COVID-19 Simulator

Policy Simulator Methodology

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Model overview

We used a validated mathematical model, the *COVID-19 Simulator* (www.covid19sim.org), to model the epidemiology of COVID-19 at the state-level in the U.S. Since May 2020, the Centers for Disease Control and Prevention (CDC) has incorporated our model outputs in its weekly COVID-19 forecasts.[1]

COVID-19 Simulator is a compartmental SEIR[2] model with compartments for Susceptible, Exposed, Infectious, Recovered, and Dead individuals, stratified by Pol status (unvaccinated, partially vaccinated, fully vaccinated). Input data includes reported cases and deaths[3], hospitalizations and ICU occupancy[4], vaccine administration history[5], and estimates for epidemiological parameters from clinical studies. The model is calibrated to reproduce historic trends in daily reported cases and deaths, and updated weekly as new data and evidence arise.

Model structure

A schematic of our compartmental model is shown in Figure 1.

$$\alpha_1 = \frac{\#\text{ first doses per day}}{S+E+I+R}$$

$$\alpha_2 = \frac{\#\text{ second doses per day}}{S_{1\text{dose}}+E_{1\text{dose}}+I_{1\text{dose}}+R_{1\text{dose}}}$$

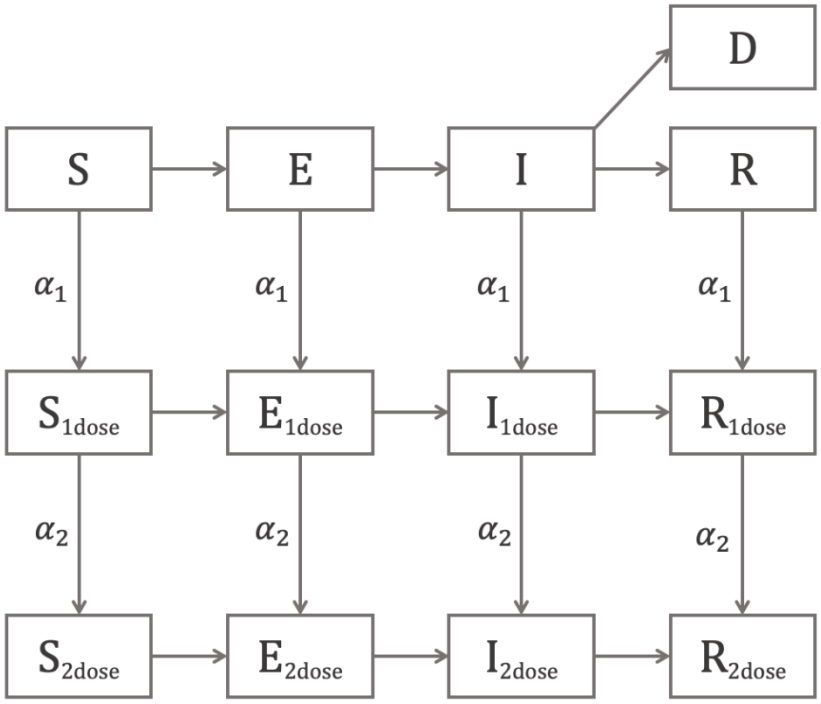

Figure 1. Schematic of the COVID-19 Simulator *compartmental model.*

The model is described by the following system of ordinary differential equations:

$$S'(t) = -R_E \frac{I + I_{1\text{dose}} + I_{2\text{dose}}}{p_I} \cdot \frac{S}{N} - \alpha_1 S$$

$$E'(t) = R_E \frac{I + I_{1\text{dose}} + I_{2\text{dose}}}{p_I} \cdot \frac{S}{N} - \frac{E}{d_E} - \alpha_1 E$$

$$I'(t) = \frac{E}{p_E} - \frac{I}{p_I} - \alpha_1 I$$
$$R'(t) = (1 - IFR) \cdot \frac{I}{p_I} - \alpha_1 R$$
$$D'(t) = IFR \cdot \frac{I}{p_I}$$
$$S'_{1\text{dose}}(t) = -R_E \frac{I + I_{1\text{dose}} + I_{2\text{dose}}}{p_I} \cdot \frac{S_{1\text{dose}}}{N} + \alpha_1 S - \alpha_2 S_{1\text{dose}}$$
$$I'_{1\text{dose}}(t) = R_E \frac{I + I_{1\text{dose}} + I_{2\text{dose}}}{p_I} \cdot \frac{S_{1\text{dose}}}{N} - \frac{E_{1\text{dose}}}{p_E} + \alpha_1 E - \alpha_2 E_{1\text{dose}}$$
$$E'_{1\text{dose}}(t) = \frac{E_{1\text{dose}}}{p_E} - \frac{I_{1\text{dose}}}{p_I} + \alpha_1 I - \alpha_2 I_{1\text{dose}}$$
$$R'_{1\text{dose}}(t) = \frac{I_{1\text{dose}}}{p_I} + \alpha_1 R - \alpha_2 R_{1\text{dose}}$$
$$S'_{2\text{dose}}(t) = -R_E \frac{I + I_{1\text{dose}} + I_{2\text{dose}}}{p_I} \cdot \frac{S_{2\text{dose}}}{N} + \alpha_2 S_{1\text{dose}}$$
$$E'_{2\text{dose}}(t) = R_E \frac{I + I_{1\text{dose}} + I_{2\text{dose}}}{p_I} \cdot \frac{S_{2\text{dose}}}{N} - \frac{E_{2\text{dose}}}{p_E} + \alpha_2 E_{1\text{dose}}$$
$$I'_{2\text{dose}}(t) = \frac{E_{2\text{dose}}}{p_E} - \frac{I_{2\text{dose}}}{p_I} + \alpha_2 I_{1\text{dose}}$$
$$R'_{2\text{dose}}(t) = \frac{I_{2\text{dose}}}{p_I} + \alpha_2 R_{1\text{dose}}$$

