

Supplement Tables and Figures

Supplementary Table 1: Vaccination, previous SARS-CoV-2, symptom, and treatment data of SARS-CoV-2 enrolled cases, April–November 2023.

	Resident (N=63)	Staff (N=23)	Overall (N=86)
COVID-19 Vaccine Doses			
1-2	9 (14%)	2 (9%)	11 (13%)
3	6 (10%)	4 (17%)	10 (12%)
≥4	43 (68%)	16 (70%)	59 (69%)
Missing	5 (8%)	1 (4%)	6 (7%)
Previous SARS-CoV-2 Diagnoses			
Never	25 (40%)	8 (35%)	33 (38%)
1	16 (25%)	7 (30%)	23 (27%)
2	3 (5%)	3 (13%)	6 (7%)
≥3	2 (3%)	2 (9%)	4 (5%)
Yes, but number of times unknown	9 (14%)	0 (0%)	9 (10%)
Unknown	8 (13%)	2 (9%)	10 (12%)
Missing	0 (0%)	1 (4%)	1 (1%)
Days with Symptoms			
Mean (SD)	4.27 (3.91)	6.39 (4.65)	4.84 (4.20)
Median [Min, Max]	3.00 [0, 14.0]	7.00 [0, 15.0]	4.00 [0, 15.0]
Treatment for Current SARS-CoV-2 Episode			
Molnupiravir	16 (25%)	0 (0%)	16 (19%)

Nirmatrelvir-Ritonavir	7 (11%)	3 (13%)	10 (12%)
No treatment	37 (59%)	18 (78%)	55 (64%)
Missing	3 (5%)	2 (9%)	5 (6%)

Last SARS-CoV-2 Diagnosis Before Current Episode (years)

<2 years prior	12 (19%)	7 (30%)	19 (22%)
≥2 years prior	4 (6%)	2 (9%)	6 (7%)
Missing	47 (75%)	14 (61%)	61 (71%)

Time of Last Vaccine Before Current Episode (years)

<2 weeks	2 (3%)	1 (4%)	3 (3%)
≥2 weeks and <6 months	1 (2%)	2 (9%)	3 (3%)
≥6 months	55 (87%)	17 (74%)	72 (84%)
Missing	5 (8%)	3 (13%)	8 (9%)

Nursing home (NH), standard deviation (SD), minimum (Min), maximum (Max)

Supplementary Table 2: Comorbidities of SARS-CoV-2 enrolled cases, April–November 2023.

	Resident (N=63)	Staff (N=23)	Overall (N=86)
Comorbidity Data Reported	N=61 (97%)	N=9 (39%)	N=70 (81%)
Alcohol Abuse	5 (8%)	0 (0%)	5 (7%)
Anemia	11 (18%)	0 (0%)	11 (16%)
Cardiac Arrhythmia	18 (30%)	0 (0%)	18 (26%)
Cerebrovascular Disease	19 (31%)	0 (0%)	19 (27%)
Coagulopathy	2 (3%)	0 (0%)	2 (3%)

Chronic Pulmonary Disease	19 (31%)	0 (0%)	19 (27%)
Congestive Heart Failure	12 (20%)	0 (0%)	12 (17%)
Connective Tissue Disorder	1 (2%)	0 (0%)	1 (1%)
Dementia	13 (21%)	0 (0%)	13 (19%)
Diabetes (Complicated)	5 (8%)	0 (0%)	5 (7%)
Diabetes (Uncomplicated)	16 (26%)	6 (67%)	22 (31%)
Fluid and Electrolyte Disorders	5 (8%)	0 (0%)	5 (7%)
Gastric or Peptic Ulcer	1 (2%)	0 (0%)	1 (1%)
Hemiplegia	4 (7%)	0 (0%)	4 (6%)
Hypertension	46 (75%)	3 (33%)	49 (70%)
Metastatic Solid Tumor	1 (2%)	0 (0%)	1 (1%)
Moderate or Severe Liver Disease	1 (2%)	0 (0%)	1 (1%)
Moderate or Severe Renal Disease	9 (15%)	0 (0%)	9 (13%)
Myocardial Infarction	5 (8%)	0 (0%)	5 (7%)
Non Metastatic Solid Tumor	1 (2%)	0 (0%)	1 (1%)
Peripheral Vascular Disease	6 (10%)	0 (0%)	6 (9%)
Pulmonary Circulation Disorders	3 (5%)	0 (0%)	3 (4%)
Renal Failure	2 (3%)	0 (0%)	2 (3%)
Comorbidity Data Not Reported	N=2 (3%)	N=14 (61%)	N=16 (19%)

Supplementary Table 3: Demographic information for all participants who enrolled across 24 NHs during April–November 2023.

	Resident (N=275)	Staff (N=312)	Overall (N=587)
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Age (years)

18-39	0 (0%)	97 (31%)	97 (17%)
40-59	14 (5%)	125 (40%)	139 (24%)
60-79	134 (49%)	39 (12%)	173 (29%)
≥80	125 (45%)	1 (0%)	126 (21%)
Missing	2 (1%)	50 (16%)	52 (9%)

Sex

Female	179 (65%)	232 (74%)	411 (70%)
Male	94 (34%)	33 (11%)	127 (22%)
Unknown	0 (0%)	1 (0%)	1 (0%)
Missing	2 (1%)	46 (15%)	48 (8%)

Race

American Indian or Alaska Native	1 (0%)	2 (1%)	3 (1%)
Asian	0 (0%)	11 (4%)	11 (2%)
Black or African American	50 (18%)	100 (32%)	150 (26%)
Native Hawaiian or Other Pacific Islander	0 (0%)	2 (1%)	2 (0%)
White	220 (80%)	124 (40%)	344 (59%)
Multiple race categories selected	1 (0%)	8 (3%)	9 (2%)
Other	0 (0%)	12 (4%)	12 (2%)
Unknown	1 (0%)	6 (2%)	7 (1%)
Missing	2 (1%)	47 (15%)	49 (8%)

Ethnicity

Hispanic	3 (1%)	21 (7%)	24 (4%)
Non-Hispanic	265 (96%)	230 (74%)	495 (84%)
Unknown	5 (2%)	11 (4%)	16 (3%)
Missing	2 (1%)	50 (16%)	52 (9%)

Charlson Comorbidity Index (CCI)¹⁷

Mean (SD)	5.81 (2.33)	0.696 (0.920)	3.32 (3.12)
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Median [Min, Max]	6.00 [1.00, 13.0]	0 [0, 4.00]	3.00 [0, 13.0]
Missing	2 (1%)	52 (17%)	54 (9%)

Nursing homes (NH), standard deviation (SD), minimum (Min), maximum (Max)

Supplementary Table 4: Vaccination and previous SARS-CoV-2 diagnoses of all participants who enrolled during April–October 2023.

