

CoP SAP 6.5 and 6.6 Appendix

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6.5 Appendix

As an appendix to section 6.5, we repeat the analysis using binned dose scores. The single-dose halved dose scores are binned as follows: 0, 1, (1, 1.5], (1.5, 2], (2, 2.5], (2.5, 3], > 3. This is being done in an attempt to improve the performance of the bootstrap confidence intervals.

Numeric viral load

Table A6.5.1: Percent of Variance Explained by Immune Virus-Specific Antibodies - Numeric Viral Load with Binned Dose Score

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
AUC BAL N1	89.94 (77.35, 100)	97.62 (93.97, 100)	89.83 (77.8, 100)	92.46 (86, 100)	79.84 (65.43, 100)	78.31 (62.9, 100)	81.76 (68.03, 100)	87.16 (76.9, 100)
AUC BAL Subgenomic	89.47 (79.75, 100)	100 (96.75, 100)	91.09 (79.44, 100)	94.19 (85.69, 100)	70.41 (51.05, 100)	64.13 (43.03, 100)	76.7 (59.65, 100)	82.07 (65.49, 100)
AUC Nasal Swab N1	93.81 (87.24, 100)	94.69 (90.04, 100)	93.42 (88.7, 100)	90.28 (84.66, 100)	85.79 (76.72, 99.7)	92.14 (85.16, 100)	93.51 (89.27, 100)	99.61 (96.63, 100)
AUC Nasal Swab Subgenomic	100 (96.71, 100)	95.68 (92.13, 100)	96.89 (92.11, 100)	93.71 (87.38, 100)	94.71 (89.26, 100)	94.32 (87.52, 100)	100 (97.49, 100)	100 (95.96, 100)
AUC OP Swab N1	99.3 (96, 100)	96.69 (92.63, 100)	97.34 (91.27, 100)	95.39 (87.77, 100)	93.31 (85.22, 100)	77.85 (40.67, 100)	94.52 (88.36, 100)	98.17 (93.52, 100)
AUC OP Swab Subgenomic	100 (88.7, 100)	95.08 (87.58, 100)	98.45 (91.08, 100)	97.52 (89.66, 100)	95.99 (86.09, 100)	66.43 (13.32, 99.1)	99.83 (93.01, 100)	100 (90.27, 100)
log VL Day2 PostChal- lenge BAL N1	87.48 (75.16, 100)	100 (96.98, 100)	73.4 (57.4, 100)	74.92 (57.72, 100)	95.72 (87.79, 100)	86.28 (74.16, 100)	90.89 (81.91, 100)	93.44 (85.86, 100)
log VL Day2 PostChal- lenge BAL Subgenomic	94.95 (87.92, 100)	100 (95.3, 100)	75.46 (58.32, 100)	77.27 (61.26, 100)	96.9 (87.34, 100)	90.61 (79.09, 100)	93.43 (83.07, 100)	95.63 (86.64, 100)
log VL Day2 PostChal- lenge OPswab N1	86.82 (76.97, 100)	81.86 (64.52, 100)	86.61 (70.85, 100)	75.55 (54.51, 100)	100 (87.5, 100)	97.27 (88.09, 100)	100 (85.8, 100)	100 (87.05, 100)
log VL Day2 PostChal- lenge OPswab Subgenomic	91.53 (80.86, 100)	91.35 (79.56, 100)	88.21 (72.61, 100)	79 (58.04, 100)	100 (90.01, 100)	100 (86.32, 100)	100 (86.44, 100)	100 (87.1, 100)
log VL Day2 PostChal- lenge NasalSwab N1	99.75 (96.53, 100)	95.94 (92.69, 100)	93.41 (88.56, 100)	88.64 (82.32, 100)	100 (97.99, 100)	96.03 (88.33, 100)	100 (94.18, 100)	100 (97.35, 100)
log VL Day2 PostChal- lenge NasalSwab Subgenomic	100 (96.59, 100)	99.9 (98.04, 100)	95.69 (91.52, 100)	90.33 (86.57, 100)	100 (98.1, 100)	97.29 (92.22, 100)	100 (93.39, 100)	100 (96.23, 100)

Binary Viral Load

Table A6.5.2: Percent of Variance Explained by Immune Virus Specific Antibodies - Binary Viral Load with Binned Dose Score

