SUPPLEMENTARY MATERIALS

The contribution of asymptomatic SARS-CoV-2 infections to transmission - a model-based analysis of the Diamond Princess outbreak.

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Methods

Data

Data for confirmed symptomatic cases was extracted from [1]. Supplementary Table 1 shows n=199 confirmed symptomatic cases by date of symptom onset for passengers and crew separately. Symptom onset dates were unavailable for a further n=115 confirmed symptomatic cases. These were accounted for in the model structure (see Supplementary Figure 1) by assuming they were distributed over time proportional to those cases with a reported date of symptom onset. The data itself was not augmented.

Date of symptom onset	Confirmed symptomatic cases		
	Passengers	Crew	Total
20-Jan	2	0	2
21-Jan	0	0	0
22-Jan	0	0	0
23-Jan	1	0	1
24-Jan	0	0	0
25-Jan	0	0	0
26-Jan	0	0	0
27-Jan	0	0	0
28-Jan	0	0	0
29-Jan	1	0	1
30-Jan	1	0	1
31-Jan	0	0	0
01-Feb	4	0	4
02-Feb	4	0	4
03-Feb	4	0	4
04-Feb	6	0	6
05-Feb	12	0	12
06-Feb	15	2	17
07-Feb	29	2	31
08-Feb	17	2	19
09-Feb	19	5	24
10-Feb	7	3	10
11-Feb	11	8	19
12-Feb	5	7	12
13-Feb	9	8	17
14-Feb	2	5	7
15-Feb	1	3	4
16-Feb	0	3	3
17-Feb	0	1	1
18-Feb	0	0	0
19-Feb	0	0	0
20-Feb	0	0	0
Total	150	49	199

Supplementary Table 1: *Confirmed symptomatic cases (n=199) by date of symptom onset for passengers and crew separately, extracted from [1]. A further n=115 confirmed symptomatic cases without symptom onset dates are not included in the table.*

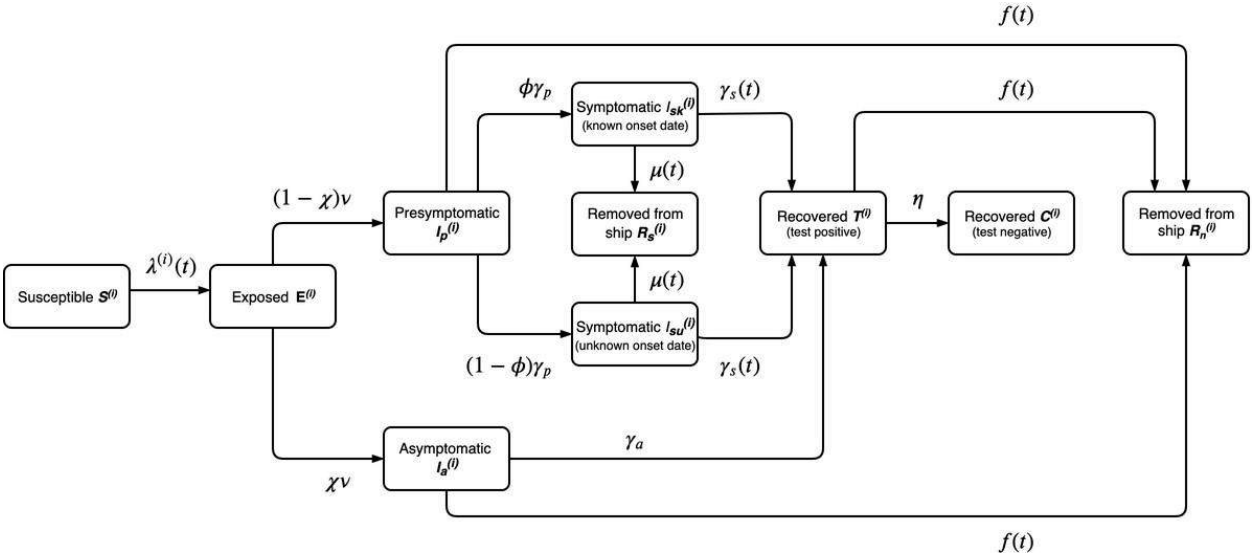
Data for confirmed pre/asymptomatic cases and symptom-agnostic testing was extracted from [2]. Supplementary Table 2 shows n=2,749 symptom-agnostic tests and n=320 confirmed pre/asymptomatic cases by date of test for passengers and crew combined, since stratification by passenger/crew was unavailable. The number of symptom-agnostic tests was inferred from the total number of tests each day, minus the number of positive results in individuals reporting symptoms in [2]. Test dates were not available for n=35 confirmed pre/asymptomatic cases between 5th-14th Feb. These were distributed proportional to the total number of tests (symptom-based and symptom-agnostic) on those days. An alternative scenario where all n=35 confirmed pre/asymptomatic cases are allocated to the last possible day (13th Feb) is explored in sensitivity analyses.

Date of test	Number of symptom agnostic tests	Number of confirmed pre/asymptomatic cases
20-Jan	0	0
21-Jan	0	0
22-Jan	0	0
23-Jan	0	0
24-Jan	0	0
25-Jan	0	0
26-Jan	0	0
27-Jan	0	0
28-Jan	0	0
29-Jan	0	0
30-Jan	0	0
31-Jan	0	0
01-Feb	0	0
02-Feb	0	0
03-Feb	0	0
04-Feb	0	0
05-Feb^{+}	23	2
06-Feb^{+}	64	3
07-Feb^{+}	138	8
08-Feb^{+}	3	0
09-Feb^{+}	54	3
10-Feb^{+}	43	5
11-Feb^{+}	0	0
12-Feb^{+}	17	3
13-Feb^{+}	188	11
14-Feb^{+}	0	0
15-Feb	188	38
16-Feb	257	38
17-Feb	475	70
18-Feb	658	65
19-Feb	596	68
20-Feb	45	6
Total	2749	320

Supplementary Table 2: *Confirmed pre/asymptomatic cases (n=320) and symptom-agnostic tests (n=2749) by date of test for passengers and crew combined, extracted from [2].* $^{+}$*Test dates were not available for n=35 confirmed pre/asymptomatic cases between 5th-14th Feb. These were distributed proportional to the total number of tests (symptom-based and symptom-agnostic) on those days.*

Model

The model described in the main text is shown in detail in Supplementary Figure 1, where passengers ($i = p$) and crew ($i = c$) are modelled separately and the annotated parameters are described in Table 1 of the main text.



Supplementary Figure 1: *Model diagram for the outbreak onboard the Diamond Princess cruise ship described in the main paper. The annotated transition parameters are defined in Table 1 of the main paper and detailed further, below. The model is stratified by i = passengers or crew. The asymptomatic, presymptomatic and symptomatic states are all assumed to be infectious and individuals would test positive during symptom-based or symptom-agnostic testing. Individuals that recover are also assumed to test positive for an average of 1-week after they are no longer infectious.*

The force of infection is given by

$$\lambda^{(i)}(t) = \sum_{j=p,c} \beta^{(ij)}(t) \frac{(\theta_a I_a^{(j)} + \theta_p I_p^{(j)} + I_{sk}^{(j)} + I_{su}^{(j)})}{N^{(j)}},$$

where the time dependent contact parameters are described by sigmoid functions

$$\beta^{(ij)}(t) = \bar{\beta} c^{(ij)} \left(1 - \frac{b_1}{1 + \mathrm{e}^{-b_2(t-\tau^{(ij)})}}\right),$$

and $\tau^{(pp)} = \tau^{(pc)} = \tau^{(cp)}$ (i.e. contact between passengers/passengers and passengers/crew is reduced at the same time, which can differ from contact between crew/crew).

The transition from exposed to presymptomatic or asymptomatic is modelled as an erlang distribution using two compartments (i.e. a shape parameter *k*=2), each with a mean duration of $1/2\nu$.

The rate of symptom agnostic testing and removal of individuals not reporting symptoms is given by the total number of symptom agnostic tests administered per day divided by the total number of individuals not presenting symptoms being tested on that day

$$f(t) = \frac{N^{\text{tests}}}{(S + E + I_a + I_p + T + C)},$$

where N^{tests} is taken from the data in Supplementary Table 2 and variables without indices represent the totals among passengers and crew (e.g. $S = S^{(p)} + S^{(c)}$)

To reflect heightened symptom awareness following quarantine, the transition rate from symptomatic infection to recovered on the ship is constant before quarantine and zero afterwards, whilst the rate of removal of individuals reporting symptoms is zero before quarantine and a constant afterwards

$$\gamma_s(t) = \gamma_s,\ \mu(t) = 0 \text{ for } t < 5\text{th Feb},$$
$$\gamma_s(t) = 0,\ \mu(t) = \mu \text{ for } t \geq 5\text{th Feb}.$$

All other model transitions are exponentially distributed.

The model is initialised with a single symptomatic passenger with a known onset date on 20th Jan, with all other individuals susceptible

$$I_{sk}^{(p)}(0) = 1, \quad S^{(p)} = N^{(p)} - 1, \quad S^{(c)} = N^{(c)}.$$

Model calibration

The model was calibrated in a Bayesian framework to fit to the two sets of empirical observations from the ship (Supplementary Tables 1 and 2). We used a Poisson likelihood for the incident symptomatic cases with a known onset date for crew and passengers separately. We used a Binomial likelihood for the number of confirmed pre- and asymptomatic infections for passengers and crew combined, using the number of tests administered per day and the prevalence of presymptomatic, asymptomatic and post-infection test-positive individuals. The complete likelihood is given by

$$L = \left(\prod_{k=1}^{K} \text{Poisson}(Z_k^{(c)}|\text{mean} = z_k^{(c)})\right)\left(\prod_{k=1}^{K} \text{Poisson}(Z_k^{(p)}|\text{mean} = z_k^{(p)})\right)\left(\prod_{k=1}^{K} \text{Binom}(Y_k|N_k^{\text{tests}}, \text{mean} = y_k)\right),$$

where $Z_k^{(i)}$ is the observed incidence of symptomatic cases with a known date of onset on day k for passengers p or crew c, $z_k^{(i)}$ is the model predicted incidence, Y_k is the observed prevalence of presymptomatic, asymptomatic and post-infection test-positive individuals (passengers and crew combined) amongst N_k^{tests} symptom-agnostic tests, and y_k is the model predicted prevalence

$$y(t) = \frac{I_a + I_p + T}{S + E + I_a + I_p + T + C}.$$

We used uniform priors for the parameters to be estimated (see Table 1 in the main text).

Model outputs

The basic reproduction number as a function of time $R_0(t)$ was calculated by first constructing the next generation matrix (NGM) at each time point using the relevant Jacobian matrices [3]. The basic reproduction number is then given by the absolute value of the dominant eigenvalue of the NGM.

The net reproduction number for a presymptomatic infection (i.e. the typical number of secondary infections caused by a single presymptomatic individual throughout both their presymptomatic and symptomatic periods) at the beginning of the outbreak is given by the respective entry in the NGM evaluated at $t = 0$.

The proportion of transmission from asymptomatics is given by the cumulative number of infections caused by asymptomatics divided by the cumulative number of total infections, evaluated at the end of the outbreak.

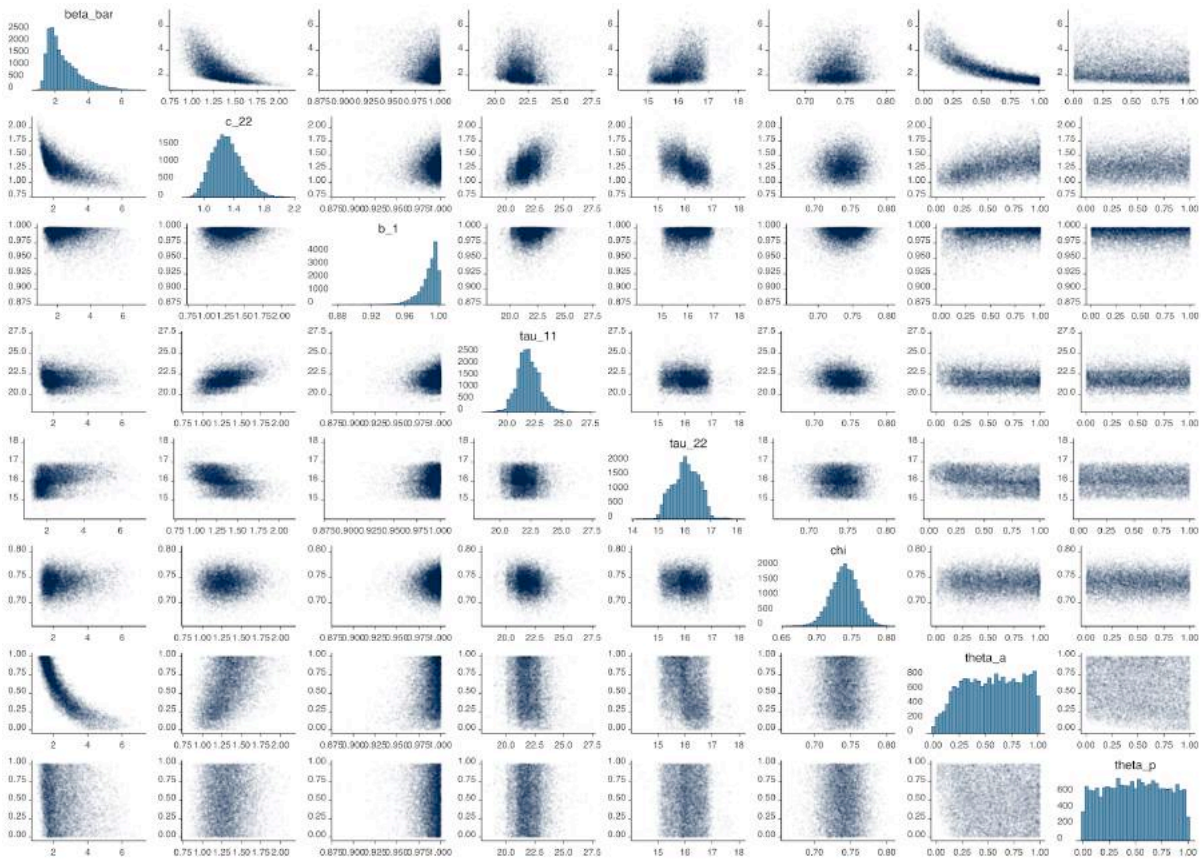
Results

Calibration

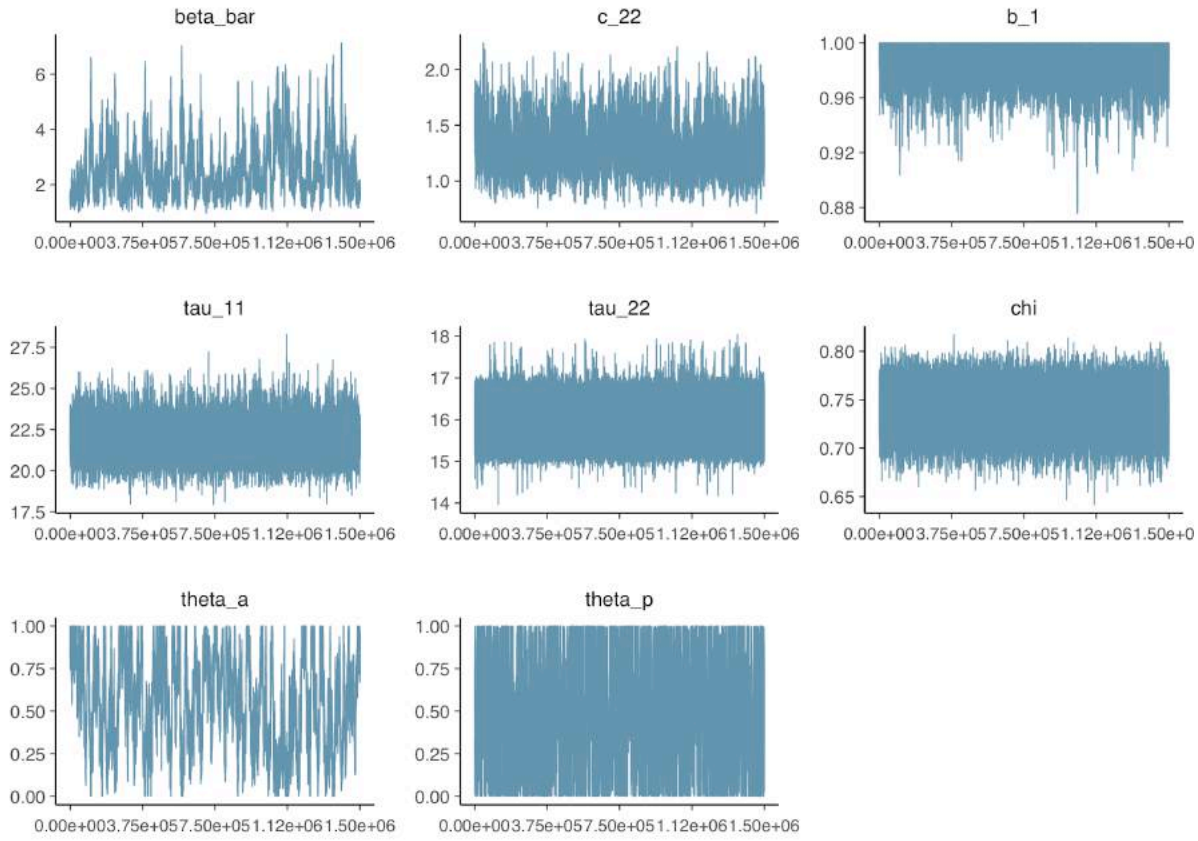
The below are further details of the model calibration for the primary analysis in the main text.

