

Robust and Intuitive Model for COVID-19 Epidemic in Slovenia

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The main goal of epidemic modelling is to support the epidemic management through forecasts and analyses of past developments. With this in mind a robust and intuitive SEIR (Susceptible, Exposed, Infectious, Recovered) type model has been developed, applied and validated during the multiple waves of the COVID-19 epidemics in Slovenia since March 2020. The model parameters were based on the general characteristics of the COVID-19 disease reported globally for the entire planet and refined with the aggregate data available mostly on a daily basis in Slovenia, as for example the number of confirmed cases, hospitalized patients, hospitalized patients in intensive care units and deceased. The Slovenian aggregate data was also used to estimate the degree of immunisation due to past infections and vaccination, which reduces the number of susceptible persons for the disease.

Examples of the model application are presented to illustrate its robustness and intuitiveness in both the forecasts and analyses of past developments. The analyses of past developments provided specific estimates of modelling parameters for Slovenia and quantified the effects of pharmaceutical and non-pharmaceutical interventions and various events on the development of the epidemics as measured through the reproduction number R . This empirically obtained information was then applied in the forecasts. Accurate forecasts are a great support for decision makers and for hospitals to plan appropriate actions in advance. The inherent uncertainties in the model and data were quantified through intuitive sensitivity analyses represented as different scenarios. The observed accuracy of the forecasts was impressively good also in demanding conditions, when various complex processes influencing the spread of the disease were going on in parallel. This demonstrates the robustness and relevance of the proposed model.

Keywords: epidemic, COVID-19, modelling, SEIR, reproduction number, public health interventions

Highlights

- Robust and intuitive susceptible, exposed, infectious, recovered (SEIR) type model has been developed.
- Model has been applied for analysis of COVID-19 epidemic in Slovenia.
- Some examples of model application are presented.
- Accuracy of forecasts is impressively good.

0 INTRODUCTION

The COVID-19 epidemic might have caught many countries and governments by surprise since its beginnings in November 2019 in Hubei province, China. Till today a huge amount of data and information have appeared online [1] to [4] and in the literature [5] to [9]. In addition, several models aiming at forecasting the spread have been developed [10] to [14].

The main goal of epidemic modelling is to support the epidemic management in real time and with the available data being far from optimal. It is crucial to get a reliable insight in the trends as early as possible to enable timely and appropriate actions by decisionmakers and for the hospitals to prepare in time.

Traditional approach for the modelling of epidemics including the COVID-19 includes compartment models. In particular, the susceptible, exposed, infectious, recovered (SEIR) model appears to be widely used [15] to [17]. In this approach the observed population (e.g., in Slovenia) is divided into four compartments, the susceptible, the exposed, the

infectious and the recovered. The transition between compartments is modelled with transition rates, which are proportional to the membership of the compartments. The SEIR model may be extended with additional compartments, like the hospitalized, the hospitalized in intensive care units (ICU) and the deceased. The time development of the membership in the compartments is usually governed by a set of ordinary differential equations, which need to be solved numerically.

Our interest was mainly in the aggregate results such as the number of infected, the number of hospitalized, the number of deceased, the reproduction number R characterizing the dynamics of the epidemic [18], and similar. Therefore, we decided to address the epidemic in Slovenia at the aggregate level and provide aggregate forecasts. Focus was on the time dependence of the aggregate results, but implicitly considering also local phenomena, including the age structure and the occasional localisation of infections. For this purpose, the SEIR type modelling approach is in principle well suited.

To perform well in realistic conditions, it is important that the model is robust and intuitive. In

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this way the uncertainties in data, like changes in the testing regimes, impact of limited testing capacity, changes in the hospitalization criteria, changes in data reporting, missing data etc. can be most appropriately considered through quantitative and qualitative approaches, as for example the modeler's expert judgment and holistic view.

With this in mind we developed an extended SEIR type model, formulated in integral form. In this framework the modelling becomes very intuitive and simple. The results, which are not distorted by numerical diffusion, become intuitively predictable and consequently strengthen the accuracy of the forecasts.

The developed robust and intuitive epidemic model is presented in the following Section 1, and then in Section 2 some examples of the model application are provided for illustration purpose.

1 MODELING

1.1 Epidemic Dynamics

The spread of a contagious disease in its early stages is an exponential process characterized by

$$N(t) = N_0 2^{t/t_2} = N_0 R^{t/\tau} \tag{1}$$

$N(t)$ is the number of exposed persons at time t , N_0 the number of exposed persons at $t=0$, t_2 the time in which the number of exposed doubles, R the reproduction number and τ the characteristic infection time. The reproduction number R is an average number of persons infected by a single person during his/her infectiousness period [18].

Epidemics will only develop if $R > 1$. When developing, the R will change with time. Gradual changes are usually consequence of immunisation, while steep changes may be related to the non-pharmaceutical interventions enforced in the observed population. If $R > 1$ we have an exponential growth, if $R = 1$ we have stagnation and if $R < 1$ we have an exponential decay (Fig. 1).

The exponential growth of the number of exposed persons will be, usually with some delay, followed by exponential growth of other aggregate parameters, e.g., number of confirmed cases, the number of hospitalized patients, the number of hospitalized patients in ICU and the number of deceased.

Early stages of the exponential growth are not easily recognized by our intuition, which appears to be better adapted to linear or linearized phenomena. Fig. 2 shows an exponential growth with doubling

time 7 days, where the aggregate parameters, e.g., the number of confirmed cases, will double every week. During the first month one could barely see anything happening, then the values start to rise and all of a sudden, the curve turns steeply upwards. This illustrates why it is so important to detect the exponential growth at the earliest possible stage.

