Supplementary Material: Epidemiological Model

The model described here builds on a previously published model of SARS-CoV-2 transmission introduced in Flaxman et al, 2020 [1], subsequently extended into a two-category framework in Faria et al, 2020 [2]. Replication code is available at `https://github.com/ImperialCollegeLondon/Delta_Variant_Delhi`.

Model Specification The model describes two categories, denoted $s \in \{1, 2\}$. The population-unadjusted reproduction number for the first category is defined as

$$R_{s=1,t} = \mu_0 \, 2 \, \sigma(X_t) \,, \tag{1}$$

where μ_0 is a scale parameter (3.3), σ is a logistic function, and X_t is an second-order autoregressive process with weekly time innovations, as specified in earlier work[3]. The population-unadjusted reproduction number of the second category is modelled as

$$R_{s=2,t} = \rho \mathbf{1}_{[t_2,\infty)} R_{1,t} \,, \tag{2}$$

with

$$\rho \sim \text{Gamma}(5, 5) \; \in [0, \infty) \,, \tag{3}$$

where ρ is a parameter defining the relative transmissibility of category 2 compared to category 1 and $\mathbf{1}_{[t_2,\infty)}$ is an indicator function taking the value of 0 prior to t_2, and 1 thereafter, highlighting that category 2 does not contribute to the observed epidemic evolution before its emergence. The prior for ρ is chosen because it weakly informative, setting 90% of prior mass a between $\times 0.4$ and $\times 1.8$ increase in transmissibility, while maintaining a neutral to conservative default in the context of increased transmissibility since it has a mean of $\times 1$ and median of $\times 0.9$.

Infections arise for each category according to a discrete renewal process [4, 5]

$$i_{s,t} = \left(1 - \frac{n_{s,t}}{N}\right) R_{s,t} \sum_{\tau < t} i_{s,\tau} g_{t-\tau} \,, \tag{4}$$

where N is the total population size, $n_{s,t}$ is the total extent of population immunity to category s present at time t, and g is the generation interval distribution.

The susceptible depletion term for category s is modelled as

$$n_{s,t} = \sum_{\tau<t} i_{s,\tau} W_{t-\tau} + \beta_s \left(1 - \alpha_{s,t}\right) \sum_{\tau<t} i_{\setminus s,\tau} W_{t-\tau} \,. \tag{5}$$

where $\setminus s$ denotes not-s, under assumptions of symmetric cross-immunity with prior

$$\beta \sim \text{Beta}(2, 1) \,. \tag{6}$$

Immune escape or the evasion of cross-immunity of Delta, as reported in the analysis, is defined as the complement of the cross-immunity parameter, that is $(1 - \beta)$. The prior for β has been chosen to reflect our default assumption that the mostly likely scenario is no evasion of cross-immunity. $W_{t-\tau}$ is the time-dependent waning of immunity elicited by previous infection, which is modelled as a Rayleigh survival-type function with Rayleigh parameter of sigma = 310, which produces 50% of individuals still immune after 1 year. The cross-immunity susceptible term $\alpha_{s,t}$ is modelled as

$$\alpha_{s,t} = \frac{(1 - \beta_s) \sum_{\tau<t} i_{s,\tau} W_{t-\tau}}{N - \beta_s \sum_{\tau<t} i_{s,\tau} W_{t-\tau}} \,. \tag{7}$$

Infections in Delhi are seeded for six days at the start of the epidemic from t_1 as

$$i_{1,t_1} \sim \text{Exponential}(1/\tau) \,, \tag{8}$$

with

$$\tau \sim \text{Exponential}(0.03) \,, \tag{9}$$

and the second category for six days from t_2, which is 14-02-2021 in the central scenario, as

$$i_{2,t_2} \sim \text{Normal}(1, 20^2) \ \in [1, \infty) \,. \tag{10}$$

Non-unit seeding of the B.1.617.2 variant and the diffuse prior represent our uncertainty in the precise date and magnitude of B.1.617.2's introduction/importation into Delhi.

The model generates deaths via the following mechanistic relationship:

$$d_t = \sum_s \text{ifr}_s \sum_{\tau<t} i_{s,\tau} \pi_{t-\tau} \,. \tag{11}$$

The infection fatality ratios of each of the categories (ifr_s) are given moderately informative priors:

$$\text{ifr}_s \sim \text{Normal}(0.25, 0.02^2) \in [0, 100] \tag{12}$$

with our central estimate based on the results of Brazeau et al [6] and adjusted for the demography of the city. We allow for variation around the estimate of 0.25 however, with the prior providing some support for IFRs in the range 0.15% - 0.35%. This range is similar to estimates by Banaji for Mumbai, a city with comparable demographics, for which an IFR is reported with 95% confidence intervals of (0.15%, 0.33%).[7] A limitation of the model is the assumption of homogeneous exposure across subsets of the population.