Parameter	2.5%	50%	97.5%
beta_bar	1.34	2.20	5.00
c_pp	0.97	1.29	1.74
b_1	0.96	0.99	1.00
tau_cc	20.2	21.8	23.9
tau_pp	15.2	16.1	16.9
chi	0.70	0.74	0.78
theta_a	0.07	0.56	0.98
theta_p	0.03	0.5	0.97

Supplementary Table 3: *Marginal posterior parameter values using 100,000 samples from the joint posterior distribution found in the primary analysis*



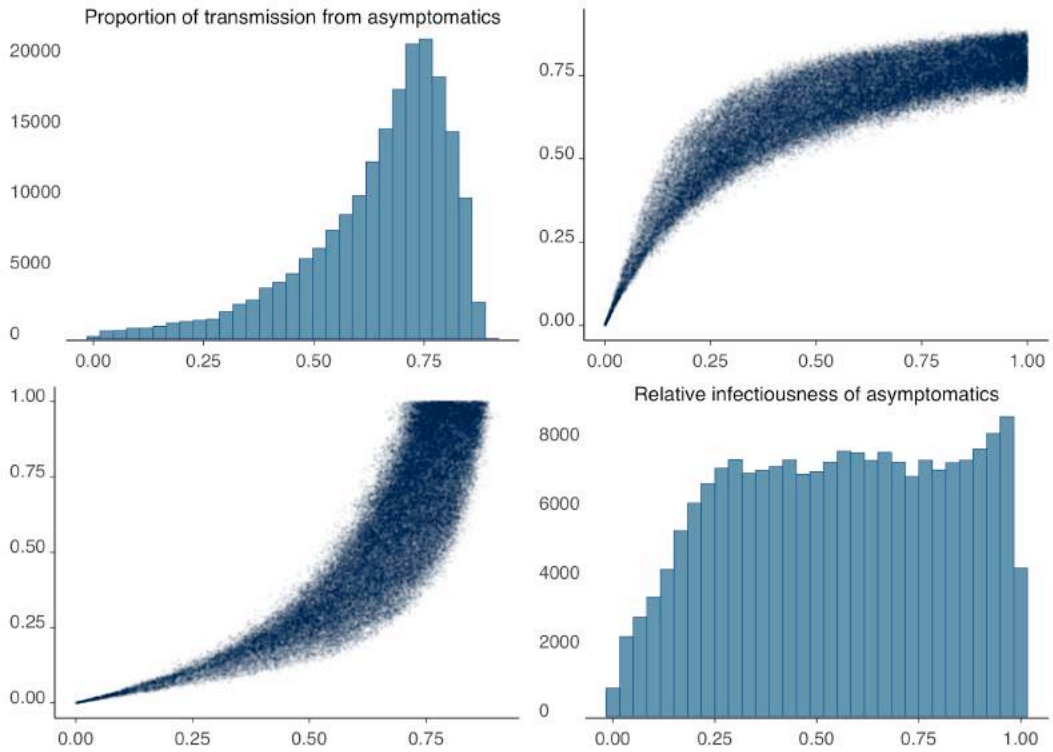
Supplementary Figure 2: *Correlation plot of parameter values from 10,000 samples of the joint posterior distribution found in the primary analysis.*



Supplementary Figure 3: *Trace plot from the MCMC for the estimated parameters in the primary analysis*

Asymptomatic infections

The below shows the correlation between the proportion of transmission from asymptomatics and their relative infectiousness, using 100,000 model runs sampled from the posterior parameters values. The relationship is non-linear, such that a modest relative infectiousness can still lead to a significant contribution to transmission.

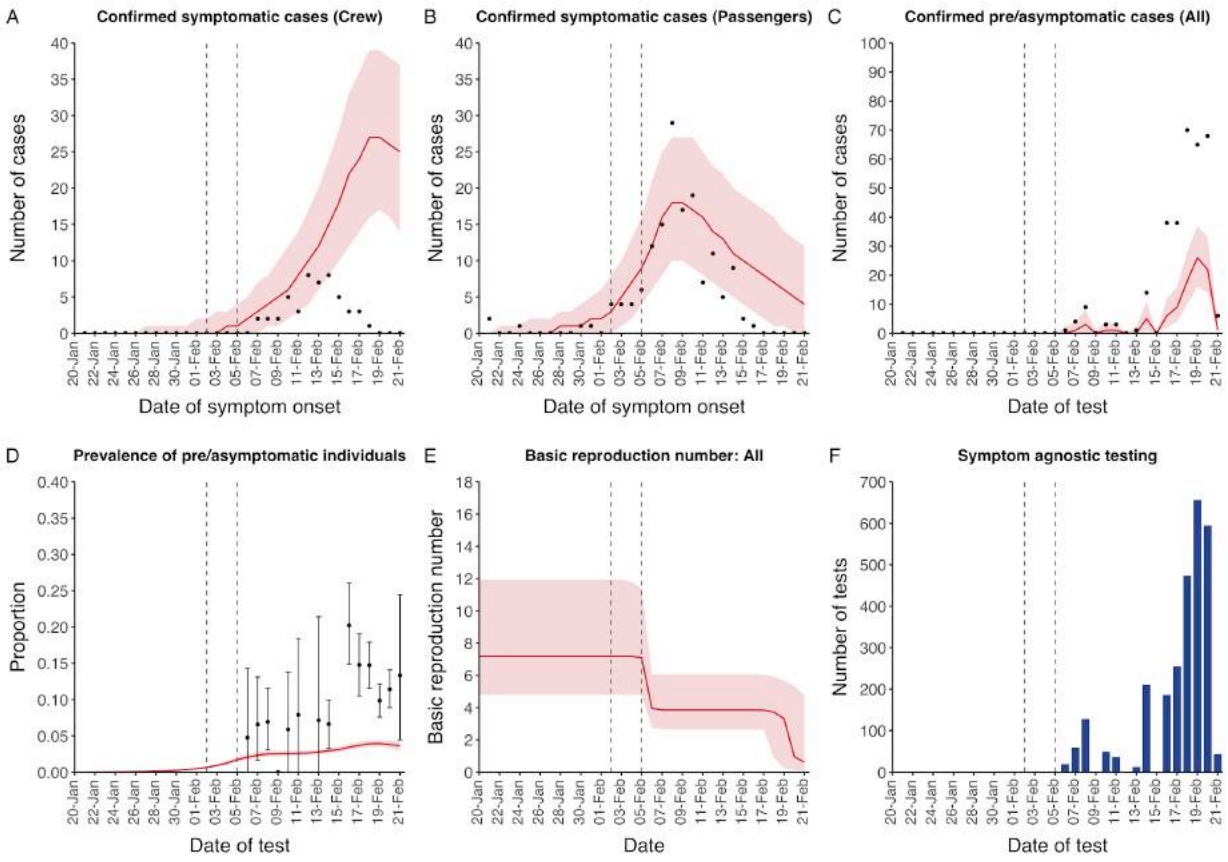


Supplementary Figure 4: *Non-linear correlation between the proportion of transmission from asymptomatics and their relative infectiousness, using 100,000 model runs with parameters sampled from the joint posterior.*

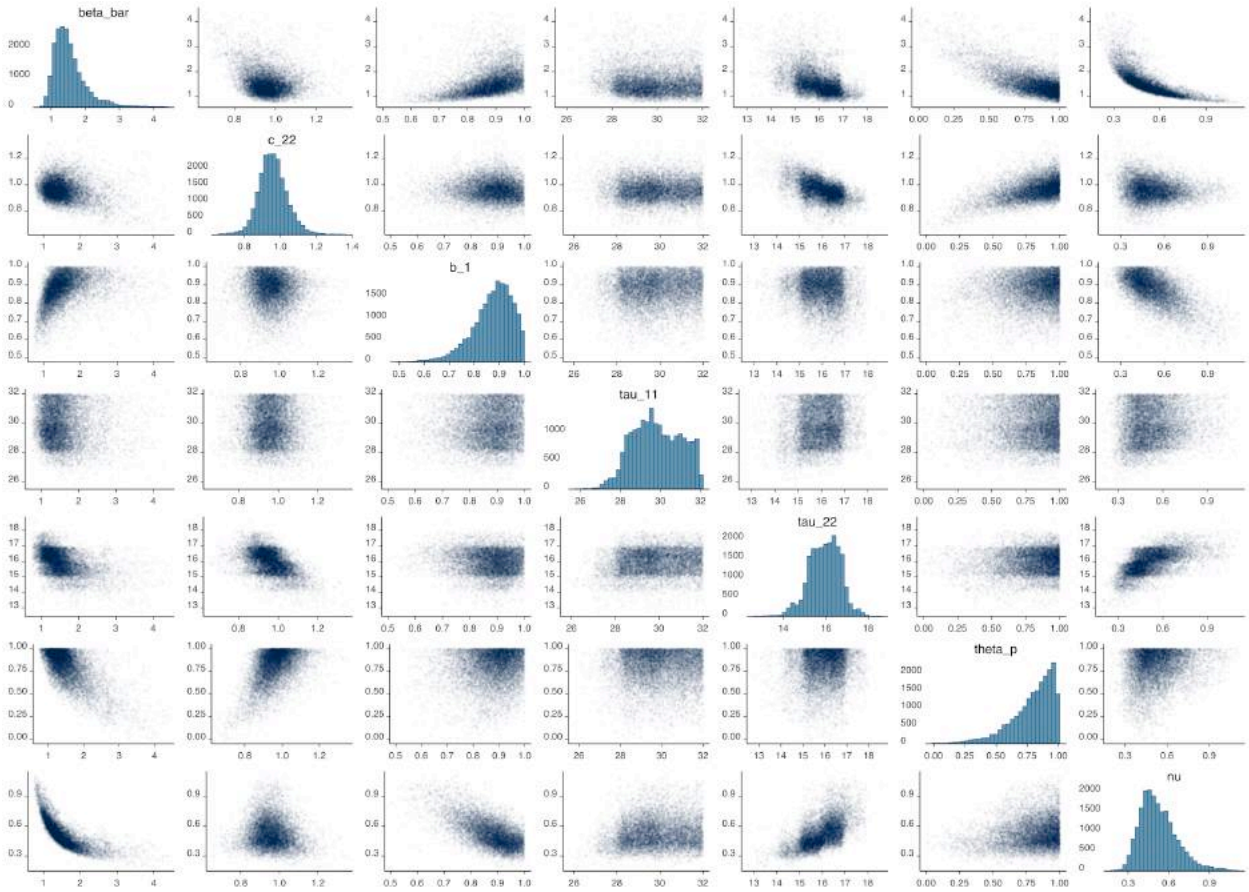
Sensitivity analyses

1. Presymptomatic infection only

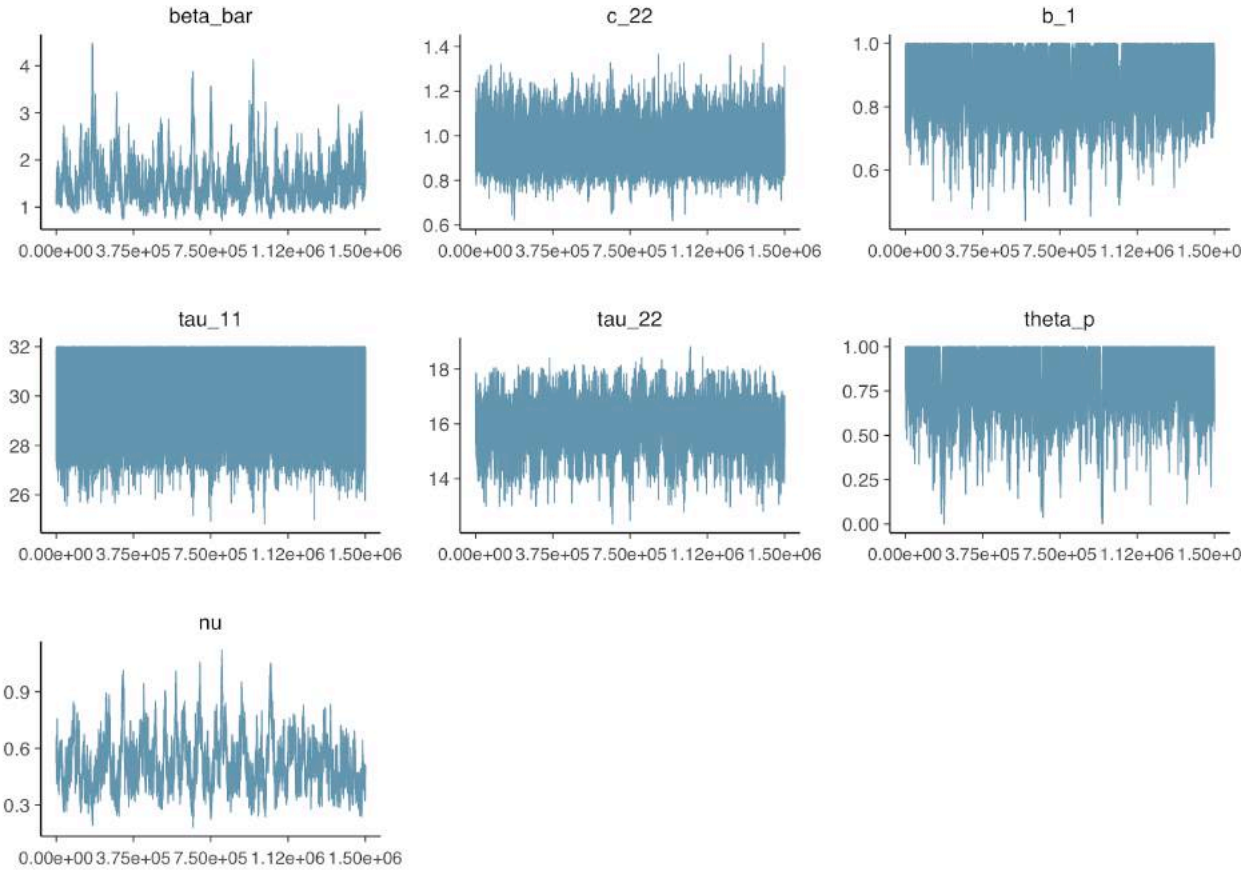
Assumes the proportion of infections that are asymptomatic and their relative infectiousness are zero ($\chi = 0$ and $\theta_a = 0$). The latent period $1/\nu$ is estimated with a uniform prior between 1 and 21 days.



