Immunity, Volume *57*

Supplemental information

SARS-CoV-2-infection- and vaccine-induced antibody responses are long lasting with an initial waning phase followed by a stabilization phase

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Supplemental Figure S1: Long-term follow up with continued dense sampling informs the structure of datasets used in analyses (related to Figure 1).

A: Study visits from each of the 496 PARIS participants are shown colored by year of study follow-up. A total of 8,041 samples were collected over the three years of the study.

B: Flow chart illustrating the data selection from PARIS study participants for the specific analyses performed. Figures in which a given dataset or subset thereof are shown are listed. Datasets based on infection data are shown in dark orange.

Supplemental Figure S2: Analysis of antibody kinetics early upon vaccination captured the impact of hybrid immunity on primary immunization but not subsequent booster vaccinations (related to Figure 2).

Early timepoints post-vaccine. Participants with hybrid immunity due to pre-vaccine SARS-CoV-2 infection are shown in orange, and those without are shown in blue. Participants with breakthrough infections are excluded. Lines connect geometric means for 5-day bins (10-day bins post-dose 4), with confidence intervals constructed by bootstrapping.

A: Longitudinal antibody data collected within 40 days after vaccination. Data from participants with (124 participants, 375 samples) and without (166 participants, 528 samples) pre-existing immunity are shown. Approximate peak timepoints for each group are indicated by dashed lines.

B: Longitudinal antibody data collected within 40 days after the third vaccine dose. Data for participants with (59 participants, 151 samples) and without (157 participants, 448 samples) prior SARS-CoV-2 infection.

C: Longitudinal antibody data collected within 40 days after the 4^{th} vaccine for participants with (12 participants, 28 samples) and without (25 participants, 57 samples) prior SARS-CoV-2 infection.

Supplemental Figure S3: The PARIS NLME model fits the observed antibody kinetics best since it considers the magnitude of the peak response and the stability of that response (related to Figure 3).

A: The three parameters of the vaccine are illustrated here, with ‘c’ representing the "steady-state" antibody level, ‘a’ representing the magnitude of the fast-decaying component, and ‘b’ representing the rate of that decay.

B: Comparison of a linear fit (grey) and the PARIS model fit (black) to the first five months of data for one representative study participant, with extrapolation from each model plotted against additional timepoints censored from model training.

