A Hybrid SEIHCRDV-UKF Model for COVID-19 Prediction. Application on real-time data

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Abstract
The prevalence of COVID-19 has been the most serious health challenge of the 21th century to date, concerning national health systems on a daily basis, since December 2019 when it appeared in Wuhan City. Prediction of pandemic spread plays an important role in effectively reducing this highly contagious disease. Nevertheless, most of the proposed mathematical methodologies, which aim to describe the dynamics of the pandemic, rely on deterministic models that are not able to reflect the true nature of the spread of COVID. In this paper, we propose a SEIHCRDV model – an extension of the classic SIR compartmental model – which also takes into consideration the populations of exposed, hospitalized, admitted in intensive care units (ICU), deceased and vaccinated cases, in combination with an unscented Kalman filter (UKF), providing a dynamic estimation of the time dependent parameters of the system. Apparently, this new consideration could be useful for examining also other pandemics. We examine the reliability of our model over a long period of 265 days, where we observe two major waves of infection, starting in January 2021 which signified the start of vaccinations in Europe, providing quite encouraging predictive performance. Finally, special emphasis is given to proving the non-negativity of SEIHCRDV model, to achieve a representative basic reproductive number $R_0$ and to investigating the existence and stability of disease equilibriums in accordance with the formula produced to estimate $R_0$.

Keywords: Epidemiology, COVID-19, Unscented Kalman Filter, State-Space Models, Compartmental Models, Dynamic Parameter Estimation

1. Introduction
The novel coronavirus SARS-CoV-2 (COVID-19) had broken out in the city of Wuhan, China during December 2019 (Muralidhar et al. 2020). The pathogenesis of the virus is characterized by respiratory tract infection, which may lead to pneumonia showing ground glass alveolar angiography. This extremely contagious disease has been declared as a pandemic from the World Health Organization since January 2020, while a year later, the virus has infected more than 100 million people (Coronavirus Research Center of John Hopkins University 2021), despite various health measures that many national governments had taken over.

The severity of the situation along with the need for early prevention, has led to an investigation of COVID’s nature through mathematical modelling. Usually, the spread of contagious diseases is described using compartmental models, where SIR (susceptible-infected-recovered) represents the most widely known model (Brauer et al. 2019). As a result, many articles base their exploration of COVID dynamics on the SIR (Cooper I. et al 2020) model, or some of its extensions like the SIRS (susceptible-infected-recovered-susceptible) (Salman A.M. et al 2021), the SEIR (susceptible-exposed-infected-recovered) (He et al. 2020) or the SEIRD (susceptible-exposed-infected-deceased) models (Rajagopal K. et al 2020). Moreover, Malkov 2020 proposed the utilization of an SEIRS (susceptible-exposed-infectious-resistant-susceptible) model with time-varying transmission rates.

However, these approaches are not able to describe the complex dynamics of this pandemic, especially for long periods of time, due to various fluctuations in the parameters of the disease. For example, the establishment of restrictive measures such as the usage of masks in closed and public environments or the initialization of lockdown in many countries around the world, reduced the daily infection rates (Atalan 2020), while the emergence of variants such as B.1.1.7 (alpha) or B.1.617.2 (delta) are associated with increased contagiousness (Kidd et al. 2021), increased risk of hospitalization and ICU admission, as well as increased mortality (Tuive et al. 2021; Veneti et al. 2021; Davies et al. 2021). In addition, Twohig et al. (2021), states that there exists a higher risk of serious illness for the unvaccinated delta-infected individuals than the alpha variant.
Since the asymptomatic infections are difficult to detect, and in addition to the false positive-negative ratio of PCR testing, we realize the existence of potential uncertainties in the reported data (Hu et al. 2020, Keeling et al. 2020). Moreover, the states and corresponding transitions of the majority of compartmental models do not take into account the complete dynamics of the disease. Therefore, the transition from a deterministic to a stochastic approach seems necessary. Singh et al. (2021) utilize the basic Kalman Filter to get estimations for the evolution of the pandemic in India, but as they state, these estimations are only reliable for a short time period. Costa et al. (2005) combine a SEIR model with an extended Kalman filter (EKF) to simulate the outbreak of the pandemic, while Ndanguza et al. (2016) include in the SEIR-EKF combination the estimation of the parameters of the epidemiological model. Zhu et al. (2021) propose an SEIRD-EKF model with dynamic parameter estimation by adding the parameters of the model in the updating process of the EKF. Song et al. (2021) combine the same two latter models, while the parameter estimation of the SEIRD takes advantage through an iterative optimization method based on maximum likelihood. Other attempts, deploy the ensemble Kalman Filter in combination with some extensions of the SIR model (Nkwayer et al. 2022; Lal et al. 2021), while Calvetti et al. (2021) adopt a SEAIR (susceptible-exposed-asymptomatic-infectious-recovered) model and utilize particle filtering methodology in order to estimate the spread of the virus in Ohio and Michigan. Finally, Marioli et al. (2021) estimate the evolution of $R_0$ using Kalman filtering.

In this paper we propose a novel hybrid of a SEIHCRDV (susceptible-exposed-infectious-hospitalized-ICU admitted-recovered-deceased-vaccinated) model with an unscented Kalman filter (UKF) with dynamic parameter estimation, that can effectively match significant variations in the spread of COVID after the opening of the vaccination period, providing a much more representative image of the daily evolution of the pandemic, due to the augmented number of suitable states and transitions.

The increase of the number of mixed differential equations, where the majority of states (6 out of 8) are observable, in combination with the dynamic parameter estimation resulting from the real time feedback of observations, prevents the occurrence of extreme parameter estimations, giving quite reliable predictions even for hidden model’s states. The proposed methodology can be easily implemented, in cases where both the observations and the system suffer from uncertainties, while we aim to eliminate unnecessary noise, providing robust estimations for both observable and unobservable states. The inclusion of the hospital and ICU admitted states in the model provides another important advantage for the analysis. COVID-19 is characterized by a high percentage of asymptomatic cases, leading to the consideration that the levels of daily active and recovered cases could be deemed as indices of low trustworthiness for the evolution of the pandemic. On the contrary, hospital and ICU admitted cases are tested/recorded thoroughly for the confirmation of COVID infection, rendering the daily observations of these two states as the most accurate indicators for assessing the fitting-predictive capacity of the proposed model. It should be noted that the addition of the aforementioned states does not impose significant computational burden to the model.

Moreover, a mathematical analysis is performed emphasizing the non-negativity of the states of the system, as long as the existence and stability of disease-free and endemic equilibriums. We even propose an alternative-improved formula for index $R_0$ – usually referred to as the basic reproduction number – based on the proposed compartmental model, drawing valuable conclusions about the nature and the future of the disease. We check the reliability of our model on the reported data of France, which cover a long period of 265 days, displaying daily estimations for the infectious, hospitalized, ICU admitted, recovered, deceased and vaccinated cases. Finally, the additional states that we added in the classic SEIR model, are selected with great care aiming to include only states with available daily observations. Specifically, except from the states of susceptible and exposed, for the remaining 6 states that are part of the proposed model, there are available observations in a daily basis, that we are able to efficiently deploy providing supplementary information to our model and enhancing significantly its fitting and predictive capacity.

The article is organized as follows: In section 2, we present the mathematical structure of the hybrid SEIHCRDV-UKF model in parallel with theoretical results based on this compartmental model. In section 3, we provide simulations for varying parameters of the model, and we test its fitting-predictive performance on the daily observations of France, starting in January of 2021 where we meet the first fully vaccinated individuals reported. In section 4 we discuss and in section 5 we conclude the main findings of our analysis with particular emphasis on the advantages that accompany our model.
2. Mathematical tools and Methods

2.1. Proposed SEIHCRDV epidemiological model

In this paragraph, we present the mathematical compartmental model SEIHCRDV, by means of which we then examine the spread of coronavirus in France using real data. As mentioned earlier, we propose an extension of the standard SIR model, by introducing five additional states and associate differential equations in order to address the exposed, hospitalized, ICU admitted, deceased and vaccinated cases.

Figure 1 that follows displays the transitions between the states of the proposed epidemiological model. The selection of the presented states and transitions has been considered with great care, aiming to manage the complexity of the examined phenomenon without significantly increasing the model’s complexity.

![Figure 1. Diagram of the SEIHCRDV epidemiological model](image)

Notice that system (2) provides a novel deterministic model of the form

\[ \dot{X}(t) = f(t, X) \]

that describes the evolution of COVID-19 spread in the population.

We denote by the variables \( S(t), E(t), I(t), H(t), C(t), R(t), D(t) \) and \( V(t) \) the susceptible, exposed, infectious, hospitalized, placed in the intense care unit (ICU), recovered, deceased and vaccinated cases, respectively, that change over time \( t \). The notation \( \beta \) denotes the transmission rate, \( \alpha \) the incubation rate, \( \gamma \) the hospitalization rate, \( \lambda \) the rate of admissions into ICU, \( \kappa \) and \( \tau \) the recovery rates of hospitalized and ICU admitted patients respectively, \( \mu \) and \( \rho \) the mortality rates of hospitalized and ICU admitted patients respectively, \( \nu \) the vaccination rate of susceptible subjects, \( \sigma \) the vaccine breakthrough infection rate of fully vaccinated subjects, \( \psi \) the re-susceptible rate and \( \omega \) the transition rate from the infectious to the recovered state that could be deemed as constant in time (Table 1). Moreover, \( \gamma, \psi \) and \( \sigma \) could be also deemed as constants, while \( 1 - \sigma \) displays the mean protection that is provided by complete vaccination.

