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A Probabilistic Description of the Impact of Vaccine-Induced Immunity in the Dynamics of COVID-19 Transmission

Javier Blecua[1,2], Juan Fernández-Recio[1], José Manuel Gutiérrez[2]

[1]Instituto de Ciencias de la Vid y del Vino (ICVV), CSIC-Universidad de La Rioja-Gobierno de La Rioja, Logroño, Spain
[2]Departamento de Matemáticas y Computación, Universidad de La Rioja, Logroño, Spain
Email: javier.blecua@icvv.es

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Abstract

The recent outbreak of COVID-19 has caused millions of deaths worldwide and a huge societal and economic impact in virtually all countries. A large variety of mathematical models to describe the dynamics of COVID-19 transmission have been reported. Among them, Bayesian probabilistic models of COVID-19 transmission dynamics have been very efficient in the interpretation of early data from the beginning of the pandemic, helping to estimate the impact of non-pharmacological measures in each country, and forecasting the evolution of the pandemic in different potential scenarios. These models use probability distribution curves to describe key dynamic aspects of the transmission, like the probability for every infected person of infecting other individuals, dying or recovering, with parameters obtained from experimental epidemiological data. However, the impact of vaccine-induced immunity, which has been key for controlling the public health emergency caused by the pandemic, has been more challenging to describe in these models, due to the complexity of experimental data. Here we report different probability distribution curves to model the acquisition and decay of immunity after vaccination. We discuss the mathematical background and how these models can be integrated in existing Bayesian probabilistic models to provide a good estimation of the dynamics of COVID-19 transmission during the entire pandemic period.

Keywords

COVID-19 Transmission Dynamics, Probabilistic Model, Bayesian Analysis, Markov Chain Monte Carlo

1. Introduction

As of 19 January 2024, over 770 million confirmed COVID-19 cases and over 7 million deaths have been reported worldwide [1]. In Spain, more than 121,000 persons have already died from the disease [2]. Although the public health emergency due to the COVID-19 pandemic is officially over, the virus is still active, and efficient mathematical models of the transmission dynamics are still needed to be ready for periodic recurrence, appearance of new virus variants, or any other unwanted future scenarios.

From the beginning of the pandemic, mathematical modelling has helped to understand the relevant factors involved in the transmission dynamics of the virus and to evaluate the effectiveness of public health measures. This has provided powerful tools for decision-makers to identify and apply effective control mechanisms in order to minimize the impact of the pandemic on public health and society. Thus, different approaches were reported to model the transmission dynamics of the virus in the population. Among them, Bayesian probabilistic models were very efficient for the estimation of the transmission parameters at the early stages of the pandemic [3], since they could use ad-hoc devised mechanistic functions in complex scenarios, like incomplete data due to low detection rates, changing conditions due to intervention measures or different compliance of such measures in each region/country. In these challenging conditions, other mathematical approaches based on differential equations were more problematic to use in practical terms.

At the beginning of the pandemic, we applied a Bayesian probabilistic model to analyse the impact of non-pharmacological measures in different countries [4], as these were the only strategies to control the spread of the disease, and found that such measures had different impact in the COVID-19 transmission in each country. The initial model was extended throughout the pandemic in order to include key features such as the possibility of defining an unlimited number of non-pharmacological measures, modelling the impact of detection rate in the transmission, or predicting cases and deaths in hospitals (manuscript in preparation). But towards the end of 2020, two key aspects had a dramatic effect on COVID-19 transmission dynamics: the massive vaccination of the population, and the appearance of different virus variants. The challenge was to efficiently include in the model the impact of vaccine-induced immunity on the evolution of the disease, taking also into account the immunity of the recovered population and considering specific transmission parameters for the different virus variants.

Different studies have estimated the evolution in time of the protection provided by vaccination based on clinical data as well as on the concentration of antibodies and other molecules of the immune system [5] [6] [7] [8]. Such studies show important aspects that need to be considered to model the impact of vaccination on transmission dynamics. Basically, after vaccination, the level of protection against infection (immunity) increases until reaching a maximum value,

which remains at a certain level during a period of time. Immunity provided by additional vaccine doses will be incremental, but at some point, if no additional doses are applied, immunity starts to decay. In addition, these studies show that immunity provided by vaccination is less effective against some variants, like omicron.

In this work, we focus on how to model the impact of the vaccination on the transmission of the disease. We define probability distribution curves to estimate the degree and duration of the vaccine-induced immunity and its impact on the transmission, considering the different vaccine doses. The approach assumes that the protective effect of the vaccination gets reflected in a reduction of the population that is susceptible of being infected, and that this reduction can be quantified by optimizing different parameters related to the impact of the vaccines, such as the percentage of the vaccine-induced immunity after each vaccine dose and the duration of this immunity. We show how these probability curves and the different vaccination parameters can be integrated in a more generic transmission model that can explain the transmission dynamics of COVID-19 over long periods of time, incorporating parameters for the most relevant factors related to the spread of the disease: non-pharmacological measures, vaccination, and individual characteristics of the different virus variants.