Supplementary Figure 5: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



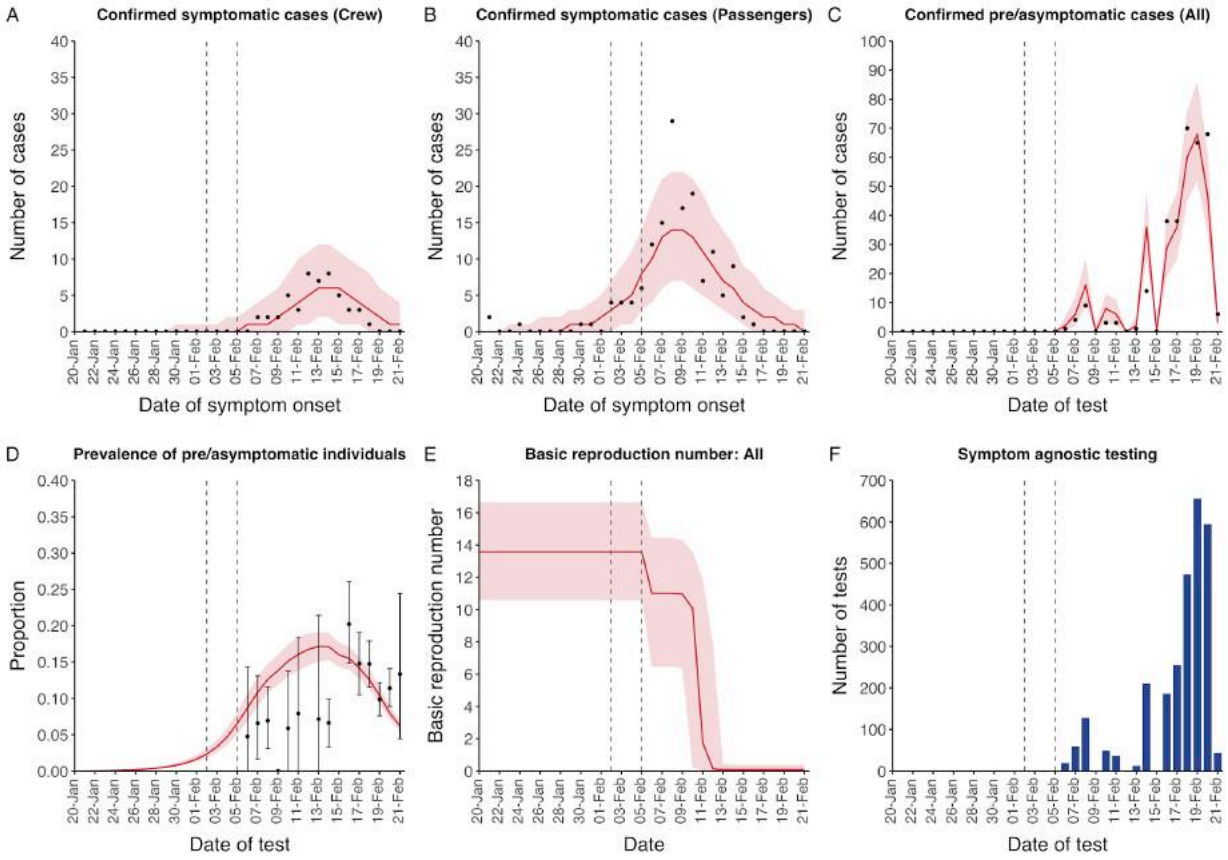
Supplementary Figure 6: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



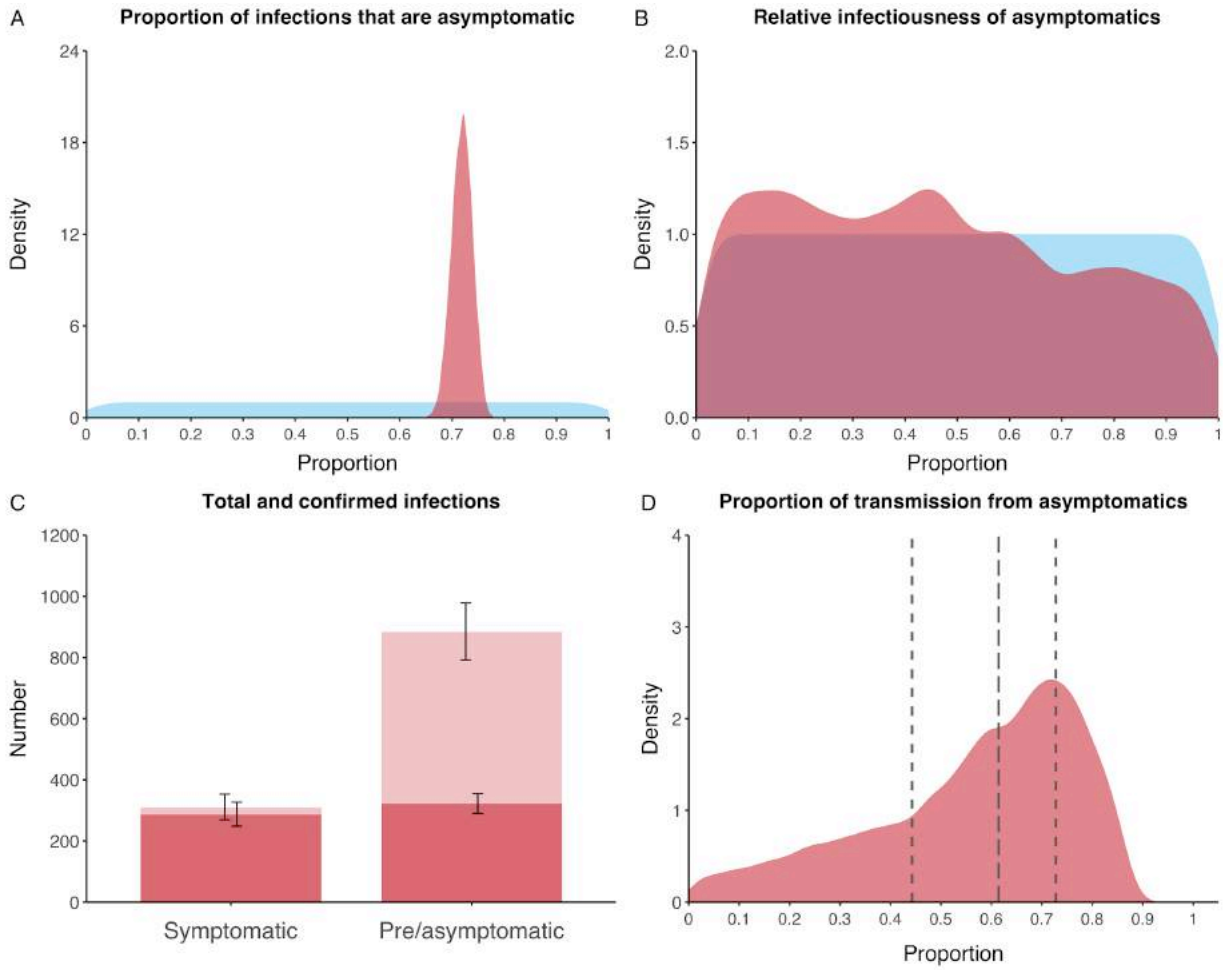
Supplementary Figure 7: *Trace plot from the MCMC for the estimated parameters*

2. ***Relative passenger-crew contact rate: X = 0.02***

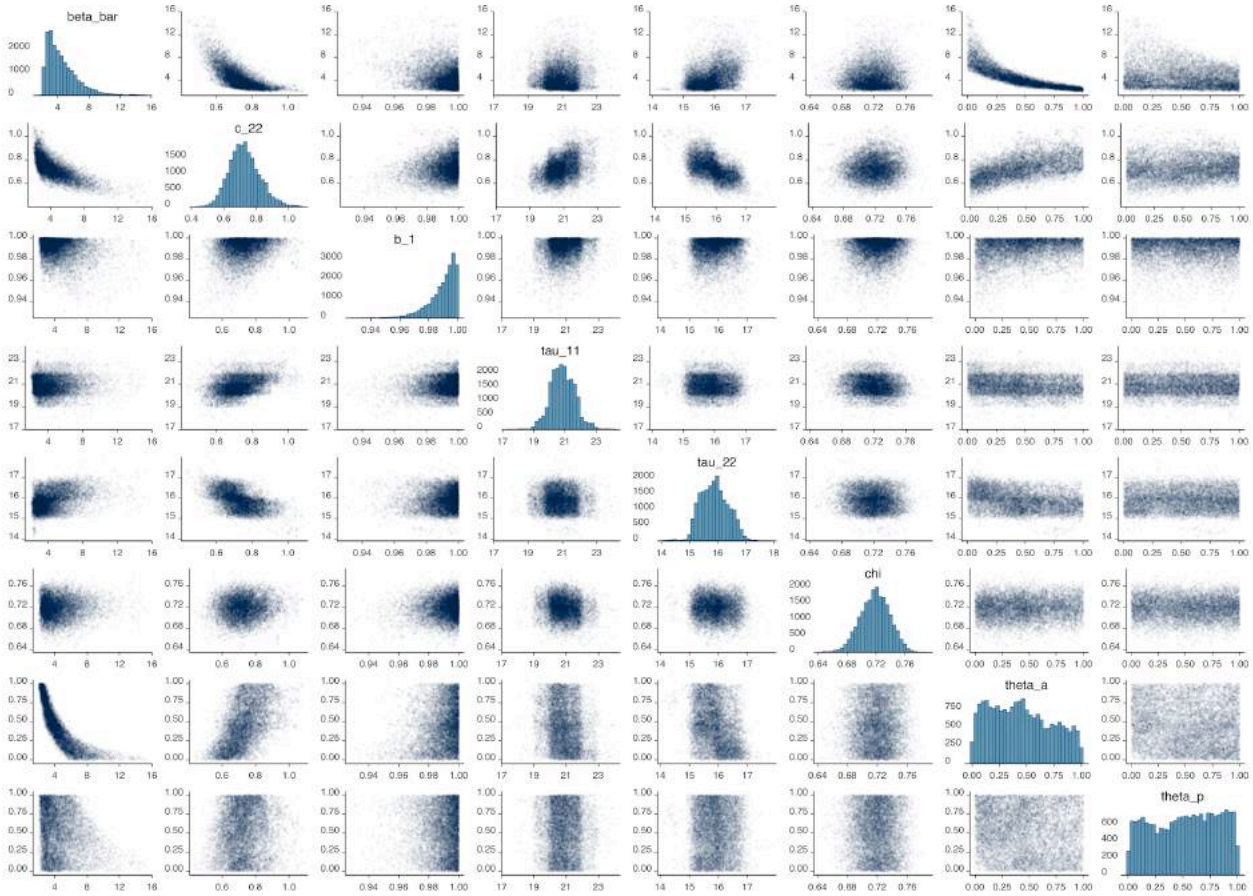
Assumes the contact rate between passengers and crew is 1/50th of contacts between crew and crew ($c^{(pc)}/c^{(cc)} = 0.02$).



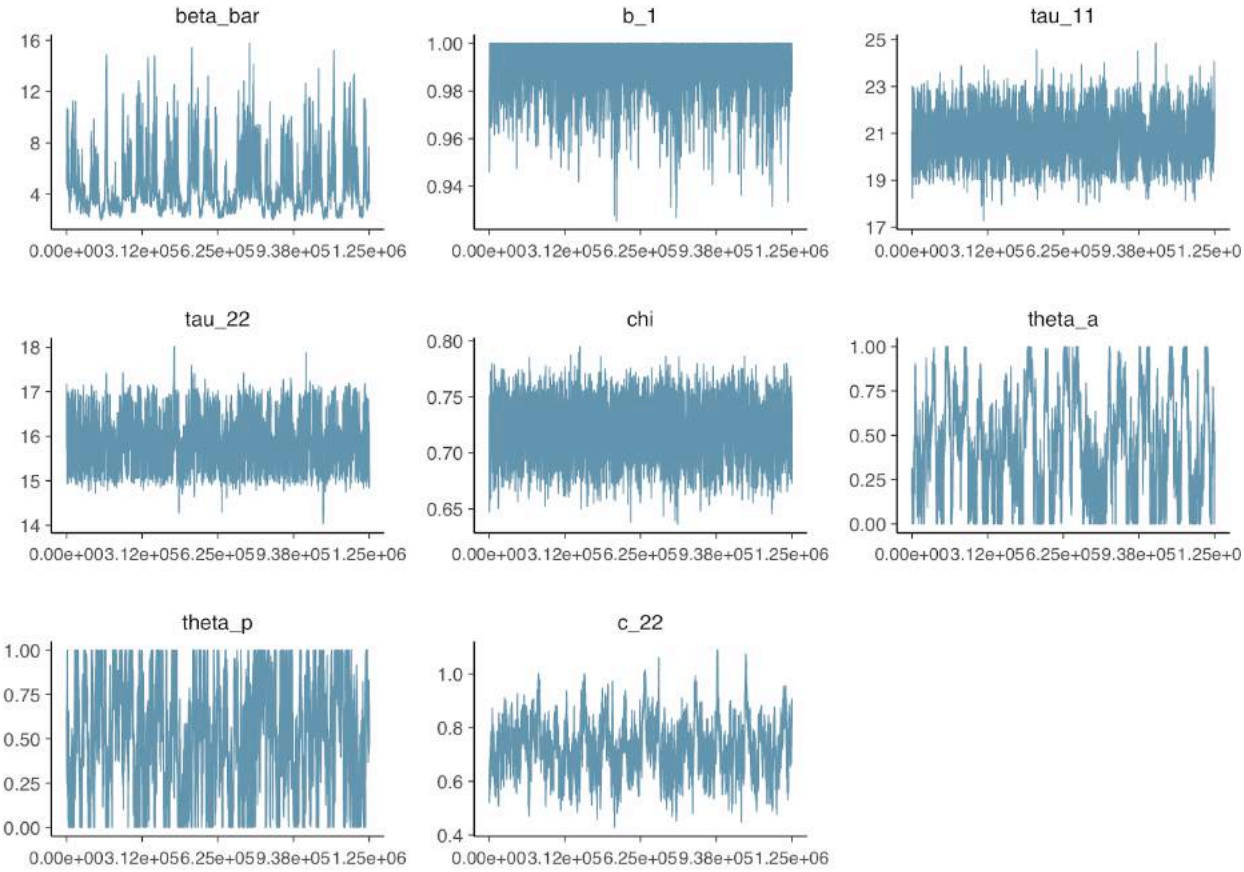
Supplementary Figure 8: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 9: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. See Figure 2 in the main text for full description.*



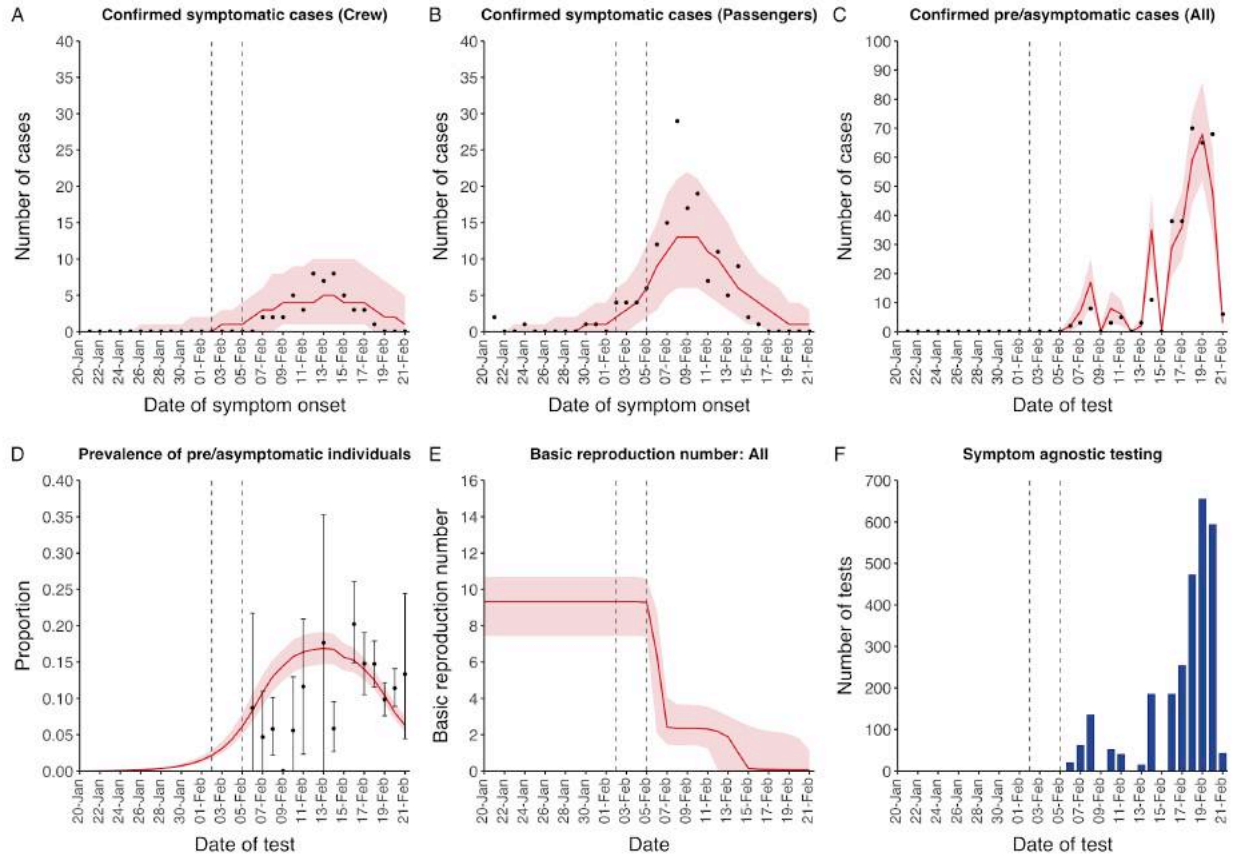
Supplementary Figure 10: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