System (2) that follows presents analytically the structure and evolution of our model,

\[
\begin{align*}
\frac{dS(t)}{dt} &= -\frac{\beta S(t)I(t)}{N} - \nu S(t) + \psi R(t) \\
\frac{dE(t)}{dt} &= \frac{\beta S(t)I(t)}{N} + \frac{\sigma \nu V(t)}{N} - aE(t) \\
\frac{dI(t)}{dt} &= aE(t) - \gamma I(t) - \omega I(t) \\
\frac{dH(t)}{dt} &= \gamma I(t) - \lambda H(t) - \kappa H(t) - \mu H(t)
\end{align*}
\]
\[
\frac{dS(t)}{dt} = \lambda H(t) - \tau C(t) - \rho C(t) \\
\frac{dR(t)}{dt} = \kappa H(t) + \tau C(t) + \omega I(t) - \psi R(t) \\
\frac{dD(t)}{dt} = \mu H(t) + \rho C(t) \\
\frac{dV(t)}{dt} = \nu S(t) - \frac{\sigma \beta V(t) I(t)}{N}
\]

where we consider population size \( N = S(t) + E(t) + I(t) + H(t) + C(t) + R(t) + D(t) + V(t) \) to be constant during the period of the pandemic. Consequently, we get that,

\[
\frac{dN}{dt} = 0 = \frac{dS(t)}{dt} + \frac{dE(t)}{dt} + \frac{dI(t)}{dt} + \frac{dC(t)}{dt} + \frac{dR(t)}{dt} + \frac{dD(t)}{dt} + \frac{dV(t)}{dt},
\]

a condition that is satisfied by the eight above ordinary differential equations (ODEs) that describe the evolution of the pandemic inside the population.

The aforementioned system of differential equations (2) could be solved by various arithmetic methods, while the most common is the 4th order Runge-Kutta method, due to its arithmetic stability. An extension of model (2) can be proposed by considering population \( N(t) \) to be non-constant, adding to model (2) a representative birth rate \( \Lambda \) and an extra mortality rate \( \delta \), due to natural, non-COVID-19 causes.

Both \( \Lambda \) and \( \delta \) may be considered as constants for relatively short time periods, while in the applied part of our analysis we deem that their impact on the population is negligible, resulting in their removal from the presented methodology and results. The consideration of these two extra parameters leads to the following model,

\[
\frac{dS(t)}{dt} = \Lambda - \frac{\beta S(t)I(t)}{N} - \nu S(t) + \psi R(t) - \delta S(t) \\
\frac{dE(t)}{dt} = \frac{\beta S(t)I(t)}{N} + \frac{\sigma \beta V(t) I(t)}{N} - aE(t) - \delta E(t) \\
\frac{dI(t)}{dt} = aE(t) - \gamma I(t) - \omega I(t) - \delta I(t) \\
\frac{dH(t)}{dt} = \gamma I(t) - \lambda H(t) - \kappa H(t) - \mu H(t) - \delta H(t) \\
\frac{dC(t)}{dt} = \lambda H(t) - \tau C(t) - \rho C(t) - \delta C(t) \\
\frac{dR(t)}{dt} = \omega I(t) + \kappa H(t) + \tau C(t) - \psi R(t) - \delta R(t) \\
\frac{dD(t)}{dt} = \mu H(t) + \rho C(t) \\
\frac{dV(t)}{dt} = \nu S(t) - \frac{\sigma \beta V(t) I(t)}{N} - \delta V(t)
\]

which is utilized during the theoretical part of our study.

Furthermore, we can convert the ODEs system of the 8 equations into a state-space representation with 7 states that could be updated during each discrete time step \( t \), as for the first differential equation we can use the relation \( S(t) = N - E(t) - I(t) - H(t) - C(t) - R(t) - D(t) - V(t) = N - \sum(E, I, H, C, D, V)(t) \). Then, the ODE system (3) can be written as
\[
\begin{align*}
\frac{dE(t)}{dt} &= \left(\frac{\beta S(t) + \sigma V(t)}{N}\right) I(t) - (a + \delta)E(t) \\
\frac{dI(t)}{dt} &= -(\gamma + \omega + \delta)I(t) + aE(t) \\
\frac{dH(t)}{dt} &= \gamma I(t) - (\lambda + \kappa + \mu + \delta)H(t) \\
\frac{dC(t)}{dt} &= \lambda H(t) - (\tau + \rho + \delta)C(t) \\
\frac{dR(t)}{dt} &= \omega I(t) + \kappa H(t) + \tau C(t) - (\psi + \delta)R(t) \\
\frac{dD(t)}{dt} &= \mu H(t) + \rho C(t) \\
\frac{dV(t)}{dt} &= v (N - \sum (E, I, H, C, R, D, V)(t)) - \frac{\sigma \beta V(t) I(t)}{N} - \delta V(t)
\end{align*}
\]

Table 1. Parameter and state definition of the proposed SEIHCRDV model

| Symbol | Definition of Parameter/State                        |
|--------|------------------------------------------------------|
| S      | Susceptible                                          |
| E      | Exposed                                              |
| I      | Infectious                                           |
| H      | Hospital admissions/Hospitalized                     |
| C      | ICU admissions                                       |
| R      | Recovered                                            |
| D      | Deceased                                             |
| V      | Vaccinated                                           |
| \Lambda| Birth rate                                           |
| \alpha | Incubation rate                                      |
| \beta  | Transmission rate                                    |
| \gamma | Rate of hospitalizations                             |
| \delta | Mortality rate due to non-COVID-19 causes            |
| \lambda| Transition rate from hospital to ICU admission       |
| \kappa | Cure rate of hospitalized cases                      |
| \mu    | Death rate of hospitalized cases                     |
| \nu    | Fully vaccination rate                               |
| \rho   | Death rate of ICU admitted cases                     |
| \sigma | Vaccine breakthrough infection rate of fully vaccinated cases |
| \tau   | Cure rate of ICU admitted cases                      |
| \psi   | Transition rate from recovered to susceptible state  |
| \omega | Cure rate of infected cases with mild symptoms       |

The displayed ODEs system adequately describes the evolution of the pandemic over continuous time. Apparently, the features of the continuous time formulation have to be derived using the discrete time observations of real-life data, rendering the discretization of the system a necessary step of this analysis. The ODEs of the system can be discretized using finite differences, i.e., \[ \frac{df(t)}{dt} = \frac{f_{k+\Delta t} - f_k}{\Delta t}, \] to derive the system,

\[
\begin{align*}
E_{k+\Delta t} &= (1 - (a + \delta) \Delta t)E_k + \frac{\beta S_k I_k}{N} \Delta t + \frac{\sigma \beta}{N} I_k V_k \Delta t \\
l_{k+\Delta t} &= (1 - \Delta t (\gamma + \omega + \delta)) l_k + \Delta t \alpha E_k \\
H_{k+\Delta t} &= (1 - \Delta t (\lambda + \kappa + \mu + \delta)) H_k + \Delta t \gamma I_k \\
C_{k+\Delta t} &= (1 - \Delta t (\tau + \rho + \delta)) C_k + \Delta t \lambda H_k \\
\end{align*}
\]
Theorem 2.2 Mathematical analysis

\[ R_{k+\Delta t} = (1 - \Delta t(\psi + \delta))R_k + \Delta t \omega I_k + \Delta t \kappa H_k + \Delta t \tau C_k \]
\[ D_{k+\Delta t} = D_k + \Delta t \mu H_k + \Delta t \rho C_k \]
\[ V_{k+\Delta t} = \left(1 - \Delta t\left(\frac{\sigma \beta}{N} I_k + \delta\right)\right)V_k + \Delta t \nu S_k \]

where the states of the model at the \( k \)-th discrete time point can be assembled in a vector \( x_k^T = [S_k \ E_k \ I_k \ H_k \ C_k \ D_k \ V_k] \). The constant parameters that accompany the above discretized system could be deemed as variables through time, resulting in an augmented state vector \( x_k^T = [S_k \ E_k \ I_k \ H_k \ C_k \ D_k \ V_k \ \theta_k^T] \), where \( \theta_k^T \) is the vector containing the parameters that can be updated during time.

We notice that – in both models (2) and (3) – there are no edges connecting the infectious cases with the state of deceased individuals. Moreover, these models contain a differential equation for the vaccinated cases, providing a representation that is more appropriate in the later stages of the pandemic, namely from January of 2021 onwards.

The period between the emergence of COVID-19 in Wuhan (December 8, 2019) (Muralidhar et al. 2020) and the initialization of the vaccination period, was sufficient to understand the risks of the disease and to inform citizens about the severity of the situation. Hence, we believe that the proportion of severely ill infected individuals that died from COVID-19 without being admitted in a hospital, or an ICU is negligible. In addition, the negligible influence of this transition, could be assumed as a part of the Gaussian noise added into the state equations, resulting into a stochastic equivalent of the above SEIHCRDV models (2), (3).

Before determining the constant parameters of system (3), we should pay attention to the value of the re-infection rate \( \psi \). Many epidemiological models do not take into account the transition from the recovered to the susceptible state – although this is mandatory – as in the occasion of COVID-19 it is known that the immunity provided by the infection is temporary. Some previous studies state that there is no significant evidence concerning the ideal selection of the re-infection rate (Salman et al. 2021; Malkov 2020), although – based on the research of Schuler et al. (2021) highlighting infected individuals with mild symptoms – the proportion of virus-neutralizing antibodies is stable for up to 6 months, providing immunity to re-infection.