2. The Model and Preliminaries

2.1. Compartmental SIR Model

Compartmental models are widely used to describe the spread of infectious diseases [9]. In these models, the population is divided into different groups (compartments), and the evolution of a disease is described by the dynamics that modulate the transition of the individuals between the different compartments.

One of the most popular compartmental approaches to describe the transmission dynamics of the COVID-19 is the SIR model (**Figure 1**), where the population is classified into the following compartments: susceptible (S), infected (I), and recovered (R).

The SIR model and other compartmental approaches are usually implemented using differential equations to describe the dynamics of the transitions between the different compartments [9]. In this model, the evolution of the population in each compartment over time can be described by the following ordinary differential equations (ODEs):

$$\mathrm{d}S/\mathrm{d}t = -\beta \cdot I \cdot S/N\,,\quad S(0) = S_0 \geq 0\,, \tag{1}$$

$$\mathrm{d}I/\mathrm{d}t = (\beta \cdot I \cdot S/N) - (\gamma \cdot I)\,,\quad I(0) = I_0 \geq 0\,, \tag{2}$$

$$\mathrm{d}R/\mathrm{d}t = \gamma \cdot I\,,\quad R(0) = R_0 \geq 0\,, \tag{3}$$

where N denotes the total population, which is a constant value, assuming no vital dynamics (births and deaths), so that $N = S(t) + I(t) + R(t)$, being $S(t)$, $I(t)$ and $R(t)$ the populations of each of the compartments at any given time.

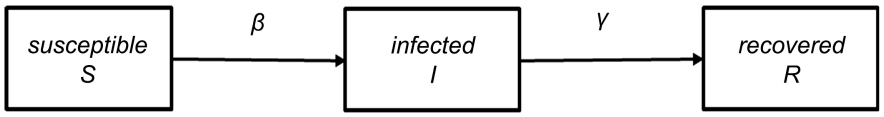

Figure 1. Scheme of a SIR model.

The identification of the values for the ODE parameters (β and γ) that best fit the observed data, usually through numerical integration, will provide the description of the factors related to the transmission of the disease. However, this approach has important limitations. This simple model does not consider different aspects of the transmission that were not evident at the beginning of the pandemic. For instance, susceptible population will be reduced due to dead individuals, recovered individuals can be susceptible again after some time when acquired immunity is lost, or the fact that infected individuals are not contagious from the moment of infection. To address these situations, SIR models were extended to the SEIR models, with an additional compartment for exposed (E), *i.e.*, individuals that have been infected but are not yet contagious, or by using of additional compartments for dead (D), or new transitions from recovered to susceptible compartments. In addition, in realistic scenarios where transmission conditions can change in time due to intervention measures or other factors, or with limited and inconsistent observed data, these mathematical models based on differential equations can become highly complex and have difficulties in estimating the key parameters for the transmission dynamics on the long term.

Here, we use a probabilistic approach based on a SIR model that has been extended by adding an additional state, dead (D), as previously described [3] [4], and where the dynamic of the transitions between the different states (susceptible, infected, recovered, dead) are described by specific parameters and probability distributions over time [3] [4]. In this model, we use a numerical integration method with a Bayesian approach and Markov Chain Monte Carlo (MCMC) simulations for the parameter estimation, which provides sets of parameter values that optimally fit the observed data.

2.2. Numerical Integration Using Probability Distributions

In our numerical integration approach, the expected number of new infections I_i occurring in each day i is defined as a function of the number of infected individuals I_j in the previous days, their probability of infecting other individuals after i-j days according to a serial interval (SI) probability density function, and the effective reproduction number (R_t) in the day i (Equation (4)).

$$I_i = \left(R_t\right)_i \cdot \sum_{j=1}^{i-1} \left(I_j \cdot SI_{i-j}\right). \tag{4}$$

The effective reproduction number (R_t) as defined here describes the total number of persons that are infected in average on a given day by each infected individual. This value changes over time and depends on different factors, such as the application of non-pharmacological measures. Values greater than 1 mean

that the disease is still spreading, while values less than 1 mean that the transmission of the disease is under control. In our model, the value of R_t at a given day *i* is determined by the basic reproduction number (R_0) and a set of factors $e^{-\alpha_k}$ that describe the effect of all non-pharmacological measures that are active on that day *i* as well as other events/conditions that can impact the virus transmission (Equation (5)).

$$\left(R_t\right)_i = R_0 \cdot e^{-\sum_k \alpha_k}. \tag{5}$$

The basic reproduction number (R_0) is the initial value of the effective reproduction number (R_t) and can be defined as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible [9]. This parameter describes the transmission rate in a susceptible population in absence of any measures. The factors that quantify the impact of the different measures that are active in a given period, defined for convenience as exponentials $e^{-\alpha_k}$, reflect the contribution of each non-pharmacological measure or event to changes in the value of the effective reproduction number. Factors with values less than 1 are related to effective measures that have contributed to a reduction in the value of the reproduction number, and therefore in the spread of the disease. Factors with values greater than 1 are associated to periods and events that have led to an increase in the reproduction number, and therefore in the number of cases. The optimal values for the basic reproduction number (R_0) and the factors $e^{-\alpha_k}$ will be estimated after fitting the model to the observed death data (see next section).