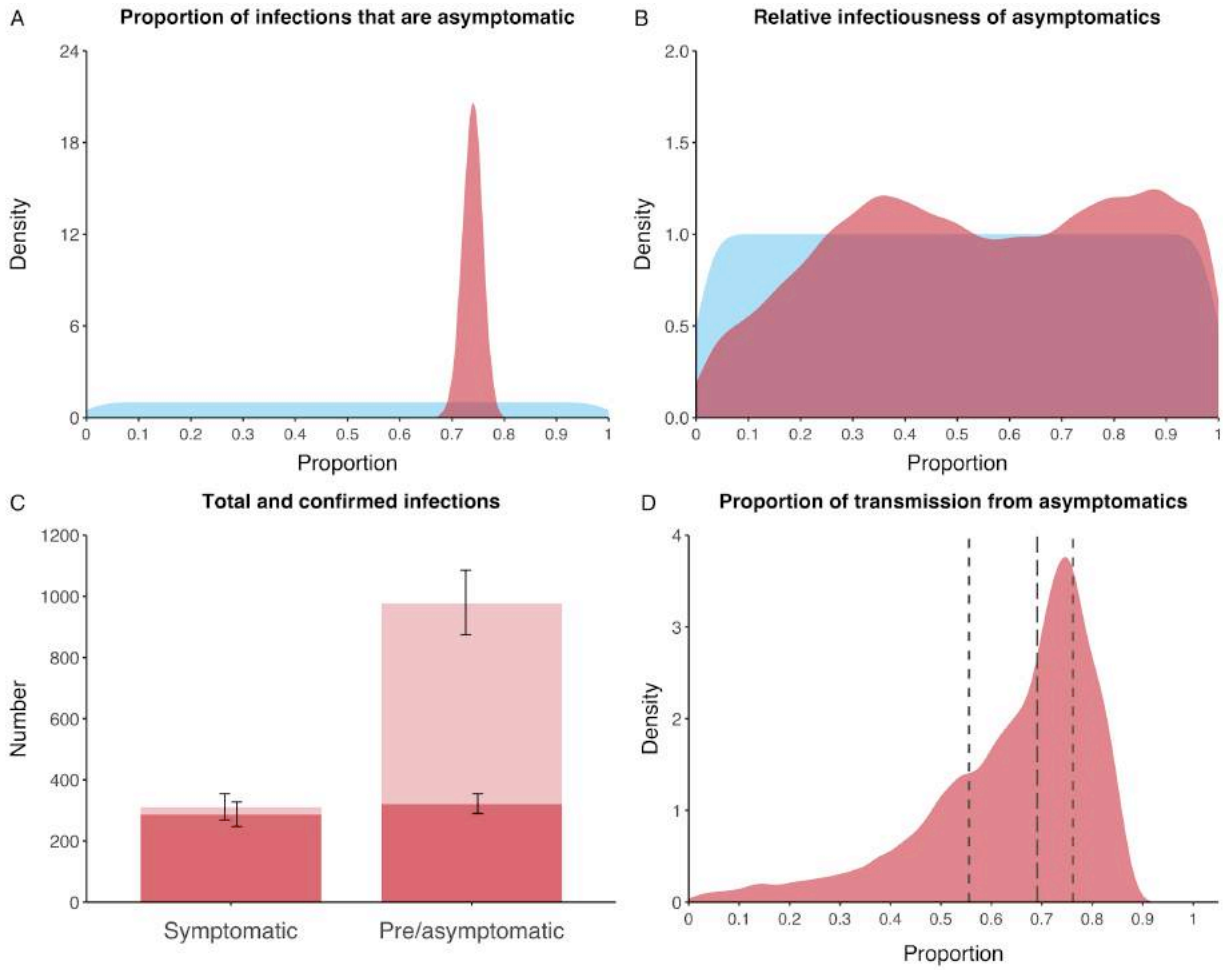
Supplementary Figure 11: *Trace plot from the MCMC for the estimated parameters*

3. *Relative passenger-crew contact rate: X = 0.5*

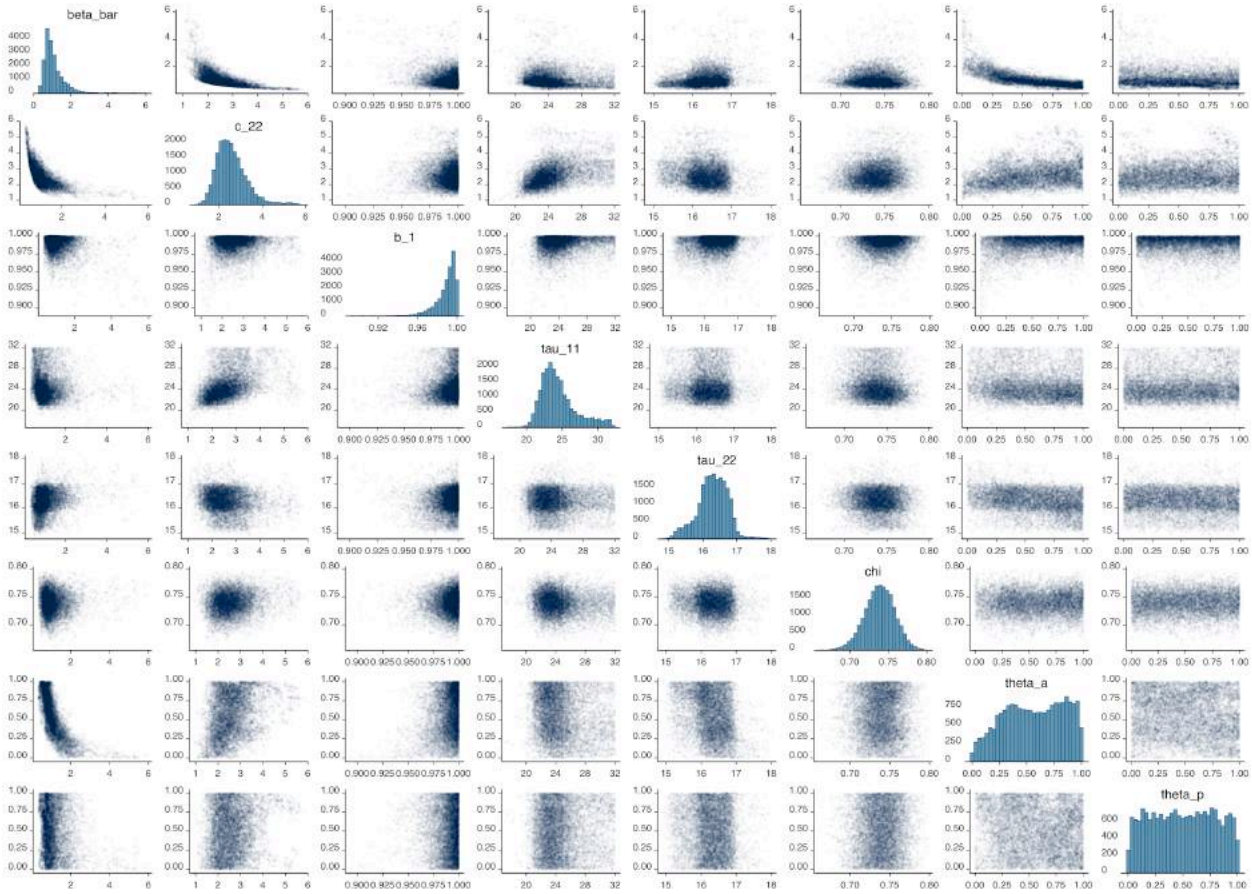
Assumes the contact rates between passengers and crew is half that of between crew and crew ($c^{(pc)}/c^{cc} = 0.5$).



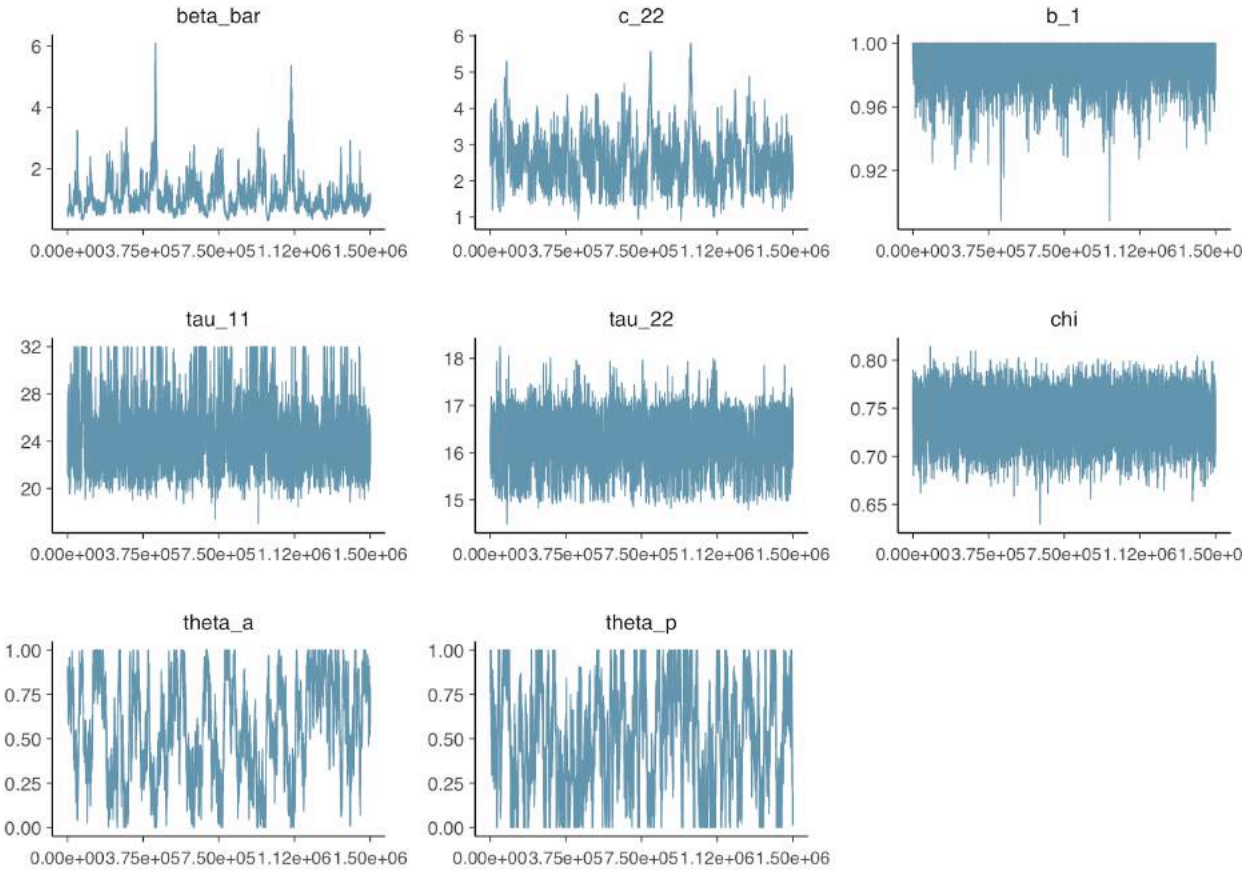
Supplementary Figure 12: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 13: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. See Figure 2 in the main text for full description.*



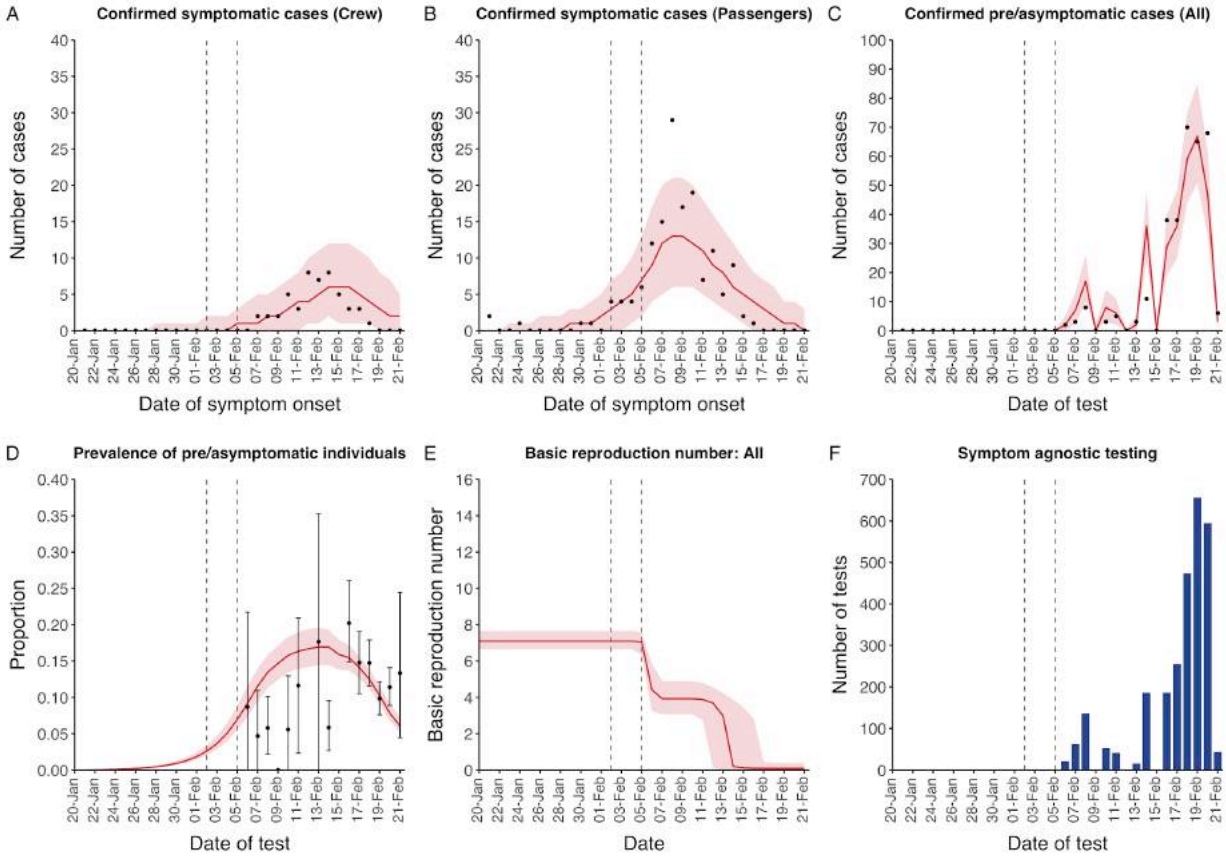
Supplementary Figure 14: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



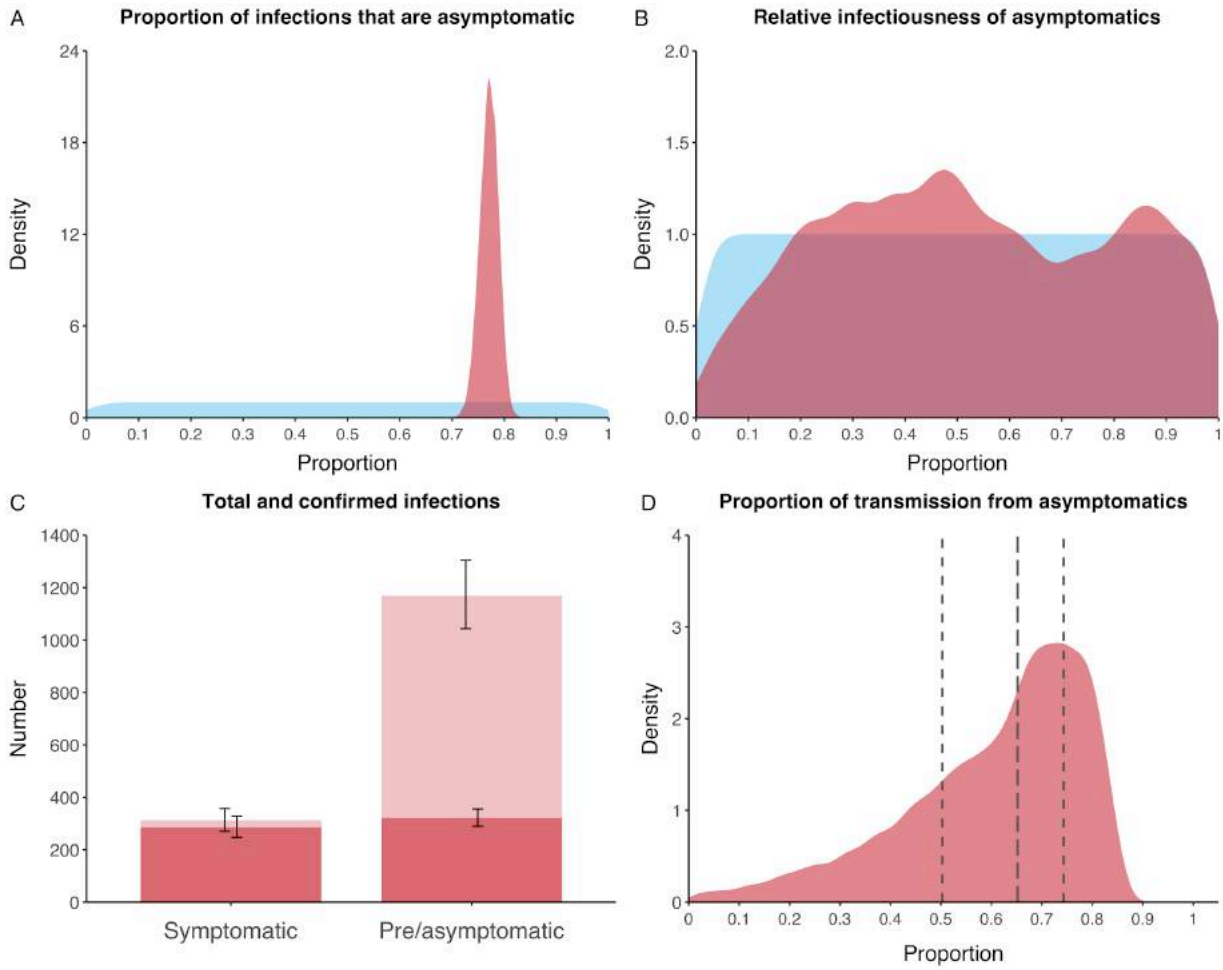
Supplementary Figure 15: *Trace plot from the MCMC for the estimated parameters*