From the 14 parameters used in our model, 7 of them could be considered as constant.

- \( 1 - \sigma \) displays the average protection provided from the vaccinations.
- Birth rate \( \Lambda \) and mortality rate \( \delta \) due to non-COVID causes may be considered as constants for a short time interval (Zamir et al. 2021; Nadeem et al. 2019).
- The incubation period can be considered as constant, and its average duration is about 5.5 days (Evensen et al. 2021). Hence, the average incubation rate is \( \alpha = \frac{2}{11} \).
- According to the above observations we assume that the virus-neutralizing antibodies of recovered patients last up to 6 months \( \approx 180 \) days. As a result, the transition rate from recovered to susceptible state is \( \psi = \frac{1}{180} \).
- The average interval that an infectious case without hospitalization passes to the recovered state, is 14 days, concluding in a constant recovery rate of \( \omega = \frac{1}{14} \) (Katul et al. 2020).
- According to the reported in France, the median value of daily fully vaccinated individuals is about 140,000, leading to a vaccination rate of \( \nu \approx 0.002 \), as the total population of France is about 65.3 million.

2.2 Mathematical analysis

**Theorem 1.** If the initial conditions of the SEIHCRDV system (3) are non-negative, i.e. \( S_0, E_0, I_0, H_0, C_0, R_0, D_0, V_0 \geq 0 \), then the respective trajectories remain non-negative for all \( t > 0 \).

**Proof.** Firstly, we note that all 14 transition rates of the SEIHCRDV system (3) are non-negative constants. From the second equation of the SEIHCRDV ODEs system, we get that
\[ E'(t) = \frac{\beta S(t) I(t)}{N} + \frac{\sigma \beta V(t) I(t)}{N} - aE(t) - \delta E(t) \geq -(a + \delta)E(t) \]

or

\[ \frac{E'(t)}{E(t)} \geq -(a + \delta) \]

and

\[ (\ln E(t))' \geq -(a + \delta). \] (6)

By integrating inequality (4), we derive

\[ E(t) \geq e^{- (a + \delta)t} \]

and thus

\[ E(t) \geq E_0 e^{- (a + \delta)t} \geq 0. \] (7)

Following similar methodology for the other equations of system (2), we result in

\[ I(t) \geq I_0 e^{- (\gamma + \omega + \delta)t} \geq 0, \] (9)

\[ H(t) \geq H_0 e^{- (\kappa + \lambda + \mu + \delta)t} \geq 0, \] (10)

\[ C(t) \geq C_0 e^{- (\tau + \rho + \delta)t} \geq 0, \] (11)

\[ R(t) \geq R_0 e^{- (\psi + \delta)t} \geq 0. \] (12)

Furthermore, for the evolution of the deceased cases described by equation 7 of system (3), we have

\[ D'(t) = \mu H(t) + \rho C(t) \geq \rho C(t) \geq \rho C_0 e^{- (\tau + \rho + \delta)t}. \] (13)

By integrating equation (13), we get

\[ D(t) \geq \rho C_0 \int_0^t e^{- (\tau + \rho + \delta)s} ds = \frac{\rho C_0}{\tau + \rho + \delta} (1 - e^{- (\tau + \rho + \delta)t}) \geq 0, \]

or

\[ D(t) \geq D_0 (1 - e^{- (\tau + \rho + \delta)t}) \geq 0, \] (14)

where \( D_0 = \frac{\rho C_0}{\tau + \rho + \delta} \).

We will prove the non-negativity of the vaccinated cases function \( V(t) \), using the infinity norm

\[ |f|_\infty = \max_{t \in [a,b]} |f(t)|. \] (15)

Thus, for the function \( V(t) \) we have
\[ V'(t) = vS(t) - \frac{\sigma \beta V(t) I(t)}{N} - \delta V(t) \geq - \left( \frac{\sigma \beta I(t)}{N} + \delta \right) V(t) \geq - \left( \frac{\sigma \beta \max_{t \in [0, \infty)} |I(t)|}{N} + \delta \right) V(t) \]

and consequently,

\[ \ln(V(t))' \geq - \frac{\sigma \beta \|I\|_\infty}{N} - \delta. \]

By integrating the above inequality and substituting for \( t = 0 \), the later inequality leads to

\[ V(t) \geq V_0 e^{-\left(\frac{\sigma \beta \|I\|_\infty}{N} + \delta\right)t} \geq 0. \] (16)

Finally, for the susceptible individuals we get in a similar way as for the vaccinated cases that

\[ S'(t) = \Lambda - \frac{\beta S(t) I(t)}{N} - vS(t) + \psi R(t) - \delta S(t) \geq - \left( \frac{\beta I(t)}{N} + v + \delta \right) S(t) \]

thus,

\[ \left( \ln S(t) \right)' \geq - \frac{\beta I(t)}{N} - v - \delta \geq - \frac{\beta \max_{t \in [0, \infty)} |I(t)|}{N} - v - \delta \geq - \left( \frac{\beta \|I\|_\infty}{N} + v + \delta \right) \]

and

\[ S(t) \geq S_0 e^{-\left(\frac{\beta \|I\|_\infty}{N} + v + \delta\right)t} \geq 0. \] (17)

Notice that \( \|I\|_\infty < \infty \), as we refer to a finite population function, \( N(t) \).

**Theorem 2.** The basic reproduction number of the proposed SEIHCRDV model (3) is

\[ R_0 = \frac{\beta a(s^0 + sv^0)}{N(\alpha + \delta)(\psi + w + \delta)} = \frac{\beta a \Lambda + sv}{N(\alpha + \delta)(\psi + w + \delta)(v + \delta)}. \]

**Proof** We will base our analysis on the utilization of the next-generation matrix proposed by Driessche and Watmough (2002) for the definition of the basic reproduction number \( R_0 \); recall that coefficient \( R_0 \) is defined as the number of new infected cases produced by another already infected individual belonging in the population.

Let \( X = (E, I, H, C)^T \) be the vector that consists of the 4 states which contain the infected cases of the system, and

\[ Y^0 = (S^0, 0, 0, 0, 0, 0, 0, v) \]

be the disease-free equilibrium (DFE), where all individuals are gathered in the susceptible and vaccinated states. We set \( X^0 = 0^T \), as there should be no cases in any of the infection states of our model during the disease-free period.

Let \( F(X) \) and \( V(X) \) be the 4x1 vectors the \( i \)-th entry of which exhibit the rate of new infections entering state \( i \) and the transfer rate of individuals out of state \( i \) or the transfer into state \( i \) by non-infection means, respectively. Moreover, we do not consider the transition of an individual between the 4 states as new infection, but rather the progression of the infected individual through the various states of the system. As a result,
\[
\dot{X} = F(X) - V(X),
\]
where
\[
F(X) = \left(\frac{BSI}{N} + \frac{\sigma \beta V I}{N}, 0, 0, 0\right)^T
\]
and
\[
V(X) = ((a + \delta)E, (y + \omega + \delta)I - aE, (\lambda + \kappa + \mu + \delta)H - \gamma I, (\tau + \rho)C - \lambda H)^T.
\]

The next-generation matrix is defined as the matrix product \(FV^{-1}\) where matrices \(F, V\) are the Jacobians of \(F(X), V(X)\) evaluated at the disease-free equilibrium \(Y^0\) (16). Hence, both \(F\) and \(V\) are 4x4 dimensional matrices of the forms
\[
F|_{Y^0} = \begin{pmatrix}
0 & \frac{\beta S^0 + \sigma \beta V^0}{N} & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
\end{pmatrix},
\]
and
\[
V|_{Y^0} = \begin{pmatrix}
\delta + a & 0 & 0 & 0 \\
-a & (y + \omega + \delta) & 0 & 0 \\
0 & -\gamma & (\lambda + \kappa + \mu + \delta) & 0 \\
0 & 0 & -\lambda & (\tau + \rho + \delta) \\
\end{pmatrix},
\]
respectively, while \(V\) is an invertible lower triangular matrix, with a non-zero determinant, which equals the product of its diagonal elements. Then, we get that
\[
V^{-1} = \begin{pmatrix}
\frac{1}{a + \delta} & 0 & 0 & 0 \\
\frac{\alpha + \delta}{(a + \delta)(y + \omega + \delta)} & \frac{1}{y + \omega + \delta} & 0 & 0 \\
\frac{\alpha + \delta}{(a + \delta)(\lambda + \mu + \delta)(y + \omega + \delta)} & \frac{\lambda}{(\lambda + \mu + \delta)(y + \omega + \delta)} & \frac{1}{\lambda} & 0 \\
\frac{\alpha + \delta}{(a + \delta)(\lambda + \mu + \delta)(\tau + \rho + \delta)} & \frac{\tau + \rho + \delta}{(\lambda + \mu + \delta)(\tau + \rho + \delta)} & \frac{1}{\tau + \rho + \delta} & 1 \\
\end{pmatrix}
\]
while \(R_0\) is the spectral radius of the next-generation matrix \(FV^{-1}\), given by
\[
R_0 = \rho(FV^{-1}) = \frac{\beta a(S^0 + \sigma V^0)}{N(a + \delta)(y + \omega + \delta)}
\]
where \(\rho(A)\) stands for the spectral radius of matrix \(A\).