The Serial Interval (*SI*) probability density distribution (**Figure 2(a)**) describes in probabilistic terms when a newly infected individual is more likely to transmit the disease to another person. This distribution was estimated as a gamma distribution $g \sim Gamma$ (6.5, 0.62) based on data from early epidemics [3].

On the other side, the expected number of deaths D_i in each day *i* is a function of the number of infections I_j occurring in the previous days, the estimated infection fatality ratio (*IFR*) for each country, and the probability of occurrence of death in day *i-j* after infection according to a previously calculated infection to death (*ITD*) probability density distribution (Equation (6)).

$$D_i = \sum_{j=1}^{i-1}\left(I_j \cdot IFR \cdot ITD_{i-j}\right). \tag{6}$$

The infection fatality ratio (*IFR*) is the probability of death for an infected case, and it has been calculated for each country from clinical data as previously described [4].

The infection to death (*ITD*) probability distribution (**Figure 2(b)**) describes when a fatality is more likely to occur after infection. This distribution was estimated as the combination of two gamma distributions, representing the incubation period (infection to onset) and the time between onset of symptoms and death (onset to death), and is given by $\pi \sim Gamma$ (5.1, 0.86) + $Gamma$ (17.8, 0.45) according to data from early epidemics [3].

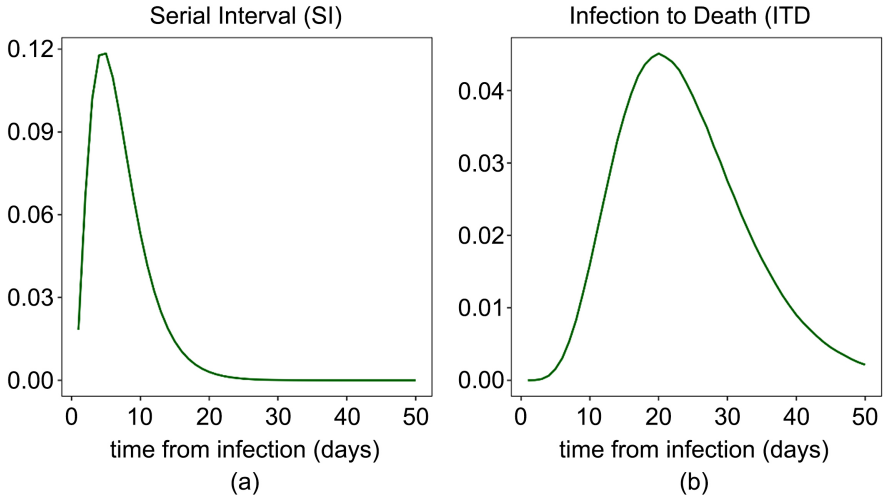

Figure 2. Probability distribution curves used in our COVID-19 transmission model: (a) Serial Interval (SI), and (b) Infection to Death (ITD).

2.3. Monte Carlo Simulations and Bayesian Estimation of Transmission Parameter Values

The above-described model (Equations (4)-(6)) estimates the new infected individuals and deaths for each day as a function of a set of parameters that will be optimized so that the model provides the best possible description of real data. These parameters are: 1) the initial infected individuals (I_0) during the first 6 days of the studied period, which usually starts 30 days before the first cumulated 10 deaths; 2) the initial value of the reproduction number (R_0), and 3) the parameters α_k that quantify the impact of the different intervention measures and conditions that are applied in each of the periods defined by the user. The values of the parameters are sampled from Bayesian prior distributions by using a Markov Chain Monte Carlo (MCMC) method in order to obtain the posterior distributions that lead to the best possible fit of the model estimations of daily deaths to the reported data, which are assumed to follow a negative binomial distribution, as previously described [3] [4]. The parameters α_k are technically grouped in two classes $(\alpha_k)_1$, related to measures that decrease transmission (e.g. lockdown), and $(\alpha_k)_2$, related to periods or events that may increase transmission of the disease (e.g. Christmas periods). Following the approach from previous works [3] [4], the prior distributions for the first class of parameters $(\alpha_k)_1$ are defined as a gamma distribution $g \sim Gamma$ (0.5, 1). This has always a value greater than 0 and ensures that the corresponding factors $e^{-\alpha_k}$ are always less than 1, which is the appropriate range of values to describe effective measures. For the second class of parameters $(\alpha_k)_2$, the prior distributions are defined as a normal $n \sim Normal$ (0, 1), which assumes a priori a neutral effect ($e^{-\alpha_k} = 1$ for the mean value $\alpha_k = 0$) and may result in a posterior distribution with all possible values for the factor $e^{-\alpha_k}$, which will allow the identification of any possible effect, either positive or negative, for the corresponding periods and events.

