

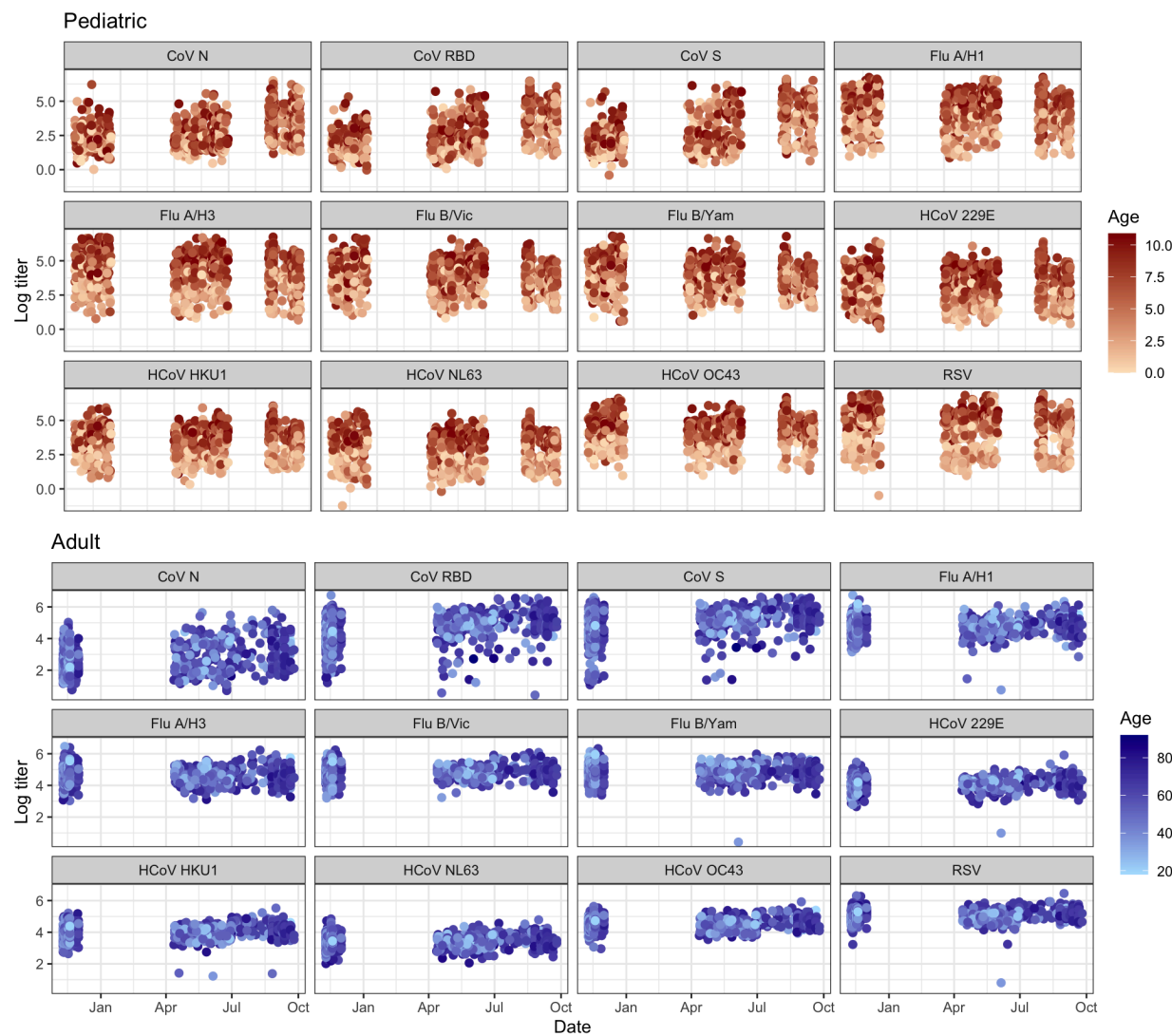
Supplementary Information: Multiplex serology reveals age-specific immunodynamics of respiratory pathogens in the wake of the COVID-19 pandemic

Supplementary Table 1

Counts by pathogen and age group			
Age group	2020 (N)	2021 (N)	2022 (N)
<1	40	42	19
1-2	70	78	61
3-4	47	69	57
5-10	166	196	154
18-49	–	128	99
50-64	–	147	134
65+	–	141	153

King County serology. Number of study participants by pathogen and age group assessed in King County, WA at the 2020, 2021, and 2022 sampling points. Participants are disaggregated by age group: <1, 1-2, 3-4, 5-10, 18-49, 50-64, and 65+.

Supplementary Fig. 1



Individual serological data in King County, WA. Individual serological data points plotted for pediatric population (top) and adult population (bottom) for each antigen against time. The color of the point corresponds to the age of the individual who provided the sample, as denoted by the figure legend.

Supplementary Table 2

Pathogen	<1 yo	1-2 yo	3-4 yo	5-10 yo
CoV-HKU1 Spike	0.1850	0.0006**	0.3516	0.4177
CoV-OC43 Spike	0.3068	0.0013*	0.0558	0.0644
Flu B Brisbane	0.1570	0.0101*	0.4138	0.0744
Flu-B-Phuket	0.2657	0.0213*	0.6430	0.0732
Flu-H1-Michigan	0.0292*	0.0120*	0.0587	0.5285
Flu-H3-HongKong	0.1007	0.0051*	0.0554	0.0595
HCoV NL63 Spike	0.0132*	0.0015*	0.0009**	0.0050*
HCoV-229E Spike	0.0130*	0.0008**	0.0013*	0.1574
RSV Pre-F	0.2251	0.0007**	0.0007*	0.0035*
SARS-CoV-2 N	0.3231	0.2574	0.3911	0.5299
SARS-CoV-2 RBD	0.2194	0.3259	0.2312	0.0586
SARS-CoV-2 Spike	0.1197	0.1934	0.2230	0.0256*

Assessing immunity debt in King County, WA, 2020-2021. Kolmogorov-Smirnov two-sided p-value results by antigen and age group comparing antibody concentration levels in 2021 to 2020 baseline for children <10 yo. 2020 represents a baseline here given that serological samples were collected shortly following a pre-pandemic respiratory season. * denotes a significant difference between antibody concentration levels by year (p-value < .05) and ** denotes a significant difference after adjustment for multiple comparisons (p-value < .00125).

Supplementary Table 3

Pathogen	<1 yo	1-2 yo	3-4 yo	5-10 yo
CoV-HKU1 Spike	0.137	0.064	0.125	0.057
CoV-OC43 Spike	0.475	0.372	0.235	0.200
Flu B Brisbane	0.020*	0.056	0.380	0.008*
Flu-B-Phuket	0.043*	0.107	0.834	0.002*
Flu-H1-Michigan	0.058	0.010*	0.045*	0.067
Flu-H3-HongKong	0.048*	0.143	0.001**	0.040*
HCoV NL63 Spike	0.252	0.302	0.043*	0.609
HCoV-229E Spike	0.161	0.122	0.530	0.547
RSV Pre-F	0.034*	0.114	0.004*	0.317
SARS-CoV-2 N	0.003*	0.000**	0.000**	0.000**
SARS-CoV-2 RBD	0.000**	0.000**	0.000**	0.000**
SARS-CoV-2 Spike	0.000**	0.000**	0.000**	0.000**

Assessing immunity debt in King County, WA, 2020-2022. Kolmogorov-Smirnov two-sided p-value results by antigen and age group comparing antibody concentration levels in 2022 to 2020 baseline for children <10 yo. 2020 represents a baseline here given that serological samples were collected shortly following a pre-pandemic respiratory season. * denotes a significant difference between antibody concentration levels by year (p-value < .05) and ** denotes a significant difference after adjustment for multiple comparisons (p-value < .00125).

Supplementary Table 4

Age group and pathogen	Antibody boost, 95% credible interval	Waning, 95% credible interval	N individuals (samples per person)
Study site: South Africa			
< 5 yo A/H3	5.50 (5.09, 5.87)	.13 (.08, .16)	91 (2)
< 5 yo A/H1	5.86 (5.31, 6.40)	0.09 (0.00, 0.15)	90 (2)
< 5 yo B/Vic	3.87 (3.12, 4.71)	.13 (.03, .21)	90 (2)
< 5 yo B/Yam	4.66 (4.17, 5.14)	.17 (.07, .25)	90 (2)
5-10 yo A/H3	2.90 (2.67, 3.13)	0.08 (0.06, 0.09)	285 (2)
5-10 yo A/H1	2.88 (2.67, 3.09)	0.04 (0.00, 0.07)	285 (2)
5-10 yo B/Vic	2.14 (1.85, 2.45)	0.04 (0.01, 0.07)	285 (2)
5-10 yo B/Yam	3.17 (2.75, 3.83)	0.09 (0.07, 0.11)	285 (2)
11-18 yo A/H3	2.30 (1.88, 2.71)	0.04 (0.03, 0.06)	445 (2)
11-18 yo A/H1	2.49 (2.14, 2.75)	0.05 (0.04, 0.06)	445 (2)
11-18 yo B/Vic	2.31 (2.01, 2.67)	0.06 (0.04, 0.07)	445 (2)

11-18 yo B/Yam	2.68 (2.23, 3.19)	0.06 (0.03, 0.08)	445 (2)
18 + A/H3	3.73 (3.52, 3.93)	0.05 (0.04, 0.05)	653 (2)
18 + A/H1	3.62 (3.48, 3.80)	0.05 (0.04, 0.06)	653 (2)
18+ B/Vic	2.77 (2.56, 2.99)	0.05 (0.05, 0.06)	653 (2)
18+ B/Yam	3.13 (2.95, 3.31)	0.06 (0.05, 0.07)	653 (2)
Study site: King County, WA			
<5 yo A/H3	4.47 (3.84, 5.72)	.16 (.05, .27)	396 (1)
<5 yo A/H1	4.11 (3.72, 4.57)	.21 (.13, .28)	406 (1)
<5 yo B/Vic	3.97 (3.42, 4.61)	.16 (.08, .24)	407 (1)
<5 yo B/Yam	4.47 (4.12, 4.84)	.25 (.18, .32)	412 (1)
<5 yo RSV	4.67 (4.29, 5.09)	0.07 (0.02, 0.12)	434 (1)
<5 yo CoV N	4.77 (4.38, 5.17)	.15 (.01, .36)	422 (1)
<5 yo CoV Spike	4.97 (4.75, 5.21)	0.05 (0.00, 0.10)	429 (1)
<5 yo CoV RBD	4.86 (4.60, 5.11)	0.11 (0.05, 0.19)	437 (1)

<5 yo HCoV 229E	4.73 (3.94, 5.33)	0.15 (0.09, 0.26)	403 (1)
<5 yo HCoV NL63	4.09 (3.85, 4.38)	0.03 (0.00, 0.08)	397 (1)
<5 yo HCoV OC43	4.36 (3.01, 4.86)	0.14 (0.09, 0.19)	334 (1)
< 5 yo HCoV HKU1	4.06 (3.68, 4.46)	0.06 (0.00, 0.13)	419 (1)
18+ yo A/H3	1.88 (1.53, 2.05)	0.01 (0.00, 0.01)	253 (2)
18+ yo A/H1	1.90 (1.57, 2.08)	0.07 (0.05, 0.08)	254 (2)
18+ yo B/Vic	1.65 (1.62, 1.69)	0.01 (0.01, 0.01)	253 (2)
18+ yo B/Yam	1.36 (1.26, 1.55)	0.03 (0.02, 0.06)	254 (2)
18+ yo RSV	2.66 (2.50, 2.72)	0.01 (0.01, 0.01)	253 (2)
18+ yo CoV N	4.02 (3.84, 4.21)	0.08 (0.01, 0.16)	245 (2)
18+ yo CoV Spike	9.35 (8.95, 9.84)	0.02 (0.00, 0.07)	243 (2)
18+ yo CoV RBD	9.99 (9.34, 10.77)	0.08 (0.00, 0.28)	245 (2)
18+ yo HCoV 229E	1.62 (1.14, 2.50)	0.01 (0.01, 0.02)	245 (2)
18+ yo HCoV NL63	1.25 (1.14, 1.42)	0.03 (0.00, 0.09)	244 (2)