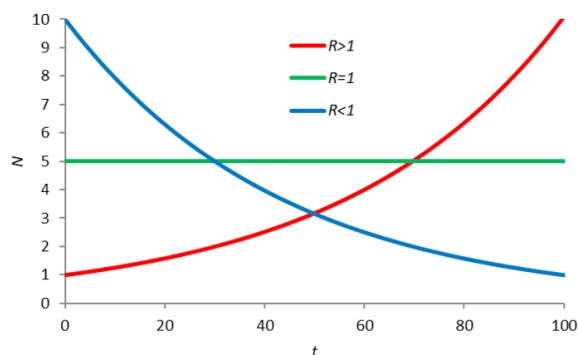


Fig. 1. Dynamics of epidemic for various reproduction numbers R

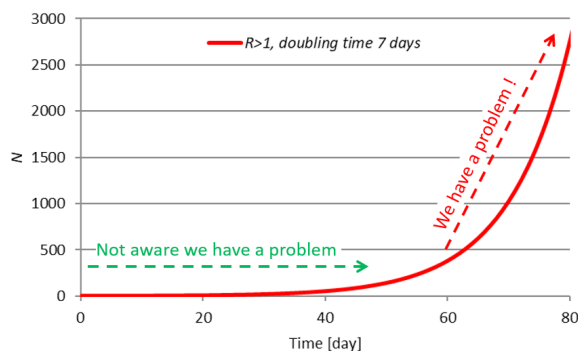


Fig. 2. Exponential growth for reproduction number $R > 1$

Fig. 3 shows the same curve as in Fig. 2 in logarithmic scale. We see that the red exponential growth curve is a rising straight line already from the beginning, and thus we know already from the very beginning where this curve will lead us if we take no action. In logarithmic scale an epidemic runs along more or less straight lines. If $R > 1$ the epidemic will grow. This growth will not stop by itself as long as there are enough susceptible persons for the disease, and at that time the capacity of the hospitals may have been already exceeded by more than an order of magnitude. Therefore, the growth of an epidemic must be stopped in time with interventions, reducing the spread of the disease, to prevent the collapse of the health care system. And here the model forecasts can be of great help.

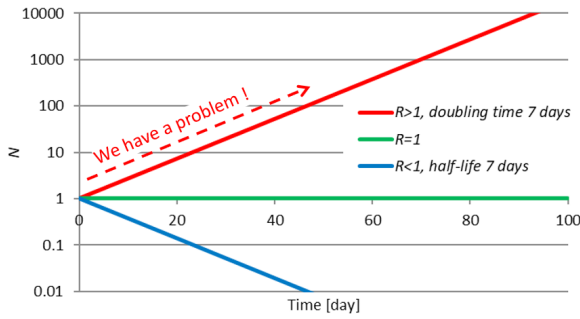


Fig. 3. Dynamics of epidemic for various reproduction numbers R in logarithmic scale

1.2 Model Setup

In this subsection the basics of the epidemic model are presented. It was strived to develop a knowledge-driven model as far as possible, with only the model parameters data-driven [19] and [20]. Therefore, the model was based on the exponential function, which is well suited for describing the spreading of an infectious disease. Eq. (1) can be written in difference form as

$$\Delta N(t) = N(t) \left(2^{\Delta t/t_2} - 1 \right), \quad (2)$$

where $\Delta N(t)$ is the change of quantity $N(t)$ during the time interval Δt . Based on the form of Eq. (2) we derived the fundamental equation of our epidemiological model as

$$\Delta E(t) = I(t) \left(2^{\Delta t/t_2} - 1 \right), \quad (3)$$

where $\Delta E(t)$ is the change of the cumulative number of exposed persons $E(t)$ in time interval Δt , $I(t)$ the number of infectious persons and t_2' a modelling parameter. $I(t)$ is calculated by

$$E(t + \Delta t) = E(t) + \Delta E(t), \quad (4)$$

$$I(t) = E(t - \tau_{inc}) - E(t - \tau_{inc} - \tau_{inf}), \quad (5)$$

where τ_{inc} is the incubation time and τ_{inf} the infectious period, as depicted in Fig. 4.



Fig. 4. Incubation time and infectious period after infection

In Fig. 5 the course of the disease is presented. Let us assume that ΔE persons are exposed at time t . After a time τ_T a fraction α_T of them are tested positive ΔT . After a time τ_H a fraction α_H of them are hospitalized ΔH . After a time τ_{ICU} a fraction α_{ICU} of them are hospitalized in intensive care units ΔICU . And after

a time τ_D a fraction α_D of them decrease ΔD . At the current stage of the modelling, the average values of all time delays τ and fractions α were considered. They may nevertheless change with time due to for example the inherent variability of different strains of SARS-CoV-2 virus.

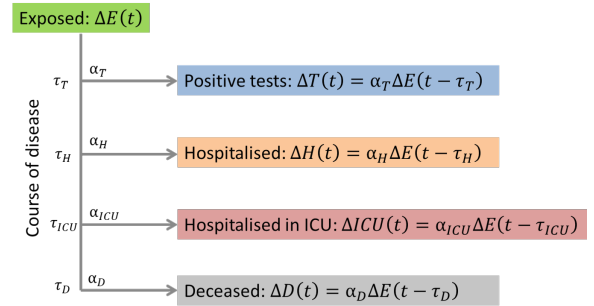


Fig. 5. Course of disease

From the number of exposed persons ΔE in a time interval Δt the time shifted number of cases ΔT , hospitalized persons ΔH , hospitalized persons in intensive care units ΔICU and deceased persons ΔD are calculated based on the equations presented in Fig. 5. The empirical estimation of parameters α and τ is described in section 1.6.

For more accurate modelling the equations in Fig. 5 may be written and solved separately for each age group i

$$\Delta T_i(t) = \alpha_T^i \Delta E(t - \tau_T), \quad (6)$$

$$\Delta H_i(t) = \alpha_H^i \Delta E(t - \tau_H), \quad (7)$$

$$\Delta ICU_i(t) = \alpha_{ICU}^i \Delta E(t - \tau_{ICU}), \quad (8)$$

$$\Delta D_i(t) = \alpha_D^i \Delta E(t - \tau_D). \quad (9)$$

The number of currently hospitalized persons H_{cur} is calculated from the number of cumulative hospitalized persons H as

$$H(t + \Delta t) = H(t) + \Delta H(t), \quad (10)$$

$$H_{cur}(t) = H(t) - H(t - \tau_{Hdur}), \quad (11)$$

where τ_{Hdur} is the average duration of hospitalization. Similarly, the number of currently hospitalized persons in intensive care units ICU_{cur} is calculated as

$$ICU(t + \Delta t) = ICU(t) + \Delta ICU(t), \quad (12)$$

$$ICU_{cur}(t) = ICU(t) - ICU(t - \tau_{Idur}), \quad (13)$$

where τ_{Idur} is the average duration of hospitalization in ICU.