3. Impact of Vaccination on Transmission Dynamics

3.1. Including Vaccine-Induced Immunity in the Transmission Model

The impact of vaccination in the transmission can be described by a reduction of the effective reproduction number by the relative amount of the initial population N_0 that is not susceptible of being infected due to the protective effect of the vaccination. The same is true also for the immunity acquired after infection. Both types of immunity contribute to the estimation of the reproduction number with a reduction factor (Equation (7)), in which Imm_{i-1} represents the total amount of immune population (calculated on the previous day for practical purposes).

$$\left(R_t\right)_i = R_0 \cdot \mathrm{e}^{-\sum_k \alpha_k} \cdot \left(1-\left(Imm_{i-1}/N_0\right)\right). \tag{7}$$

The amount of immune population (Imm_i) can be calculated as a function of the reported number of individuals vaccinated on previous days at each dose type ($Vacc1_j$, $Vacc2_j$, $Vacc3_j$), the probability of having acquired immunity in day *i-j* after vaccination according to a precalculated distribution for each dose type ($V1TImm$, $V2Timm$, $V3TImm$), and the efficiency of the vaccine against each virus variant, according to the reported proportion of variants each day ($IRvar_j$) (Equation (8)). The value Imm_i also includes the number of infected people in previous days and the probability of retaining immunity since the time of infection. To avoid double counting in the case of infected individuals that are vaccinated, here we have included only detected cases when this number is larger than the number of vaccinated people.

$$\begin{aligned} Imm_i = \sum_{j=1}^{i-1} \Big(& IRvar_j \cdot \left(Vacc1_j \cdot V1TImm_{i-j} + Vacc2_j \cdot V2TImm_{i-j}\right. \\ & \left. + Vacc3_j \cdot V3TImm_{i-j}\right) + I_j \cdot ITImm_{i-j} \Big). \end{aligned} \tag{8}$$

The $V1TImm$, $V2ITmm$, $V3TImm$ distributions will describe the probability of being immune at a given time after each vaccination dose. We will analyse here (see next section) different probability distributions based on approaches from other studies and on empirical data related to the effectiveness of the vaccines.

On the other side, the infection fatality ratio (*IFR*), assumed to be a constant value for each country during the entire studied period in the initial model, should actually be variable in time when vaccine-induced immunity is included, given that vaccinated individuals that are infected have lower probability of death. In addition, *IFR* can be different for each virus variant. Thus, *IFR* on a given day *j* will depend on the percentage of vaccinated population and on the proportion of infections for the different virus variants on that day. With this, the constant value of *IFR* used initially in Equation (6) for the estimation of the number of deaths is replaced by a variable value IFR_j (Equation (9)).

$$D_i = \sum_{j=1}^{i-1} \left(I_j \cdot IFR_j \cdot ITD_{i-j}\right). \tag{9}$$

3.2. Vaccine-Induced Immunity Probability Distributions

A key element for efficiently describing COVID-19 transmission dynamics in our Bayesian model will be the probability distributions that describe the protection against infection after vaccination ($V1TImm$, $V2Timm$, $V3TImm$), which are used for the estimation of the immune population on a given day based on the information about the vaccinated population for each dose type (Equation (8)). Based on previous studies [5] [6] [7] [8], the probability distributions that describe vaccine-induced immunity should take into account two important aspects: 1) vaccination does not provide immediate immunity; and 2) vaccinated and infected individuals are immune against infection during an undetermined period of time.

The acquisition of immunity after vaccination is not immediate, and there are many studies showing how this immunity increases over time until reaching a maximum in a period of time that depends on the vaccine type and the number of previously received doses. As an example, **Figure 3** shows empirical data with the evolution of the concentration of antibodies after 1st dose vaccination [10], which can be described as a logistic curve.

The evolution in time of vaccine-induced immunity acquired after more than one dose will require of more complex probability distribution curves. As an example, **Figure 4** shows different probability distribution curves as possible approaches to model the vaccine-induced immunity for the individuals that have received two vaccine doses on time ($V2TImm$), and how these curves describe well available data showing the evolution of antibody concentration after the two first vaccination doses, after adjusting the empirical data to the vaccination time between doses [10]. But it must be noticed that the level of the antibody concentration does not reflect necessarily the degree of immunity, especially when the