By substituting the DFE values in equation (22) we get that
\[
R_0 = \frac{\alpha \beta \lambda (\delta + \sigma \nu)}{N \delta (a + \delta)(y + \omega + \delta)(\nu + \delta)}.
\]

In a similar way, we can calculate the basic reproductive number for system (2) where we remove the impact of exogenous factors like new births and mortality due to non-COVID causes, namely,
\[
R_0 = \frac{\beta (S^0 + \sigma V^0)}{N(y + \omega)}.
\]
A dynamic equivalent of the basic reproduction number $R_0$ that can be calculated in a daily basis during the pandemic is the effective reproduction number $R_t$ that is represented by the formula

$$R_t = \frac{\beta t (S_t + \sigma V_t)}{N(y_t + \omega)}.$$  \hfill (25)

**Theorem 3.** The ratio of the evolution rates of deceased cases and ICU admissions is lower bounded, i.e., \(\frac{dD(t)}{dt} / \frac{dC(t)}{dt} \geq \frac{\mu t}{\lambda t}\), during periods of positive ICU admissions rate.

**Proof.** Firstly, using the fifth and seventh equation of system (3), that correspond to the evolution of ICU admissions and deceased individuals through time, respectively, we have

\[
\frac{dC(t)}{dt} \leq \lambda H(t), \quad \frac{dD(t)}{dt} \geq \mu H(t).
\]  \hfill (26)

Consequently,

\[
\frac{dD(t)}{dt} / \frac{dC(t)}{dt} \geq \frac{\mu}{\lambda}.
\]  \hfill (27)

while by considering the potential dynamic evolution of parameters $\mu$ and $\lambda$ we get that

\[
\frac{dD(t)}{dt} / \frac{dC(t)}{dt} \geq \frac{\mu_t}{\lambda_t}.
\]  \hfill (28)

**Theorem 4.** The proposed SEIHCRDV model leads asymptotically to a unique non-trivial endemic equilibrium when $R_0 > 1$.

**Proof.** Let $Y^* = (S^*, E^*, I^*, H^*, C^*, R^*, D^*, V^*)^T$ be the SEIHCRDV’s endemic equilibrium that may be determined after setting all differential equations of the system equal to zero. We may limit the analysis to 7 equations, as $D(t)$ can be described as a linear combination of the remaining 7 states and does not contribute to any other differential equation. We explore the existence and uniqueness of a non-trivial endemic equilibrium, as $Y^0$ obviously constitutes the disease-free equilibrium for system (3).

Moreover, for simplicity let $\beta_t = \frac{\beta}{N} > 0$. Then,

\[
\begin{align*}
\Lambda - \beta_t S^* I^* - \nu S^* + \psi R^* - \delta S^* &= 0 \\
\beta_t S^* I^* + \sigma \beta_t V^* I^* - a E^* - \delta E^* &= 0 \\
\alpha E^* - \gamma I^* - \omega I^* - \delta I^* &= 0 \\
\gamma I^* - \lambda H^* - \kappa H^* - \mu H^* - \delta H^* &= 0 \\
\lambda H^* - \tau C^* - \rho C^* - \delta C^* &= 0 \\
\omega I^* + \kappa H^* + \tau C^* - \psi R^* - \delta R^* &= 0 \\
\nu S^* - \sigma \beta_t V^* I^* - \delta V^* &= 0.
\end{align*}
\]

According to the above non-linear system, we aim to describe each state in the equilibrium as a function of $I^*$, resulting in the formulas,
\[ E^* = \frac{\gamma + \omega + \delta}{\alpha} I^* \]  
(30)

\[ H^* = \frac{\gamma}{\lambda + \kappa + \mu + \delta} I^* \]  
(31)

\[ C^* = \frac{\lambda \gamma}{(\lambda + \kappa + \mu + \delta)(\tau + \rho + \delta)} I^* \]  
(32)

\[ R^* = \frac{\omega(\lambda + \kappa + \mu + \delta)(\tau + \rho + \delta) + \kappa \gamma (\tau + \rho + \delta) + \tau \lambda \gamma}{(\psi + \delta)(\lambda + \kappa + \mu + \delta)(\tau + \rho + \delta)} I^* = c_1 I^* \]  
(33)

\[ S^* = \frac{A + \psi c_1 I^*}{\beta_1 I^* + v + \delta} \]  
(34)

\[ V^* = \frac{\nu A + \psi c_1 I^*}{(\sigma \beta_1 I^* + \delta)(\beta_1 I^* + v + \delta)} \]  
(35)

It should be noticed here that \( c_1 \in \left(0, \frac{\gamma + \omega}{\psi + \delta}\right) \); this statement could be proven easily, by rewriting \( c_1 \), appearing in (33), in the form

\[ c_1 = \frac{1}{\psi + \delta} \left[ \frac{\omega + \gamma}{(\lambda + \kappa + \mu + \delta)(\tau + \rho + \delta)} \right] < \frac{\gamma + \omega}{\psi + \delta}, \]  
(36)

as \( \lambda \tau + \kappa(\tau + \rho + \delta) < (\lambda + \kappa + \mu + \delta)(\tau + \rho + \delta) \).

By substituting relations (30), (34) and (35) into the second equation of the system, we derive the cubic equation -without constant coefficient-

\[ a \beta_1(A + \psi c_1 I^*)(\sigma \beta_1 I^* + \delta)I^* + \sigma \beta_1 \alpha \nu (A + \psi c_1 I^*)I^* \]

\[ -(\alpha + \delta)(\gamma + \omega + \delta)(\sigma \beta_1 I^* + \delta)(\beta_1 I^* + v + \delta) I^* = 0, \]  
(37)

which has one zero and two non-zero solutions. The respective quadratic equation derived from (37) to determine the aforementioned two solutions, is

\[ \sigma \beta_1^2[\alpha \psi c_1 - (\alpha + \delta)(\gamma + \omega + \delta)] I^* \]

\[ + [a \beta_1(A \beta_1 \sigma + \psi c_1(\delta + \sigma \nu)) - \beta_1(\alpha + \delta)(\gamma + \omega + \delta)(\sigma \delta + \delta + \sigma \nu)] I^* \]

\[ + a \beta_1\Lambda(\delta + \sigma \nu) - \delta(\alpha + \delta)(\gamma + \omega + \delta)(\delta + v) = 0. \]  
(38)

Using Vieta’s formulas, we can determine the sign of the two real solutions of equation (38). Let \( l_1^* \) and \( l_2^* \) be the solutions of (38) with

\[ l_1^* l_2^* = \frac{a \beta_1 \Lambda(\delta + \sigma \nu) - \delta(\alpha + \delta)(\gamma + \omega + \delta)(\delta + v)}{\sigma \beta_1^2[\alpha \psi c_1 - (\alpha + \delta)(\gamma + \omega + \delta)]}. \]  
(39)

The denominator of (39) is strictly negative as

\[ a \psi c_1 < a \frac{\psi}{\psi + \delta}(\omega + \gamma) < \alpha(\omega + \gamma) < (\alpha + \delta)(\gamma + \omega + \delta). \]
On the other hand, the numerator of (39) is positive when
\[ a\beta_1 A(δ + σv) - δ(α + δ)(γ + Ω + δ)(δ + 0), \]
thus, according to (23),
\[ R_0 > 1. \]  
(40)

Consequently, if \( R_0 > 1 \), we have solutions with opposite sign, leading to a unique endemic equilibrium, as the negative solution must be rejected according to Theorem 1. Using relations (30) – (35) we can calculate the remaining quantities of the endemic equilibrium.

When \( R_0 < 1 \) , based on Vieta’s formulas we are led to solutions of the same sign. We note that the term
\[ a\beta_1(A\beta_1\sigma + \psi c_1(δ + σv)) - β_1(α + δ)(γ + Ω + δ)(σδ + δ + σv) \]
is also negative as
\[ a\beta_1\psi c_1(δ + νσ) < a\beta_1 \frac{ψ}{ψ + δ}(γ + ω)(δ + νσ) < β_1(α + δ)(γ + Ω + δ)(δ + νσ) \]
and
\[ A\beta_1^2 σδ < β_1(α + δ)(γ + Ω + δ)σδ. \]

According to the Routh-Hurwitz criterion for second order polynomials, the solutions of (38) are lying on the left side of the complex plane, leading to the rejection of both \( I_1 \) and \( I_2 \), due to Theorem 1. Thus, only the zero solution of DFE \( Y^0 \) is valid for the cubic polynomial (34). As a result, we conclude that the proposed SEIHCRDV model has a unique endemic equilibrium.

Another important issue here is the exploration of the stability of system (3) examined on the disease-free equilibrium \( Y^0 = (S^0, 0, 0, 0, 0, 0, V^0) = (\frac{A}{v + δ}, 0, 0, 0, 0, 0, \frac{vA}{δ(v + δ)}). \) This DFE is obtained after equating the ODEs of system (3) with zero, namely \( f(t, X) = 0 \), while setting \( I = 0 \) (Brauer et al. 2019). We prove the local stability of the proposed system based on the value of the basic reproduction number \( R_0 \), using the formula provided by Theorem 2. More specifically, when \( R_0 < 1 \), the stability of the model indicates a recursion of system (3) to the initial state when time tends to infinity.