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
bin VL Day2 PostChal- lenge BAL N1	100 (47.52, 100)	70.74 (33.51, 100)	57.51 (13.39, 100)	36.28 (6.21, 100)	100 (59.88, 100)	100 (23.05, 100)	100 (47.68, 100)	94.71 (60.67, 100)
bin VL Day2 PostChal- lenge BAL Subgenomic	96.86 (94.05, 100)	100 (93.56, 100)	63.4 (45.07, 100)	59.58 (40.07, 100)	100 (95.05, 100)	89.43 (81.2, 100)	90.74 (82.85, 100)	97.98 (92.51, 100)
bin VL Day2 PostChal- lenge OPswab N1	100 (87.74, 100)	100 (61.56, 100)	100 (56.95, 100)	100 (55.34, 100)	92.26 (57.18, 100)	100 (68.52, 100)	100 (52.8, 100)	100 (58.82, 100)
bin VL Day2 PostChal- lenge OPswab Subgenomic	56.34 (31.89, 100)	45.05 (18.62, 100)	35.52 (5.86, 97.38)	26.85 (0.04, 79.58)	73.99 (56.21, 100)	85.89 (75.34, 100)	69.65 (50.72, 100)	69.65 (50.55, 100)
bin VL Day2 PostChal- lenge NasalSwab N1	6.4 (0, 100)	17.42 (4.34, 53.78)	0 (0, 100)	0 (0, 100)	9.83 (0, 100)	47.69 (0, 100)	6.47 (0, 100)	1.08 (0, 17.12)
bin VL Day2 PostChal- lenge NasalSwab Subgenomic	100 (81.4, 100)	100 (71.15, 100)	100 (70.98, 100)	100 (59.65, 100)	100 (84.95, 100)	100 (84.07, 100)	100 (64.4, 100)	100 (77.18, 100)

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SAP section 6.6 is also repeated using larger bins of the single dose halved dose scores: 0, 1, (1, 2], >2. This was done to increase the amount of data in each bin, after splitting by vaccine.

Numeric Viral Load

Table A6.6.1: Differential Vaccine Effect - Numeric Viral Load with Binned Dose Score

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
AUC BAL N1	90.83 (81.78, 100)	100 (98.74, 100)	82.2 (71.22, 98.49)	91.12 (86.59, 100)	90.05 (83.97, 100)	94.08 (90.6, 100)	88.38 (83.09, 100)	99.17 (97.17, 100)
AUC BAL Subgenomic	98.51 (90.88, 100)	100 (92.39, 100)	89.43 (81.26, 100)	99 (96.66, 100)	100 (94.17, 100)	100 (91.02, 100)	92.67 (85.28, 100)	100 (88.47, 100)
AUC Nasal Swab N1	73.23 (59.49, 88.79)	74.78 (63.87, 90.93)	74.87 (61.2, 89.12)	82.1 (73.1, 94.6)	76.63 (64.24, 91.77)	77.08 (65.82, 92.99)	74.05 (61.4, 88.19)	79.03 (67.49, 92.75)
AUC Nasal Swab Subgenomic	86.82 (79.81, 99.26)	88.36 (82.25, 100)	81.52 (71.94, 96.26)	87.33 (80.52, 100)	83.36 (74.84, 98.07)	82.26 (71.21, 96.1)	81.41 (72.29, 96.06)	89.08 (83.46, 100)
AUC OP Swab N1	67.88 (41.02, 92)	71.5 (41.39, 94.19)	62.24 (36.79, 84.79)	63.52 (36.06, 86.59)	65.89 (38.49, 91.26)	66.53 (37.82, 91.12)	62.73 (35.27, 87.41)	71.23 (42.62, 94.61)
AUC OP Swab Subgenomic	51.83 (23.64, 87.28)	56.75 (25.5, 90.21)	43.9 (19, 76)	46.46 (22.26, 82.3)	46.93 (22.19, 86.66)	45.59 (13.27, 75.82)	43.66 (17.72, 80.29)	51.15 (21.64, 88.04)
log VL Day2 PostChal- lenge BAL N1	91.18 (82.72, 100)	90.76 (86.8, 100)	84.13 (75.23, 100)	91.05 (87.88, 100)	95.2 (91.94, 100)	88.34 (82.62, 100)	93.02 (88.59, 100)	95.63 (91.83, 100)
log VL Day2 PostChal- lenge BAL Subgenomic	100 (95.7, 100)	100 (96.58, 100)	93.02 (90.62, 100)	97.3 (95.77, 100)	100 (93.43, 100)	100 (93.65, 100)	100 (99.31, 100)	100 (96.05, 100)
log VL Day2 PostChal- lenge OPswab N1	62.63 (44.15, 100)	48.73 (24.74, 84.16)	58.13 (40.65, 100)	57.89 (37.44, 90.53)	64.07 (43.9, 100)	48.9 (26.66, 81.38)	66.93 (49.33, 100)	74.42 (60.09, 100)
log VL Day2 PostChal- lenge OPswab Subgenomic	75.54 (62.13, 100)	65.74 (48.9, 100)	67.52 (51.14, 100)	65.49 (46.92, 96.61)	78.98 (67.89, 100)	61.01 (40.18, 92.85)	75.14 (63.65, 100)	86.95 (78.79, 100)
log VL Day2 PostChal- lenge NasalSwab N1	100 (94.25, 100)	85.43 (77.89, 100)	97.27 (94.49, 100)	100 (95, 100)	100 (92.94, 100)	92.92 (87.79, 100)	100 (95.48, 100)	100 (93.38, 100)
log VL Day2 PostChal- lenge NasalSwab Subgenomic	99.79 (96.45, 100)	85.99 (81.05, 100)	96.38 (94.04, 100)	98.43 (95.07, 100)	100 (96.82, 100)	86.83 (79.01, 100)	100 (96.66, 100)	100 (97.14, 100)

