



A Review of Mathematical Modeling in the Pandemic Age

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Abstract— This study is a primer for formulating, analysing and simulating mathematical models for understanding the dynamics of COVID-19, the novel corona virus that emerged from Wuhan city in December 2019. A basic modeling framework, based on using a simple compartmental deterministic epidemic modeling a homogeneous population, is illustrated for gaining insight into the transmission dynamics of COVID-19 which is also developed to stochastic case. This simple model can be extended to include the population-level impact of a COVID-19 vaccine.

Keywords— COVID-19, mathematical modeling, transmission dynamics, simulation, vaccine.

I. Introduction

There exists a wide class of mathematical models that analyse the spread of epidemic diseases, either deterministic or stochastic, and may involve many factors such as infectious agents, mode of transmission, incubation periods, infectious periods, quarantine periods, etc. [4]. A basic model of infectious disease population dynamics, consisting of susceptible (S), infective (I) and recovered (R) individuals were first considered in a deterministic model by Kermack and McKendric (1927). Since then, various epidemic deterministic models have been developed, with or without a time delay [5]. At the same time, many stochastic models have been considered: discrete time models [6], continuous time Markov chain models and diffusion models [7]. The models obtained in these three categories have increasing mathematical complexity and allow us to study important aspects of the epidemics. A variety of mathematical model types, including statistical, deterministic, stochastic, network and agent-based models, have been used to study the transmission dynamics and control of COVID-19 [1].

The rest of paper is as follows. In first section some basic compartmental epidemic model have been studied. Section 2 includes fundamental ideas of vaccination models. In section 3 the model is extended to include vaccination.

II. Basic compartmental epidemic model for COVID-19 dynamic

To design the basic epidemic model for COVID-19, let $N(t)$ be the total human population size at time t . This population is divided into the compartments of susceptible $S(t)$ (i.e. people who are at risk of acquiring infection, but have not yet contracted the disease), exposed $E(t)$ (i.e. newly-infected individuals who are incubating the disease), symptomatically-infectious $I_s(t)$ (i.e. infectious people showing clinical symptoms of the disease), asymptotically-infectious $I_a(t)$ (i.e. infectious people showing no clinical symptoms of the disease), hospitalized $I_h(t)$, recovered $R(t)$ individuals and $D(t)$ stands for the deceased individuals [1]. Thus,

$$N(t) = S(t) + E(t) + I_s(t) + I_a(t) + I_h(t) + R(t) + D(t).$$

A major feature of COVID-19 is that a large fraction of infections is generated by infected individuals who do not show clinical symptoms of the disease (i.e. individuals in the I_a compartment). This important feature of asymptomatic transmission, makes the effort to control the disease more difficult and at the very least, the model should incorporate this feature [1].

In order to formulate the basic epidemic model for COVID-19, it should be noted that infection occurs when a susceptible individual (i.e. someone in the S compartment) has an effective contact with an infectious individual in either the asymptomatic I_a , symptomatic I_s , or hospitalized I_h class. Based on this fact and noting the flow diagram in Fig. 1, the basic model for COVID-19 transmission dynamics in a community is given by the following deterministic system of nonlinear differential equations (where a dot represents differentiation with respect to time t) [1]:

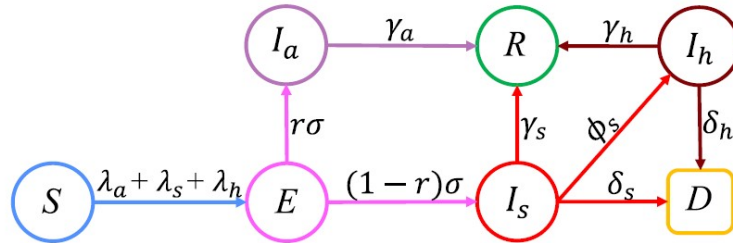


Fig. 1. Flow diagram of the model.

