

# Extended COVID-19 Models

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## Abstract

The paper discusses how to extend the SEICUR model with a description of migration. Next, the SEICUR model is extended with a description of age distribution, for the case that infection and serious illness depends on age. Finally, the SEICUR model is extended with models of vaccination. Simulation of the SEICUR model for Italy and Spain indicated that the number of migrants per day between the two countries need to be relatively large before a significant change in infection is noticed. However, this was based on the assumption of average spreaders among the migrants. The age distribution model is mainly of use when considering serious illness and death, and was not pursued further. Vaccination data for Italy, Spain, and Norway, shows that for countries with a low fraction of infected (e.g., Norway), vaccination allows for a noticeable relaxation in mitigation, while for countries which already have a high fraction of infected (e.g., Spain), the effect of vaccination is relatively smaller due to the larger fraction of people already recovered. The extended models allow for a more realistic study of COVID-19 spread, and how to optimize mitigation policies vs. vaccination.

*Keywords: COVID-19 models, deterministic models, complex models, vaccination policy*

## 1 Introduction

### 1.1 Background

The COVID-19<sup>1</sup> pandemic spreading in 2020 initially caused fear, irrational hoarding of consumer goods, uncertainty about future food supply, and economic depression, but also spawned a renewed interest in epidemiology to understand how infections spread, and a massive effort in development of virus medicine and vaccines. Policy making and society saw challenges hardly faced before on how to adapt to the development in real time.

More than one year after the pandemic outbreak in February/March 2020, fitted epidemic macro models are becoming more reliable due to large amounts of data, and vaccination is well underway in some countries. Still, for accurate mitigation policy, the models have shortcomings. Current mitigation models have poor description of seasonal variations, genetic/health variations, cultural variations, and demographic variations. In addition, relations

<sup>1</sup>COVID-19 is the Corona Virus Disease originating in 2019. The World Health Organization and Wikipedia.com both appear to write COVID-19 in all caps.

between infection, treatment, and death is lacking in understanding.

Spreading by migration is clearly important, with travel restrictions and lock-downs being key instruments in taming infection spread. Data from the past year has shown that age distribution is an important determining factor for serious illness/death. Data from Europe and USA indicate that a combination of genetics, nutrition, health care, culture, and living conditions put some groups more at risk. But seasonal variation in temperature, solar irradiation, humidity, etc. also plays an important role, whether this is directly by influencing infection rates, or indirectly by keeping people more outdoor and therefore reducing infection rates.

In Europe, the initial spread in the winter/spring of 2020 saw a dramatic reduction starting in late May/June 2020, and lasting until late September 2020. Most likely, this was a combination of improved hygiene and some social distancing. But it is almost certain that there also was a seasonal element in this reduction. The winter/spring of 2021 has been marked by vigorous vaccination in Europe and North America, and again: the number of infected is going down.

Both for COVID-19 and for future epidemics, it is of interest to study how extended infection models can be developed.

### 1.2 Previous work

Classical epidemiology models were developed in the decade following the “Spanish Flu”. A renewed *public* interest in epidemic models started with the AIDS/HIV epidemic some decades ago; these models have been used to study other infectious diseases, e.g., (Brauer et al., 2019). (Lie, 2021a) gives a brief overview of such general models from a process engineering point of view.

Many COVID-19 models are available on the internet, e.g., from the *IHME COVID-19 Forecasting Team*<sup>2</sup>, see (Reiner et al., 2021)<sup>3</sup>. (Zlojutro et al., 2019) give a general framework for reducing spread via migration. Early work at Imperial College London<sup>4</sup> was important in stressing the importance of mitigation policy. Some relatively complete *macro* models include that of (López and Rodó,

<sup>2</sup>The Institute for Health Metrics and Evaluation (IHME) is an independent global health research center at the University of Washington

<sup>3</sup><https://covid19.healthdata.org/united-states-of-america?view=cumulative-deaths&tab=trend>

<sup>4</sup><https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/covid-19-planning-tools/>

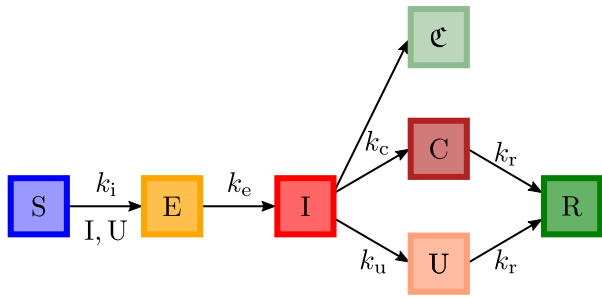


Figure 1. Flow of SEICUR reactions.