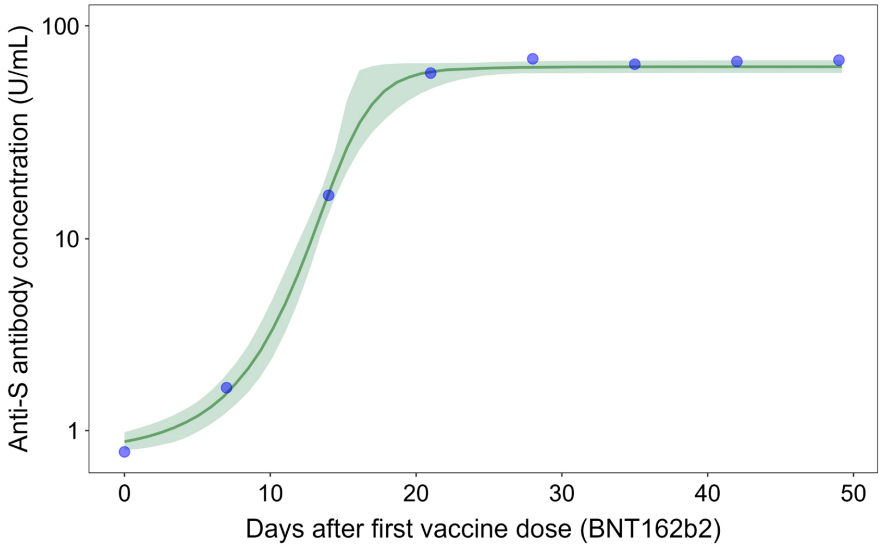

Figure 3. Logistic curve fit (median with 95% confidence interval in green) to antibody concentration levels after vaccination with BNT162b2 (blue dots, extracted manually from **Figure 1** in reference [10]).

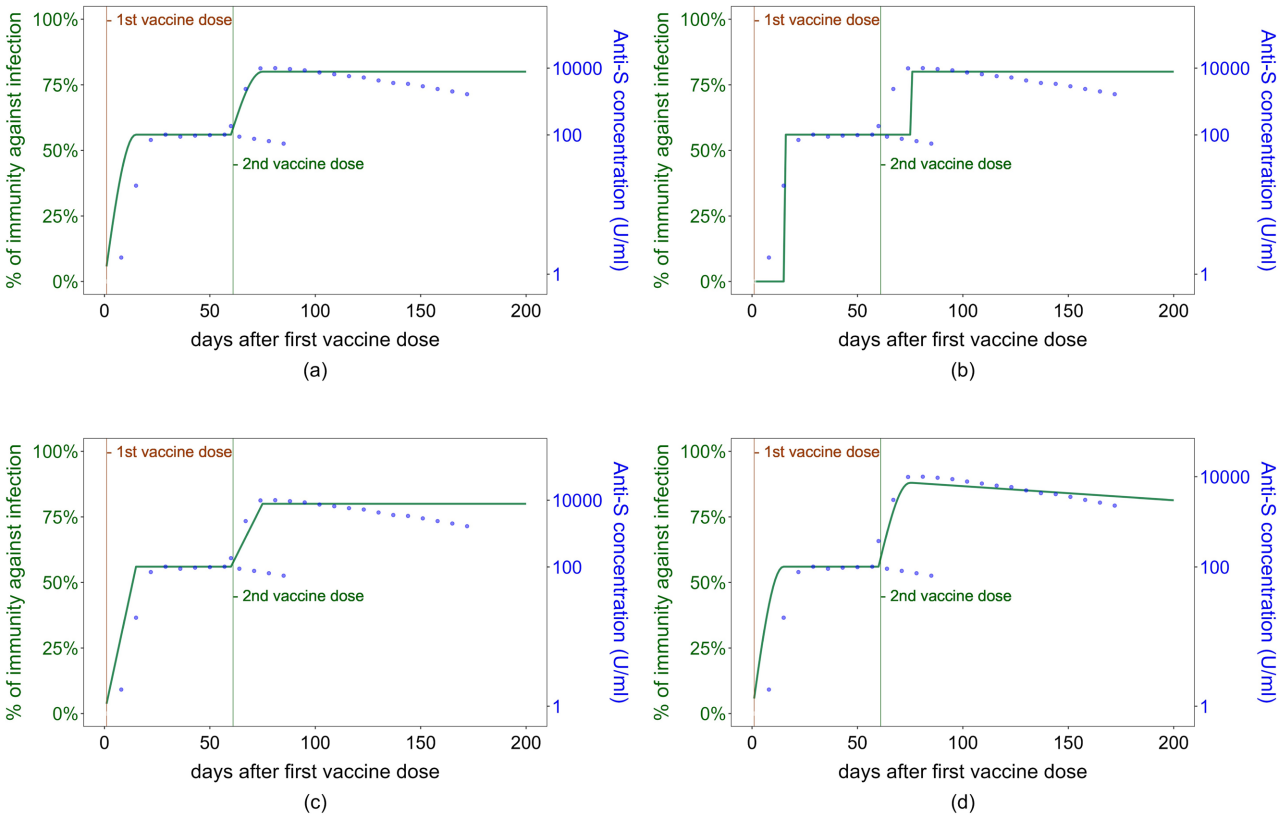

Figure 4. Examples of probability distribution curves (*V2TImm*) that describe the evolution of vaccine-induced immunity when the two first vaccine doses are applied on time: (a) smooth increase of the immunity defined by truncated gaussians; (b) using a step function, assuming an activation of the immunity some days after vaccination; (c) successive increase of the degree of immunity after vaccination; and (d) smooth increase of immunity after vaccination following the trend of a truncated gaussian, the maximum level of immunity starts to decay immediately after the second dose to get a best fit to the concentration of antibodies. For comparison, an empirical example with the evolution of the antibody concentration levels after vaccination is shown (blue dots, representing data extracted from **Figure 1** in reference [10] for the evolution of antibodies after vaccination with BNT162b2).

highest level of protection is reached. In this situation, according to some studies, the immunity will be kept as long as the antibody concentration remains above a defined protective threshold (see details, for example, in reference [11]). For this reason, the most adequate immunity curve will not be automatically the one that best fits the values of the concentration of antibodies.

