***2.1.c. SAPHIRE model***

*Overview:* This model (13) extends the classic SEIR model to estimate COVID-related transmission parameters, in addition to projecting COVID-19 counts, while accounting for pre-symptomatic infectiousness, time-varying ascertainment rates, transmission rates and population movements. *Figure 3*provides a schematic diagram of the compartments and transitions conceptualized in this model. The model includes seven compartments: susceptible (S), exposed (E), pre-symptomatic infectious (P), ascertained infectious (I), unascertained infectious (A), isolation in hospital (H) and removed (R). Compared with the classic SEIR model, SAPHIRE explicitly models population movement and introduce two additional compartments (A and H) to account for the fact that only ascertained cases would seek medical care and thus be quarantined by hospitalization. The model described and implemented here relies on the same methodology and arguments as presented by the authors of the SAPHIRE model. The only difference is that while the original model analyzed data from China over a time period of December 2019 to March 2020 (which constituted the initial days of the pandemic in China), we analyze data from India, for the initial period of the pandemic in India. Additionally, the original manuscript adjusted the model to account for population movement. With the lockdown in India being severe (several states closed their respective borders) and data on population movement not being available, we make no such modifications. Additionally, described in greater detail in the subsequent sections, we note that the SAPHIRE model returns reported and unreported cumulative COVID-case counts, in addition to cumulative counts of the removed compartment. As such, for the purpose of comparisons, the SAPHIRE model is used only to study cumulative COVID-case counts, and not active case counts or cumulative death counts. The R package for implementing this general model for understanding disease dynamics is publicly available at*https://github.com/chaolongwang/SAPHIRE.*

*Formulation:* The dynamics of the 7 compartments described above at time are described by the set of ordinary differential equations

in which is the transmission rate for ascertained cases (defined as the number of individuals that an ascertained case can infect per day), is the ratio of the transmission rate of unascertained cases to that of ascertained cases, is the ascertainment rate, is the latent period, is the pre-symptomatic infectious period, is the symptomatic infectiousness period, is the duration from illness onset to isolation and is the isolation period in the hospital.



Figure : The SAPHIRE model with separate compartments for the latent, unascertained and ascertained cases.

Under this setup, reproductive number (as presented in the original manuscript) may be expressed as

in which the three terms represent infections contributed by pre-symptomatic individuals, unascertained cases and ascertained cases, respectively. The model adjusts the infectious periods of each type of case by taking population movement () and isolation into account. For the case of India, we set

Initial states and parameter settings: We set α=0.55, assuming lower transmissibility for unascertained cases1. Compartment contains both ascertained and unascertained cases in the pre-symptomatic phase. We set the transmissibility of to be the same as unascertained cases, because it has been reported that the majority of cases are unascertained1. We assumed an incubation period of 5.2 days and a pre-symptomatic infectious period =2.3 days2,3. Thus, the latent period was =2.9 days. Because pre-symptomatic infectiousness was estimated to account for 44% of the total infections from ascertained cases2, we set the mean of total infectious period as (+)=/0.44=5.2 days, assuming constant infectiousness across the pre-symptomatic and symptomatic phases of ascertained cases4 – thus the mean symptomatic infectious period was =2.9 days. We set an isolation period of =17 days based on the study investigating the hospital stay in Karnataka5, but this parameter has no effect on the model fitting procedure, or the final parameter estimates as we fit daily new cases under this method. The duration from the onset of symptoms to isolation was estimated to be =7 days6,7. On the basis of the parameter settings above, the initial state of the model is specified on March 15. The initial number of ascertained symptomatic cases 𝐼(0) is specified as the number ascertained cases in which individuals experienced symptom onset during 12-14 March. The initial ascertainment rate is assumed to be ( = 0.10)8, and thus the initial number of unascertained cases is 𝐴(0) =(1−)𝐼(0). (0) and (0) denote the numbers of ascertained cases in which individuals experienced symptom onset during 15–16 March and 17–19 March, respectively. Then, the initial numbers of exposed and pre-symptomatic individuals are set as 𝐸(0)=(0) and 𝑃(0)=(0), respectively. The initial number of the hospitalized cases 𝐻(0) is set as half of the cumulative ascertained cases on 8 March since =7 days and there would be more severe cases among the ascertained cases in the early phase of the epidemic.