	Resident (N=275)	Staff (N=312)	Overall (N=587)
COVID-19 Vaccine Doses			
1-2	19 (7%)	70 (22%)	89 (15%)
3	24 (9%)	88 (28%)	112 (19%)
≥4	220 (80%)	95 (30%)	315 (54%)
Missing	12 (4%)	59 (19%)	71 (12%)
Previous SARS-CoV-2 Diagnoses			
Never	93 (34%)	77 (25%)	170 (29%)
1	83 (30%)	114 (37%)	197 (34%)
2	33 (12%)	49 (16%)	82 (14%)
≥3	9 (3%)	16 (5%)	25 (4%)
Yes, but number of times unknown	36 (13%)	0 (0%)	36 (6%)
Unknown	21 (8%)	9 (3%)	30 (5%)
Missing	0 (0%)	47 (15%)	47 (8%)

Supplementary Table 5: Number of SARS-CoV-2 enrolled cases at each academic partner site, April–November 2023.

	Resident (N=63)	Staff (N=23)	Overall (N=86)
Site (Number of Nursing Homes)			
Site 1 (3)	25 (40%)	4 (17%)	29 (34%)
Site 2 (3)	14 (22%)	6 (26%)	20 (23%)
Site 3 (5)	9 (14%)	0 (0%)	9 (10%)
Site 4 (3)	8 (13%)	9 (39%)	17 (20%)
Site 5 (3)	6 (10%)	0 (0%)	6 (7%)
Site 6 (2)	1 (2%)	0 (0%)	1 (1%)
Site 7 (3)	0 (0%)	2 (9%)	2 (2%)
Site 8 (2)	0 (0%)	2 (9%)	2 (2%)

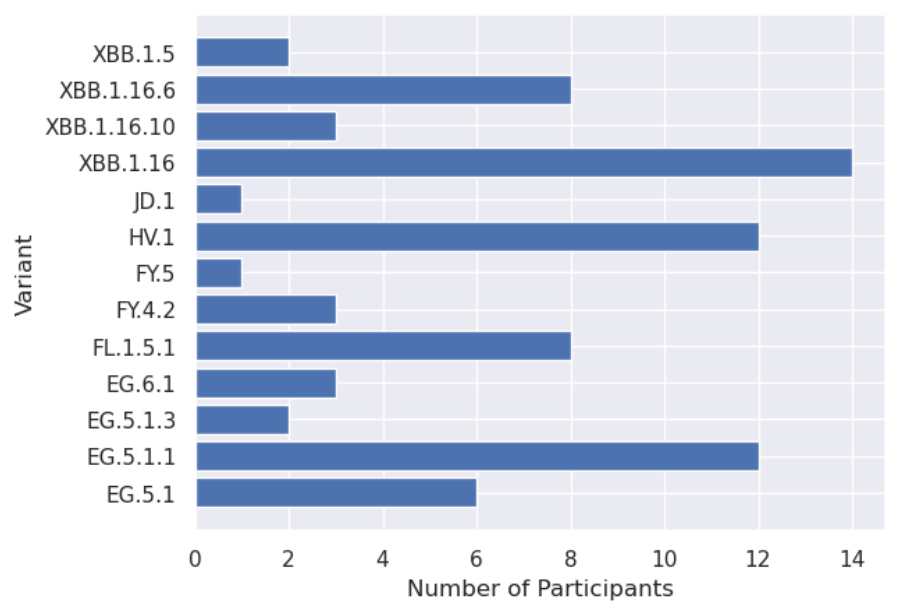
Supplementary Table 6: Number of participants enrolled at each academic partner site, April–November 2023.

	Resident (N=275)	Staff (N=312)	Overall (N=587)
Site (Number of Nursing Homes)			
Site 1 (3)	49 (18%)	23 (7%)	72 (12%)
Site 2 (3)	61 (22%)	108 (35%)	169 (29%)
Site 3 (5)	52 (19%)	18 (6%)	70 (12%)
Site 4 (3)	49 (18%)	39 (12%)	88 (15%)
Site 5 (3)	33 (12%)	29 (9%)	62 (11%)
Site 6 (2)	18 (7%)	13 (4%)	31 (5%)
Site 7 (3)	7 (3%)	60 (19%)	67 (11%)
Site 8 (2)	6 (2%)	22 (7%)	28 (5%)

Supplementary Table 7: List of academic partner sites.

Partner Sites	
Brown University	BU
Case Western Reserve University	CWRU
Emory University	EU
Johns Hopkins University	JHU
Oregon State University	OSU
University of Michigan	UoM
University of Pittsburgh	UoP
University of Wisconsin	UoW

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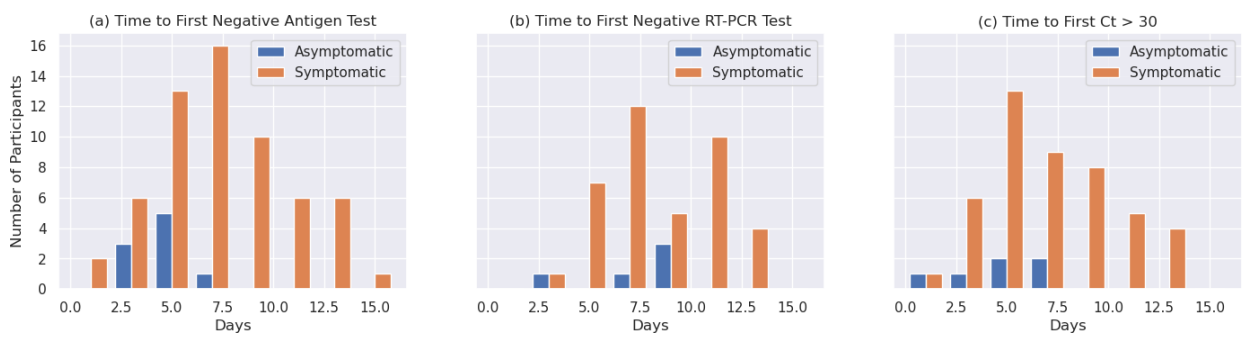
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Supplementary Figure 1: Distribution of SARS-CoV-2 variants among study participants, April–November 2023.