where

$S,\ S_{1\text{dose}},\ S_{2\text{dose}}$ = Number of susceptible individuals at time t,
$E,\ E_{1\text{dose}},\ E_{2\text{dose}}$ = Number of exposed (latent) individuals at time t,
$I,\ I_{1\text{dose}},\ I_{2\text{dose}}$ = Number of infectious individuals at time t,
$R,\ R_{1\text{dose}},\ R_{2\text{dose}}$ = Number of recovered individuals at time t,
D = Number of dead individuals at time t,
R_E = Effective reproduction number at time t,
N = Total population,
p_I = Duration of the infectiousness period,
p_E = Duration of the exposed (latent) period,
α_1 = Rate of first vaccine dose administration,
α_2 = Rate of second vaccine dose administration.

The variable subscripts "1dose", "2dose" differentiate individuals in the susceptible, exposed, infected, and recovered populations who have received one or two doses of the vaccine.

Model programming is performed in R (version 3.6.2). We use numerical solvers from the R package "deSolve".[6]

Effective reproduction number

The transmission force of a pandemic under a given non-pharmaceutical intervention (NPI) is described by a parameter called the *effective reproduction number,* R_E, defined as the average number of secondary infections per infectious case in a population made up of both susceptible and non-susceptible people. To reproduce the historic trends in cases and deaths, we allowed R_E to be a function of time to capture the effect of tightening and relaxing NPIs as the pandemic progresses. Specifically, we specify a stepwise function $R_E(t)$ with 11 joinpoints $\tau_1, \tau_2, \ldots, \tau_{11}$ (time points at which R_E takes on a new value). We let the first 10 joinpoints be distributed uniformly over the historic time horizon from March 1, 2020, to the date of the latest data. We set τ_{11} to be 12 days before the date of the latest data point to capture the R of current interventions.

Reinfection

We assume reinfection is not possible within the time frame of the simulation based on the opinions of experts and emerging evidence that re-infections are rare.[7–9]

Infection fatality rate

For all states, we assume an average IFR of 0.005 based on the CDC COVID-19 Pandemic Planning Scenarios[10] current best estimates, weighted by the national population age distribution. The model infers the curve of total new infections (diagnosed and undiagnosed) over time based on the curve of deaths and the chosen infection fatality rate.

Vaccine effects

Starting from February 2021, *COVID-19 Simulator* accounts for vaccination rollout. The model captures the reduced fatality rate and susceptibility of vaccinated individuals. We assume 100% reduction in the infection fatality rate, along with 80% reduction in susceptibility of first-dose recipients and 90% reduction in susceptibility for second-dose recipients. Due to lack of data on disease status at the time of vaccination, we conservatively assume uniform distribution of vaccines across the susceptible, exposed, infected, and recovered populations. [11–13] Projecting forward, we fix vaccination rates at the latest rate from data.

Calibration of unobserved parameters

Because several parameters in the model are not directly observable, we estimate their values using a calibration approach. We begin by defining clinically plausible ranges:

- Initial number of infections I_0: 0–1,000 cases
- Latent period duration p_E: 2–10 days[14]
- Infectious period duration p_I: 0.1–10 days[15]
- Effective reproduction number R_E: 0.5–4.00 secondary cases per infectious case

We calibrate using generalized simulated annealing (R package "GenSA"[16]) to the curve of historic new deaths as the calibration target and mean squared error as the objective function. To account for uncertainty in the calibrated values, we repeat the calibration 100 times with different random seeds, resulting in 100 unique sets of parameter values and fitted curves. At each time point, we take the median to be the point estimate and compute the 95% credible interval.

Hospital beds capacity

Data on hospital beds capacity was extracted from the Centers for Medicare & Medicaid Services (CMS) annual cost reports (fiscal years 2016 through 2019). The data in these reports is accessible via CMS's Healthcare Cost Report Information System (HCRIS)[17]. Data from four years was pooled for analysis to allow for correction of missing and inaccurate data. Hospitals that were deemed unlikely to be able to assist in a pandemic were not counted (e.g., alcohol and drug treatment hospitals, psychiatric hospitals, mental health hospitals, hospices, religious non-medical hospitals, skilled nursing facilities and homecare). For the estimation of ICU bed capacity, we included beds in similar units that could be repurposed for general intensive care in the event of a pandemic (e.g., cardiac critical care, burn ICU, surgical ICU).

We estimated the total number of hospital/ICU beds available to COVID-19 patients on a given day using hospitals' reported bed days and inpatient days for each bed type. If a hospital reported bed numbers but not bed utilization numbers, we used the average occupancy rate over all states that provided this data.

Intervention Strategies

COVID-19 Simulator can model four different non-pharmaceutical interventions:

1. *Current intervention:* $R_E =$ the calibrated value over the last 12 days of data.
2. *Stay-at-home orders:* $R_E =$ the minimum observed value during the period of nationwide stay-at-home orders between March and August 2020, as estimated by rt.live[18].
3. *Lockdown:* $R_E = 0.3$, the estimated value in Wuhan after lockdown of the region.[19] This intervention assumes a complete ban on international, inter-state, and local travel, except for essential trips such as grocery shopping and filling prescriptions.
4. *Minimal restrictions:* $R_E = 3.6$. *This intervention assumes minimal social distancing but there is a* level of learned social awareness (handwashing, avoiding close contact when sick, etc.).

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