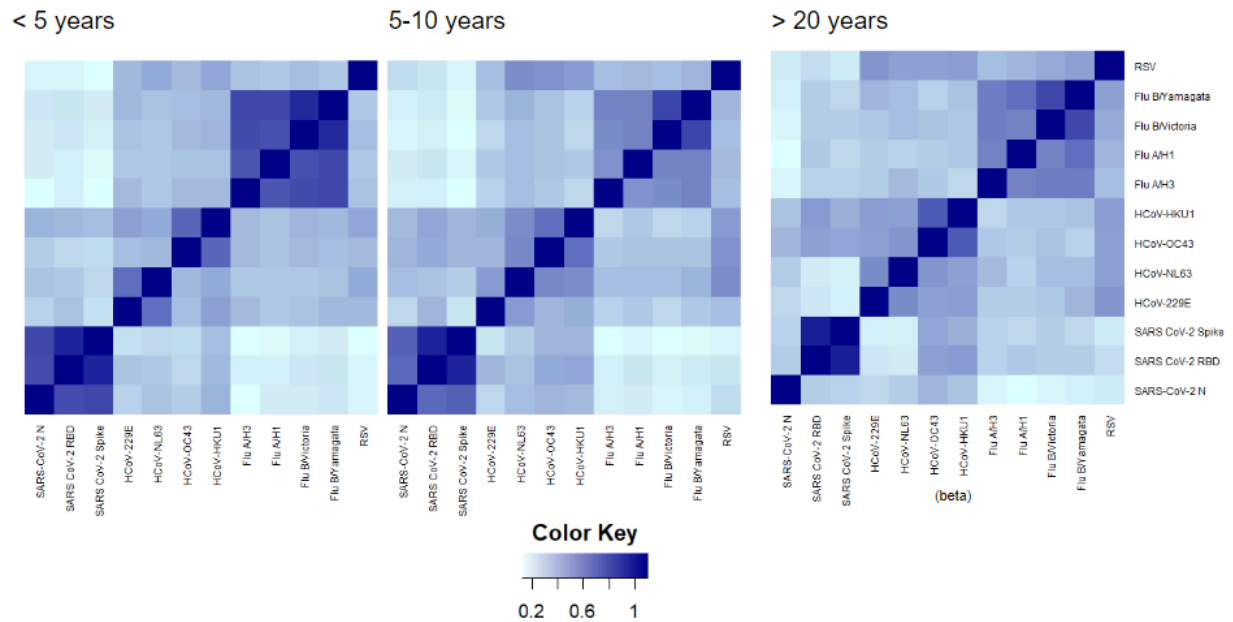
18+ yo HCoV OC43	1.23 (1.12, 1.73)	0.01 (0.00, 0.04)	243 (2)
18+ yo HCoV HKU1	2.55 (2.40, 2.80)	0.01 (0.01, 0.02)	246 (2)

Antibody kinetics estimation based on the Serosolver model. Model estimates for antibody boost, waning rate, and sample size for each age group, location, and pathogen analyzed. Models were run with a minimum of three chains and 500,000 iterations per chain.

Supplementary Methods 1

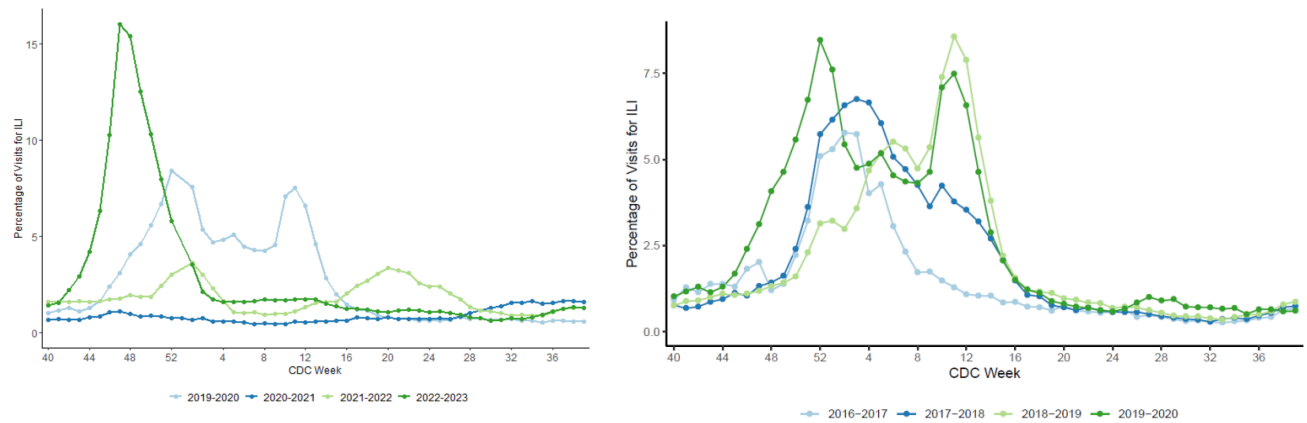
We used the serosolver modeling framework to interrogate whether differences in age-specific waning rates may be biased by age-specific difference in infection rates. We set up an experiment where we fixed the prior on the infection rate to be the same between children and adults at 10% and then another where we set the infection rates to be 2x higher in children than adults based on plausible upper bound differences from published serological studies. We tested our experiment with the influenza AH3 data from King County. We found that under the scenario where infection rates for children were 2x that of adults (mean attack rate over time = 20%), the waning rate was 0.19 (CrI: 0.14, 0.26), compared to 0.16 (CrI: 0.05, 0.27) for the scenario where we fixed the mean attack rate to be 10%. These estimates overlapped in their credible intervals and were significantly greater than the waning rate estimated for adults. These findings suggest quicker waning estimates for children are robust to a range of plausible attack rates.

Supplementary Fig. 2



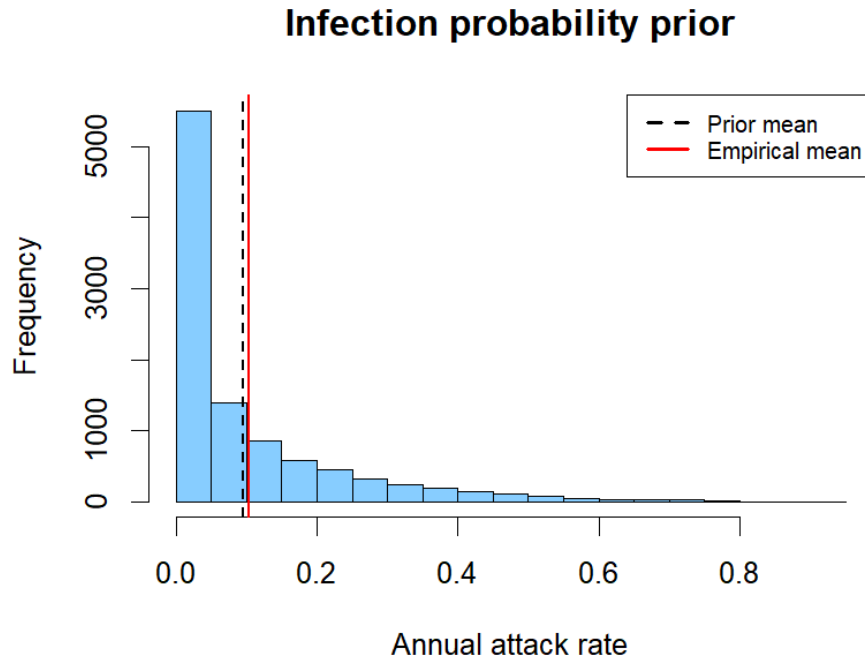
Pairwise correlations in antibody concentration levels. Each panel represents the correlation between antibody levels for two pathogens in the same individual at any of the sampled time points, grouped by age band: <5 years, 5-10 years, > 20 years in King County, WA. Darker blue represents higher correlations, more prominently shown across SARS-CoV-2 antigens, alpha and beta coronavirus antigens, and influenza antigens.

Supplementary Fig. 3



Seasonal incidence of influenza-like illness (ILI) in WA. Percentage of clinic visits positive for ILI in the state of Washington from 2016-2020 and 2019-2023 as reported by CDC surveillance.

