) | 323 | 0.2363 (-0.1843, 0.3762) | 1193 | 0.8007 ( 0.7213, 0.8263) | 4685 | 0.9569 ( 0.9468, 0.9658) |
| 75 | -1.3732 (-2.2244,-0.8739) | 341 | 0.2729 (-0.1300, 0.4048) | 1257 | 0.8117 ( 0.7394, 0.8355) | 4889 | 0.9590 ( 0.9492, 0.9676) |
| 79 | -1.2978 (-2.1350,-0.8146) | 359 | 0.3082 (-0.0772, 0.4323) | 1325 | 0.8222 ( 0.7564, 0.8443) | 5151 | 0.9613 ( 0.9520, 0.9697) |
| 83 | -1.2235 (-2.0467,-0.7562) | 378 | 0.3420 (-0.0258, 0.4587) | 1359 | 0.8272 ( 0.7644, 0.8484) | 5427 | 0.9636 ( 0.9547, 0.9716) |
| 88 | -1.1505 (-1.9595,-0.6990) | 399 | 0.3745 ( 0.0241, 0.4842) | 1396 | 0.8322 ( 0.7724, 0.8526) | 5718 | 0.9657 ( 0.9572, 0.9734) |
| 92 | -1.0786 (-1.8733,-0.6429) | 420 | 0.4056 ( 0.0726, 0.5087) | 1471 | 0.8415 ( 0.7874, 0.8604) | 6024 | 0.9676 ( 0.9596, 0.9751) |
| 97 | -1.0080 (-1.7883,-0.5878) | 442 | 0.4355 ( 0.1195, 0.5322) | 1549 | 0.8504 ( 0.8015, 0.8679) | 6347 | 0.9695 ( 0.9619, 0.9768) |
| 103 | -0.9387 (-1.7043,-0.5339) | 466 | 0.4640 ( 0.1649, 0.5547) | 1633 | 0.8588 ( 0.8148, 0.8750) | 6688 | 0.9713 ( 0.9639, 0.9784) |
| 108 | -0.8706 (-1.6214,-0.4811) | 491 | 0.4914 ( 0.2087, 0.5763) | 1720 | 0.8668 ( 0.8272, 0.8818) | 7046 | 0.9729 ( 0.9658, 0.9798) |
| 114 | -0.8039 (-1.5397,-0.4294) | 500 | 0.5005 ( 0.2234, 0.5835) | 1812 | 0.8743 ( 0.8388, 0.8885) | 7245 | 0.9738 ( 0.9668, 0.9806) |
| 120 | -0.7384 (-1.4592,-0.3788) | 517 | 0.5175 ( 0.2510, 0.5970) | 1909 | 0.8814 ( 0.8496, 0.8954) | 7424 | 0.9745 ( 0.9676, 0.9812) |
| 126 | -0.6742 (-1.3798,-0.3293) | 545 | 0.5424 ( 0.2917, 0.6169) | 2012 | 0.8881 ( 0.8598, 0.9019) | 7822 | 0.9760 ( 0.9694, 0.9825) |
| 133 | -0.6114 (-1.3019,-0.2810) | 574 | 0.5663 ( 0.3308, 0.6359) | 2120 | 0.8945 ( 0.8687, 0.9081) | 8241 | 0.9774 ( 0.9710, 0.9837) |
| 140 | -0.5500 (-1.2266,-0.2338) | 605 | 0.5890 ( 0.3683, 0.6540) | 2233 | 0.9005 ( 0.8767, 0.9138) | 8683 | 0.9787 ( 0.9725, 0.9848) |
| 148 | -0.4899 (-1.1524,-0.1872) | 638 | 0.6106 ( 0.4042, 0.6714) | 2353 | 0.9061 ( 0.8839, 0.9192) | 9149 | 0.9799 ( 0.9740, 0.9858) |
| 156 | -0.4313 (-1.0794,-0.1415) | 643 | 0.6140 ( 0.4099, 0.6741) | 2479 | 0.9115 ( 0.8907, 0.9243) | 9639 | 0.9811 ( 0.9754, 0.9868) |
| 164 | -0.3740 (-1.0076,-0.0969) | 672 | 0.6312 ( 0.4386, 0.6879) | 2612 | 0.9165 ( 0.8972, 0.9290) | 10156 | 0.9822 ( 0.9767, 0.9877) |
| 173 | -0.3182 (-0.9369,-0.0536) | 708 | 0.6509 ( 0.4714, 0.7038) | 2752 | 0.9213 ( 0.9032, 0.9335) | 10156 | 0.9822 ( 0.9767, 0.9877) |
| 182 | -0.2639 (-0.8674,-0.0114) | 746 | 0.6695 ( 0.5027, 0.7189) | 2876 | 0.9251 ( 0.9079, 0.9371) | 10156 | 0.9822 ( 0.9767, 0.9877) |
| 192 | -0.2110 (-0.7990, 0.0296) | 786 | 0.6873 ( 0.5325, 0.7333) | 2900 | 0.9258 ( 0.9087, 0.9377) | 10156 | 0.9822 ( 0.9767, 0.9877) |
| 202 | -0.1596 (-0.7319, 0.0694) | 828 | 0.7042 ( 0.5608, 0.7470) | 3055 | 0.9301 ( 0.9140, 0.9416) | 10156 | 0.9822 ( 0.9767, 0.9877) |
| 213 | -0.1096 (-0.6660, 0.1081) | 872 | 0.7202 ( 0.5877, 0.7601) | 3219 | 0.9341 ( 0.9189, 0.9453) | 707.9 | .6509 (.4714,.7038) |
| 224 | -0.0612 (-0.6013, 0.1455) | 919 | 0.7355 ( 0.6132, 0.7725) | 3392 | 0.9379 ( 0.9235, 0.9488) | 2233 | .9005 (.8767,.9138) |
| 236 | -0.0142 (-0.5379, 0.1819) | 922 | 0.7364 ( 0.6147, 0.7733) | 3573 | 0.9414 ( 0.9279, 0.9520) | 4180 | .9510 (.9396,.9606) |
| 249 | 0.0312 (-0.4757, 0.2171) | 968 | 0.7499 ( 0.6374, 0.7844) | 3765 | 0.9448 ( 0.9320, 0.9550) | | |

Table 6.6: Controlled VE with sensitivity analysis as functions of Day 57 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 57.7 | -0.3732 (-0.8288,-0.0847) | 262 | 0.3555 ( 0.0140, 0.4781) | 1000 | 0.7861 ( 0.6915, 0.8153) | 3967 | 0.9480 ( 0.9359, 0.9579) |
| 61 | -0.3497 (-0.8045,-0.0660) | 276 | 0.3785 ( 0.0454, 0.4957) | 1020 | 0.7901 ( 0.6982, 0.8185) | 4180 | 0.9510 ( 0.9396, 0.9606) |
| 64 | -0.3259 (-0.7796,-0.0471) | 291 | 0.4011 ( 0.0768, 0.5130) | 1075 | 0.8002 ( 0.7153, 0.8268) | 4404 | 0.9538 ( 0.9430, 0.9630) |
| 67 | -0.3019 (-0.7543,-0.0280) | 307 | 0.4232 ( 0.1080, 0.5299) | 1133 | 0.8098 ( 0.7315, 0.8347) | 4640 | 0.9564 ( 0.9462, 0.9654) |
| 71 | -0.2775 (-0.7285,-0.0087) | 323 | 0.4448 ( 0.1391, 0.5465) | 1193 | 0.8191 ( 0.7470, 0.8423) | 4685 | 0.9569 ( 0.9467, 0.9658) |
| 75 | -0.2529 (-0.7022, 0.0107) | 341 | 0.4660 ( 0.1701, 0.5628) | 1257 | 0.8279 ( 0.7618, 0.8496) | 4889 | 0.9589 ( 0.9491, 0.9675) |
| 79 | -0.2280 (-0.6754, 0.0303) | 359 | 0.4867 ( 0.2007, 0.5787) | 1325 | 0.8364 ( 0.7759, 0.8567) | 5151 | 0.9612 ( 0.9519, 0.9695) |
| 83 | -0.2029 (-0.6483, 0.0499) | 378 | 0.5068 ( 0.2311, 0.5943) | 1359 | 0.8405 ( 0.7825, 0.8601) | 5427 | 0.9634 ( 0.9545, 0.9714) |
| 88 | -0.1776 (-0.6207, 0.0696) | 399 | 0.5264 ( 0.2612, 0.6095) | 1396 | 0.8445 ( 0.7892, 0.8634) | 5718 | 0.9654 ( 0.9569, 0.9732) |
| 92 | -0.1522 (-0.5927, 0.0894) | 420 | 0.5455 ( 0.2909, 0.6243) | 1471 | 0.8523 ( 0.8019, 0.8699) | 6024 | 0.9673 ( 0.9592, 0.9749) |
| 97 | -0.1265 (-0.5642, 0.1092) | 442 | 0.5641 ( 0.3201, 0.6388) | 1549 | 0.8597 ( 0.8139, 0.8761) | 6347 | 0.9691 ( 0.9614, 0.9765) |
| 103 | -0.1008 (-0.5354, 0.1291) | 466 | 0.5821 ( 0.3489, 0.6528) | 1633 | 0.8668 ( 0.8252, 0.8821) | 6688 | 0.9708 ( 0.9633, 0.9780) |
| 108 | -0.0749 (-0.5063, 0.1490) | 491 | 0.5996 ( 0.3771, 0.6665) | 1720 | 0.8736 ( 0.8360, 0.8879) | 7046 | 0.9724 ( 0.9651, 0.9794) |
| 114 | -0.0489 (-0.4768, 0.1689) | 500 | 0.6055 ( 0.3867, 0.6711) | 1812 | 0.8801 ( 0.8462, 0.8936) | 7245 | 0.9732 ( 0.9661, 0.9802) |
| 120 | -0.0228 (-0.4469, 0.1887) | 517 | 0.6166 ( 0.4048, 0.6798) | 1909 | 0.8863 ( 0.8558, 0.8997) | 7424 | 0.9739 ( 0.9669, 0.9808) |
| 126 | 0.0032 (-0.4168, 0.2086) | 545 | 0.6330 ( 0.4318, 0.6927) | 2012 | 0.8922 ( 0.8649, 0.9055) | 7822 | 0.9753 ( 0.9685, 0.9820) |
| 133 | 0.0293 (-0.3865, 0.2284) | 574 | 0.6488 ( 0.4582, 0.7052) | 2120 | 0.8978 ( 0.8729, 0.9110) | 8241 | 0.9766 ( 0.9701, 0.9831) |
| 140 | 0.0554 (-0.3569, 0.2481) | 605 | 0.6642 ( 0.4839, 0.7173) | 2233 | 0.9032 ( 0.8801, 0.9162) | 8683 | 0.9779 ( 0.9715, 0.9842) |
| 148 | 0.0815 (-0.3270, 0.2681) | 638 | 0.6790 ( 0.5089, 0.7291) | 2353 | 0.9083 ( 0.8866, 0.9211) | 9149 | 0.9791 ( 0.9729, 0.9852) |
| 156 | 0.1074 (-0.2968, 0.2881) | 643 | 0.6814 ( 0.5128, 0.7309) | 2479 | 0.9132 ( 0.8929, 0.9258) | 9639 | 0.9802 ( 0.9742, 0.9861) |
| 164 | 0.1332 (-0.2664, 0.3081) | 672 | 0.6933 ( 0.5331, 0.7405) | 2612 | 0.9179 ( 0.8988, 0.9302) | 10156 | 0.9812 ( 0.9755, 0.9870) |
| 173 | 0.1589 (-0.2358, 0.3278) | 708 | 0.7071 ( 0.5565, 0.7515) | 2752 | 0.9223 ( 0.9045, 0.9344) | 10156 | 0.9812 ( 0.9755, 0.9870) |
| 182 | 0.1844 (-0.2050, 0.3474) | 746 | 0.7204 ( 0.5792, 0.7621) | 2876 | 0.9259 ( 0.9089, 0.9377) | 10156 | 0.9812 ( 0.9755, 0.9870) |
| 192 | 0.2098 (-0.1740, 0.3667) | 786 | 0.7332 ( 0.6011, 0.7724) | 2900 | 0.9266 ( 0.9097, 0.9383) | 10156 | 0.9812 ( 0.9755, 0.9870) |
| 202 | 0.2348 (-0.1429, 0.3859) | 828 | 0.7455 ( 0.6221, 0.7823) | 3055 | 0.9306 ( 0.9146, 0.9421) | 10156 | 0.9812 ( 0.9755, 0.9870) |
| 213 | 0.2596 (-0.1116, 0.4049) | 872 | 0.7573 ( 0.6424, 0.7919) | 3219 | 0.9344 ( 0.9193, 0.9456) | 707.9 | .6509 (.4714,.7038) |
| 224 | 0.2841 (-0.0803, 0.4236) | 919 | 0.7687 ( 0.6618, 0.8011) | 3392 | 0.9381 ( 0.9238, 0.9489) | 2233 | .9005 (.8767,.9138) |
| 236 | 0.3083 (-0.0489, 0.4420) | 922 | 0.7694 ( 0.6630, 0.8017) | 3573 | 0.9415 ( 0.9280, 0.9521) | 4180 | .9510 (.9396,.9606) |
| 249 | 0.3321 (-0.0174, 0.4602) | 968 | 0.7796 ( 0.6804, 0.8100) | 3765 | 0.9448 ( 0.9321, 0.9551) | | |

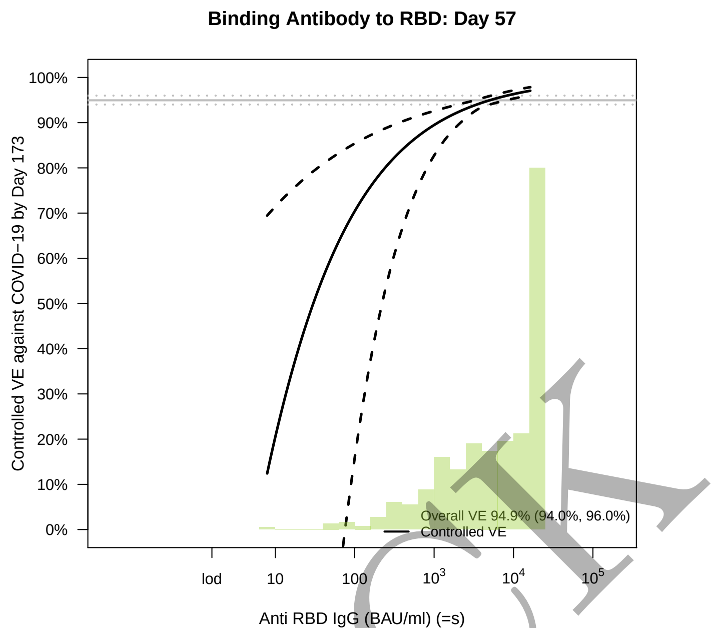



(a) Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

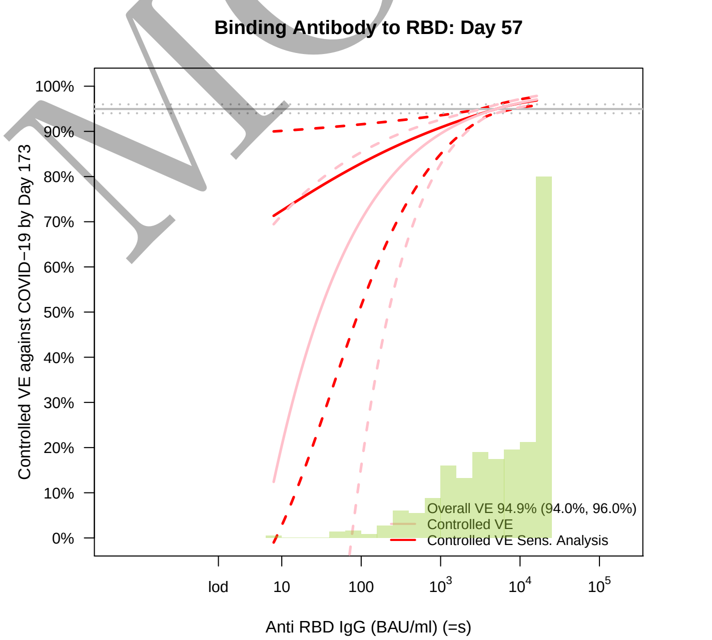



(b) Marginalized cumulative risk by Day 173 as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 6.9: Marginalized cumulative risk curves (=s).

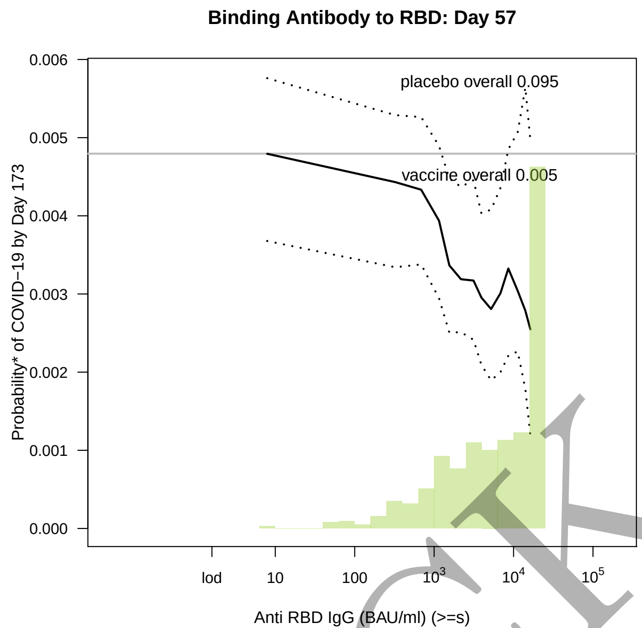



(a) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

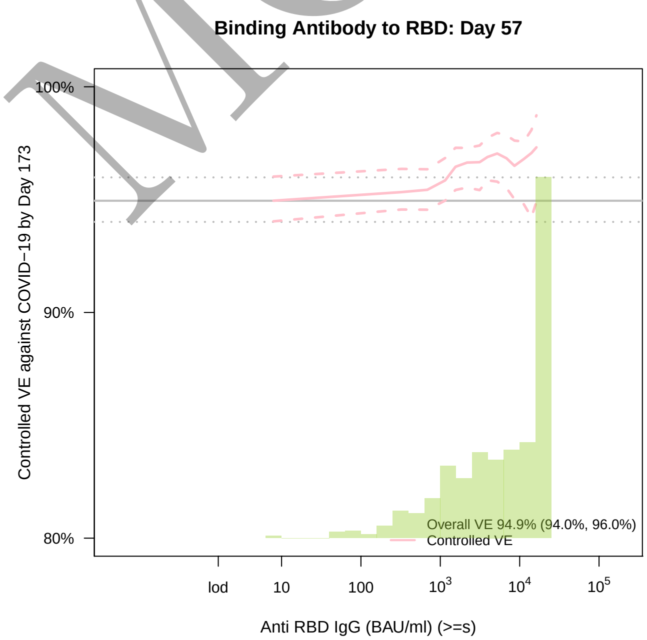



(b) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 6.10: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 173 post Day 57 visit as functions of Day 57 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.




(b) Controlled VE as functions of Day 57 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 6.11: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 6.7: Marginalized cumulative risk by Day 173 as functions of Day 57 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

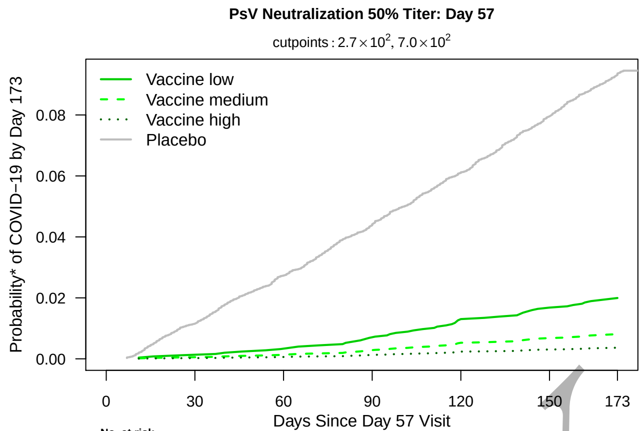
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 7.9 | .0832 (.0293,.2959) | 68 | .0332 (.0156,.1021) | 548 | .0131 (.0085,.0255) | 3483 | .0057 (.0046,.0069) |
| 9 | .0806 (.0286,.2872) | 74 | .0321 (.0153,.0974) | 592 | .0127 (.0083,.0241) | 3762 | .0055 (.0044,.0066) |
| 9 | .0781 (.0280,.2785) | 80 | .0310 (.0150,.0929) | 639 | .0122 (.0081,.0228) | 3798 | .0054 (.0044,.0065) |
| 10 | .0757 (.0274,.2700) | 86 | .0300 (.0146,.0886) | 690 | .0118 (.0079,.0216) | 4064 | .0053 (.0042,.0063) |
| 11 | .0733 (.0268,.2616) | 93 | .0290 (.0143,.0845) | 743 | .0114 (.0077,.0205) | 4389 | .0051 (.0041,.0061) |
| 12 | .0710 (.0262,.2533) | 101 | .0280 (.0140,.0805) | 746 | .0114 (.0077,.0204) | 4741 | .0049 (.0039,.0059) |
| 13 | .0687 (.0256,.2451) | 109 | .0271 (.0137,.0766) | 806 | .0110 (.0075,.0193) | 5121 | .0047 (.0038,.0058) |
| 14 | .0666 (.0251,.2370) | 117 | .0262 (.0134,.0730) | 870 | .0106 (.0074,.0183) | 5531 | .0046 (.0036,.0056) |
| 15 | .0645 (.0245,.2291) | 127 | .0253 (.0131,.0694) | 940 | .0103 (.0072,.0173) | 5974 | .0044 (.0035,.0054) |
| 16 | .0624 (.0240,.2213) | 137 | .0244 (.0128,.0660) | 1000 | .0100 (.0070,.0166) | 6453 | .0043 (.0033,.0053) |
| 17 | .0604 (.0234,.2137) | 148 | .0236 (.0125,.0628) | 1015 | .0099 (.0070,.0164) | 6791 | .0042 (.0033,.0052) |
| 18 | .0585 (.0229,.2061) | 160 | .0228 (.0122,.0597) | 1096 | .0096 (.0068,.0155) | 6970 | .0041 (.0032,.0051) |
| 20 | .0566 (.0224,.1988) | 172 | .0221 (.0119,.0567) | 1152 | .0094 (.0067,.0149) | 7528 | .0040 (.0031,.0050) |
| 22 | .0548 (.0219,.1915) | 186 | .0213 (.0117,.0538) | 1184 | .0092 (.0067,.0146) | 8131 | .0038 (.0030,.0049) |
| 23 | .0530 (.0214,.1844) | 201 | .0206 (.0114,.0511) | 1279 | .0089 (.0065,.0138) | 8782 | .0037 (.0028,.0047) |
| 25 | .0513 (.0210,.1775) | 217 | .0199 (.0111,.0485) | 1382 | .0086 (.0064,.0131) | 9486 | .0036 (.0027,.0046) |
| 27 | .0496 (.0205,.1707) | 235 | .0192 (.0109,.0460) | 1492 | .0083 (.0062,.0124) | 10246 | .0035 (.0026,.0045) |
| 29 | .0480 (.0200,.1641) | 254 | .0186 (.0106,.0437) | 1612 | .0080 (.0061,.0117) | 11067 | .0033 (.0025,.0044) |
| 32 | .0465 (.0196,.1576) | 274 | .0179 (.0104,.0414) | 1625 | .0080 (.0060,.0117) | 11504 | .0033 (.0024,.0043) |
| 34 | .0449 (.0192,.1513) | 296 | .0173 (.0102,.0393) | 1741 | .0078 (.0059,.0111) | 11953 | .0032 (.0024,.0043) |
| 37 | .0435 (.0187,.1452) | 319 | .0167 (.0099,.0372) | 1880 | .0075 (.0058,.0105) | 12911 | .0031 (.0023,.0042) |
| 40 | .0420 (.0183,.1392) | 345 | .0162 (.0097,.0353) | 2031 | .0072 (.0056,.0099) | 13945 | .0030 (.0022,.0041) |
| 43 | .0407 (.0179,.1334) | 373 | .0156 (.0095,.0335) | 2194 | .0070 (.0055,.0094) | 15063 | .0029 (.0021,.0040) |
| 47 | .0393 (.0175,.1278) | 403 | .0151 (.0093,.0317) | 2369 | .0067 (.0054,.0089) | 16269 | .0028 (.0020,.0039) |
| 50 | .0380 (.0171,.1223) | 435 | .0146 (.0091,.0300) | 2559 | .0065 (.0052,.0085) | 16269 | .0028 (.0020,.0039) |
| 54 | .0368 (.0167,.1170) | 470 | .0141 (.0089,.0284) | 2764 | .0063 (.0051,.0080) | 16269 | .0028 (.0020,.0039) |
| 59 | .0355 (.0164,.1118) | 500 | .0137 (.0087,.0272) | 2986 | .0061 (.0049,.0076) | 16269 | .0028 (.0020,.0039) |
| 63 | .0344 (.0160,.1069) | 507 | .0136 (.0087,.0269) | 3225 | .0059 (.0047,.0073) | 16269 | .0028 (.0020,.0039) |

Table 6.8: Controlled VE as functions of Day 57 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 173 days post Day 57 was 0.005 in vaccine recipients compared to 0.095 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 96.0%).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 7.9 | .1241 (-2.0838,.6945) | 74 | .6618 (-0.0152,.8402) | 639 | .8712 ( 0.7618,.9154) | 4064 | .9445 ( 0.9351,.9545) |
| 9 | .1512 (-1.9925,.7011) | 80 | .6731 ( 0.0315,.8438) | 690 | .8756 ( 0.7746,.9173) | 4389 | .9464 ( 0.9372,.9561) |
| 9 | .1776 (-1.9024,.7077) | 86 | .6840 ( 0.0764,.8473) | 743 | .8797 ( 0.7862,.9191) | 4741 | .9483 ( 0.9389,.9578) |
| 10 | .2032 (-1.8135,.7141) | 93 | .6946 ( 0.1196,.8507) | 746 | .8798 ( 0.7867,.9192) | 5121 | .9501 ( 0.9406,.9594) |
| 11 | .2282 (-1.7257,.7203) | 101 | .7048 ( 0.1612,.8540) | 806 | .8840 ( 0.7982,.9210) | 5531 | .9518 ( 0.9422,.9609) |
| 12 | .2524 (-1.6392,.7265) | 109 | .7147 ( 0.2012,.8573) | 870 | .8880 ( 0.8091,.9228) | 5974 | .9535 ( 0.9438,.9624) |
| 13 | .2760 (-1.5539,.7325) | 117 | .7243 ( 0.2396,.8605) | 940 | .8918 ( 0.8194,.9246) | 6453 | .9551 ( 0.9454,.9638) |
| 14 | .2989 (-1.4700,.7383) | 127 | .7336 ( 0.2765,.8636) | 1000 | .8948 ( 0.8273,.9259) | 6791 | .9561 ( 0.9464,.9647) |
| 15 | .3211 (-1.3874,.7441) | 137 | .7425 ( 0.3118,.8667) | 1015 | .8955 ( 0.8291,.9263) | 6970 | .9566 ( 0.9469,.9652) |
| 16 | .3427 (-1.3062,.7497) | 148 | .7512 ( 0.3457,.8697) | 1096 | .8991 ( 0.8384,.9279) | 7528 | .9581 ( 0.9483,.9666) |
| 17 | .3637 (-1.2264,.7552) | 160 | .7596 ( 0.3781,.8726) | 1152 | .9014 ( 0.8441,.9290) | 8131 | .9596 ( 0.9497,.9680) |
| 18 | .3841 (-1.1480,.7606) | 172 | .7677 ( 0.4091,.8755) | 1184 | .9026 ( 0.8472,.9296) | 8782 | .9610 ( 0.9511,.9694) |
| 20 | .4039 (-1.0711,.7659) | 186 | .7756 ( 0.4387,.8783) | 1279 | .9059 ( 0.8555,.9312) | 9486 | .9623 ( 0.9524,.9707) |
| 22 | .4231 (-0.9957,.7711) | 201 | .7832 ( 0.4670,.8810) | 1382 | .9092 ( 0.8634,.9329) | 10246 | .9636 ( 0.9537,.9719) |
| 23 | .4417 (-0.9219,.7762) | 217 | .7905 ( 0.4941,.8837) | 1492 | .9123 ( 0.8706,.9345) | 11067 | .9649 ( 0.9549,.9731) |
| 25 | .4598 (-0.8496,.7811) | 235 | .7977 ( 0.5199,.8863) | 1612 | .9153 ( 0.8775,.9360) | 11504 | .9655 ( 0.9555,.9737) |
| 27 | .4773 (-0.7790,.7860) | 254 | .8045 ( 0.5445,.8888) | 1625 | .9156 ( 0.8781,.9362) | 11953 | .9661 ( 0.9560,.9742) |
| 29 | .4943 (-0.7099,.7907) | 274 | .8112 ( 0.5680,.8913) | 1741 | .9183 ( 0.8840,.9376) | 12911 | .9673 ( 0.9571,.9754) |
| 32 | .5108 (-0.6426,.7953) | 296 | .8176 ( 0.5903,.8938) | 1880 | .9211 ( 0.8901,.9391) | 13945 | .9684 ( 0.9582,.9765) |
| 34 | .5268 (-0.5769,.7999) | 319 | .8238 ( 0.6116,.8962) | 2031 | .9238 ( 0.8959,.9405) | 15063 | .9695 ( 0.9592,.9775) |
| 37 | .5423 (-0.5129,.8043) | 345 | .8298 ( 0.6319,.8985) | 2194 | .9264 ( 0.9014,.9419) | 16269 | .9706 ( 0.9602,.9785) |
| 40 | .5573 (-0.4506,.8087) | 373 | .8356 ( 0.6512,.9008) | 2369 | .9290 ( 0.9067,.9433) | 16269 | .9706 ( 0.9602,.9785) |
| 43 | .5718 (-0.3901,.8129) | 403 | .8412 ( 0.6695,.9030) | 2559 | .9314 ( 0.9116,.9448) | 16269 | .9706 ( 0.9602,.9785) |
| 47 | .5859 (-0.3313,.8171) | 435 | .8466 ( 0.6869,.9052) | 2764 | .9338 ( 0.9163,.9462) | 16269 | .9706 ( 0.9602,.9785) |
| 50 | .5996 (-0.2742,.8212) | 470 | .8519 ( 0.7035,.9074) | 2986 | .9361 ( 0.9207,.9476) | 16269 | .9706 ( 0.9602,.9785) |
| 54 | .6129 (-0.2189,.8251) | 500 | .8560 ( 0.7163,.9091) | 3225 | .9383 ( 0.9249,.9492) | 68.4 | .6501 (-0.0635,.8366) |
| 59 | .6257 (-0.1654,.8290) | 507 | .8570 ( 0.7192,.9094) | 3483 | .9404 ( 0.9288,.9510) | 1096 | .8991 ( 0.8384,.9279) |
| 63 | .6381 (-0.1136,.8329) | 548 | .8619 ( 0.7342,.9115) | 3762 | .9425 ( 0.9323,.9528) | 5121 | .9501 ( 0.9406,.9594) |
| 68 | .6501 (-0.0635,.8366) | 592 | .8666 ( 0.7483,.9135) | 3798 | .9427 ( 0.9327,.9530) | | |