Binary Viral Load

Table A6.6.2: Differential Vaccine Effect - Binary Viral Load with Binned Dose Score

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
bin VL Day2 PostChal- lenge BAL N1	17.07 (0, 100)	66.37 (0, 100)	100 (0, 100)	92.78 (0, 100)	0 (0, 100)	0 (0, 100)	58.01 (0, 100)	49.78 (0, 100)
bin VL Day2 PostChal- lenge BAL Subgenomic	100 (85.16, 100)	93.71 (77.39, 100)	100 (85.49, 100)	100 (85.75, 100)	100 (81.14, 100)	94.91 (73.11, 100)	97.26 (81.69, 100)	81.44 (58.53, 100)
bin VL Day2 PostChal- lenge OPswab N1	0 (0, 100)	0 (0, 100)	45.43 (0, 100)	57.14 (0, 100)	18.7 (0, 100)	0 (0, 100)	100 (42.36, 100)	96.29 (30.1, 100)
bin VL Day2 PostChal- lenge OPswab Subgenomic	74.61 (53.24, 100)	56.8 (28.02, 100)	72.56 (54.35, 100)	84.63 (63.06, 100)	73.26 (50.9, 100)	53.93 (26.98, 100)	58.52 (30.87, 100)	95 (76.2, 100)
bin VL Day2 PostChal- lenge NasalSwab N1	14.84 (0, 100)	100 (100, 100)	0 (0, 100)	0 (0, 100)	16.01 (0, 100)	5.99 (0, 100)	17.23 (0, 100)	6.45 (0, 100)
bin VL Day2 PostChal- lenge NasalSwab Subgenomic	93.78 (51.33, 100)	100 (55.08, 100)	69.36 (24.17, 100)	92.69 (50.38, 100)	76.48 (39.88, 100)	50.8 (19.12, 100)	0 (0, 100)	58.87 (0, 100)

Additional Analysis - Base+Dose+Vacc vs. Base

As an additional analysis for the appendix, we compare the base model to the base+dose+vacc model. Details of the base model are explained in the SAP section 6.5. The base+dose+vacc model used here is slightly different than that described in SAP section 6.6. In this model, the single dose halved dose score is used as a numeric value, with a separate effect for each vaccine manufacturer. Linear models for numeric viral load (e.g., Section 6.4.1) or logistic models for binary viral load (more complicated models, regardless of what was selected by the cross-validation procedure in section 6.4.2, are not used) will be employed. The percentage of variance (PVE) is 100 times the adjusted R square value from the base model over the adjusted R squared values from the base+dose+vacc model. Confidence intervals on the PVE are calculated by using bias-adjusted nonparametric bootstrap methods (using 5000 replicates).

Numeric Viral Load

Table A6.6.3: Compare Base to Base, Dose, Vacc - Numeric Viral Load with Binned Dose Score