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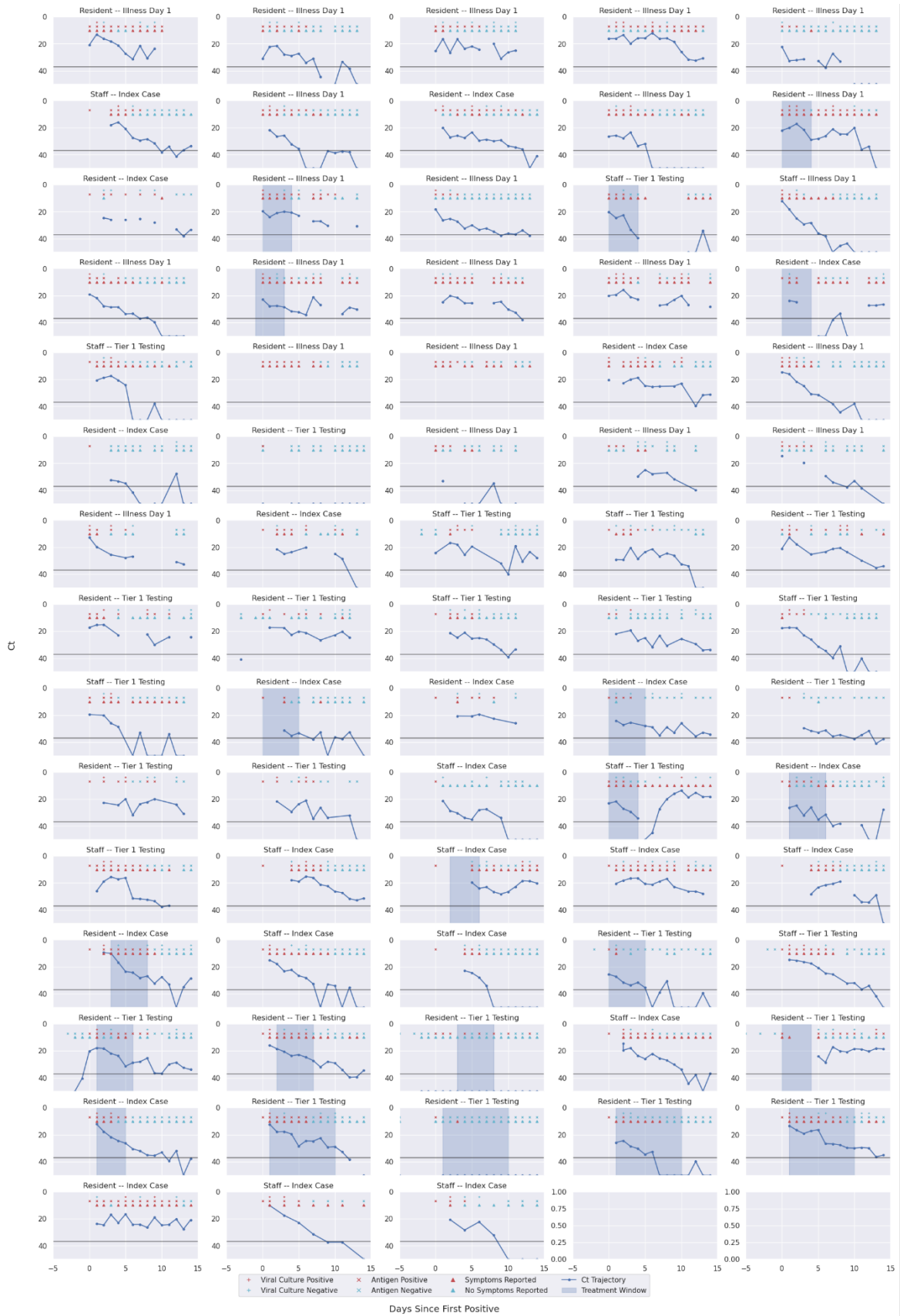
Supplementary Figure 2: Time to first negative test antigen test (a), first negative RT-PCR test (b), and first Ct > 30 (c) for asymptomatic (n = 9) vs symptomatic (n = 62) participants, April–November 2023.

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(a) Distribution of day to first negative antigen test for asymptomatic and symptomatic participants. One symptomatic participant was censored. One symptomatic participant was not included due to lack of follow-up. By the log rank test the differences in the corresponding survival curves are significant ($p < 0.001$). **(b)** Distribution of day to the first negative RT-PCR test for asymptomatic and symptomatic participants. Fourteen symptomatic participants and two asymptomatic participants were censored. Nine symptomatic participants and two asymptomatic participants were not included due to lack of follow-up or lack of initial RT-PCR positive result. By the log rank test the differences in the corresponding survival curves are not significant ($p = 0.994$). **(c)** Distribution of day to the first Ct > 30 test for asymptomatic and symptomatic participants. Five symptomatic participants and no asymptomatic participants were censored. Eleven symptomatic participants and three

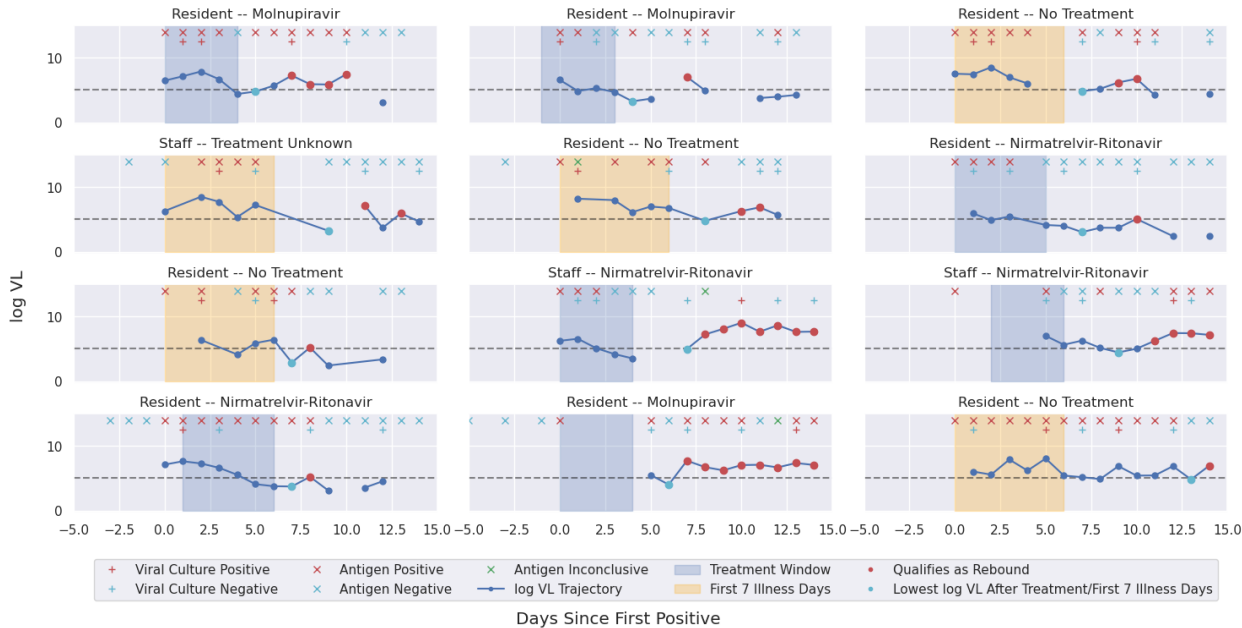
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43 asymptomatic participants were not included due to lack of follow up or lack of initial $Ct < 30$. By
44 the log rank test the differences in the corresponding survival curves are significant ($p = 0.013$).
45 Reverse transcription polymerase chain reaction (RT-PCR), cycle threshold (Ct)
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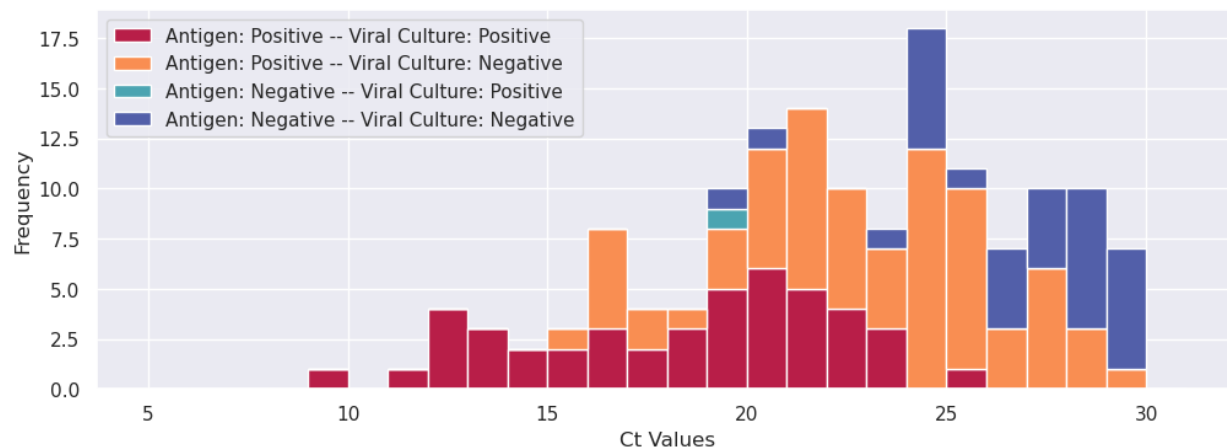