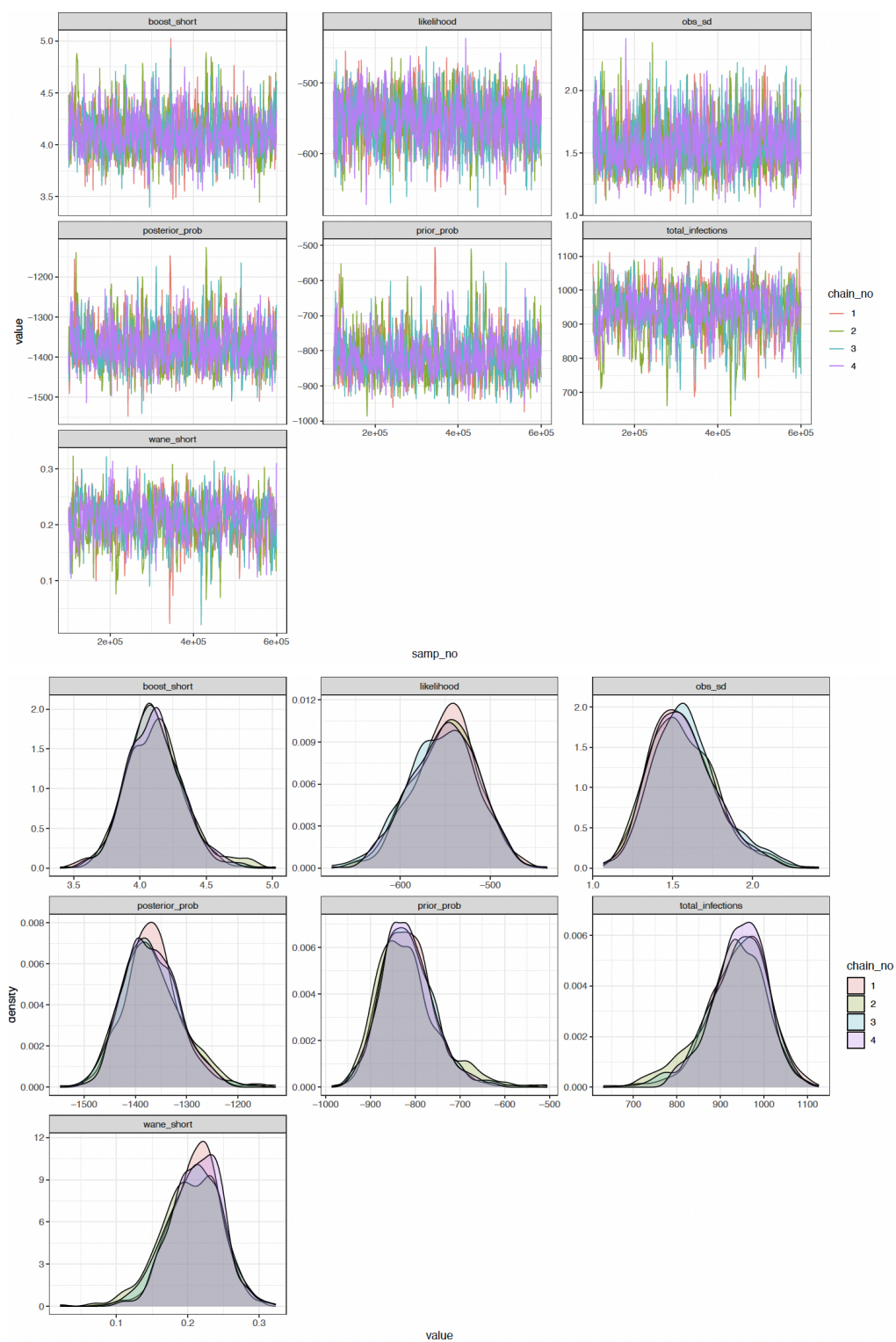
Supplementary Fig. 4



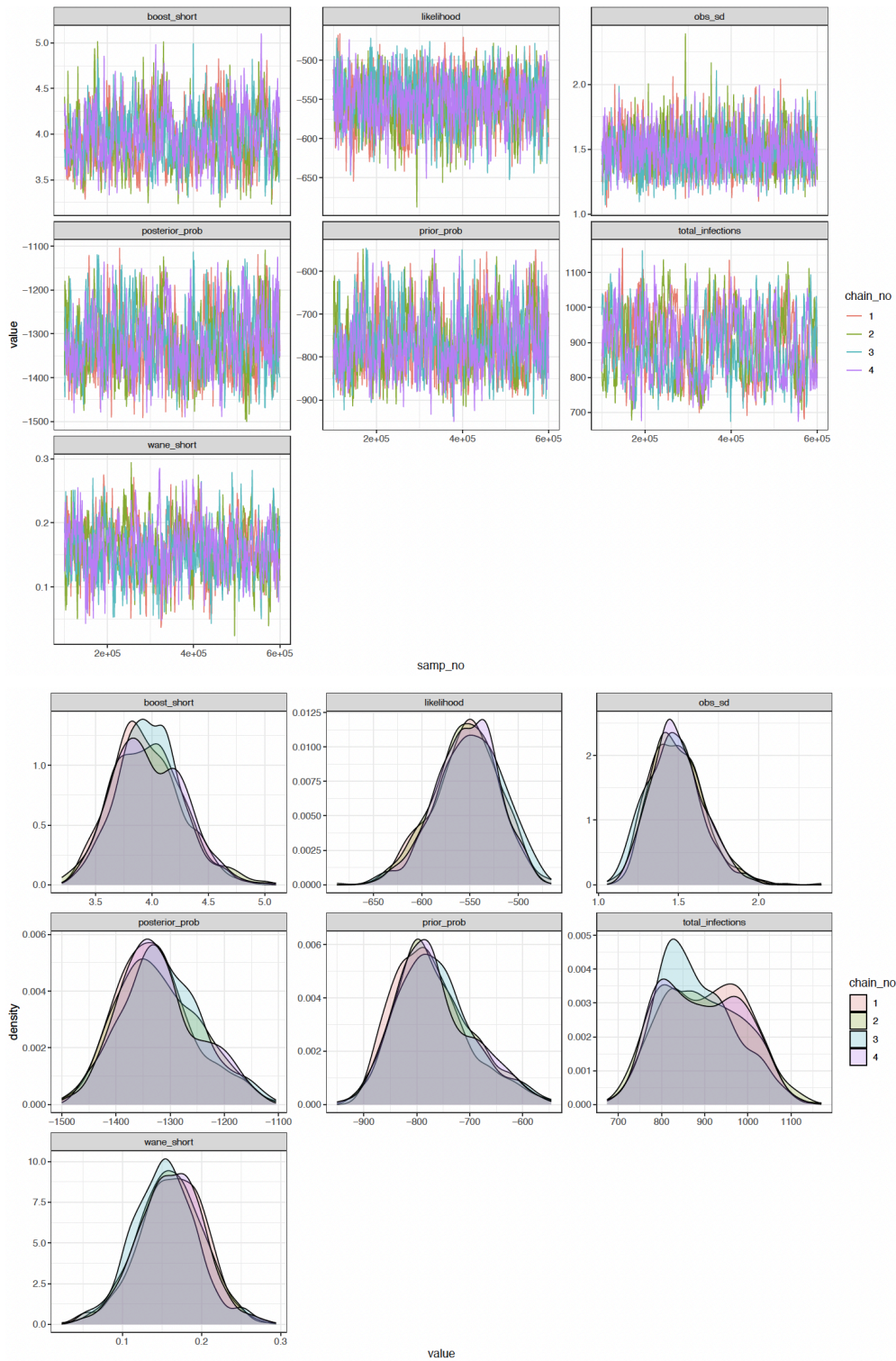
Infection probability prior for Serosolver model. To set the prior on the infection probability in the Serosolver model, we inferred the distribution of influenza population attack rates from PCR-confirmed data collected through the PHIRST study. Annual attack rates were right-skewed with a mean of 10% standard deviation of 13%; we used this to define our infection probability prior for all endemic respiratory pathogens across both study locations. Thus the population probability of infection $P(\phi)$ is defined by a beta distribution in which we have set $\alpha = 0.37$ and $\beta = 3.5$ (mean: 0.10, standard deviation: 0.13). Here we simulated 10,000 distributions with these specifications and compared to observed attack rate.

Supplementary Figs. 5

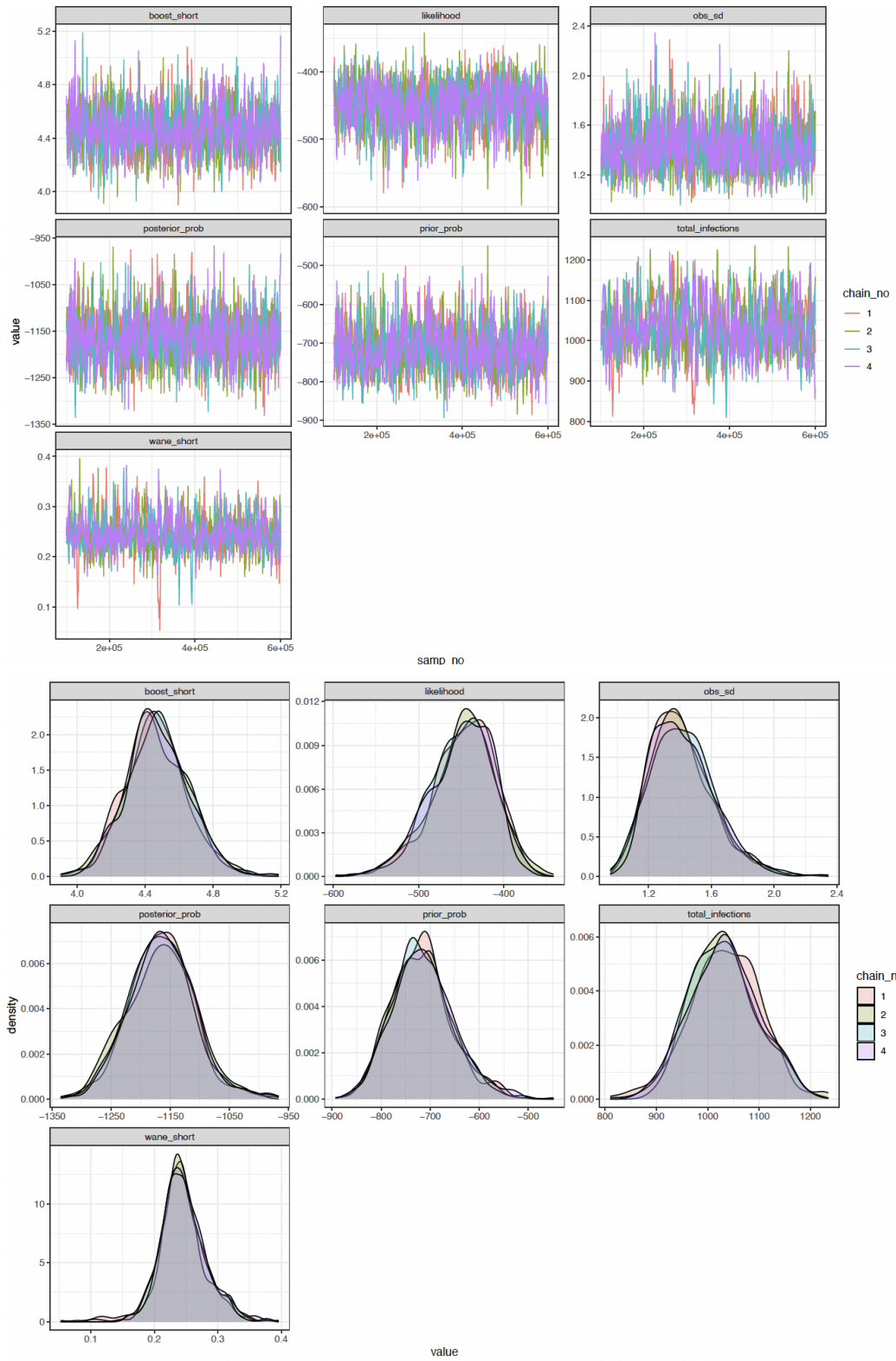
King County, < 5 yo, Influenza AH1



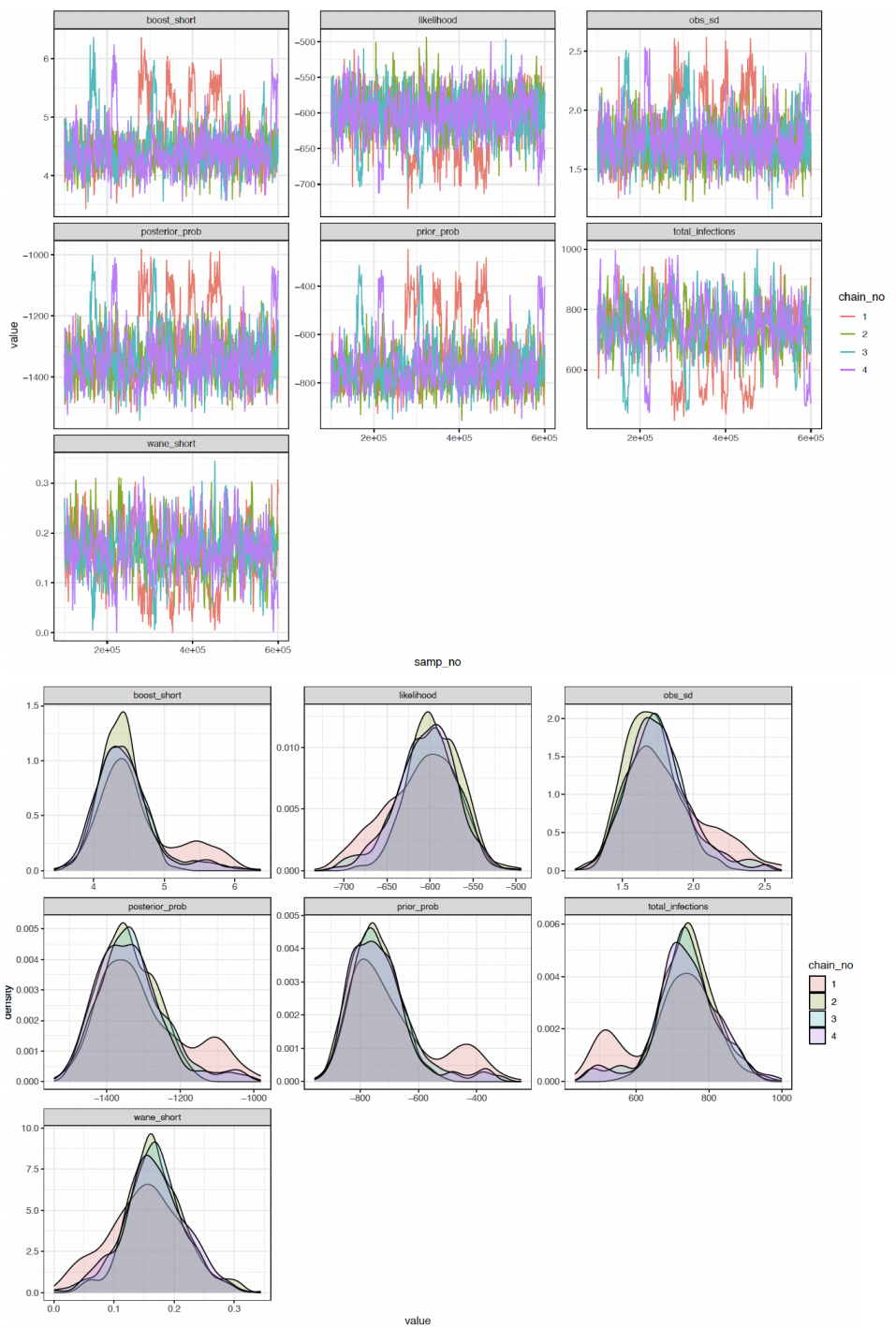
King County, < 5 yo, Influenza B/Victoria