*Likelihood and MCMC algorithm:* Considering the time-varying strength of control measures implemented in India over the four lockdown periods, the model assumes that the value of corresponding to the lockdown period is The observed number of ascertained cases in which individuals experience symptom onset on day – denoted by – is assumed to follow a Poisson distribution with rate , with denoting the expected number of pre-symptomatic individuals on day . The following likelihood equation is used to fit the model using observed data from March 15 ( to October 15 .

and the model is used to predict COVID-counts from October 16 to December 31, 2020. A non-informative prior of is used for and. For , an informative prior of 8is used, by matching the first two moments of the estimate using data from Singapore, as done by the authors of the SAPHIRE model. Re-parameterizing as

where is the standard logit function. In the MCMC, A burn-in period of 100,000 iterations is fixed, with a total of 200,000 iterations being run.

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***3. RESULTS***

***3.1. Estimation of reproduction number***

From*Table 2****,*** we compare the mean of the time-varying effective reproduction number over the four phases of lockdown in India. The eSIR model does not return phase-specific values but returns a mean value of 2.08 (95% CI: 1.41 to 2.12) over the entire lockdown period. The mean (and 95% CI) values returned by the SAPHIRE model is 2.79 (95% CI: 2.08 to 3.50) during phase one of the lockdown, 0.77 (95% CI: 0.63 to 1.07) for phase two, 1.28 (95% CI: 1.11 to 1.71) for phase three and 1.40 (95% CI: 1.15 to 1.84) for the fourth and final lockdown phase. The SEIR-*fansy* notes that the mean drops from 4.09 (95% CI: 3.99 to 4.20) during the first phase of lockdown, to 1.72 (95% CI: 1.70 to 1.76) during the fourth lockdown phase. The ICM-based mean values fluctuate, from 1.41 (95% CI: 1.12 to 1.77) during the first lockdown phase, followed by 1.20 (95% CI: 0.92 to 1.50), then dropping to 1.29 (95% CI: 1.01 to 1.59) and finally rising to 1.41 again (95% CI: 1.11, 1.77) for the fourth phase of lockdown. In terms of agreement of reported values, SAPHIRE, SEIR-*fansy* and ICM report the highest mean for phase one of the lockdown. While values reported by SEIR-*fansy* show a steady decrease over subsequent lockdown phases, both SAPHIRE and ICM report a drop in intermediate lockdown phases, followed by a rise. While SAPHIRE reports the lowest value of for phase three, ICM reports the lowest value of for phase two.

Table 2: Comparison of projections and prediction accuracies of the models under consideration.

|  |  |  |  |
| --- | --- | --- | --- |
|  | | SAPHIRE | |
|  | ***(ascertained rate)*** |
| Estimated mean [95% CI] | **Lockdown 1.0**  ***(March 25 – April 14)*** | 2.79  [2.08, 3.50] | 1.13  [0.47, 2.84] |
| **Lockdown 2.0**  ***(April 15 – May 3)*** | 0.77  [0.63, 1.07] | 0.98  [0.23, 3.32] |
| **Lockdown 3.0**  ***(May 4 – May 17)*** | 1.28  [1.11, 1.71] | 4.22  [1.71, 13.12] |
| **Lockdown 4.0**  ***(May 18 – May 31)*** | 1.40  [1.15, 1.84] | 3.80  [0.80, 14.30] |
| **Unlock 1.0 (June 1 - June 30)** | 1.23  [1.19, 1.29] | 4.21  [0.74, 17.05] |
| **Unlock 2.0 (July 1 - July 31)** | 1.34  [1.25, 1.45] | 4.42  [0.72, 18.05] |
| **Unlock 3.0 (August 1 - August 31)** | 1.30  [1.09, 1.56] | 4.03  [0.62, 16.77] |
| **Unlock 4.0 (September 1 - September 30)** | 1.55  [1.01, 2.40] | 4.73  [0.62, 20.07] |
| **Unlock 5.0 (Octorber 1 - Octorber 15)** | 1.92  [0.92, 3.80] | 4.44  [0.80,18.85] |







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