Supplementary Figure 3: Ct trajectories, antigen results, viral culture results, treatment with an antiviral, and symptoms over time, April–November 2023. Title for individual plots is the participant type and the participants tier at the time of first positive test result.

Cycle threshold (Ct)

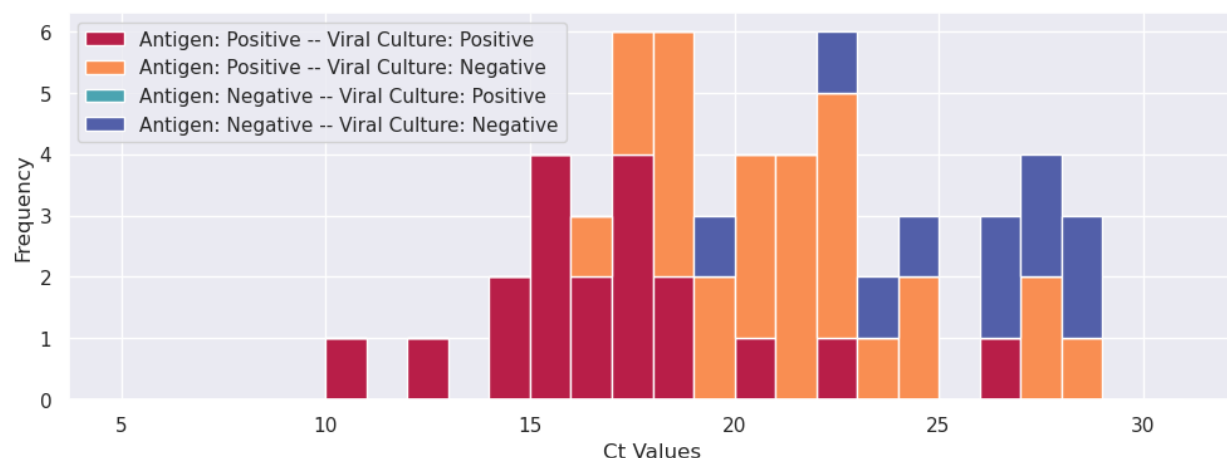


Supplementary Figure 4: Trajectories of log viral load of participants who met the criteria for rebound, April–November 2023. Individual log viral load (VL) trajectories are plotted in blue. Antiviral treatment period, antigen results, and viral culture results are included. The horizontal dashed line is at 5 log copies / ml which is the amount the viral load must pass to be considered rebound. Nine residents and three staff met the criteria for rebound. Ct measurements that qualify a participant for rebound are plotted in red. To meet the criteria for rebound a Ct value must be a 10-fold increase to or above five log copies per mL from the lowest measured Ct value (plotted in cyan) after the completion of SARS-CoV-2 antiviral treatment or, if untreated, seven days after the initial positive test.



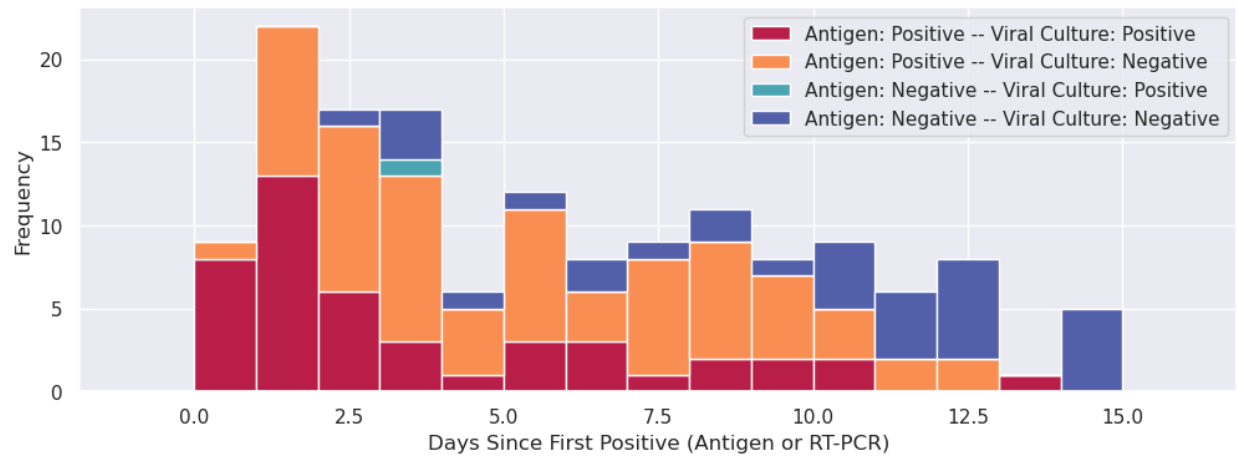
Supplementary Figure 5: Concordance between antigen and viral culture results by Ct value for resident participants, April–November 2023. Dark red denotes both antigen and viral culture results are positive while purple denotes that both antigen and viral culture results are negative. There are higher levels of positive agreement at lower Ct values and higher levels of negative agreement at higher Ct values.

