

A Mathematical Model to Investigate How Vaccination Affect the Reproduction Number for COVID-19

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Abstract: In this paper a mathematical model that investigates how vaccination affects the dynamics of COVID-19 was considered. More particularly the model takes into account the waning rate of immunity after vaccination as well as administration of booster vaccine. Posititivity and boundedness of solutions of the model were proved. The disease free equilibrium of the model was determined and by using the next generation matrix method both the basic and effective reproduction numbers of the model were determined. Further, from the effective reproduction number, the minimum critical value of individuals to be vaccinated for containment of the diseases was determined. It was found that the value is less for a perfect vaccine compared to an imperfect vaccine. Numerical simulation of the model was done to determine how the parameters of interest in the study (waning rate of immunity, vaccination rate, administration of booster vaccine and efficacy of the vaccine) affect the effective reproduction number. The results show that increasing the rates of vaccination, administering booster vaccine will decrease the effective reproduction number while an increase in waning rate of immunity increases the effective reproduction number.

Keywords: Vaccination, Reproduction Number, COVID-19, Mathematical Model, Re-infection, Waning of Immunity

1. Introduction

Corona Virus Disease of 2019 (COVID-19) is a novel corona virus that was first identified in December 2019 in China. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [5]. Covid-19 is likened to the severe acute respiratory syndrome(SARS) occurred in 2003 [7]. However covid-19 is more contagious than (SARS)of 2003 as within 3 months of outbreak there were more than 100,000 confirmed cases and more than 3000 death cases [7]. In addition, in February 2020, it was found that, the reproduction number of COVID-19 was about 3.28, which is higher as compared to 2.79 of (SARS) [7]. As much as the virus is a threat to everyone, symptoms vary from person to person. Most individuals experience fever, coughing and shortness of breath, while others may face savere symptoms

such as damage to the lungs, acute respiratory failure [5] or others end up dying. Other symptoms include, fatigue, muscle aches, headache, loss of taste, sore throat, nausea and runny nose. The virus has since spread rapidly resulting in about 770 million confirmed cases and 6.9 million deaths world wide [18].

Several interventions were put into place in order to reduce the spread of the disease. One potential solution that was proposed is the implementation of non-pharmaceutical measures which include; wearing face mask, public event bans, school and workplace closure, keeping social distance, public transport shutdowns, restrictions on internal movement, international travel controls and stay at home requirements [3, 7, 10]. Implementation of these measures have shown to be effective in containing the spread of other viruses, such as SARS-Cov [20]. And hence these measures can also be used to contain the spread of COVID-19 since they fall in the same group. However, implementation of these measures can negatively affect the economy and other health outcomes, including mental health and chronic conditions [1]. Vaccination is the common method that is relied on apart from the measures above. Vaccination not only provides protection for the individual it also provides it for the community at large since it keeps the effective reproduction rate below the level which would allow an epidemic to start, hence the so called 'herd immunity' [16]. As viruses are constantly changing, including the one that causes COVID-19, there is need for people to get vaccinated since the changes can lead to emergence of variants that can increase the risk of reinfection [6].

Many mathematical models for example in yellowAli M, George K and Kate F's research [2, 11, 13] have been used to describe the dynamics of COVID-19. In the study done by Kate F [13] they first considered an SEIR model with no vaccine and then incorporated a vaccine compartment. The vaccine considered was imperfect meaning individuals who are vaccinated can still contract the virus but at a reduced rate. The model considered in this paper not only incorpoarates vaccination but also administration of booster vaccination as well as waning of immunity after vaccination.

2. Formulation of the Model

2.1. Assumptions of the Model

The population under study is divided into the following compartments; S(t) which denote a fraction of individuals who are susceptible to COVID-19 but not yet infected at time t, E(t) a fraction of exposed individuals who are infected but not yet infectious at time t, I(t) a fraction of infective individuals, R(t) a fraction of booster vaccinated and recovered individuals, and V(t) fraction of vaccinated individuals. For notational convenient we define the following variables; S(t); = S, E(t); = E, V(t); = V, I(t); = I and R(t); = R