More complex is the description of the vaccine-induced immunity decay after a given period of time. Many studies have shown that the level of immunity can start to decay months after the vaccination, although the extent of this decay is less clear. Besides, the starting time of such decay depends on the number and type of vaccine doses, which increases the complexity of the description. Thus, several factors define the parameters of the immunity probability distribution curves related to the vaccination: time to reach the highest immunity after each vaccine dose, highest immunity against infection after each vaccine dose, period of highest immunity after each vaccine dose, period of immunity decay from highest to lowest immunity, and lowest immunity against infection after im-

munity decay. We have evaluated here different probability distribution curves describing the evolution of vaccine-induced immunity after several doses, according to the following requirements: consistency with information available from other studies, good fit of empirical data, and convenience for a flexible implementation.

Figure 5 shows some examples of the immunity curves used in the current version of the model for the individuals that have received 2 or 3 doses (*V2TImm*, *V3TImm*) when using specific values for the different parameters in different scenarios. Delaying (or suppressing) the application of the booster dose shows a relevant impact in the decay of the immunity. Figure 5 also includes the probability distribution curve describing the evolution of immunity in infected people (*ITImm*). The periods of increase and decrease of immunity are defined as truncated gaussians, and the periods of maximum and minimum immunity are just constant values.

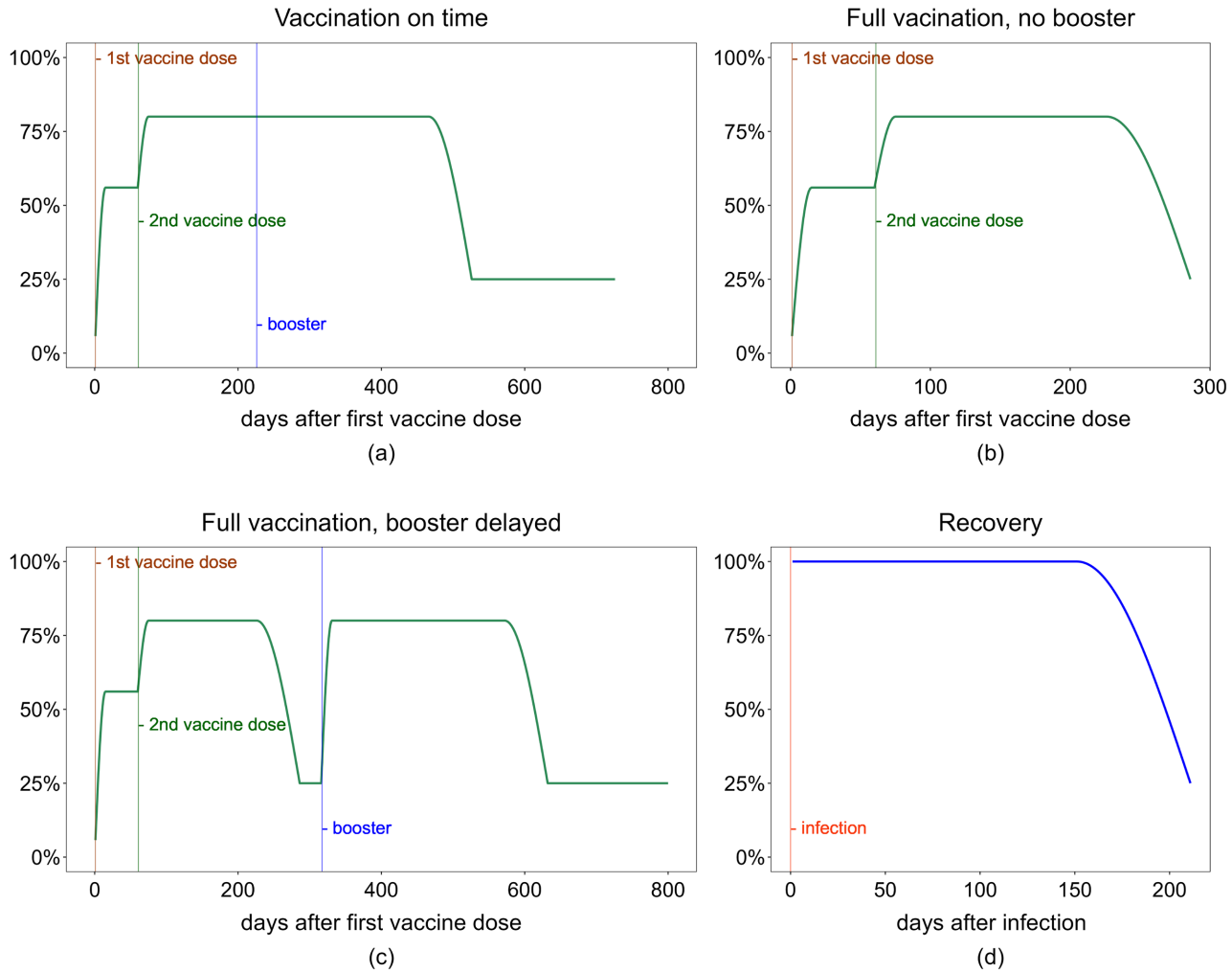

Figure 5. Probability distribution curves describing the evolution of vaccine-induced immunity in different possible scenarios: (a) when all vaccine doses are applied on time; (b) when only two vaccine doses (no booster) are applied; (c) when the booster is delayed; and (d) curve for immunity decay in infected people (*ITImm*).

4. COVID-19 Transmission Model Including Vaccine-Induced Immunity: Application to Reported Data

4.1. Defining the Optimal Parameters for the Immunity Probability Curves

The model has been applied to available data from a total of 30 European countries using different combinations of the parameters that define the vaccination immunity curves. Initial values for these parameters have been obtained from empirical data documented in different sources [12] and from available information about the effectiveness of the vaccines obtained from a systematic review of 65 studies from 19 different countries [13], which is considered a good starting point for the definition of the initial values used to fit and optimize the model. From these initial values, the optimal combination of parameters has been found by adjusting some of them to get the best fit results of the model for different countries. The values of the parameters that provide the best fit for the majority of the European countries are shown in **Table 1**.