Likelihood component 1. The observation model uses three types of data from four sources. In the first, the likelihood for the expected deaths D_t, is modelled as negative-binomially distributed,

$$D_t \sim \text{NegativeBinomial}(d_t(1-\omega), d_t + \frac{d_t^2}{\phi}) \,, \tag{13}$$

with mortality data d_t and dispersion prior

$$\phi \sim \text{Normal}(0, 5^2) \in [0, \infty) \,. \tag{14}$$

and underreporting factor ω, which describes the degree of death underascertainment, e.g. a value of 0.25 means 25% of COVID-19 deaths are not reported (due, e.g. to limited testing). The central scenario chosen for death underreporting is 50%, due to the wide range values reported in available literature for Delhi and India.[8, 9, 10, 7, 11, 12] To mitigate the effect of the uncertainty in death underreporting, sensitivity tests are carried out a range of values, ω in {10%, 33%, 50%, 66%}, to ensure inferences are robust.

Likelihood component 2. The second likelihood is based on genomic data from individuals where infections were sequenced and where the sequence was uploaded to GISAID. Specifically, the proportion of sequenced genomes identified as B.1.617.2 at time t are modelled with a binomial likelihood

$$G_t^+ \sim \text{Binomial}(G_t^+ + G_t^-, \theta_t) \,, \tag{15}$$

with positive counts for B.1.617.2 denoted G_t^+ and counts for lineages not belonging to B.1.617.2 recorded as G_t^-. The success probability for B.1.617.2 positivity is modelled as the infection ratio

$$\theta_t = \frac{\tilde{i}_{2,t}}{\tilde{i}_{1,t} + \tilde{i}_{2,t}} \,, \tag{16}$$

where $\tilde{i}_{s,t}$ is given by

$$\tilde{i}_{s,t} = \sum_{\tau \leq t} i_{s,\tau} \, \kappa_{t-\tau} \,, \tag{17}$$

to account for the time varying PCR positivity displayed over the natural course of a COVID-19 infection. The distribution κ describes the probability of being PCR positive over time following infection, and is based on [13].

Likelihood component 3. Serological data are incorporated in our modelling framework, using results from the survey presented in this work, and from Velumani et al..[14] The observed seropositivity (S_t) on a given day, t, is modelled as follows

$$S_t^+ \sim \text{Binomial}(S_t^+ + S_t^-\,,\, \nu_t \sum_{\tau \leq t} i_{s,\tau} C_{t-\tau})\,, \tag{18}$$

where $C_{t-\tau}$ is the cumulative probability of an individual infected on day τ having seroconverted less seroreverted by time t. This distribution is empirical and based on [15]. The term ν_t is a multiplicative random effect specified to mitigate likely biases in the serological data

$$\nu_t = 2\sigma(Y_t)\,, \quad Y_t \sim \mu + \eta_t\,, \quad \mu \sim N(0,1)\,, \quad \eta_t \sim N(0,\delta)\,, \quad \delta \sim N^+(0,1)\,, \tag{19}$$

where σ is the logistic function.

Eq (4) can be modified to account for population effects (decreasing susceptible population over time) such that no over-shooting happens due to discretization as follows [16, 17]:

$$i_{s,t} = (N - n_{s,t}) \left(1 - \exp\left(-\frac{i_{s,t}}{N}\right)\right), \tag{20}$$

The formula for $i_{s,t}$ is derived from a continuous time model on $[t-1, t]$. This is to avoid discrete time effects such as infections going above the total population N. Specifically, we assume that the infections $i(\Delta t)$ in $[t-1, t-1+\Delta t]$ are given by the differential equation $\partial i(\Delta t)/\partial \Delta t = i_t(1 - (n_{s,t} + i(\Delta t))/N)$, which has the solution $i(1) = i_t$ as above.

Modelling limitations Inferences from the model are subject multiple limitations, arising from biases in the data, and in our choices of priors. In particular, the level of underreporting in Delhi is poorly characterised. This uncertainty is mitigated by sensitivity testing, as described in the Supplementary Information. Similarly, uncertainty in the temporal waning of immunity, the date of when Delta was first introduced to Delhi, and the IFRs of SARS-CoV-2 variants in Delhi, all provide sources of bias that we currently only mitigate through sensitivity testing. Furthermore, we note serological data is likely to be systematically biased. This is partially addressed through the inclusion of an additional term in the serology likelihood that provides a multiplicative random effect.

Computational notes The analysis uses R version 3.6.3. Inferences are based on 2000 iterations of Hamiltonian Monte Carlo using 2 chains, with rhat statis-

tics confirmed to be less than 1.02. The inference is performed using rstan version 2.21.2. Replication code and data are available at `https://github.com/ImperialCollegeLondon/Delta_Variant_Delhi`.

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