Table 6.9: Controlled VE with sensitivity analysis as functions of Day 57 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 7.9 | .7131 (-0.0101,.8999) | 74 | .8168 ( 0.4500,.9134) | 639 | .8952 ( 0.8062,.9312) | 4064 | .9448 ( 0.9355,.9548) |
| 9 | .7169 ( 0.0018,.9003) | 80 | .8200 ( 0.4667,.9140) | 690 | .8975 ( 0.8143,.9319) | 4389 | .9466 ( 0.9374,.9563) |
| 9 | .7207 ( 0.0142,.9007) | 86 | .8232 ( 0.4831,.9145) | 743 | .8998 ( 0.8219,.9326) | 4741 | .9483 ( 0.9390,.9578) |
| 10 | .7244 ( 0.0270,.9011) | 93 | .8263 ( 0.4994,.9151) | 746 | .8999 ( 0.8222,.9327) | 5121 | .9501 ( 0.9406,.9594) |
| 11 | .7282 ( 0.0402,.9015) | 101 | .8294 ( 0.5154,.9157) | 806 | .9022 ( 0.8298,.9334) | 5531 | .9518 ( 0.9422,.9609) |
| 12 | .7320 ( 0.0538,.9019) | 109 | .8325 ( 0.5311,.9162) | 870 | .9045 ( 0.8372,.9342) | 5974 | .9534 ( 0.9438,.9624) |
| 13 | .7357 ( 0.0678,.9024) | 117 | .8356 ( 0.5466,.9168) | 940 | .9067 ( 0.8443,.9350) | 6453 | .9550 ( 0.9453,.9637) |
| 14 | .7395 ( 0.0822,.9028) | 127 | .8386 ( 0.5617,.9174) | 1000 | .9085 ( 0.8498,.9356) | 6791 | .9560 ( 0.9462,.9646) |
| 15 | .7432 ( 0.0969,.9032) | 137 | .8416 ( 0.5766,.9180) | 1015 | .9090 ( 0.8511,.9357) | 6970 | .9565 ( 0.9467,.9651) |
| 16 | .7469 ( 0.1120,.9036) | 148 | .8446 ( 0.5912,.9186) | 1096 | .9112 ( 0.8577,.9365) | 7528 | .9579 ( 0.9480,.9664) |
| 17 | .7506 ( 0.1274,.9041) | 160 | .8475 ( 0.6055,.9192) | 1152 | .9126 ( 0.8618,.9371) | 8131 | .9592 ( 0.9493,.9677) |
| 18 | .7543 ( 0.1432,.9045) | 172 | .8504 ( 0.6194,.9198) | 1184 | .9133 ( 0.8640,.9373) | 8782 | .9605 ( 0.9505,.9690) |
| 20 | .7580 ( 0.1592,.9050) | 186 | .8533 ( 0.6331,.9204) | 1279 | .9155 ( 0.8701,.9382) | 9486 | .9617 ( 0.9516,.9701) |
| 22 | .7616 ( 0.1754,.9054) | 201 | .8561 ( 0.6463,.9210) | 1382 | .9176 ( 0.8760,.9391) | 10246 | .9628 ( 0.9527,.9713) |
| 23 | .7653 ( 0.1920,.9059) | 217 | .8589 ( 0.6593,.9217) | 1492 | .9197 ( 0.8815,.9400) | 11067 | .9639 ( 0.9536,.9723) |
| 25 | .7689 ( 0.2087,.9064) | 235 | .8617 ( 0.6719,.9223) | 1612 | .9218 ( 0.8868,.9409) | 11504 | .9644 ( 0.9541,.9728) |
| 27 | .7725 ( 0.2256,.9068) | 254 | .8645 ( 0.6842,.9229) | 1625 | .9220 ( 0.8873,.9410) | 11953 | .9650 ( 0.9545,.9733) |
| 29 | .7760 ( 0.2427,.9073) | 274 | .8672 ( 0.6962,.9236) | 1741 | .9238 ( 0.8919,.9418) | 12911 | .9660 ( 0.9553,.9743) |
| 32 | .7796 ( 0.2599,.9078) | 296 | .8699 ( 0.7078,.9242) | 1880 | .9259 ( 0.8968,.9428) | 13945 | .9669 ( 0.9561,.9753) |
| 34 | .7831 ( 0.2772,.9083) | 319 | .8725 ( 0.7191,.9249) | 2031 | .9279 ( 0.9015,.9437) | 15063 | .9678 ( 0.9569,.9762) |
| 37 | .7866 ( 0.2946,.9088) | 345 | .8752 ( 0.7300,.9256) | 2194 | .9298 ( 0.9060,.9446) | 16269 | .9687 ( 0.9576,.9771) |
| 40 | .7900 ( 0.3120,.9093) | 373 | .8778 ( 0.7406,.9262) | 2369 | .9318 ( 0.9104,.9456) | 16269 | .9687 ( 0.9576,.9771) |
| 43 | .7935 ( 0.3295,.9098) | 403 | .8803 ( 0.7509,.9269) | 2559 | .9337 ( 0.9146,.9466) | 16269 | .9687 ( 0.9576,.9771) |
| 47 | .7969 ( 0.3469,.9103) | 435 | .8829 ( 0.7609,.9276) | 2764 | .9356 ( 0.9186,.9477) | 16269 | .9687 ( 0.9576,.9771) |
| 50 | .8003 ( 0.3644,.9108) | 470 | .8854 ( 0.7706,.9283) | 2986 | .9375 ( 0.9225,.9488) | 16269 | .9687 ( 0.9576,.9771) |
| 54 | .8036 ( 0.3817,.9113) | 500 | .8874 ( 0.7782,.9289) | 3225 | .9394 ( 0.9262,.9501) | 68.4 | .6501 (-0.0635,.8366) |
| 59 | .8070 ( 0.3990,.9118) | 507 | .8879 ( 0.7799,.9290) | 3483 | .9412 ( 0.9297,.9517) | 1096 | .8991 ( 0.8384,.9279) |
| 63 | .8103 ( 0.4161,.9124) | 548 | .8903 ( 0.7890,.9297) | 3762 | .9430 ( 0.9329,.9532) | 5121 | .9501 ( 0.9406,.9594) |
| 68 | .8135 ( 0.4332,.9129) | 592 | .8928 ( 0.7977,.9305) | 3798 | .9432 ( 0.9333,.9534) | | |



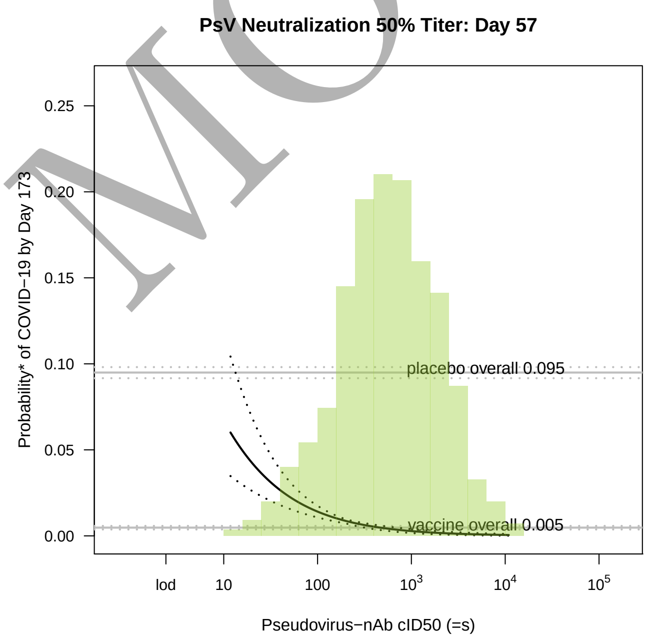

**No. at risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Low: | 3724 | 3637 | 3597 | 3561 | 3523 | 3450 | 2751 |
| Med: | 3726 | 3725 | 3673 | 3614 | 3560 | 3536 | 2908 |
| High: | 3712 | 3675 | 3650 | 3643 | 3621 | 3540 | 2732 |
| Plac: | 11301 | 11054 | 10708 | 10369 | 10023 | 9635 | 7815 |

**Cumulative No. of COVID−19 Endpoints**

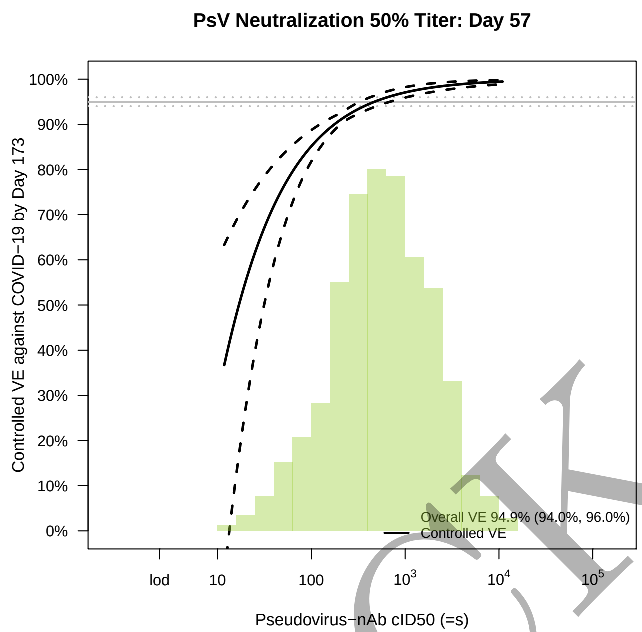
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Low: | 0 | 1 | 3 | 8 | 15 | 20 | 23 |
| Med: | 0 | 1 | 3 | 5 | 8 | 12 | 16 |
| High: | 0 | 1 | 2 | 4 | 11 | 12 | 12 |
| Plac: | 0 | 131 | 305 | 489 | 672 | 869 | 1010 |

(a) Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

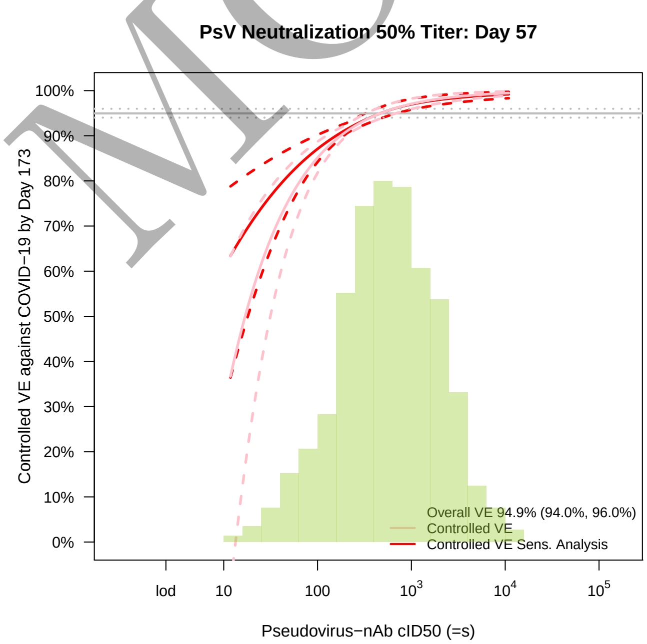



(b) Marginalized cumulative risk by Day 173 as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

Figure 6.12: Marginalized cumulative risk curves (=s).

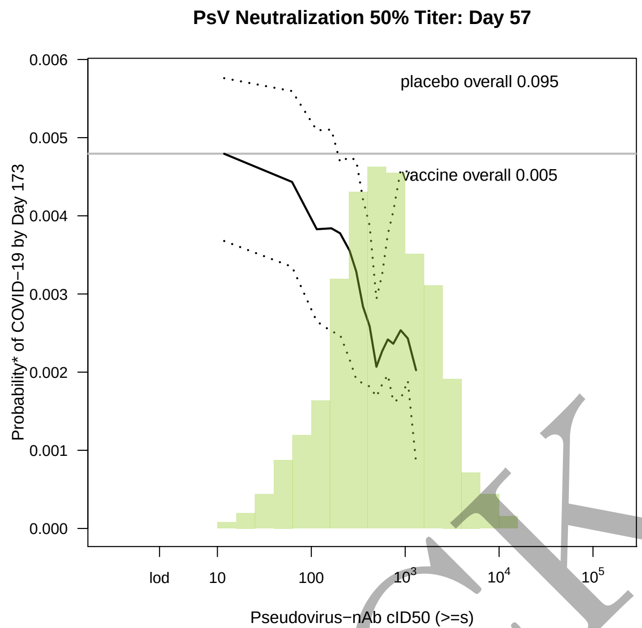



(a) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

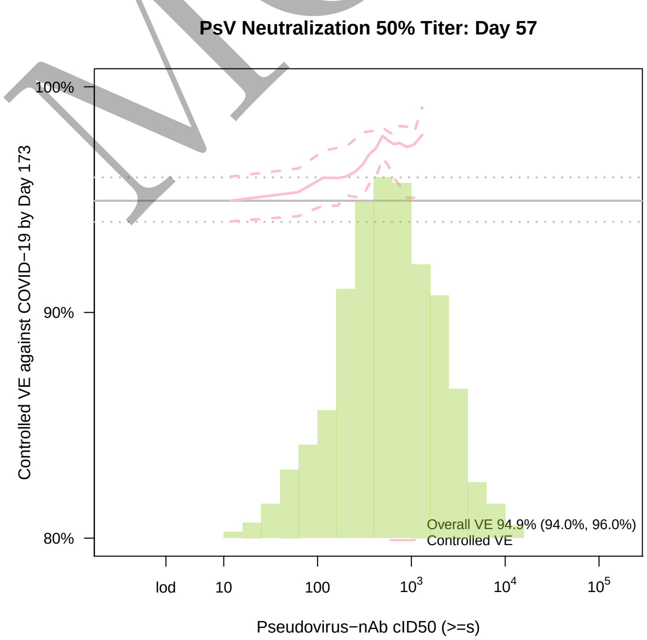



(b) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

Figure 6.13: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 173 post Day 57 visit as functions of Day 57 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.




(b) Controlled VE as functions of Day 57 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =2.4.

Figure 6.14: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 6.10: Marginalized cumulative risk by Day 173 as functions of Day 57 Pseudovirus-nAb cID50 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

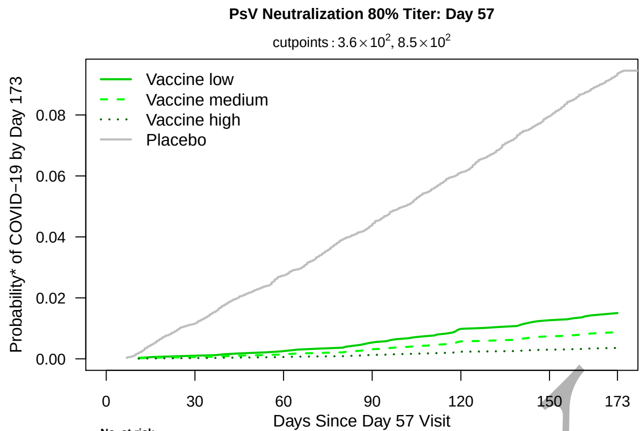
| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 11.8 | .0601 (.0348,.1043) | 81 | .0163 (.0120,.0208) | 427 | .0051 (.0037,.0063) | 1946 | .0017 (.0009,.0027) |
| 13 | .0575 (.0335,.0989) | 87 | .0155 (.0115,.0196) | 457 | .0049 (.0035,.0060) | 1948 | .0017 (.0009,.0027) |
| 14 | .0549 (.0323,.0939) | 93 | .0148 (.0111,.0185) | 489 | .0046 (.0033,.0058) | 2085 | .0017 (.0008,.0026) |
| 15 | .0525 (.0311,.0890) | 100 | .0141 (.0107,.0174) | 490 | .0046 (.0033,.0058) | 2234 | .0016 (.0008,.0025) |
| 16 | .0502 (.0300,.0843) | 107 | .0134 (.0103,.0164) | 500 | .0046 (.0032,.0058) | 2393 | .0015 (.0007,.0024) |
| 17 | .0479 (.0289,.0798) | 115 | .0128 (.0099,.0155) | 525 | .0044 (.0031,.0056) | 2519 | .0014 (.0007,.0024) |
| 18 | .0458 (.0278,.0756) | 118 | .0126 (.0098,.0152) | 562 | .0042 (.0029,.0054) | 2564 | .0014 (.0007,.0024) |
| 19 | .0437 (.0268,.0715) | 123 | .0122 (.0095,.0146) | 602 | .0040 (.0027,.0052) | 2747 | .0014 (.0006,.0023) |
| 20 | .0418 (.0258,.0676) | 132 | .0116 (.0091,.0137) | 645 | .0038 (.0025,.0050) | 2944 | .0013 (.0006,.0022) |
| 22 | .0399 (.0248,.0639) | 141 | .0111 (.0088,.0129) | 655 | .0038 (.0025,.0050) | 3154 | .0012 (.0005,.0021) |
| 24 | .0381 (.0239,.0604) | 152 | .0106 (.0085,.0122) | 691 | .0036 (.0024,.0048) | 3379 | .0012 (.0005,.0020) |
| 25 | .0364 (.0230,.0570) | 162 | .0101 (.0081,.0115) | 741 | .0035 (.0022,.0046) | 3621 | .0011 (.0005,.0020) |
| 27 | .0347 (.0222,.0538) | 164 | .0100 (.0081,.0114) | 794 | .0033 (.0021,.0045) | 3879 | .0011 (.0004,.0019) |
| 29 | .0331 (.0214,.0508) | 174 | .0096 (.0078,.0108) | 850 | .0031 (.0019,.0043) | 4156 | .0010 (.0004,.0018) |
| 31 | .0316 (.0206,.0479) | 186 | .0091 (.0075,.0102) | 911 | .0030 (.0018,.0041) | 4453 | .0010 (.0004,.0017) |
| 33 | .0302 (.0198,.0452) | 200 | .0087 (.0072,.0097) | 927 | .0029 (.0018,.0041) | 4771 | .0009 (.0004,.0017) |
| 36 | .0288 (.0190,.0426) | 205 | .0085 (.0071,.0095) | 976 | .0028 (.0017,.0040) | 5112 | .0009 (.0003,.0016) |
| 38 | .0274 (.0183,.0401) | 214 | .0083 (.0068,.0092) | 1000 | .0028 (.0017,.0039) | 5477 | .0008 (.0003,.0016) |
| 41 | .0262 (.0176,.0378) | 229 | .0079 (.0064,.0088) | 1046 | .0027 (.0016,.0038) | 5868 | .0008 (.0003,.0015) |
| 44 | .0250 (.0170,.0356) | 246 | .0075 (.0060,.0085) | 1121 | .0026 (.0015,.0037) | 6288 | .0008 (.0003,.0015) |
| 47 | .0238 (.0163,.0336) | 263 | .0072 (.0057,.0082) | 1201 | .0025 (.0014,.0036) | 6737 | .0007 (.0003,.0014) |
| 50 | .0227 (.0157,.0316) | 282 | .0068 (.0053,.0079) | 1286 | .0023 (.0013,.0034) | 7218 | .0007 (.0002,.0014) |
| 54 | .0217 (.0151,.0297) | 302 | .0065 (.0050,.0076) | 1378 | .0022 (.0012,.0033) | 7733 | .0007 (.0002,.0013) |
| 58 | .0207 (.0146,.0280) | 324 | .0062 (.0047,.0073) | 1477 | .0021 (.0011,.0032) | 8286 | .0006 (.0002,.0013) |
| 62 | .0197 (.0140,.0264) | 345 | .0059 (.0044,.0071) | 1569 | .0020 (.0011,.0031) | 8878 | .0006 (.0002,.0012) |
| 66 | .0188 (.0135,.0249) | 347 | .0059 (.0044,.0070) | 1582 | .0020 (.0011,.0031) | 9512 | .0006 (.0002,.0012) |
| 71 | .0179 (.0130,.0234) | 372 | .0056 (.0042,.0068) | 1695 | .0019 (.0010,.0030) | 10191 | .0005 (.0002,.0011) |
| 76 | .0171 (.0125,.0221) | 398 | .0054 (.0039,.0065) | 1816 | .0018 (.0009,.0028) | 10919 | .0005 (.0002,.0011) |

Table 6.11: Controlled VE as functions of Day 57 Pseudovirus-nAb cID50 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 173 days post Day 57 was 0.005 in vaccine recipients compared to 0.095 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 96.0%).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 11.8 | .3671 (-0.0995,.6331) | 87 | .8366 ( 0.7953,.8782) | 489 | .9513 ( 0.9397,.9647) | 2234 | .9834 ( 0.9738,.9919) |
| 13 | .3948 (-0.0434,.6465) | 93 | .8443 ( 0.8071,.8829) | 490 | .9513 ( 0.9397,.9647) | 2393 | .9842 ( 0.9747,.9924) |
| 14 | .4215 ( 0.0103,.6594) | 100 | .8516 ( 0.8182,.8873) | 500 | .9520 ( 0.9404,.9654) | 2519 | .9847 ( 0.9754,.9928) |
| 15 | .4471 ( 0.0619,.6718) | 107 | .8586 ( 0.8287,.8916) | 525 | .9536 ( 0.9419,.9670) | 2564 | .9849 ( 0.9757,.9929) |
| 16 | .4717 ( 0.1112,.6838) | 115 | .8652 ( 0.8386,.8958) | 562 | .9558 ( 0.9441,.9691) | 2747 | .9856 ( 0.9766,.9934) |
| 17 | .4952 ( 0.1583,.6954) | 118 | .8673 ( 0.8416,.8971) | 602 | .9579 ( 0.9462,.9711) | 2944 | .9863 ( 0.9774,.9938) |
| 18 | .5178 ( 0.2034,.7066) | 123 | .8716 ( 0.8477,.8997) | 645 | .9599 ( 0.9482,.9730) | 3154 | .9870 ( 0.9783,.9942) |
| 19 | .5394 ( 0.2464,.7174) | 132 | .8776 ( 0.8562,.9036) | 655 | .9604 ( 0.9486,.9734) | 3379 | .9876 ( 0.9791,.9946) |
| 20 | .5601 ( 0.2874,.7279) | 141 | .8834 ( 0.8643,.9073) | 691 | .9618 ( 0.9501,.9747) | 3621 | .9882 ( 0.9798,.9949) |
| 22 | .5800 ( 0.3265,.7380) | 152 | .8889 ( 0.8719,.9108) | 741 | .9637 ( 0.9519,.9764) | 3879 | .9888 ( 0.9806,.9952) |
| 24 | .5990 ( 0.3637,.7477) | 162 | .8941 ( 0.8791,.9142) | 794 | .9654 ( 0.9537,.9779) | 4156 | .9893 ( 0.9813,.9955) |
| 25 | .6172 ( 0.3991,.7570) | 164 | .8947 ( 0.8799,.9146) | 850 | .9670 ( 0.9554,.9793) | 4453 | .9898 ( 0.9820,.9958) |
| 27 | .6346 ( 0.4327,.7661) | 174 | .8991 ( 0.8859,.9175) | 911 | .9686 ( 0.9571,.9806) | 4771 | .9903 ( 0.9827,.9961) |
| 29 | .6512 ( 0.4647,.7748) | 186 | .9039 ( 0.8923,.9207) | 927 | .9690 ( 0.9575,.9810) | 5112 | .9908 ( 0.9833,.9964) |
| 31 | .6672 ( 0.4950,.7832) | 200 | .9084 ( 0.8984,.9237) | 976 | .9701 ( 0.9587,.9819) | 5477 | .9912 ( 0.9839,.9966) |
| 33 | .6824 ( 0.5238,.7913) | 205 | .9102 ( 0.9008,.9251) | 1000 | .9706 ( 0.9592,.9823) | 5868 | .9916 ( 0.9845,.9968) |
| 36 | .6970 ( 0.5510,.7991) | 214 | .9127 ( 0.9037,.9270) | 1046 | .9715 ( 0.9602,.9831) | 6288 | .9920 ( 0.9851,.9970) |
| 38 | .7109 ( 0.5768,.8067) | 229 | .9169 ( 0.9079,.9312) | 1121 | .9729 ( 0.9617,.9842) | 6737 | .9924 ( 0.9856,.9972) |
| 41 | .7242 ( 0.6013,.8139) | 246 | .9208 ( 0.9118,.9353) | 1201 | .9742 ( 0.9631,.9852) | 7218 | .9928 ( 0.9861,.9974) |
| 44 | .7369 ( 0.6244,.8209) | 263 | .9246 ( 0.9152,.9391) | 1286 | .9754 ( 0.9645,.9861) | 7733 | .9931 ( 0.9866,.9976) |
| 47 | .7491 ( 0.6463,.8277) | 282 | .9281 ( 0.9184,.9427) | 1378 | .9766 ( 0.9658,.9870) | 8286 | .9934 ( 0.9871,.9977) |
| 50 | .7607 ( 0.6670,.8342) | 302 | .9315 ( 0.9214,.9461) | 1477 | .9777 ( 0.9671,.9879) | 8878 | .9938 ( 0.9876,.9979) |
| 54 | .7718 ( 0.6865,.8404) | 324 | .9348 ( 0.9243,.9492) | 1569 | .9786 ( 0.9681,.9886) | 9512 | .9941 ( 0.9880,.9980) |
| 58 | .7824 ( 0.7050,.8465) | 345 | .9377 ( 0.9269,.9520) | 1582 | .9788 ( 0.9683,.9887) | 10191 | .9943 ( 0.9885,.9981) |
| 62 | .7925 ( 0.7224,.8523) | 347 | .9379 ( 0.9271,.9522) | 1695 | .9798 ( 0.9695,.9894) | 10919 | .9946 ( 0.9889,.9983) |
| 66 | .8022 ( 0.7388,.8579) | 372 | .9408 ( 0.9298,.9550) | 1816 | .9807 ( 0.9706,.9901) | 28.9 | .6512 (.4647,.7748) |
| 71 | .8114 ( 0.7544,.8632) | 398 | .9436 ( 0.9324,.9576) | 1946 | .9817 ( 0.9717,.9907) | 174 | .8991 (.8859,.9175) |
| 76 | .8202 ( 0.7690,.8684) | 427 | .9463 ( 0.9349,.9601) | 1948 | .9817 ( 0.9717,.9907) | 457 | .9489 (.9374,.9625) |
| 81 | .8286 ( 0.7828,.8734) | 457 | .9489 ( 0.9374,.9625) | 2085 | .9825 ( 0.9727,.9913) | | |