We make the following assumptions for the model

- (i) Individuals in each compartment are uniformly mixed.
- (ii) Susceptible individuals are vaccinated at a rate η . However, we assume that immunity induced by vaccination wanes at a rate ε following vaccination. Since the vaccines are not perfect, the efficacy of vaccine is represented by ρ . Thus individuals in compartment V can be infected if they make contact with individuals in compartments E and I as the vaccines are imperfect.
- (iii) Infectivity rate of exposed individuals is reduced by a factor λ_E
- (iv) Individuals in E and I compartments recover at rates r_E and r_I respectively. There is death due to COVID-19 in compartment I with a mortality rate d.
- (v) Individuals in compartment R who were administered a booster vaccine are considered to have protective immunity at a longer period of time otherwise they can

be reinfected at a rate ω . The rate of administering booster vaccination is b

(vi) The total population size in consideration is a constant N

The following parameters will be used in the model

- (i) β is the transmission rate of the disease, it describes the number of new cases that arise from each existing case.
- (ii) λ_E is the infection rate of exposed individuals
- (iii) η is the rate at which individuals are vaccinated while ρ is the efficacy of the vaccine
- (iv) γ is the rate at which exposed members become infectious
- (v) r_E and r_I are the rates at which exposed and infective members recover respectively. However, individulas in I may die due to COVID-19 at a mortality rate d. In addition, μ is the natural death rate in each compartment. ω is the rate at which individuals in R become susceptible to the disease again.

The schematic diagram for the model is as shown below. The arrows indicate individuals progressing from one compartment to another



Figure 1. Schematic diagram showing the progression from one compartment to another.

2.2. The Model

Using the assumptions, parameters schematic diagram above and evolution of individuals from one compartment to another, we form the following system of differential equations describing the model

$$\begin{aligned} \frac{dS}{dt} &= \phi - \beta S(\lambda_E E + I) - (\eta + \mu)S + \varepsilon V + \omega R, \\ \frac{dV}{dt} &= \eta S - (1 - \rho)\beta V[\lambda_E E + I] - (b + \mu + \varepsilon)V, \\ \frac{dE}{dt} &= \beta S(\lambda_E E + I) + (1 - \rho)\beta V[\lambda_E E + I)] \quad (1) \\ &- (\gamma + r_E + \mu)E, \\ \frac{dI}{dt} &= \gamma E - (r_I + d + \mu)I, \\ \frac{dR}{dt} &= r_E E + r_I I - (\omega + \mu)R + bV \end{aligned}$$

Equation (1) is subject to the initial conditions $S(0) \ge 0$, $V(0) \ge 0$, $E(0) \ge 0$, $I(0) \ge 0$, and $R(0) \ge 0$. We analyze the system in (1), first starting with its basic properties, positivity

and boundedness of solutions, which we describe as follows.

3. Model analysis

3.1. Postivity and Boundedness of Solutions

Since we are dealing with human population, the solutions set $\{S(t), V(t), E(t), I(t), R(t)\}$ must be positive and bounded. We therefore state and prove the following theorems with respect to our model.

Theorem 3.1. The solutions set $\{S(t), V(t), E(t), I(t), R(t)\}$ for the equation (1) is positive with the initial conditions $\{S(0) \geq 0\}$ $0, V(0) \ge 0, E(0) \ge 0, I(0) \ge 0, H(0) \ge 0, R(0) \ge 0$ for all t > 0 and all nonnegative parameters. *Proof* For $\frac{dS}{dt}$ we have

$$\frac{dS}{dt} = \phi - \beta S(\lambda_E E + I) - (\eta + \mu)S + \varepsilon V + \omega R$$

= $\phi + \varepsilon V + \omega R - \beta S(\lambda_E E + I) - (\eta + \mu)S$
 $\geq -S(\beta \lambda_E E + \beta I + \eta + \mu)$

Letting $\psi(t) = \beta \lambda_E E + \beta I + \eta + \mu$ we have

$$\frac{dS}{dt} \geq -S\psi(t)$$

Just like a separable differential equation, the inequality is separable. We thus use separation of variables technique to solve the inequality. That is,

$$\int \frac{dS}{S} \geq \int -\psi(t)dt$$

We integrate from 0 to t to obtain

 $[lnS]_o^t \geq -\int_0^t \psi(\tau)d\tau$

$$S(t) \geq S(0)exp\left(-\int_0^t \psi(\tau)d\tau\right)$$

Since $S(0) \ge 0$ and an exponential function is always positive we have that S(t) > 0

Similarly, we can prove that V(t), E(t), I(t) and R(t) are all nonnegative.