Cycle threshold (Ct)

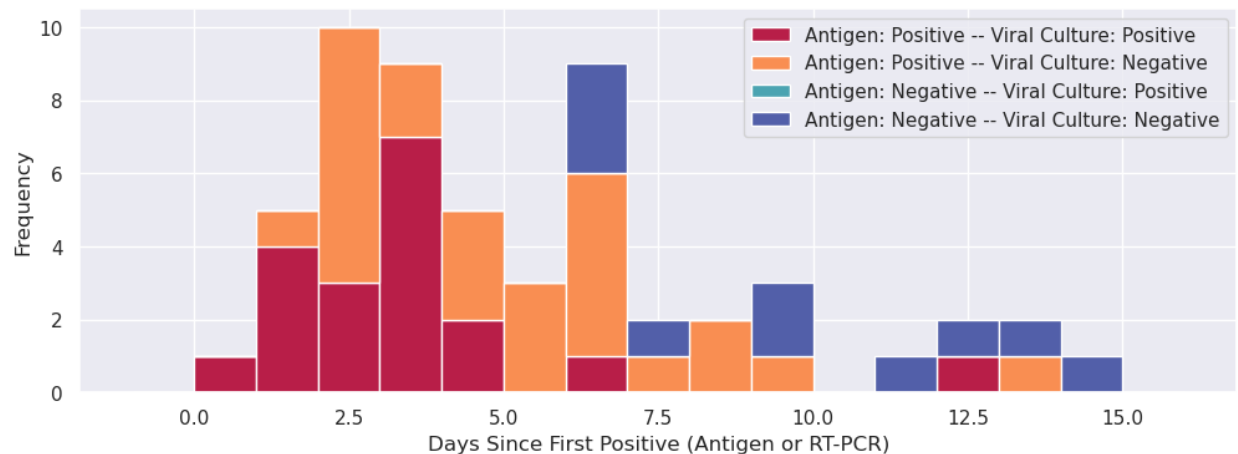


Supplementary Figure 6: Concordance between antigen and viral culture results by Ct value for staff participants, April–November 2023. Dark red denotes both antigen and viral culture results are positive while purple denotes that both antigen and viral culture results are negative. There are higher levels of positive agreement at lower Ct values and higher levels of negative agreement at higher Ct values.

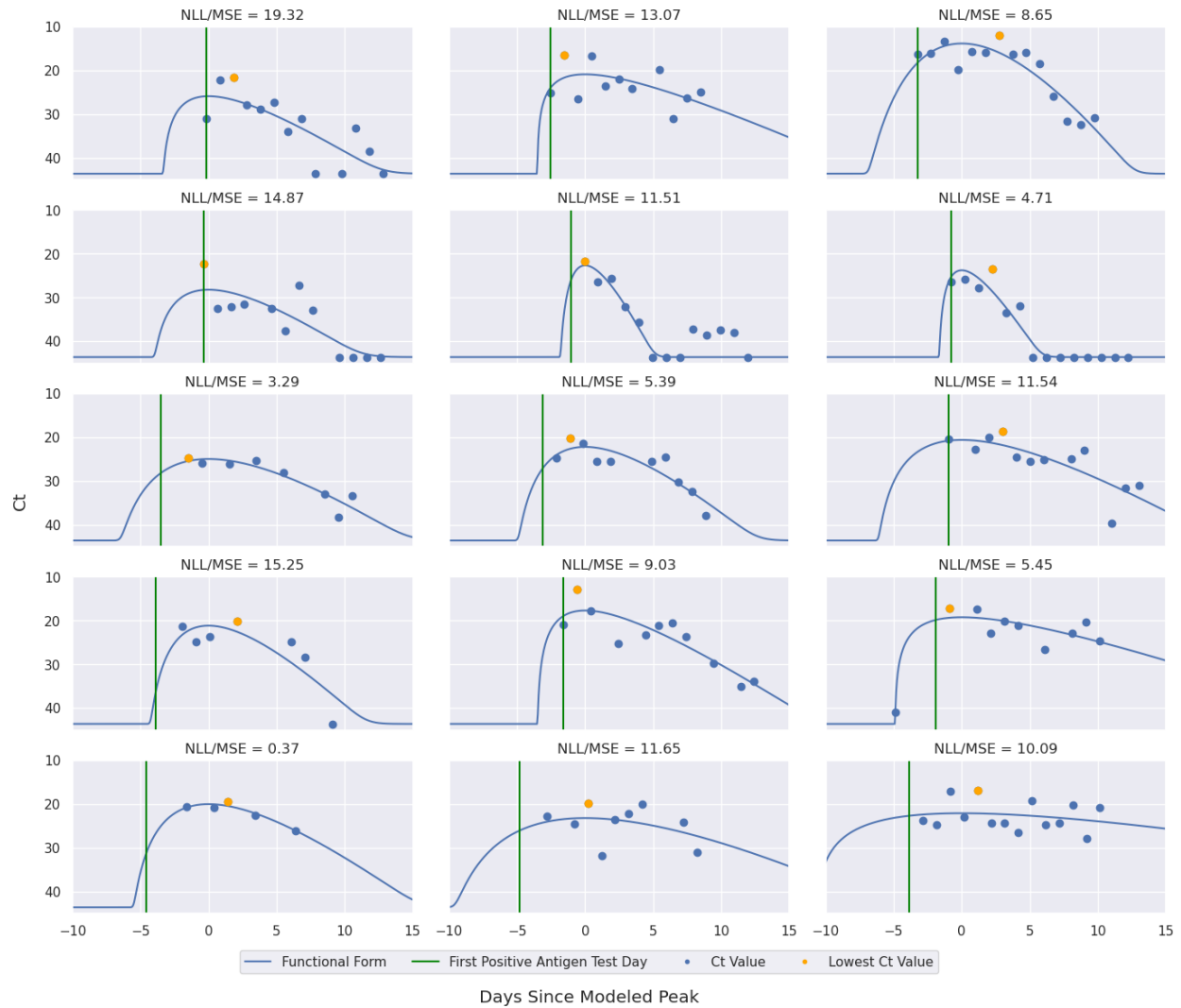
Cycle threshold (Ct)