Table 6.12: Controlled VE with sensitivity analysis as functions of Day 57 Pseudovirus-nAb cID50 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 11.8 | .6340 (.3643,.7879) | 87 | .8610 (.8259,.8964) | 489 | .9513 (.9397,.9647) | 2234 | .9812 (.9703,.9908) |
| 13 | .6448 (.3875,.7925) | 93 | .8661 (.8341,.8993) | 490 | .9513 (.9397,.9647) | 2393 | .9819 (.9711,.9913) |
| 14 | .6553 (.4102,.7970) | 100 | .8711 (.8421,.9021) | 500 | .9520 (.9404,.9654) | 2519 | .9824 (.9717,.9917) |
| 15 | .6656 (.4325,.8015) | 107 | .8759 (.8497,.9049) | 525 | .9536 (.9419,.9670) | 2564 | .9826 (.9719,.9918) |
| 16 | .6756 (.4543,.8059) | 115 | .8805 (.8570,.9076) | 562 | .9558 (.9440,.9691) | 2747 | .9832 (.9726,.9922) |
| 17 | .6855 (.4756,.8102) | 118 | .8820 (.8592,.9085) | 602 | .9578 (.9460,.9710) | 2944 | .9839 (.9734,.9927) |
| 18 | .6951 (.4963,.8145) | 123 | .8851 (.8637,.9103) | 645 | .9597 (.9479,.9729) | 3154 | .9845 (.9741,.9931) |
| 19 | .7045 (.5166,.8187) | 132 | .8894 (.8701,.9129) | 655 | .9602 (.9483,.9732) | 3379 | .9850 (.9747,.9934) |
| 20 | .7137 (.5363,.8229) | 141 | .8937 (.8763,.9155) | 691 | .9616 (.9497,.9745) | 3621 | .9856 (.9754,.9938) |
| 22 | .7227 (.5554,.8270) | 152 | .8978 (.8822,.9180) | 741 | .9633 (.9514,.9761) | 3879 | .9861 (.9760,.9941) |
| 24 | .7315 (.5740,.8310) | 162 | .9018 (.8879,.9205) | 794 | .9649 (.9530,.9776) | 4156 | .9866 (.9766,.9944) |
| 25 | .7400 (.5920,.8350) | 164 | .9023 (.8885,.9207) | 850 | .9664 (.9546,.9789) | 4453 | .9871 (.9772,.9947) |
| 27 | .7484 (.6094,.8389) | 174 | .9057 (.8934,.9229) | 911 | .9678 (.9560,.9802) | 4771 | .9876 (.9778,.9950) |
| 29 | .7565 (.6263,.8428) | 186 | .9095 (.8986,.9253) | 927 | .9682 (.9564,.9805) | 5112 | .9880 (.9784,.9953) |
| 31 | .7645 (.6426,.8466) | 200 | .9131 (.9036,.9276) | 976 | .9692 (.9574,.9814) | 5477 | .9885 (.9789,.9955) |
| 33 | .7722 (.6584,.8503) | 205 | .9146 (.9056,.9287) | 1000 | .9697 (.9579,.9818) | 5868 | .9889 (.9794,.9958) |
| 36 | .7797 (.6736,.8540) | 214 | .9166 (.9080,.9303) | 1046 | .9705 (.9588,.9825) | 6288 | .9893 (.9799,.9960) |
| 38 | .7871 (.6883,.8576) | 229 | .9201 (.9115,.9338) | 1121 | .9717 (.9601,.9835) | 6737 | .9896 (.9804,.9962) |
| 41 | .7942 (.7025,.8612) | 246 | .9234 (.9146,.9374) | 1201 | .9729 (.9613,.9845) | 7218 | .9900 (.9808,.9964) |
| 44 | .8012 (.7161,.8647) | 263 | .9266 (.9175,.9407) | 1286 | .9740 (.9625,.9854) | 7733 | .9904 (.9813,.9966) |
| 47 | .8079 (.7293,.8681) | 282 | .9297 (.9202,.9439) | 1378 | .9751 (.9636,.9862) | 8286 | .9907 (.9817,.9968) |
| 50 | .8145 (.7419,.8715) | 302 | .9327 (.9228,.9470) | 1477 | .9761 (.9647,.9870) | 8878 | .9910 (.9821,.9969) |
| 54 | .8209 (.7540,.8748) | 324 | .9356 (.9253,.9499) | 1569 | .9769 (.9656,.9876) | 9512 | .9913 (.9825,.9971) |
| 58 | .8272 (.7657,.8780) | 345 | .9383 (.9276,.9525) | 1582 | .9770 (.9657,.9877) | 10191 | .9916 (.9829,.9972) |
| 62 | .8332 (.7769,.8812) | 347 | .9385 (.9278,.9527) | 1695 | .9779 (.9667,.9884) | 10919 | .9919 (.9833,.9974) |
| 66 | .8391 (.7876,.8844) | 372 | .9412 (.9303,.9553) | 1816 | .9788 (.9676,.9891) | 28.9 | .6512 (.4647,.7748) |
| 71 | .8448 (.7979,.8875) | 398 | .9439 (.9327,.9578) | 1946 | .9796 (.9685,.9897) | 174 | .8991 (.8859,.9175) |
| 76 | .8504 (.8078,.8905) | 427 | .9464 (.9351,.9602) | 1948 | .9796 (.9686,.9897) | 457 | .9489 (.9374,.9625) |
| 81 | .8558 (.8172,.8935) | 457 | .9489 (.9374,.9625) | 2085 | .9804 (.9694,.9903) | | |



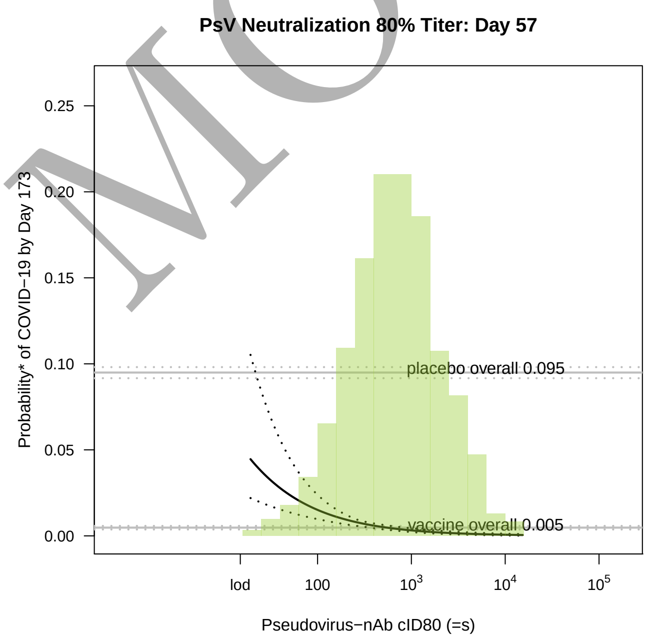

**No. at risk**

| | 0 | 30 | 60 | 90 | 120 | 150 | 173 |
|---|---|---|---|---|---|---|---|
| Low: | 3722 | 3619 | 3532 | 3489 | 3411 | 3342 | 2815 |
| Med: | 3720 | 3703 | 3680 | 3634 | 3630 | 3571 | 2812 |
| High: | 3721 | 3716 | 3707 | 3694 | 3664 | 3611 | 2765 |
| Plac: | 11301 | 11054 | 10708 | 10369 | 10023 | 9635 | 7815 |

**Cumulative No. of COVID−19 Endpoints**

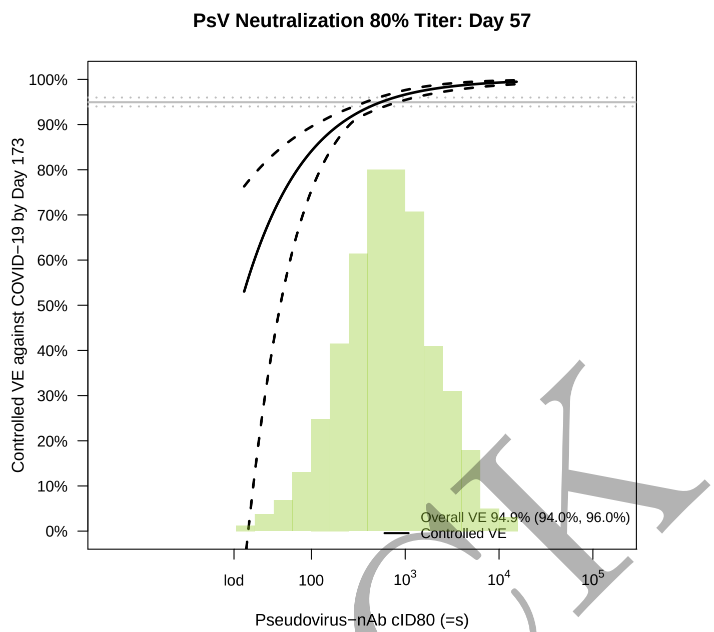
| | 0 | 30 | 60 | 90 | 120 | 150 | 173 |
|---|---|---|---|---|---|---|---|
| Low: | 0 | 1 | 2 | 7 | 15 | 18 | 21 |
| Med: | 0 | 2 | 5 | 8 | 14 | 17 | 19 |
| High: | 0 | 0 | 1 | 2 | 5 | 8 | 11 |
| Plac: | 0 | 131 | 305 | 489 | 672 | 869 | 1010 |

(a) Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

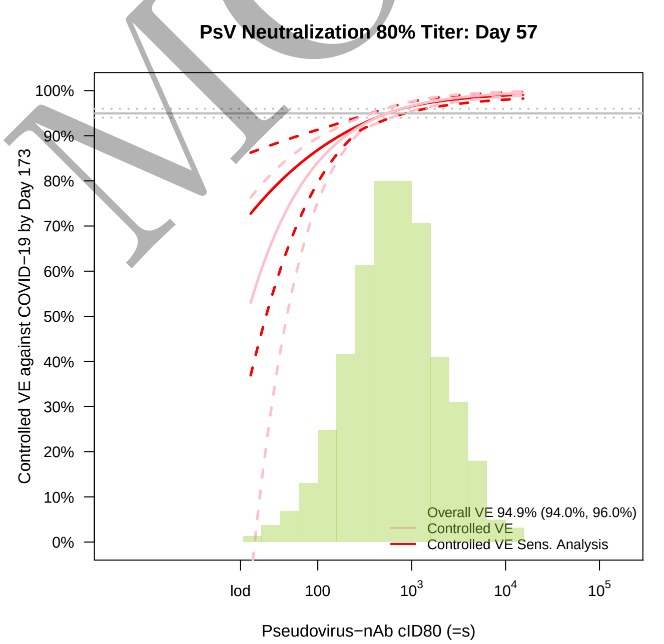



(b) Marginalized cumulative risk by Day 173 as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

Figure 6.15: Marginalized cumulative risk curves (=s).

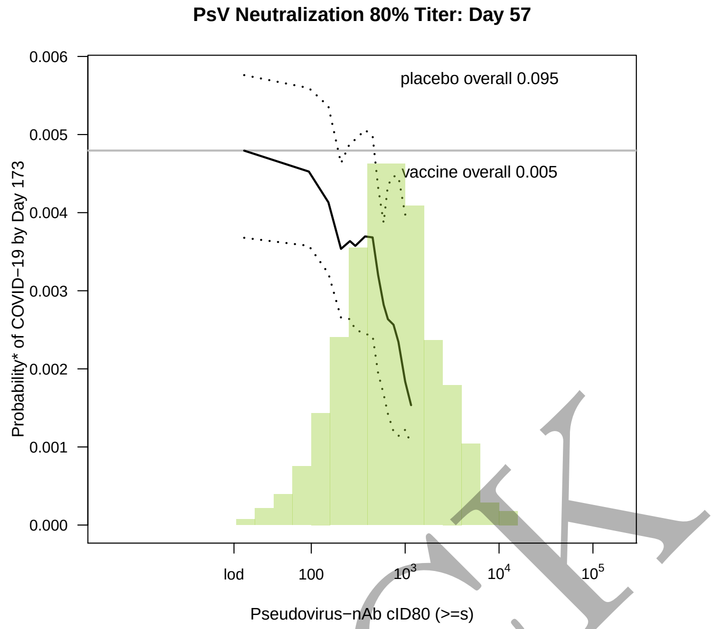



(a) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

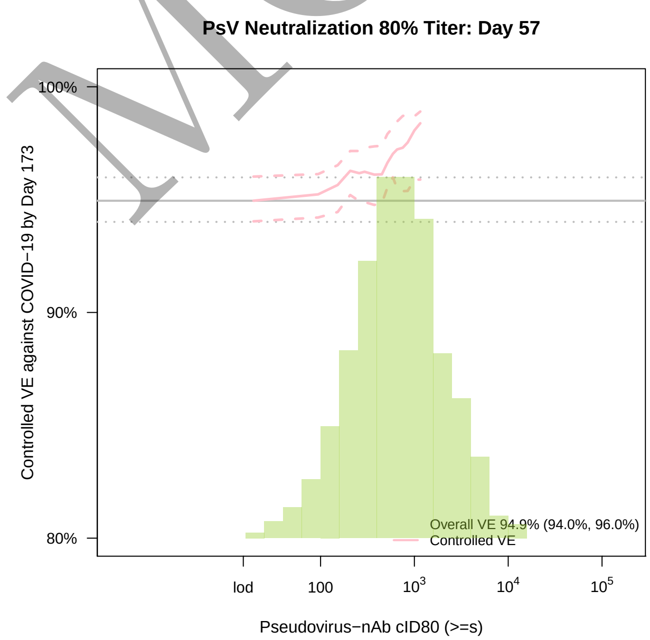



(b) Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

Figure 6.16: Controlled VE curves (=s).




(a) Marginalized cumulative risk by Day 173 post Day 57 visit as functions of Day 57 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.




(b) Controlled VE as functions of Day 57 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =15.

Figure 6.17: Marginalized cumulative risk curves and controlled VE curves (>=s).

Table 6.13: Marginalized cumulative risk by Day 173 as functions of Day 57 Pseudovirus-nAb cID80 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 19.3 | .0446 (.0220,.1052) | 128 | .0128 (.0086,.0189) | 584 | .0046 (.0034,.0059) | 2659 | .0016 (.0010,.0026) |
| 21 | .0427 (.0213,.0994) | 137 | .0123 (.0083,.0178) | 602 | .0045 (.0033,.0058) | 2787 | .0016 (.0009,.0025) |
| 22 | .0409 (.0206,.0939) | 146 | .0117 (.0080,.0167) | 644 | .0043 (.0032,.0056) | 2844 | .0016 (.0009,.0025) |
| 24 | .0391 (.0199,.0887) | 156 | .0112 (.0077,.0156) | 689 | .0041 (.0030,.0054) | 3043 | .0015 (.0008,.0024) |
| 25 | .0375 (.0193,.0837) | 160 | .0110 (.0076,.0153) | 738 | .0039 (.0029,.0052) | 3255 | .0014 (.0008,.0023) |
| 27 | .0359 (.0186,.0789) | 167 | .0107 (.0074,.0146) | 756 | .0039 (.0028,.0051) | 3482 | .0014 (.0007,.0022) |
| 29 | .0343 (.0180,.0744) | 179 | .0102 (.0071,.0137) | 789 | .0037 (.0027,.0050) | 3725 | .0013 (.0007,.0022) |
| 31 | .0328 (.0174,.0701) | 191 | .0098 (.0069,.0129) | 844 | .0036 (.0026,.0048) | 3986 | .0012 (.0007,.0021) |
| 33 | .0314 (.0168,.0661) | 205 | .0093 (.0066,.0121) | 903 | .0034 (.0024,.0046) | 4264 | .0012 (.0006,.0020) |
| 35 | .0301 (.0163,.0622) | 207 | .0093 (.0066,.0119) | 966 | .0033 (.0023,.0045) | 4561 | .0011 (.0006,.0019) |
| 38 | .0288 (.0158,.0586) | 219 | .0089 (.0064,.0113) | 1000 | .0032 (.0022,.0044) | 4880 | .0011 (.0005,.0019) |
| 41 | .0275 (.0152,.0551) | 234 | .0085 (.0061,.0106) | 1014 | .0032 (.0022,.0044) | 5221 | .0010 (.0005,.0018) |
| 43 | .0263 (.0147,.0519) | 251 | .0081 (.0059,.0099) | 1034 | .0031 (.0022,.0043) | 5585 | .0010 (.0005,.0017) |
| 46 | .0252 (.0142,.0488) | 262 | .0079 (.0058,.0095) | 1106 | .0030 (.0020,.0042) | 5975 | .0009 (.0004,.0017) |
| 50 | .0241 (.0138,.0459) | 268 | .0078 (.0057,.0093) | 1183 | .0028 (.0019,.0040) | 6392 | .0009 (.0004,.0016) |
| 53 | .0230 (.0133,.0431) | 287 | .0074 (.0055,.0088) | 1266 | .0027 (.0018,.0039) | 6838 | .0009 (.0004,.0015) |
| 57 | .0220 (.0129,.0405) | 307 | .0071 (.0053,.0085) | 1354 | .0026 (.0017,.0037) | 7316 | .0008 (.0004,.0015) |
| 61 | .0210 (.0125,.0381) | 328 | .0068 (.0051,.0081) | 1448 | .0025 (.0016,.0036) | 7826 | .0008 (.0003,.0014) |
| 65 | .0201 (.0120,.0358) | 351 | .0065 (.0049,.0078) | 1550 | .0024 (.0015,.0035) | 8373 | .0008 (.0003,.0014) |
| 70 | .0192 (.0117,.0336) | 376 | .0062 (.0047,.0075) | 1570 | .0023 (.0015,.0034) | 8957 | .0007 (.0003,.0013) |
| 74 | .0184 (.0113,.0315) | 402 | .0059 (.0044,.0072) | 1658 | .0023 (.0014,.0033) | 9582 | .0007 (.0003,.0013) |
| 80 | .0176 (.0109,.0296) | 430 | .0057 (.0042,.0069) | 1773 | .0022 (.0014,.0032) | 10251 | .0007 (.0003,.0013) |
| 85 | .0168 (.0105,.0278) | 445 | .0055 (.0041,.0068) | 1897 | .0021 (.0013,.0031) | 10967 | .0006 (.0003,.0012) |
| 91 | .0161 (.0102,.0261) | 460 | .0054 (.0040,.0067) | 1993 | .0020 (.0012,.0030) | 11733 | .0006 (.0002,.0012) |
| 97 | .0154 (.0098,.0245) | 492 | .0052 (.0038,.0065) | 2030 | .0020 (.0012,.0030) | 12552 | .0006 (.0002,.0011) |
| 104 | .0147 (.0095,.0230) | 500 | .0051 (.0038,.0064) | 2171 | .0019 (.0012,.0029) | 13428 | .0005 (.0002,.0011) |
| 111 | .0140 (.0092,.0215) | 526 | .0049 (.0037,.0062) | 2323 | .0018 (.0011,.0028) | 14365 | .0005 (.0002,.0011) |
| 119 | .0134 (.0089,.0202) | 563 | .0047 (.0035,.0060) | 2485 | .0017 (.0010,.0027) | 15368 | .0005 (.0002,.0010) |

Table 6.14: Controlled VE as functions of Day 57 Pseudovirus-nAb cID80 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 173 days post Day 57 was 0.005 in vaccine recipients compared to 0.095 in placebo recipients, with cumulative vaccine efficacy 94.9% (95% CI 94.0 to 96.0%).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 19.3 | .5303 (-0.0872,.7632) | 137 | .8709 ( 0.8166,.9102) | 644 | .9547 ( 0.9423,.9656) | 3043 | .9842 ( 0.9751,.9911) |
| 21 | .5503 (-0.0274,.7709) | 146 | .8766 ( 0.8280,.9134) | 689 | .9568 ( 0.9443,.9675) | 3255 | .9849 ( 0.9760,.9917) |
| 22 | .5695 ( 0.0295,.7784) | 156 | .8821 ( 0.8388,.9165) | 738 | .9587 ( 0.9463,.9693) | 3482 | .9856 ( 0.9769,.9922) |
| 24 | .5879 ( 0.0838,.7856) | 160 | .8839 ( 0.8423,.9176) | 756 | .9594 ( 0.9470,.9699) | 3725 | .9863 ( 0.9777,.9927) |
| 25 | .6055 ( 0.1354,.7926) | 167 | .8873 ( 0.8489,.9196) | 789 | .9605 ( 0.9483,.9710) | 3986 | .9869 ( 0.9785,.9931) |
| 27 | .6224 ( 0.1845,.7994) | 179 | .8923 ( 0.8583,.9225) | 844 | .9623 ( 0.9501,.9726) | 4264 | .9875 ( 0.9793,.9936) |
| 29 | .6387 ( 0.2311,.8060) | 191 | .8971 ( 0.8672,.9253) | 903 | .9640 ( 0.9519,.9741) | 4561 | .9880 ( 0.9801,.9940) |
| 31 | .6542 ( 0.2754,.8123) | 205 | .9017 ( 0.8756,.9280) | 966 | .9656 ( 0.9537,.9756) | 4880 | .9886 ( 0.9808,.9943) |
| 33 | .6692 ( 0.3174,.8185) | 207 | .9025 ( 0.8770,.9285) | 1000 | .9664 ( 0.9545,.9763) | 5221 | .9891 ( 0.9815,.9947) |
| 35 | .6835 ( 0.3572,.8244) | 219 | .9060 ( 0.8834,.9307) | 1014 | .9667 ( 0.9549,.9766) | 5585 | .9896 ( 0.9821,.9950) |
| 38 | .6972 ( 0.3949,.8302) | 234 | .9102 ( 0.8907,.9332) | 1034 | .9671 ( 0.9553,.9769) | 5975 | .9900 ( 0.9828,.9953) |
| 41 | .7103 ( 0.4305,.8358) | 251 | .9142 ( 0.8976,.9356) | 1106 | .9686 ( 0.9569,.9782) | 6392 | .9905 ( 0.9834,.9956) |
| 43 | .7229 ( 0.4643,.8412) | 262 | .9167 ( 0.9017,.9371) | 1183 | .9700 ( 0.9585,.9794) | 6838 | .9909 ( 0.9840,.9959) |
| 46 | .7350 ( 0.4961,.8464) | 268 | .9180 ( 0.9037,.9379) | 1266 | .9714 ( 0.9600,.9806) | 7316 | .9913 ( 0.9845,.9961) |
| 50 | .7465 ( 0.5263,.8515) | 287 | .9217 ( 0.9093,.9401) | 1354 | .9727 ( 0.9614,.9816) | 7826 | .9917 ( 0.9851,.9964) |
| 53 | .7576 ( 0.5547,.8563) | 307 | .9252 ( 0.9132,.9423) | 1448 | .9739 ( 0.9628,.9827) | 8373 | .9921 ( 0.9856,.9966) |
| 57 | .7682 ( 0.5815,.8611) | 328 | .9285 ( 0.9168,.9443) | 1550 | .9750 ( 0.9641,.9836) | 8957 | .9924 ( 0.9861,.9968) |
| 61 | .7783 ( 0.6068,.8656) | 351 | .9317 ( 0.9198,.9470) | 1570 | .9753 ( 0.9644,.9838) | 9582 | .9928 ( 0.9866,.9970) |
| 65 | .7880 ( 0.6307,.8701) | 376 | .9347 ( 0.9227,.9495) | 1658 | .9762 ( 0.9654,.9845) | 10251 | .9931 ( 0.9870,.9972) |
| 70 | .7973 ( 0.6532,.8744) | 402 | .9377 ( 0.9255,.9519) | 1773 | .9772 ( 0.9667,.9854) | 10967 | .9934 ( 0.9875,.9974) |
| 74 | .8062 ( 0.6743,.8785) | 430 | .9404 ( 0.9281,.9541) | 1897 | .9783 ( 0.9679,.9862) | 11733 | .9937 ( 0.9879,.9976) |
| 80 | .8147 ( 0.6943,.8825) | 445 | .9418 ( 0.9294,.9552) | 1993 | .9790 ( 0.9687,.9868) | 12552 | .9940 ( 0.9883,.9977) |
| 85 | .8229 ( 0.7131,.8864) | 460 | .9431 ( 0.9307,.9563) | 2030 | .9792 ( 0.9690,.9870) | 13428 | .9943 ( 0.9887,.9979) |
| 91 | .8307 ( 0.7307,.8901) | 492 | .9456 ( 0.9332,.9583) | 2171 | .9802 ( 0.9701,.9878) | 14365 | .9945 ( 0.9891,.9980) |
| 97 | .8382 ( 0.7473,.8938) | 500 | .9462 ( 0.9338,.9588) | 2323 | .9811 ( 0.9712,.9885) | 15368 | .9948 ( 0.9895,.9981) |
| 104 | .8453 ( 0.7630,.8973) | 526 | .9481 ( 0.9356,.9603) | 2485 | .9819 ( 0.9723,.9892) | 30.9 | .6542 (.2754,.8123) |
| 111 | .8521 ( 0.7776,.9007) | 563 | .9504 ( 0.9379,.9622) | 2659 | .9827 ( 0.9733,.9899) | 205 | .9017 (.8756,.9280) |
| 119 | .8587 ( 0.7914,.9039) | 584 | .9516 ( 0.9391,.9631) | 2787 | .9833 ( 0.9739,.9903) | 563 | .9504 (.9379,.9622) |
| 128 | .8649 ( 0.8044,.9071) | 602 | .9526 ( 0.9401,.9639) | 2844 | .9835 ( 0.9742,.9905) | | |

Table 6.15: Controlled VE with sensitivity analysis as functions of Day 57 Pseudovirus-nAb cID80 (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

| s | Estimate | s | Estimate | s | Estimate | s | Estimate |
|---|---|---|---|---|---|---|---|
| 19.3 | .7276 (.3694,.8626) | 137 | .8875 (.8403,.9218) | 644 | .9547 (.9422,.9656) | 3043 | .9813 (.9705,.9895) |
| 21 | .7349 (.3943,.8649) | 146 | .8914 (.8486,.9237) | 689 | .9566 (.9442,.9674) | 3255 | .9819 (.9712,.9900) |
| 22 | .7421 (.4186,.8672) | 156 | .8951 (.8566,.9258) | 738 | .9585 (.9461,.9692) | 3482 | .9825 (.9719,.9905) |
| 24 | .7491 (.4423,.8695) | 160 | .8963 (.8592,.9264) | 756 | .9591 (.9467,.9698) | 3725 | .9831 (.9726,.9910) |
| 25 | .7560 (.4653,.8717) | 167 | .8987 (.8642,.9277) | 789 | .9602 (.9479,.9708) | 3986 | .9836 (.9733,.9914) |
| 27 | .7628 (.4877,.8740) | 179 | .9023 (.8714,.9297) | 844 | .9619 (.9496,.9723) | 4264 | .9842 (.9739,.9919) |
| 29 | .7694 (.5094,.8762) | 191 | .9057 (.8783,.9316) | 903 | .9634 (.9512,.9737) | 4561 | .9847 (.9745,.9923) |
| 31 | .7759 (.5304,.8784) | 205 | .9091 (.8849,.9335) | 966 | .9649 (.9527,.9751) | 4880 | .9852 (.9751,.9926) |
| 33 | .7823 (.5508,.8806) | 207 | .9097 (.8861,.9338) | 1000 | .9656 (.9534,.9757) | 5221 | .9857 (.9757,.9930) |
| 35 | .7885 (.5705,.8827) | 219 | .9124 (.8912,.9353) | 1014 | .9659 (.9537,.9760) | 5585 | .9861 (.9762,.9933) |
| 38 | .7946 (.5896,.8848) | 234 | .9156 (.8972,.9371) | 1034 | .9663 (.9541,.9763) | 5975 | .9865 (.9767,.9937) |
| 41 | .8006 (.6080,.8870) | 251 | .9187 (.9029,.9389) | 1106 | .9676 (.9555,.9775) | 6392 | .9870 (.9773,.9940) |
| 43 | .8064 (.6257,.8890) | 262 | .9207 (.9064,.9401) | 1183 | .9688 (.9568,.9786) | 6838 | .9874 (.9777,.9943) |
| 46 | .8121 (.6428,.8911) | 268 | .9217 (.9080,.9407) | 1266 | .9700 (.9581,.9797) | 7316 | .9878 (.9782,.9946) |
| 50 | .8177 (.6593,.8932) | 287 | .9247 (.9128,.9424) | 1354 | .9712 (.9593,.9806) | 7826 | .9881 (.9786,.9948) |
| 53 | .8232 (.6752,.8952) | 307 | .9276 (.9160,.9441) | 1448 | .9722 (.9605,.9816) | 8373 | .9885 (.9791,.9951) |
| 57 | .8285 (.6904,.8972) | 328 | .9304 (.9190,.9458) | 1550 | .9733 (.9616,.9824) | 8957 | .9889 (.9795,.9953) |
| 61 | .8337 (.7051,.8992) | 351 | .9331 (.9215,.9481) | 1570 | .9735 (.9618,.9826) | 9582 | .9892 (.9799,.9956) |
| 65 | .8388 (.7192,.9012) | 376 | .9358 (.9239,.9503) | 1658 | .9742 (.9626,.9833) | 10251 | .9895 (.9803,.9958) |
| 70 | .8438 (.7327,.9032) | 402 | .9384 (.9263,.9524) | 1773 | .9752 (.9637,.9841) | 10967 | .9898 (.9807,.9960) |
| 74 | .8486 (.7457,.9051) | 430 | .9409 (.9287,.9545) | 1897 | .9761 (.9646,.9848) | 11733 | .9902 (.9811,.9962) |
| 80 | .8534 (.7581,.9070) | 445 | .9422 (.9299,.9555) | 1993 | .9767 (.9653,.9853) | 12552 | .9904 (.9814,.9964) |
| 85 | .8580 (.7700,.9089) | 460 | .9434 (.9310,.9565) | 2030 | .9769 (.9656,.9855) | 13428 | .9907 (.9818,.9965) |
| 91 | .8626 (.7814,.9108) | 492 | .9458 (.9334,.9585) | 2171 | .9777 (.9665,.9863) | 14365 | .9910 (.9821,.9967) |
| 97 | .8670 (.7923,.9127) | 500 | .9463 (.9339,.9589) | 2323 | .9785 (.9673,.9870) | 15368 | .9913 (.9825,.9969) |
| 104 | .8713 (.8028,.9145) | 526 | .9481 (.9356,.9603) | 2485 | .9792 (.9682,.9877) | 30.9 | .6542 (.2754,.8123) |
| 111 | .8755 (.8128,.9164) | 563 | .9504 (.9379,.9622) | 2659 | .9800 (.9690,.9883) | 205 | .9017 (.8756,.9280) |
| 119 | .8796 (.8224,.9182) | 584 | .9516 (.9391,.9631) | 2787 | .9804 (.9695,.9887) | 563 | .9504 (.9379,.9622) |
| 128 | .8836 (.8315,.9200) | 602 | .9526 (.9401,.9639) | 2844 | .9806 (.9698,.9889) | | |

# Chapter 7

# Univariate CoR: Nonparametric Threshold Modeling (>=s)



An extension of the unadjusted nonparametric threshold-searching approach developed in Donovan, Hudgens, and Gilbert (2019), the covariate-adjusted TMLE-based approach developed by van der Laan, Zhang, Gilbert (submitted) is used to estimate the so-called threshold-response function $E_X[E[Y \mid S \geq s, X, A = 1] \mid A = 1]$ for a range of thresholds $s$.Here, $X$ is a set of baseline characteristics, $A = 1$ represents the vaccine group, $S$ is the biomarker/immune-response/correlate of interest, and $Y$ is the indicator of COVID disease before some time point $t_f$. This parameter can be viewed as a causal/covariate-adjusted version of the parameter $P(Y = 1 \mid S \geq s, A = 1)$. Intuitively, the threshold-response at a given threshold is the expected probability of obtaining COVID disease if one experiences a marker/immune-response value above that threshold. The threshold-response function is estimated for each of the four Day 57 antibody markers, in each case adjusting for the baseline covariates: baseline risk score, high risk indicator, and underrepresented minority status. A restrictive but flexible specification of the Highly Adaptive Lasso estimator is used for the covariate adjustment. A number of plots and tables are reported:

1. A plot and table with risk estimates and point-wise 95% confidence intervals
2. A plot and table with risk estimates and simultaneous 95% confidence bands
3. Monotone-corrected versions of 1 and 2.