Theorem 3.2. The solution set of the equation (1) is bounded within the invariant region $\Omega \in \mathbb{R}^5_+$. Where $\Omega =$ $\left\{ (S, V, E, I, R) : N \le \frac{\phi}{\mu} \right\}$

Before the proof let's define what an invariant set is

Definition 3.1. A set Ω is said to be invariant if any solution with initial condition in the set remains in the set for all time $t \ge 0.$

We now prove the theorem.

Proof Adding the differential equations in system (1), we

have

$$N' = S' + V' + E' + I' + R$$

Where $l_{i} = \frac{d}{dt}$ From equation (1) we have

$$N' = \phi - \mu S - \mu V - \mu E - (d + \mu)I - \mu R$$

= $\phi - \mu (S + V + E + I + R) - dI$
= $\phi - \mu N - dI$

If there is an infection in the population I(t) > 0. And since $I \leq N \implies dI \leq dN$. Thus,

$$N' \geq \phi - \mu N - dN = \phi - (\mu + d)N$$

$$N' \geq \phi - (\mu + d)N$$
(2)

If there is no infection, then I(t)=0. Thus,

$$N' \leq \phi - \mu N \tag{3}$$

From (2) and (3) we obtain

$$\phi - (\mu + d)N \leq N' \leq \phi - \mu N$$

By the variation of constant formulae and taking the limits of integration from 0 to t we have

$$e^{-(\mu+d)t} \left[N(0) + \int_0^t \phi e^{(\mu+d)\tau} d\tau \right]$$

$$\leq N \leq e^{-\mu t} \left[N(0) + \int_0^t \phi e^{\mu\tau} d\tau \right]$$
(4)

Upon integration and simplifying we obtain

$$\frac{\phi}{\mu+d} + e^{-(\mu+d)t} \left(N(0) - \frac{\phi}{\mu+d} \right)$$

$$\leq N \leq \frac{\phi}{\mu} + e^{-\mu t} \left(N(0) - \frac{\phi}{\mu} \right)$$
(5)

As t approaches ∞ we have

$$\frac{\phi}{\mu+d} \leq N \leq \frac{\phi}{\mu} \tag{6}$$

Therefore from (6) we conclude that the solution sets for system (1) are bounded within the invariant region Ω

3.2. The Basic Reproduction Number

The basic reproduction number, usually denoted by R_o , is the average number of secondary cases produced by one infected individual introduced into a population of susceptible individuals without any interventions in place[4]. If interventions like vaccination are put in place then we will determine effective reproduction number analogous to R_o , which we will denote as R_e . Therefore both R_o and R_e

will help us know how many individuals one infected person can transmit the disease to. Which in turn help us know if an epidemic will occur or not. For instance if $R_0 > 1$ or $R_e > 1$ there will be an epidemic, that is, the disease persist in the population for some period. However if $R_o < 1$ or $R_e < 1$ then the disease will die out. To compute the basic reproduction number, we use the next generation matrix method which we describe.

The next generation matrix method

This method is based on dividing the compartments under study into two;

- (i) Disease compartment- This is the compartment in which individuals are infected
- (ii) Non-disease compartment- Individuals here are disease free.

Following [4] we assume that there are n disease compartments and m non-disease compartments. We also assume that there are x and y subpopulations in each of the compartments n and m respectively. That is, $x \in \mathbb{R}^n$ and $y \in \mathbb{R}^m$. We then denote the rate at which new infections increase the i^{th} infected compartment by F_i while V_i denote the rate of decrease in the i^{th} compartment by disease progression, death and recovery. The general compartmental model thus take the form;

$$x_i = F_i(x, y) - V_i(x, y), i = 1, 2, ..., n$$

$$y_j = g_j(x, y), \ j = 1, 2, ..., m$$
(7)

Next we put some conditions on F_i and V_i ;

 $F_i(x, y) \ge 0$ for all $x \ge 0, y \ge 0$ and i = 1, 2, ..., n. Since F represent new infections and therefore it is nonnegative

 $V_i(x, y) \leq 0$ provided $x_i = 0$ for i = 1, 2, ..., n. V_i is the net outflow from compartment i hence it must be negative whenever the compartment is empty

 $\sum_{i=1}^{n} V_i(x, y) \ge 0$ for all $x \ge 0, y \ge 0$. This represent the total outflow from all infected compartments.