4. Duration of asymptomatic infection: 2.5 days

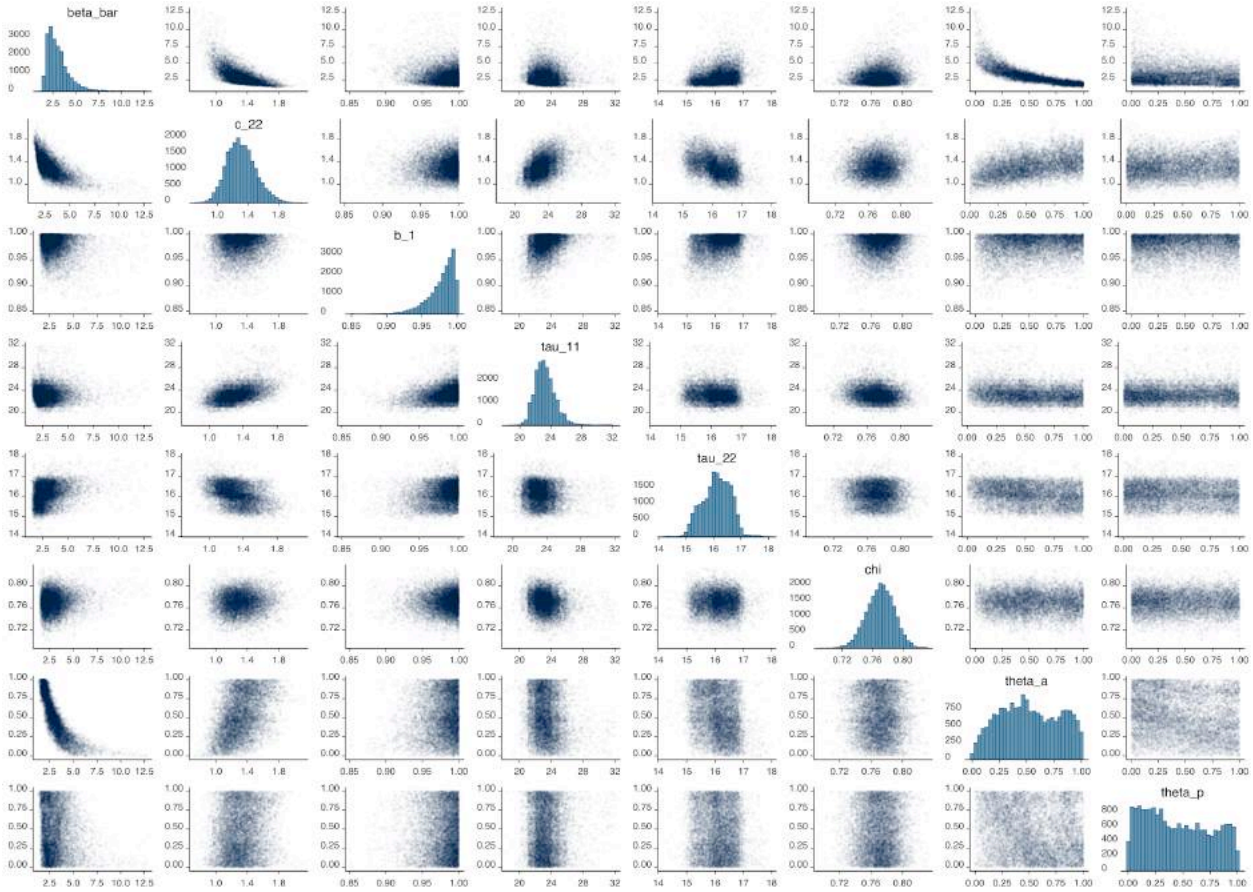
Assumes the average duration of asymptomatic infection is $1/\gamma_a = 2.5$ days, compared to 5 days in the primary analysis.



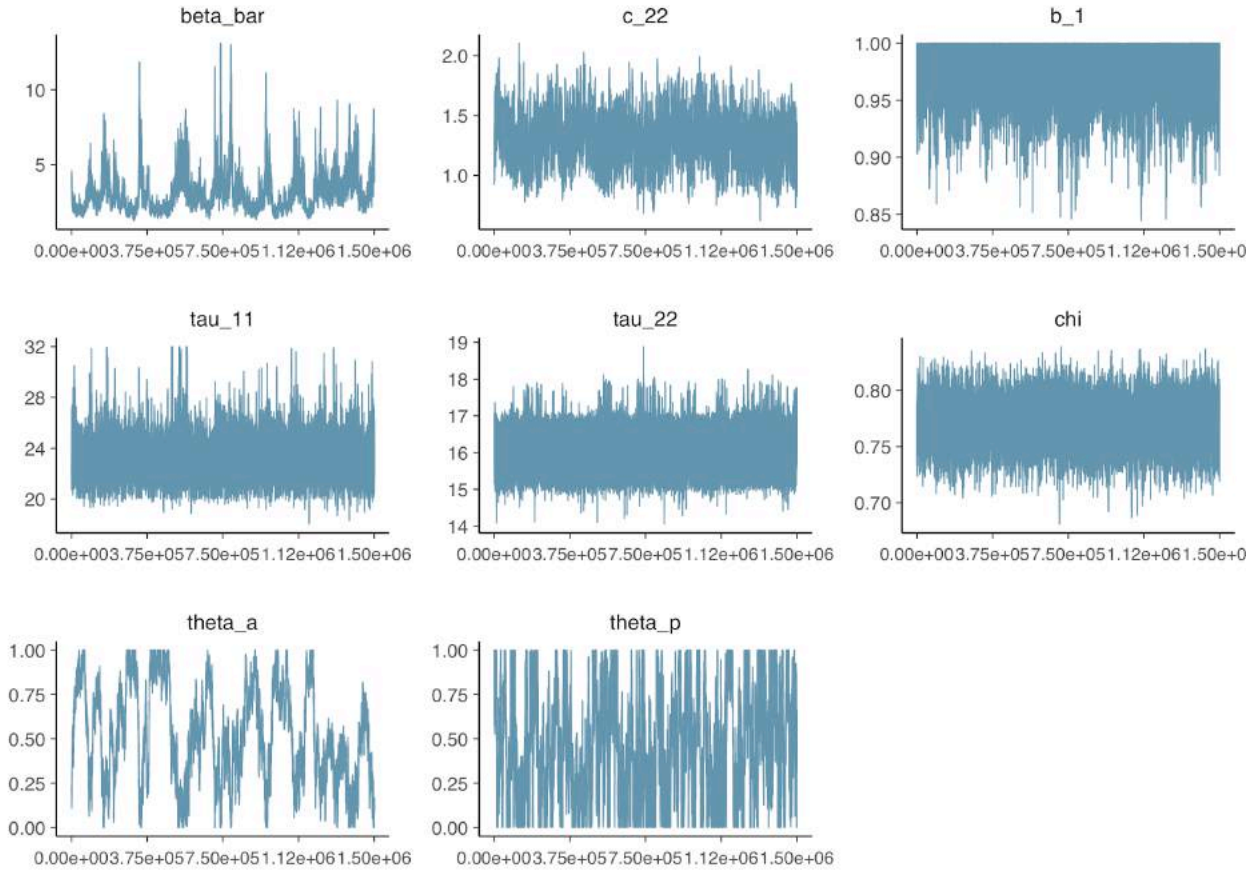
Supplementary Figure 16: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 17: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. See Figure 2 in the main text for full description.*



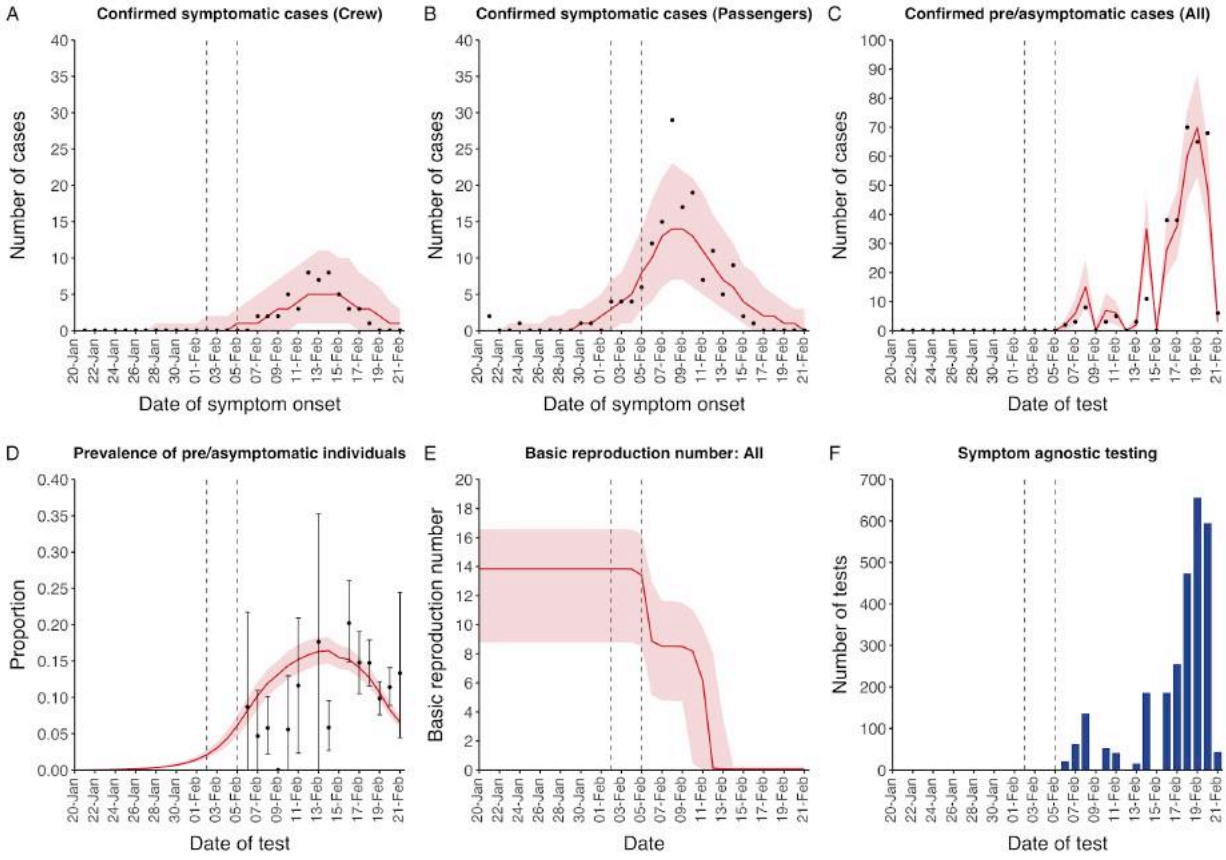
Supplementary Figure 18: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



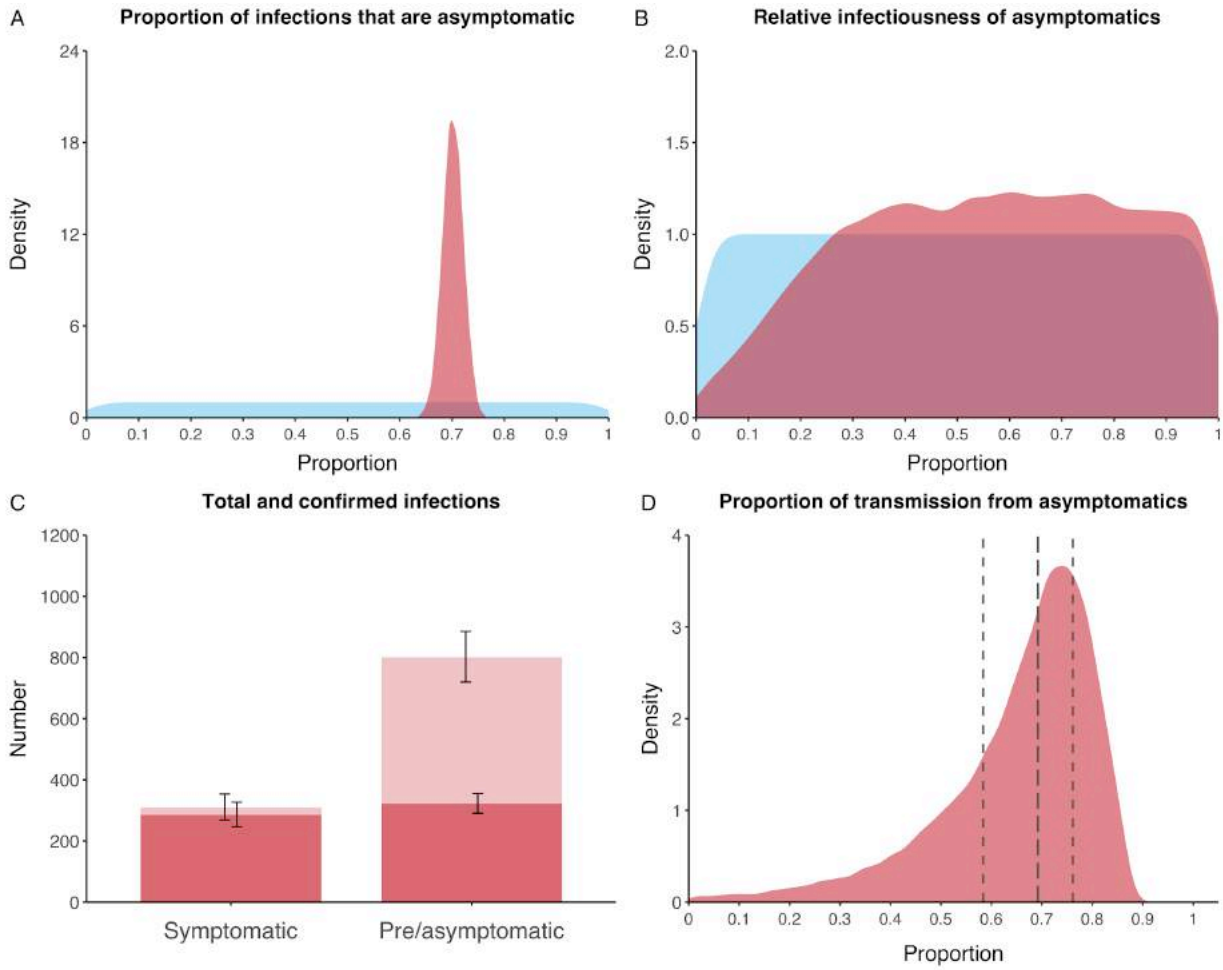
Supplementary Figure 19: *Trace plot from the MCMC for the estimated parameters*

5. *Duration of asymptomatic infection: 10 days*

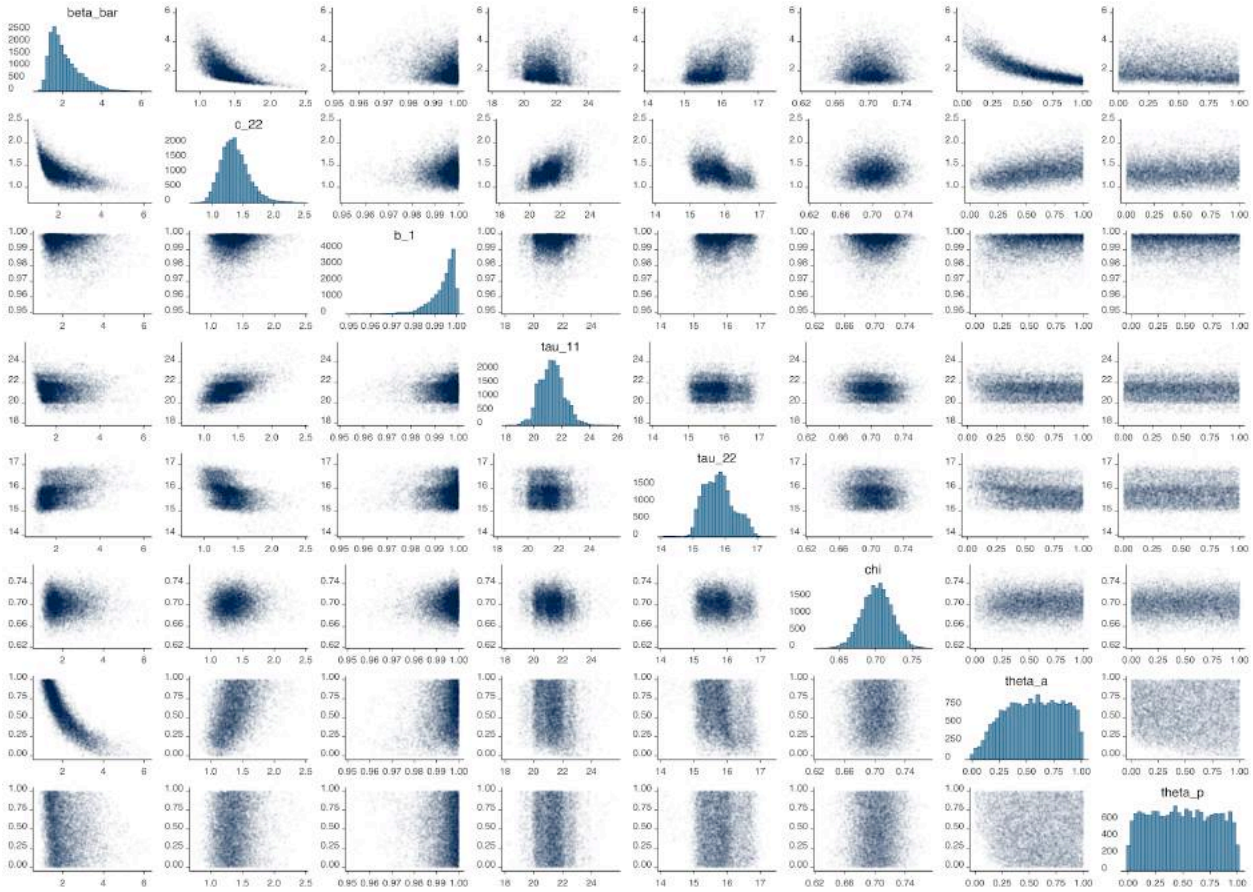
Assumes the average duration of asymptomatic infection is $1/\gamma_a = 10$ days, compared to 5 days in the primary analysis.