2020), (Liu et al., 2020b,a,c), (Øyvann, 2020), and others. (Lie, 2021b) gives an overview of how to fit the SEIRU (SEICUR) model to cumulative confirmed infected data, with applications to Italy, Spain, and Norway.

### 1.3 Scope

Here, the focus is on extending a model from (Lie, 2021b) to be (i) more general, and (ii) more useful. Extensions relate to network models/distributed models, and to age dependent models. Network models can also be used to study the effect of migration/tourism. A further extension is the effect of vaccination. By combining vaccination rates and mitigation policy, control engineering may suggest an “optimal” return to normalcy

In Section 2, the SEICUR model is extended with migration terms, and with age distribution. Some simple models of vaccination are proposed. In Section 3, the SEICUR model is studied with migration between some countries, and with vaccination. In Section 4, the results are discussed, and some conclusions are drawn.

All computations in the paper are carried out using language Julia, with packages `DifferentialEquations.jl` for solving models, (Rackauckas and Nie, 2017a), (Rackauckas and Nie, 2017b), (Rackauckas and Nie, 2018), `BlackBoxOptim.jl` for fitting mitigation policy, and `Plots.jl` for plotting results.

## 2 Materials and Methods

### 2.1 Reaction mechanism

A SEIR model with the I population extended to (I,C,U) was proposed for COVID-19 in (Liu et al., 2020b; Lie, 2021b) Figure 1.

The above, proposed mechanism implies that *susceptibles* S are infected by some “pre-infected” I and the non-quarantined *unconfirmed* U leading to the *exposed* phase E, which is infected but not yet infectious. These exposed E then are converted to the “pre-infected” I class, which then either become more serious cases and are *confirmed* infected C, or stay as *unconfirmed* U. Finally, the confirmed infected and the unconfirmed end up in the *recovered* population R (which includes those who die). We will refer to this model as the SEICUR model.

For class X, let X denote the number of people in that

class, and  $\check{X}$  the number of people per capita. The following mechanism describes the reactions; :

$$\begin{aligned} \mathcal{E}_i : S &\xrightarrow{I+U k_i} E, & r_i &= k_i (\check{I} + \check{U}) \check{S} \\ \mathcal{E}_e : E &\xrightarrow{k_e} I, & r_e &= k_e \check{E} \\ \mathcal{E}_c : I &\xrightarrow{k_c} C, & r_c &= k_c \check{I} \\ \mathcal{E}_u : I &\xrightarrow{k_u} U, & r_u &= k_u \check{I} \\ \mathcal{E}_{cr} : C &\xrightarrow{k_r} R, & r_{cr} &= k_r \check{C} \\ \mathcal{E}_{ur} : U &\xrightarrow{k_r} R, & r_{ur} &= k_r \check{U}. \end{aligned}$$

We introduce

$$\begin{aligned} k_{cu} &= k_c + k_u \\ k_c &= \eta k_{cu}. \end{aligned}$$

Thus, specifying  $k_{cu}$  and  $\eta$ , we can find

$$\begin{aligned} k_c &= \eta k_{cu} \\ k_u &= (1 - \eta) k_{cu}. \end{aligned}$$

(Lie, 2021b) details how to fit the model to cumulative confirmed infection cases, and how to find initial states.

### 2.2 Migration

We consider the response in infection when compartments open up for migration exchange at rate  $\dot{N}$  people per day. With  $X_i$  denoting a general population state,  $X_i \in (S, E, I, C, U, R)$ , the emigration rate of class  $X_i$  is

$$\dot{X}_i^e = \dot{N} \check{X}_i = \dot{N} \cdot X_i / N$$

where we have assumed homogeneous mixing of the population. The balance equation for class  $X_i$  with constant population  $N$  is then

$$\frac{dX_i}{dt} = \dot{X}_i^i - \dot{X}_i^e + N \left( v^T r \right)_i$$

where  $v$  is the *stoichiometric matrix*, (Lie, 2021a), and  $r$  is the vector of rates of reaction for the events, (Lie, 2021a,b). For a constant population  $N = \sum_i X_i$ , it is required that  $\sum_i \dot{X}_i^i = \sum_i \dot{X}_i^e$ .