1.3 Reproduction Number

Eq. (3) can be expressed as a function of the time dependent reproduction number $R(t)$ as

$$\Delta E(t) = I(t)R(t)\frac{\Delta t}{\tau_{inf}}, \quad R(t) = \frac{\Delta E(t)\tau_{inf}}{I(t)\Delta t}, \quad (14)$$

assuming that the infection rate during the infectious period τ_{inf} is constant. The incubation time and the infectious period in this simplified approach were adjusted to result in the correct serial interval, i.e. the time between successive cases in a chain of transmission [21]. Considering Eq. (5) the reproduction number can be calculated from

$$R(t) = \frac{\Delta E(t)}{E(t - \tau_{inc}) - E(t - \tau_{inc} - \tau_{inf})} \frac{\tau_{inf}}{\Delta t}. \quad (15)$$

As the number of confirmed cases ΔT , hospitalized persons ΔH , hospitalized persons in intensive care units ΔICU and deceased persons ΔD is a linear function of the number of exposed persons ΔE (see equations in Fig. 5), the reproduction number can be calculated from these quantities by substituting them in Eq. (15). Thus, based on the number of daily ΔT and cumulative T cases one obtains the following expression

$$R(t - \tau_T) = \frac{\Delta T(t)}{T(t - \tau_{inc}) - T(t - \tau_{inc} - \tau_{inf})} \frac{\tau_{inf}}{\Delta t}, \quad (16)$$

where the reproduction number is being estimated for the time τ_T in the past. The current estimate of R from the number of confirmed cases is therefore valid for the time in the past, characterized by an (average) time needed from infection to a confirmation by test. Similarly, the reproduction numbers can be estimated for the past also from the data of hospitalizations, hospitalizations in ICU and deceased, with a time delay from infection till the data, replacing in Eq. (16) T with H , ICU or D , and τ_T with τ_H , τ_{ICU} or τ_D .

Due to the predominantly weekly rhythm of the society, the data shows strong daily variations with a weekly period. Weekly averages of the aggregate parameters in the equations could therefore make the results more stable and reliable.

1.4 Immunity

Immunity may be obtained by infection or vaccination. The number of exposed people is reduced by the fraction of people which obtained immunity due to past infections according to

$$\Delta E_{inf}(t) = \left(1 - \frac{e_E E(t)}{N_{pop}}\right) \Delta E(t), \quad (17)$$

where e_E is the efficiency of immunization due to past infections and N_{pop} is the number of all people in the considered population (e.g., 2.1 million for Slovenia). Similarly, the number of exposed people is reduced by the fraction of people which obtained immunity due to vaccination as

$$\Delta E_{vac}(t) = \left(1 - \frac{e_V V(t)}{N_{pop}}\right) \Delta E(t), \quad (18)$$

where e_V is the efficiency of immunization due to vaccination and V is the number of vaccinated people. The efficiency of immunisation due to past infections and vaccination is obtained from global data available in the literature. The population with past infection and the vaccinated population partly overlap. This is considered with the following general equation

$$\Delta E_{im}(t) = \left(1 - \frac{IM(t)}{N_{pop}}\right) \Delta E(t), \quad (19)$$

where IM is the equivalent number of totally immunized people, which may be calculated from E and V considering their efficiencies of immunisation and overlapping.

Vaccination does not reduce only the number of susceptible people but may also change the age structure of the exposed. The vaccination was namely prioritizing the more vulnerable elders. The fractions of exposed, which need hospitalization, intensive care or die, depend strongly on the age structure of the infected, which changes due to vaccination. The influence of vaccination therefore depends on the fraction of vaccinated v_i in each age group i and the relative contribution of this age group, which may be described with weights w_i . Thus, the time dependent fraction of exposed people who need hospitalization considering the vaccination dynamics may be calculated as

$$\alpha_{Hvac}(t) = \alpha_H \sum_{i=1}^n w_H^i (1 - v_i(t)), \quad (20)$$

where w_H^i are the weights for hospitalisation, which may be obtained from Eq. (7) as

$$w_H^i = \alpha_H^i / \alpha_H. \quad (21)$$

Similarly, the influence of vaccination on the corresponding fractions for hospitalizations in ICU and deaths can be calculated by replacing in Eq. (20) and Eq. (21) α_H with α_{ICU} or α_D , α_H^i with α_{ICU}^i or α_D^i , and w_H^i with w_{ICU}^i or w_D^i .

1.5 Virus Variants

The spreading of various virus variants is considered by modelling each variant separately and then summing the results. The variants share the same susceptible population or part of it, depending on the cross-immunity of the variants. The characteristics of the variants are obtained from global data available in the literature. For practical reasons, in the model the characteristics of the variants are expressed by the characteristics of the chosen basic variant multiplied by a constant proportionality factor to enable a straightforward fitting of the model parameters to data. Consequently, only the characteristics of the basic variant are independent variables and so the same fitting procedure can be applied as when treating only a single variant. Typically, only two variants are of interest at the same time. Thus, the equations are presented for the parallel treatment of two variants, but the approach could be easily extended for the general parallel treatment of more variants.