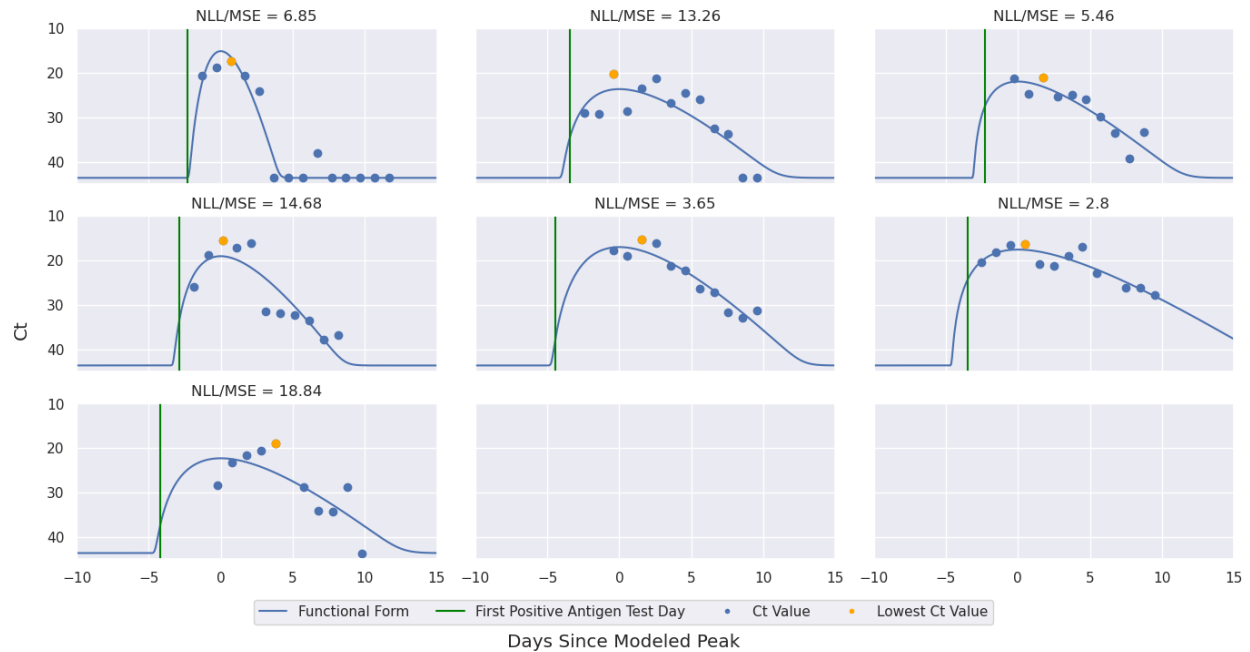
Supplementary Figure 7: Concordance between antigen and viral culture results over time for resident participants, April–November 2023. Dark red denotes both antigen and viral culture results are positive while purple denotes that both antigen and viral culture results are negative. There are higher levels of positive agreement early in time and higher levels of negative agreement later in time. The viral culture positive after day 10 was a resident who experienced rebound.



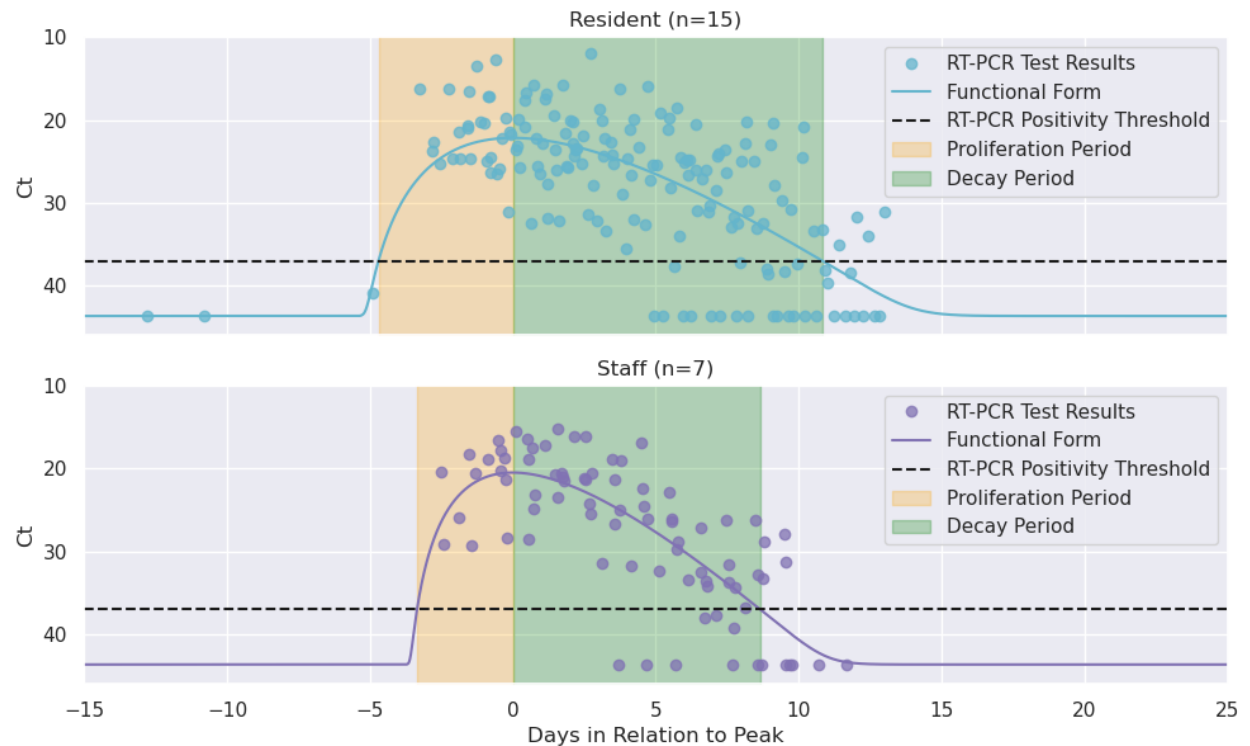
Supplementary Figure 8: Concordance between antigen and viral culture results over time for staff participants, April–November 2023. Dark red denotes both antigen and viral culture results are positive while purple denotes that both antigen and viral culture results are negative. There are higher levels of positive agreement early in time and higher levels of negative agreement later in time. The viral culture positive after day 10 was a resident who experienced rebound.



Supplementary Figure 9: Modeled Ct Trajectories of Residents with At Least One Data Point Before Modeled Peak, April–November 2023. Modeled resident Gamma distribution functional forms and measured Ct values are plotted in blue. The lowest measured Ct value is plotted in orange. The day of the first positive antigen test is denoted by the vertical green line. All plotted Gamma distribution functional forms are plotted such that the modeled peak is aligned with $t=0$.