Without loss of generality, consider two compartments, each with constant populations  $N_1$  and  $N_2$ , which have open borders with migration rate  $\dot{N}$  between each other and closed borders to every other compartment. Neglecting the possibility of people staying on the border, it follows that we must require

$$\dot{X}_{i,1}^i = \dot{X}_{i,2}^e;$$

the number of people per day of class  $i$  immigrating to compartment 1 must equal the number of people per day of class  $i$  emigrating from compartment 2.

If we also include a model for equivalent mitigation policy as in (Lie, 2021b), the SEICUR model for compartment  $j \in \{1, 2\}$  is then

$$\begin{aligned} \frac{dS_j}{dt} &= \dot{N} \left( \frac{S_{\bar{j}}}{N_{\bar{j}}} - \frac{S_j}{N_j} \right) - k_i^{0,j} x_{fm}^j (I_j + U_j) S_j / N_j \\ \frac{dE_j}{dt} &= \dot{N} \left( \frac{E_{\bar{j}}}{N_{\bar{j}}} - \frac{E_j}{N_j} \right) + k_i^{0,j} x_{fm}^j (I_j + U_j) S_j / N_j - k_e E_j \\ \frac{dI_j}{dt} &= \dot{N} \left( \frac{I_{\bar{j}}}{N_{\bar{j}}} - \frac{I_j}{N_j} \right) + k_e E_j - k_{cu} I_j \\ \frac{dC_j}{dt} &= k_c I_j - k_r C_j \\ \frac{dU_j}{dt} &= \dot{N} \left( \frac{U_{\bar{j}}}{N_{\bar{j}}} - \frac{U_j}{N_j} \right) + k_a I_j - k_r U_j \\ \frac{dR_j}{dt} &= \dot{N} \left( \frac{R_{\bar{j}}}{N_{\bar{j}}} - \frac{R_j}{N_j} \right) + k_r (C_j + U_j) \\ \frac{dx_{fm}^j}{dt} &= \frac{1}{T_{fm}^j} (u_{fm}^j - x_{fm}^j) \end{aligned}$$

Here,  $\bar{j}$  denotes the complement of  $j$ , i.e., if  $j = 1$ , then  $\bar{j} = 2$ , and vice versa. In the model above, it has been assumed that the confirmed infected are quarantined, and are not allowed to travel. Furthermore, it has been assumed that model parameters  $k_e$ ,  $k_{cu}$ ,  $k_a$ , and  $k_r$  are independent of the compartment.

### 2.3 Demographic distribution

Most likely, infection rates, severity of infection, and recovery time vary with demographic distribution of the population. Here, we focus on age distribution. Description of demographic distribution is mainly of interest when the model is extended with a distribution in the severity of infections, such as a separate class for the number of deaths.

Without loss of generality, suppose we divide the population into a young population of  $N_y$  people with SEICUR members  $S_y, E_y, I_y, C_y, U_y$ , and  $R_y$ , and an old population of  $N_o = N - N_y$  people with members  $S_o, E_o, I_o, C_o, U_o, R_o$ . For simplicity, assume both  $N$  and  $N_y = \gamma N$  are constant, with  $\gamma$  being the fraction of young.

We assume that young people are infected at equal rate  $k_i^y$  when meeting either young or old infected, and that old people are infected at equal rate  $k_i^o$  when meeting either young or old infected. Similarly, we assume that young and old recover at rates  $k_r^y$  and  $k_r^o$ , respectively. Furthermore, we assume that people become confirmed and unconfirmed infected at rates  $k_c^y, k_u^y$  and  $k_c^o, k_u^o$ , respectively.