A reverse cumulative distribution function curve estimated by the IPW NPMLE of the marker values is superimposed on the threshold-response plots and a dashed red line is added to mark the threshold value after which no more events are observed.

The blue dots on the plots represent the risk predictions at marker values where there was an observed COVID-19 case.

## 7.1 Plots and Tables with estimates and pointwise confidence intervals for Day 57

### 7.1.1 Day 57 bindSpike

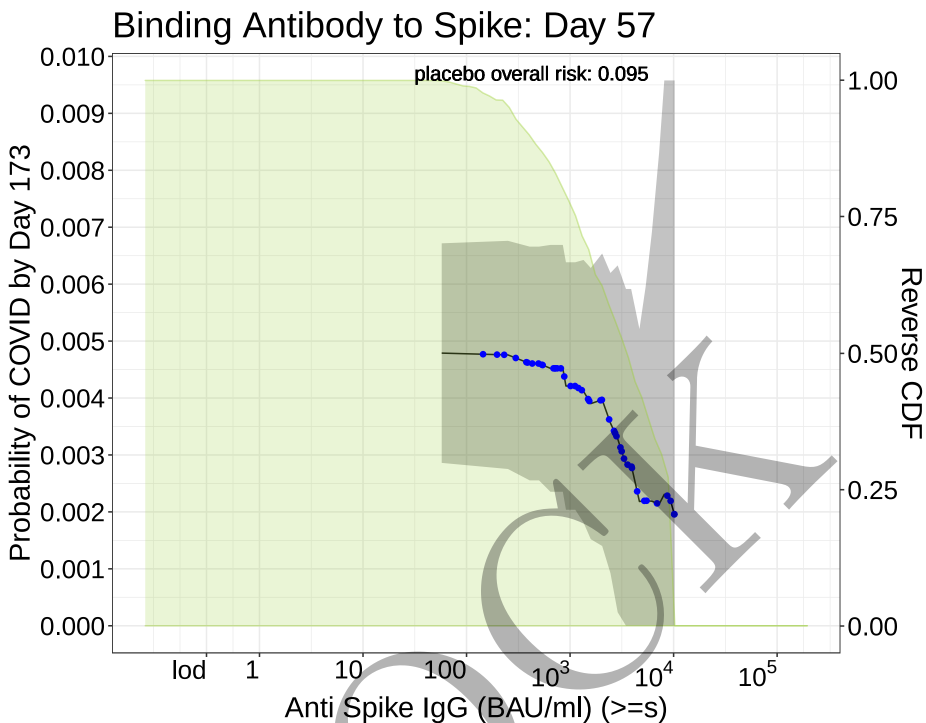



Figure 7.1: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindSpike levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.



Table 7.1: Table of risk estimates for a range of thresholds of Day 57 Day57bindSpike levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.761 | $5.77 * 10^1$ | 0.00479 | 0.00286 | 0.00672 |
| 2.699 | $5.00 * 10^2$ | 0.00461 | 0.00255 | 0.00666 |
| 2.808 | $6.43 * 10^2$ | 0.00452 | 0.00235 | 0.00669 |
| 2.965 | $9.23 * 10^2$ | 0.00421 | 0.00204 | 0.00638 |
| 3.000 | $1.00 * 10^3$ | 0.00421 | 0.00204 | 0.00638 |
| 3.133 | $1.36 * 10^3$ | 0.00412 | 0.00181 | 0.00643 |
| 3.459 | $2.88 * 10^3$ | 0.00328 | 0.00024 | 0.00633 |
| 3.671 | $4.69 * 10^3$ | 0.00218 | 0.00000 | 0.00521 |
| 3.860 | $7.24 * 10^3$ | 0.00213 | 0.00000 | 0.00831 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |

### 7.1.2 Day 57 bindRBD

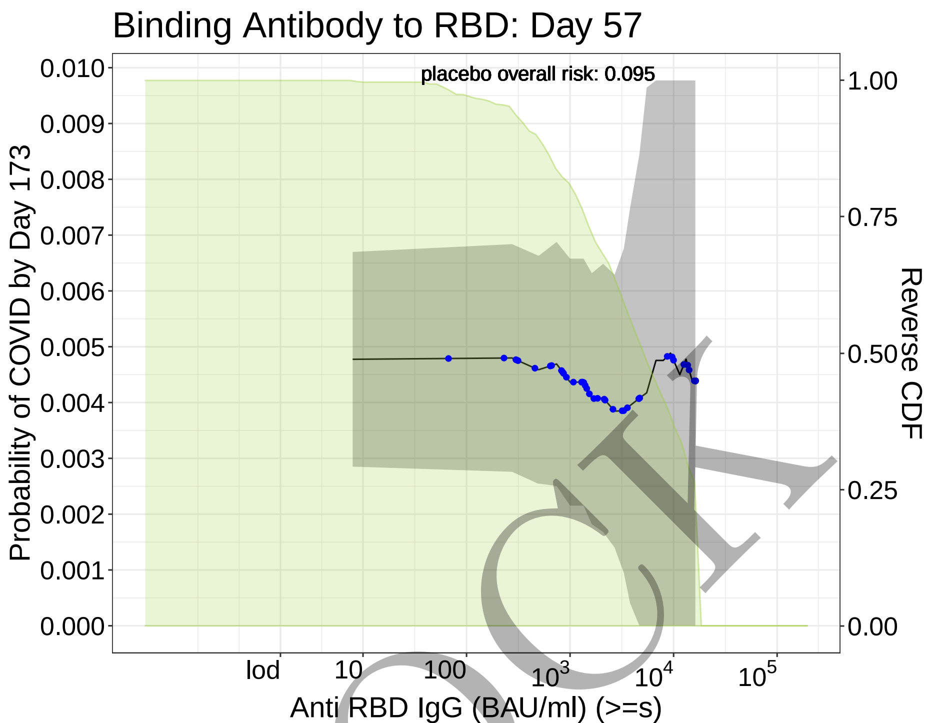



Figure 7.2: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindRBD levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.



Table 7.2: Table of risk estimates for a range of thresholds of Day 57 Day57bindRBD levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.898 | $7.91 * 10^0$ | 0.00478 | 0.00285 | 0.00670 |
| 2.699 | $5.00 * 10^2$ | 0.00459 | 0.00255 | 0.00663 |
| 2.871 | $7.43 * 10^2$ | 0.00469 | 0.00251 | 0.00688 |
| 3.000 | $1.00 * 10^3$ | 0.00437 | 0.00215 | 0.00658 |
| 3.062 | $1.15 * 10^3$ | 0.00437 | 0.00215 | 0.00658 |
| 3.211 | $1.63 * 10^3$ | 0.00407 | 0.00182 | 0.00632 |
| 3.580 | $3.80 * 10^3$ | 0.00395 | 0.00040 | 0.00749 |
| 3.832 | $6.79 * 10^3$ | 0.00475 | 0.00000 | 0.01193 |
| 4.061 | $1.15 * 10^4$ | 0.00450 | 0.00000 | 0.01635 |
| 4.211 | $1.63 * 10^4$ | 0.00439 | 0.00000 | 0.03856 |
| 4.211 | $1.63 * 10^4$ | 0.00439 | 0.00000 | 0.03856 |
| 4.211 | $1.63 * 10^4$ | 0.00439 | 0.00000 | 0.03856 |
| 4.211 | $1.63 * 10^4$ | 0.00439 | 0.00000 | 0.03856 |
| 4.211 | $1.63 * 10^4$ | 0.00439 | 0.00000 | 0.03856 |

### 7.1.3 Day 57 pseudoneutid50

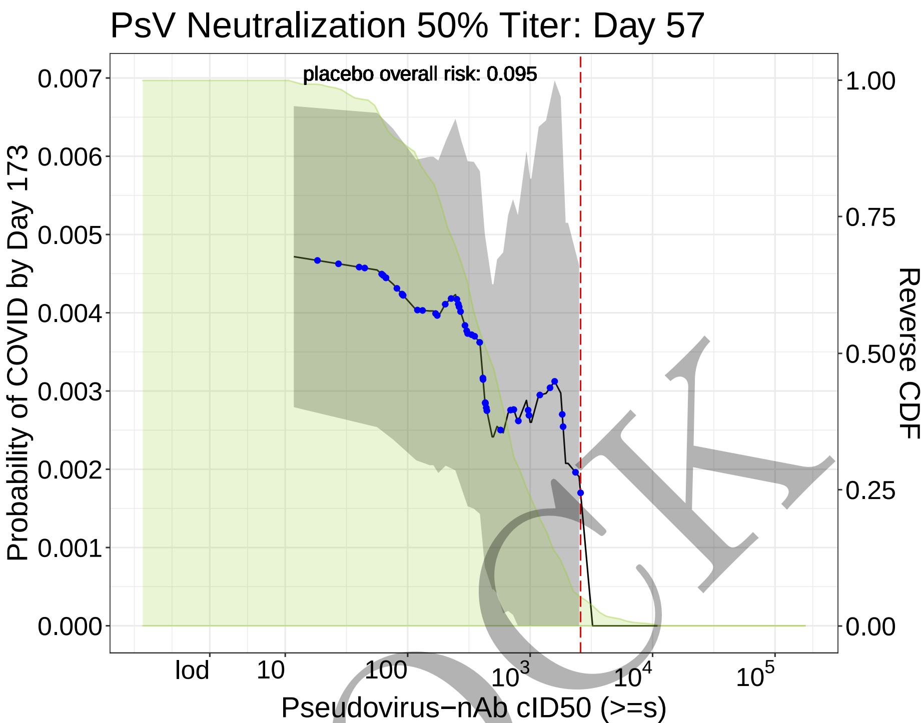



Figure 7.3: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid50 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.



Table 7.3: Table of risk estimates for a range of thresholds of Day 57 Day57pseudoneutid50 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.072 | $1.18 * 10^1$ | 0.00472 | 0.00279 | 0.00664 |
| 2.070 | $1.17 * 10^2$ | 0.00404 | 0.00211 | 0.00596 |
| 2.214 | $1.64 * 10^2$ | 0.00402 | 0.00205 | 0.00599 |
| 2.313 | $2.06 * 10^2$ | 0.00412 | 0.00205 | 0.00619 |
| 2.538 | $3.45 * 10^2$ | 0.00371 | 0.00150 | 0.00593 |
| 2.690 | $4.90 * 10^2$ | 0.00241 | 0.00047 | 0.00436 |
| 2.699 | $5.00 * 10^2$ | 0.00241 | 0.00047 | 0.00436 |
| 2.817 | $6.56 * 10^2$ | 0.00272 | 0.00019 | 0.00525 |
| 2.967 | $9.27 * 10^2$ | 0.00288 | 0.00000 | 0.00607 |
| 3.000 | $1.00 * 10^3$ | 0.00260 | 0.00000 | 0.00571 |
| 3.196 | $1.57 * 10^3$ | 0.00312 | 0.00000 | 0.00697 |
| 3.290 | $1.95 * 10^3$ | 0.00208 | 0.00000 | 0.00515 |
| 3.401 | $2.52 * 10^3$ | 0.00191 | 0.00000 | 0.00460 |
| 4.038 | $1.09 * 10^4$ | 0.00000 | NA | NA |

### 7.1.4 Day 57 pseudoneutid80

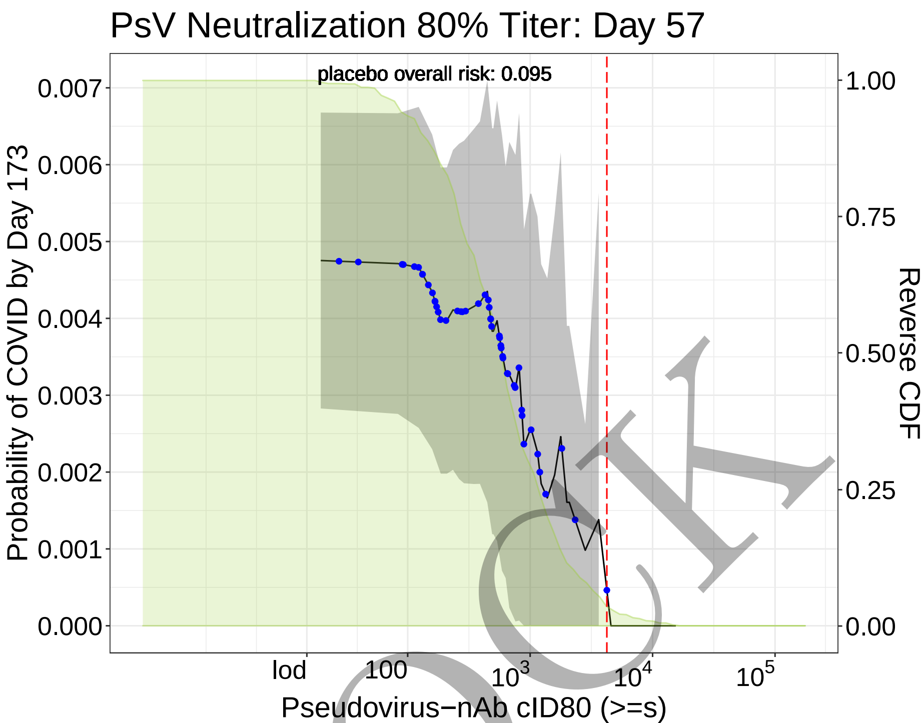



Figure 7.4: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid80 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 7.4: Table of risk estimates for a range of thresholds of Day 57 Day57pseudoneutid80 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.285 | $1.93 * 10^1$ | 0.00475 | 0.00283 | 0.00668 |
| 2.204 | $1.60 * 10^2$ | 0.00434 | 0.00230 | 0.00639 |
| 2.316 | $2.07 * 10^2$ | 0.00397 | 0.00198 | 0.00596 |
| 2.418 | $2.62 * 10^2$ | 0.00409 | 0.00191 | 0.00627 |
| 2.648 | $4.45 * 10^2$ | 0.00435 | 0.00161 | 0.00710 |
| 2.699 | $5.00 * 10^2$ | 0.00383 | 0.00119 | 0.00647 |
| 2.766 | $5.83 * 10^2$ | 0.00355 | 0.00072 | 0.00639 |
| 2.878 | $7.55 * 10^2$ | 0.00309 | 0.00006 | 0.00613 |
| 3.000 | $1.00 * 10^3$ | 0.00255 | 0.00000 | 0.00562 |
| 3.006 | $1.01 * 10^3$ | 0.00255 | 0.00000 | 0.00562 |
| 3.196 | $1.57 * 10^3$ | 0.00196 | 0.00000 | 0.00535 |
| 3.299 | $1.99 * 10^3$ | 0.00161 | 0.00000 | 0.00390 |
| 3.445 | $2.79 * 10^3$ | 0.00098 | 0.00000 | 0.00263 |
| 4.187 | $1.54 * 10^4$ | 0.00000 | NA | NA |

## 7.2 Plots and Tables with estimates and pointwise confidence intervals for Day 57 (monotone-corrected)

### 7.2.1 Day 57 bindSpike

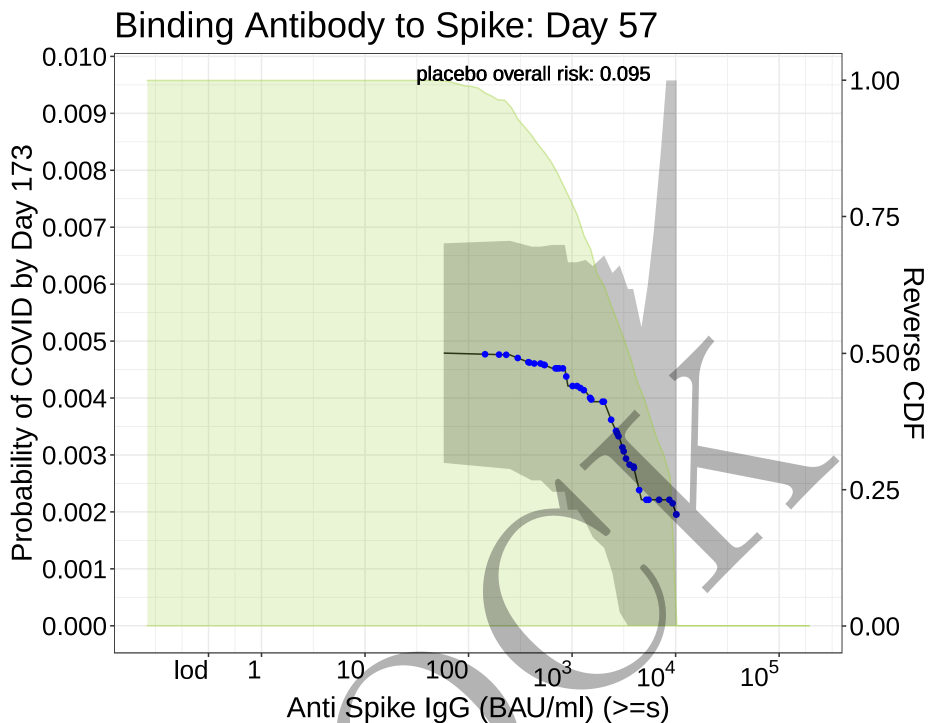



Figure 7.5: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindSpike levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.5: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57bindSpike levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.761 | $5.77 * 10^1$ | 0.00479 | 0.00286 | 0.00672 |
| 2.699 | $5.00 * 10^2$ | 0.00461 | 0.00255 | 0.00666 |
| 2.808 | $6.43 * 10^2$ | 0.00452 | 0.00235 | 0.00669 |
| 2.965 | $9.23 * 10^2$ | 0.00421 | 0.00204 | 0.00638 |
| 3.000 | $1.00 * 10^3$ | 0.00421 | 0.00204 | 0.00638 |
| 3.133 | $1.36 * 10^3$ | 0.00412 | 0.00181 | 0.00643 |
| 3.459 | $2.88 * 10^3$ | 0.00328 | 0.00024 | 0.00633 |
| 3.671 | $4.69 * 10^3$ | 0.00221 | 0.00000 | 0.00524 |
| 3.860 | $7.24 * 10^3$ | 0.00221 | 0.00000 | 0.00839 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.02958 |

### 7.2.2 Day 57 bindRBD

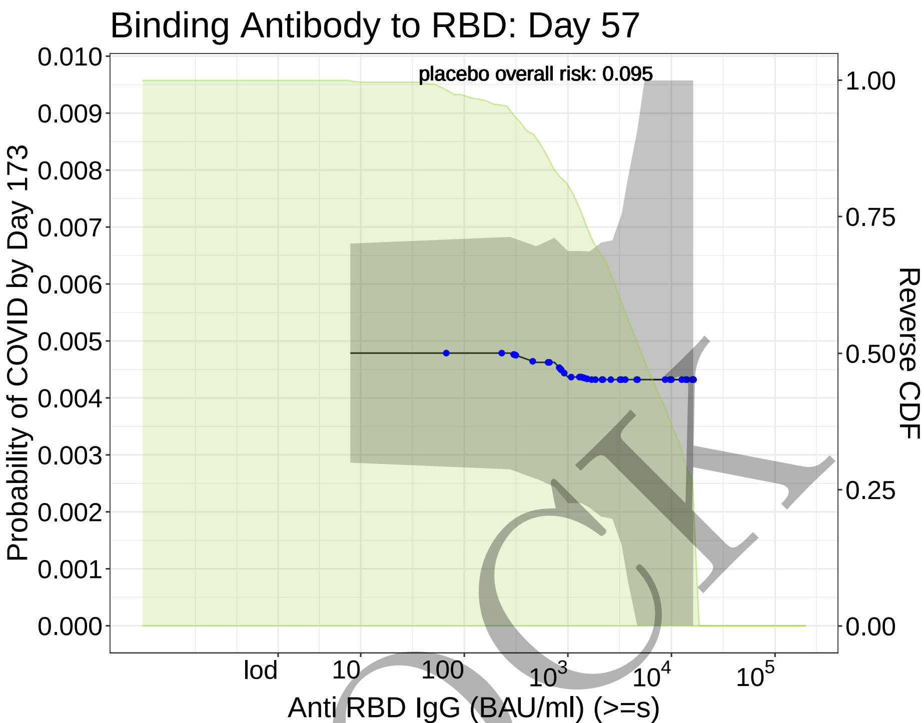





Figure 7.6: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindRBD levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.6: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57bindRBD levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.898 | $7.91 * 10^0$ | 0.00479 | 0.00286 | 0.00671 |
| 2.699 | $5.00 * 10^2$ | 0.00462 | 0.00258 | 0.00667 |
| 2.871 | $7.43 * 10^2$ | 0.00462 | 0.00244 | 0.00681 |
| 3.000 | $1.00 * 10^3$ | 0.00437 | 0.00215 | 0.00658 |
| 3.062 | $1.15 * 10^3$ | 0.00437 | 0.00215 | 0.00658 |
| 3.211 | $1.63 * 10^3$ | 0.00432 | 0.00207 | 0.00657 |
| 3.580 | $3.80 * 10^3$ | 0.00432 | 0.00078 | 0.00786 |
| 3.832 | $6.79 * 10^3$ | 0.00432 | 0.00000 | 0.01150 |
| 4.061 | $1.15 * 10^4$ | 0.00432 | 0.00000 | 0.01617 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.03849 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.03849 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.03849 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.03849 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.03849 |

### 7.2.3 Day 57 pseudoneutid50

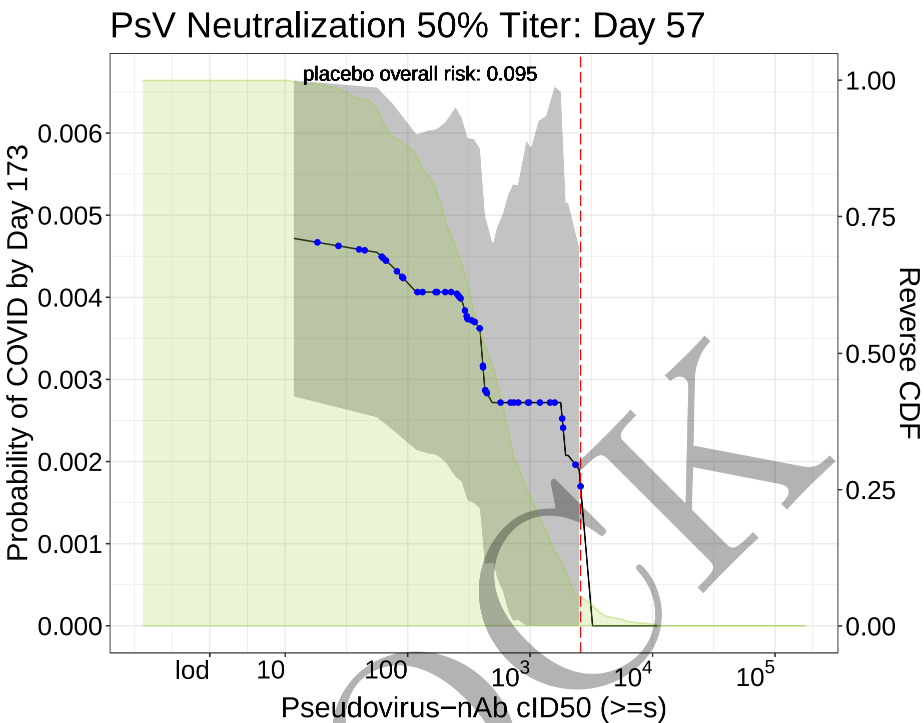



Figure 7.7: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid50 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.7: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57pseudoneutid50 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.072 | $1.18 * 10^1$ | 0.00472 | 0.00279 | 0.00664 |
| 2.070 | $1.17 * 10^2$ | 0.00406 | 0.00214 | 0.00599 |
| 2.214 | $1.64 * 10^2$ | 0.00406 | 0.00209 | 0.00603 |
| 2.313 | $2.06 * 10^2$ | 0.00406 | 0.00199 | 0.00614 |
| 2.538 | $3.45 * 10^2$ | 0.00371 | 0.00150 | 0.00593 |
| 2.690 | $4.90 * 10^2$ | 0.00272 | 0.00077 | 0.00467 |
| 2.699 | $5.00 * 10^2$ | 0.00272 | 0.00077 | 0.00467 |
| 2.817 | $6.56 * 10^2$ | 0.00272 | 0.00019 | 0.00525 |
| 2.967 | $9.27 * 10^2$ | 0.00272 | 0.00000 | 0.00590 |
| 3.000 | $1.00 * 10^3$ | 0.00272 | 0.00000 | 0.00583 |
| 3.196 | $1.57 * 10^3$ | 0.00272 | 0.00000 | 0.00656 |
| 3.290 | $1.95 * 10^3$ | 0.00208 | 0.00000 | 0.00515 |
| 3.401 | $2.52 * 10^3$ | 0.00191 | 0.00000 | 0.00460 |
| 4.038 | $1.09 * 10^4$ | 0.00000 | NA | NA |

### 7.2.4 Day 57 pseudoneutid80

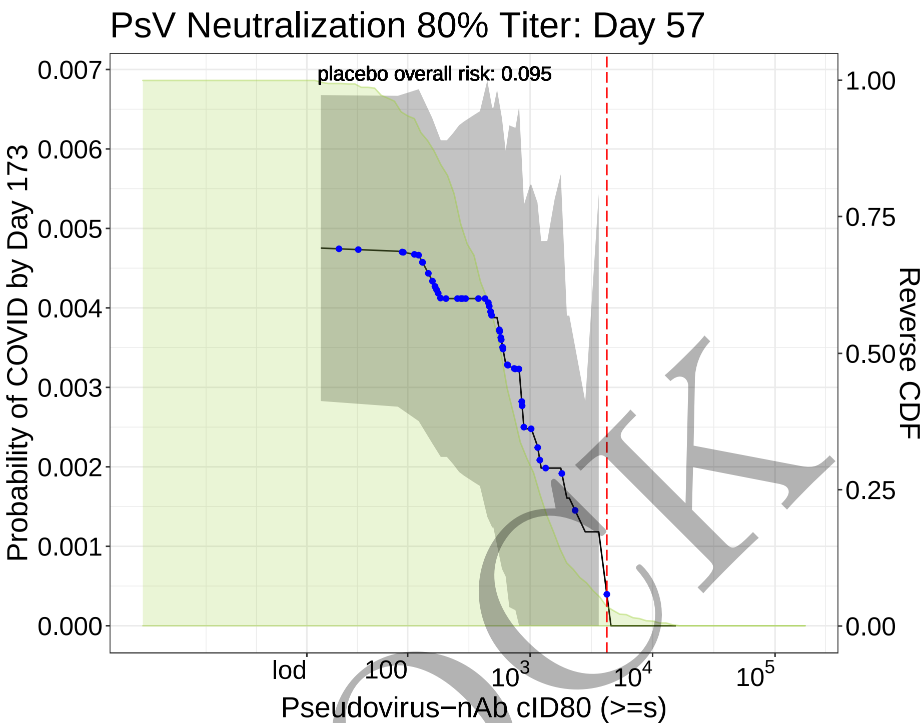



Figure 7.8: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid80 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.8: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57pseudoneutid80 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.285 | $1.93 * 10^1$ | 0.00475 | 0.00283 | 0.00668 |
| 2.204 | $1.60 * 10^2$ | 0.00434 | 0.00230 | 0.00639 |
| 2.316 | $2.07 * 10^2$ | 0.00412 | 0.00212 | 0.00611 |
| 2.418 | $2.62 * 10^2$ | 0.00412 | 0.00194 | 0.00630 |
| 2.648 | $4.45 * 10^2$ | 0.00412 | 0.00137 | 0.00686 |
| 2.699 | $5.00 * 10^2$ | 0.00388 | 0.00124 | 0.00652 |
| 2.766 | $5.83 * 10^2$ | 0.00355 | 0.00072 | 0.00639 |
| 2.878 | $7.55 * 10^2$ | 0.00323 | 0.00020 | 0.00627 |
| 3.000 | $1.00 * 10^3$ | 0.00248 | 0.00000 | 0.00555 |
| 3.006 | $1.01 * 10^3$ | 0.00248 | 0.00000 | 0.00555 |
| 3.196 | $1.57 * 10^3$ | 0.00198 | 0.00000 | 0.00537 |
| 3.299 | $1.99 * 10^3$ | 0.00161 | 0.00000 | 0.00390 |
| 3.445 | $2.79 * 10^3$ | 0.00118 | 0.00000 | 0.00282 |
| 4.187 | $1.54 * 10^4$ | 0.00000 | NA | NA |