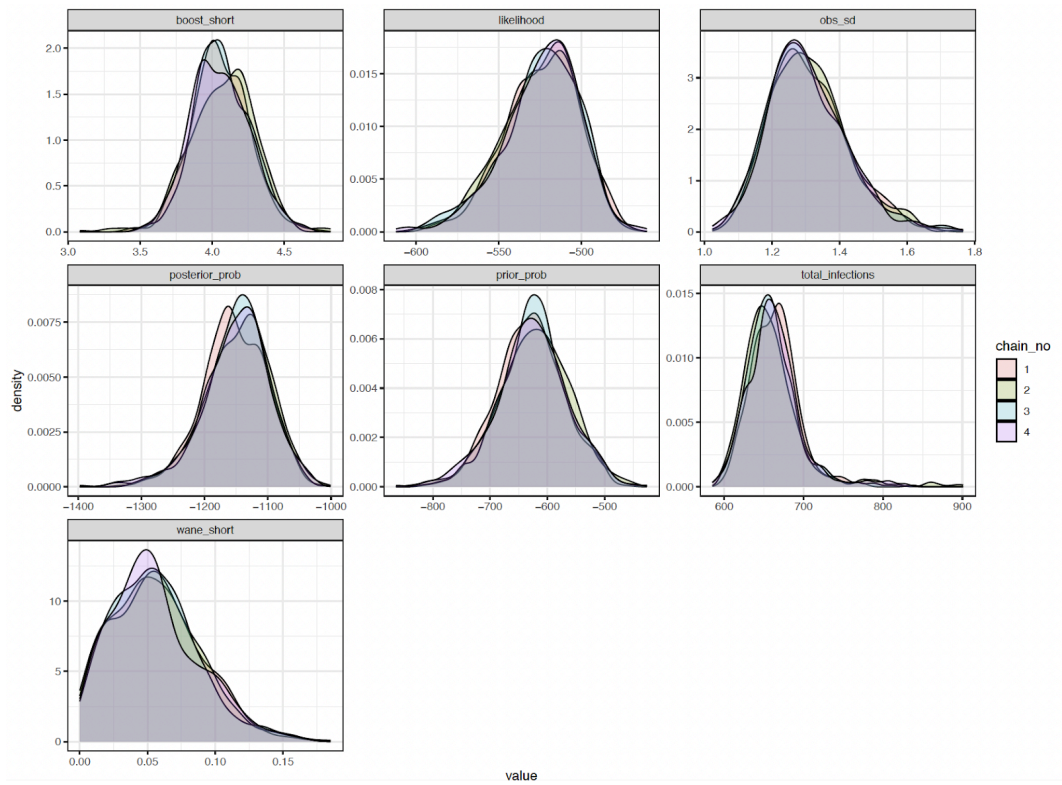
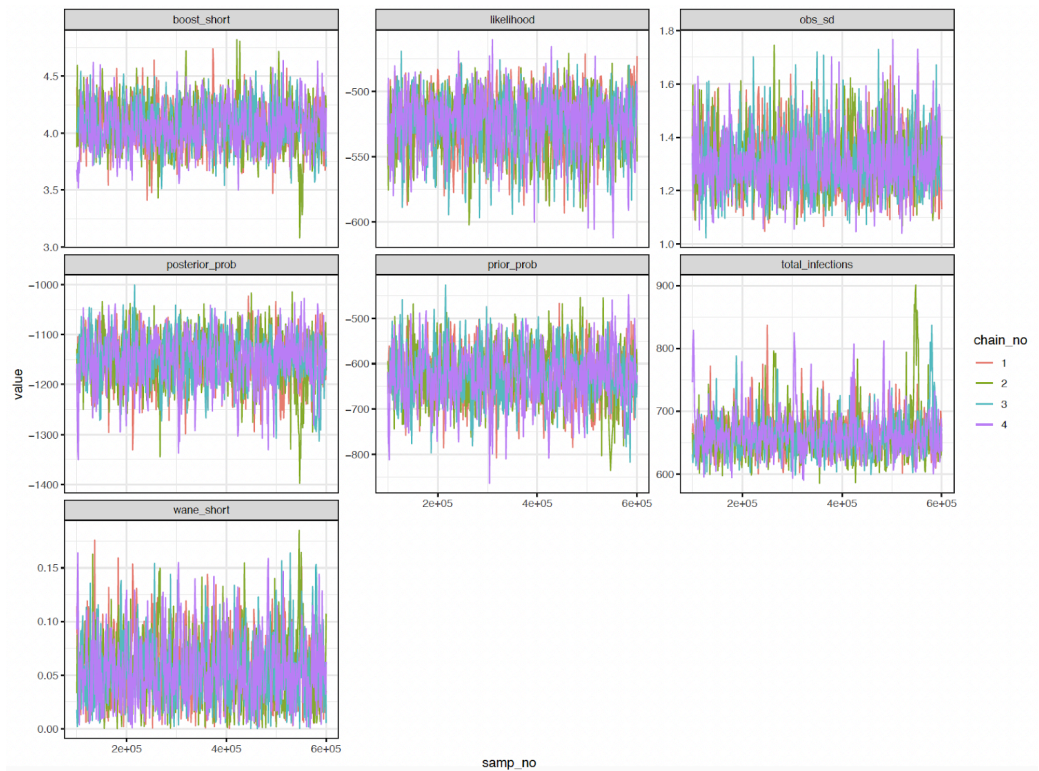
King County, < 5 yo, Influenza B/Yamagata



