Simulator of interventions for COVID-19

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Abstract

The COVID-19 simulator is a graphical user interface aimed to provide a decision support framework. Here, we describe the mathematical model used for the COVID-19 simulator. In addition to this documentation, the simulator code is freely available for download.

The modeling framework is an age-stratified $S(IQ)^K HR$ model. The key differences we present in this work include the explicit account of contact tracing, and accounting for partial compliance of the public.

1 Introduction

The rapid spread of the coronavirus (COVID-19) pandemic led many countries to take unprecedented measures to prevent uncontrolled endemic spread. Large scale lockdowns were proven to be effective for short periods of time, but are not sustainable on longer time scales. A variety of long term policies to address COVID-19 were suggested, including shielding of elderly, lockdown intervals, contact-tracing systems, limitation on schools, workplaces or other places, social distancing and finally local measures. Policymakers are required to design a policy that is likely to be based on one of the above policies or on a combination of them. To allow policy makers to make informed decisions regarding COVID-19 policy, they need a single tool that can assess the impact of a variety of long-term policies or of their combinations. Here, we present a model of non-pharmaceutical interventions to address epidemic spread.

A key application of this work is a COVID-19 simulator aimed to provide a decision support framework. It is implemented in a graphical user interface that makes the model accessible to non-experts. The interface and default parameters are tuned to Israel, but can be applied anywhere. A key value we emphasize in this work is transparency. The tool itself, as well as full documentation and code, is freely available to the public, as it is also available to policymakers. A vital component in any long-term policy chosen is public awareness and compliance. We believe that transparency helps maintain high levels of public awareness and leads to higher compliance.

2 Modeling framework

The modeling framework is an age-stratified $S(IQ)^K HR$ model. It is very much based on the framework presented in [1, 2, 3, 4]. The key differences we present in this work include the explicit account of contact tracing, and accounting for partial compliance of the public. We choose to model disease stages by temporal compartments. This choice allows us to combine the temporal profile of the disease (especially infectiousness) with the delays associated with contact tracing. We thus monitor the daily progress of the disease by considering the group of compartments $\{I^k\}_{k=1}^K$ for infected individuals at day k since infection. The daily resolution of the disease timeline allows us to directly account for the infectiousness profile, rather than only accounting for an incubation/latent period and an infected period.

In order to account for partial compliance we consider subgroups. Namely, each age group is divided to subgroups of compliant/disobedient individuals. Roughly speaking, disobedient individuals in quarantine behave as if they were not in quarantine, and disobedient individuals in the community have a higher chance of infecting or getting infected, e.g., since they are less compliant with healthcare orders. We, therefore, choose

to account for sub-groups of disobedient individuals in a way that allows exploration of various intervention options while assessing their sensitivity to obedience.

The introduction of subgroups can be used to introduce additional details. Indeed, we further divide each age group to subgroups of low-risk (healthy)/high-risk (background disease) individuals.

2.1 Flow diagram, variables and parameters

The model consists of n age groups, each divided to four sub-groups consisting of low-risk (healthy)/high-risk (background disease) and obedient/disobedient sub-groups. For each age group, the model consists of