where

$$\lambda_a = \beta_a I_a / N, \lambda_s = \beta_s I_s / N, \text{ and } \lambda_h = \beta_h I_h / N.$$

and

$$\begin{aligned}
 \dot{S} &= - \left(\frac{\beta_a I_a + \beta_s I_s + \beta_h I_h}{N} \right) S, \\
 \dot{E} &= \left(\frac{\beta_a I_a + \beta_s I_s + \beta_h I_h}{N} \right) S - \sigma E, \\
 \dot{I}_a &= r \sigma E - \gamma_a I_a, \\
 \dot{I}_s &= (1 - r) \sigma E - (\varphi_s + \gamma_s + \delta_s) I_s, \\
 \dot{I}_h &= \varphi_s I_s - (\gamma_h + \delta_h) I_h, \\
 \dot{R} &= \gamma_s I_s + \gamma_a I_a + \gamma_h I_h, \\
 \dot{D} &= \delta_s I_s + \delta_h I_h.
 \end{aligned}
 \tag{1}$$

In (1), the parameters β_a , β_s and β_h respectively represent, the rate at which asymptotically-infectious, symptomatically-infectious, and hospitalized individuals transmit COVID-19 to susceptible individuals. Generally $\beta_a \neq \beta_s \neq \beta_h$. Exposed individuals progress out of the E class at a rate σ (i.e., $1/\sigma$ is the intrinsic incubation period of COVID-19). It is assumed that a proportion, $0 < r \leq 1$, of exposed individuals show no clinical symptoms of COVID-19 (and move to the (I_a) compartment) at the end of the incubation period. The remaining proportion, $1 - r$, show clinical symptoms and move to the (I_s) compartment at the end of the incubation period. Individuals in the I_s (I_a) (I_h) compartment recover from COVID-19 infection at a rate (γ_s) (γ_a) and (γ_h) . Infectious individuals are hospitalized (or isolated either at home or in hospital) at a rate ϕ_s . Individuals in the symptomatically-infectious (I_s) and hospitalized (I_h) compartments die of COVID-19 at a rate δ_s and δ_h , respectively.

III. Mathematical Model of Vaccination

Mathematical models of the impact of vaccination is one of the important epidemiology concerns. In 1760, Swiss mathematician Daniel Bernoulli published a study of the predicted impact of immunization with cowpox upon the expectation of life of the immunised population. Nearly 150 years later, around the time of the First World War, Ronald Ross produced a series of mathematical models of the spread of malaria that laid the foundations of the modern theory of the control of infectious disease. For vaccination strategies, some of the simplest questions that arise are: (i) what fraction of the population must be successfully vaccinated to eradicate the infectious agent; (ii) what happens if the target coverage for eradication is not met; (iii) does it matter if vaccine induced immunity wanes with time; and (iv) what happens if there are vaccine resistant sub-types? [3] In the following we review mathematical models to address some of these questions.

Amplification Factors and Eradication Thresholds

All that is required for the incidence of an infectious disease to go into decline is that each case should generate, on average, less than one other case. The number of secondary infections caused by one infectious individual is often referred to as the effective reproductive number and denoted by R . Epidemics often peak and go into decline as R falls below 1 because the pool of susceptible individuals has been temporarily exhausted. For the trajectory of incidence to remain on a downward course until the agent is eradicated requires that the effective reproductive rate should remain below 1, even when the number of susceptible individuals is at its maximum. There are two further amplification factors that stated in Tab. (??). R_0 , the basic reproductive number is the number of secondary cases caused by one primary case introduced

into a population that is wholly susceptible. R_{0p} , the basic reproductive number under vaccination is the number of secondary cases caused by one primary case introduced into a population in which a proportion p have been vaccinated. For a perfect vaccine that confers life-long protection [3]

$$R_{0p} = (1 - p)R_0$$

The critical vaccination proportion that will achieve eradication, p_c , is that for which the basic reproductive number under vaccination is just equal to 1. This yields:

$$p_c = 1 - \frac{1}{R_0}$$

Amplification factor	Name	Definition
R_0	Basic reproductive number	Number of secondary case caused by one primary case introduced into a population that is wholly susceptible
R_{0p}	Basic reproductive number under vaccination	Number of secondary cases caused by one primary case introduced into a population in which a proportion p have been vaccinated
R	Effective reproductive number	The number of secondary cases caused by one primary case in a population with the extant susceptible population