If variant v_1 is chosen as the basic variant, then the characteristics of the other variant v_2 are expressed by the characteristics of variant v_1 as follows. Different contagiousness of both variants is considered by linking the reproduction numbers R_{v_2} and R_{v_1} of both variants as

$$R_{v_2} = r_{v_2} R_{v_1}, \tag{22}$$

where r_{v_2} is a constant proportionality factor and R_{v_1} is the independent variable. Different severities of the disease for both variants are considered by linking the fractions of the exposed for hospitalization α_H , hospitalisation in ICU α_{ICU} and death α_D for both variants as

$$\alpha_H^{v_2} = A_H^{v_2} \alpha_H^{v_1}, \tag{23}$$

$$\alpha_{ICU}^{v_2} = A_{ICU}^{v_2} \alpha_{ICU}^{v_1}, \tag{24}$$

$$\alpha_D^{v_2} = A_D^{v_2} \alpha_D^{v_1}, \tag{25}$$

where $A_H^{v_2}$, $A_{ICU}^{v_2}$ and $A_D^{v_2}$ are the corresponding constant proportionality factors and $\alpha_H^{v_1}$, $\alpha_{ICU}^{v_1}$ and $\alpha_D^{v_1}$ are the independent variables. Similarly, also different time delays from infection to hospitalisation, hospitalisation in ICU and death may be considered for both variants.

The aggregate results are then obtained by summing the results over all considered variants v_i , presented here for the exposed, as

$$\Delta E(t) = \sum_{v_i} \Delta E_{v_i}(t). \tag{26}$$

Similarly, the aggregate results for the other considered quantities are obtained by replacing in Eq. (26) ΔE with ΔT , ΔH , ΔICU or ΔD .

The time development of fraction f_{v_i} of variant v_i is obtained from

$$f_{v_i}(t) = \Delta E_{v_i}(t) / \Delta E(t). \tag{27}$$

1.6 Model Parameters

If the data is presented in logarithmic scale, we realise that the data curves for the daily positive tests, hospitalized, hospitalized in ICU and the deceased are in the simplified case just shifted curves of the infected (Fig. 6). The slope of all these curves is the same and depends on the reproduction number R . From the slope of these curves we can estimate the reproduction number, as presented in Section 1.3.

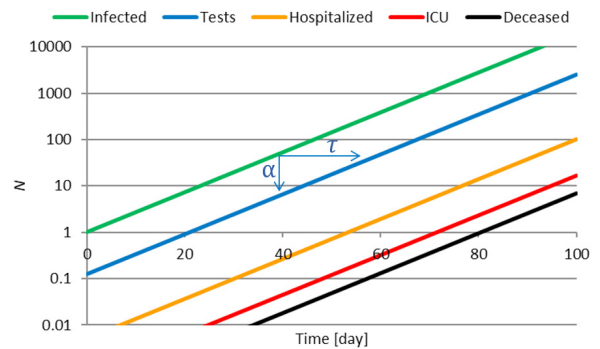


Fig. 6. Presentation of data in logarithmic scale; example with straight lines

The curves are shifted vertically and horizontally. They are shifted vertically due to the fractions α in the equations presented in Fig. 5, i.e. the fraction of the infected α_T that are tested positive, the fraction of the infected α_H that are hospitalized, the fraction of the infected α_{ICU} that are hospitalized in ICU, and the fraction of the infected α_D that die. Further, they are shifted horizontally due to the time delays τ , i.e. the time τ_T from infection to a positive test, the time τ_H from infection to hospitalization, the time τ_{ICU} from infection to hospitalization in ICU and the time τ_D from infection to death.

It may be observed in Fig. 6 that the fractions α and time delays τ cannot be determined uniquely, because e.g. from the green curve of infected we can come to the blue curve of positive tests with different combinations of vertical and horizontal shifts. These shifts could be determined uniquely only if there

would be a change in the slope of the curves defining a reference point.

Fig. 7 presents an example, where the curves are kinked due to the sudden introduction of non-pharmaceutical interventions, which reduce the reproduction number R to 1 and change the slope of the curves from an exponential growth to horizontal stagnation. In this case both, the fractions α and time delays τ can be determined uniquely, as there is a reference point, i.e. the kink in the curves, which occurs when the non-pharmaceutical interventions are implemented. The fractions α can be determined from the vertical shifts of the kinks in the curves and the time delays τ can be determined from the horizontal shifts.

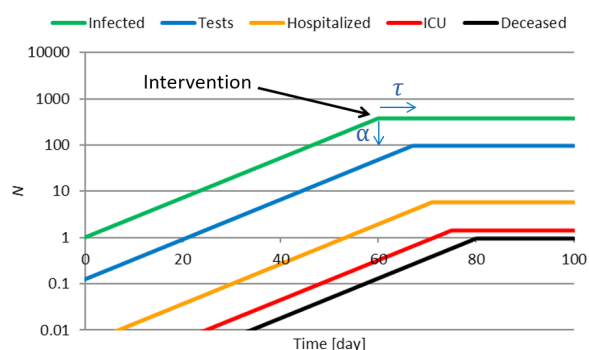


Fig. 7. Presentation of data in logarithmic scale; example with kinked lines due to non-pharmaceutical intervention

The easiest way to estimate the fractions α is when the epidemic stagnates, as we are not limited only to the kinks in the curves, but we can determine it in the entire stagnation area (Fig. 7). The time delays τ are most easily estimated when very stringent non-pharmaceutical interventions are implemented maximizing the change in the slope of the curves.

With this approach the fractions α can be established also for age groups, as addressed in Section 1.2. This information is also needed to consider the influence of age group specific vaccination, as presented in Section 1.4.