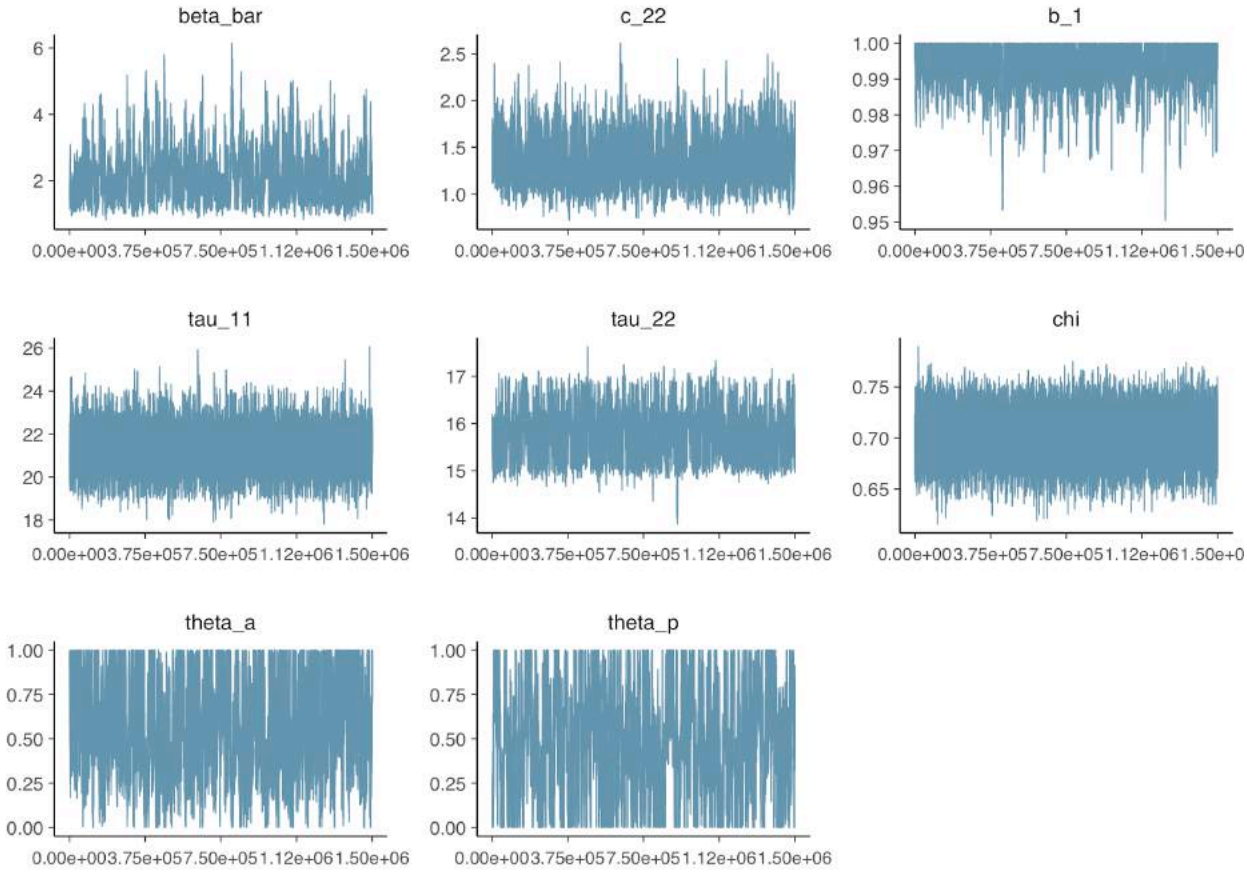
Supplementary Figure 20: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 21: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. See Figure 2 in the main text for full description.*



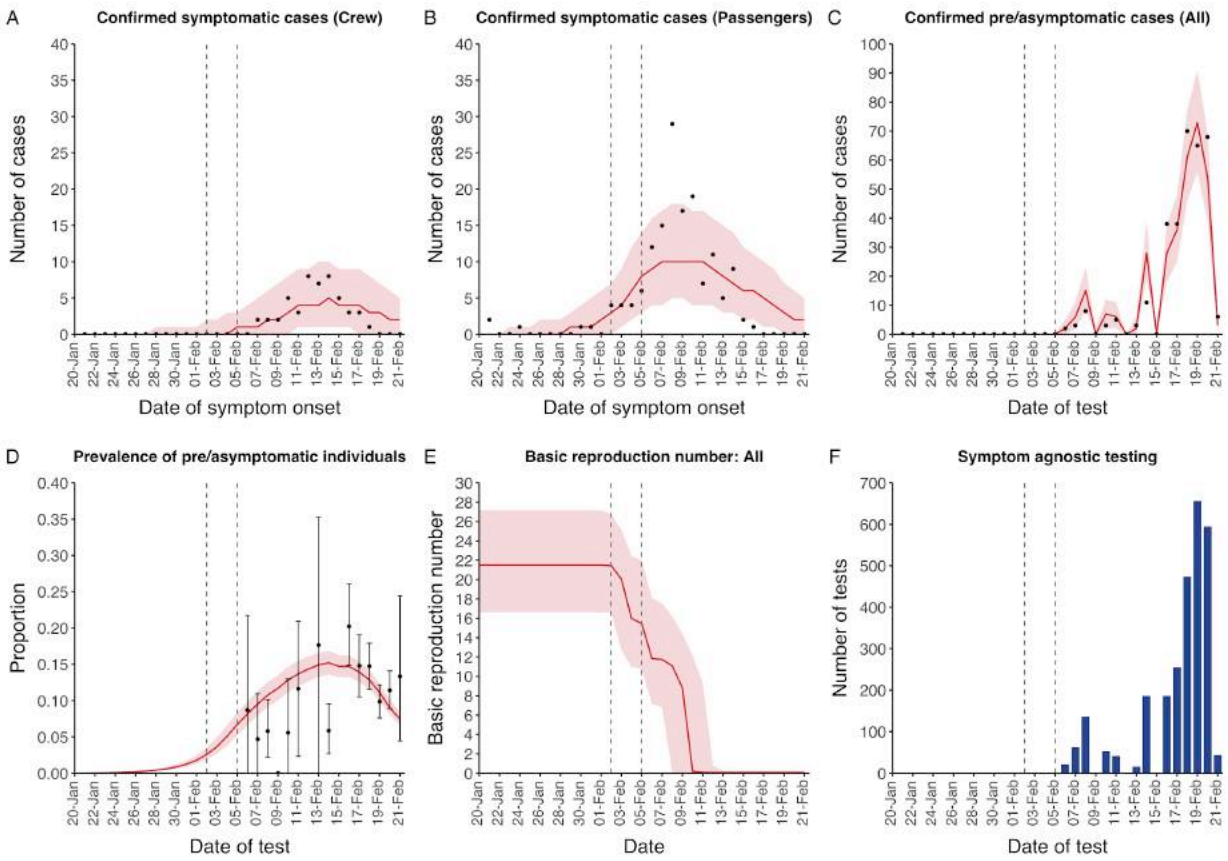
Supplementary Figure 22: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



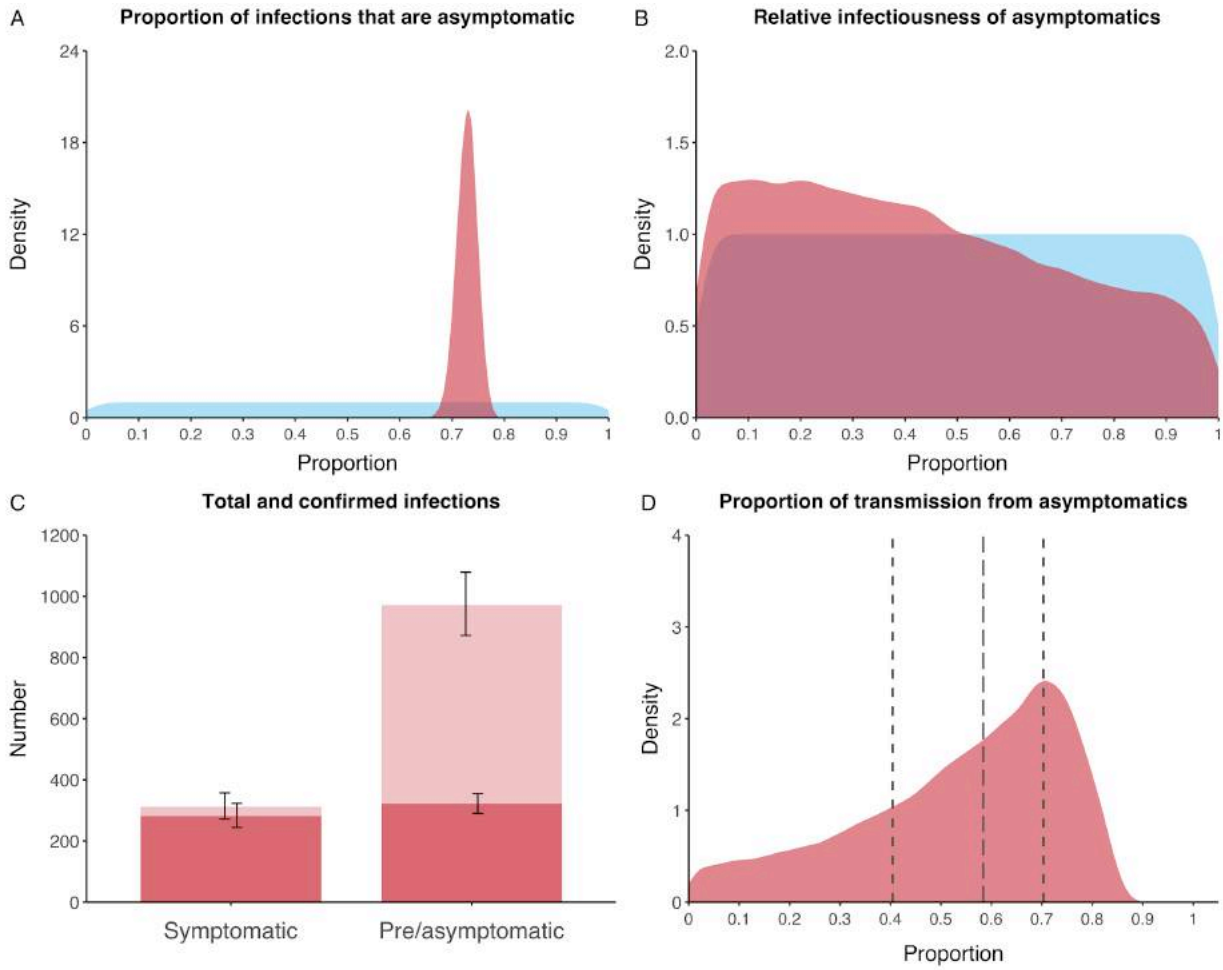
Supplementary Figure 23: *Trace plot from the MCMC for the estimated parameters*

6. *Duration of latent period: 8.8 days*

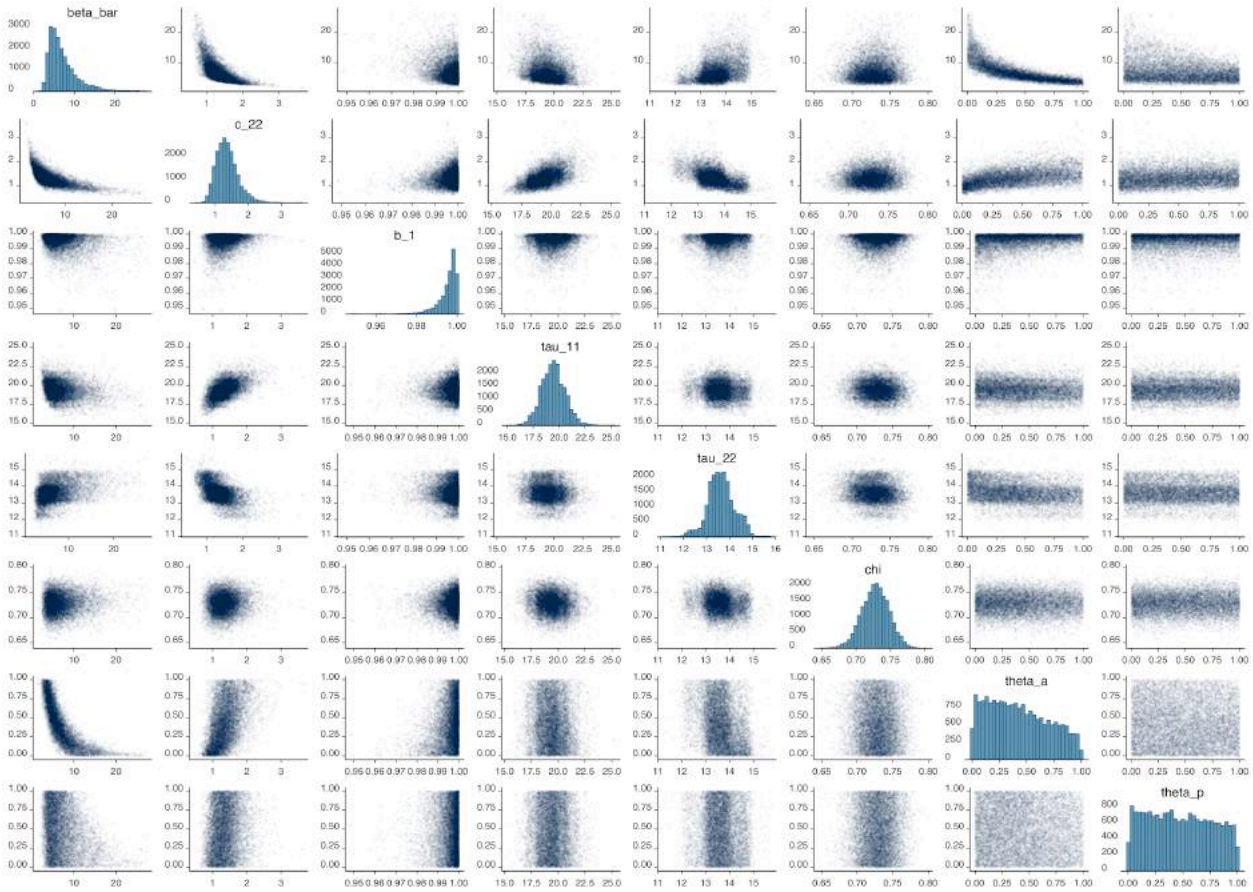
Assumes the average duration for the latent period is $1/\nu = 8.8$ days [4], compared to 4.3 in the primary analysis.