Table I. Different amplification factors in mathematical models of vaccination

Post-vaccination Dynamics

To study the predicted dynamics of infection after the introduction of a vaccination program requires the use of mathematical models of transmission dynamics. The simplest model that can be used to study the impact of vaccination keeps track of three groups of individuals: susceptible, S ; infected, I ; and recovered R . The model we study here includes a fourth group; those who have been vaccinated, V (Fig. (2)). This refinement allows the investigation of the impact of waning immunity as well. If vaccine induced immunity is life-long, then the equations of this SVIR model are [3]:

$$\begin{aligned}
 \dot{S} &= (1 - ep)\mu N - \beta IS - \mu S, \\
 \dot{V} &= ep\mu N - \mu V, \\
 \dot{I} &= \beta IS - \gamma I - \mu I, \\
 \dot{R} &= \gamma I - \mu R.
 \end{aligned}$$

Here, N is the total population size. The transitions described by each term of the equations of this model are as labeled and the model's parameters are described in Tab. (??)

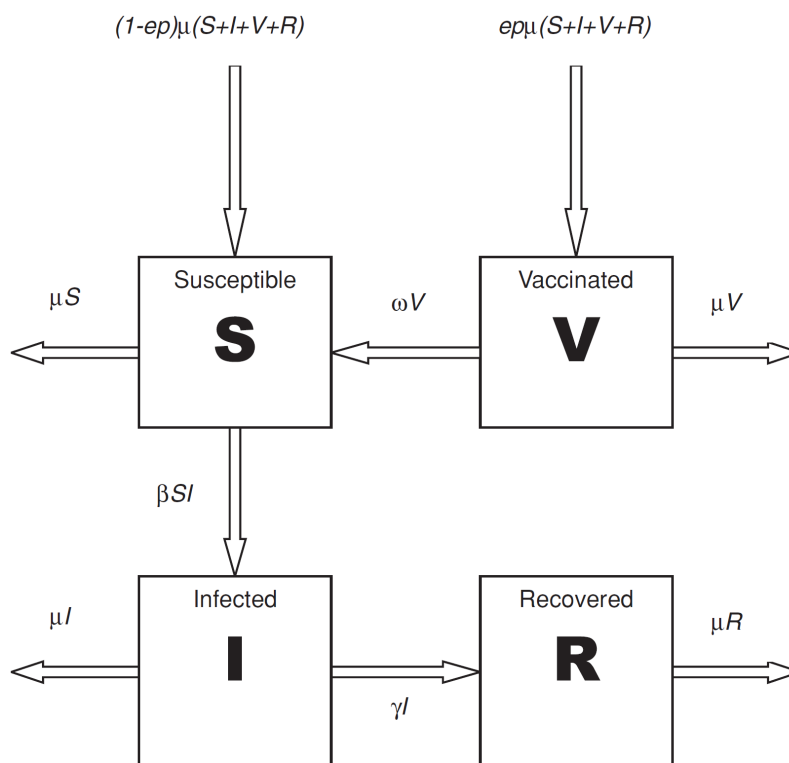


Fig. 2. Modeling childhood vaccination

Parameter	Interpretation
N	Population size
β	Force of infection
μ	Death rate
γ	Rate of recovery
e	Vaccine take, the fraction of vaccinated population protected by the vaccine
ρ	Fraction of population vaccinated at birth
ω	Rate of loss of vaccine induced immunity