Once we estimate the fractions α for age groups one can use Eq. (6) to Eq. (9) for short-term estimations of hospitalizations, hospitalizations in ICU and deaths based on the known number of confirmed cases in age groups in the last period as

$$\Delta H(t) = \sum_{i=1}^n \frac{\alpha_H^i}{\alpha_T^i} \Delta T(t - (\tau_H - \tau_T)), \quad (28)$$

$$\Delta ICU(t) = \sum_{i=1}^n \frac{\alpha_{ICU}^i}{\alpha_T^i} \Delta T(t - (\tau_{ICU} - \tau_T)), \quad (29)$$

$$\Delta D(t) = \sum_{i=1}^n \frac{\alpha_D^i}{\alpha_T^i} \Delta T(t - (\tau_D - \tau_T)). \quad (30)$$

The model parameters were estimated based on the following daily and cumulative available aggregate data for Slovenia [4], [22] to [26]:

- Number of positive tests, share of positive tests, number of PCR and rapid antigen tests, age structure of persons with confirmed infection.
- Daily admissions and discharges from hospitals and ICU, current and cumulative number of hospitalized patients and hospitalized patients in ICU, age structure of hospitalized patients and hospitalized patients in ICU.
- Number of deceased, age structure of deceased.
- Share of SARS-CoV-2 virus variants.
- Concentration of SARS-CoV-2 virus in sewage.

The ratio of confirmed cases and all cases α_T was estimated based on seroprevalence data of SARS-CoV-2 virus for Slovenia [27] and expert judgement. The fractions α and time delays τ were estimated regularly at changes of the trend of the epidemic, considering also the age structure. The duration of hospitalizations and hospitalizations in ICU were estimated based on the known data of daily admissions and the current number of hospitalized patients and hospitalized patients in ICU. The reproduction number was estimated based on the daily number of positive tests, admissions in hospitals and ICU, and deceased. When estimating the model parameters, we tried to consider all available data in a holistic way, considering also soft data, like the social climate affecting the consistent implementation of non-pharmaceutical interventions.

2 RESULTS

The developed model was applied for the analysis of the COVID-19 epidemic situation in Slovenia and to forecast the epidemic development [28]. In this section some examples of the model application are provided for illustration purpose.

The forecasts were performed in the following way. If no major change in people's behaviour in near future influencing the disease transmission was expected, it was assumed that the model parameters will not change. In this case the disease transmission is influenced only by changes in the immunity of the population due to vaccination and past infections, as described in Section 1.4.

Planned implementation or release of non-pharmaceutical interventions and important changes

in people's behaviour, such as the beginning or end of holidays, are taken into account by changing the reproduction number R based on past experience in Slovenia or other countries, or expert judgement. Similarly, also the influence of weather, where e.g. in colder conditions people stay indoors enhancing disease transmission, was considered. We tried to consider as far as possible also soft data, i.e. information that is not given in form of numbers, like the social climate affecting the consistent implementation of non-pharmaceutical interventions, or that the virus entered a retirement home generating an outbreak within a specific age structure.

The initial part of the forecast is checked with the short-term prediction based on the known number of confirmed cases in age groups in the last period, as described in Section 1.6.

2.1 Scenarios

Fig. 8 shows a typical example of an epidemic forecast with different scenarios, when approaching the peak of the second wave in Slovenia end of year 2020. On October 26, 2020 stringent non-pharmaceutical

interventions were implemented [4]. Before that some non-pharmaceutical interventions were already implemented and the reproduction number was estimated to be $R = 1.5$.

In the forecast three scenarios are presented for the number of hospitalized patients, hospitalized patients in ICU and deceased. The dotted curves present the scenario without additional non-pharmaceutical interventions. In this case the epidemic continues to growth with the reproduction number R , that gradually decreases due to the build up of immunity in the population caused by past infections. When the reproduction number is reduced to $R = 1$ the peak is reached and after that the curves start to decrease, except for the deceased, where the cumulative number is shown.

The dashed line shows the scenario with successful non-pharmaceutical interventions, reducing the reproduction number to $R = 0.9$. Because $R < 1$, the epidemic starts to decrease and consequently with the time delays τ also the number of hospitalized patients and hospitalized patients in ICU decreases.

The full line presents the forecast, where it is estimated that the non-pharmaceutical interventions