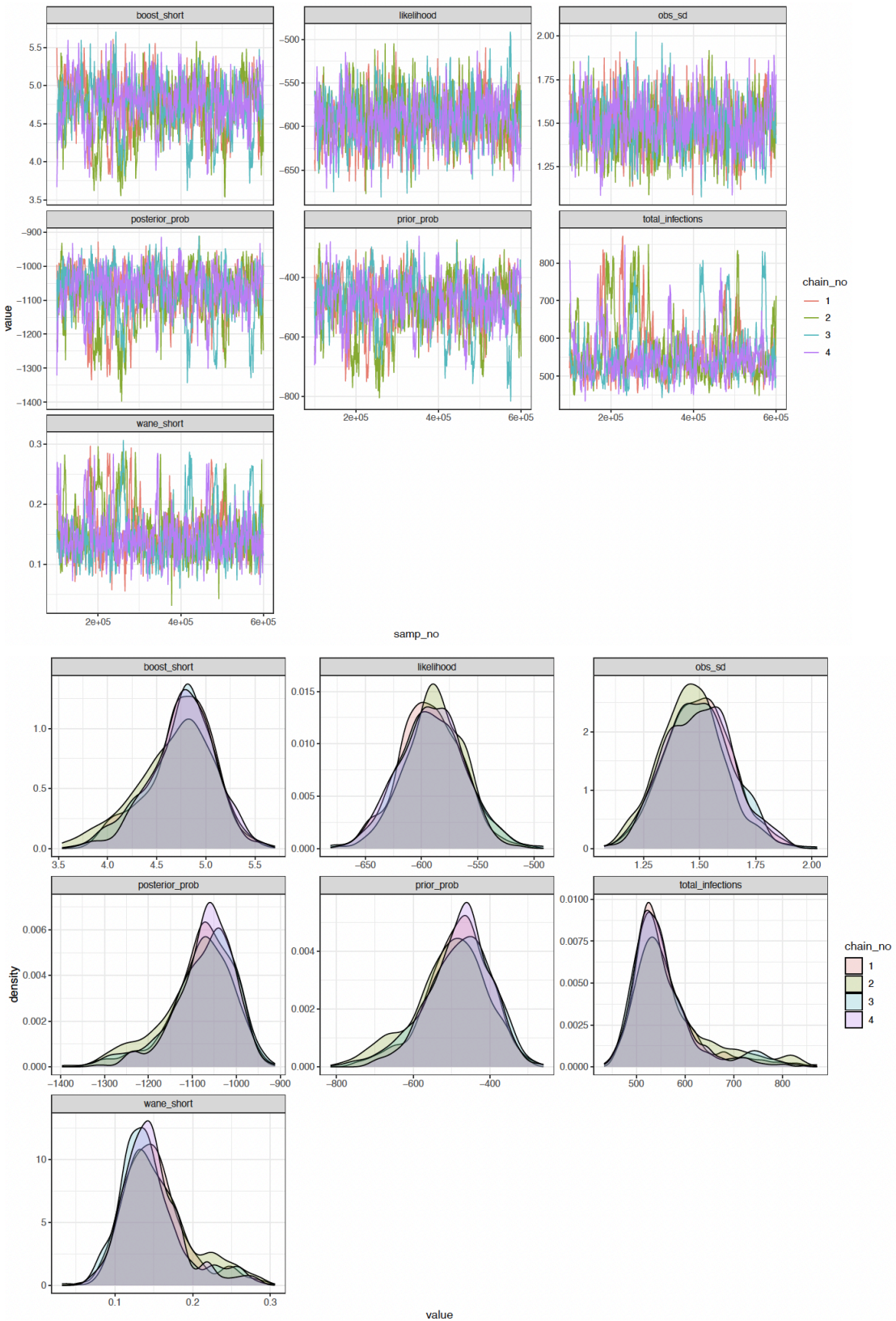
King County, < 5 yo, Influenza AH3



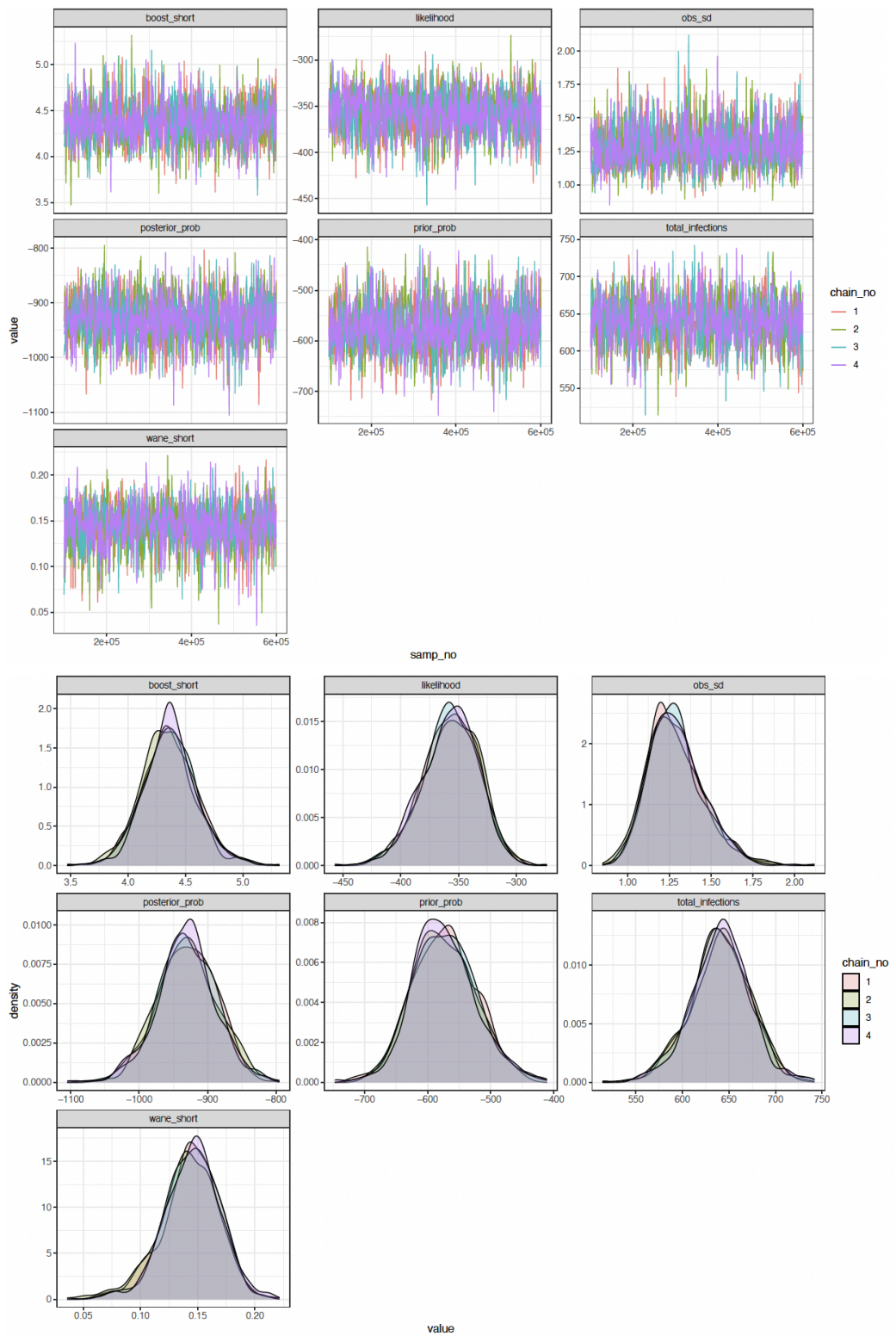
King County, < 5 yo, HCoV HKU1



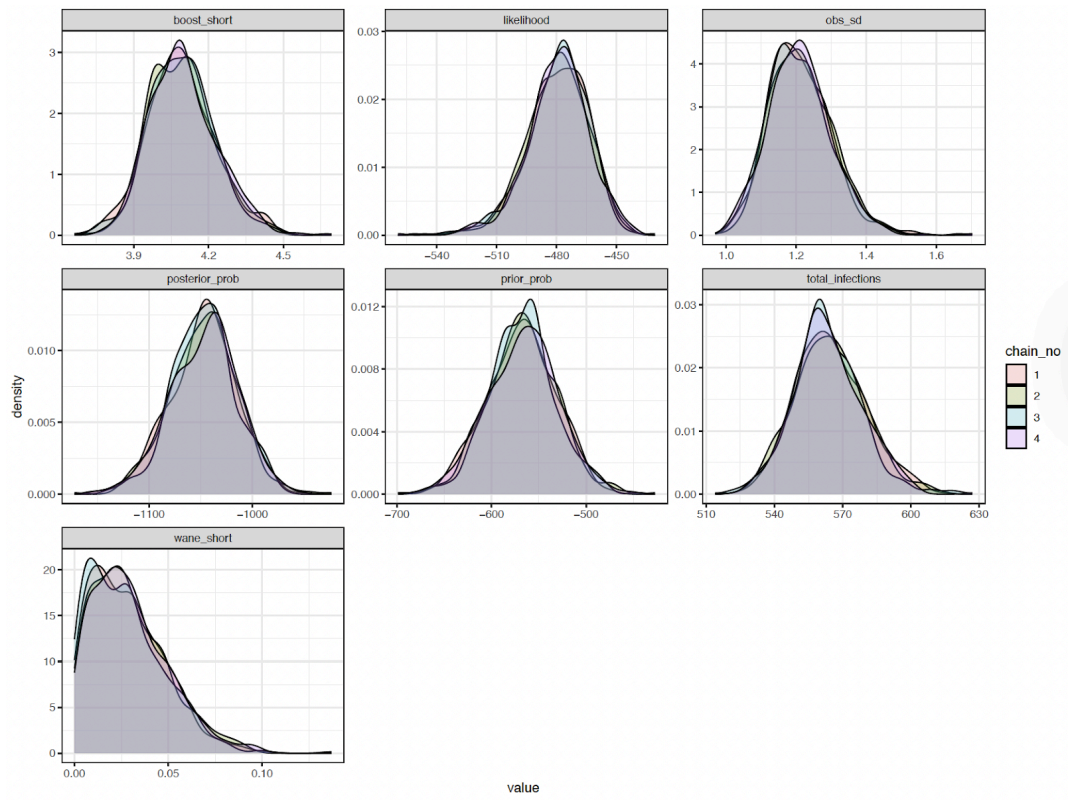
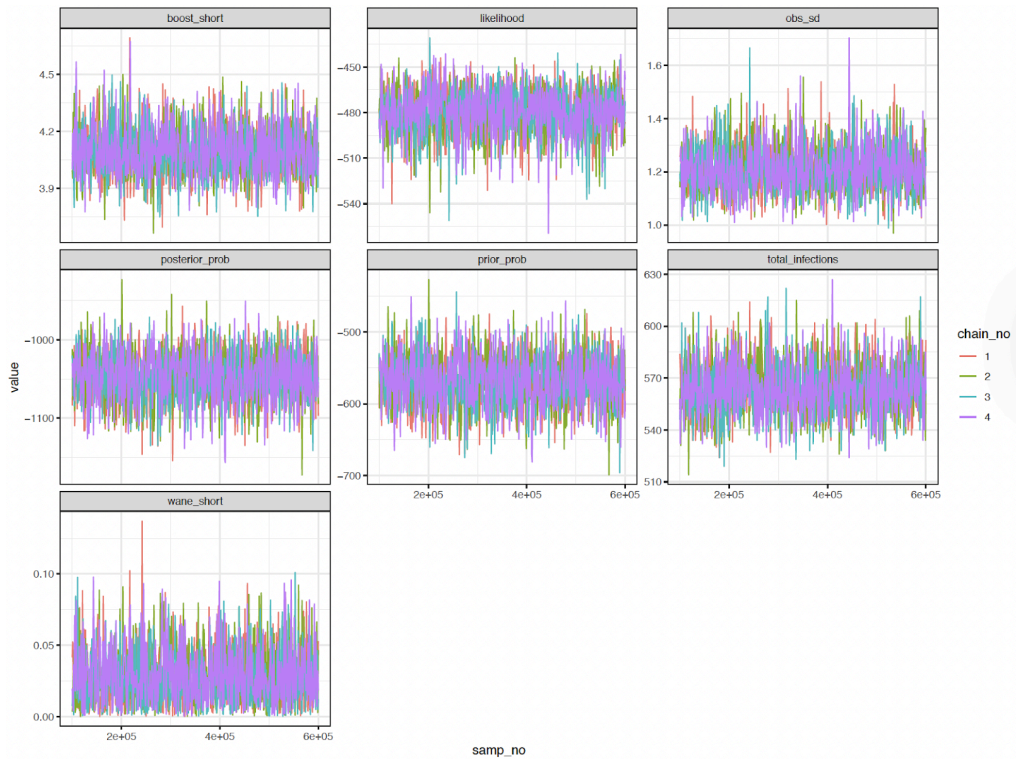
King County, < 5 yo, HCoV 229E



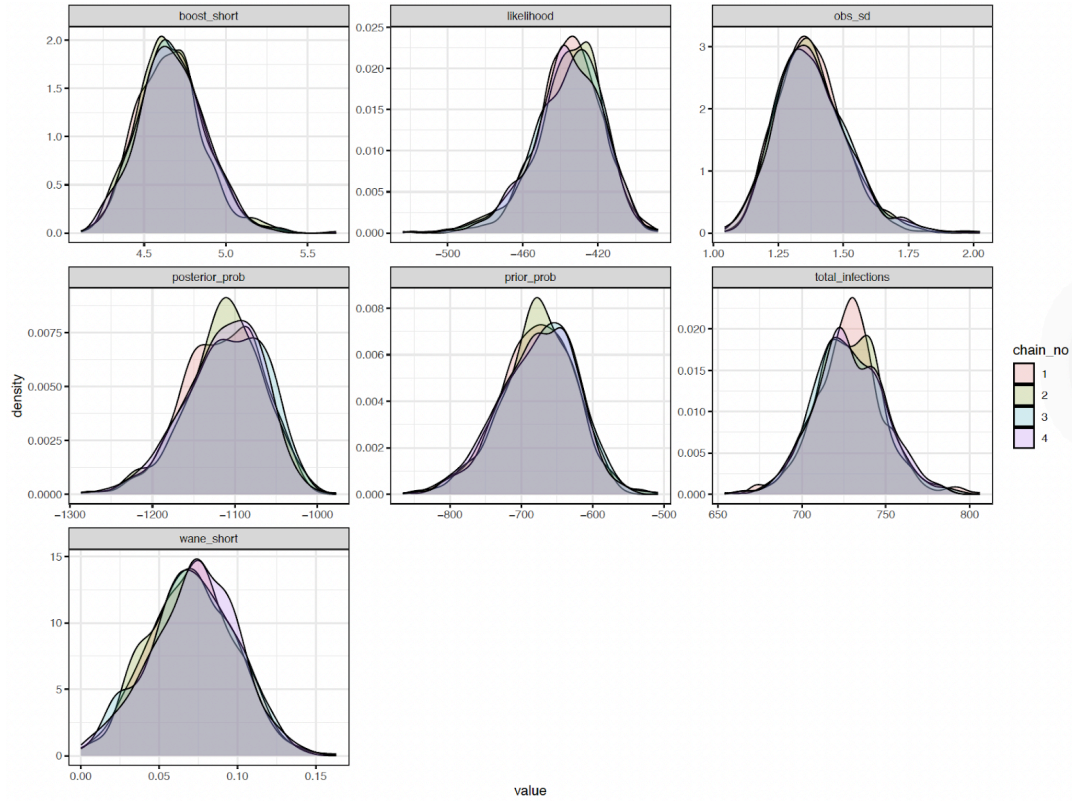
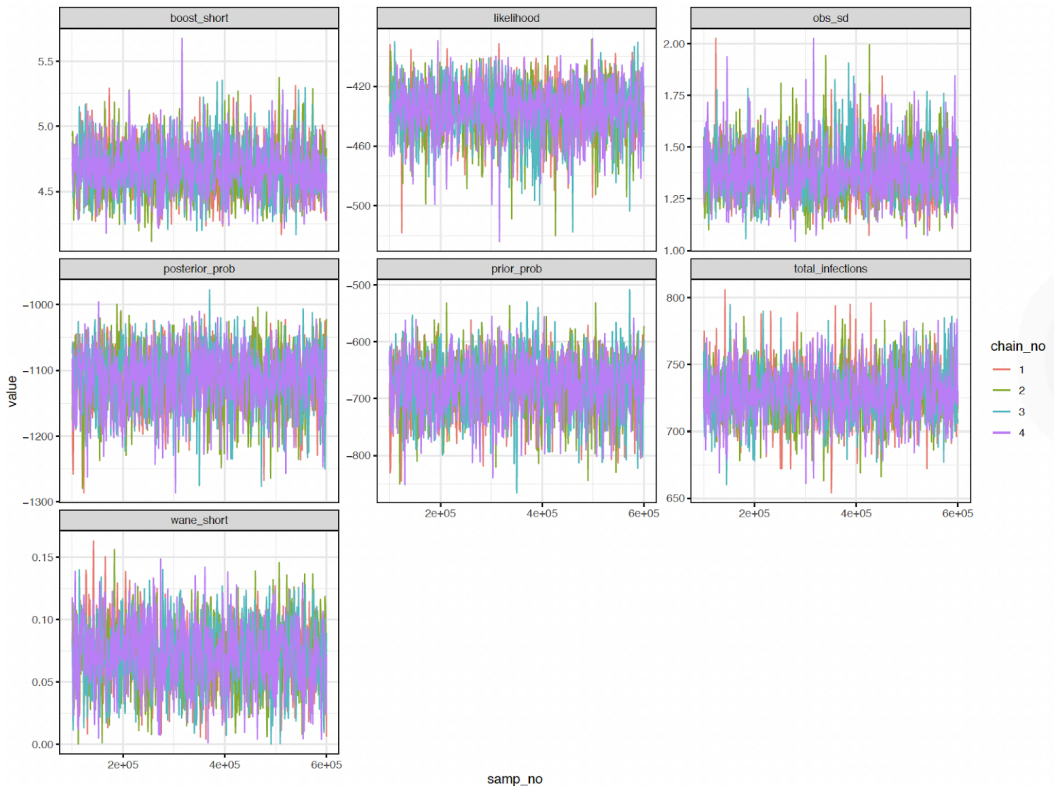
King County, < 5 yo, HCoV OC43