Relative to the rates in Section 2.1, for simplicity we assume that young infected  $I_y, U_y$  and old infected  $I_o, U_o$  infect the young susceptibles at equal rate. The same assumption is made for the old susceptibles, but the infection rate constants may differ. Thus, with  $I = I_y + I_o$  and  $U = U_y + U_o$ , this implies that the infection rates are,  $j \in \{y, o\}$  :

$$r_1^j = k_1^j (I + U) S_j / N^2.$$

The other rates remain as in Section 2.1. In the rate expression  $N \cdot r_1^j$ , we need to use the full population if we assume that the mixture of young and old population is perfectly homogeneous.

Finally, we need to take into account that people are born at a rate  $\dot{N}_b$  and die at a rate  $\dot{N}_d$ ; for a constant population,  $\dot{N}_d = \dot{N}_b$ . This means that people are transferred from young to old at a rate  $\dot{N}_b$ . For young people ( $j = y$ ), we have

$$\dot{S}_y^b = \dot{N}_b;$$

people are born as young, and all are assumed to be susceptible at birth. Similarly, the susceptible “die”, or rather age from young to old, as

$$\dot{S}_y^d = \dot{N}_b \frac{S_y}{N_y}.$$

Note that we need to use the number of young susceptibles per young population here, i.e., the correct fraction is  $\frac{S_y}{N_y}$ . For all other classes in the SEICUR model,  $\dot{X}_y^b \in \{\dot{E}_y^b, \dot{I}_y^b, \dot{C}_y^b, \dot{U}_y^b, \dot{R}_y^b\}$ , it follows that

$$\dot{X}_y^b \equiv 0.$$

Ageing from “dying” young into “born” old implies

$$\begin{aligned} \dot{E}_y^d &= \dot{N}_b \frac{E_y}{N_y} = \dot{E}_o^b \\ \dot{I}_y^d &= \dot{N}_b \frac{I_y}{N_y} = \dot{I}_o^b \\ \dot{C}_y^d &= \dot{N}_b \frac{C_y}{N_y} = \dot{C}_o^b \\ \dot{U}_y^d &= \dot{N}_b \frac{U_y}{N_y} = \dot{U}_o^b \\ \dot{R}_y^d &= \dot{N}_b \frac{R_y}{N_y} = \dot{R}_o^b. \end{aligned}$$

Old people die out of their classes at rates due to ageing:

$$\begin{aligned} \dot{S}_o^d &= \dot{N}_b \frac{S_o}{N_o} \\ \dot{E}_o^d &= \dot{N}_b \frac{E_o}{N_o}, \\ \dot{I}_o^d &= \dot{N}_b \frac{I_o}{N_o} \\ \dot{C}_o^d &= \dot{N}_b \frac{C_o}{N_o} \\ \dot{U}_o^d &= \dot{N}_b \frac{U_o}{N_o} \\ \dot{R}_o^d &= \dot{N}_b \frac{R_o}{N_o}. \end{aligned}$$

For  $j \in \{y, o\}$ , we thus have

$$\begin{aligned} \frac{dS_j}{dt} &= S_j^b - S_j^d - k_i^j (I + U) S_j / N \\ \frac{dE_j}{dt} &= E_j^b - E_j^d + k_i^j (I + U) S_j / N - k_e^j E_j \\ \frac{dI_j}{dt} &= I_j^b - I_j^d + k_e^j E_j - k_{cu}^j I_j \\ \frac{dC_j}{dt} &= C_j^b - C_j^d + k_{cu}^j I_j - k_r^j C_j \\ \frac{dU_j}{dt} &= U_j^b - U_j^d + k_u^j I_j - k_r^j U_j \\ \frac{dR_j}{dt} &= R_j^b - R_j^d + k_r^j (C_j + U_j) \end{aligned}$$

where we have used that  $N(r_c^j + r_u^j) = (k_c^j + k_u^j) I_j = k_{cu}^j I_j$ . Here,  $N_o = N - N_y = (1 - \gamma) N$ .

To take advantage of this demographic extension of the SEICUR model, it is really necessary to extend the model and split the recovered class into those surviving, and those dying. This extension is relatively straightforward, but is not pursued here, since it requires fitting this extended model to additional data of cumulative deaths.

## 2.4 Extinction of COVID-19

### 2.4.1 Herd immunity

So-called *herd immunity* is reached when there are too few susceptible left to drive the infection growth. Just before herd immunity is reached, the infection rate increases dramatically, before dying out. When herd immunity is reached, a large fraction of the population will have become recovered; in the SEICUR model, the class of recovered includes those who die.