For determination of the basic reproduction number using this method we only consider the infected compartments. Moreover, determining R_o involves the linearization of the ODEs in the infected compartments about the disease free equilibrium(DFE). The disease free equilibrium for the above general model will be $(0, y_o)$. After linearization about the DFE, we obtain two matrices F and V given by

$$F = \frac{\partial F_i(0, y_o)}{\partial x_i} \quad V = \frac{\partial V_i(0, y_o)}{\partial x_i}$$

The matrix given by FV^{-1} is known as the next generation matrix. The spectral radius of this matrix is what we refer as the basic reproduction number. With this knowledge on the next generation matrix, we are now ready to compute the effective reproduction number but first we determine the disease free equilibrium(DFE) since we will need it for determination of F and V. The DFE is determined by equating each of the equations in (1) to 0 and taking E,I,R to be equal to 0 since there is no disease in the population. After these simple steps we only remain with two equations thus

$$\phi - (\eta + \mu)S_o + \varepsilon V_o = 0 \tag{8}$$
$$\eta S_o - (b + \mu + \varepsilon)V_o = 0 \tag{9}$$

$$\eta S_o - (b + \mu + \varepsilon) V_o = 0 \tag{9}$$

Solving (8) and (9) for S_o and V_o we obtain

$$S_o = \frac{\phi(b+\mu+\varepsilon)}{(b+\mu)(\eta+\mu)+\mu\varepsilon}$$
$$V_o = \frac{\phi\eta}{(b+\mu)(\eta+\mu)+\mu\varepsilon}$$

With S_o and V_o as given above the DFE becomes $(S_o, V_o, 0, 0, 0)$. For our model in (1) the disease compartments are E and I. Therefore we will only focus on the differential equations;

$$\frac{dE}{dt} = \beta S(\lambda_E E + I) + (1 - \rho(t))\beta V[\lambda_E E + I)] -(\gamma + r_E + \mu)E, \qquad (10)$$
$$\frac{dI}{dt} = \gamma E - (r_I + d + \mu)I$$

From (10) we form F_i and V_i which will help us determine F and V. Since we only have two disease compartments, i = 1, 2. Therefore we have for F_i

$$F_1 = \beta S(\lambda_E E + I) + (1 - \rho)\beta V[\lambda_E E + I)],$$

$$F_2 = 0$$
(11)

 $F_2 = 0$ in equation (11) is due to the fact that there are no new infections in compartment I. For V_i we have

$$V_1 = (\gamma + r_E + \mu)E$$

$$V_2 = (r_I + \mu + d)I - \gamma E$$
(12)

Letting $\gamma + r_E + \mu = c_1$, $r_I + \mu + d = c_2$ and linearizing systems (11) and (12) about the DFE ($S_o, V_o, 0, 0, 0$) we obtain matrices F and V. That is;

$$\mathbf{F} = \begin{pmatrix} \beta \lambda_E [S_o + (1-\rho)V_o] & \beta [S_o + (1-\rho)V_o] \\ 0 & 0 \end{pmatrix} \\ \mathbf{V} = \begin{pmatrix} c_1 & 0 \\ -\gamma & c_2 \end{pmatrix}$$

To determine the basic reproduction number we have to find FV^{-1} . First, we determine V^{-1} . We first determine if determinant of V, |V|, exists and $|V| \neq 0$ so that V^{-1} exists. We easily compute |V| as follows

$$|V| = \begin{vmatrix} c_1 & 0 \\ -\gamma & c_2 \end{vmatrix} = c_1 c_2 \neq 0.$$
 Thus V^{-1} exists and it is given by

$$V^{-1} = \frac{1}{c_1 c_2} \begin{pmatrix} c_2 & c_1 \\ \gamma & c_1 \end{pmatrix}$$