## 7.3 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected)

### 7.3.1 Day 29 bindSpike

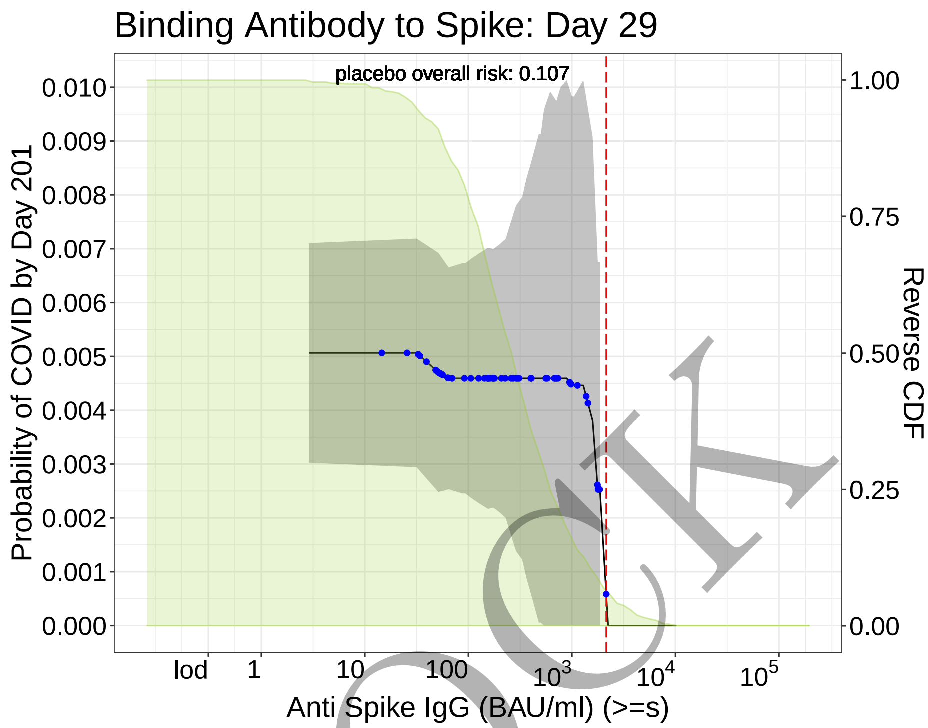



Figure 7.9: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.9: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.459 | $2.88 * 10^{0}$ | 0.00507 | 0.00303 | 0.00710 |
| 1.805 | $6.38 * 10^{1}$ | 0.00459 | 0.00253 | 0.00665 |
| 1.967 | $9.27 * 10^{1}$ | 0.00459 | 0.00246 | 0.00673 |
| 2.114 | $1.30 * 10^{2}$ | 0.00459 | 0.00226 | 0.00692 |
| 2.356 | $2.27 * 10^{2}$ | 0.00459 | 0.00200 | 0.00718 |
| 2.518 | $3.30 * 10^{2}$ | 0.00459 | 0.00123 | 0.00796 |
| 2.675 | $4.73 * 10^{2}$ | 0.00459 | 0.00005 | 0.00913 |
| 2.699 | $5.00 * 10^{2}$ | 0.00459 | 0.00005 | 0.00913 |
| 2.850 | $7.08 * 10^{2}$ | 0.00459 | 0.00000 | 0.00975 |
| 3.000 | $1.00 * 10^{3}$ | 0.00446 | 0.00000 | 0.00983 |
| 3.112 | $1.29 * 10^{3}$ | 0.00446 | 0.00000 | 0.01072 |
| 3.250 | $1.78 * 10^{3}$ | 0.00253 | 0.00000 | 0.00675 |
| 3.350 | $2.24 * 10^{3}$ | 0.00000 | NA | NA |
| 4.007 | $1.02 * 10^{4}$ | 0.00000 | NA | NA |

### 7.3.2 Day 29 bindRBD

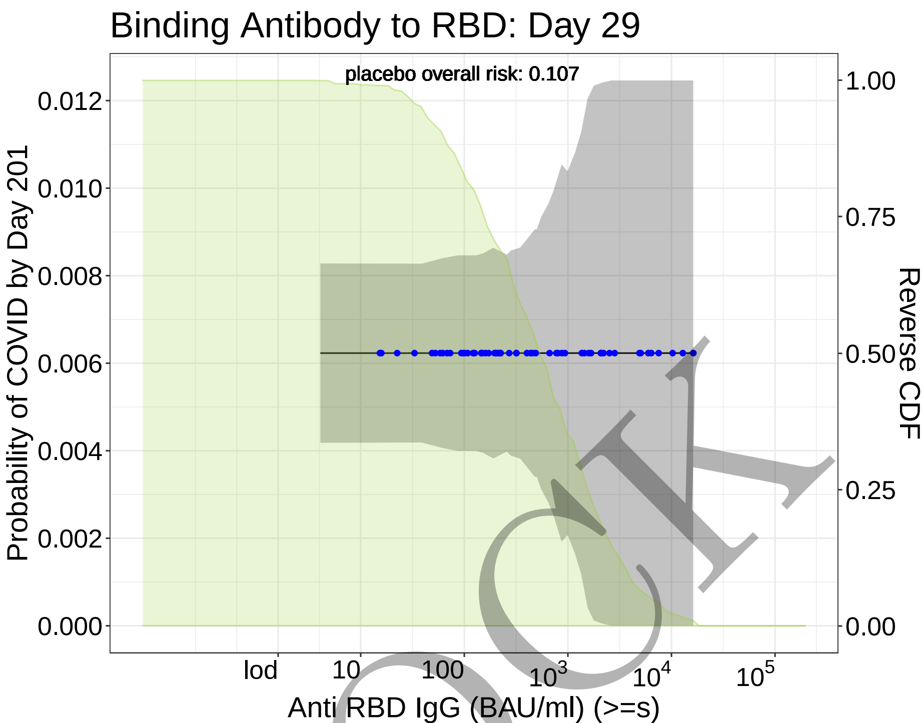



Figure 7.10: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.10: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.609 | $4.06 * 10^0$ | 0.00623 | 0.00418 | 0.00828 |
| 1.940 | $8.71 * 10^1$ | 0.00623 | 0.00400 | 0.00846 |
| 2.110 | $1.29 * 10^2$ | 0.00623 | 0.00400 | 0.00846 |
| 2.281 | $1.91 * 10^2$ | 0.00623 | 0.00382 | 0.00864 |
| 2.610 | $4.07 * 10^2$ | 0.00623 | 0.00361 | 0.00885 |
| 2.699 | $5.00 * 10^2$ | 0.00623 | 0.00340 | 0.00906 |
| 2.811 | $6.47 * 10^2$ | 0.00623 | 0.00283 | 0.00964 |
| 2.991 | $9.79 * 10^2$ | 0.00623 | 0.00206 | 0.01040 |
| 3.000 | $1.00 * 10^3$ | 0.00623 | 0.00206 | 0.01040 |
| 3.192 | $1.56 * 10^3$ | 0.00623 | 0.00042 | 0.01204 |
| 3.489 | $3.08 * 10^3$ | 0.00623 | 0.00000 | 0.01356 |
| 3.613 | $4.10 * 10^3$ | 0.00623 | 0.00000 | 0.01532 |
| 3.759 | $5.74 * 10^3$ | 0.00623 | 0.00000 | 0.01393 |
| 4.211 | $1.63 * 10^4$ | 0.00623 | 0.00000 | 0.03897 |

### 7.3.3 Day 29 pseudoneutid50

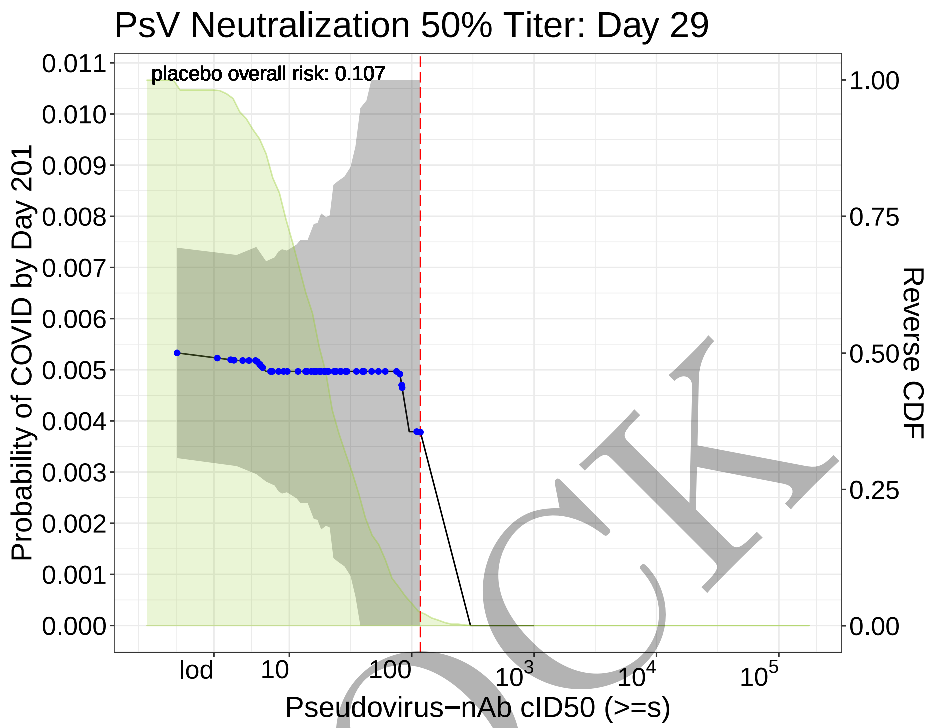



Figure 7.11: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid50 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.11: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid50 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.083 | $1.21 * 10^0$ | 0.00533 | 0.00327 | 0.00739 |
| 0.814 | $6.52 * 10^0$ | 0.00497 | 0.00281 | 0.00712 |
| 0.912 | $8.17 * 10^0$ | 0.00497 | 0.00263 | 0.00731 |
| 0.985 | $9.66 * 10^0$ | 0.00497 | 0.00261 | 0.00733 |
| 1.200 | $1.58 * 10^1$ | 0.00497 | 0.00208 | 0.00785 |
| 1.304 | $2.01 * 10^1$ | 0.00497 | 0.00195 | 0.00798 |
| 1.404 | $2.54 * 10^1$ | 0.00497 | 0.00124 | 0.00869 |
| 1.537 | $3.44 * 10^1$ | 0.00497 | 0.00057 | 0.00936 |
| 1.730 | $5.37 * 10^1$ | 0.00497 | 0.00000 | 0.01112 |
| 1.811 | $6.47 * 10^1$ | 0.00497 | 0.00000 | 0.01205 |
| 1.905 | $8.04 * 10^1$ | 0.00497 | 0.00000 | 0.01161 |
| 2.481 | $3.03 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

### 7.3.4 Day 29 pseudoneutid80

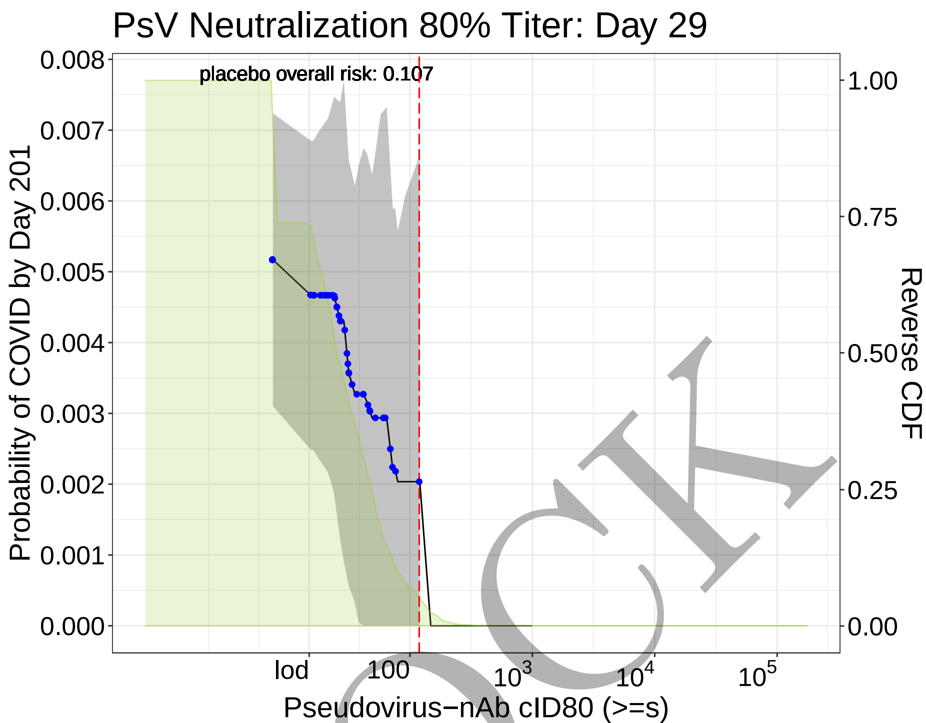



Figure 7.12: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid80 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.12: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid80 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00310 | 0.00724 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00310 | 0.00724 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00310 | 0.00724 |
| 1.185 | $1.53 * 10^1$ | 0.00467 | 0.00249 | 0.00685 |
| 1.334 | $2.16 * 10^1$ | 0.00467 | 0.00217 | 0.00717 |
| 1.425 | $2.66 * 10^1$ | 0.00430 | 0.00121 | 0.00739 |
| 1.548 | $3.53 * 10^1$ | 0.00327 | 0.00033 | 0.00621 |
| 1.652 | $4.49 * 10^1$ | 0.00316 | 0.00000 | 0.00667 |
| 1.806 | $6.40 * 10^1$ | 0.00294 | 0.00000 | 0.00733 |
| 1.877 | $7.53 * 10^1$ | 0.00220 | 0.00000 | 0.00589 |
| 1.962 | $9.16 * 10^1$ | 0.00203 | 0.00000 | 0.00607 |
| 2.529 | $3.38 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

## 7.4 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected)

### 7.4.1 Day 29 bindSpike

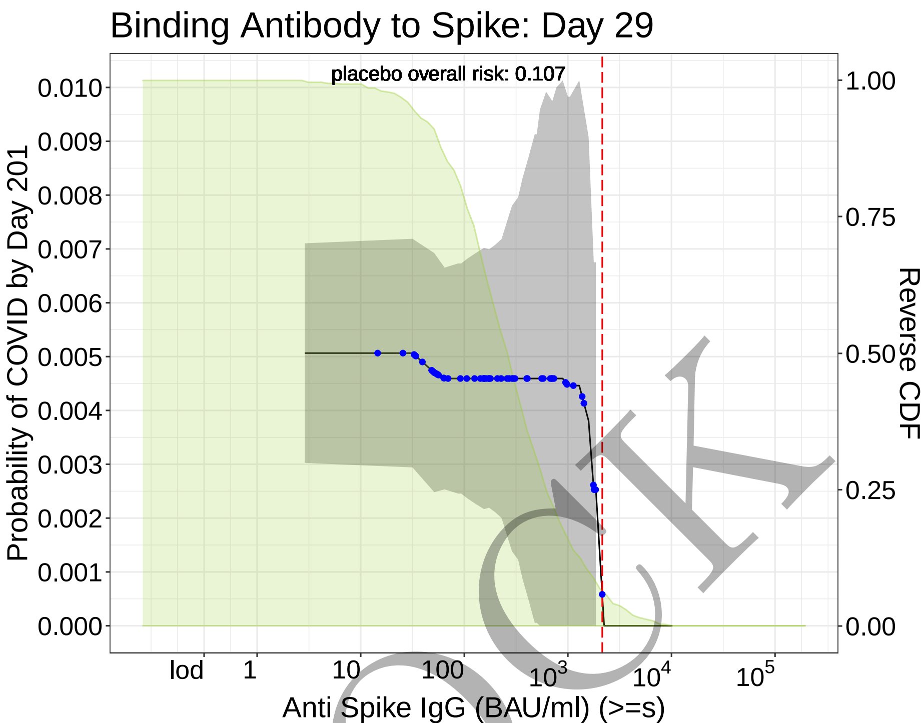



Figure 7.13: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.13: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---:|---|---:|---:|---:|
| 0.459 | $2.88 * 10^0$ | 0.00507 | 0.00303 | 0.00710 |
| 1.805 | $6.38 * 10^1$ | 0.00459 | 0.00253 | 0.00665 |
| 1.967 | $9.27 * 10^1$ | 0.00459 | 0.00246 | 0.00673 |
| 2.114 | $1.30 * 10^2$ | 0.00459 | 0.00226 | 0.00692 |
| 2.356 | $2.27 * 10^2$ | 0.00459 | 0.00200 | 0.00718 |
| 2.518 | $3.30 * 10^2$ | 0.00459 | 0.00123 | 0.00796 |
| 2.675 | $4.73 * 10^2$ | 0.00459 | 0.00005 | 0.00913 |
| 2.699 | $5.00 * 10^2$ | 0.00459 | 0.00005 | 0.00913 |
| 2.850 | $7.08 * 10^2$ | 0.00459 | 0.00000 | 0.00975 |
| 3.000 | $1.00 * 10^3$ | 0.00446 | 0.00000 | 0.00983 |
| 3.112 | $1.29 * 10^3$ | 0.00446 | 0.00000 | 0.01072 |
| 3.250 | $1.78 * 10^3$ | 0.00253 | 0.00000 | 0.00675 |
| 3.350 | $2.24 * 10^3$ | 0.00000 | NA | NA |
| 4.007 | $1.02 * 10^4$ | 0.00000 | NA | NA |

### 7.4.2 Day 29 bindRBD

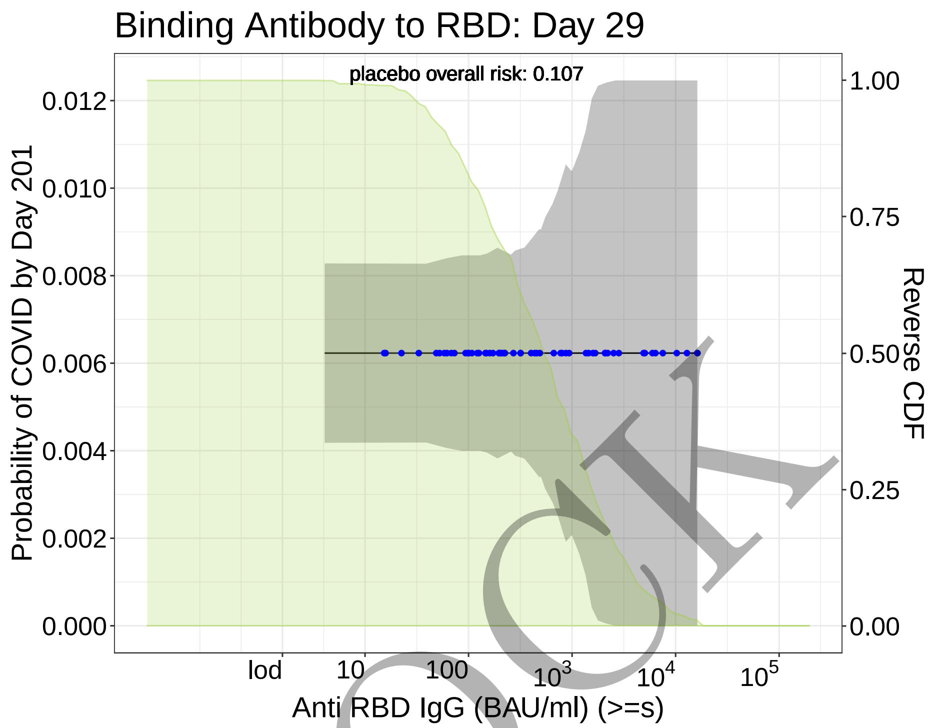





Figure 7.14: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.14: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.609 | $4.06 * 10^0$ | 0.00623 | 0.00418 | 0.00828 |
| 1.940 | $8.71 * 10^1$ | 0.00623 | 0.00400 | 0.00846 |
| 2.110 | $1.29 * 10^2$ | 0.00623 | 0.00400 | 0.00846 |
| 2.281 | $1.91 * 10^2$ | 0.00623 | 0.00382 | 0.00864 |
| 2.610 | $4.07 * 10^2$ | 0.00623 | 0.00361 | 0.00885 |
| 2.699 | $5.00 * 10^2$ | 0.00623 | 0.00340 | 0.00906 |
| 2.811 | $6.47 * 10^2$ | 0.00623 | 0.00283 | 0.00964 |
| 2.991 | $9.79 * 10^2$ | 0.00623 | 0.00206 | 0.01040 |
| 3.000 | $1.00 * 10^3$ | 0.00623 | 0.00206 | 0.01040 |
| 3.192 | $1.56 * 10^3$ | 0.00623 | 0.00042 | 0.01204 |
| 3.489 | $3.08 * 10^3$ | 0.00623 | 0.00000 | 0.01356 |
| 3.613 | $4.10 * 10^3$ | 0.00623 | 0.00000 | 0.01532 |
| 3.759 | $5.74 * 10^3$ | 0.00623 | 0.00000 | 0.01393 |
| 4.211 | $1.63 * 10^4$ | 0.00623 | 0.00000 | 0.03897 |

### 7.4.3 Day 29 pseudoneutid50

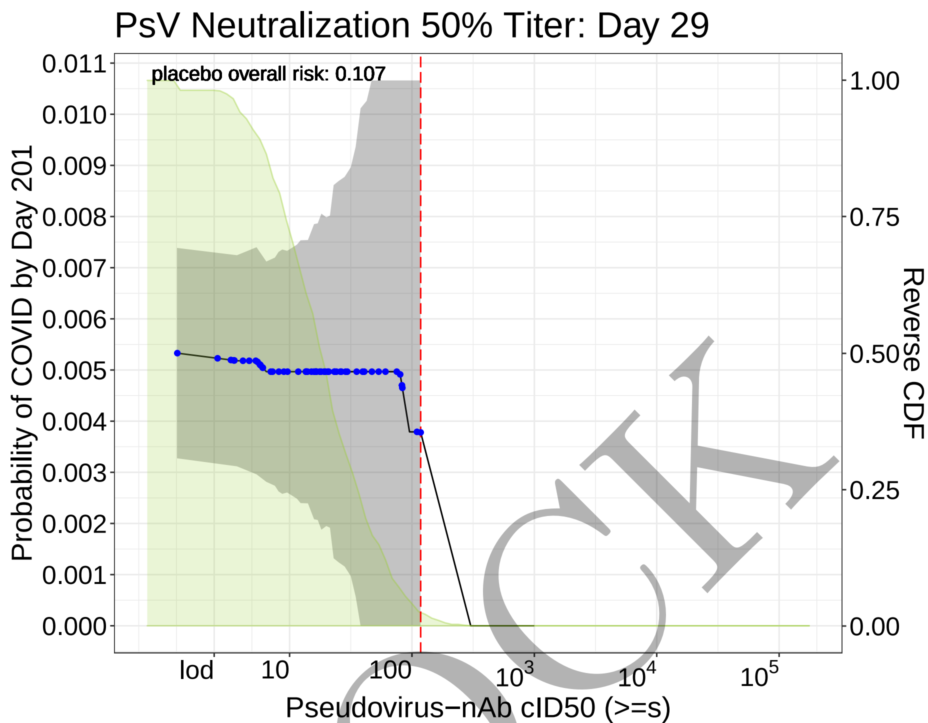



Figure 7.15: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid50 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.15: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid50 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.083 | $1.21 * 10^0$ | 0.00533 | 0.00327 | 0.00739 |
| 0.814 | $6.52 * 10^0$ | 0.00497 | 0.00281 | 0.00712 |
| 0.912 | $8.17 * 10^0$ | 0.00497 | 0.00263 | 0.00731 |
| 0.985 | $9.66 * 10^0$ | 0.00497 | 0.00261 | 0.00733 |
| 1.200 | $1.58 * 10^1$ | 0.00497 | 0.00208 | 0.00785 |
| 1.304 | $2.01 * 10^1$ | 0.00497 | 0.00195 | 0.00798 |
| 1.404 | $2.54 * 10^1$ | 0.00497 | 0.00124 | 0.00869 |
| 1.537 | $3.44 * 10^1$ | 0.00497 | 0.00057 | 0.00936 |
| 1.730 | $5.37 * 10^1$ | 0.00497 | 0.00000 | 0.01112 |
| 1.811 | $6.47 * 10^1$ | 0.00497 | 0.00000 | 0.01205 |
| 1.905 | $8.04 * 10^1$ | 0.00497 | 0.00000 | 0.01161 |
| 2.481 | $3.03 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

### 7.4.4 Day 29 pseudoneutid80

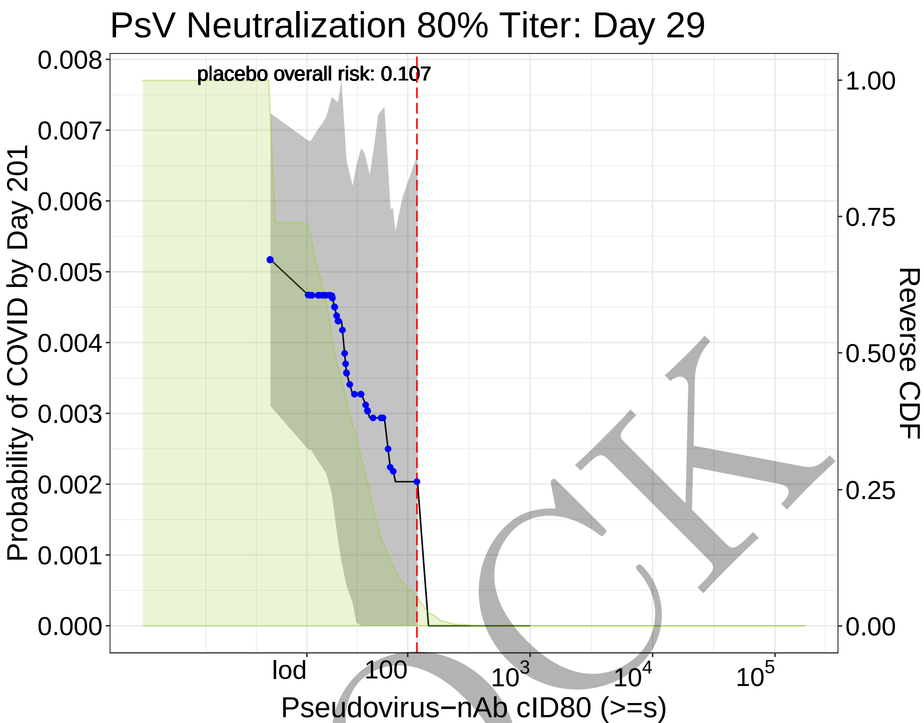



Figure 7.16: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid80 levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.16: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid80 levels with pointwise 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00310 | 0.00724 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00310 | 0.00724 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00310 | 0.00724 |
| 1.185 | $1.53 * 10^1$ | 0.00467 | 0.00249 | 0.00685 |
| 1.334 | $2.16 * 10^1$ | 0.00467 | 0.00217 | 0.00717 |
| 1.425 | $2.66 * 10^1$ | 0.00430 | 0.00121 | 0.00739 |
| 1.548 | $3.53 * 10^1$ | 0.00327 | 0.00033 | 0.00621 |
| 1.652 | $4.49 * 10^1$ | 0.00316 | 0.00000 | 0.00667 |
| 1.806 | $6.40 * 10^1$ | 0.00294 | 0.00000 | 0.00733 |
| 1.877 | $7.53 * 10^1$ | 0.00220 | 0.00000 | 0.00589 |
| 1.962 | $9.16 * 10^1$ | 0.00203 | 0.00000 | 0.00607 |
| 2.529 | $3.38 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