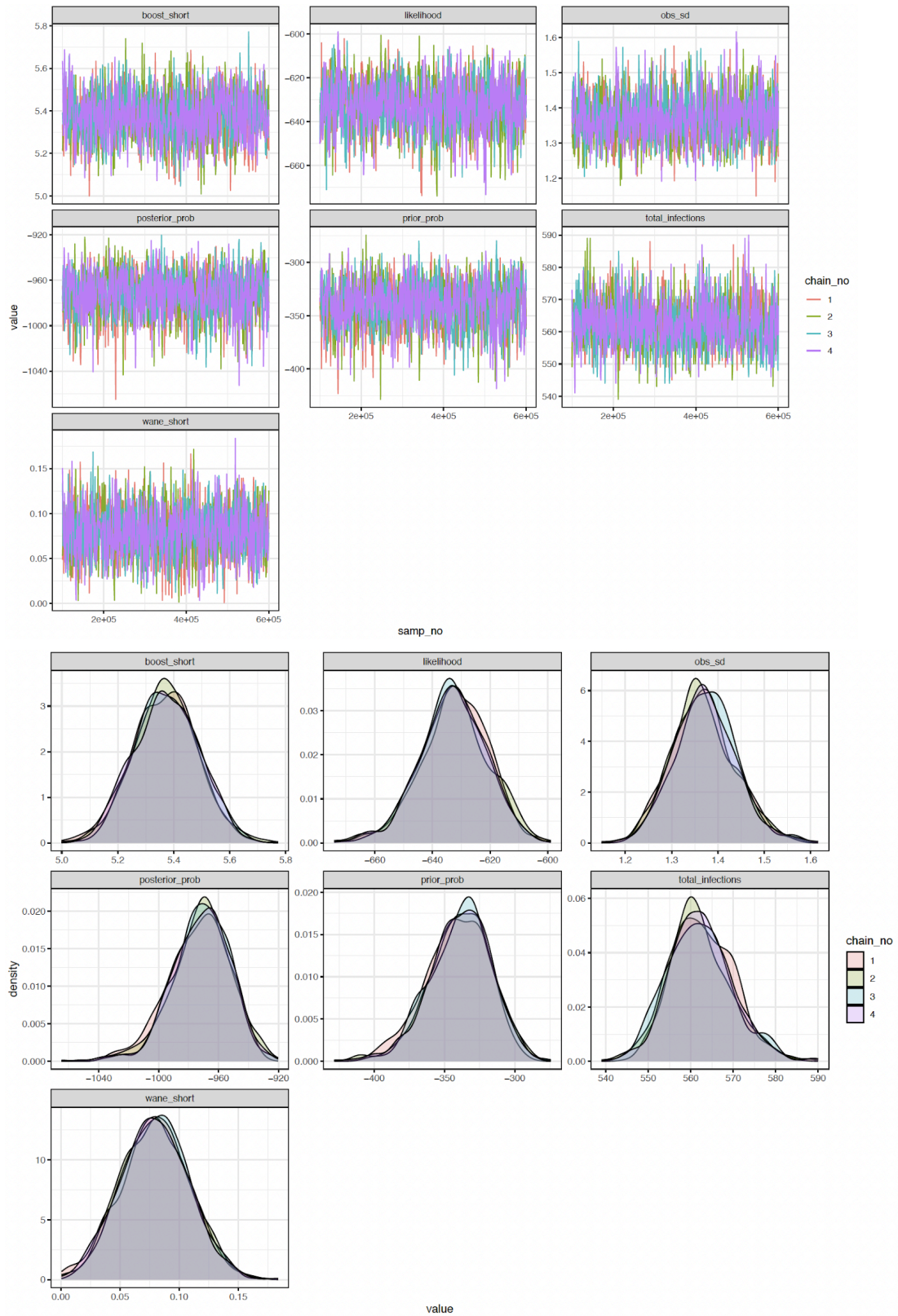
King County, < 5 yo, HCoV NL63



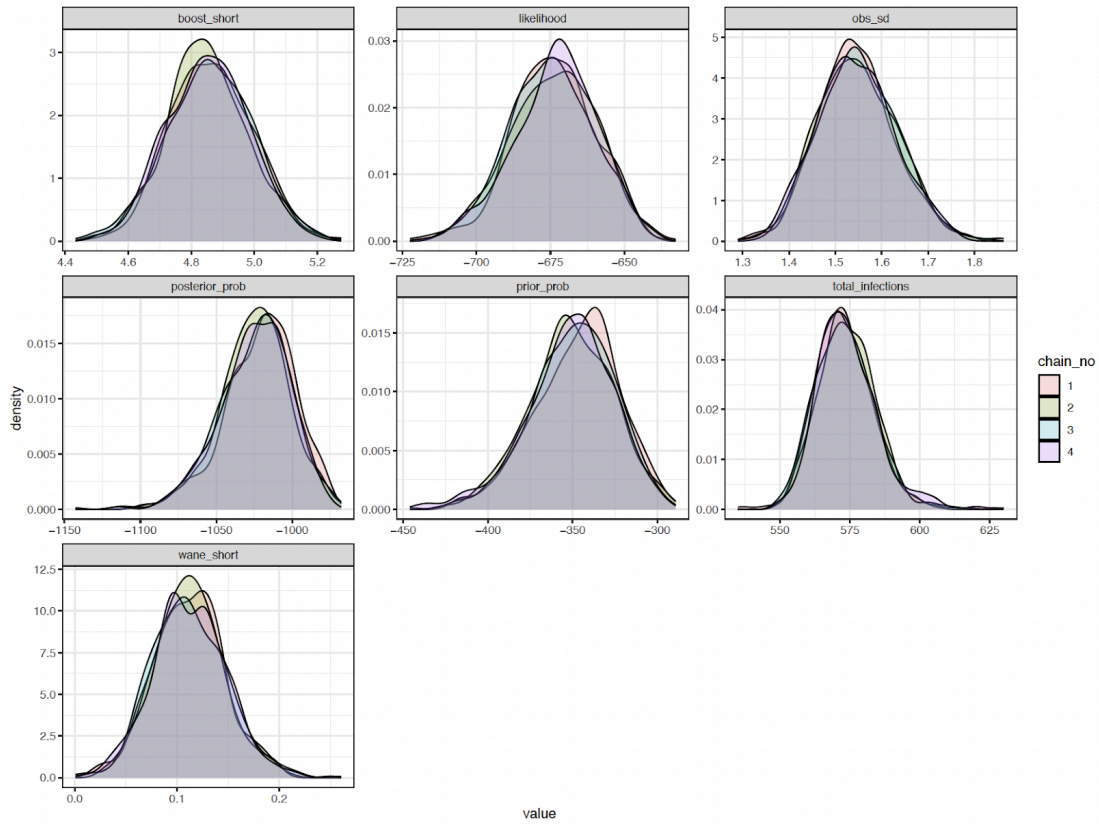
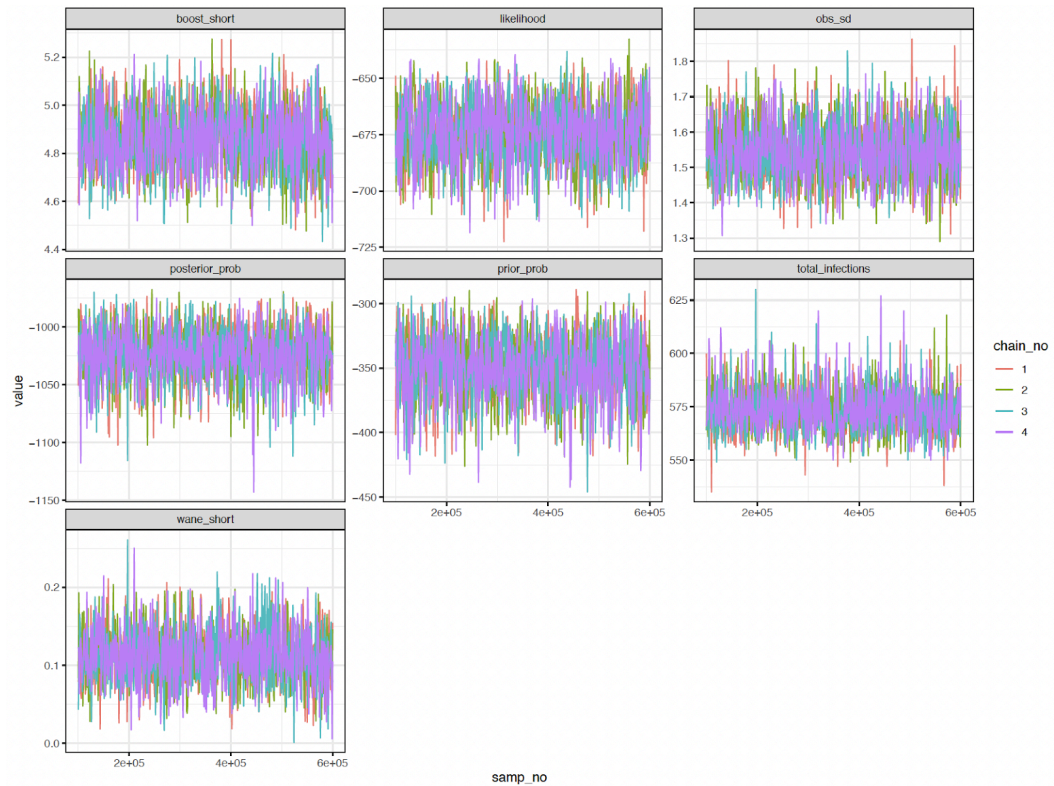
King County, <5 yo, RSV



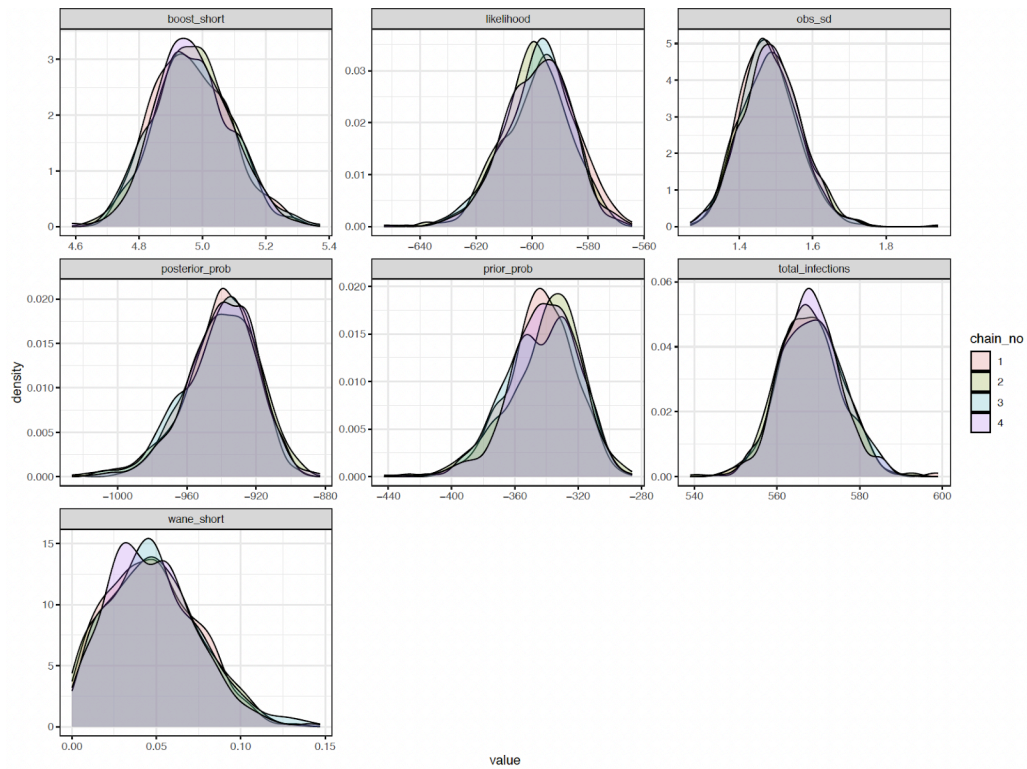
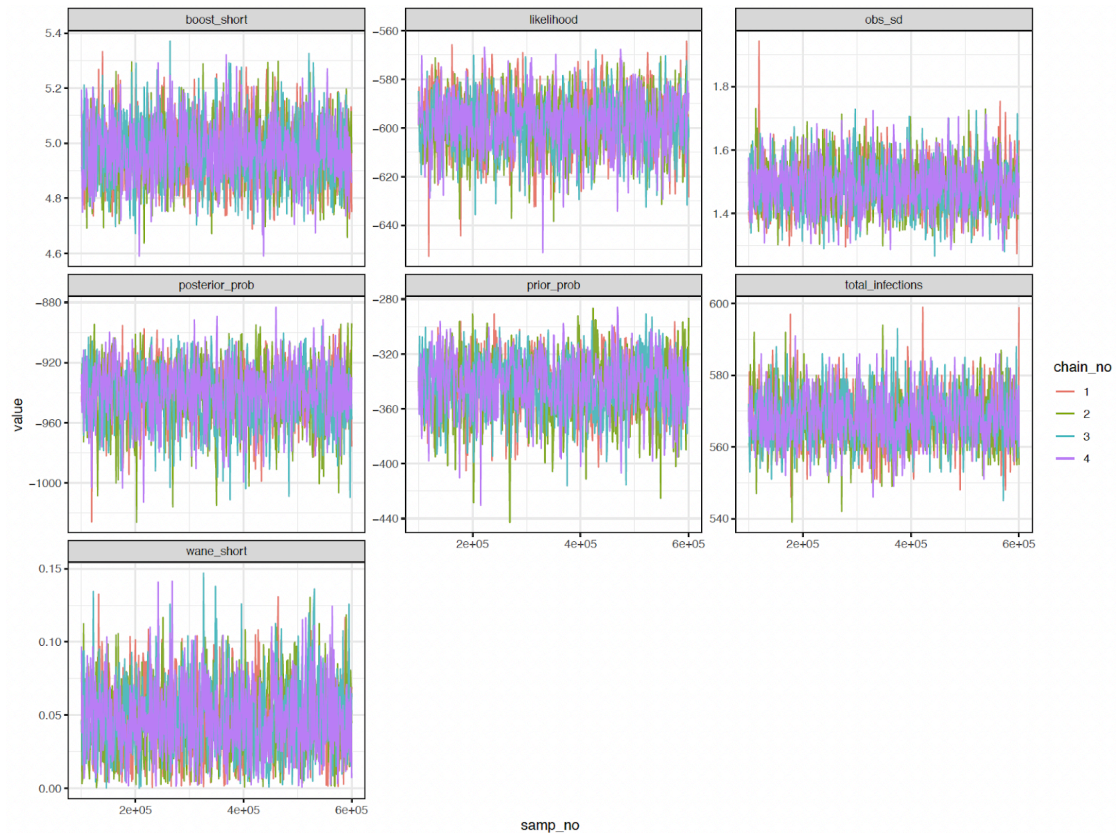
King County, < 5 yo, SARS-CoV-2 N