4.2. A Case Study: Application of the Model to COVID-19 Transmission Dynamics in Spain

The above-described model, including the effect of vaccine-induced immunity, has been applied to the available data of COVID-19 pandemic in Spain in the period from January 1st, 2020 to October 31st, 2022. The vaccination immunity model has been adjusted using the best values for the parameters from **Table 1** (*best-fit scenario*), as well as using different values in three of the parameters to describe another potential situation with a reduced impact of vaccination impact in the disease transmission reduction (*pessimistic scenario*). **Table 2** shows the parameter values used here for these two scenarios.

Figure 6 shows the predicted cumulative number of deaths (median with 95% credible interval) for the two above-described scenarios in comparison with the real data. Remarkably, using the values from **Table 1** (best-fit scenario), the predictions from the model replicate well the evolution of the number of reported deaths along the entire period of time since the beginning of the pandemic (from 01/01/2020 to 31/10/2022). In the pessimistic scenario, the predictions deviate from the real data in the first months of 2021, when the massive vaccination of the population started. This analysis indicates that vaccination showed a clear positive impact on reducing the spread of the disease and the parameter values shown in **Table 1** suggest a consistent description of the evolution of acquired immunity after vaccination.

Figure 7 shows the evolution of the values for daily infection fatality rate (IFR_j) in Spain, considering the percentage of vaccinated population and the proportion of infections for the different virus variants on a given day. This value gradually decreases since beginning of 2021, when massive vaccination of population starts, and dramatically drops towards the end of 2021, when the omicron variant becomes dominant.

Table 1. Optimal values for the parameters of the vaccine-induced immunity probability distribution curves within the COVID-19 transmission model.

Parameter	Value
Time to reach the highest immunity after each vaccine dose	15 days
Highest immunity against infection after first dose	56%
Highest immunity against infection after second dose	80%
Highest immunity against infection after booster	80%
Period of highest immunity after second dose	150 days
Period of highest immunity after booster	240 days
Period of immunity decay from highest to lowest immunity	60 days
Lowest immunity against infection after immunity decay	25%
Reduction factor of the previous immunity values for infections with the variant omicron	0.5

Table 2. Parameter values of the vaccination immunity curves used in two potential scenarios regarding the impact of vaccination.

Parameter	Best-fit	Pessimistic
Highest immunity against infection after second dose	80%	70%
Highest immunity against infection after booster	80%	70%
Period of highest immunity after second dose	150 days	120 days