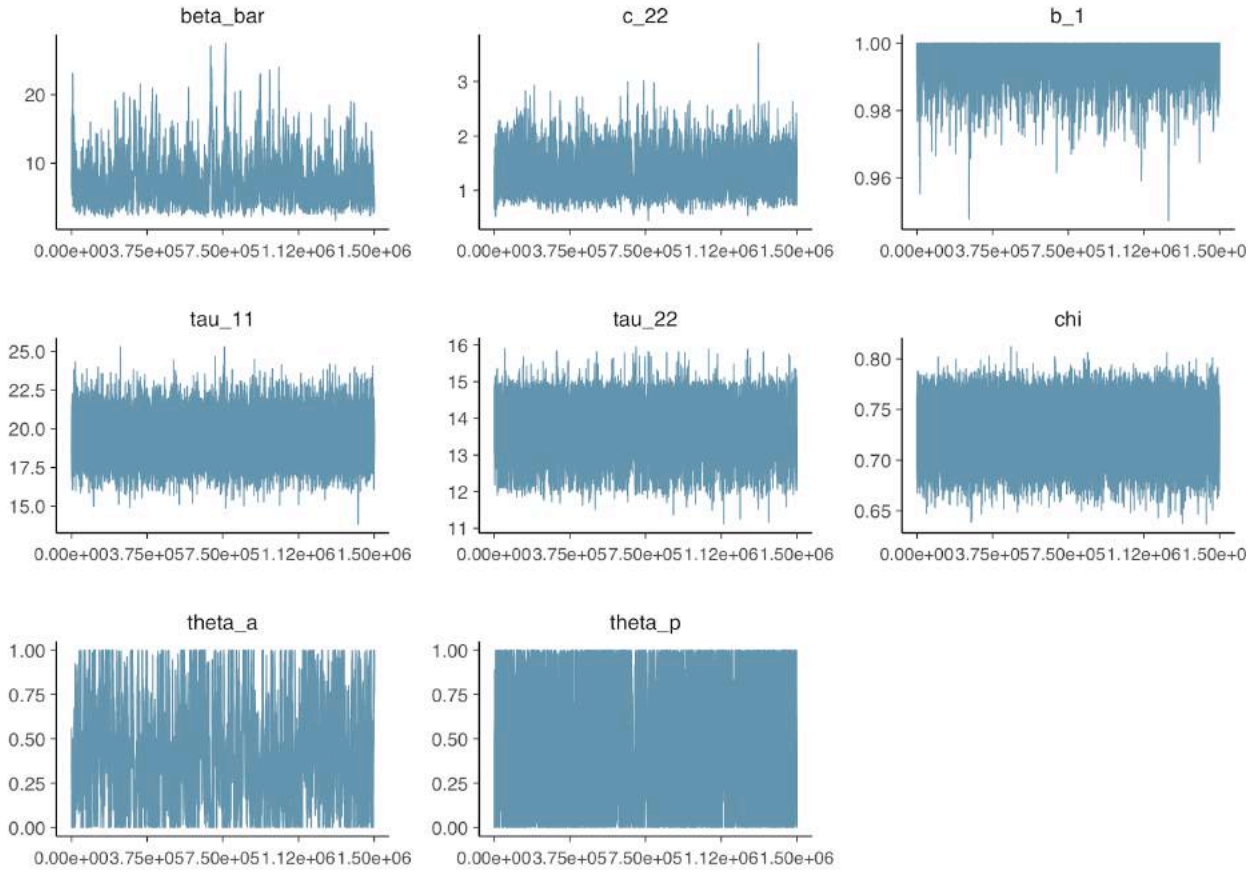
Supplementary Figure 24: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 25: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. See Figure 2 in the main text for full description.*



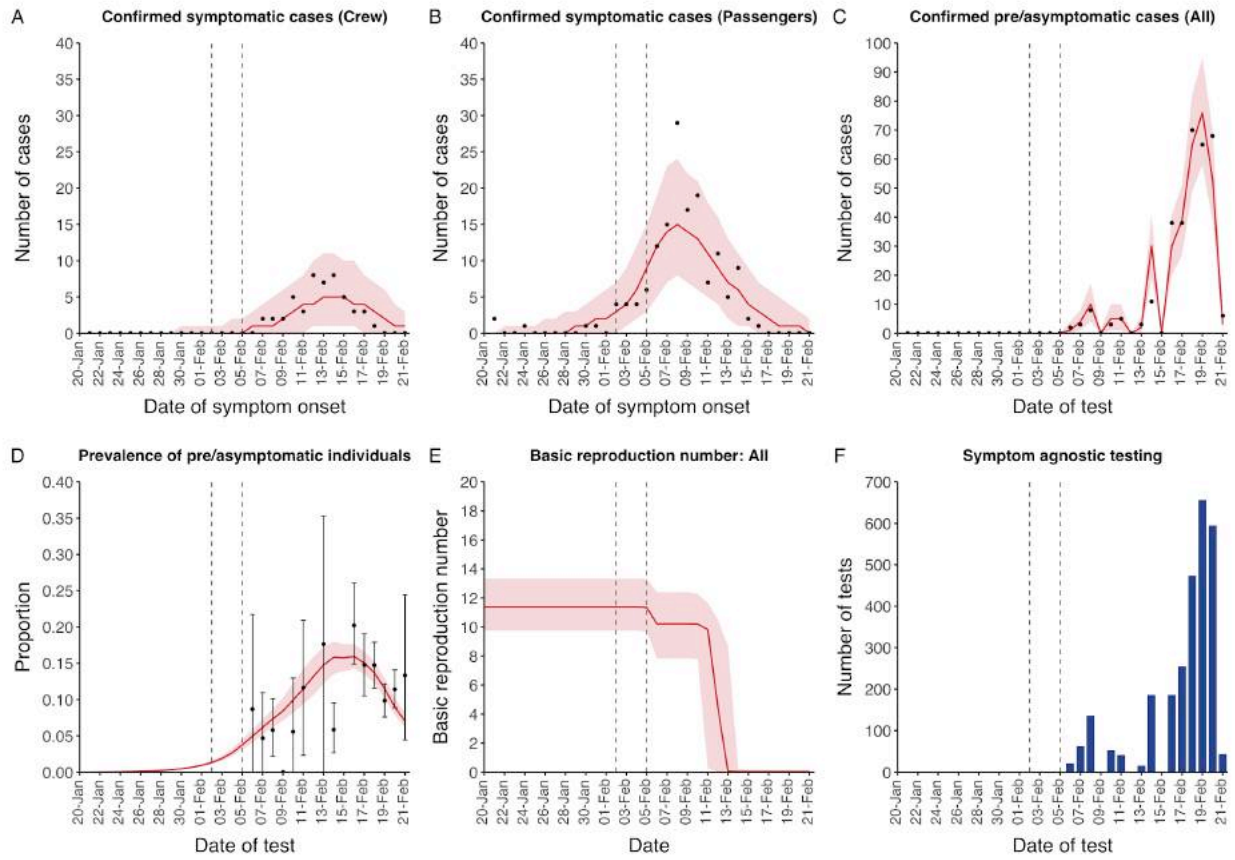
Supplementary Figure 26: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



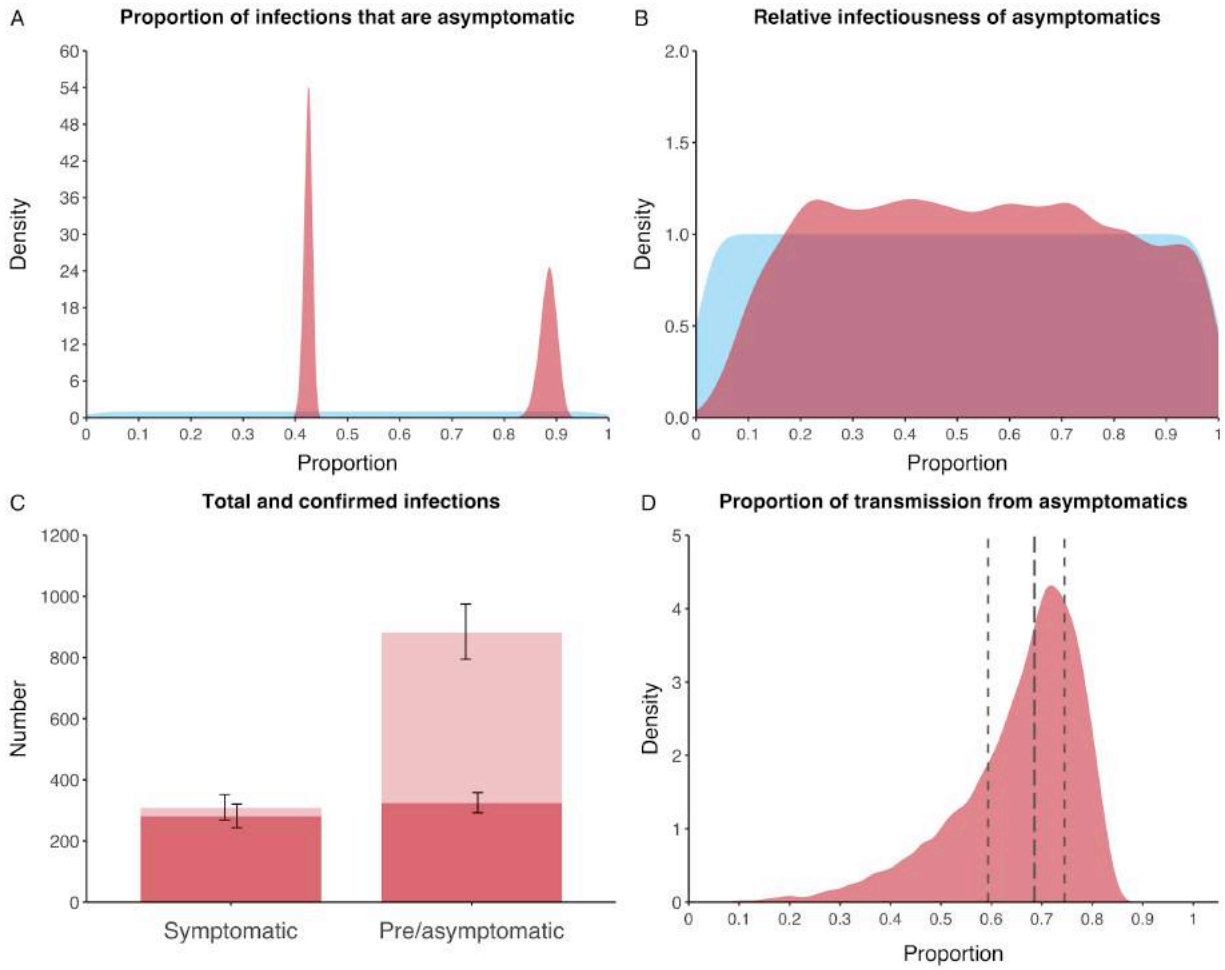
Supplementary Figure 27: *Trace plot from the MCMC for the estimated parameters*

7. *Age dependent proportion asymptomatic*

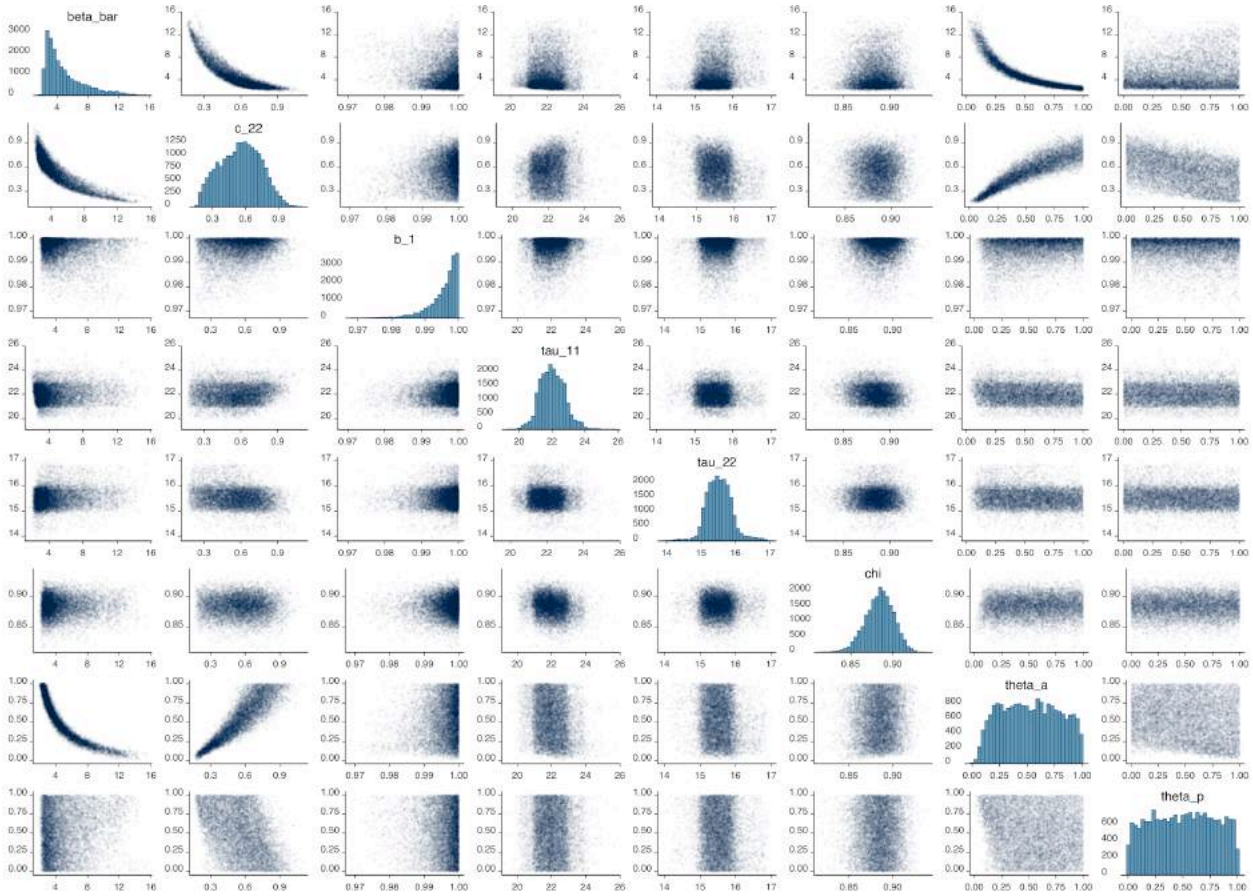
Assumes separate asymptomatic proportions for crew ($\chi^{(c)}$) and passengers ($\chi^{(p)}$) to reflect their different age demographics (median ages of 36 and 69 respectively), compared to a single asymptomatic proportion in the primary analysis. The ratio $\chi^{(p)}/\chi^{(c)}$ was fixed at 0.48 using the results for asymptomatic proportion by age from a model fitted to epidemic data in six countries by Davies et al. [5]



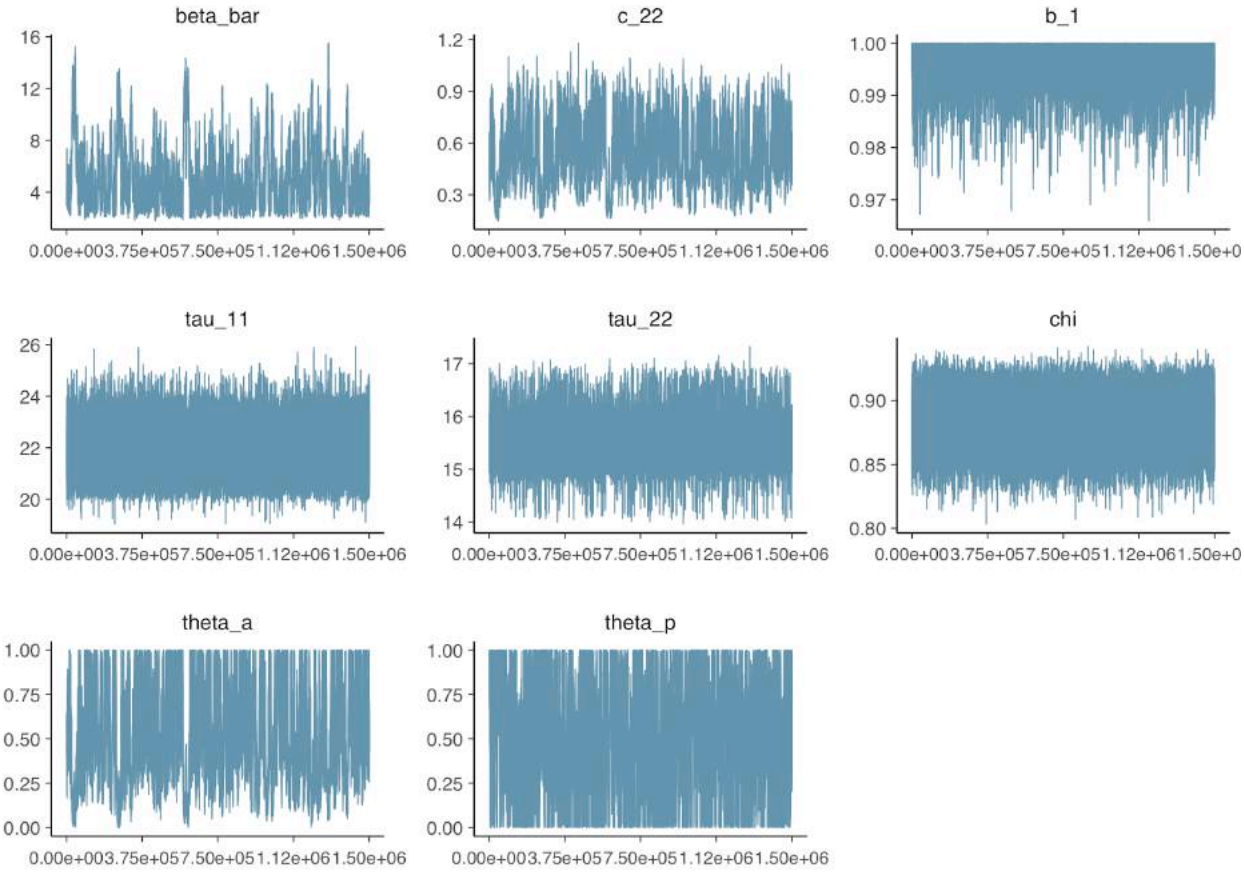
Supplementary Figure 28: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 29: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. The left hand peak in* ***A*** *is for passengers, whilst the right hand peak is for crew. See Figure 2 in the main text for full description.*