**Theorem 5.** The disease-free equilibrium (DFE) \( Y^0 \) is asymptotically stable if and only if \( R_0 < 1 \), marginally stable when \( R_0 = 1 \) and unstable otherwise.

**Proof.** Firstly, we remove the equation presenting the flow of the deceased cases from system (3), as \( D(t) \) does not take part in the remaining 7 differential equations and may be calculated based on the statement \( D(t) = N - \sum(S, E, I, H, C, R, V)(t) \). We linearize system (3), by taking the respective Jacobian matrix evaluated on the disease-free equilibrium \( Y^0 \).

\[
J_{DFE} = \begin{pmatrix}
-(v + δ) & 0 & -β_1 S^0 & 0 & 0 & ψ & 0 \\
0 & -(α + δ) & β_1 S^0 + σV^0 & 0 & 0 & 0 & 0 \\
0 & α & -(γ + Ω + δ) & 0 & 0 & 0 & 0 \\
0 & 0 & γ & -(λ + κ + μ + δ) & 0 & 0 & 0 \\
0 & 0 & 0 & λ & -(τ + ρ + δ) & 0 & 0 \\
0 & 0 & ω & κ & τ & -(ψ + δ) & 0 \\
v & 0 & -σβ_1 V^0 & 0 & 0 & 0 & -δ
\end{pmatrix}. \]  
(41)
System (3) is asymptotically stable when all the eigenvalues of the Jacobian $J_{DFE}$ lay on the left side of the complex plane, thus having negative real parts. The characteristic polynomial of $J_{DFE}$ is

$$p(s) = \det(J_{DFE} - sI_{7 \times 7})$$

$$= (s + \delta)(s + \lambda + \kappa + \mu + \delta)(s + \tau + \rho + \delta)(s + \delta + \psi)
\quad (s^2 + (a + \gamma + \omega + 2\delta)s + \delta(a + \gamma + \delta + \omega) + \alpha(y + \omega - \beta_1 S^0 - \sigma \beta_1 V^0) = 0, (42)$$

leading to 5 negative eigenvalues, namely

$s_1 = -\delta, s_2 = -(\lambda + \kappa + \mu + \delta), s_3 = -(\tau + \rho + \delta), s_4 = -(\tau + \rho + \delta)$ and $s_5 = -(\delta + \psi)$.

For the quadratic polynomial (42), we apply the second-order Routh-Hurwitz criterion, where the roots of the quadratic polynomial, lay on the left-hand side of the complex plane when coefficients $(a + \gamma + \omega + 2\delta)$ and $\delta(a + \gamma + \delta + \omega) + \alpha(y + \omega - \beta_1 S^0 - \sigma \beta_1 V^0)$ are both positive. As $(a + \gamma + \omega + 2\delta) > 0$, then the Routh-Hurwitz criterion is satisfied if and only if

$$\delta(a + \gamma + \delta + \omega) + \alpha(y + \omega - \beta_1 S^0 - \sigma \beta_1 V^0) > 0$$

or

$$\beta_1 a(S^0 + \sigma V^0) < a(y + \omega + \delta) + \delta(y + \omega + \delta)$$

or

$$\beta_1 a(S^0 + \sigma V^0) < (a + \delta)(y + \omega + \delta)$$

and, consequently,

$$R_0 < 1, \quad (43)$$

showing that system (3) is locally asymptotically stable if and only if $R_0 < 1$.

In case where $R_0 = 1$, the quadratic polynomial (42) takes the form

$$s^2 + (a + \gamma + \omega + 2\delta)s = 0, \quad (44)$$

leading to the real solutions

$$s_1 = 0, \quad s_2 = -(a + \gamma + \omega + 2\delta) < 0.$$

Solution $s_1$ is laying on the imaginary axis $\gamma'y$, characterizing a marginally stable system, as the remaining 6 eigenvalues are laying at the left-hand side of the complex plane. For $R_0 > 1$ the quadratic equation has roots with positive real parts, thus rendering system (3) to be unstable; this means that the existence of even a small number of infections can lead to a rapid increase of contagiousness.

2.3 Unscented Kalman Filter

The EKF is an extended version of the widely used Kalman Filter that is ideal for systems that can by approximated using linear dynamics. EKF makes use of the Jacobian matrices that describe both state and observation systems, aiming to locally linearize the non-linear dynamics of the model. Hence, EKF provides adequate estimations in nonlinear problems that do not exhibit a strong nonlinear behavior (Einicke and White 1999).

The Unscented Kalman Filter (UKF) is a version of Kalman filter that aims to eliminate the problems caused by the nonlinearities of the system by utilizing a set of sigma-points, trying to accurately describe the distribution of the states and the observations. The purpose of both EKF and UKF is the efficient elimination of the noise that accompanies the above observations aiming to reveal the true evolution of the states, while the comparison of these
2 methodologies provides valuable inferences about the appropriateness of these methodologies in the examination of epidemiological models. Relations (45) and (46) represent the state and observation equations, where \( \mathbf{x}_k = [S_k \ E_k \ I_k \ H_k \ C_k \ D_k \ V_k] \) is the state vector that describes the evolution of susceptible, exposed, infectious, hospitalized, ICU admitted, recovered, deceased and vaccinated cases. Equation (45) that follows, is derived by the discretization of the ODEs system presented in (5) and the addition of Gaussian noise, while (46) represents the observation equation

\[
\mathbf{x}_k = f(\mathbf{x}_{k-1}) + \mathbf{v}_k, \quad (45)
\]

\[
\mathbf{y}_k = h(\mathbf{x}_k) + \mathbf{w}_k. \quad (46)
\]

The addition of the noises \( \mathbf{v}_k \) and \( \mathbf{w}_k \) in (45) and (46), indicates the transition from the deterministic to the stochastic point of view; in addition, the random vectors \( \mathbf{v}_k \) and \( \mathbf{w}_k \) are considered to be white noises, i.e., to have zero means and finite covariance matrices \( Q \) and \( R \), respectively.

Firstly, we assume an initialization of the state and the corresponding covariance matrix with \( \mathbf{\bar{x}}_0 = E[\mathbf{x}_0] \) and \( \mathbf{P}_0 = E[(\mathbf{x}_0 - \mathbf{\bar{x}}_0)(\mathbf{x}_0 - \mathbf{\bar{x}}_0)^T] \). For the implementation of the UKF methodology, we construct a series of sigma points \( \mathbf{s}_i \) with corresponding first order weights \( w_i^0 \) where

\[
E[\mathbf{x}_i] = \sum_{i=0}^{N} w_i^0 \mathbf{s}_{i,j}, \quad j = 1, \ldots, L \quad (47)
\]

and second-order weights \( w_i^L \), where

\[
E[\mathbf{x}_j|\mathbf{x}_i] = \sum_{i=0}^{N} w_i^L \mathbf{s}_{i,l}\mathbf{s}_{i,j}, \quad j, l = 1, \ldots, L. \quad (48)
\]

The \( 2L + 1 \) sigma points can be calculated as

\[
\mathbf{s}_0 = \mathbf{\bar{x}}_{k-1|k-1}
\]

\[
w_i^0 = \frac{a^2 \kappa - L}{a^2 \kappa} \quad (50)
\]

\[
w_i^c = w_i^0 + 1 - a^2 + \beta \quad (51)
\]

\[
s_i = \mathbf{\bar{x}}_{k-1|k-1} + a \sqrt{\kappa} \mathbf{A}_i, \quad i = 1, \ldots, L \quad (52)
\]

\[
s_{L+i} = \mathbf{\bar{x}}_{k-1|k-1} - a \sqrt{\kappa} \mathbf{A}_i, \quad i = 1, \ldots, L \quad (53)
\]

\[
w_i^d = w_i^c = \frac{1}{2a^2 \kappa}, \quad i = 1, \ldots, 2L \quad (54)
\]

(Wan and Van der Merwe 2000). The vector \( \mathbf{A}_i \) is the \( i \)-th column of matrix \( \mathbf{A} \) of \( \mathbf{P}_{k-1|k-1} = \mathbf{A} \mathbf{A}^T \), while \( \mathbf{A} \) can be calculated using the Cholesky decomposition. Indexes \( \alpha \) and \( \kappa \) determine the spread of sigma points around the mean state \( \mathbf{\bar{x}} \) and are usually defined as \( \alpha = 0.001 \) and \( \kappa = 1 \). Parameter \( \beta \) is used to determine the prior knowledge of the distribution of \( \mathbf{x} \), and for Gaussian distributions the optimal value is \( \beta = 2 \) (Wan and Van der Merwe 2000).