With F and V^{-1} we compute the next generation matrix FV^{-1} . That is;

$$FV^{-1} = \frac{1}{c_1 c_2} \begin{pmatrix} \beta \lambda_E [S_o + (1-\rho)V_o] & \beta [S_o + (1-\rho)V_o] \\ 0 & 0 \end{pmatrix} \begin{pmatrix} c_2 & 0 \\ \gamma & c_1 \end{pmatrix} \\ = \frac{1}{c_1 c_2} \begin{pmatrix} c_2 \beta \lambda_E [S_o(1-\rho)V_o] + \gamma \beta [S_o + (1-\rho)V_o] & c_1 \beta [S_o + (1-\rho)V_o] \\ 0 & 0 \end{pmatrix}$$

The effective reproduction number, R_e , is the dominant eigenvalue of the matrix FV^{-1} . Thus we have

$$R_{e} = \frac{1}{c_{1}c_{2}} \{c_{2}\beta\lambda_{E}[S_{o}(1-\rho)V_{o}]\} + \frac{1}{c_{1}c_{2}} \{\gamma\beta[S_{o}+(1-\rho)V_{o}]\}$$

$$= \frac{1}{c_{1}}\beta\lambda_{E}S_{o} + \frac{\gamma}{c_{1}}\frac{1}{c_{2}}\beta S_{o} + \frac{1}{c_{1}}\beta\lambda_{E}(1-\rho)V_{o} + \frac{\gamma}{c_{1}}\frac{1}{c_{2}}\beta(1-\rho)V_{o}$$
(13)

We can clearly see that the effective reproduction number is as a result of unvaccinated susceptible individuals and vaccinated individuals. Thus we can express it as

$$R_e = R_o^{S_o} + R_o^{V_o} \tag{14}$$

Where

$$R_o^{S_o} = \frac{1}{c_1}\beta\lambda_E S_o + \frac{\gamma}{c_1}\frac{1}{c_2}\beta S_o \text{ and } R_o^{V_o} = \frac{1}{c_1}\beta\lambda_E(1-\rho)V_o + \frac{\gamma}{c_1}\frac{1}{c_2}\beta(1-\rho)V_o$$

After substituting c_1 and c_2 as we had let earlier we get

$$R_o^{S_o} = \frac{1}{\gamma + r_E + \mu} \beta \lambda_E S_o + \frac{\gamma}{\gamma + r_E + \mu} \frac{1}{r_I + \mu + d} \beta S_o$$
(15)

$$R_{o}^{V_{o}} = \frac{1}{\gamma + r_{E} + \mu} \beta \lambda_{E} (1 - \rho) V_{o} + \frac{\gamma}{\gamma + r_{E} + \mu} \frac{1}{r_{I} + \mu + d} \beta (1 - \rho) V_{o}$$
(16)

With no interventions, from the effective reproduction number we obtain the basic reproduction number as

$$R_o = \frac{1}{\gamma + r_E + \mu} \beta \lambda_E S_o + \frac{\gamma}{\gamma + r_E + \mu} \frac{1}{r_I + \mu + d} \beta S_o \tag{17}$$

Where $S_o = \frac{\phi}{\mu} = 1$. What this means is that before the disease invasion, the susceptible population is equal to the total population.

Next we express the effective reproduction number in terms of R_o for ease of determination of the minimum critical value to be vaccinated to contain the disease. Note that from now in our analysis we are going to assume that the rates of recovery of exposed individuals and infected individuals are equal, thus we take $r_E = r_I = r$. In addition we take $1 - \rho = \psi$. After substituting $S_o = \frac{\phi}{\mu} = 1$ in the equation for R_o we obtain

$$R_o = \frac{\beta \lambda_E}{(\gamma + r + \mu)} + \frac{\gamma \beta}{(\gamma + r + \mu)(r + \mu + d)}$$
(18)

We can express R_e in terms of R_o as follows

$$R_o^{S_o} = \frac{(b+\mu+\varepsilon)\phi}{(b+\mu)(\eta+\mu)+\mu\varepsilon} (R_o) \text{ and } R_o^{V_o} = \frac{\phi\psi\eta}{(b+\mu)(\eta+\mu)+\mu\varepsilon} (R_o)$$

Thus

$$R_e = \frac{\phi R_o}{(b+\mu)(\eta+\mu)+\mu\varepsilon} \left[b+\mu+\varepsilon+\eta\psi\right] = (S_o+\psi V_o)R_o$$