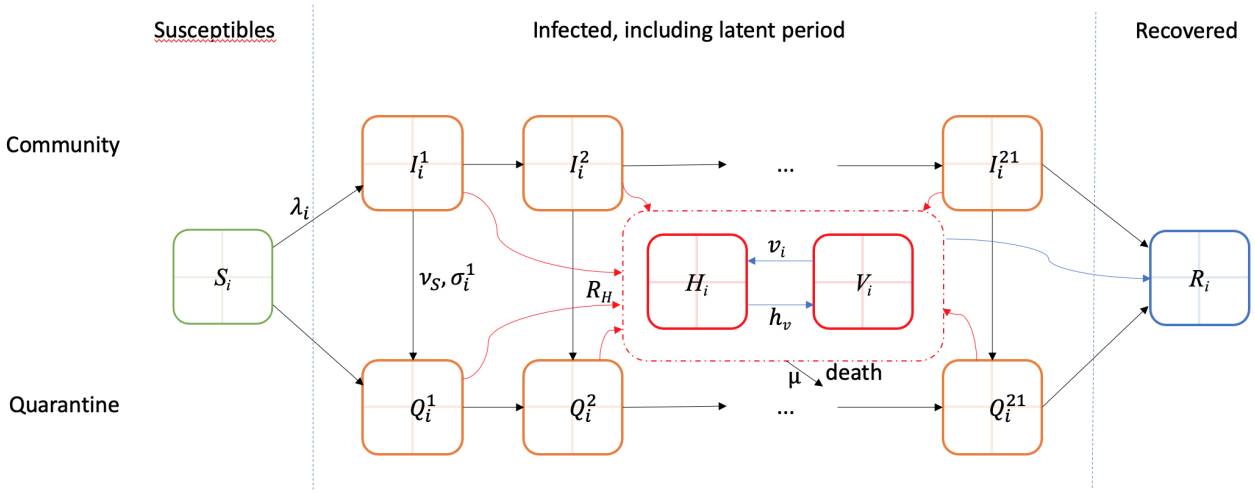

Figure 1: Schematic flow diagram for the age, obedience and condition-structured $S(QI)^K HR$ model. The model consists of n age groups, each divided to four sub-groups consisting of low-risk (healthy)/high-risk (background disease) and obedient/disobedient sub-groups ($i = 1 \cdots 4n$). For each group, the model consists of susceptible S_i and recovered R_i compartments, as well as compartments $\{I_i^k\}_{k=1}^K$ for infected individuals at day k since infection, up to $K = 21$ days which is considered the maximal duration of the disease for non-hospitalized infected individuals. These compartments represent groups of individuals who reside in the community. Infected individuals in quarantine are represented by corresponding compartments $\{Q_i^k\}_{k=1}^{21}$. Additionally, individuals who are hospitalized are represented by compartments H_i (hospitalized) and V_i (ventilated).

compartments of susceptible $\mathbf{S}_i$ and recovered R_i individuals, as well as compartments $\{I_i^k\}_{k=1}^K$ of infected individuals at day k since infection, where K is the maximal duration in days of the disease for non-hospitalized infected individuals. The latter group of compartments $\{I_i^k\}_{k=1}^K$ represent the disease timeline for an individual from infection to recovery in a daily resolution. The main motivation for such a fine resolution of the disease timeline is to be able to account for contact tracing whose efficiency is sensitive to the number of days from the identification of a new infection to contact tracing and quarantine of the individuals who are potentially infected by that individual. The above compartments represent groups of individuals who reside in the community. Infected individuals that are in quarantine are represented by corresponding compartments $\{Q_i^k\}_{k=1}^K$. We assume that the number of susceptible and recovered individuals in quarantine are negligible with respect to the total number of susceptible and recovered individuals, respectively. Therefore, we consider only infected individuals in quarantine. Additionally, individuals who are hospitalized are represented by compartments H_i (hospitalized) and V_i (ventilated).

Finally, to account for sub-groups, each variable is a vector of size $s = 4$

$$\mathbf{X}_i = \begin{bmatrix} X_i^{LO} \\ X_i^{LD} \\ X_i^{HO} \\ X_i^{HD} \end{bmatrix}$$

where $X_i^{LO}, X_i^{HO}, X_i^{LD}, X_i^{HD}$ corresponds to low-risk/obedient, high-risk/obedient, low-risk/disobedient, and

high-risk/disobedient, respectively. The state flow diagram for one of the $4n$ groups is illustrated in Figure 1. Interactions between groups are due to infection and contact tracing, as will be detailed below.

3 Model derivation

We assume a closed population, namely, we neglect incoming traveling individuals, as well as births and deaths that are not due to the disease. Under this condition, we adopt [4], and describe the spread of disease between the $4n$ groups.

3.1 Temporal profile of the disease

Following [5], we define γ_k as the relative infectiousness at day k, with $\sum_k \gamma_k = 1$ (See Figure 1 in [5]). Similar to [6],We also define the effective number of infected and quarantined individuals as:

$$J_i = \sum_{k=1}^{K} \gamma_k I_i^k, \quad J_i^Q = \sum_{k=1}^{K} \gamma_k Q_i^k,$$

.