Some researchers and politicians have suggested that one should let COVID-19 go its natural course, and aim for herd immunity. The alternative is to impose mitigation policies to reduce the number of infected at any time, while waiting for vaccines.

Clearly, aiming for herd immunity with no mitigation would have put an end to COVID-19 relatively quickly. However, the number of seriously ill from the infection would have completely overwhelmed the hospital system, leading to a high fraction of deaths among the infected. Aiming for herd immunity has rarely been an explicit policy, but a few countries have at times lost control of the infection growth, with near collapse in the health system. The main idea behind a mitigation policy is to attempt to keep the number of seriously infected at any time within the capacity of the health system and thus minimize the number of deaths.

### 2.4.2 Vaccination

Let  $V$  denote the class of vaccinated, and let  $\dot{V}$  denote the vaccination rate for a compartment. We will assume that only susceptible  $S$  are vaccinated.

**Crude model** In a *crude* vaccination model, we assume that vaccinated *immediately* become recovered, with efficacy  $\eta$ . For the SEICUR model, vaccination only changes the expressions for  $S$  and  $R$ , which become

$$\begin{aligned} \frac{dS}{dt} &= -\eta \dot{V} - k_i (I + U) S / N \\ \frac{dR}{dt} &= \eta \dot{V} + k_r (C + U). \end{aligned}$$

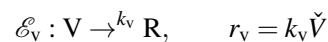
**Semi-crude model** A *slightly less crude* model could utilize that it takes a certain time interval  $\tau_v$  before good vaccine protection is achieved, and then operate with a *filtered* vaccination rate

$$\frac{d\dot{V}_f}{dt} = \frac{1}{\tau_v} (\dot{V} - \dot{V}_f)$$

with expressions for  $S$  and  $R$  now becoming

$$\begin{aligned} \frac{dS}{dt} &= -\eta \dot{V}_f - k_i (I + U) S / N \\ \frac{dR}{dt} &= \eta \dot{V}_f + k_r (C + U). \end{aligned}$$

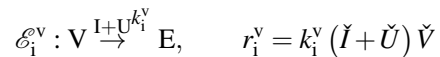
**Mechanistic model** In a more *realistic* mechanistic vaccination model, vaccinated are still partially susceptible, and it takes a certain time  $\tau_v$  before full vaccination is achieved. This transformation of vaccinated into recovered can be described by the reaction



with  $k_v = 1/\tau_v$ . The number of recovered is then modified to

$$\frac{dR}{dt} = k_v V + k_r (C + U).$$

The vaccinated population  $V$  will still be susceptible, but with a relatively low average infection rate over the time constant  $\tau_v$ . This implies that there will be an additional infection reaction



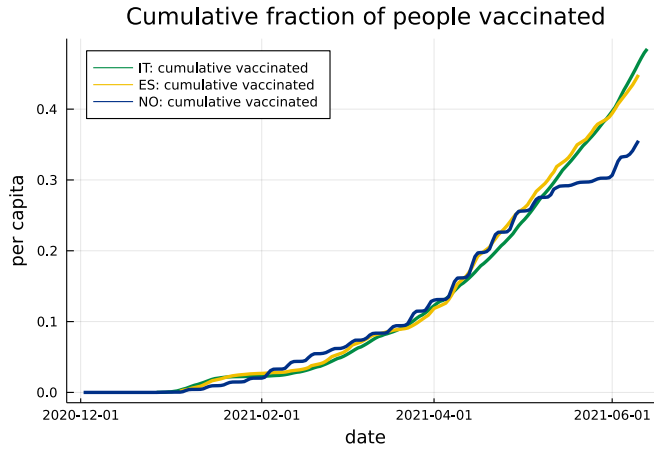
where  $k_i^v$  is considerably smaller than  $k_i$  for an efficient vaccine. The total expression for  $V$  is then

$$\begin{aligned} \frac{dV}{dt} &= \dot{V} - N \cdot r_v - N \cdot r_i^v \\ &\Downarrow \\ \frac{dV}{dt} &= \dot{V} - k_v V - k_i^v (I + U) V / N. \end{aligned}$$

The expressions for the number of exposed  $E$  becomes

$$\frac{dE}{dt} = k_i (I + U) S / N + k_i^v (I + U) V / N - k_e E.$$

The remainder of the model is as before.