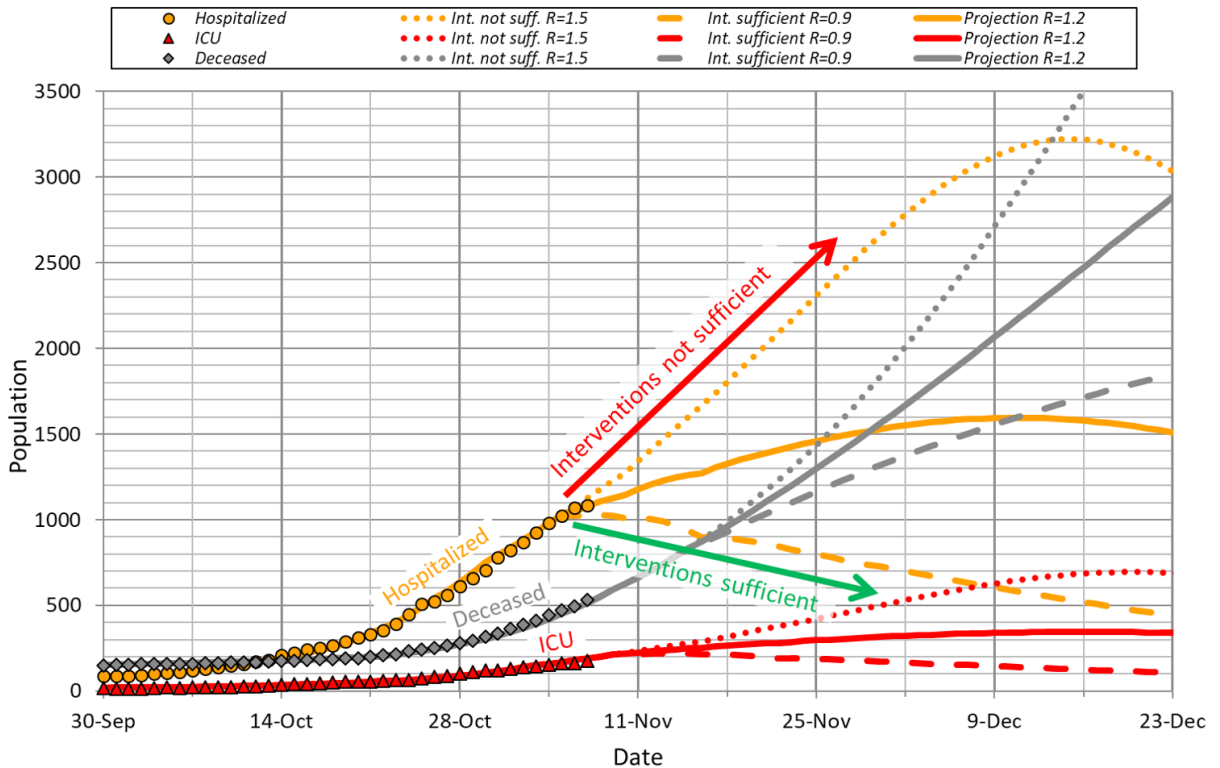


Fig. 8. Forecast with different scenarios for the second wave in Slovenia end of year 2020; the following scenarios are presented: without any additional non-pharmaceutical interventions (dotted line), with successful non-pharmaceutical interventions (dashed line) and forecast (full line); the curves show the number of hospitalized patients (orange curves), hospitalized in ICU (red curves) and deceased (gray curves)

reduce the reproduction number to $R = 1.2$. In this case the epidemic still rises, but the peak is significantly lower than without any additional non-pharmaceutical interventions.

The purpose of presenting such scenarios is to get an impression about the uncertainties of the forecasts, the characteristic times, the possible maximal values of the presented results, the possible course of events etc. The calculated curves serve primarily for the qualitative and quantitative orientation of the possible development of the epidemic.

2.2 Analysis

As an example of an epidemic analysis the second wave in Slovenia end of year 2020 and beginning of year 2021 is analyzed in Fig. 9. The orange dots and curves show the number of hospitalized patients and the blue curve shows the estimated reproduction number R .

Already at the end of August 2020 the reproduction number R was bigger than one due to the end of holidays. It then increased sharply due to the start of the school year and then declined due awareness rising and some non-pharmaceutical interventions, but remained above 1, meaning that

the epidemic grew during all that time. As a result, the number of confirmed cases became so large, that the capacity for epidemiological contact tracing was gradually exceeded, which significantly increased R . In addition, during this period the share of the more contagious variant B.1.258 significantly increased, further contributing to the rise of R . As a consequence, the epidemic started to grow extremely fast with a doubling time of only about one week. With a series of increasingly stringent non-pharmaceutical interventions Slovenia finally managed to stop the growth, but the numbers remained high. The epidemic then began to slowly decline due increased immunity of the population caused by past infections. During the Christmas and New Year holidays, the epidemic started again to rise due to more contacts among people. After that it started to decline faster and faster due to mass testing with rapid antigen tests, past infections and vaccination. First the vulnerable population was vaccinated, which significantly reduced the number of hospitalizations. The decline of the epidemic was then slowed down by some relaxation of non-pharmaceutical interventions. Then the more contagious alpha variant occurred and the epidemic started again to rise. The rise was so fast that in April 2021 a short lockdown had to be implemented,

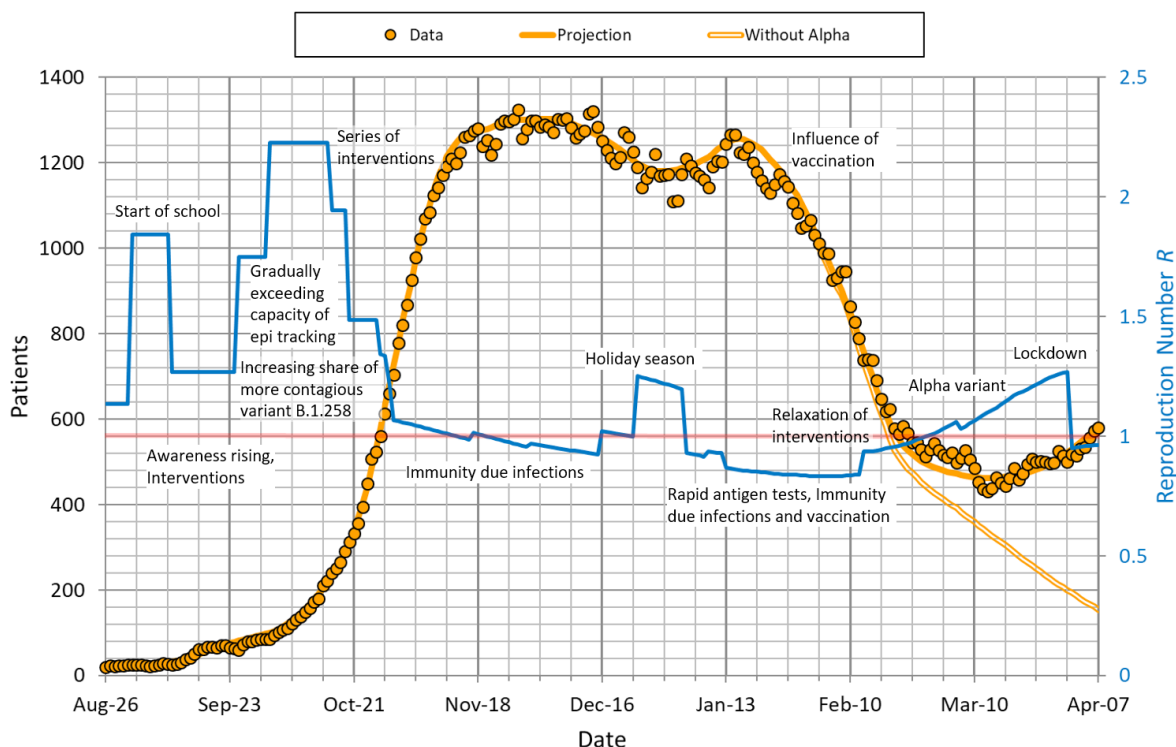


Fig. 9. Analysis of second wave in Slovenia end of year 2020 and beginning of year 2021; the orange dots and curves show the number of hospitalized patients; the blue curve shows the estimated reproduction number R

which successfully contained the epidemic. Without the alpha variant the epidemic would just continue to decline and no non-pharmaceutical interventions would be needed.