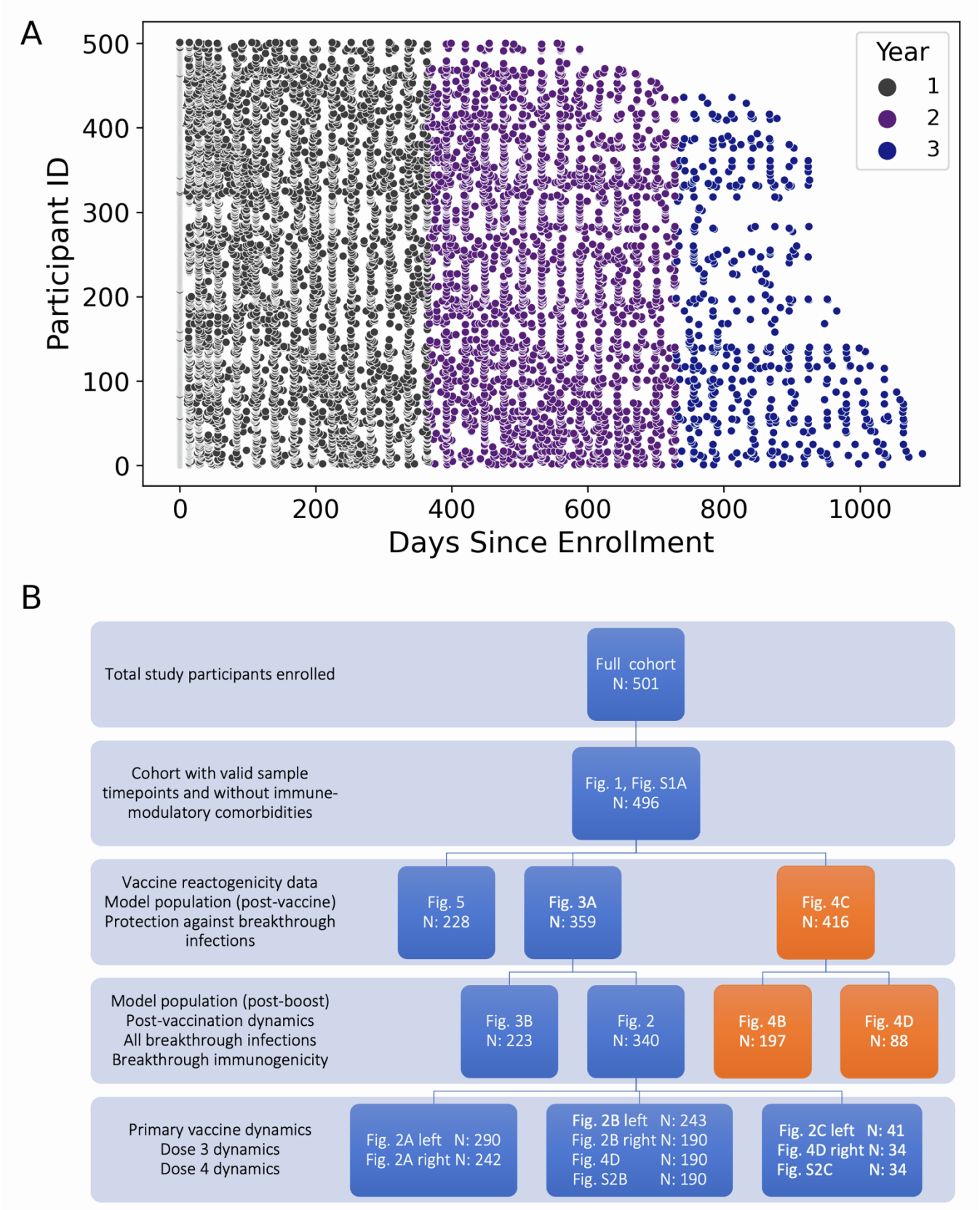
Supplemental Figure S4: The PARIS NLME model allows for more precise modeling of antibody kinetics compared to alternate model structures (related to Figure 3).

Geometric mean titers for the primary two-component model as well as for alternate model structures such as a simple exponential decay and a power law model to both post-vaccine (A) and post-boost (B) data are shown. The simple exponential decay (linear fit in the log-linear space) and power law (linear fit in the log-log space) models were fit using the NLMIXED procedure with two random effects (in each case, allowing the slope and intercept to vary for each participant). Data was stratified by SARS-CoV-2 infection status prior to vaccination, with the vaccine-only immunity group shown in blue and the hybrid immunity group shown in orange.