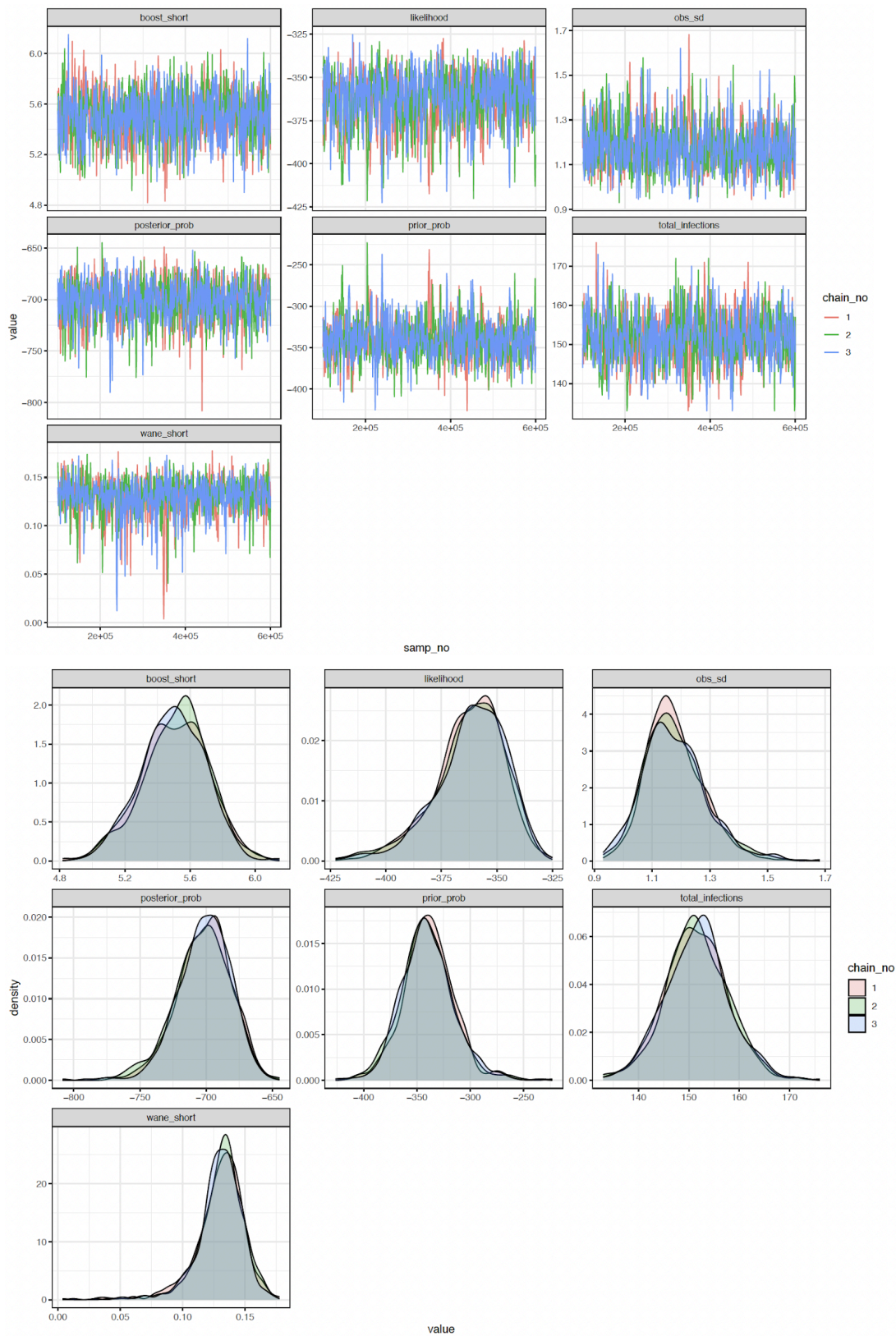
King County, <5 yo, SARS-CoV-2 RBD



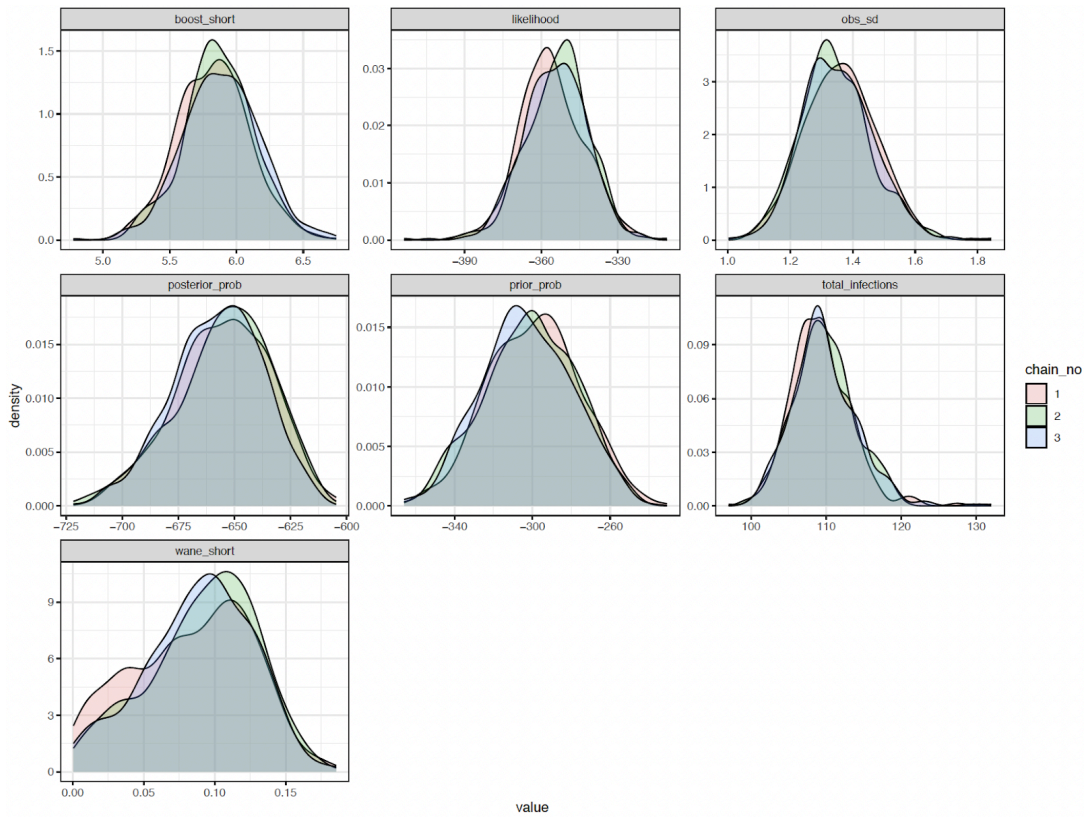
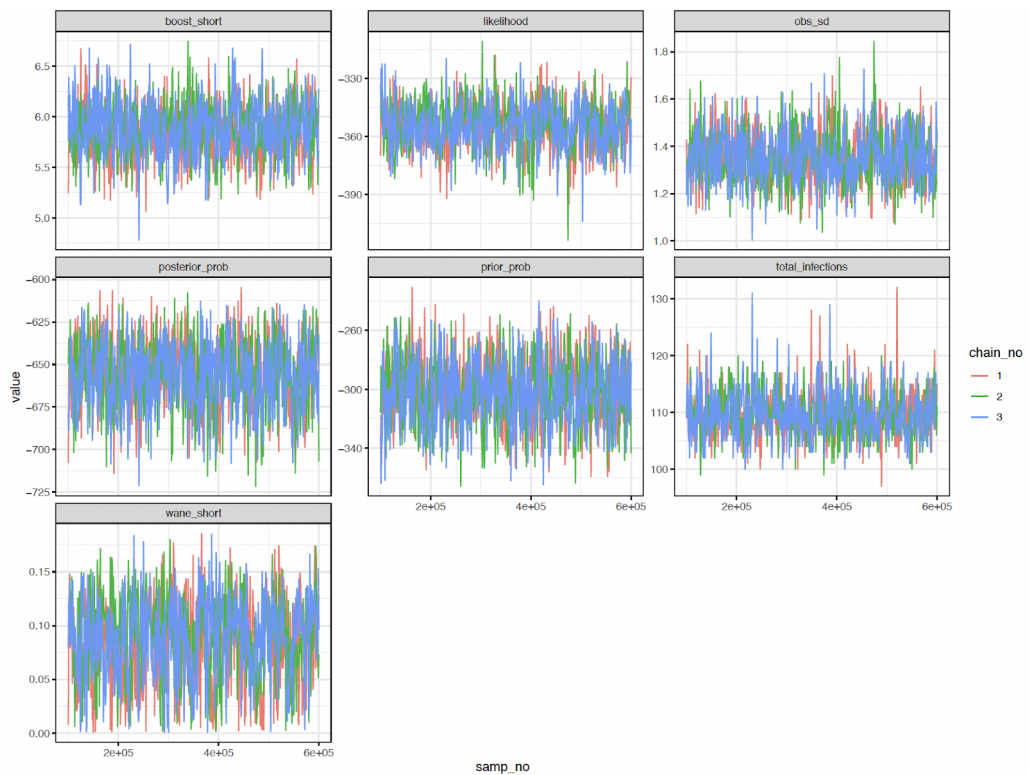
King County, < 5 yo, SARS-CoV-2 Spike