Similarly, as with other Kalman filter methods, the UKF utilizes an iterative prediction-update algorithm aiming to provide the best possible estimations. During the prediction process the algorithm takes advantage of the sigma points by propagating them through the nonlinear function \( \mathbf{x}_i = f(\mathbf{s}_i), i = 0, \ldots, 2L \) and calculates a weighted mean and covariance matrix for the \( k \) prediction step,
\[
\bar{x}_{k|k-1} = \sum_{i=0}^{2L} w_i^0 x_i
\]  
\[
P_{k|k-1} = \sum_{i=0}^{2L} w_i^0 (x_i - \bar{x}_{k|k-1}) (x_i - \bar{x}_{k|k-1})^T + Q.
\]  

Given the mean and error covariance matrix at the k prediction step, \( \bar{x}_{k|k-1} \) and \( P_{k|k-1} \), new sigma points propagate in the k update step through the observation function \( y_i = h(s_i), i = 0, \ldots, 2L \). Then the weighted mean and the covariance of the transformed points are calculated (Sarkka 2007)

\[
\bar{y} = \sum_{i=0}^{2L} w_i^0 y_i
\]  
\[
S_k = \sum_{i=0}^{2L} w_i^0 (y_i - \bar{y}) (y_i - \bar{y})^T + R.
\]  

In addition, the cross covariance and the Kalman gain matrices can be calculated,

\[
C_{sz} = \sum_{i=0}^{2L} w_i^0 (s_i - \bar{x}_{k|k-1}) (y_i - \bar{y})^T,
\]
\[
K_k = C_{sz} S_k^{-1}.
\]

Finally, the updated mean and error covariance matrix are derived:

\[
\bar{x}_{k|k} = \bar{x}_{k|k-1} + K_k (y_k - \bar{y}),
\]
\[
P_{k|k} = P_{k|k-1} - K_k S_k K_k^T.
\]

3. Results

3.1. Deterministic SEIHCRDV model and comparison with the conventional SEIRD model

In this section, we explore the dynamics of the above ODEs system (1) using the numerical method of 4th-order Runge-Kutta, which is a widely used numerical method for solving ODEs systems. For the purposes of this analysis, we consider the parameters of the model as constant. According to the above observations, let \( \sigma = 0.05 \), considering that the average protection rate from the vaccination is 95\% (Polack et al. 2020). Moreover, let \( \alpha = \frac{2}{11}, \psi = \frac{1}{186}, \omega = \frac{1}{14} \) and let \( \nu = 0.002 \) represent the mean vaccination rate. As the average time intervals of the transitions from the hospitalized to the recovered or the deceased state are 5 and 16 days, respectively, we set \( \kappa = \frac{1}{5} \) and \( \mu = \frac{1}{16} \) (Evensen et al. 2021). Similarly, the mean intervals between ICU admissions and the transitions to the recovered or deceased state are 8 and 15 days, respectively (Roquetaillade et al. 2021), while we deem the average transition rate between the hospitalized and ICU states as 0.1. As a result we set \( \tau = \frac{1}{8}, \rho = \frac{1}{15} \), while \( \lambda = 0.1 \). Based on Thompson et al. (2020) we can consider that the mean duration of the transitions from the infectious to the hospitalized state is 6.5 days, providing that \( \gamma = \frac{2}{13} \). In addition, Faes et al. (2020) state that in a study concerning 14,618 hospitalized patients in Belgium, the mean duration between the onset of symptoms and hospitalization was...
3 to 10.4 days, thus validating the selection $\gamma = \frac{2}{13}$. Finally, we also deem that the infection rate and the total population are constants, with $\beta = 1$ and $N = 100,000$.

The following simulated results are derived utilizing the model provided by system (2) with constant population, considering the impact of daily births compared to the daily mortality from non-COVID causes as negligible. In figure 2, we present the evolution of the pandemic according to the proposed SEIHCRDV model using the 4th-order Runge-Kutta method.

![Figure 2. Numerical solution of the proposed SEIHCRDV model using 4th-order Runge-Kutta algorithm](image)

We run the simulation for 400 days, using the abovementioned constant parameters. This simulation produces two waves of infection, where the first, most prevalent reaches its peak after 56 days and the second less severe after 265 days. Considering constant parameters, we restrict our model into providing a pandemic scenario, which does not take into account external measures, such as masks or lockdowns that suppress the spread of the disease. In addition, this assumption excludes cases like the emergence of COVID-19 variants, which may affect the rate of hospital or ICU admissions, as well as the death and recovery rates of infectious individuals.

The hospital and ICU admissions curves imitate the infection curve with a relatively short delay of 3 and 8 days, respectively, during the first most prevalent infection wave. We find similar behavior in the second wave. The cumulative recovery curve reaches its first peak after about 87 days, following the increasing trend of the infection curve, while the displayed decrease until day 240 is due to the transition from the recovered to the susceptible state, as we consider that the antibodies produced by an individual from the infection last up to 6 months (180 days) on average.

We also notice that the curve of deceased cases shows an increasing trend following the emergence of the two infection waves, displaying a much more intense increase during the first infection wave, as expected. Finally, the vaccination curve follows a rarely linear increasing trend, as we refer to the cumulative number of fully vaccinated individuals.

In figure 3, we observe the state evolution based on the conventional and widely-used SEIRD model, aiming to describe the characteristics of the pandemic using only five major states. The five diagrams that constitute figure 3, are constructed according to the numerical solution of the ODEs system of SEIRD model, using the 4th-order
Runge-Kutta algorithm. This examination helps us to realize the differentiations between the conventional SEIRD model and the proposed one in combination with the added value that accompanies the proposed SEIHCRDV model. In Table 2, we present the constant transition parameters for the implementation of the SEIRD and the proposed SEIHCRDV model.

**Table 2. Respective parameters for the conventional SEIRD and the proposed SEIHCRDV model**

|                  | $\alpha$ | $\beta$ | $\tau$ | $\rho$ | $\gamma$ | $\lambda$ | $\kappa$ | $\mu$ | $\psi$ | $\sigma$ | $\nu$ | $\omega$ |
|------------------|----------|---------|--------|--------|----------|-----------|----------|-------|--------|----------|-------|----------|
| SEIRD model      | $\frac{2}{11}$ | 1 | $\frac{1}{6}$ | $\frac{1}{15}$ | $-$ | $-$ | $-$ | $-$ | $-$ | $-$ | $-$ | $-$ |
| Proposed SEIHCRDV model | $\frac{2}{11}$ | 1 | $\frac{1}{8}$ | $\frac{1}{15}$ | $\frac{2}{13}$ | $\frac{1}{10}$ | $\frac{1}{5}$ | $\frac{1}{16}$ | $\frac{1}{180}$ | 0.05 | 0.002 | 1 | 14 |

The three extra differential equations included in our model provide a more detailed and realistic representation of the COVID-19 spread in the population, as we can explore the transfers of hospitalizations, ICU admissions and number of fully vaccinated people in a daily basis. Another interesting fact is that the widely used SEIRD model cannot cope with the emergence of more than one infection waves. In figure 3, there is only one infection wave that reaches its peak after 54 days, while the system reaches its equilibrium around day 100, thus indicating the end of the pandemic. On the other hand, our model produces additional waves of reduced intensity, a phenomenon that results from the potential reinfection of the recovered individuals. During the 400 days simulation, the curve of the recovered cases declines slightly after the appearance of the two prominent infection peaks.

**Figure 3.** Numerical solution of the conventional SEIRD model using 4th-order Runge-Kutta method
3.2 Impact of vaccination

An important question that can be investigated is how the various vaccination rates affect the evolution of the pandemic. In this paragraph, we variate the parameter $v$ corresponding to the vaccination rate over a time interval of 400 days of pandemic. In figure 4, we observe the fluctuations in the infectious cases, the hospital and ICU admissions and the cumulative number of deaths from day 1 to 400. In each graph, there are four curves produced according to vaccination rates $v = 0.002$, $v = 0.003$, $v = 0.004$ and $v = 0.005$, representing an increasing vaccination tendency.

![Figure 4. Infectious, deceased, hospitalized and ICU admissions curves, for increased vaccination rates](image)

By increasing the vaccination rate from $v = 0.002$ to $v = 0.005$, the number of infectious cases, hospitalizations, ICU admissions and deceased individuals, falls gradually revealing an inversely proportional relation between the increase in the number of fully vaccinated individuals and the spread of the pandemic through the affected population. The hospitalization and ICU admission curves follow the behavior of the infectious curve, a phenomenon that is highly expected, as the fewer the infectious cases, the less the hospital and ICU admissions.

An important observation is that the usage of a vaccination rate of $v = 0.005$, not only mitigates the first wave of COVID-19 spread, but almost extinguishes the second wave of the pandemic leading to a stabilization of the disease. Theoretically, this significant deterioration of the pandemic spread could be achieved through a daily relative raise of 1.5% in fully vaccinated cases, confirming the importance of applying a rapid vaccination process.

3.3 Impact of an increase in hospital and ICU admissions

Following the methodology mentioned in the paragraph of vaccination’s impact, we variate the parameter $\lambda$ that is responsible for the transition rate between the hospitalized and ICU states, as long as the rate of hospitalizations; these rates may be influenced by the prevalence of COVID’s variants like B.1.1.7, B.1.351 (Veneti et al. 2021) or B.1.617.2 (Kidd et al. 2021). More specifically, we utilized a $\lambda = 0.1$ for the creation of the initial timeseries of ICU admissions. Hence, we constructed three more curves by increasing the average transition rate by 0.1.
Concerning the hospitalization rate, the initial simulated timeseries is constructed using $\gamma = \frac{2}{13}$ derived from the average time interval from the emergence of symptoms to hospital admission. We aim to examine the pandemic evolution, when this average time interval decreases from 6.5 to 6, 5.5 and 5 days respectively. This procedure may help us examine the differentiation caused by a highly realistic alteration as there are many COVID-19 variants that significantly deteriorate the health of the infectious individuals, leading to intensified hospital and ICU admission rates. In Figure 5, we notice the differentiations concerning the hospitalized, ICU admitted, recovered and deceased cases.