## 7.5 Plots and Tables with estimates and simultaneous confidence intervals for Day 57 (monotone-corrected)

### 7.5.1 Day 57 bindSpike

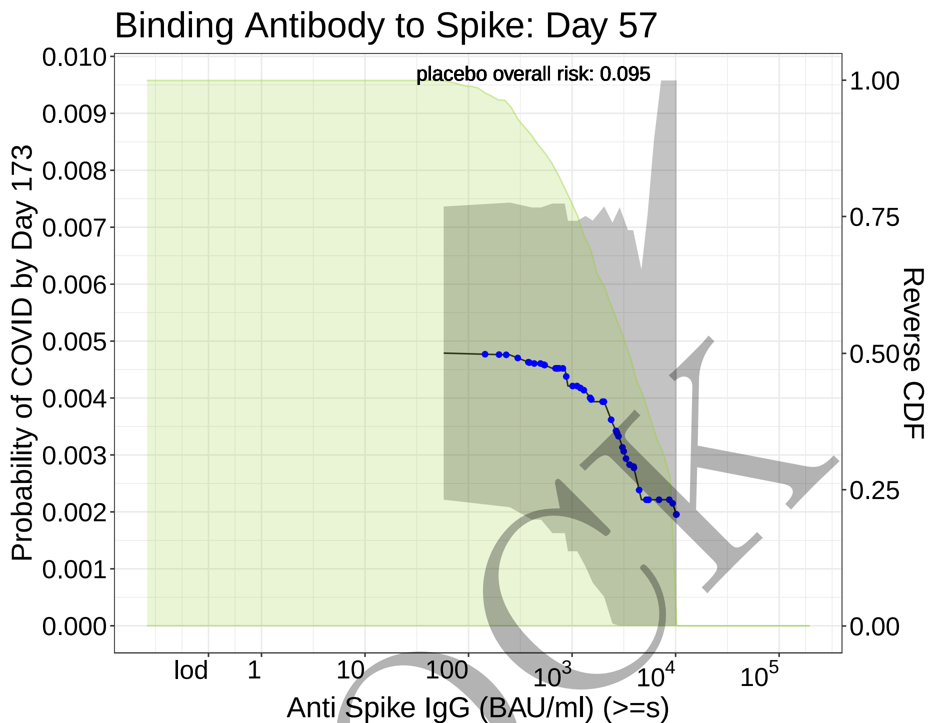



Figure 7.17: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindSpike levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.17: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57bindSpike levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.761 | $5.77 * 10^1$ | 0.00479 | 0.00221 | 0.00736 |
| 2.699 | $5.00 * 10^2$ | 0.00461 | 0.00187 | 0.00735 |
| 2.808 | $6.43 * 10^2$ | 0.00452 | 0.00163 | 0.00742 |
| 2.965 | $9.23 * 10^2$ | 0.00421 | 0.00131 | 0.00711 |
| 3.000 | $1.00 * 10^3$ | 0.00421 | 0.00131 | 0.00711 |
| 3.133 | $1.36 * 10^3$ | 0.00412 | 0.00104 | 0.00720 |
| 3.459 | $2.88 * 10^3$ | 0.00328 | 0.00000 | 0.00735 |
| 3.671 | $4.69 * 10^3$ | 0.00221 | 0.00000 | 0.00626 |
| 3.860 | $7.24 * 10^3$ | 0.00221 | 0.00000 | 0.01045 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |

### 7.5.2 Day 57 bindRBD

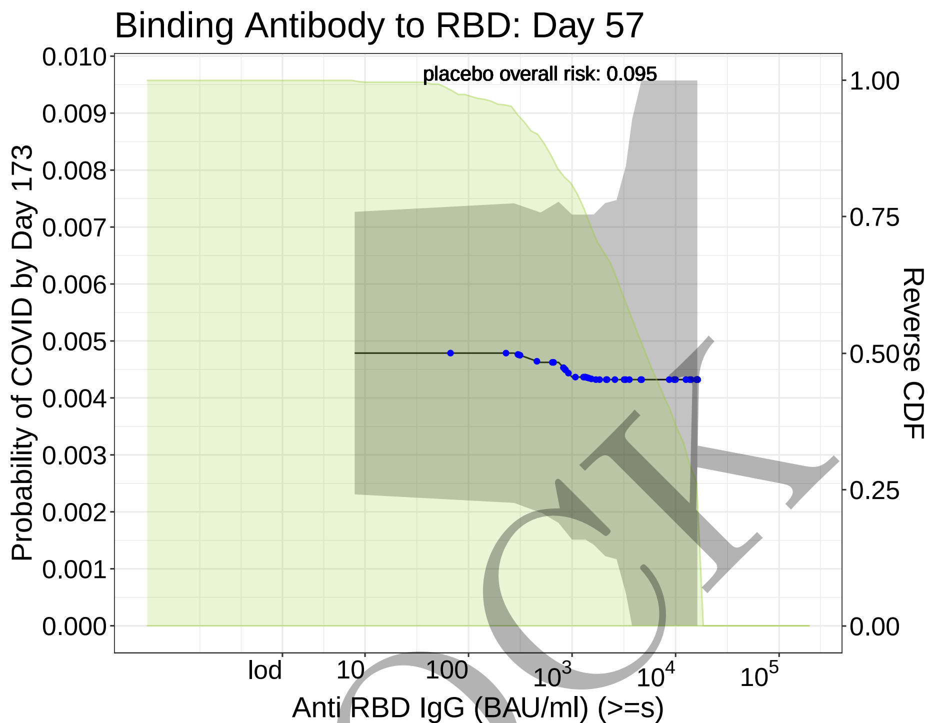



Figure 7.18: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindRBD levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.18: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57bindRBD levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.898 | $7.91 * 10^0$ | 0.00479 | 0.00231 | 0.00727 |
| 2.699 | $5.00 * 10^2$ | 0.00462 | 0.00199 | 0.00726 |
| 2.871 | $7.43 * 10^2$ | 0.00462 | 0.00181 | 0.00744 |
| 3.000 | $1.00 * 10^3$ | 0.00437 | 0.00151 | 0.00722 |
| 3.062 | $1.15 * 10^3$ | 0.00437 | 0.00151 | 0.00722 |
| 3.211 | $1.63 * 10^3$ | 0.00432 | 0.00142 | 0.00722 |
| 3.580 | $3.80 * 10^3$ | 0.00432 | 0.00000 | 0.00889 |
| 3.832 | $6.79 * 10^3$ | 0.00432 | 0.00000 | 0.01357 |
| 4.061 | $1.15 * 10^4$ | 0.00432 | 0.00000 | 0.01960 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |

### 7.5.3 Day 57 pseudoneutid50

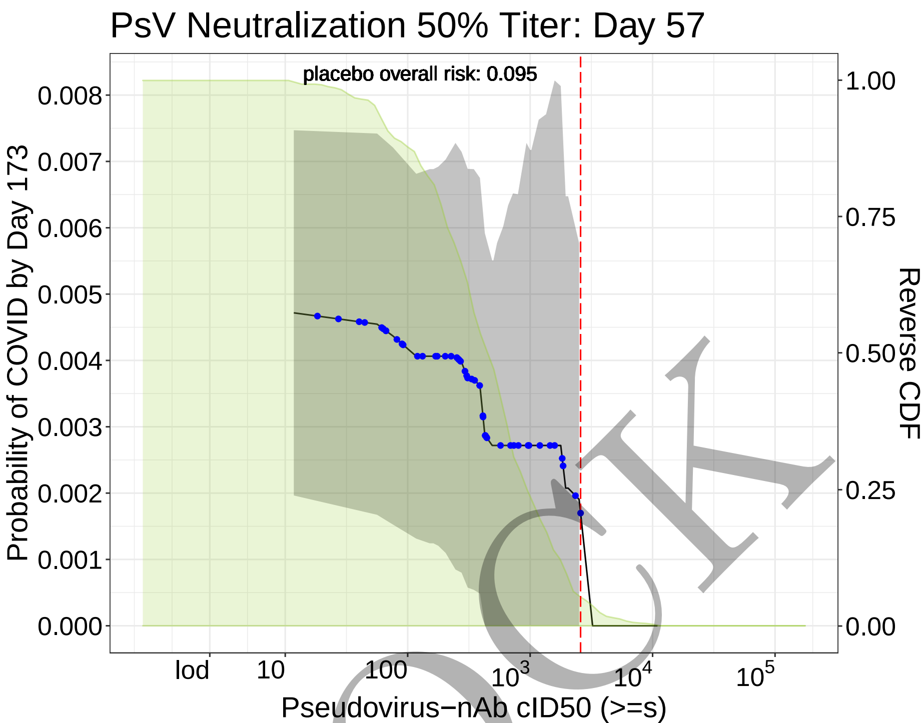



Figure 7.19: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid50 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.19: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57pseudoneutid50 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.072 | $1.18 * 10^1$ | 0.00472 | 0.00196 | 0.00747 |
| 2.070 | $1.17 * 10^2$ | 0.00406 | 0.00131 | 0.00681 |
| 2.214 | $1.64 * 10^2$ | 0.00406 | 0.00124 | 0.00688 |
| 2.313 | $2.06 * 10^2$ | 0.00406 | 0.00110 | 0.00703 |
| 2.538 | $3.45 * 10^2$ | 0.00371 | 0.00054 | 0.00688 |
| 2.690 | $4.90 * 10^2$ | 0.00272 | 0.00000 | 0.00551 |
| 2.699 | $5.00 * 10^2$ | 0.00272 | 0.00000 | 0.00551 |
| 2.817 | $6.56 * 10^2$ | 0.00272 | 0.00000 | 0.00634 |
| 2.967 | $9.27 * 10^2$ | 0.00272 | 0.00000 | 0.00728 |
| 3.000 | $1.00 * 10^3$ | 0.00272 | 0.00000 | 0.00717 |
| 3.196 | $1.57 * 10^3$ | 0.00272 | 0.00000 | 0.00822 |
| 3.290 | $1.95 * 10^3$ | 0.00208 | 0.00000 | 0.00648 |
| 3.401 | $2.52 * 10^3$ | 0.00191 | 0.00000 | 0.00577 |
| 4.038 | $1.09 * 10^4$ | 0.00000 | NA | NA |

### 7.5.4 Day 57 pseudoneutid80

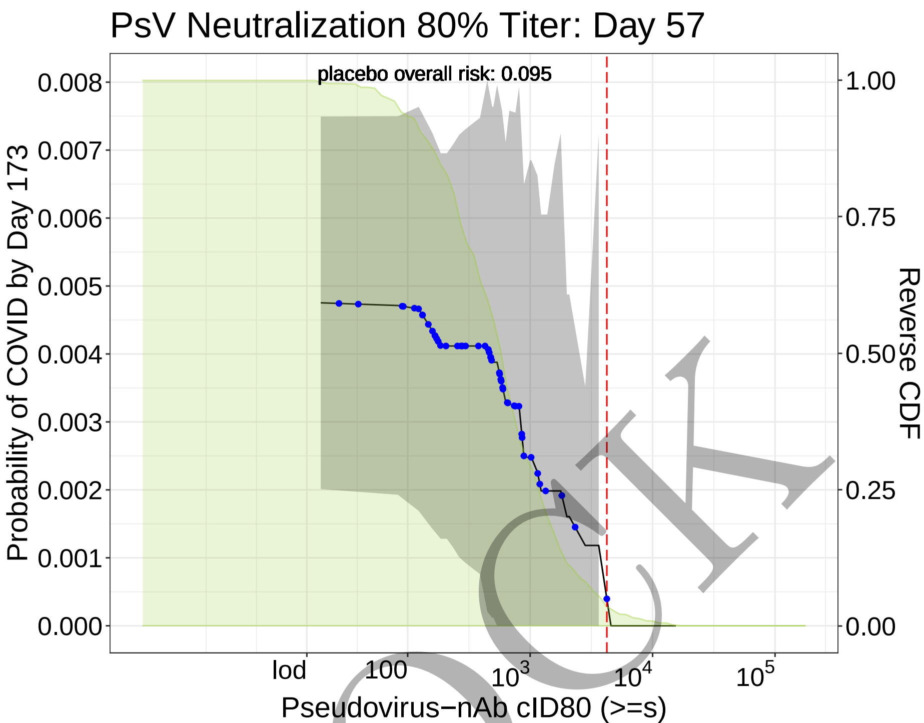



Figure 7.20: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid80 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.20: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57pseudoneutid80 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.285 | $1.93 * 10^1$ | 0.00475 | 0.00201 | 0.00749 |
| 2.204 | $1.60 * 10^2$ | 0.00434 | 0.00143 | 0.00726 |
| 2.316 | $2.07 * 10^2$ | 0.00412 | 0.00128 | 0.00695 |
| 2.418 | $2.62 * 10^2$ | 0.00412 | 0.00101 | 0.00722 |
| 2.648 | $4.45 * 10^2$ | 0.00412 | 0.00021 | 0.00803 |
| 2.699 | $5.00 * 10^2$ | 0.00388 | 0.00012 | 0.00764 |
| 2.766 | $5.83 * 10^2$ | 0.00355 | 0.00000 | 0.00759 |
| 2.878 | $7.55 * 10^2$ | 0.00323 | 0.00000 | 0.00755 |
| 3.000 | $1.00 * 10^3$ | 0.00248 | 0.00000 | 0.00685 |
| 3.006 | $1.01 * 10^3$ | 0.00248 | 0.00000 | 0.00685 |
| 3.196 | $1.57 * 10^3$ | 0.00198 | 0.00000 | 0.00680 |
| 3.299 | $1.99 * 10^3$ | 0.00161 | 0.00000 | 0.00488 |
| 3.445 | $2.79 * 10^3$ | 0.00118 | 0.00000 | 0.00352 |
| 4.187 | $1.54 * 10^4$ | 0.00000 | NA | NA |

## 7.6 Plots and Tables with estimates and simultaneous confidence intervals for Day 57 (monotone-corrected)

### 7.6.1 Day 57 bindSpike

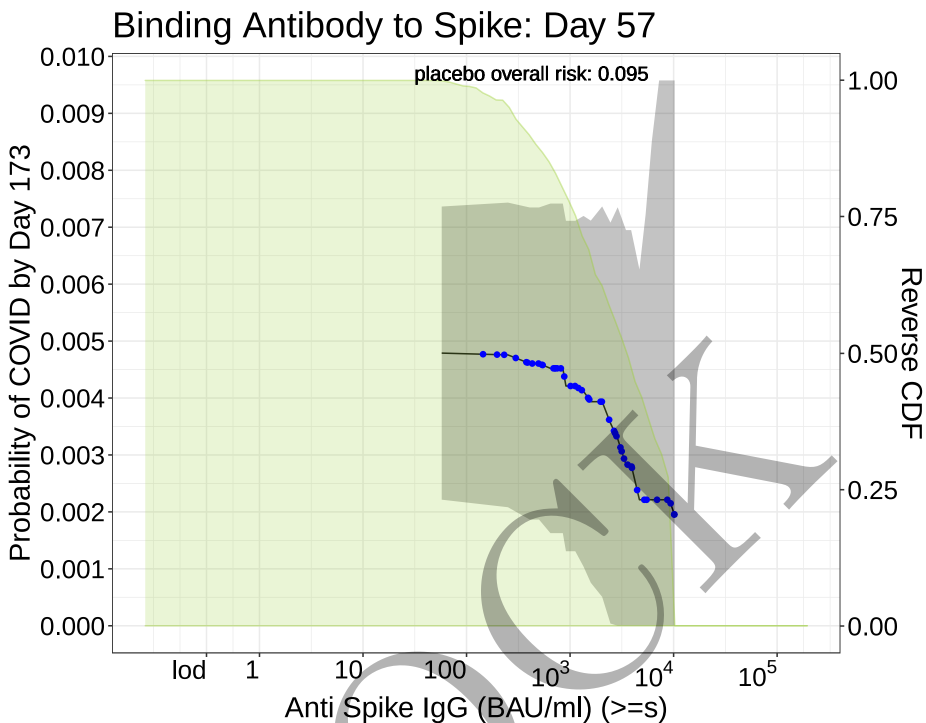



Figure 7.21: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindSpike levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.21: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57bindSpike levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.761 | $5.77 * 10^1$ | 0.00479 | 0.00221 | 0.00736 |
| 2.699 | $5.00 * 10^2$ | 0.00461 | 0.00187 | 0.00735 |
| 2.808 | $6.43 * 10^2$ | 0.00452 | 0.00163 | 0.00742 |
| 2.965 | $9.23 * 10^2$ | 0.00421 | 0.00131 | 0.00711 |
| 3.000 | $1.00 * 10^3$ | 0.00421 | 0.00131 | 0.00711 |
| 3.133 | $1.36 * 10^3$ | 0.00412 | 0.00104 | 0.00720 |
| 3.459 | $2.88 * 10^3$ | 0.00328 | 0.00000 | 0.00735 |
| 3.671 | $4.69 * 10^3$ | 0.00221 | 0.00000 | 0.00626 |
| 3.860 | $7.24 * 10^3$ | 0.00221 | 0.00000 | 0.01045 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |
| 4.007 | $1.02 * 10^4$ | 0.00194 | 0.00000 | 0.03884 |

### 7.6.2 Day 57 bindRBD

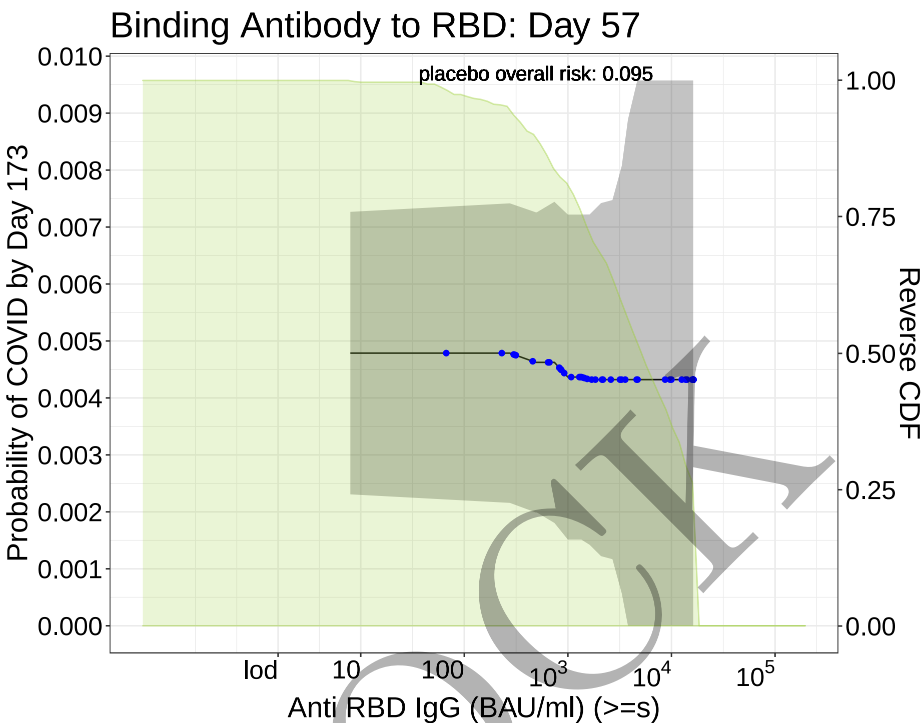



Figure 7.22: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57bindRBD levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.22: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57bindRBD levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.898 | $7.91 * 10^0$ | 0.00479 | 0.00231 | 0.00727 |
| 2.699 | $5.00 * 10^2$ | 0.00462 | 0.00199 | 0.00726 |
| 2.871 | $7.43 * 10^2$ | 0.00462 | 0.00181 | 0.00744 |
| 3.000 | $1.00 * 10^3$ | 0.00437 | 0.00151 | 0.00722 |
| 3.062 | $1.15 * 10^3$ | 0.00437 | 0.00151 | 0.00722 |
| 3.211 | $1.63 * 10^3$ | 0.00432 | 0.00142 | 0.00722 |
| 3.580 | $3.80 * 10^3$ | 0.00432 | 0.00000 | 0.00889 |
| 3.832 | $6.79 * 10^3$ | 0.00432 | 0.00000 | 0.01357 |
| 4.061 | $1.15 * 10^4$ | 0.00432 | 0.00000 | 0.01960 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |
| 4.211 | $1.63 * 10^4$ | 0.00432 | 0.00000 | 0.04838 |

### 7.6.3 Day 57 pseudoneutid50

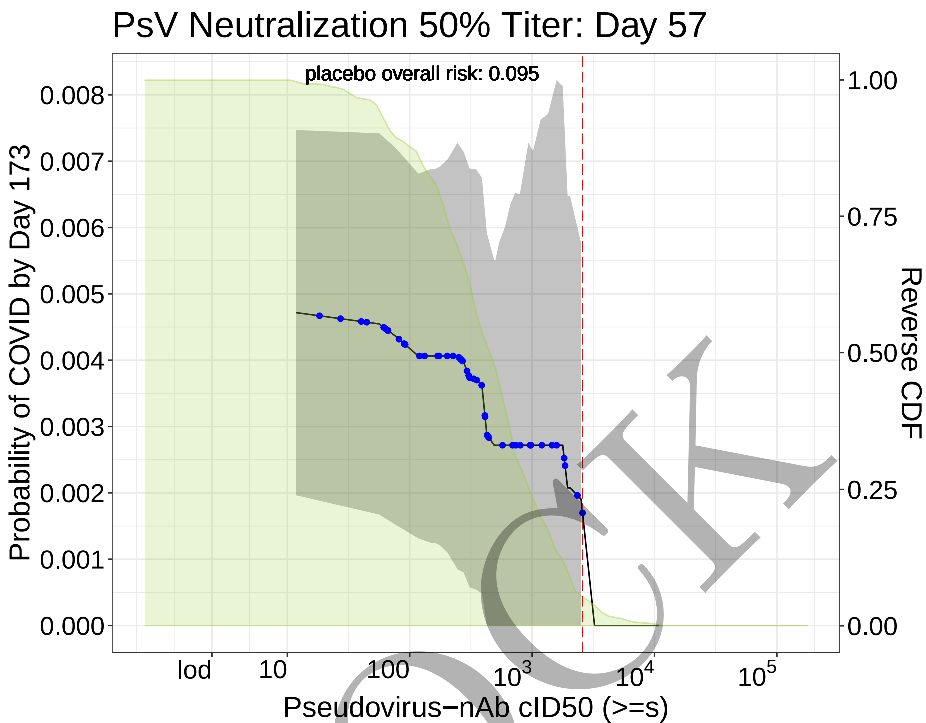



Figure 7.23: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid50 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.23: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57pseudoneutid50 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.072 | $1.18 * 10^1$ | 0.00472 | 0.00196 | 0.00747 |
| 2.070 | $1.17 * 10^2$ | 0.00406 | 0.00131 | 0.00681 |
| 2.214 | $1.64 * 10^2$ | 0.00406 | 0.00124 | 0.00688 |
| 2.313 | $2.06 * 10^2$ | 0.00406 | 0.00110 | 0.00703 |
| 2.538 | $3.45 * 10^2$ | 0.00371 | 0.00054 | 0.00688 |
| 2.690 | $4.90 * 10^2$ | 0.00272 | 0.00000 | 0.00551 |
| 2.699 | $5.00 * 10^2$ | 0.00272 | 0.00000 | 0.00551 |
| 2.817 | $6.56 * 10^2$ | 0.00272 | 0.00000 | 0.00634 |
| 2.967 | $9.27 * 10^2$ | 0.00272 | 0.00000 | 0.00728 |
| 3.000 | $1.00 * 10^3$ | 0.00272 | 0.00000 | 0.00717 |
| 3.196 | $1.57 * 10^3$ | 0.00272 | 0.00000 | 0.00822 |
| 3.290 | $1.95 * 10^3$ | 0.00208 | 0.00000 | 0.00648 |
| 3.401 | $2.52 * 10^3$ | 0.00191 | 0.00000 | 0.00577 |
| 4.038 | $1.09 * 10^4$ | 0.00000 | NA | NA |

### 7.6.4 Day 57 pseudoneutid80

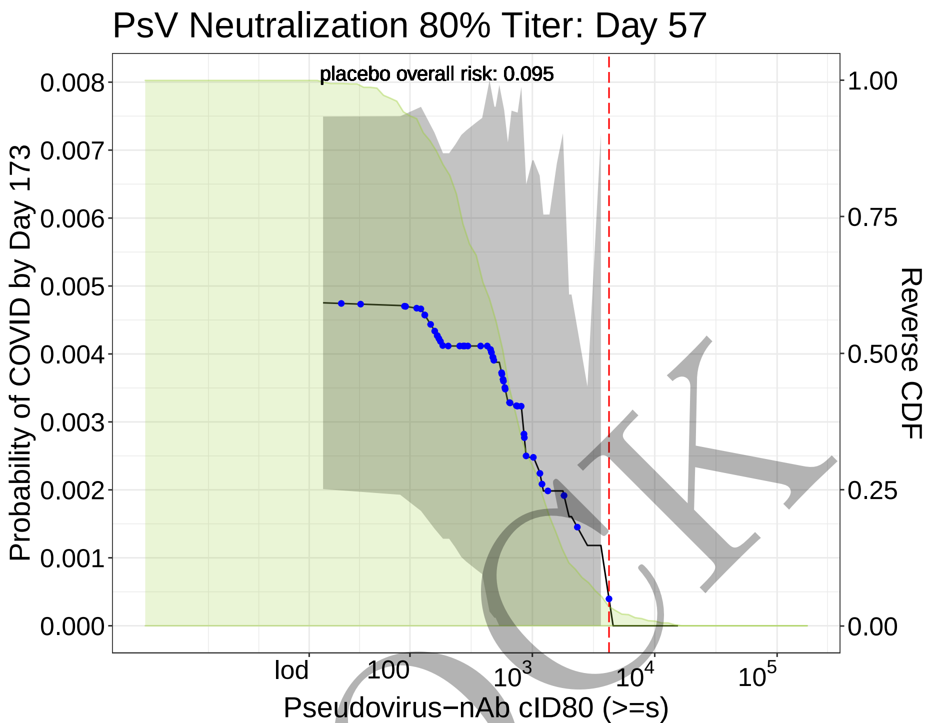



Figure 7.24: Adjusted threshold-response function for a range of thresholds of the Day 57 Day57pseudoneutid80 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.24: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Day57pseudoneutid80 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 1.285 | $1.93 * 10^1$ | 0.00475 | 0.00201 | 0.00749 |
| 2.204 | $1.60 * 10^2$ | 0.00434 | 0.00143 | 0.00726 |
| 2.316 | $2.07 * 10^2$ | 0.00412 | 0.00128 | 0.00695 |
| 2.418 | $2.62 * 10^2$ | 0.00412 | 0.00101 | 0.00722 |
| 2.648 | $4.45 * 10^2$ | 0.00412 | 0.00021 | 0.00803 |
| 2.699 | $5.00 * 10^2$ | 0.00388 | 0.00012 | 0.00764 |
| 2.766 | $5.83 * 10^2$ | 0.00355 | 0.00000 | 0.00759 |
| 2.878 | $7.55 * 10^2$ | 0.00323 | 0.00000 | 0.00755 |
| 3.000 | $1.00 * 10^3$ | 0.00248 | 0.00000 | 0.00685 |
| 3.006 | $1.01 * 10^3$ | 0.00248 | 0.00000 | 0.00685 |
| 3.196 | $1.57 * 10^3$ | 0.00198 | 0.00000 | 0.00680 |
| 3.299 | $1.99 * 10^3$ | 0.00161 | 0.00000 | 0.00488 |
| 3.445 | $2.79 * 10^3$ | 0.00118 | 0.00000 | 0.00352 |
| 4.187 | $1.54 * 10^4$ | 0.00000 | NA | NA |