On the basis of such analyses it is possible to find out how pharmaceutical (e.g. vaccination) and non-pharmaceutical interventions (e.g. masks, lockdowns) and various events (e.g. holidays) affect the reproduction number R . Such empirically obtained information was successfully applied in forecasts, as presented in the next Section.

2.3 Accuracy of Forecasts

To get an impression how accurate the forecasts are, some examples are provided for the third wave in Slovenia in the year 2021.

Fig. 10 presents the share of the alpha variant in Slovenia, which displaced the B.1.258.17 variant. Based on the data from Denmark [1], the model parameters of the alpha variant were determined. It was assumed that the ratio of the contagiousness of the alpha variant and the at that time dominant variant in Slovenia is the same as it was in Denmark and that consequently the dynamics of the alpha variant share will be the same in Slovenia as it was in Denmark. Based on that the green curve of the alpha variant share was calculated. When the data for Slovenia became available [24] and [25], the calculated curve was fitted to that data by accordingly time shifting it horizontally. Based on our calculations we forecasted already end of January 2021 that the third wave in Slovenia will probably start mid March, which turned out to be true. It may be seen that the agreement of the green curve with the data is nearly perfect, which means that the alpha variant share increased in Slovenia like it did in Denmark. This is also the reason why our forecast was so accurate.

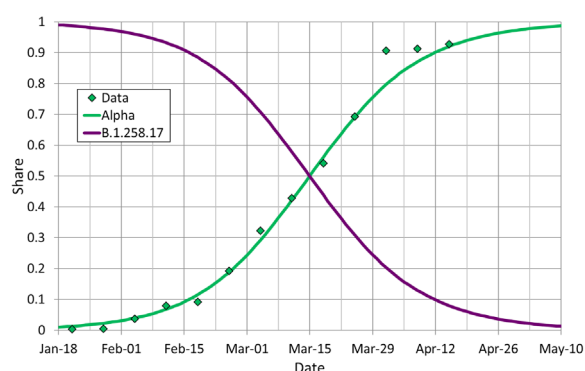


Fig. 10. Share of alpha variant in the year 2021

Figs. 11 and 12 show a demanding forecast for the third wave in Slovenia for hospitalizations and hospitalizations in ICU, considering the implemented non-pharmaceutical interventions, the spreading of the alpha variant, and the immunity due to past infections and vaccination. The forecast was prepared on March 31, 2021 before the 11 days lockdown, which was implemented on April 1, 2021 [4]. Based on past experience, where a similar set of non-pharmaceutical interventions was released as was now implemented in the lockdown, we estimated that during the lockdown the reproduction number R will be reduced by 25 % and then after the lockdown increased by 10 % according to the Slovenian COVID-19 traffic light non-pharmaceutical intervention system.

The epidemic modelling in this period was very demanding as various processes were going on in parallel: non-pharmaceutical interventions were implemented, the share of the alpha variant was rising, the people were extensively vaccinated and the rate of infections was high, both importantly increasing the immunity of the population. Due to all these complex parallel processes it was anticipated that the uncertainties of the forecasts will be large. To capture them, in the presented scenarios the reproduction number R was varied by approximately ± 10 % in regard to the projection, which had a large effect on the results, as may be seen on the figures.

In Figs. 11 and 12 with green dots the actual data after the forecast was prepared is plotted. We see that till the time, when it is anticipated that the non-pharmaceutical interventions have an influence, i.e. the point when the curves for various scenarios start to separate, the forecasts are in nearly perfect agreement with the data. Also later, the agreement is impressively good, especially for the hospitalizations in ICU. Thus, it seems that with an appropriate modelling approach it is possible to make quite accurate medium-term forecasts also for a few months. It may be observed that without the alpha variant (and later new variants) the epidemic would end already in May 2021.

During our epidemic modelling we realized that at an extensive epidemic epistemic uncertainties dominate, like the influence of interventions and events significantly affecting people's behaviour, e.g. start of holidays or school. The impact of aleatory uncertainties, such as random infections, is much smaller than one would expect based on the observed large daily variations of data. Namely, these daily variations are often only a consequence of the weekly rhythm of the society, and if we average the data over one week the average values become very smooth and much more predictable.