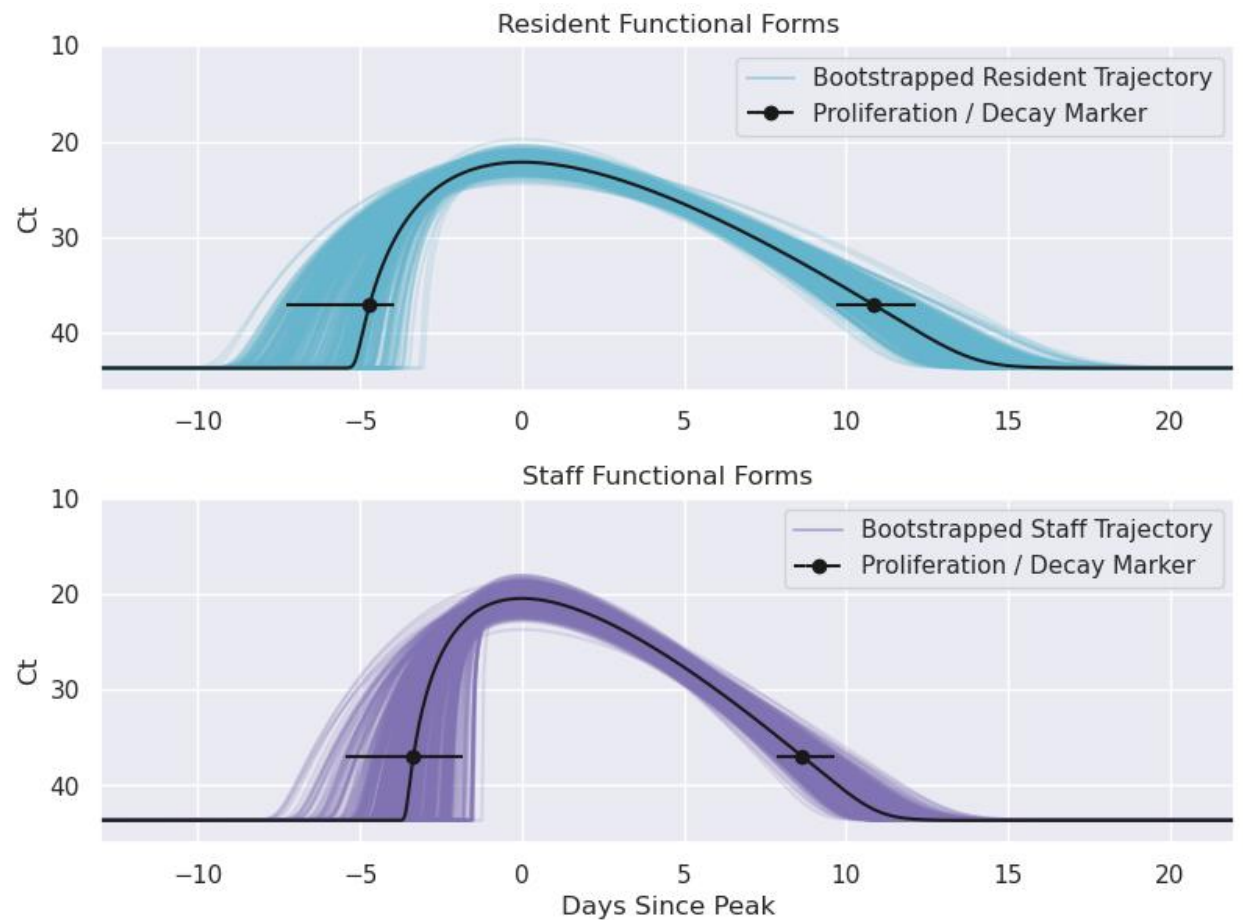


Supplementary Figure 10: Modeled Ct Trajectories of Staff with At Least One Data Point Before Modeled Peak, April–November 2023. Modeled staff Gamma distribution functional forms and measured Ct values are plotted in blue. The lowest measured Ct value is plotted in orange. The day of the first positive antigen test is denoted by the vertical green line. All plotted Gamma distribution functional forms are plotted such that the modeled peak is aligned with $t=0$.

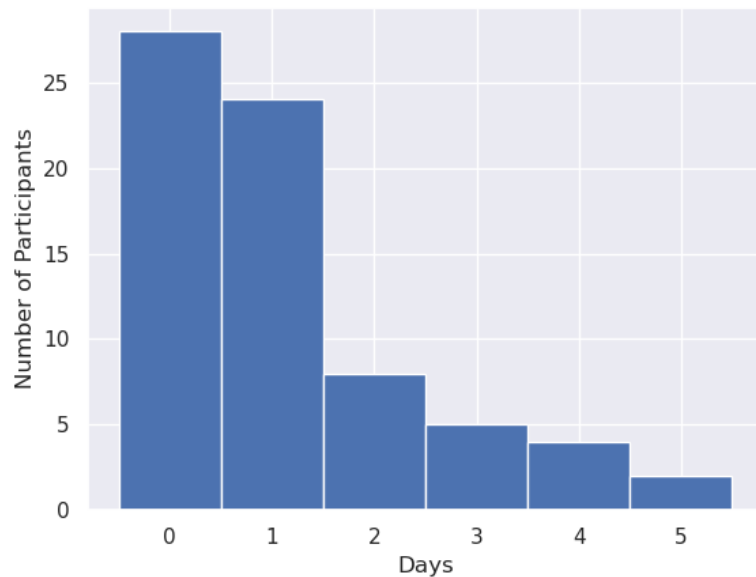


Supplementary Figure 11: Population Level Gamma Distribution Functional Form for Residents and Staff, April–November 2023. Resident (in blue) and staff (in purple) population level gamma distribution functional forms. The Ct measurements are plotted in the dots of the corresponding color. The dashed line shows the RT-PCR positivity threshold. The proliferation period is shaded in orange and the decay period is shaded in green.

Reverse transcription polymerase chain reaction (RT-PCR), cycle threshold (Ct)



Supplementary Figure 12: Gamma Distribution Functional Forms for Residents and Staff fit to bootstrapped data, April–November 2023. We show the resident (blue) and staff (purple) population-level Gamma distribution functional forms fitted to bootstrapped data. The bootstrapped data was randomly sampled from the 15 residents and seven staff who met criteria for individual functional form fitting and inclusion in the population level model. The functional forms fitted from the original data is plotted in black. The black dots denote where the proliferation periods began, and the decay period ended while the lines correspond to the non-parametric 95% confidence intervals.



Supplementary Figure 13: Distribution of time to first RT-PCR test after testing positive, April–November 2023. Most participants received an RT-PCR test within one day of initial positive (day 0: 28/73, 38%, day 1: 24/73, 33%). Two participants never received an RT-PCR test.