![Figure 5. Infectious, ICU admitted, recovered, and deceased curves for increased hospital and ICU admission rates](image)

According to Figure 5, we observe the descending tendency of hospitalized cases, as we increased the transition rate from the hospitalized to ICU state more rapidly than the respective rate of hospitalizations. Furthermore, the higher levels of hospital and ICU admissions seem to result in significantly lower cumulative recovered cases, while the cumulative daily deceased cases reveal an inversely proportional behavior in comparison with the equivalent recovered cases.

### 3.4 Resistance of antibodies produced by infection

As mentioned earlier, the period of maintenance of the antibodies produced by the infection varies considerable between different individuals and is highly affected by the individual’s immune system as well as the COVID-19 variant that infected it. Hence, we investigate the impact of the re-infection period on the spread of the disease in the population. Figure 6 shows the evolution of infectious, recovered, deceased and vaccinated cases over a re-infection period of 3, 6, 9 and 12 months. According to the graphs, we conclude that longer re-infection periods result into a delay in the emergence of the second wave, while the number of recovered cases constantly increases. The resulting outcome concerning the evolution of vaccinated cases is interesting, as longer maintenance of antibodies seems to lead to reduced vaccination levels. We may deem that longer re-infection periods moderate the desire of people to be vaccinated as they feel protected by the antibodies of their immune system. However, the need for vaccination reappears for each of the examined four re-infection rates, shortly after the antibody levels have weakened.
Figure 6. The impact of the resistance of antibodies produced by infection

3.5 Comparison of UKF and EKF efficiency on simulated data

During this part of analysis, we investigate the predictive efficiency of the Extended Kalman Filter (EKF) and the Unscented Kalman Filter (UKF) algorithms based on the aforementioned simulated data generated using the 4th-order Runge-Kutta numerical solution. The purpose of this section is the identification of the actual states of our model at each time step, during a time interval of 400 days, when we add to the original data a Gaussian noise providing a stochastic equivalent of the proposed deterministic SEIHRCDV model.

We produce the necessary observations for the EKF and UKF models, by adding white noise of zero mean and standard deviation equal to the 10% of each original timeseries’ standard deviation, to the six observable timeseries produced by the Runge-Kutta numerical method. We do not examine the performance of UKF and EKF on the susceptible or the exposed cases, as these cases are usually considered as hidden states for the system in most articles dealing with combined epidemiological state-space models.
Figure 7. Actual simulated data produced by the 4th-order Runge-Kutta method for each of the six model’s observable states and the respective time series after the addition of the Gaussian noise.

The purpose of using EKF or UKF, is to efficiently eliminate the effect of noise that accompanies the above observations, to reveal the evolution of the true states; in addition, the comparison of these 2 methodologies will give us valuable inferences about their appropriateness in examining epidemiological models. In figure 7, we observe the filtering efficiency of EKF and UKF, especially in areas where noise-free timeseries display a relatively linear behavior.

The second goal of this section is to compare the efficiency of the Extended and the Unscented Kalman Filter on simulated data. As a result, we considered for both algorithms the same noise covariance matrices $Q$ and $R$, as well as the same initial state vectors, $x_0$, and the corresponding initial covariance matrix $P_0$, to ensure the comparability of the resulting estimations. In figure 8, we can visually compare the estimation capability of EKF and UKF on the simulated pandemic data. In Table 3 we present the RMSE values between the six examined timeseries produced by the proposed SEIHCRDV model, the noisy equivalent of these timeseries and the produced estimations of EKF and UKF. In all six cases, the filtering efficacy of UKF overcomes the EKF’s, while the widest difference is noticed for the recovered individuals. The EKF provides a greater overestimation of true infectious, hospitalized and ICU admitted cases compared to the UKF, during the emergence of the infection waves.
**Figure 8.** Examination of the filtering efficacy of EKF and UKF algorithms on simulated noisy data

**Table 3.** RMSEs for noisy data, EKF, UKF estimations and actual simulated data produced by the numerical solution of the proposed SEIHCRDV model

|            | Infectious | Hospitalized | ICU  | Recovered | Deceased | Vaccinated |
|------------|------------|--------------|------|-----------|----------|------------|
| Noisy Data | 317.61     | 129.77       | 67.28| 1683.66   | 720.14   | 541.65     |
| EKF        | 270.78     | 116.44       | 57.89| 916.84    | 215.73   | 151.06     |
| UKF        | 262.56     | 112.13       | 54.65| 858.50    | 200.52   | 138.53     |

3.6 **Evaluation of COVID-19 pandemic in France based on UKF with dynamic parameter estimation**

This section highlights the fitting and predictive capacity of the dynamic UKF algorithm based on the proposed SEIHCRDV model, applied to real daily COVID-19 observations in France. We explore the evolution of the pandemic in France from January 16 to October 7, 2021, providing a time interval of 265 days. We choose January 16 as the starting point for our analysis, as it is the first day that fully vaccinated cases have been recorded.

The fully vaccinated cases represent individuals who have received two doses of Pfizer or Astra Zeneca or one dose of Johnson & Johnson or Moderna vaccines. The observation data used, including infectious (active), hospitalized, ICU admitted, recovered, deceased and vaccinated cases, are collected from the datasets contained in the data.europa.eu webpage; a daily updated webpage that includes the official, daily COVID-19 observations for all European Union’s members that are collected from national resources.

The examined time period reveals two infection waves that reach their peak around day 80 (April 5) and 210 (August 15), while they are accompanied by respective waves of hospital and ICU admissions. The declining tendency of the first infection wave can be strongly influenced by the daily lockdowns imposed in 16 departments in France, while the curfew hours were shifted nationally between 7pm and 6am every day (March 20).
The appearance of the second wave around the first week of July (day 170) is highly related to the relaxation of the restrictive measures such as the re-opening of restaurants/bars/cafes with 50% capacity (June 9), the outdoor relaxation of mask-wearing (June 17) and the lifting of the night traffic ban (June 20). Another important factor for the second COVID-19 spread in France is the monitoring of the delta variant in the country, where according to G. Attal (2021), the highly contagious delta variant represents 40% of new COVID-19 infections.

Based on the results presented in figure 9, in addition to the first wave examined, the second wave of infection is also prevalent, while the corresponding waves of hospital and ICU admissions are significantly attenuated. This phenomenon shows the improvement of the French medical system against COVID-19, as the experience gained from previous infection waves helped the experts to understand more details about the characteristics of the disease leading to more targeted and effective treatment techniques. Moreover, the constantly increasing number of fully vaccinated cases plays a key role in the aforementioned phenomenon, since it reduces (figure 9) the likelihood of severe COVID-19 infections, leading to fewer hospitalizations and ICU admissions. At the same time, we observe an increase in the total number of deceased individuals but with a strongly declining trend, while the recovery rates are increasing along with the appearance of the two examined infection waves, indicating the more effective treatment of COVID-19 in new cases.

Figure 9. The evolution of infectious, hospitalized, ICU admissions, recovered, deceased and vaccinated cases during COVID-19 pandemic in France

After the first conclusions derived from the visual examination of Figure 9, we then investigate the fitting – predictive efficiency of the UKF applied to the daily COVID-19 observations in France. Specifically, we perform a
comparative analysis between an UKF algorithm based on the SEIHCRDV model with constant parameters, a dynamic EKF – SEIHCRDV and a dynamic UKF – SEIHCRDV model with 7 varying parameters that aim to describe more efficiently the dynamics characterizing the spread of COVID-19 in France, after the start of vaccinations. In figure 10, we present the fitting capacity of UKF and UKF with dynamic parameter estimation using the timeseries of infectious (active), hospitalized, ICU admitted, recovered, deceased and vaccinated cases in France. The most characteristic difference is that the standard UKF – with constant parameters – displays an underestimation of infectious cases especially during the two infection waves in April and August and a more intense overestimation in the respective number of hospital and ICU admissions, compared to the results derived from the dynamic UKF – SEIHCRDV model.

Figure 10. Performance comparison of UKF and the UKF with dynamic parameter estimation based on the proposed SEIHCRDV model, on the transmission states of COVID-19 in France; Infectious, Hospitalized, ICU admissions, Recovered, Deceased, Vaccinated
In parallel with figure 10, we present in Table 4 the respective normalized root mean squared errors (NRMSEs) of the numerical solution of the deterministic SEIHCRDV and the three abovementioned stochastic equivalents of UKF, EKF and UKF with dynamic parameter estimation. The presented NRMSE values are calculated according to the formula presented in (Papageorgiou and Tsaklidis 2021; Pal 2016). Both UKF, dynamic EKF and UKF significantly outperform the deterministic SEIHCRDV equivalent. Furthermore, the proposed UKF with dynamic parameter estimation provides the most accurate description of the pandemic evolution in France, rarely in all 6 observable states. In particular, the dynamic UKF – SEIHCRDV model produces 145.17%, 337.16%, 149.62%, 26.17% and 33.12% lower NRMSE values compared to UKF, and 24.41%, 286.71%, 44.83%, 18.32% and 19.88% compared to the dynamic EKF for the infectious (active), hospitalized, ICU admitted, recovered and deceased cases respectively.

|                  | Infectious | Hospitalized | ICU    | Recovered | Deceased | Vaccinated |
|------------------|------------|--------------|--------|-----------|----------|------------|
| Numerical        | 0.868560   | 0.960792     | 0.997148 | 0.967693  | 0.998600 | 0.846578   |
| UKF              | 0.214439   | 0.256795     | 0.098419 | 0.026397  | 0.092463 | 0.015045   |
| Dynamic EKF-SEIRD| 0.131866   | -            | -      | 0.024213  | 0.246692 | -          |
| Dynamic EKF-SEIHCRDV | 0.108814 | 0.227158     | 0.057104 | 0.024754  | 0.083265 | 0.015059   |
| Dynamic UKF-SEIHCRDV | 0.087466 | 0.058741     | 0.039427 | 0.020921  | 0.069456 | 0.015074   |

An important characteristic that verifies the robustness of the proposed dynamics of UKF – SEIHCRDV models is the monitoring of the parameter updates (Figure 11). First, the transmission rate $\beta$, follows the existence of the two infection waves that we observe within the period of 250 days, especially on the occasion of the second wave where the increase of rate $\beta$ and the number of infectious-active cases begin simultaneously. The transition parameters $\gamma$ and $\lambda$ display a relatively decreasing behavior during the evolution of the pandemic, which also seems to be in agreement with the observable timeseries. This phenomenon underlines the declining risk of COVID-19 infection as we proceed deeper into the period of vaccination.