**Figure 2.** Cumulative fraction of people that have received at least one vaccine dose vs. time (IT = Italy, ES = Spain, NO = Norway; line color refers to a key color in national flags).

The efficacy  $\eta$  is now determined indirectly by  $k_1^V$ . One possible definition of the efficacy is unity minus the fraction of the rate at which vaccinated get infected, and the rate at which susceptible get infected,

$$\eta = 1 - \frac{k_1^V(I+U)V/N}{k_1(I+U)S/N} = 1 - \frac{k_1^V V}{k_1 S}.$$

We assume an efficient vaccine, so that in steady state,  $|\dot{V} - k_v V| \gg k_1^V(I+U)V/N$ , thus  $dV/dt \rightarrow 0$  leads to

$$V = \frac{1}{k_v} \dot{V} = \tau_v \dot{V}.$$

Then, approximately,

$$k_1^V = (1 - \eta) k_1 \frac{S}{\tau_v \dot{V}}.$$

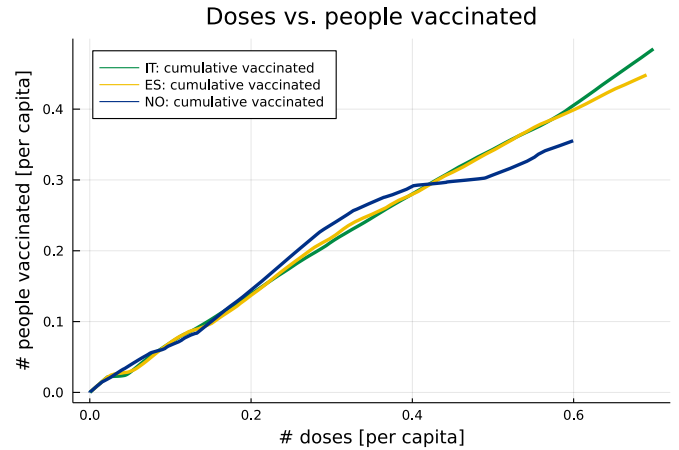
This expression is not entirely satisfactory, as  $k_1^V$  depends on the remaining number of susceptible  $S$  and the vaccination rate  $\dot{V}$ . A simpler expression is

$$k_1^V = (1 - \eta) k_1.$$

**Vaccination rate** Figure 2 shows the cumulative number of *people* having received at least one vaccine dose (per capita) in Italy, Spain, and Norway. The ripples in the data are due to slower vaccination in week-ends.

Figure 3 shows the *actual* cumulative fraction of administered *doses* vs. the cumulative fraction of *people* receiving at least one vaccine dose, for Italy, Spain, and Norway.

Efficacy varies with vaccine types, where mRNA based vaccines (e.g., those of Pfizer and Moderna) seem to provide 95+% efficacy, while vector based vaccines (e.g., AstraZeneca, Sputnik, etc.) seem to provide in the range 50-85% efficacy. These numbers have been reduced with the emergence of more aggressive mutations such as the Delta variant.



**Figure 3.** Cumulative fraction of doses vs. people that have received at least one vaccine dose (IT = Italy, ES = Spain, NO = Norway; line color refers to a key color in national flags).

Typically, full vaccination is assumed 1–3 weeks after the final dose; for most vaccines, two doses are required. In Norway, initially, two dose vaccines were given with 3 week intervals. Then this was changed to 4 weeks, then to 6 weeks, then to 12 weeks, then moved back to 9 weeks, etc. Thus,  $\tau_v$  may vary with time to some degree.