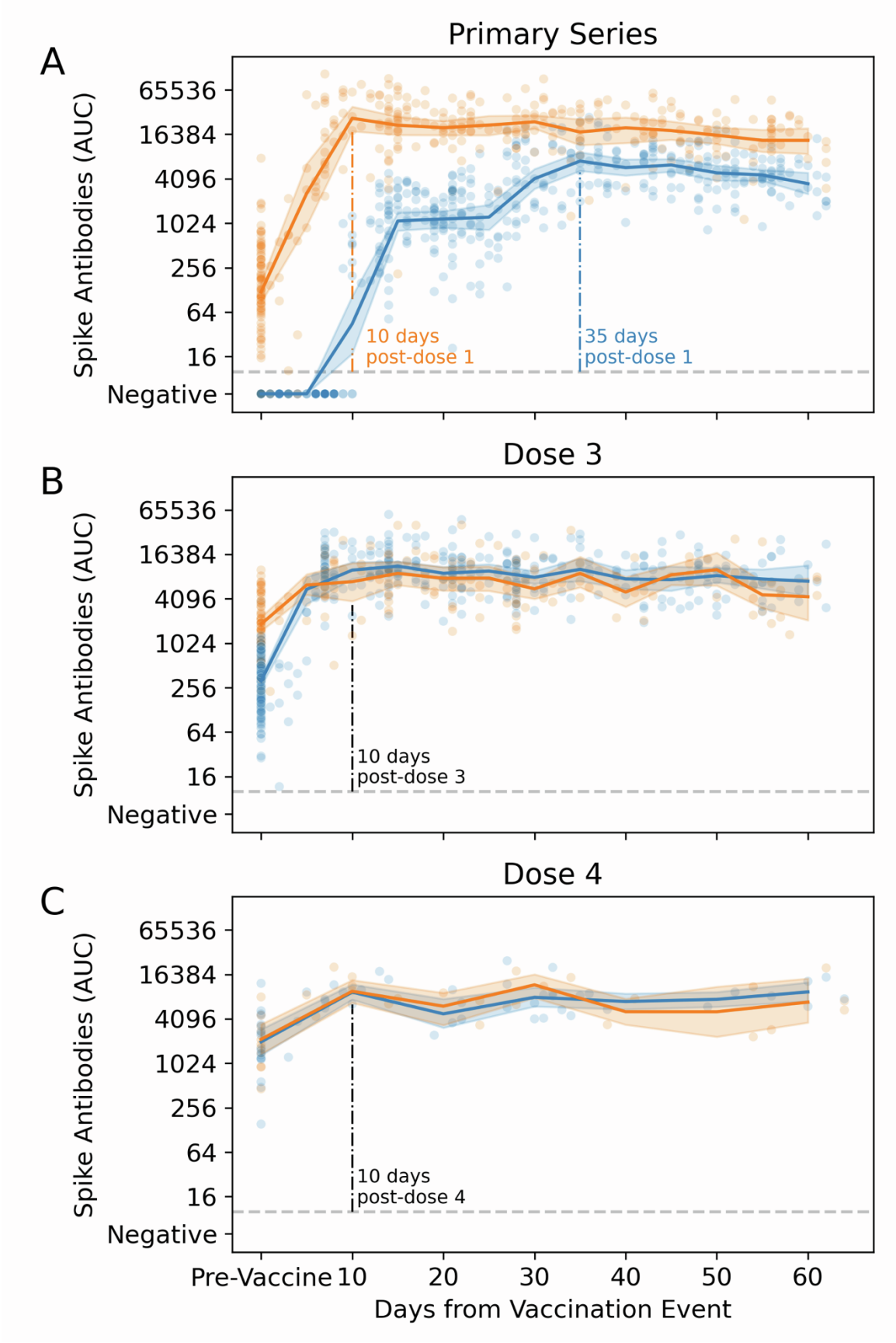
Supplemental Figure S5: Hybrid immunity determines the frequency of mild, moderate, and severe side effects reported after SARS-CoV-2 vaccine doses 1, 2 and 3 (related to Figure 5).

Local and systemic side effects were recorded after the first (A), second (B) and third vaccine (C) doses in PARIS participants with (right, yellow) and without (left, blue) pre-existing immunity. 230 participants completed all three surveys. Symptom severity was self-reported and classified as mild, moderate, or severe based on description and duration.