## 7.7 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected)

### 7.7.1 Day 29 bindSpike

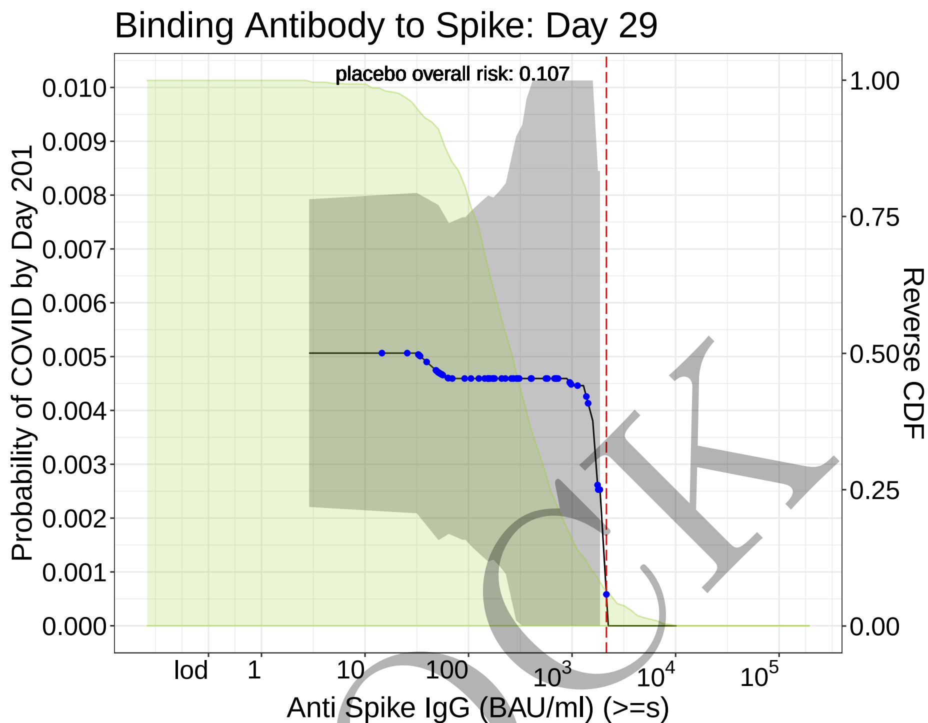




Figure 7.25: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.25: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.459 | $2.88 * 10^0$ | 0.00507 | 0.00221 | 0.00792 |
| 1.805 | $6.38 * 10^1$ | 0.00459 | 0.00171 | 0.00748 |
| 1.967 | $9.27 * 10^1$ | 0.00459 | 0.00160 | 0.00759 |
| 2.114 | $1.30 * 10^2$ | 0.00459 | 0.00133 | 0.00786 |
| 2.356 | $2.27 * 10^2$ | 0.00459 | 0.00096 | 0.00822 |
| 2.518 | $3.30 * 10^2$ | 0.00459 | 0.00000 | 0.00931 |
| 2.675 | $4.73 * 10^2$ | 0.00459 | 0.00000 | 0.01095 |
| 2.699 | $5.00 * 10^2$ | 0.00459 | 0.00000 | 0.01095 |
| 2.850 | $7.08 * 10^2$ | 0.00459 | 0.00000 | 0.01181 |
| 3.000 | $1.00 * 10^3$ | 0.00446 | 0.00000 | 0.01198 |
| 3.112 | $1.29 * 10^3$ | 0.00446 | 0.00000 | 0.01323 |
| 3.250 | $1.78 * 10^3$ | 0.00253 | 0.00000 | 0.00845 |
| 3.350 | $2.24 * 10^3$ | 0.00000 | NA | NA |
| 4.007 | $1.02 * 10^4$ | 0.00000 | NA | NA |

### 7.7.2 Day 29 bindRBD

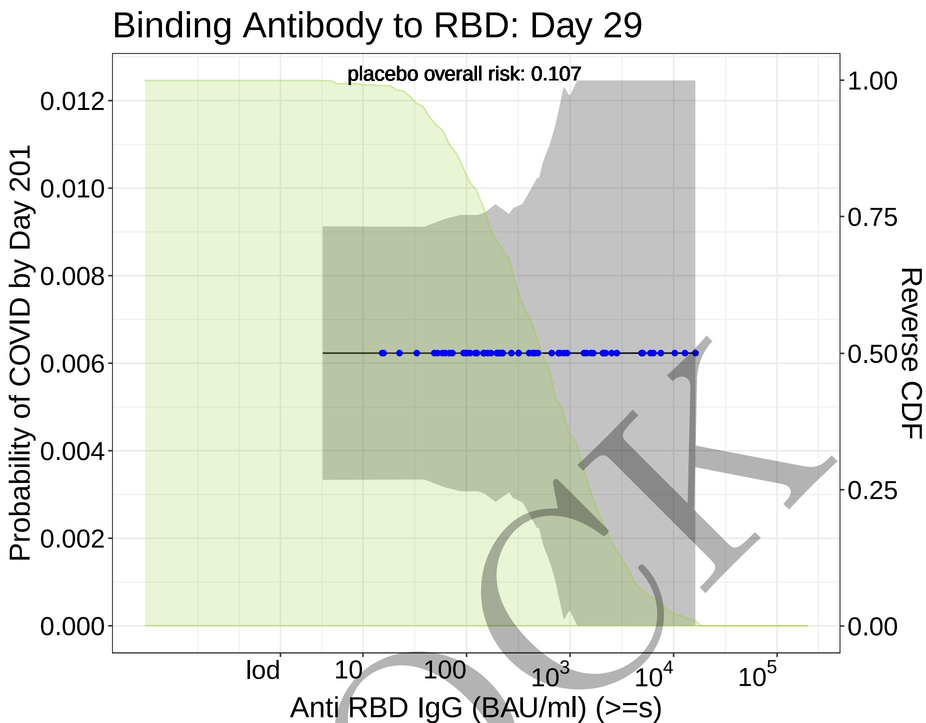



Figure 7.26: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.26: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.609 | $4.06 * 10^0$ | 0.00623 | 0.00333 | 0.00913 |
| 1.940 | $8.71 * 10^1$ | 0.00623 | 0.00307 | 0.00939 |
| 2.110 | $1.29 * 10^2$ | 0.00623 | 0.00307 | 0.00939 |
| 2.281 | $1.91 * 10^2$ | 0.00623 | 0.00283 | 0.00963 |
| 2.610 | $4.07 * 10^2$ | 0.00623 | 0.00253 | 0.00993 |
| 2.699 | $5.00 * 10^2$ | 0.00623 | 0.00223 | 0.01023 |
| 2.811 | $6.47 * 10^2$ | 0.00623 | 0.00142 | 0.01104 |
| 2.991 | $9.79 * 10^2$ | 0.00623 | 0.00034 | 0.01212 |
| 3.000 | $1.00 * 10^3$ | 0.00623 | 0.00034 | 0.01212 |
| 3.192 | $1.56 * 10^3$ | 0.00623 | 0.00000 | 0.01445 |
| 3.489 | $3.08 * 10^3$ | 0.00623 | 0.00000 | 0.01659 |
| 3.613 | $4.10 * 10^3$ | 0.00623 | 0.00000 | 0.01908 |
| 3.759 | $5.74 * 10^3$ | 0.00623 | 0.00000 | 0.01711 |
| 4.211 | $1.63 * 10^4$ | 0.00623 | 0.00000 | 0.05251 |

### 7.7.3 Day 29 pseudoneutid50

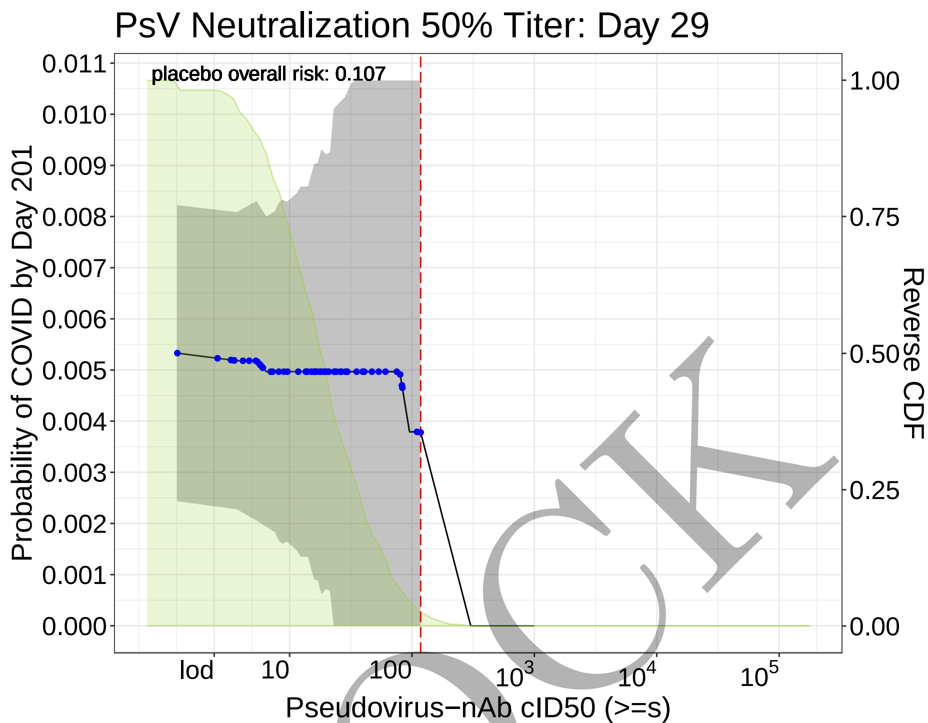





Figure 7.27: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid50 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.27: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid50 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.083 | $1.21 * 10^0$ | 0.00533 | 0.00244 | 0.00822 |
| 0.814 | $6.52 * 10^0$ | 0.00497 | 0.00194 | 0.00800 |
| 0.912 | $8.17 * 10^0$ | 0.00497 | 0.00167 | 0.00826 |
| 0.985 | $9.66 * 10^0$ | 0.00497 | 0.00164 | 0.00829 |
| 1.200 | $1.58 * 10^1$ | 0.00497 | 0.00091 | 0.00903 |
| 1.304 | $2.01 * 10^1$ | 0.00497 | 0.00072 | 0.00921 |
| 1.404 | $2.54 * 10^1$ | 0.00497 | 0.00000 | 0.01021 |
| 1.537 | $3.44 * 10^1$ | 0.00497 | 0.00000 | 0.01116 |
| 1.730 | $5.37 * 10^1$ | 0.00497 | 0.00000 | 0.01362 |
| 1.811 | $6.47 * 10^1$ | 0.00497 | 0.00000 | 0.01494 |
| 1.905 | $8.04 * 10^1$ | 0.00497 | 0.00000 | 0.01431 |
| 2.481 | $3.03 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

### 7.7.4 Day 29 pseudoneutid80

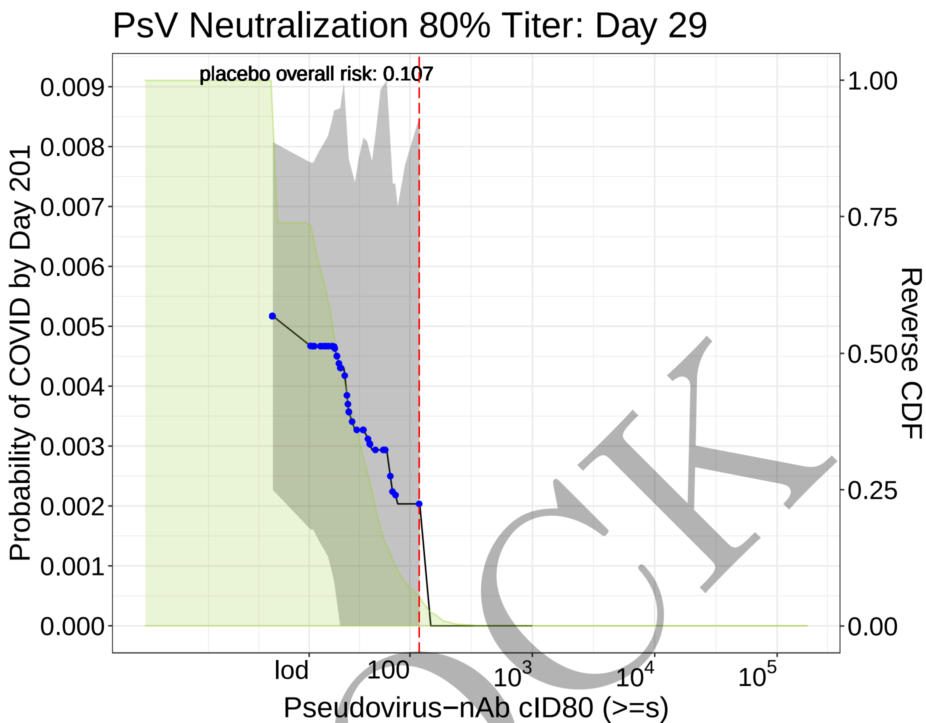



Figure 7.28: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid80 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.28: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid80 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00227 | 0.00807 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00227 | 0.00807 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00227 | 0.00807 |
| 1.185 | $1.53 * 10^1$ | 0.00467 | 0.00160 | 0.00773 |
| 1.334 | $2.16 * 10^1$ | 0.00467 | 0.00116 | 0.00818 |
| 1.425 | $2.66 * 10^1$ | 0.00430 | 0.00000 | 0.00864 |
| 1.548 | $3.53 * 10^1$ | 0.00327 | 0.00000 | 0.00740 |
| 1.652 | $4.49 * 10^1$ | 0.00316 | 0.00000 | 0.00809 |
| 1.806 | $6.40 * 10^1$ | 0.00294 | 0.00000 | 0.00910 |
| 1.877 | $7.53 * 10^1$ | 0.00220 | 0.00000 | 0.00738 |
| 1.962 | $9.16 * 10^1$ | 0.00203 | 0.00000 | 0.00770 |
| 2.529 | $3.38 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

## 7.8 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected)

### 7.8.1 Day 29 bindSpike

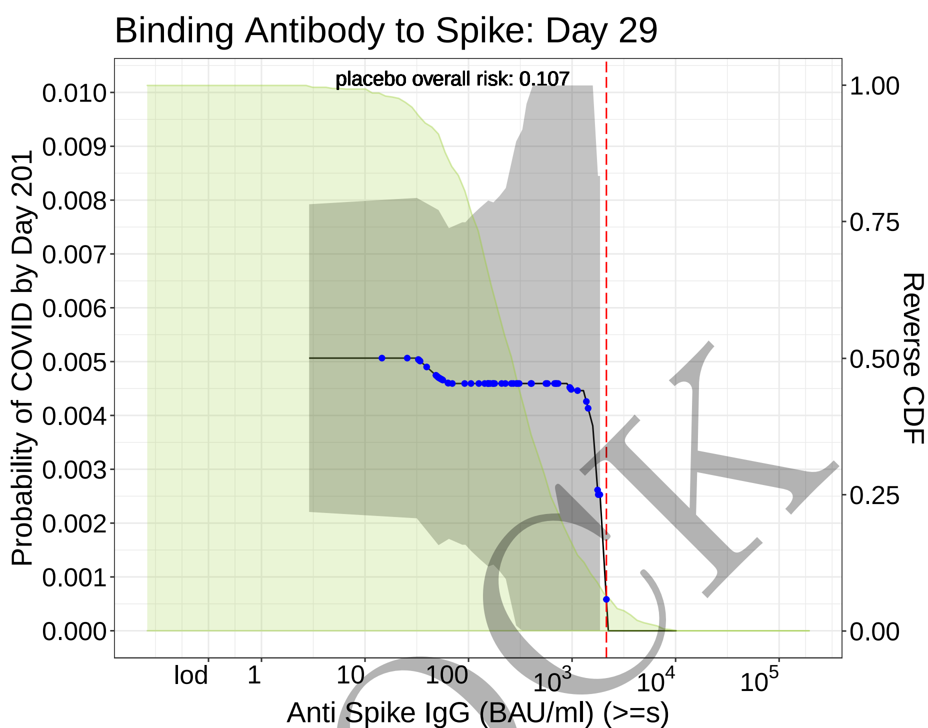



Figure 7.29: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.



Table 7.29: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.459 | $2.88 * 10^0$ | 0.00507 | 0.00221 | 0.00792 |
| 1.805 | $6.38 * 10^1$ | 0.00459 | 0.00171 | 0.00748 |
| 1.967 | $9.27 * 10^1$ | 0.00459 | 0.00160 | 0.00759 |
| 2.114 | $1.30 * 10^2$ | 0.00459 | 0.00133 | 0.00786 |
| 2.356 | $2.27 * 10^2$ | 0.00459 | 0.00096 | 0.00822 |
| 2.518 | $3.30 * 10^2$ | 0.00459 | 0.00000 | 0.00931 |
| 2.675 | $4.73 * 10^2$ | 0.00459 | 0.00000 | 0.01095 |
| 2.699 | $5.00 * 10^2$ | 0.00459 | 0.00000 | 0.01095 |
| 2.850 | $7.08 * 10^2$ | 0.00459 | 0.00000 | 0.01181 |
| 3.000 | $1.00 * 10^3$ | 0.00446 | 0.00000 | 0.01198 |
| 3.112 | $1.29 * 10^3$ | 0.00446 | 0.00000 | 0.01323 |
| 3.250 | $1.78 * 10^3$ | 0.00253 | 0.00000 | 0.00845 |
| 3.350 | $2.24 * 10^3$ | 0.00000 | NA | NA |
| 4.007 | $1.02 * 10^4$ | 0.00000 | NA | NA |

### 7.8.2 Day 29 bindRBD

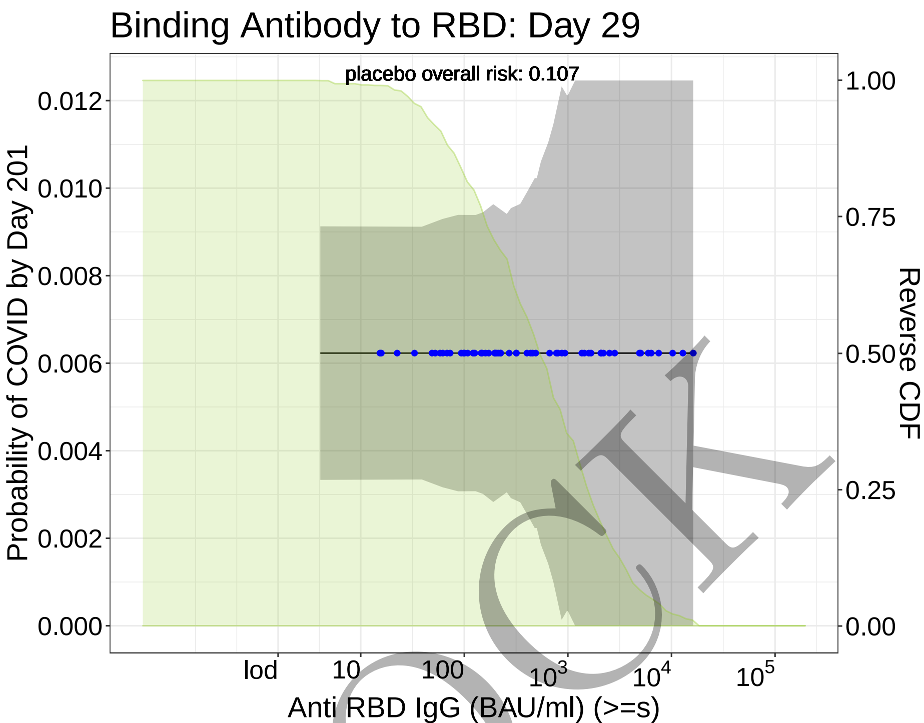



Figure 7.30: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.30: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.609 | $4.06 * 10^0$ | 0.00623 | 0.00333 | 0.00913 |
| 1.940 | $8.71 * 10^1$ | 0.00623 | 0.00307 | 0.00939 |
| 2.110 | $1.29 * 10^2$ | 0.00623 | 0.00307 | 0.00939 |
| 2.281 | $1.91 * 10^2$ | 0.00623 | 0.00283 | 0.00963 |
| 2.610 | $4.07 * 10^2$ | 0.00623 | 0.00253 | 0.00993 |
| 2.699 | $5.00 * 10^2$ | 0.00623 | 0.00223 | 0.01023 |
| 2.811 | $6.47 * 10^2$ | 0.00623 | 0.00142 | 0.01104 |
| 2.991 | $9.79 * 10^2$ | 0.00623 | 0.00034 | 0.01212 |
| 3.000 | $1.00 * 10^3$ | 0.00623 | 0.00034 | 0.01212 |
| 3.192 | $1.56 * 10^3$ | 0.00623 | 0.00000 | 0.01445 |
| 3.489 | $3.08 * 10^3$ | 0.00623 | 0.00000 | 0.01659 |
| 3.613 | $4.10 * 10^3$ | 0.00623 | 0.00000 | 0.01908 |
| 3.759 | $5.74 * 10^3$ | 0.00623 | 0.00000 | 0.01711 |
| 4.211 | $1.63 * 10^4$ | 0.00623 | 0.00000 | 0.05251 |

### 7.8.3 Day 29 pseudoneutid50

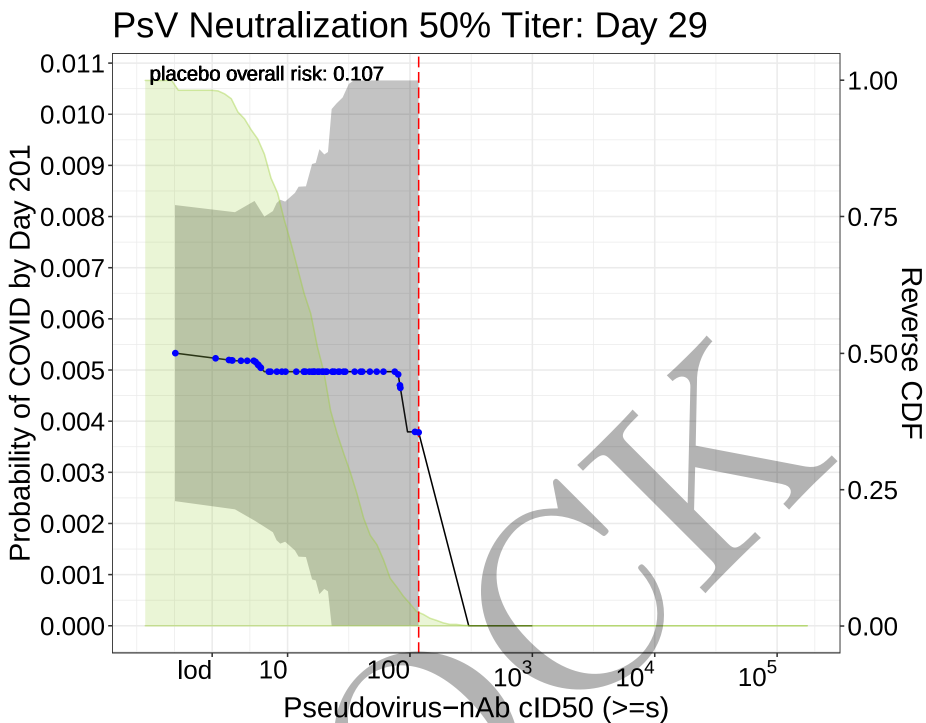



Figure 7.31: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid50 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.31: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid50 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.083 | $1.21 * 10^0$ | 0.00533 | 0.00244 | 0.00822 |
| 0.814 | $6.52 * 10^0$ | 0.00497 | 0.00194 | 0.00800 |
| 0.912 | $8.17 * 10^0$ | 0.00497 | 0.00167 | 0.00826 |
| 0.985 | $9.66 * 10^0$ | 0.00497 | 0.00164 | 0.00829 |
| 1.200 | $1.58 * 10^1$ | 0.00497 | 0.00091 | 0.00903 |
| 1.304 | $2.01 * 10^1$ | 0.00497 | 0.00072 | 0.00921 |
| 1.404 | $2.54 * 10^1$ | 0.00497 | 0.00000 | 0.01021 |
| 1.537 | $3.44 * 10^1$ | 0.00497 | 0.00000 | 0.01116 |
| 1.730 | $5.37 * 10^1$ | 0.00497 | 0.00000 | 0.01362 |
| 1.811 | $6.47 * 10^1$ | 0.00497 | 0.00000 | 0.01494 |
| 1.905 | $8.04 * 10^1$ | 0.00497 | 0.00000 | 0.01431 |
| 2.481 | $3.03 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

### 7.8.4 Day 29 pseudoneutid80

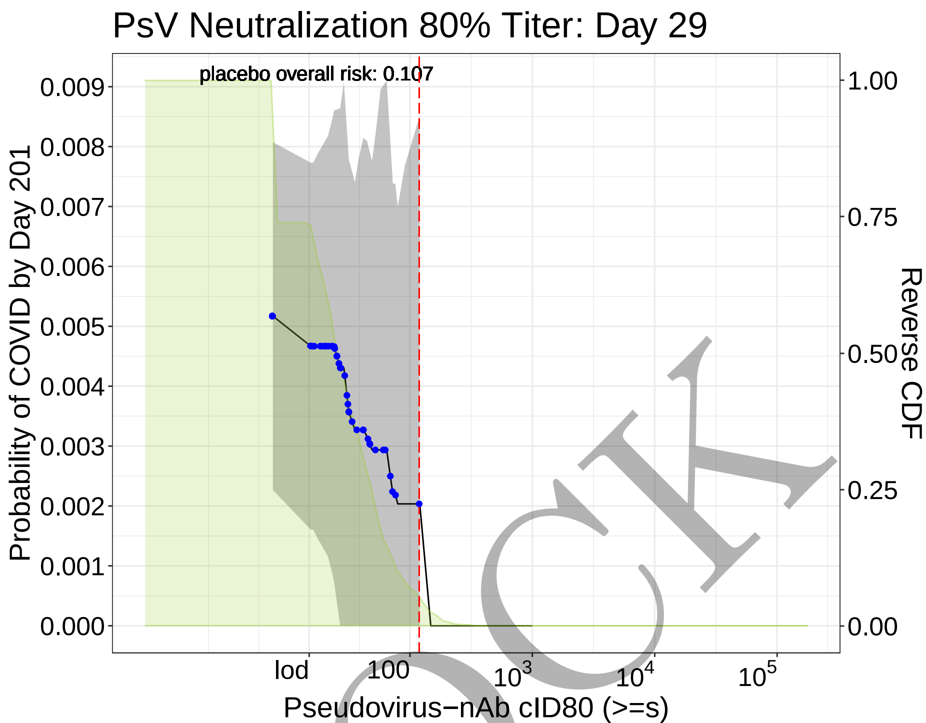



Figure 7.32: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29pseudoneutid80 levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 7.32: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29pseudoneutid80 levels with simultaneous 95% confidence intervals.

| $\log_{10}$-Threshold | Threshold | Risk estimate | CI left | CI right |
|---|---|---|---|---|
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00227 | 0.00807 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00227 | 0.00807 |
| 0.876 | $7.52 * 10^0$ | 0.00517 | 0.00227 | 0.00807 |
| 1.185 | $1.53 * 10^1$ | 0.00467 | 0.00160 | 0.00773 |
| 1.334 | $2.16 * 10^1$ | 0.00467 | 0.00116 | 0.00818 |
| 1.425 | $2.66 * 10^1$ | 0.00430 | 0.00000 | 0.00864 |
| 1.548 | $3.53 * 10^1$ | 0.00327 | 0.00000 | 0.00740 |
| 1.652 | $4.49 * 10^1$ | 0.00316 | 0.00000 | 0.00809 |
| 1.806 | $6.40 * 10^1$ | 0.00294 | 0.00000 | 0.00910 |
| 1.877 | $7.53 * 10^1$ | 0.00220 | 0.00000 | 0.00738 |
| 1.962 | $9.16 * 10^1$ | 0.00203 | 0.00000 | 0.00770 |
| 2.529 | $3.38 * 10^2$ | 0.00000 | NA | NA |
| 2.699 | $5.00 * 10^2$ | 0.00000 | NA | NA |
| 3.000 | $1.00 * 10^3$ | 0.00000 | NA | NA |

# Chapter 8

# Univariate CoR: Nonparametric Threshold Modeling (<=s)



The same methodology as the previous section is apply to estimate the "below" threshold-response function $E_W E[Y = 1|A = 1, X, S \leq s]$.

# Chapter 9

# Day D29 Univariate CoR: Nonlinear modeling



To explore nonlinear association and threshold modeling, we fit smoothing spline models with degrees of freedom selected by cross-validation using the mgcv R package.

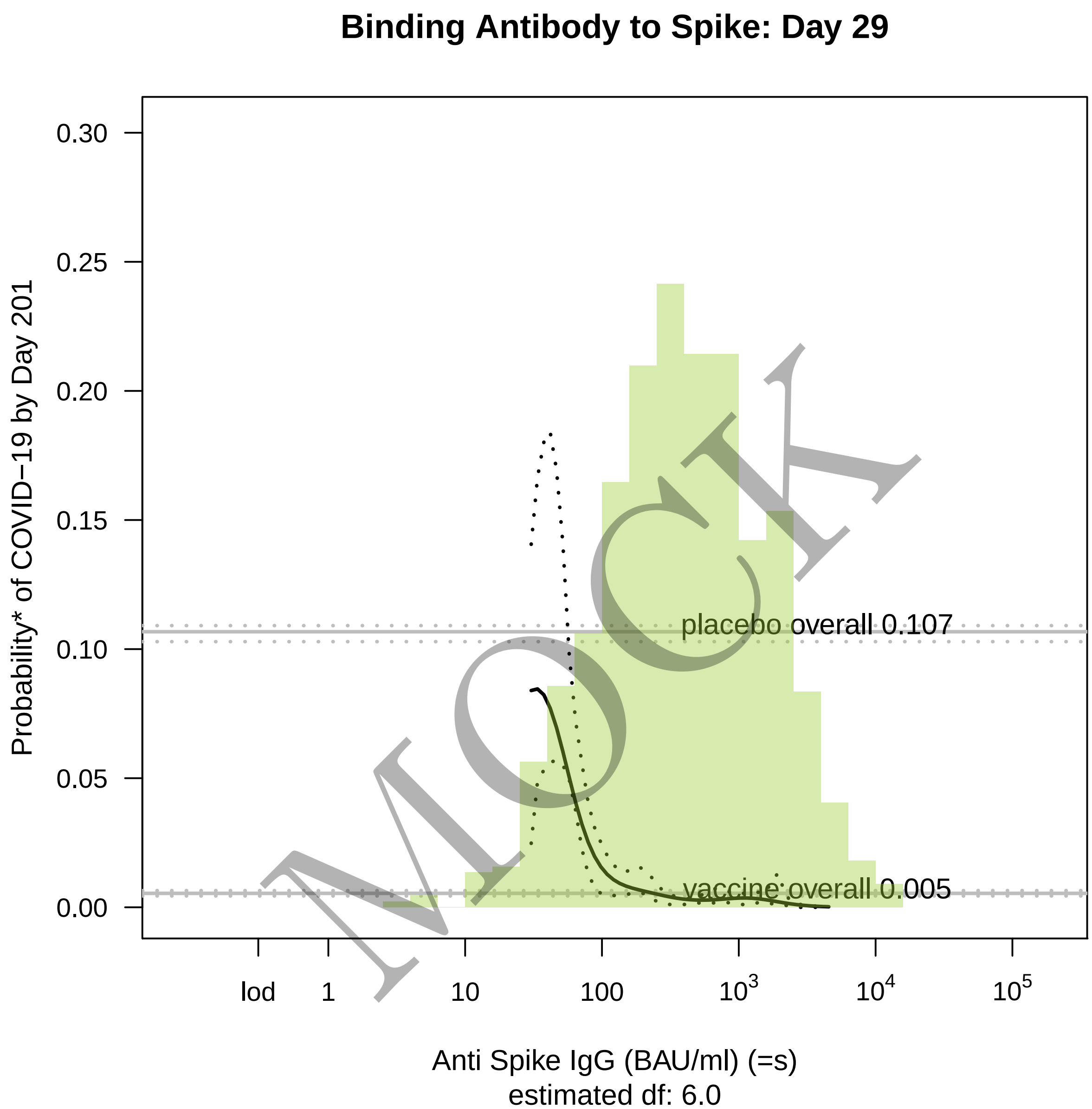



Figure 9.1: Marginalized risk as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 201  and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 0.3.