#### 2.4.3 Qualitative effect of mitigation + vaccination

Initial requirement for stability for the disease-free case is that the basic reproduction number is less than unity,  $R_0 < 1$ , (Lie, 2021a,b). This requirement is based on the assumption that the entire population is susceptible, i.e., that  $\check{S}(0) = S(0)/N = 1$ . If the infection dies out, and then is in the process of re-starting, the requirement for stability is that  $\check{S}(0)R < 0$ . Here, it should be noted that  $R \propto k_1$ , the infection rate constant, where  $k_1 = k_1^0 \cdot u_{fm}$  in the steady state of the mitigation policy;  $k_1^0$  is the infection rate constant *without* mitigation, and  $u_{fm} \in [0, 1]$  is the equivalent mitigation policy which depends on seasonal variations, etc. Thus,  $R = R_0 u_{fm}$ , and the infection is kept under control when

$$\check{S}(0) R_0^0 u_{fm} < 1.$$

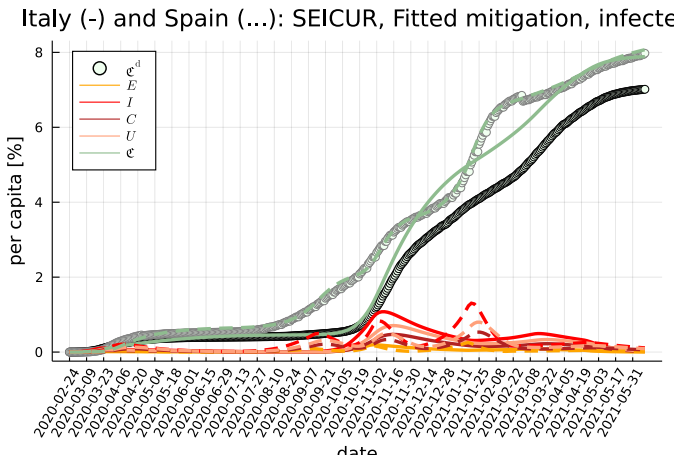
It follows that with  $\check{S}(0) = 1$ , the equivalent mitigation policy  $u_{fm}$  must be chosen such that

$$u_{fm} \leq 1/R_0^0.$$

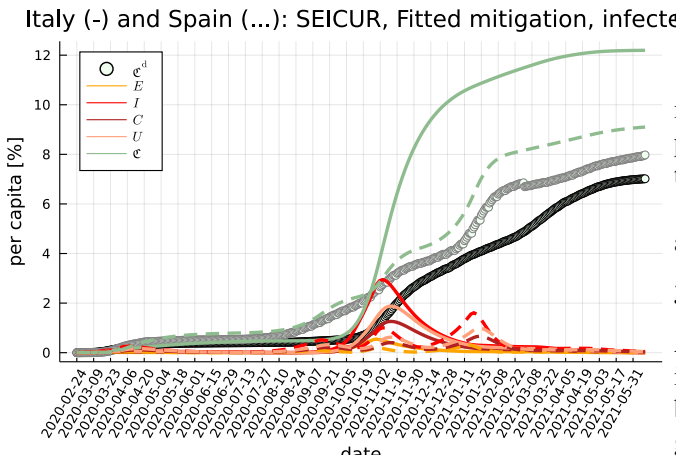
Some initial estimates of  $R_0^0$  from March 2020 suggested that  $R_0^0 \in [2.2, 2.7]$  or so<sup>5</sup>. Some of the more recent virus mutations (British, South-African, Indian) are more infectious, with the Delta mutant having  $R_0 = 6$  or even higher. This could indicate that  $R_0^0$  is as a minimum  $R_0^0 = 5$  at the moment, leading to the requirement that  $u_{fm} \leq 0.2$ .

The effect of vaccination, on the other hand, is essentially to reduce  $\check{S}(0)$ . It follows that to go back to the normal, pre-COVID-19 situation with  $u_{fm} = 1$ , we need to

<sup>5</sup>Early estimates from China indicated values up to 4 or 5.



**Figure 4.** SEICUR models for Italy (solid) and Spain (dotted) with fitted mitigation, and with  $\dot{N} = 10^4$  persons/day exchange rate.



**Figure 5.** SEICUR models for Italy (solid) and Spain (dotted) with fitted mitigation, and with  $\dot{N} = 10^5$  persons/day exchange rate.

reduce  $\check{S}(0)$  to  $\check{S}(0) \leq 0.2$ , which implies that 80% of the population must be vaccinated.