3.2 Force of infection

For a susceptible individual in group i to be infected by an individual from group j requires a contact between the groups, parametrized by $\mathrm{C}_{ij}^{\mathrm{eff}}$. This is also modulated by group-specific susceptibility and transmission factors β_i and α_i. The overall force of infection is therefore:

$$\lambda_i = \beta_s \beta_i \sum_{j=1}^{n} \frac{\alpha_j}{N_j} \left(J_j + \alpha_Q J_j^Q \right) S_i C_{ij}^{\mathrm{eff}}$$

where β_s is the global transmission rate per interaction , N_j is the size of group j and α_Q is the reduction of contacts by individuals in quarantine.

3.3 Transitions within groups

Figure 1 shows the major transitions of the model, along with the parameters and variables characterizing them.

Infections move individuals from susceptible to the first day of infection:

$$\frac{d}{dt} S_i = -\lambda_i$$

The number of infected individuals on their first day of infection satisfies

$$\frac{d}{dt} I_i^1 = \lambda_i - I_i^1 - \sigma_i^1(I_i^1, I_i^2, \cdots, I_i^K),$$

where σ_i^k is the rate at which infected individuals at day k from their infection are quarantined as a result of contact tracing. Similarly, the number of infected individuals at day 1 in quarantine satisfies

$$\frac{d}{dt} Q_i^1 = I_i^1 - Q_i^1 + \sigma_i^1(I_i^1, I_i^2, \cdots, I_i^K).$$

Infected individuals on days $k = 2, \cdots, K$ from their infection satisfy

$$\frac{d}{dt} I_i^{k+1} = I_i^k - I_i^{k+1} - \sigma_i^{k+1}(I_i^1, I_i^2, \cdots, I_i^K) - \nu_S^{k+1} I_i^{k+1} - r_{i,H}^{k+1} I_i^{k+1}, \quad k = 1, \cdots, K-1,$$

where ν_S^k is the rate of self-quarantine due to the appearance of symptoms, and $r_{i,H}^k$ is the rate at which infected individuals at day k are hospitalized. Similarly, infected individuals in quarantine satisfy

$$\frac{d}{dt} Q_i^{k+1} = Q_i^k - Q_i^{k+1} + \sigma_i^{k+1}(I_i^1, I_i^2, \cdots, I_i^K) + \nu_S^{k+1} Q_i^{k+1} - r_{i,H}^{k+1} Q_i^{k+1}, \quad k = 1, 2, \cdots K-1.$$

Hospitalized patients follow

$$\frac{d}{dt}H_i = \sum_{k=1}^{K} r_{i,H}^k (I_i^k + Q_i^k) - h_i^R H_i - h_i^V H_i + v_H V_i - \mu_i^H H_i,$$

where h_i^R is the recovery (and discharge) rate for group age i, h_i^V is the rate at which hospitalized patient require ventilation, v_i is the rate at which ventilated patients are return to hospitalization with no ventilation, and μ_i^H is the death rate of hospitalized patients.

Ventilated patients satisfy

$$\frac{d}{dt}V_i = h_i^V H_i - v_H V_i - \mu_i^V V_i,$$

where μ_i^V is the death rate of ventilated patients.

Finally, the number of recovered individuals in the community satisfies

$$\frac{d}{dt}R_i = I_i^K + Q_i^K + h_i^R H_i.$$

3.4 The effective contact matrix

In the absence of demographic shielding and quarantine, the average number of contacts made per day by an individual in group i with an individual in class j is given by the effective contact matrix C_{ij}^{reff} where

$$C_{ij}^{\text{eff}} = \eta_{\text{home}} C_{ij}^{\text{home}} + \eta_{\text{school}} C_{ij}^{\text{school}} + \eta_{\text{work}} C_{ij}^{\text{work}} + \eta_{\text{other}} C_{ij}^{\text{other}}. \tag{1}$$

Regular contact patterns correspond to all coefficients equal to one. Interventions may reduce one or more of the coefficients. For example, school closure will reduce η_{school} to zero, and spontaneous reduction of contacts by the public will lead to a reduction in η_{other}.