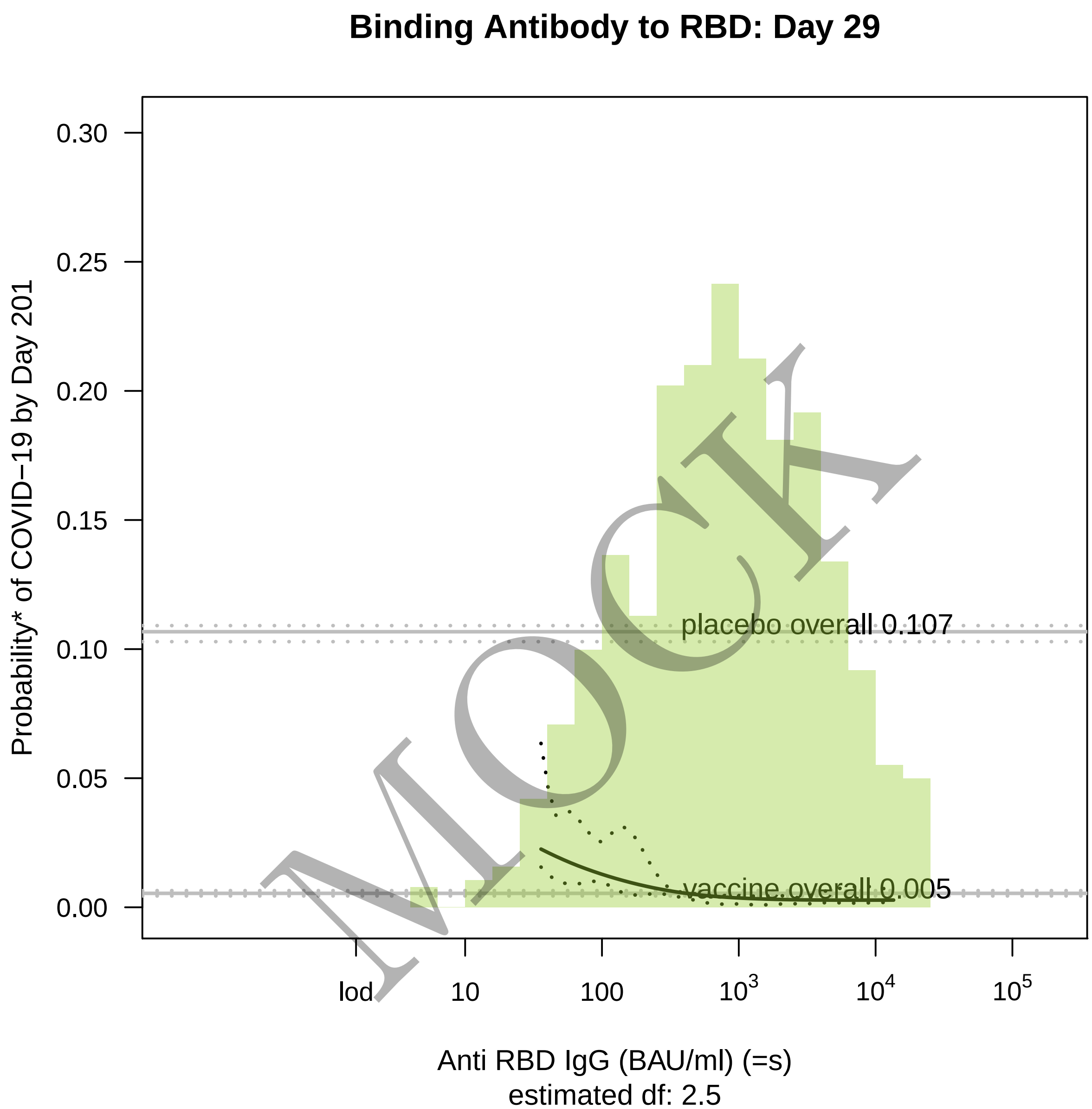



Figure 9.2: Marginalized risk as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 201  and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 1.6.

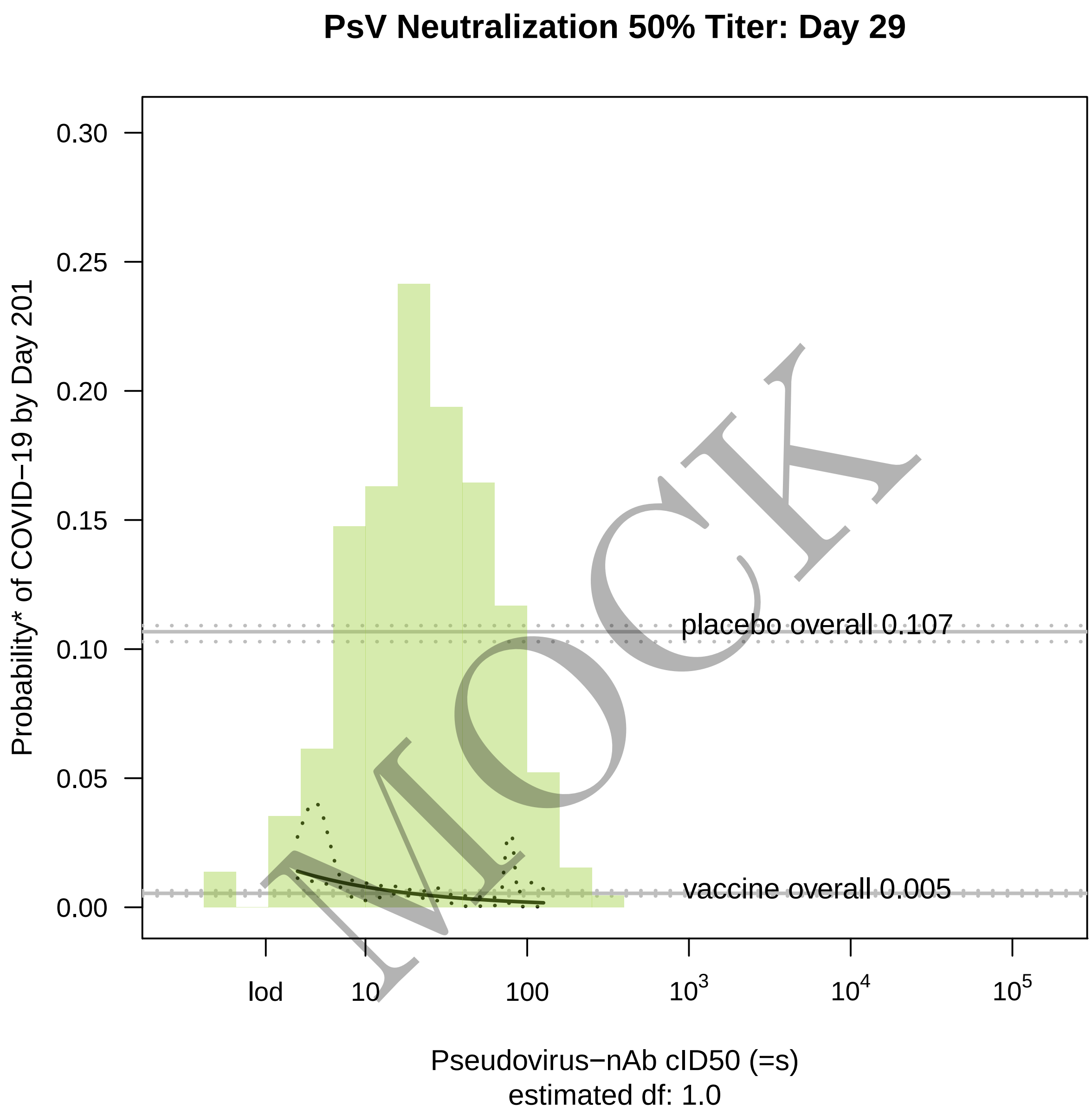



Figure 9.3: Marginalized risk as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 201 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 2.4.

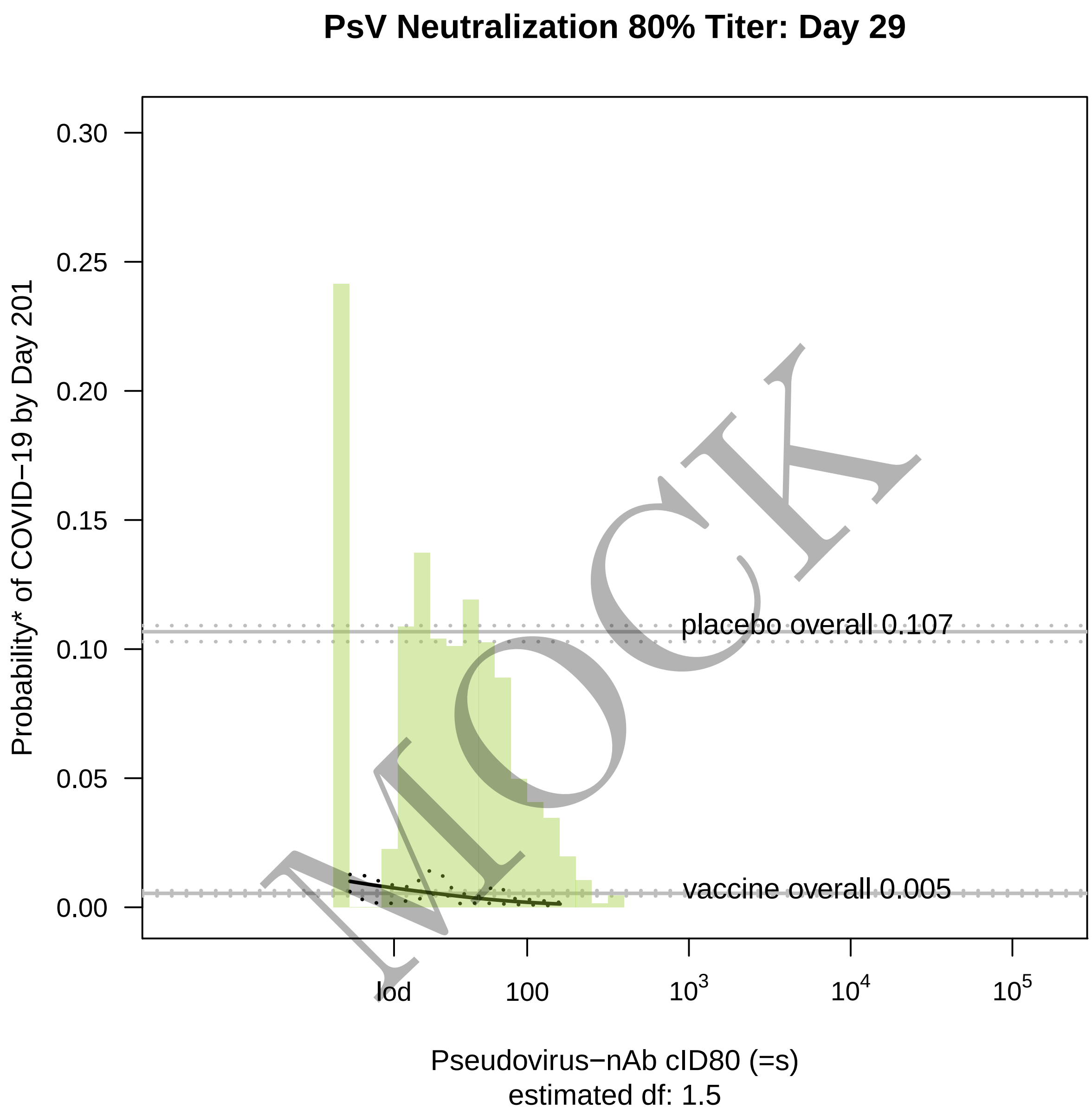



Figure 9.4: Marginalized risk as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 201  and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 15.

# Chapter 10

# Day D57 Univariate CoR: Nonlinear modeling



To explore nonlinear association and threshold modeling, we fit smoothing spline models with degrees of freedom selected by cross-validation using the mgcv R package.

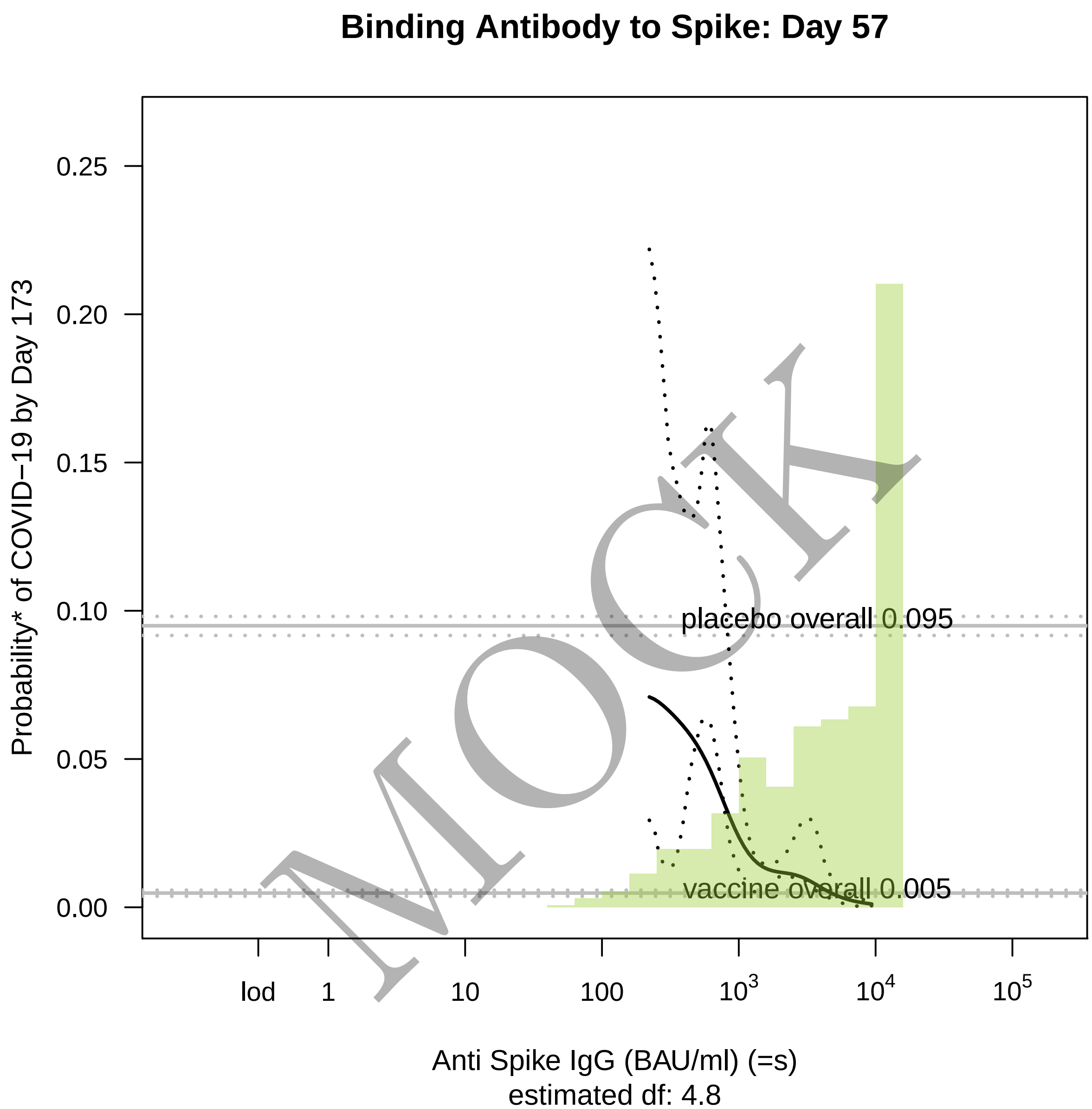



Figure 10.1: Marginalized risk as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 0.3.

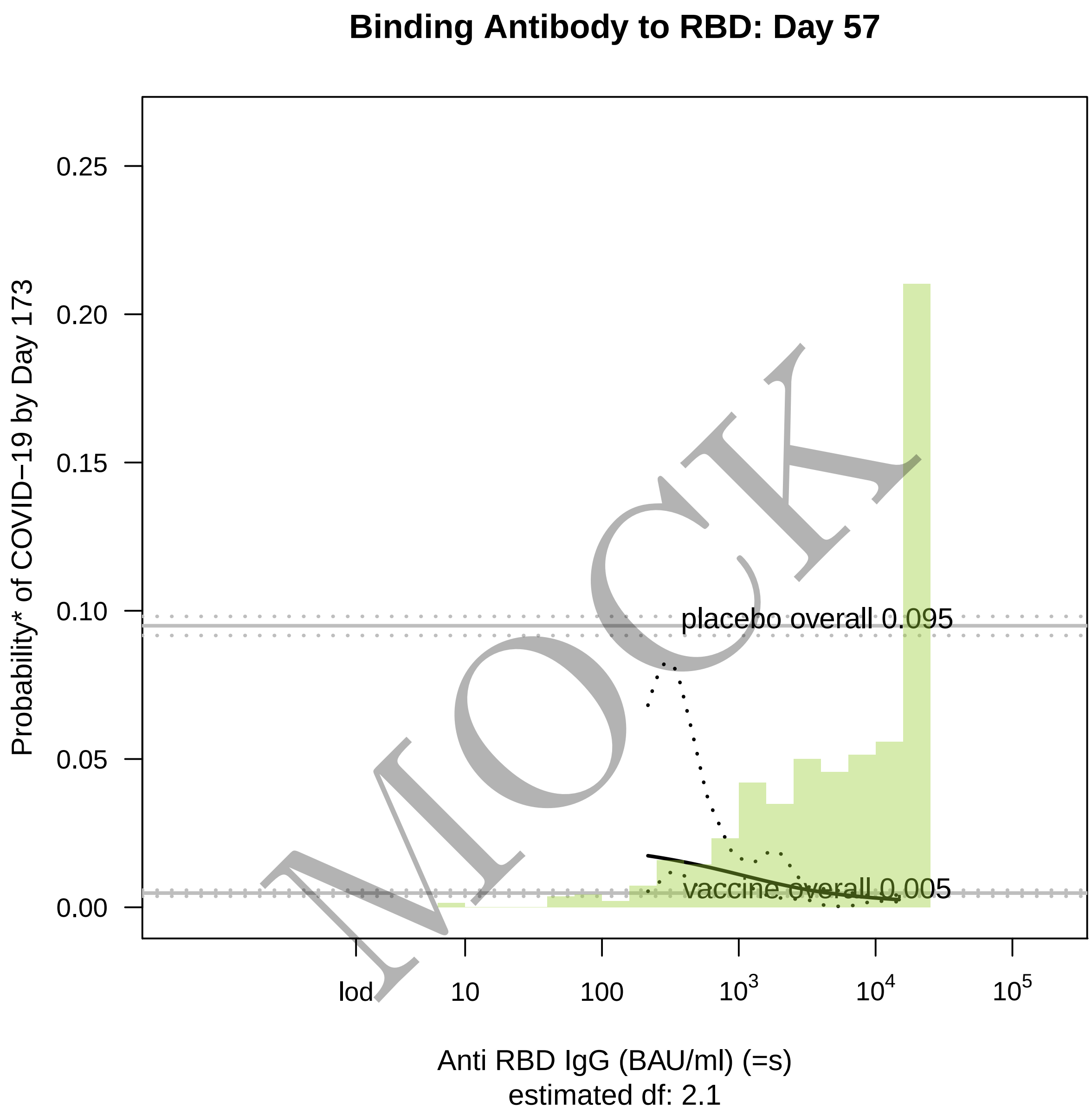



Figure 10.2: Marginalized risk as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 173 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 1.6.

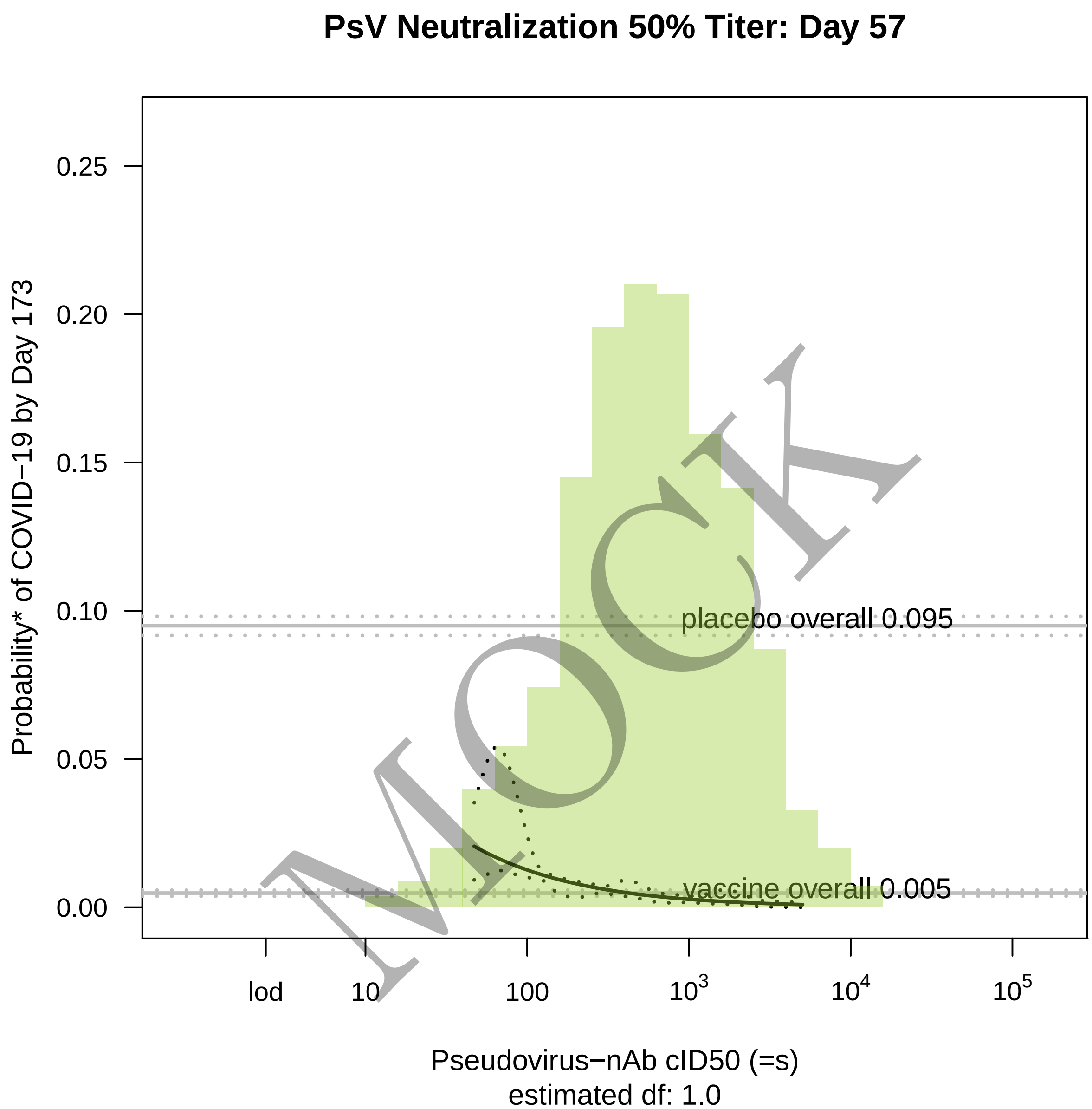



Figure 10.3: Marginalized risk as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 173  and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 2.4.

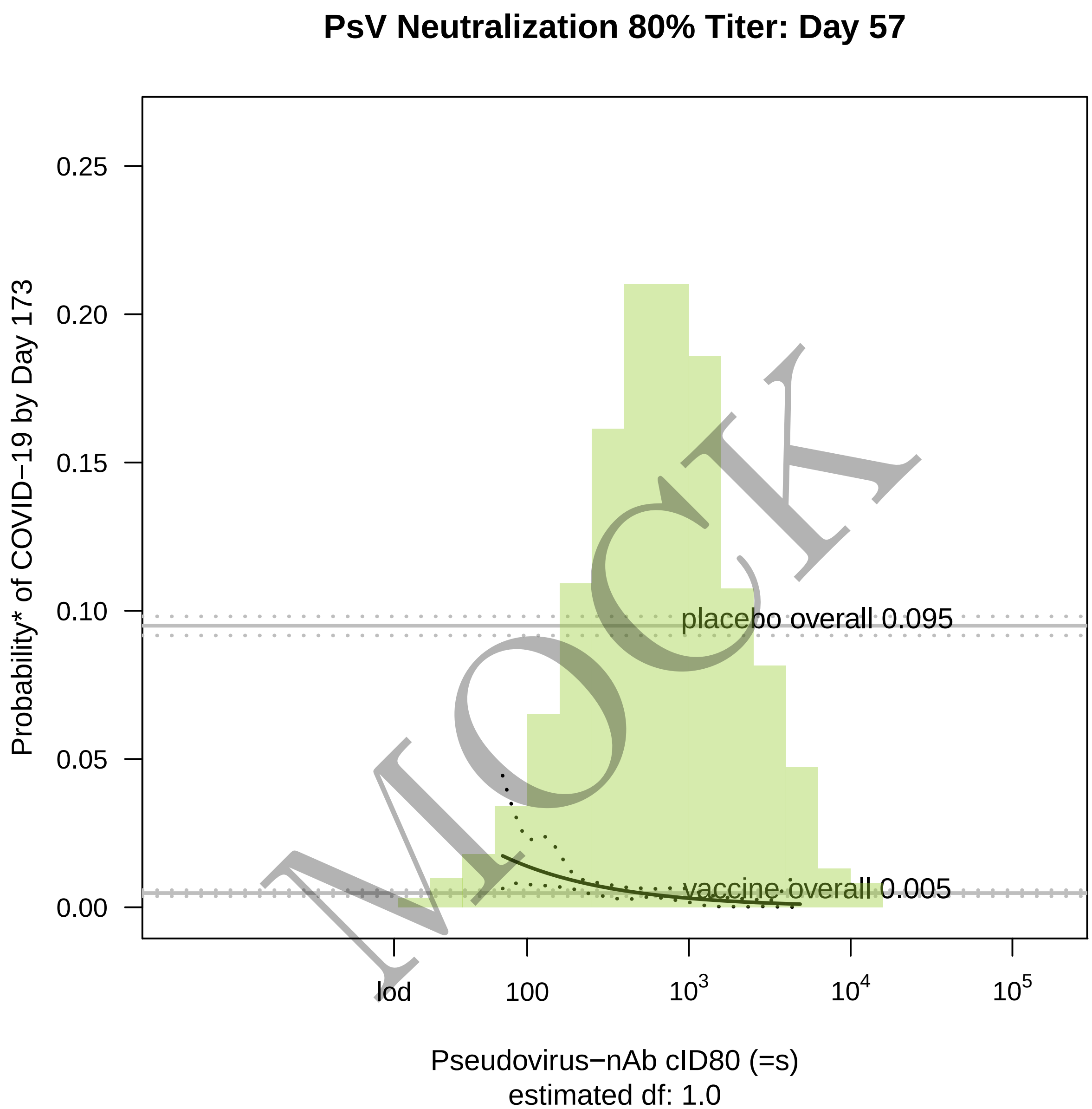



Figure 10.4: Marginalized risk as functions of Day 57 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10  replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: MinorityInd + HighRiskInd + Age. The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 173  and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 15.

# Chapter 11

# Appendix

```
#> [1] "reading data from moderna_mock_data_processed_with_riskscore.csv"
```

- This report was built from the `CoVPN/correlates_reporting` repository with commit hash 59a25c72d817e44e6ae60a113fac7cfc8046b57a. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/59a25c72d817e44e6ae60a113fac7cfc8046b57a
- The sha256 hash sum of the processed file, "moderna_mock_data_processed_with_riskscore.csv": c29963d581d8d6b7c13fecc9ca9b60a505a187b34fae117ebc0ad747cff1b26a