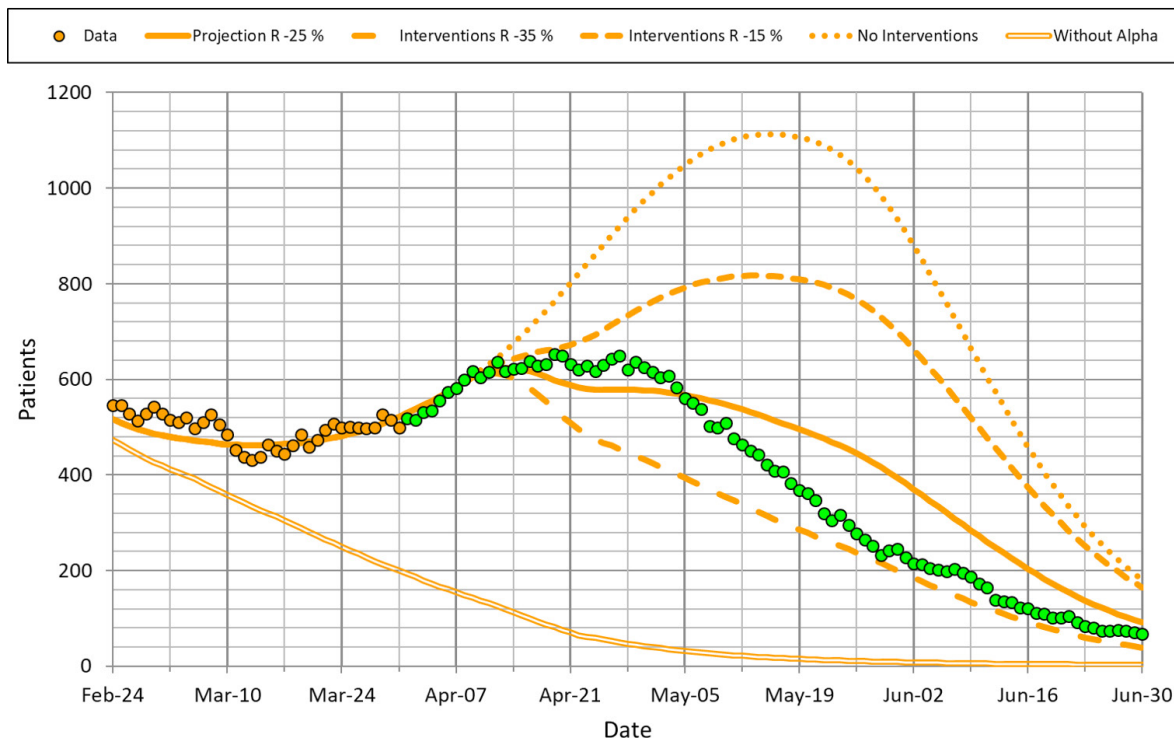


Fig. 11. Forecast for third wave in Slovenia in the year 2021 for hospitalizations, considering the implemented non-pharmaceutical interventions, spreading of alpha variant, and immunity due to past infections and vaccination; the green dots show data after the forecast was prepared, which are in good agreement with the projection

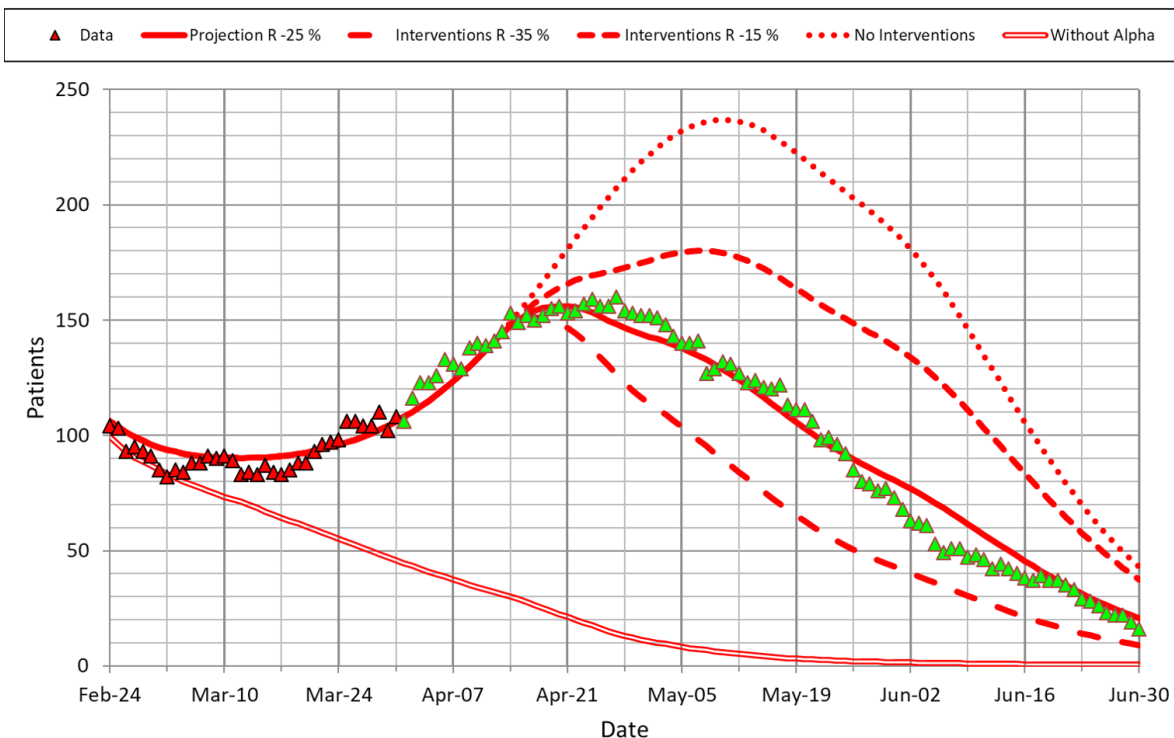


Fig. 12. Forecast for third wave in Slovenia in the year 2021 for hospitalizations in ICU, considering the implemented non-pharmaceutical interventions, spreading of alpha variant, and immunity due to past infections and vaccination; the green dots show data after the forecast was prepared, which are in good agreement with the projection

3 CONCLUSIONS

An epidemic is a complex nonlinear time dependent phenomenon. While it appears to be governed by a number of random processes and events, it is also reasonably predictable on the aggregate (e.g., country) level using purely deterministic models.

The main goal of epidemic modelling is to support the epidemic management through forecasts and analyses of past developments. Modelling during a developing epidemic must rely on the data available in real time, which may not be always optimal and might also change with time significantly. A robust and intuitive SEIR type epidemic model was developed, applied and tested in the realistic conditions of the COVID-19 epidemic developments in Slovenia since March 2020.

The model, formulated in the integral form for better robustness and intuitiveness, is described. Examples of applications include the analysis of the past epidemic situation in Slovenia and a forecast of the epidemic development.

Analyses of past epidemic developments help to explain the effect of non-pharmaceutical interventions and various events on the development of the epidemics characterized through the reproduction number R . This empirically obtained information was then used in the simulation of different scenarios, providing valuable qualitative and quantitative insight of the possible future development of the epidemic.

The accuracy of the forecasts of the number of hospitalized patients and hospitalized patients in ICU was impressively good also in demanding conditions, when various complex processes influencing the spread of the disease were going on in parallel. This demonstrates the robustness and relevance of the proposed model.

Accurate forecasts offered valuable support for decision makers and for hospitals to plan appropriate actions in advance.

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