3.5 Contact tracing

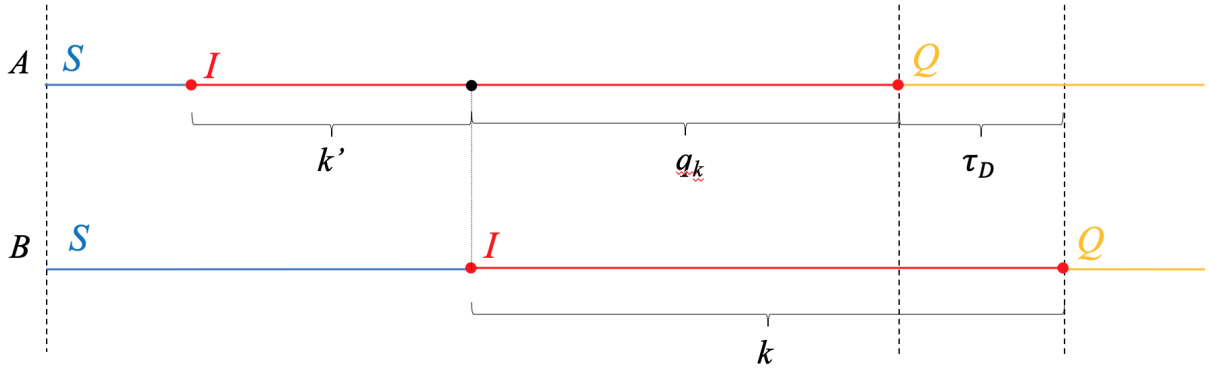

Figure 2: Schematic timeline of a contact tracing procedure. Individual B is infected by individual A on day k' from his infection. Individual A develops symptoms on day $k' + q_k$ from his infection, at which stage a contact tracing procedure is initiated. The overall duration of the procedure is τ_D days after which the contacts of individual A, and in particular individual B, are quarantined.

The timeline of a contact tracing procedure starts when an infected individual becomes symptomatic. We assume that symptomatic individuals self-quarantine themselves and proceed to be tested for COVID-19. We account for a delay of τ_D days from the appearance of symptoms to the return of lab results and the conclusion of the epidemiological investigation. The epidemiological investigation traces all contacts made by the individual in the last two weeks and quarantines them. We only consider the effect of quarantining infected individuals, and do not account for the healthy contacts who were also quarantined.

In the following, we consider a chain of infections starting from an infected individual A from group j where the timeline reference is the day of his/her infection. Let us start with the first generation from group i: On day k', the infected individual infects on average

$$\beta_s \alpha_j \frac{\gamma_{k'}}{N_j} C_{ij}^{\text{eff}} I_j^{k'} S_i$$

individuals from group i. Here, we assume that S_i doesn't change significantly over a typically duration of contact tracing. Let us now assume that after q_k days, individual A develops symptoms, reports and initiates contact tracing. The probability density of such an event is given by

$$\nu_{\text{self}}^{k'+q_k}.$$

Therefore, a successful contact tracing under the above condition (infection occurs on day k' and self-quarantine of day $k'+q_k$) will result in the quarantine of

$$\beta_s \frac{\alpha_j}{N_j} C_{ij}^{\text{eff}} \gamma_{k'} \nu_{\text{self}}^{k'+q_k} I_j^{k'} S_i$$

individuals from group i at day $q_k + \tau_d$ from *their* infection. To compute the number of individuals from group i that are contact traced at day k from *their* infection, let $q_k = k - \tau_D$,

$$\sigma_i^k = -c_s \beta_s S_i \sum_{k'=1}^{K-k+\tau_D} \sum_{j=1}^{n} \frac{\alpha_j}{N_j} \nu_{\text{self}}^{k'+k-\tau_D} \gamma_{k'} I_j^{k'} C_{ij}^{\text{eff}},$$

where c_s is the percent of successful traces that lead to quarantine. Define

$$J_i^k = \sum_{k'=1}^{K-k+\tau_D} \nu_{\text{self}}^{k'+k-\tau_D} \gamma_{k'} I_i^{k'}$$

Then,

$$\sigma_i^k = -c_s \beta_s S_i \sum_{j=1}^{n} \frac{\alpha_j}{N_j} J_j^k C_{ij}^{\text{eff}}.$$

3.6 Computation of R^{eff}

To compute R^{eff}, we follow [7]. We consider only the equations for I_i and Q_i, namely, assume that the contribution of hospitalized individuals on the effective reproduction rate is negligible.