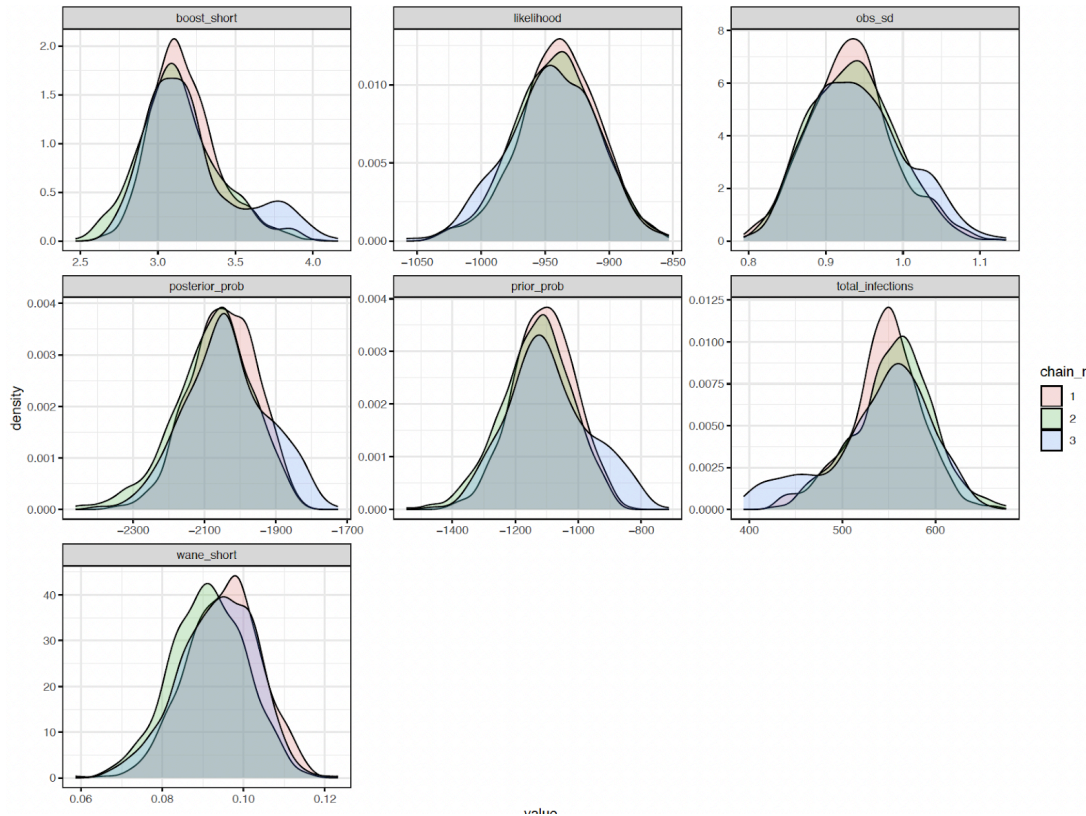
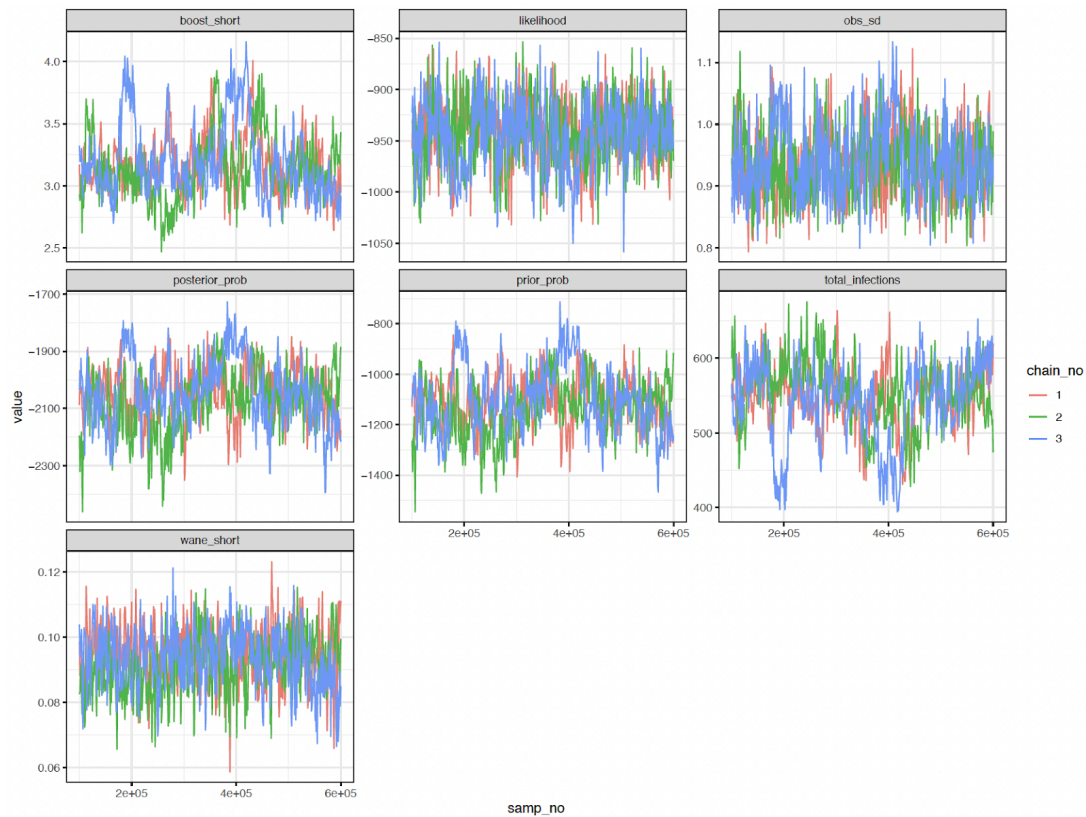
South Africa, <5 yo, Influenza AH3



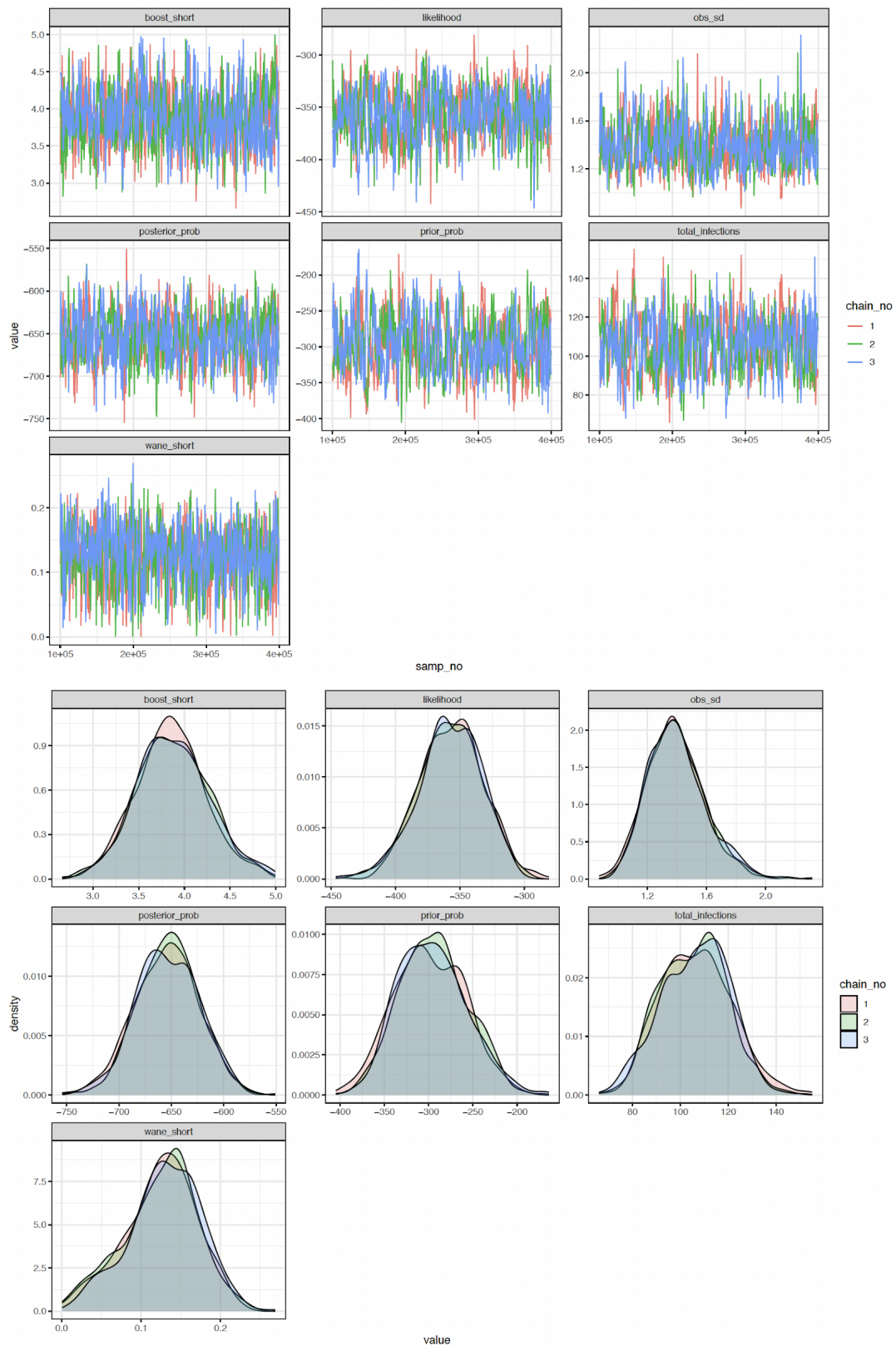
South Africa, < 5 yo, Influenza AH1



South Africa, < 5 yo, Influenza B/Yamagata



South Africa, < 5 yo, Influenza B/Victoria



Serosolver MCMC diagnostic plots. Serosolver MCMC diagnostic plots that demonstrate 1) trace plots showing chain mixing and 2) posterior density plots for estimated parameters for all runs for children <5 yo in King County and South Africa. Each antigen tested is shown separately.

Supplementary Table 5

Model Parameters	Definition	Source	Value
$1/\nu$	Duration of immunity (years)	Fixed	4
β_1	Amplitude of seasonal forcing	Fit	.28
$1/Y$	Infectious period (days)	Fixed	2.3
$1/\delta$	Latent period (days)	Fixed	2
Φ	Phase shift	Fit	4.59
β_0	Transmission coefficient	Fit	.53
$\sigma_{1, 2, 3}$	Proportion of reduced susceptibility via maternal antibodies in months 1,2,3 of infancy	Fixed	.08, .45, .45
h_1, h_2, h_3, h_4	Age-specific hospitalization rates for 0-5, 5-10, 20-64, 65+ age groups	Fit	.12, .09, .06, .10
c_1, c_2	Reduced transmissibility via lockdowns March 2020-March 2021, April 2021-April 2022	Fit	.57, .73

Influenza transmission model parameter table. Parameter estimates, definitions, and information on whether the parameter was fixed or fitted for the SEIRS model with uniform immunity structure (null model).

Supplementary Table 6

Model Parameters	Definition	Source	Value
$1/v$	Duration of immunity (years) in individuals > 5 yrs	Fixed	4
r	Change in duration of immunity in children < 5yrs, relative to older individuals (duration of immunity in children is r/v)	Fit	0.49
β_1	Amplitude of seasonal forcing	Fit	.32
$1/Y$	Infectious period (days)	Fixed	2.27
$1/\delta$	Latent period (days)	Fixed	2
ϕ	Phase shift	Fit	4.61
β_0	Transmission coefficient	Fit	.51
$\sigma_{1, 2, 3}$	Proportion of reduced susceptibility via maternal antibodies in months 1,2,3 of infancy	Fixed	.08, .45, .45
h_1, h_2, h_3, h_4	Age-specific hospitalization rates for 0-5, 5-10, 20-64, 65+ age groups	Fit	.13, .20, .08, .08
c_1, c_2	Reduced transmissibility via lockdowns March 2020-March 2021, April 2021-April 2022	Fit	.50, .61

Influenza transmission model parameter table. Parameter estimates, definitions, and information on whether the parameter was fixed or fitted for the SEIRS model with tiered immunity structure.