Reverse transcription polymerase chain reaction (RT-PCR)

Supplemental Information on the Gamma Distribution Functional Form

Individual Fits

Individualized Gamma distribution functional forms were fitted to participants who had a minimum of 5 measured Ct values and were not treated with antivirals. There are 27 residents and 16 staff that meet these criteria. Participants with negative RT-PCR test result but no Ct values were filled with Ct values that were approximately $\log VL \sim 0$. Participants with Ct values larger than $\log VL \sim 0$ were filled with Ct values that were approximately $\log VL \sim 0$. Individual participant data was fit using the following equation for the gamma distribution functional form:

$$\widehat{Ct}_i(t; \beta_i, k_i, \theta_i, loc_i) = -\log_2(\beta_i F(t_i; k_i, \theta_i, loc_i) + 2^{\log VL \sim 0}) \text{ where:}$$

- $F(t_i; k_i, \theta_i, loc_i)$ is the underlying Gamma distribution modeling viral load with individual-level shape, scale, and location parameters k_i, θ_i, loc_i .
- β_i is a coefficient that scales the infectiousness profile to the Ct values
- $\log VL \sim 0$ is Ct value that corresponds to a log VL of 0

Parameters $(\beta_i, k_i, \theta_i, loc_i)$ are learned for each participant by minimizing the negative log-likelihood (NLL). This is equivalent to minimizing the mean squared error (MSE) as we assume the errors are normally distributed. This is also equivalent to maximizing the likelihood. We use constrained optimization with the following initial conditionals and bounds.

Initial conditions and bounds:

- $k_i \sim Unif(5, 15)$ $k_i \in [1.5, \infty)$
- $\theta_i = \frac{5}{k_i - 1}$ $\theta_i \in [0, \infty)$
- $loc_i = -3$ $loc_i \in [t_{i0}^+ - 7, t_{i0}^+ - 1]$
- $\beta_i \sim Unif(2^{-23}, 2^{-10})$ $\beta_i \in [0, 1]$
- t_{i0}^+ is the day of the first positive test. If a participant tests antigen positive and RT-PCR positive on the same day, then $t_{i0}^+ = 0$. If a participant tests antigen positive before testing RT-PCR positive, then $t_{i0}^+ < 0$. Distribution of time to first RT-PCR test after initial positive test is shown in Supplemental Figure 10.

We bound k_i , the shape parameter of the gamma distribution, to be ≥ 1.5 because a shape parameter of 1 would make the distribution exponential. This would imply no viral proliferation period, which is not biologically feasible. We bound θ_i , the scale parameter of the gamma distribution, to be > 0 , this is a requirement of the distribution parameter. We bound loc_i , the location parameter of the Gamma distribution, to be one day to one week before the first positive test result. If a participant tests antigen positive before testing RT-PCR positive there will be no Ct value, but we would expect the Gamma distribution to be defined on this day. Since the Gamma distribution is only defined for $t \geq loc_i$, loc_i must be at least one day and up to a week before the first positive test. Finally, we bound β_i , the coefficient parameter, to be between zero and one. A coefficient of zero would force the functional form to be flat with a Ct value that is approximately $\log VL \sim 0$. A coefficient of one would require the peak of the underlying Gamma distribution to be approximately $1.4 \cdot 10^{-3}$ to achieve a Ct = 9.48, the lowest measured Ct value. With this peak value it would take over 357 days to capture less than 50%

172 of the area under the distribution curve. Given the Kaplan-Meier survival analysis, this would be
 173 unreasonable. In order to match the height of the functional form to match the peak Ct value, β_i
 174 must be small.

175 For each participant we run the optimization with ten randomized initial conditions, drawn from
 176 the above distributions or set to give values. Out of the optimizations that converge, we use the
 177 parameters that correspond to the smallest NLL. Since there is significant left censoring in the
 178 data, several of the learned distributions are only fit to the decaying section of the gamma
 179 distribution and some fits resulted in nearly nonexistent proliferation periods and/or modeled Ct
 180 values < 0 , which is biologically implausible.

181 To focus on learned functional forms that capture some element of both the proliferation and
 182 decay period, we restrict to participants where there is at least one measured data point before
 183 the learned peak of the Gamma distribution functional form. There are 15 residents and 7 staff
 184 profiles that meet this requirement. We center the data so that the functional form peak is at $t =$
 185 0. This is accomplished by shifting each participant's timeframe by $(k_i - 1)\theta_i$, which is a
 186 function of the shape and scale parameters of their individually fit Gamma distribution functional
 187 form.

188 Population Fits

189 The population gamma distribution functional forms were fitted similarly to the individual level
 190 forms with a slight modification. Instead of including a location parameter, we pin the peak of the
 191 functional form to occur at $t = 0$ by shifting the input t by $(k - 1)\theta$. Here k and θ are population
 192 level shape and scale parameters that are shared across participant group (residents vs. staff).

193 $\widehat{Ct}(t; \beta, k, \theta) = -\log_2(\beta F(t + (k - 1)\theta; k, \theta) + 2^{\log VL \sim 0})$ where:

- 194 • $F(x; k, \theta)$ is the underlying gamma distribution modeling infectiousness with shape and
 195 scale parameters k, θ .
- 196 • β is a coefficient that scales the infectiousness profile to the Ct values
- 197 • $\log VL \sim 0$ is Ct value that corresponds to a log VL of 0

198 Parameters (β, k, θ) are learned using a negative log-likelihood approach which simplifies to the
 199 sum of squared errors (in the code we take the mean). We use constrained optimization with the
 200 following initial conditionals and bounds.

201 Initial conditions and bounds:

- 202 • $k \sim Unif(5, 15)$ $k \in [1.5, \infty)$
- 203 • $\theta = \frac{5}{k-1}$ $\theta \in [10^{-5}, \infty)$
- 204 • $\beta \sim Unif(2^{-23}, 2^{-10})$ $\beta \in [0, 1]$

205 The initial conditions and bounds are very similar to the individual function forms. A slight
 206 modification was made to the θ lower bound to ensure convergence.

207 Nonparametric confidence intervals were calculated for the resident and staff populations using
 208 resampling. The data shown in Supplementary Figure 11 was bootstrapped 1000 times and

209 Gamma distribution functional forms were fitted for each data set. The proxies for the
210 proliferation period and decay period were calculated for each functional form. Proliferation and
211 decay period were calculated as described in the Methods section of the main manuscript. The
212 95% confidence intervals were calculated to capture 95% of the 1000 proliferation and decay
213 periods.

214 The Gamma distribution functional forms were fitted using Python 3.9.13 and packages numpy
215 (1.23.2), pandas (1.4.3), and scipy (1.9.0).

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