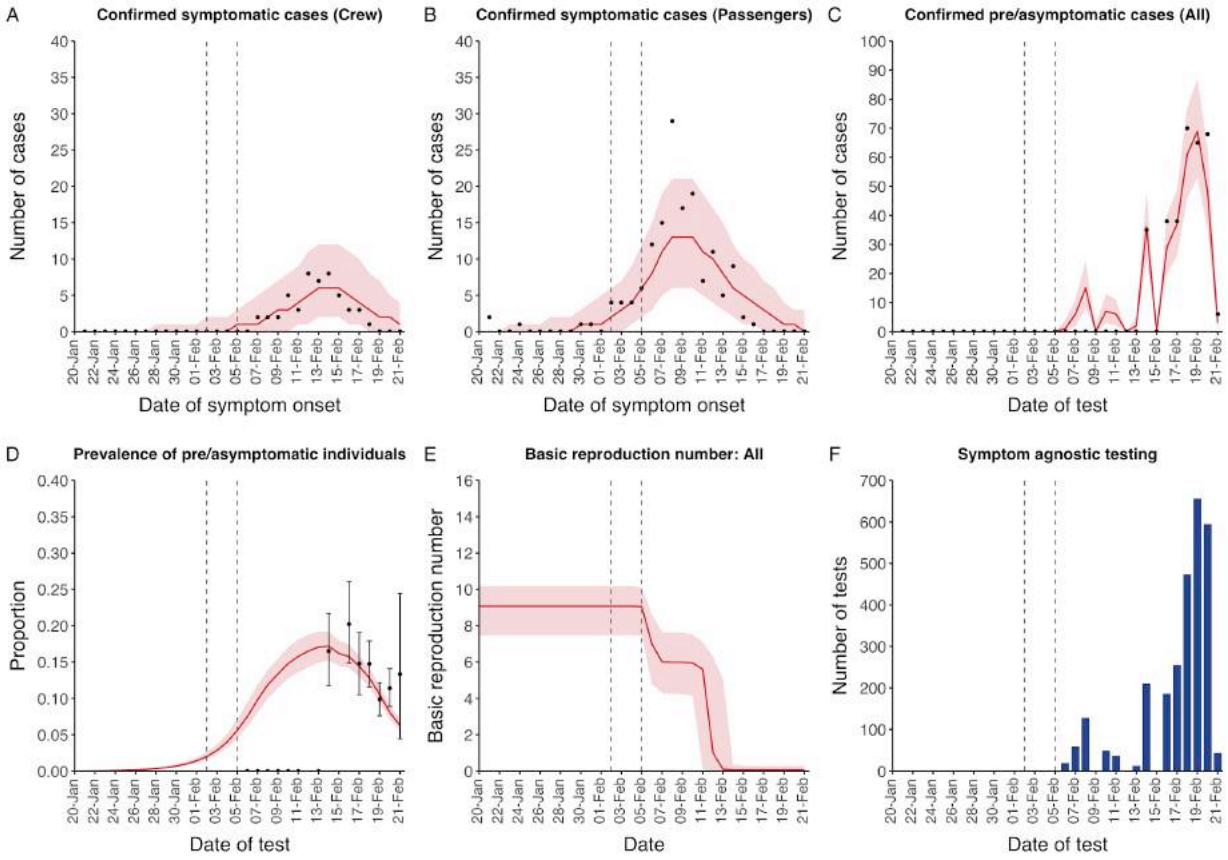
Supplementary Figure 30: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



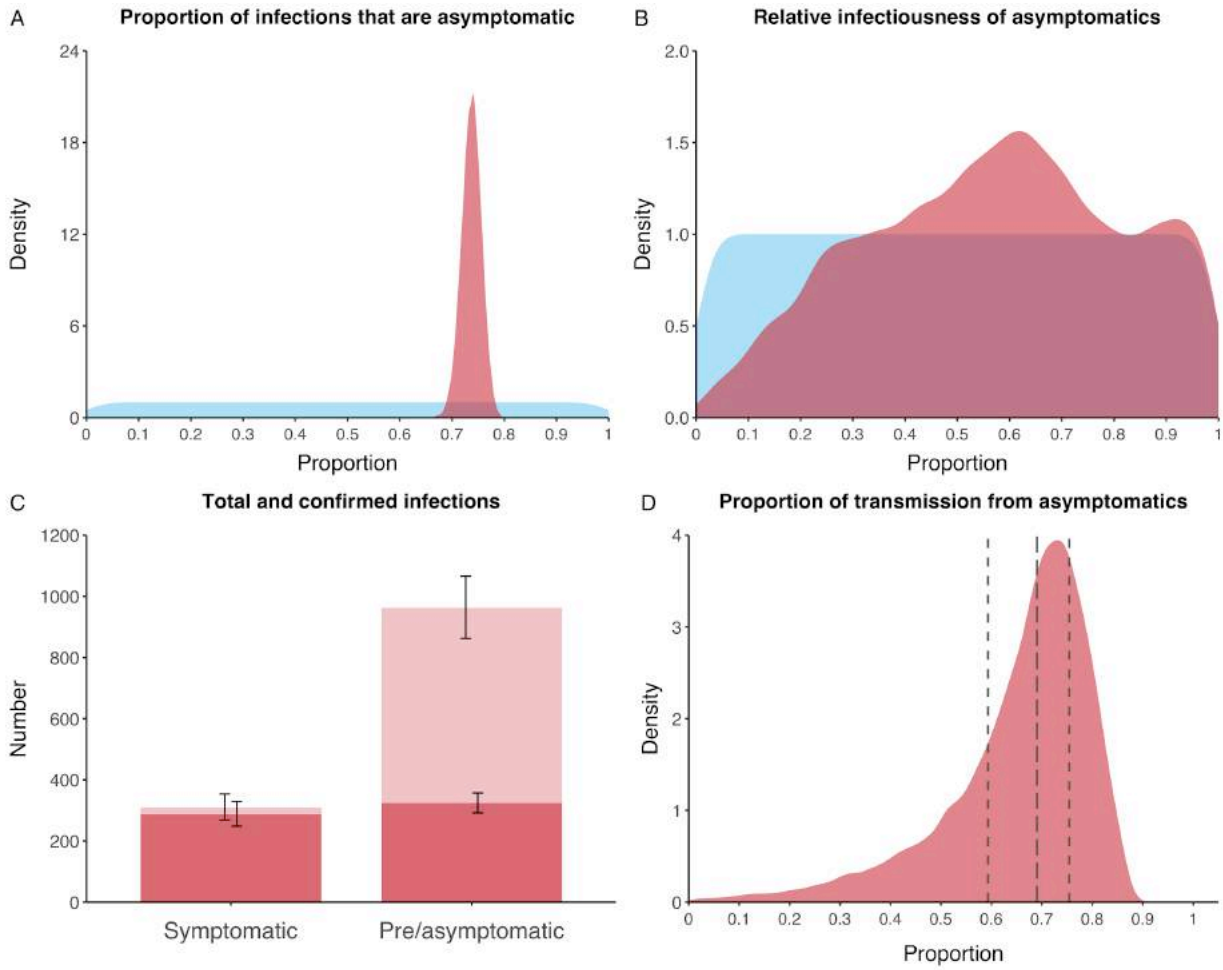
Supplementary Figure 31: *Trace plot from the MCMC for the estimated parameters*

8. Alternative distribution of n=35 confirmed pre/asymptomatic cases

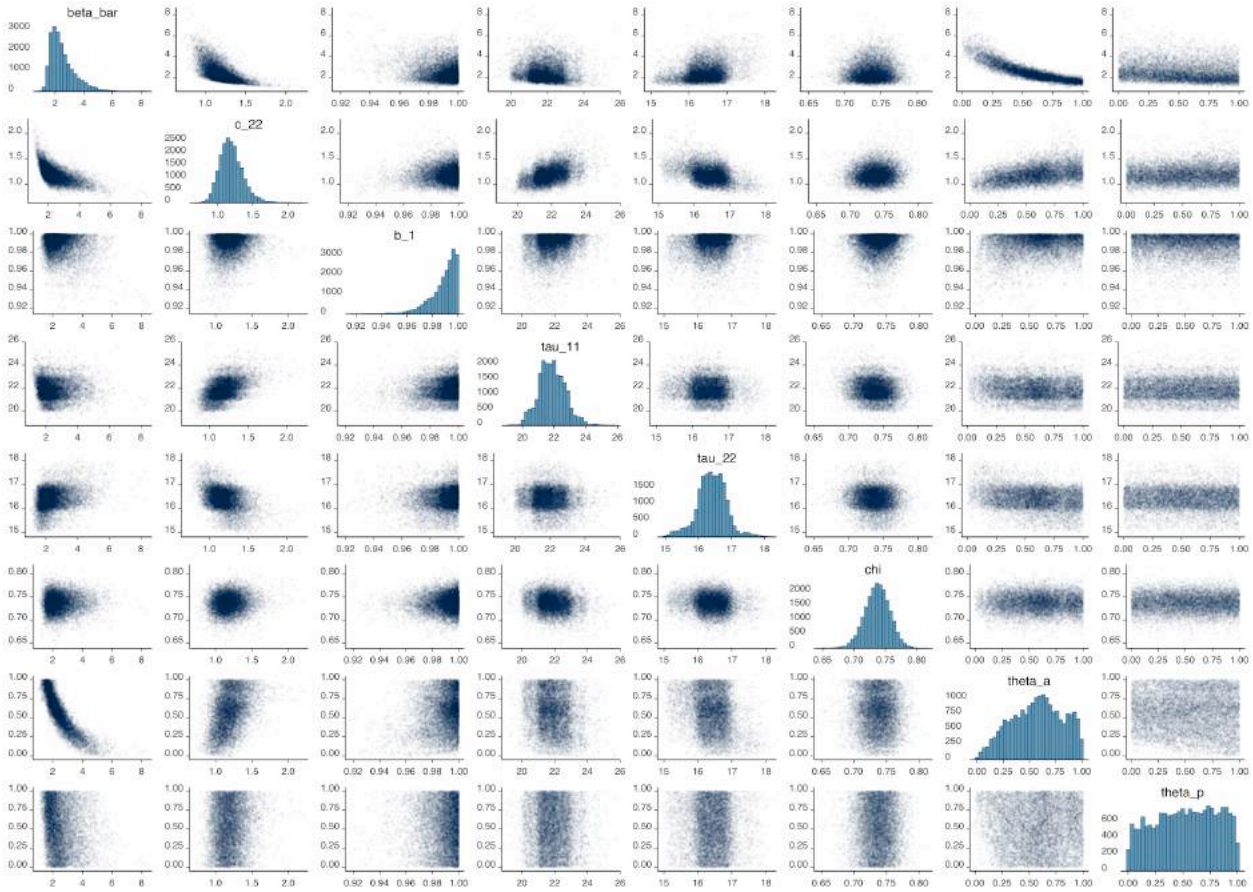
Assumes that n=35 confirmed pre/asymptomatic cases without a test are apportioned to the last possible day (13th Feb), compared to proportional to the total number of tests administered over 6th-13th Feb in the primary analysis.



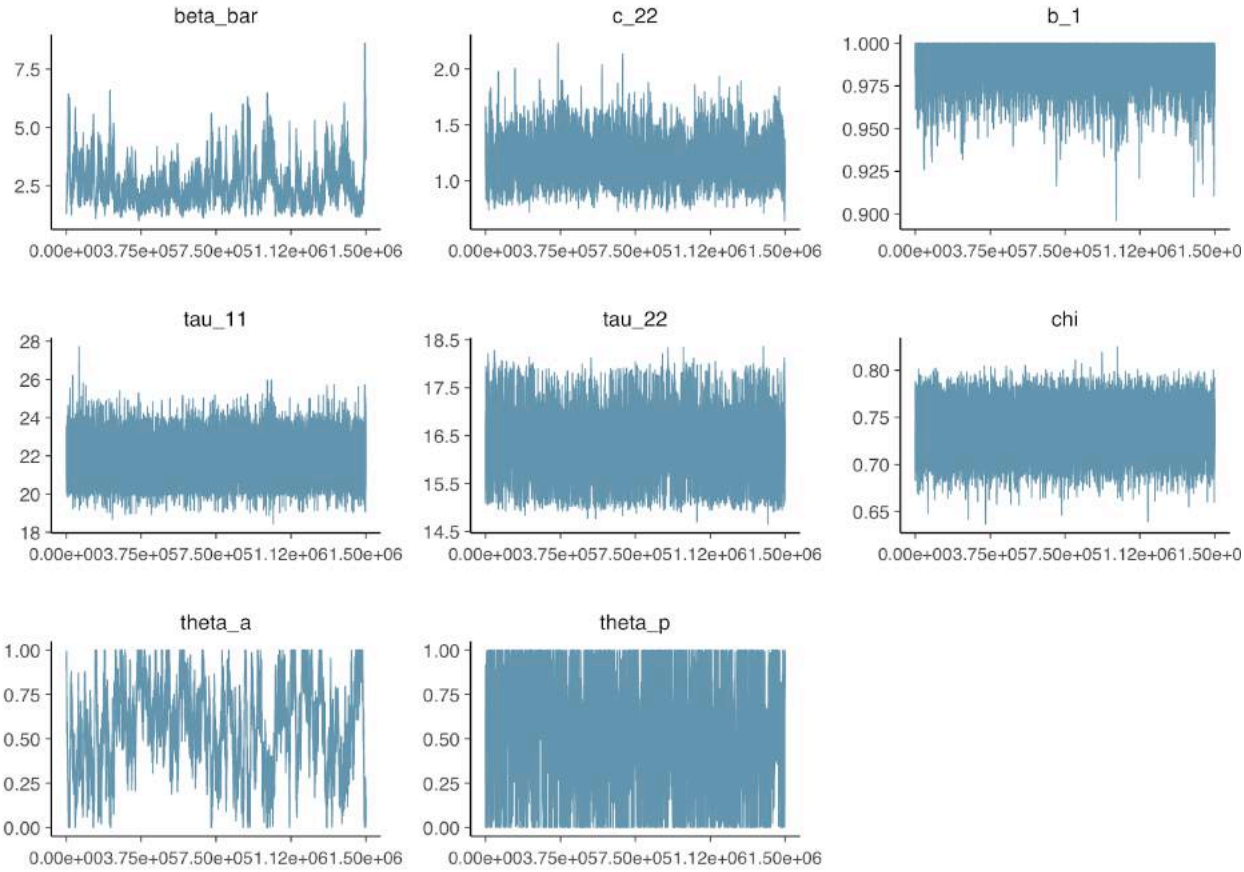
Supplementary Figure 32: *Data from the Diamond Princess and results from model calibration. See Figure 1 in the main text for full description.*



Supplementary Figure 33: *Marginal posterior parameter distributions and results for total/confirmed infections and contribution of asymptomatics to transmission. See Figure 2 in the main text for full description.*



Supplementary Figure 34: *Correlation plot of parameters values from 10,000 samples of the joint posterior distribution.*



Supplementary Figure 35: *Trace plot from the MCMC for the estimated parameters*

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