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
AUC BAL N1	88.8 (81.23, 100)	98.2 (96.63, 100)	77.71 (62.88, 96.09)	85.42 (76.65, 100)	71.53 (62.09, 94.64)	71.43 (60.72, 98.51)	75.08 (66.23, 100)	85.9 (79.74, 100)
AUC BAL Subgenomic	91.92 (85.6, 100)	97.25 (93.52, 100)	80.09 (63.3, 100)	89.19 (77.58, 100)	67.32 (56.23, 100)	63.02 (49.37, 100)	72.22 (60.1, 100)	83.68 (73.51, 100)
AUC Nasal Swab N1	77.44 (67.5, 91.85)	78.51 (69.86, 95.34)	72.73 (62.82, 86.61)	74.44 (65.03, 88.82)	74.32 (64.72, 90.73)	74.52 (65.38, 91.74)	76.64 (67.79, 91.24)	84.57 (76.9, 98.19)
AUC Nasal Swab Subgenomic	88.38 (82.98, 99.07)	85.29 (79.61, 99.33)	73.88 (62.91, 90.36)	76.66 (66.94, 91.73)	80.07 (73.37, 94.77)	77.34 (67.72, 93.07)	81.68 (74.48, 92.93)	90.64 (86.61, 99.56)
AUC OP Swab N1	82.53 (72.82, 100)	92.28 (86.48, 100)	76.81 (62.11, 94.82)	83.08 (71.26, 100)	76.46 (69.89, 95.33)	71.1 (54.25, 94.11)	83.63 (79, 100)	90.88 (86.33, 100)
AUC OP Swab Subgenomic	82.55 (70.55, 100)	77.24 (44.5, 100)	71.52 (47.11, 94.7)	79.33 (58.84, 100)	70.62 (59.3, 98.01)	50.29 (13.47, 80.26)	78.56 (69.63, 100)	82.46 (73.29, 100)
log VL Day2 PostChal- lenge BAL N1	83.29 (75.83, 100)	98.13 (97.55, 100)	65.1 (51.39, 91.13)	73.82 (65.47, 97.18)	90.1 (87.76, 100)	84.45 (81.57, 100)	88.23 (84.16, 100)	92.5 (91.65, 100)
log VL Day2 PostChal- lenge BAL Subgenomic	86.67 (80.05, 100)	100 (98.36, 100)	64.54 (48.56, 91.14)	70.41 (56.83, 100)	90.11 (84.84, 100)	87.88 (82.15, 100)	89.44 (82.98, 100)	89.96 (83.45, 100)
log VL Day2 PostChal- lenge OPswab N1	74.66 (65.32, 100)	69.86 (59.88, 100)	60.18 (43.55, 100)	51.88 (33.83, 100)	76.82 (65.84, 100)	74.18 (62.21, 100)	82.62 (75.78, 100)	92.8 (85.98, 100)
log VL Day2 PostChal- lenge OPswab Subgenomic	77.99 (66.4, 100)	78.61 (71.45, 100)	68.61 (51.21, 100)	59.14 (39.53, 100)	88.5 (84.59, 100)	84.97 (80.16, 100)	88.99 (84.86, 100)	100 (97.59, 100)
log VL Day2 PostChal- lenge NasalSwab N1	99.78 (94.37, 100)	100 (98.13, 100)	81.02 (73.62, 100)	78.98 (69.81, 100)	100 (98.32, 100)	96.45 (93.61, 100)	100 (95.88, 100)	100 (93.21, 100)
log VL Day2 PostChal- lenge NasalSwab Subgenomic	97.53 (93.73, 100)	99.21 (97.65, 100)	81.3 (76.45, 100)	78.89 (72.7, 100)	97.15 (96.18, 100)	93.08 (88.54, 100)	99.74 (99.11, 100)	100 (96.06, 100)

Binary Viral Load

Table A6.6.4: Compare Base to Base, Dose, Vacc - Binary Viral Load with Binned Dose Score

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
bin VL Day2 PostChal- lenge BAL N1	100 (41.59, 100)	100 (58.73, 100)	47.52 (19.33, 100)	39.4 (21.56, 100)	100 (54.98, 100)	100 (40.25, 100)	100 (31.39, 100)	94.41 (52.57, 100)
bin VL Day2 PostChal- lenge BAL Subgenomic	78.31 (72.4, 100)	100 (93.43, 100)	56.34 (42.3, 95.48)	56.84 (42.28, 93.22)	91.82 (91.8, 100)	95.69 (99.49, 100)	80.1 (75.17, 100)	90.63 (90.36, 100)
bin VL Day2 PostChal- lenge OPswab N1	67.02 (36.22, 100)	100 (66.55, 100)	47.13 (14.31, 100)	48.92 (18.68, 100)	46.6 (19.47, 100)	63.65 (28.73, 100)	65.52 (32.43, 100)	75.53 (43.28, 100)
bin VL Day2 PostChal- lenge OPswab Subgenomic	51.17 (37.48, 100)	41.56 (23.17, 100)	28.27 (8.39, 68.77)	29.51 (8.48, 72.69)	62.51 (50.62, 100)	66.49 (59.65, 100)	53.74 (41.58, 100)	74.4 (67.48, 100)
bin VL Day2 PostChal- lenge NasalSwab N1	0 (0, 100)	17.42 (4.5, 58.69)	0 (0, 100)	0 (0, 100)	3.85 (0, 100)	0 (0, 100)	2.92 (0, 100)	0 (0, 100)
bin VL Day2 PostChal- lenge NasalSwab Subgenomic	67.83 (60.21, 100)	83.21 (81.79, 100)	58.96 (47.45, 100)	69.04 (60.12, 100)	76.23 (63.96, 100)	58.64 (45.14, 100)	100 (98.45, 100)	78.05 (70.11, 100)