Another notable observation is the descending trend of mortality rates $\mu$ and $\rho$ during the 250 days examined, where the mortality rate of hospitalized cases $\mu$ becomes lower than the mortality rate $\rho$ of ICU admissions – which is quite expected – as the total number of deceased cases increases with a descending trend (Figure 9) and the mortality probability of ICU cases is comparatively higher that the respective mortality of hospitalized cases. Finally, the behavior of the recovery rates $\kappa$ and $\tau$ validates the trustworthiness of our model, as both increase significantly over time, emphasizing the impact of vaccination and the adaptability of the national medical system of France to the challenges posed by this new virus. Hence, the hospitalization’s recovery rate $\kappa$ is displaying an ascending trend while constantly reaching higher levels during the 250 days in comparison with the ICU recovery rate $\tau$. In figure 12, we display the evolution of the effective reproduction number $R_t$ according to formula (25) presented in theorem 2, during the examined period of 250 days. According to this formula and the ability to dynamically calculate the parameters of model (2), we are able to estimate $R_t$ quite efficiently on a daily basis, providing a robust index concerning the spread of COVID-19.
Figure 11. Evolution of the 7 non-constant parameters of the model SEIHCRDV, that originate from the implementation of the dynamic UKF algorithm on daily data of France.

Figure 12. Evolution of the effective reproduction number during 250 days after the first reported fully vaccinated individuals.

Finally, we test the predictive efficiency of the proposed model on new observations. We use the NRMSE that constitutes a reliable indicator of the predictive ability of the model, as for values less than one the proposed model provides better estimations in comparison with the historic mean of the timeseries. In figure 13, we present the corresponding estimations of the dynamic SEIHCRDV-UKF model for 15 days ahead. All NRMSE values for the 6 observable states seem highly promising, as these values are quite close to zero, emphasizing the appropriateness of our model in describing and modelling real epidemic data.
More specifically, we achieve NRMSE values of 0.24756, 0.44588, 0.32585, 0.45927, 0.39823 and 0.18285 for the infectious, hospital and ICU admitted, recovered, deceased and vaccinated individuals, respectively. The higher NRMSE value corresponds to the recovered cases where the dynamic UKF – SEIHCRDV model displays a small overestimation as we move further into future states. This overestimation is influenced by the short underestimations in the hospitalized and ICU admitted cases, as these two states are linearly associated in the SEIHCRDV model with the recovered one. Hence, all 6 NRMSE values are much smaller than 1, leading to the conclusion that our model can efficiently handle the prediction of future states – even for half a month ahead – especially for the number of infectious cases, hospital – ICU admissions and deaths, which are the most important variables in assessing the severity of the pandemic.

![Graphs showing predictive efficiency of dynamic SEIHCRDV-UKF for half a month ahead](image)

**Figure 13.** Predictive efficiency of the dynamic SEIHCRDV-UKF for half a month ahead

4. Discussion

The new SARS-CoV-2 coronavirus, which has spread rapidly around the world, is causing serious problems for many national health systems. As a result, accurate understanding of the disease along with efficient prediction, can offer significant benefits in tackling and preventing this persistent life-threatening danger that continues to exacerbate the global economic situation. Usually, mathematical modelling of contagious diseases relies on
deterministic approaches, which often use a slight extension of the standard SIR model, by adding differential equations for the exposed and diseased cases. However, this deterministic approach fails to handle the complex dynamics of COVID-19, as the parameters of the models vary significantly in accordance with the introduction of health restrictive measures such as lockdowns and masks, or the constant emergence of variants. In addition, the existence of uncertainties in the reported data is justified by the asymptomatic infections, which are difficult to detect, and the false positive-negative ratio of the PCR test. Hence, we consider the establishment of a dynamic model that can manage these alterations.

In this paper, we introduce a novel, hybrid SEIHCRDV-UKF model with dynamic parameter estimation, aiming to address all the mentioned restrictions of the deterministic equivalent compartmental models while enhancing their predictive capacity dramatically. We extend the standard SIR model by increasing adequately the number of differential equations of the system to eight, taking into account exposed, hospital and ICU admitted, deceased and vaccinated cases. The inclusion of the hospital and ICU admitted states in the model has an additional major advantage. In the occasion of COVID-19 that is characterized by high percentages of asymptomatic individuals, the daily active and recovered reported cases could be deemed as low accuracy indices for the pandemic’s evolution. On the other hand, individuals admitted to hospital and ICUs are tested thoroughly for COVID infection, rendering the daily observations of these two states the most trustworthy data for the validation of the fitting-predictive ability of the proposed model.

The additional states that we have included in the classic SEIR model, leading to the extended compartmental version proposed in this article, have been selected with significant care aiming to encompass only states with available daily observations. Except from the states of susceptible and exposed, for the remaining 6 states that take place in our model, there are valuable available observations in a daily basis, that we efficiently deploy providing supplementary information to our epidemiological model while enhancing significantly its fitting and predictive capacity.

Furthermore, the UKF methodology deploys the daily reported observations for a more drastic treatment of the constant parameter variation, leading to a stochastic approach. The inclusion of model’s parameters in the estimation-updating of the filtering process helps us to follow the alterations in pandemics. The presented results of the fitting and prediction of the disease’s spread in France – even for half a month ahead – confirm the trustworthiness of our model.

We argue that this stochastic approach is necessary, as errors in the daily reported observations are known, and the encapsulation of all possible transitions of the pandemic would lead to a very complex model, making the process computationally expensive and the fitting-predictive performance unreliable. For example, transitions characterized by negligible rates, such as the transition from infection directly to ICU admission or from infection directly to death, are included in the system’s additive noise. The parameter initialization process in non-linear methodologies should be performed with great care. Dynamic parameter estimation addresses this necessity effectively, enhancing the trustworthiness of our model.

The simulations performed in the results section, help us to notice the differences between our SEIHCRDV and the frequently used SEIRD model. They also help us understand the severity of certain important parameters such as the re-infection rate or the increased ICU admission and deceased rate introduced by some variants, while our simulations validate the effectiveness of vaccination against the unwanted effects of COVID-19. Even a small increase in the vaccination rate would be of great benefit to the control of the coronavirus, while the effects of the vaccination are noticeable during the two infection waves of the period under consideration in France.

The theoretical analysis based on the proposed SEIHCRDV model, results into the revelation of valuable conclusions about the spread of the pandemic. The derived formula for $R_0$ provides a more representative image concerning the spread of pandemic, while we gain important conclusions about its evolution based on the value of $R_0$. According to previously mentioned studies, COVID’s $R_0$ is much higher than 1, and its value can be reduced only with decisive interferences such as lockdowns. Given this situation – at least for the foreseeable future – we should emphasize the deterioration of the heavily infectious and deceased rates, as the limitation of the disease’s contagiousness seems quite challenging so far, revealing once again the importance of full vaccination in the population.

The presented methodology can be easily applied to many other already existed or novel epidemics like ebola, influenza, yellow fever etc., as the proposed states and transitions are representative for most of them. At the same time, this methodology is ideal in cases where both the dynamics of the system and the corresponding observations
in real time cannot accurately capture the spread of an epidemic due to uncertainties, aiming to eliminate the noises affecting the evolution of the states and the observations.

5. Conclusion

This article establishes a novel hybrid SEIHCRDV-UKF epidemiological model with dynamic parameter estimation that takes into account the populations of susceptible, exposed, infectious, hospitalized, ICU admitted, recovered, deceased and vaccinated cases, providing trustworthy fitting and prediction, even for half a month ahead. We note that this new consideration could be useful for examining other pandemics too. The state-space augmentation that encapsulates seven time-varying parameters in the updating procedure provides a much more reliable description of the spread of the pandemic in France, for a long-time interval of 265 days. The emergence of two infection waves in this period reflects more challenging dynamics; nevertheless, our model is able to deal with the challenging dynamics successfully, due to the real time parameter estimation.

The mathematical analysis performed according to the novel compartmental model, offers valuable results and conclusions about the nature of the pandemic. The construction of a more representative basic and effective reproductive number will also be a helpful aid in predicting and preventing outbreaks of infection, while the exploration of equilibriums and their stability informs us of the nature of the disease. Finally, the simulations provided in our paper, help us to monitor the severity of an increased re-infection or ICU admission rate, and reveal the importance of COVID-19 vaccination.

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Availability of data and material: The data is included in an online repository
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