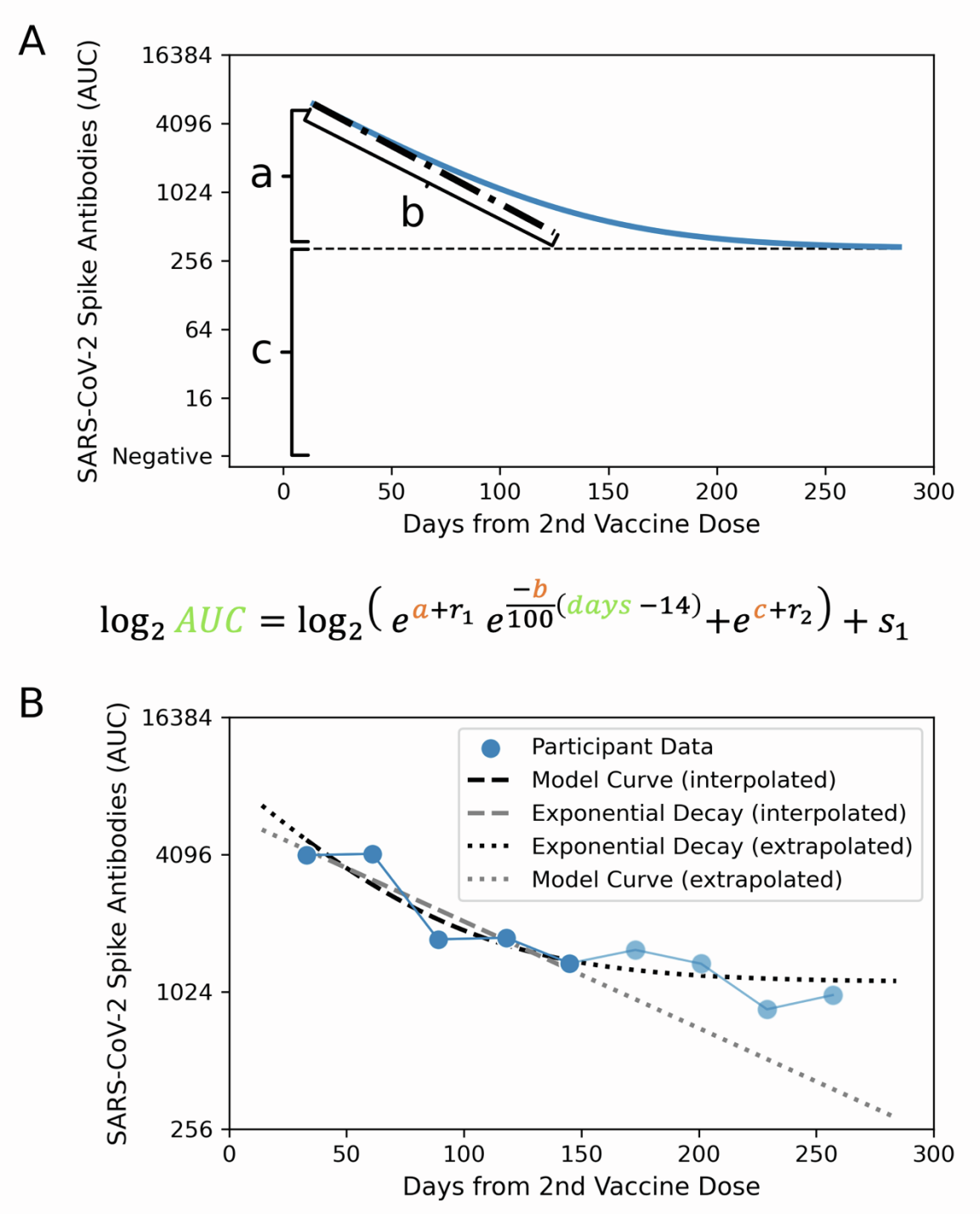
Supplemental Figure 1:



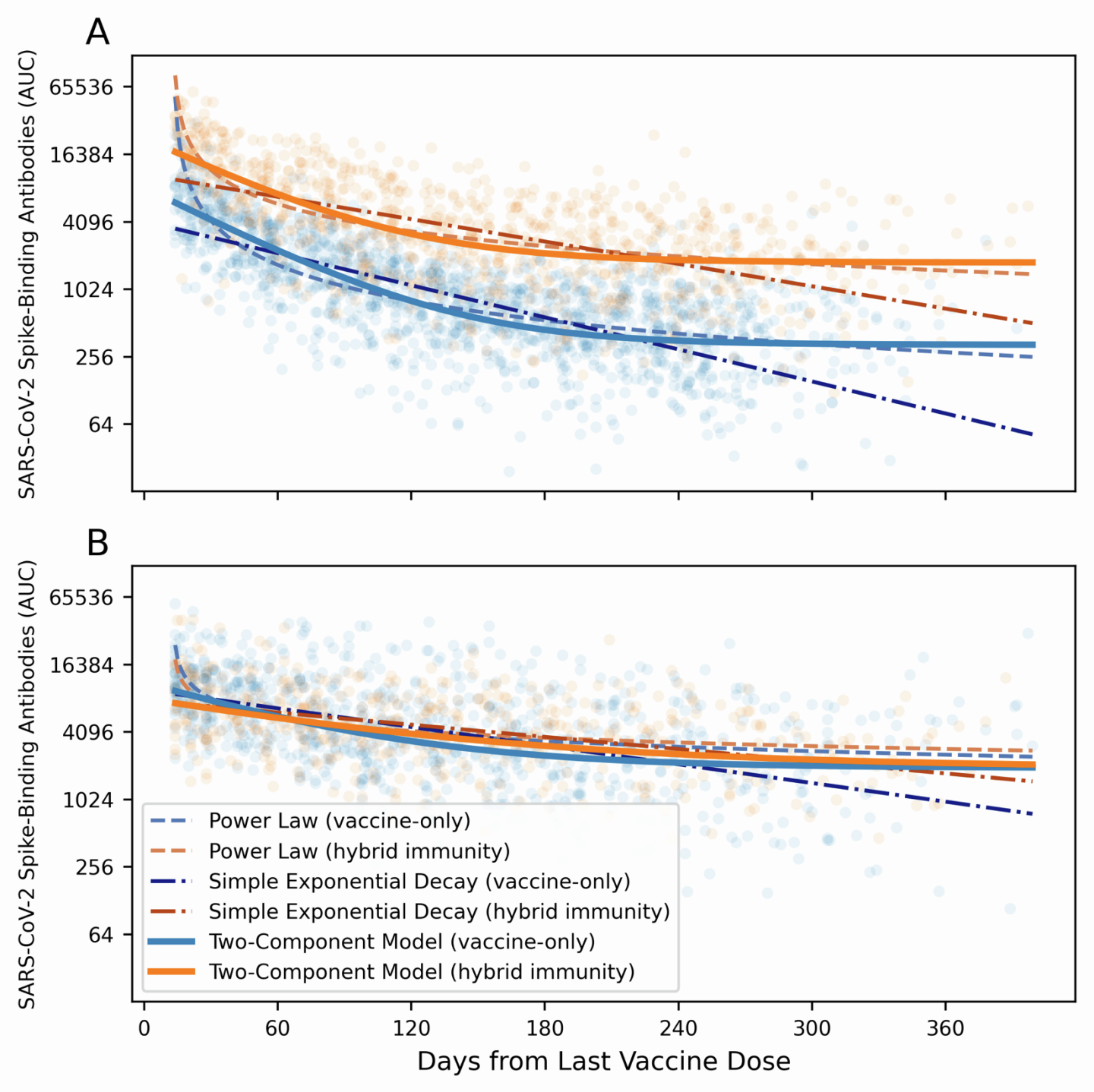
Supplemental Figure 2:



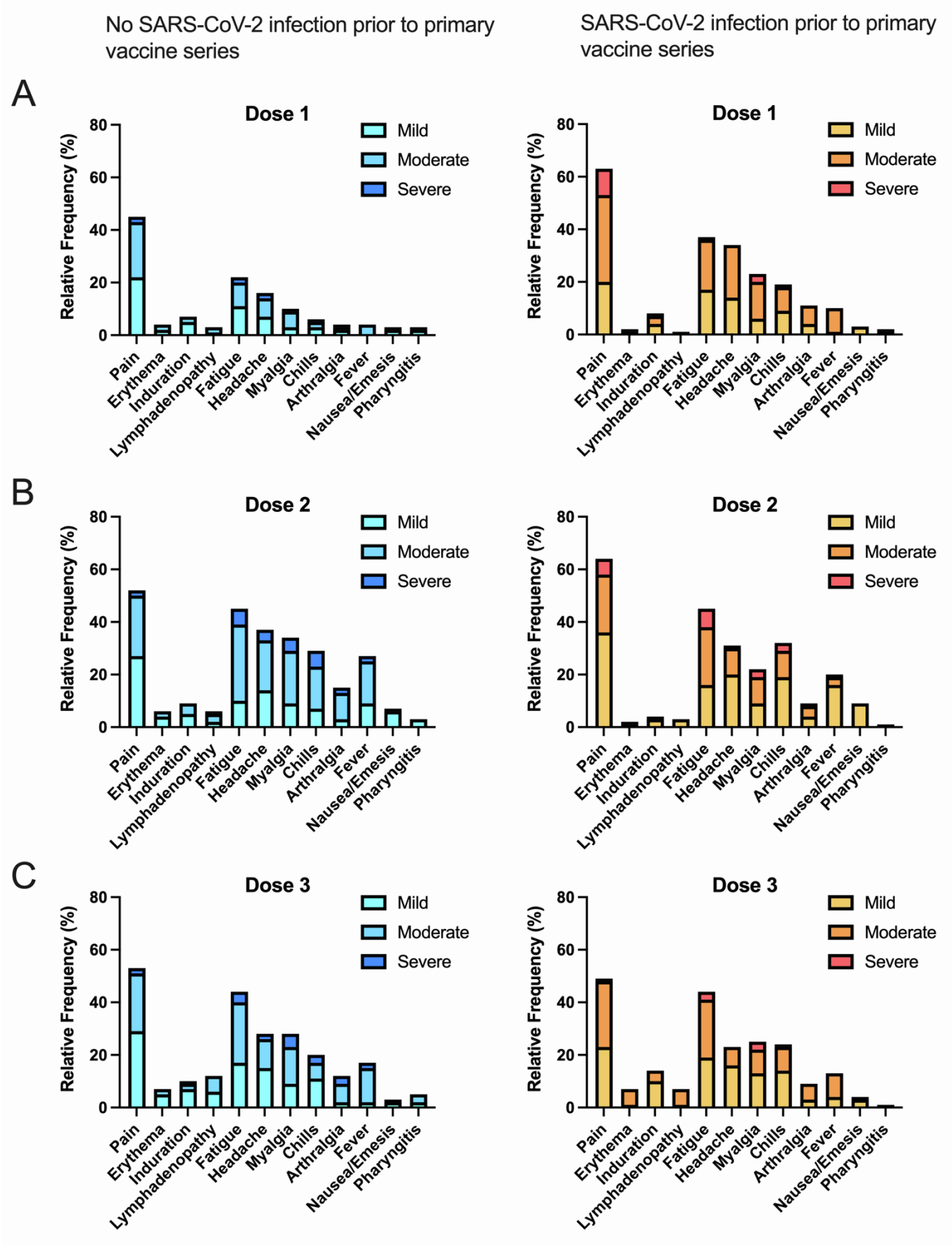
Supplemental Figure 3:



Supplemental Figure 4:



Supplemental Figure 5:



Supplemental Table S2: Akaike Information Criterion (AIC) differences from best-fit model for each dataset (related to Fig. 3).

Group	Two-Component	Power Law	Simple Exponential Decay
Post-Vaccine, Vaccine-Only	0	261.1	427.9
Post-Vaccine, Hybrid Immunity	0	77.5	336.6
Post-Boost, Vaccine-Only	0	135.9	33.8
Post-Boost, Hybrid Immunity	0	48	3.8

Supplemental Table S3: Distributions of vaccination series and infection histories in side effect survey respondents (related to Fig. 5 and Fig. S5).