Table II. Parameters of the model

IV. Stochastic Model with Vaccination

Vaccination is universally considered to be the best hope to effectively curtail or eliminate COVID-19 globally. The vaccines are expected to offer some protective but not perfect efficacy against COVID-19 infection. Thus, a model like Eq. (1), which allows for human demography (births/deaths processes) is an

appropriate tool for accounting for long-term outcomes. Consequently, to assess the impact of such a vaccine on the dynamics of COVID-19, the model (1) will be extended to incorporate vital dynamics (births and deaths). Further, the susceptible population ($S(t)$) will be split into two sub-populations, namely the sub-population of unvaccinated susceptible (denoted by $S_u(t)$) and vaccinated susceptible ($S_v(t)$) individuals. It is assumed that the potential COVID-19 vaccine is imperfect, so that breakthrough infection (i.e. the infection of vaccinated susceptible individuals) can occur but at a reduced rate, compared to the infection of unvaccinated susceptible individuals. It is also assumed that the vaccine-induced immunity may not last a lifetime. To incorporate a vaccine into the basic model (1), the first two equations are replaced by:

$$\begin{aligned}
 \dot{S}_u &= \Lambda + \omega_v S_v - \left(\frac{\beta_s I_s + \beta_a I_a + \beta_h I_h}{N} \right) S_u - (\mu + \xi_v) S_u - \sigma_{EIS_v} I E S_v \dot{W}_t, \\
 \dot{S}_v &= \xi_v S_u - (1 - \epsilon_v) \left(\frac{\beta_s I_s + \beta_a I_a + \beta_h I_h}{N} \right) S_v - (\mu + \omega_v) S_v + b \sigma_{EIS_v} I E S_v \dot{W}_t, \\
 \dot{E} &= \left(\frac{\beta_s I_s + \beta_a I_a + \beta_h I_h}{N} \right) S_u + (1 - \epsilon_v) \left(\frac{\beta_s I_s + \beta_a I_a + \beta_h I_h}{N} \right) S_v - (\mu + \sigma) E + b \sigma_{EIS_v} I E S_v \dot{W}_t, \\
 \dot{I}_s &= (1 - r) \sigma E - (\mu + \varphi_s + \gamma_s + \delta_s) I_s - \sigma_{IR} I_s R \dot{W}_t, \\
 \dot{I}_a &= r \sigma E - (\mu + \gamma_a) I_a - \sigma_{IR} I_a R \dot{W}_t, \\
 \dot{I}_h &= \varphi_s I_s - (\mu + \gamma_h + \delta_h) I_h - \sigma_{IR} I_h R \dot{W}_t, \\
 \dot{R} &= \gamma_s I_s + \gamma_a I_a + \gamma_h I_h - \mu R + \rho_1 \sigma_{IR} (I_s + I_a + I_h) R \dot{W}_t, \\
 \dot{D} &= \delta_s I_s + \delta_h I_h + \rho_2 \sigma_{IR} (I_s + I_a + I_h) R \dot{W}_t,
 \end{aligned}
 \tag{2}$$

This model is stochastic. The fact behind the motivation for generating the stochastic dynamic model is the stochastic nature of the COVID-19 dynamics, which differs everywhere and has unpredictable characteristics. We start by adding white noise terms satisfying Wiener process (W_t) properties to the dynamic model. The newly added diffusion terms are used to reach more probabilistic positions covering a wide range of probable viral wave dynamics. Two positive diffusion coefficients are assumed to study how the 8 classes are stochastically affected by each other. The first diffusion coefficients the exposed-infected-vaccinated coefficient (σ_{EIV}) which measures the probabilistic effect of exposed, infected, vaccinated, and susceptible individuals on each other. The σ_{EIV} is stochastically affecting vaccinated people through the assumed constant weights b [2]. The second diffusion coefficient is the infected-recovered coefficient (σ_{IR}) which measures the stochastic diffusion effect of the recovered, deaths, and infected individuals on each other. ρ_1 and ρ_2 are constant weights that describe the partial effect of the σ_{IR} on the recovered and deaths class respectively. Also, β_h represents the rate at which hospitalized individuals transmit COVID-19 to susceptible individuals, ξ_v is the vaccination rate, $0 < \epsilon_v \leq 1$ is the vaccine efficacy to protect against breakthrough infection (in vaccinated susceptible individuals), and ω_v is rate of loss of vaccine-induced immunity. All other parameters in Eq. (2) are as defined before. It is assumed, for simplicity, that the imperfect vaccine does not wane during the chosen time duration for the model simulations. It is also assumed that vaccine-induced protection can wane at a constant rate.

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