Let us decompose the system into two column vectors, $\mathcal{F}$ and $\mathcal{V}$ of length $2snK$. The vector $\mathcal{F}$ presents the rate at which new infections appear in compartment F_i^k, and the vector $\mathcal{V}$ presents transitions between compartments.

$$\mathcal{F} = \begin{bmatrix} -\lambda_1 S_1^0 \\ -\lambda_2 S_2^0 \\ \vdots \\ -\lambda_n S_n^0 \\ 0 \\ \vdots \\ 0 \\ \hline 0 \\ \vdots \\ 0 \end{bmatrix}, \qquad \mathcal{V} = \begin{bmatrix} -I_1^1 - r_{1,H}^1 I_1^2 - \sigma_1^1 \\ -I_2^1 - r_{2,H}^1 I_1^2 - \sigma_2^1 \\ \vdots \\ -I_n^1 - r_{n,H}^1 I_1^2 - \sigma_n^1 \\ I_1^1 - I_1^2 - r_{1,H}^2 I_1^2 - \sigma_1^2 \\ I_2^1 - I_2^2 - r_{2,H}^2 I_2^2 - \sigma_2^2 \\ \vdots \\ I_n^1 - I_n^2 - r_{n,H}^2 I_n^2 - \sigma_n^2 \\ \vdots \\ I_1^{K-1} - I_1^K - r_H^K I_1^K - \sigma_1^K \\ I_2^{K-1} - I_2^K - r_H^K I_2^K - \sigma_2^K \\ \vdots \\ I_n^{K-1} - I_n^K - r_H^2 I_n^K - \sigma_n^K \\ \hline -Q_1^1 - r_{1,H}^1 Q_1^2 + \sigma_n^1 \\ \vdots \\ Q_n^{K-1} - Q_n^K - r_H^n Q_n^K + \sigma_1^K \end{bmatrix},$$

where

$$\lambda_i = \beta_s \beta_i \sum_{j=1}^{n} \frac{\alpha_j}{N_j} \left(J_j + \alpha_Q J_j^Q \right) S_i C_{ij}^{\text{eff}}.$$

Let F be the Jacobian of $\mathcal{F}$, and let V be the Jacobian of $\mathcal{V}$. Then, R^{eff} is the spectral radius of the matrix FV^{-1},

$$R^{\text{eff}} = \rho(FV^{-1}).$$

4 Interventions

The following table summarizes the interventions which the model accounts for and their implementation.

Intervention	Details
Social distancing	The tendency to adhere with healthcare instruction such wearing masks, washing hands is reflected by a decrease in the transmission factor per interaction β_s. The tendency to avoid contacts outside of work and school, e.g., restaurants, religious meetings or sports events is reflected by a decrease in η_{other}. Namely, a decrease in the number of contacts that do not originate from school, work or home.
Contact tracing	Contact tracing is embedded in the model and controlled by the parameters τ_D (delay from test to trace and quarantine), and c_s (percent of potentially infected contacts that are traced and quarantines).
Demographic shielding	Demographic shielding is implemented by adjusting the effective contact matrix such that all contacts involving groups which are shielded is decreased by a factor of α_D.
Workplace or school closure	These closures are implemented by decreasing η_{work} and η_{school}, respectively. Namely, adjusting the effective contact matrix so that contacts that originate from work/school are partially or fully eliminated.
Lockdown intervals	During a lockdown interval, the effective contact matrix reduce to C_{ij}^{home}, namely all contacts except those that originate from home are eliminated.

5 Concluding remarks

We have presented an age-stratified $S(IQ)^K HR$ framework. This framework is very much based on the framework presented in [1, 2, 3, 4], with the key differences that this work includes an explicit account of contact tracing, and also accounts for partial compliance of the public.