Infection History	Vaccination Series	Male	Female	Unknown	Total
Naïve (N=149)	Pfizer BNT162b2	26	73	1	100
	Moderna mRNA-1273	12	24	1	37
	Heterogenous	6	5	1	12
Hybrid Immunity (N=63)	Pfizer BNT162b2	15	27	1	43
	Moderna mRNA-1273	1	7	0	8
	Heterogenous	5	7	0	12
Breakthrough Infection (N=11)	Pfizer BNT162b2	1	9	0	10
	Moderna mRNA-1273	0	1	0	1
	Heterogenous	0	0	0	0
Pre-Vaccine and Breakthrough Infection (N=5)	Pfizer BNT162b2	1	3	0	4
	Moderna mRNA-1273	0	1	0	1
	Heterogenous	0	0	0	0
Total		67	157	4	228

Supplemental Table 4: Symptom frequency after any dose, stratified by serostatus pre-vaccine and vaccine type (Moderna mRNA-1273, Pfizer BNT162b2, related to Fig. 5 and Fig. S5).

	Serostatus by Vaccine Type				**Total by Vaccine Type**		**Total by Serostatus**	
	Naïve (N=160)		**Hybrid Immunity (N=68)**		**Total (N=228)**		**Total (N=228)**	
	Moderna (N=42)	**Pfizer (N=118)**	**Moderna (N=15)**	**Pfizer (N=53)**	**Moderna (N=57)**	**Pfizer (N=171)**	**Naïve (N=160)**	**Hybrid Immunity (N=68)**
Local Symptoms (n [%])								
Pain	33 (79)	86 (73)	14 (93)	41 (77)	47 (82)	127 (74)	119 (74)	55 (81)
Erythema	7 (17)	14 (12)	3 (20)	5 (9)	10 (18)	19 (11)	21 (13)	8 (12)
Induration	11 (26)	17 (14)	7 (47)	7 (13)	18 (32)	24 (14)	28 (18)	14 (21)
Lymphadenopathy	4 (10)	23 (19)	1 (7)	4 (8)	5 (9)	27 (16)	27 (17)	5 (7)
Other	1 (2)	6 (5)	4 (27)	1 (2)	5 (9)	7 (4)	7 (4)	5 (7)
Any Local	33 (79)	90 (76)	14 (93)	42 (79)	47 (82)	132 (77)	123 (77)	56 (82)
Systemic Symptoms (n [%])								
Fatigue	24 (57)	80 (68)	13 (87)	31 (58)	37 (65)	111 (65)	104 (65)	44 (65)
Headache	27 (64)	56 (47)	9 (60)	25 (47)	36 (63)	81 (47)	83 (52)	34 (50)
Myalgia	19 (45)	56 (47)	10 (67)	21 (40)	29 (51)	77 (45)	75 (47)	31 (46)
Chills	17 (40)	43 (36)	11 (73)	20 (38)	28 (49)	63 (37)	60 (38)	31 (46)
Arthralgia	14 (33)	19 (16)	7 (47)	7 (13)	21 (37)	26 (15)	33 (21)	14 (21)
Fever	19 (45)	36 (31)	9 (60)	11 (21)	28 (49)	47 (27)	55 (34)	20 (29)
Nausea/Emesis	7 (17)	11 (9)	2 (13)	7 (13)	9 (16)	18 (11)	18 (11)	9 (13)
Pharyngitis	4 (10)	11 (9)	1 (7)	3 (6)	5 (9)	14 (8)	15 (9)	4 (6)
Other	6 (14)	5 (4)	0 (0)	3 (6)	6 (11)	8 (5)	11 (7)	3 (4)
Any Systemic	33 (79)	88 (75)	13 (87)	40 (75)	46 (81)	128 (75)	121 (76)	53 (78)