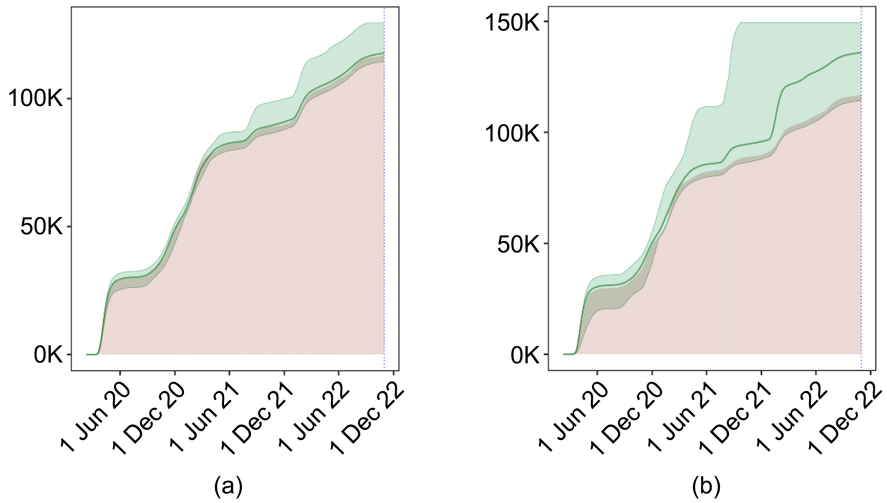

Figure 6. Cumulated number of deaths in Spain predicted by our COVID-19 transmission model (green line is the median and green shadow indicates the 95% confidence interval of the predictions) using different vaccination parameters: (a) best-fit scenario with parameter values from Table 1, and (b) pessimistic scenario, as a result of assuming a reduced effect of the vaccination. Reported cumulated number of deaths is shown in brown bars.

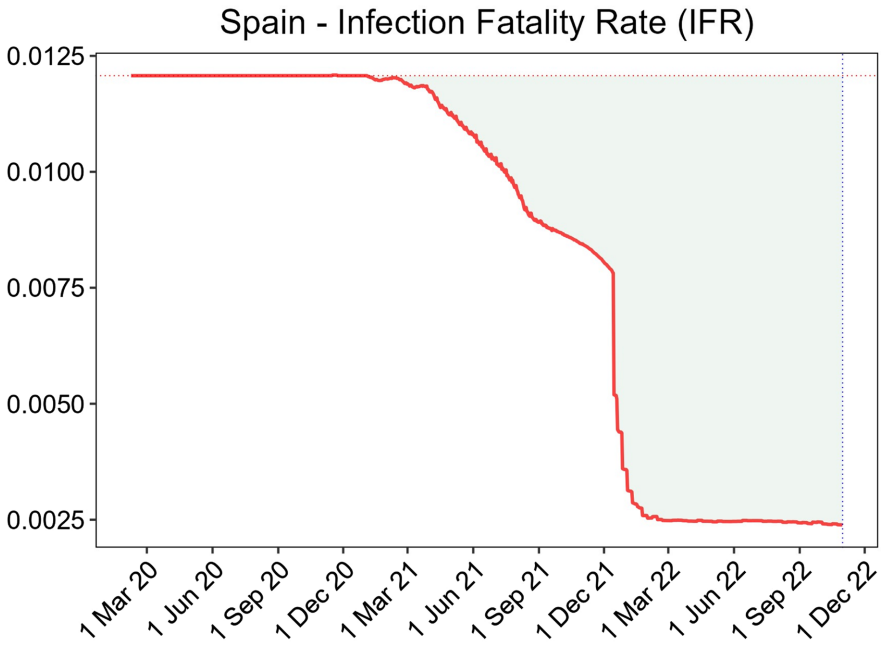

Figure 7. Evolution of daily infection fatality rate (IFR_j) estimated for Spain data, considering the percentage of vaccinated population and the proportion of infections for the different virus variants on every day.

5. Discussion and Conclusions

We have explored here different probability models to include the impact of vaccination in a previously described Bayesian COVID-19 transmission model [4]. The use of probability distribution curves with parameters from empirical data to describe the evolution of vaccine-induced immunity provides estimations that optimally fit the reported data. However, while working well in general terms, our approach has some limitations. For instance, there is evidence that there are differences in the effect of the vaccination between seropositive (*i.e.*, recovered from a COVID-19 infection) and seronegative individuals [8], and that this effect is also different depending on the age [14]. These factors are not considered in our model, where we assume common vaccination parameters for the whole population. This is consistent with other simplifications of the model, in which, for example, age weighted values for the initial value of the infection fatality ratio (*IFR*) are used.

On the other side, while the initial value of the reproduction number (R_0) and the factors that quantify the impact of the non-pharmacological interventions are optimised during the fitting process, the parameters that define the vaccination immunity curves are predefined as constant values in each fit run, according to empirical data as described in previous sections. Future versions of the model will include these parameters to be optimized during the fitting process. The challenge is the limited availability of epidemiological data for the majority of countries, which is increasingly scarce since the COVID-19 pandemic is officially over.

In summary, Bayesian inference models are very efficient to model transmission dynamics of infectious agents in complex scenarios, like COVID-19. These models can be used to estimate the impact of non-pharmacological measures or other events that can affect the virus transmission. The versatility of these models makes it feasible to include different scenarios like vaccination or new variants. We have used a realistic distribution probability curve to describe the acquisition of immunity after vaccination, which provides very good fitting of the model to the available epidemiological data. Now that the public health emergency due to the COVID-19 pandemic is officially over and COVID-19 data are not published regularly, the challenge is to estimate the evolution of the vaccine-induced immunity in the long term. The tool presented here can be easily adapted to estimate future potential scenarios and can be used for the planning of long-term vaccination strategies, e.g. considering the need of additional boosters periodically due to the decay of the vaccine-induced immunity, or to the appearance of new virus variants with specific transmission dynamics.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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