Contact tracing, as it is described in this work, is initiated by the onset of symptoms. Accordingly, it is sensitive to the portion of asymptomatic cases, and its efficiency drops if the vast majority of the invectives are asymptomatic.

The contact tracing mechanism presented in this work refers to the tracing of the immediate contacts of the infected person. It is more efficient to further test those immediate contact for infection, and trace their contacts in case they are infected. Further details and an extension of the contact tracing component will be published elsewhere.

Finally, this work does not consider over-dispersion and rather assumes that all people are equally infectious, except perhaps an age-dependent factor. We will present the effect of over-dispersion in a subsequent version of this work.

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A Table of parameters

Parameter	Name	Description
	Demographic	
n	Number of age groups	
N_i	Size of the i^{th} age groups	
s	Number of sub-groups per age group	
$P_{\text{high}}(i)$	Percent of population in high-risk per age group	
$P_{\text{compliance}}$	Percent of compliant population	
	Clinical development of a single case	
K	Duration of disease (days)	Number of days from infection to full recovery for infected individuals that are not hospitalized
β_s	Maximal transmission rate per interaction	The transmission rate per interaction attained in the most infectious stage of the disease
β_i	Age factor for susceptibility	See below.
α_i	Age factor for transmission rate	Age factor such that $\beta_s\beta_i\alpha_j$ is the transmission rate per interaction between an infected individual in age group j, and a susceptible in age group i, attained in the most infectious stage of the disease.
γ_k	Infectiousness factor of infected individuals of stage k in the community, $k = 1, \cdots K$	The relative transmission rate such that $\beta_s\beta_i\alpha_j\gamma_k$ is the transmission rate per interaction between an infected individual in age group j on day k from his/her infection, and a susceptible in age group i.
ν^k_{self}	Probability density of self-quarantine due to symptoms onset on day k from infection.	Note that this parameter encompasses the proportion of asymptomatic people c_{rmI2C}.
	Epidemics	
R_0	Basic reproduction number	
	Medical	
$R^{\text{cases,k}}_{i,L/H}$	Hospitalization rate	Rate at which low risk and high risk confirmed cases from group age i at day k, respectively, are hospitalized.
c_{I2C}	Infected to Case ratio	Percent of cases from infected
$R^k_{i,L/H}$	Hospitalization rate	Rate at which low risk and high risk infected individuals from group age i at day k, respectively, are hospitalized. Equals $R^k_{i,L/H} = c_{I2C}R^{\text{cases,k}}_{i,L/H}$.
h^R_i	Recovery (and discharge) rate for group age i	Rate at which hospitalized patients are discharged.
h^V_i	Rate at which hospitalized patient require ventilation	
v_i	Rate at which ventilated patients return to hospitalization	
μ^H_i	Death rate of hospitalized patients	
μ^V_i	Death rate of ventilated patients	
	Interaction matrices	
C^{home}_{ij}	Home related interaction matrix in the community	$sn \times sn$ matrix of the average number of interactions between group age i to j.
C^{school}_{ij}	School related interaction matrix	$sn \times sn$ matrix of the average number of interactions between group age i to j.
C^{work}_{ij}	Work related interaction matrix	$sn \times sn$ matrix of the average number of interactions between group age i to j.
C^{other}_{ij}	Matrix of interactions that do not correspond to home, school or work.	$sn \times sn$ matrix of the average number of interactions between group age i to j.
η	Coefficients η_{home}, η_{school}, η_{work} and η_{other} of effective contact matrix.	See (1).

Parameter	Name	Description
	Interventions	
α_P	Transmission factor of disobedient individuals in the community	
α_Q	Transmission factor of compliant individuals in quarantine	
α_D	Transmission factor of an compliant individuals in demographic quarantine	
τ_D	The delay (days) in contact tracing.	The number of days from self-quarantine of an infected individual due to the appearance of symptoms to the completion of an epidemiological investigation, contact tracing and quarantine of potentially infected contacts.
c_s	The percent of potentially infected contacts quarantined via the process of contact tracing	