For the minimum value to archive elimination as seen in [14], $R_e = 1$. Therefore

$$\frac{\phi R_o}{(b+\mu)(\eta+\mu)+\mu\varepsilon} \left[b+\mu+\varepsilon+\eta\psi\right] = 1$$

$$\phi R_o(b + \mu + \varepsilon + \eta \psi) = (b + \mu)(\eta + \mu) + \mu \varepsilon$$
(19)

Our aim is determining the critical value η_c which is easily archived by making η the subject in equation (19). After some simple algebra we obtain

$$\eta_c = \frac{\phi(b+\mu+\varepsilon)(R_o-1)}{b+\mu-\phi\psi R_o}$$
(20)

This is the minimum critical value that need to be vaccinated in order to contain the disease. If there is no booster vaccination we have

$$\eta_c = \frac{(\mu + \varepsilon)(R_o - 1)}{1 - \psi R_o} \tag{21}$$

For a perfect vaccine and there is no booster vaccination, that is, for $1 - \rho = \psi = 0$ and b=0 we have

$$\eta_c = (\mu + \varepsilon)(R_o - 1) \tag{22}$$

For a perfect vaccine we expect the critical value to be vaccinated to be less compared to when the vaccine is imperfect. Thus, it should be clear that the expression for η_c in equation (21) should be greater than the expression for η_c in equation (22). In deed this is true. Let's prove this by contradiction. Let's assume that

 $(\mu + \varepsilon)(R_o - 1) > \frac{(\mu + \varepsilon)(R_o - 1)}{1 - \psi R_o}$ $1 > \frac{1}{1 - \psi R_o}$ $1 - \psi R_o > 1$ $\psi R_0 < 0$

We know that ψ and R_o are nonnegative thus $\psi R_0 < 0$ is false, hence our assumption is false. Therefore

$$(\mu + \varepsilon)(R_o - 1) < \frac{(\mu + \varepsilon)(R_o - 1)}{1 - \psi R_o}$$

4. Numerical Simulations

In this section we carry out numerical simulation of our model. Particularly to know how R_e varies with parameters. The table below shows the values of the parameters used in simulation.

<i>Table 1.</i> Parameter value	Table	1.	Parameter	Vai	ue.
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Parameter	Value	Source
ϕ	0.00005	[8]
β	0.5	[11]
λ_E	0.314	[11]
η	0.0005	[19]
μ	0.00005	Assumed
ω	0.0033	[9]
ε	0.0042	[15]
ψ	0.2	Assumed
b	0.0001	Assumed
γ	0.1667	[12]
r	0.1	[5]
d	0.0016	[11]

With the parameters above R_o and R_e are 3.6625 and 2.7860 respectively. Also we can determine the numerical value for η_c , that is

$$\eta_c = \frac{\phi(b+\mu+\varepsilon)(R_o-1)}{b+\mu-\phi\psi R_o} = 0.0051$$

Without booster vaccine, that is for b=0, we have

 $\eta_c = 0.0423$

We can clearly see that when booster vaccination is included, the critical value to be vaccinated to achieve elimination of the disease is less compared to when there is no booster vaccination.

The Figures below show how R_e varies with our parameters of interest, that is, the rate of vaccination, the rate of administering booster vaccine, the waning rate of immunity after vaccination and the efficacy of the vaccine









0.0051 and 0.0101 respectively will reduce R_e and in turn prevent an epidemic to occur. From Figure 4 we observe that R_e increases as ε increases. Therefore, if the immunity after vaccination wanes at a higher rate the disease will remain in the population. From Figure 5, when the vaccine is perfect($\psi =$ 0), $R_e = 2.725 > 1$. Thus there will be an epidemic even if the vaccine is perfect. This is due to the waning rate of immunity after vaccination which makes individuals exposed to the infection. We can also see that as the efficacy of the vaccine reduces ($\psi > o$), R_e increases.

5. Conclusion and Recommendation

5.1. Conclusion

Booster vaccination reduces the critical value needed to be vaccinated in order to contain the disease. Moreover, booster vaccination increases the period of protection against the disease. Even when the vaccine is perfect the disease still persist in the population due to the waning rate of immunity.

5.2. Recommendation

The model considered never incorporated how the effect of environmental factors such as climate affect the spread of the disease. Moreover, a model that takes into account the waning of immunity that depends on time is recommended.

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Conflicts of Interest

The authors declare no conflict of interest.

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