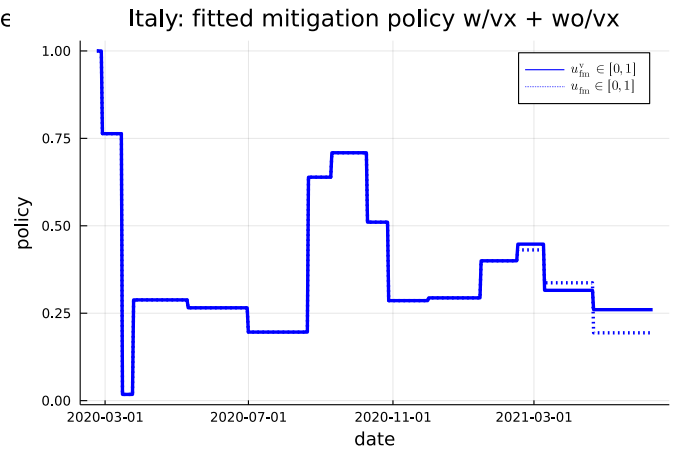
Because the most vulnerable, those that have a high risk of dying, probably are vaccinated early, society may function more or less as normal with fewer than 80% vaccinated — but must then accept that there is a certain number of infected at any time.

### 3 Results

#### 3.1 Migration

Figures 4 and 5 display resulting change in infections caused by migration between Italy and Spain when these countries are assumed closed for other countries, first with  $\dot{N} = 10^4$  persons/day, Figure 4, and with  $\dot{N} = 10^5$  persons/day, Figure 5.

The results in Figs. 4, 5 indicate that migration needs to be considerable to give an effect. The results should be used with caution, though: (i) data used in equivalent mitigation policy fitting already has some interaction with



**Figure 6.** Fitted equivalent mitigation policy  $u_{fm}^v$  for Italy based on SEICUR model *extended* with *semi-crude* vaccination model, compared to fitted equivalent mitigation policy  $u_{fm}$  based on the pure SEICUR model (Lie, 2021b). Vaccine is administered according to Figure 2.

multiple countries, and (ii) “super-spreaders” (in densely populated bars, discoteques, ...) are perhaps more likely to migrate than average spreaders.

The idea of interaction between countries as indicated above, is the basis for *network models*.

#### 3.2 Herd immunity

Although not shown here, using the fitted mitigation policy for Italy for the period February 2020 – late October 2020, and making forecasts while keeping the mitigation policy at the level of late October 2020 into the future, those forecasts indicated that Italy would have reached herd immunity before Christmas 2020. The consequence would have been a health system with considerably higher strain than in April 2020. Italy introduced restrictions/lock-downs ca. October/November 2020 which reduced the infection spread sufficiently to avoid this situation, see (Lie, 2021b).

#### 3.3 Vaccination

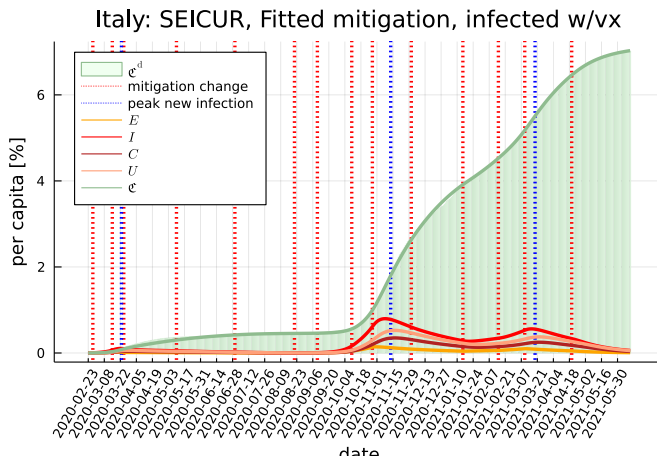
Here, we consider the simplified case of (i) use of the fitted mitigation policy, (ii) use of the “semi-crude” vaccination model with  $\eta_v = 0.8$  and  $\tau_v = 28$  d, and (iii) actual vaccination rates.

The resulting equivalent mitigation policy for Italy *with* vaccination,  $u_{fm}^v$ , vs. *without* vaccination,  $u_{fm}$ , is displayed in Figure 6.  $u_{fm}^v$  is the *real* equivalent policy, while  $u_{fm}$  is a hypothetical policy when neglecting vaccination.

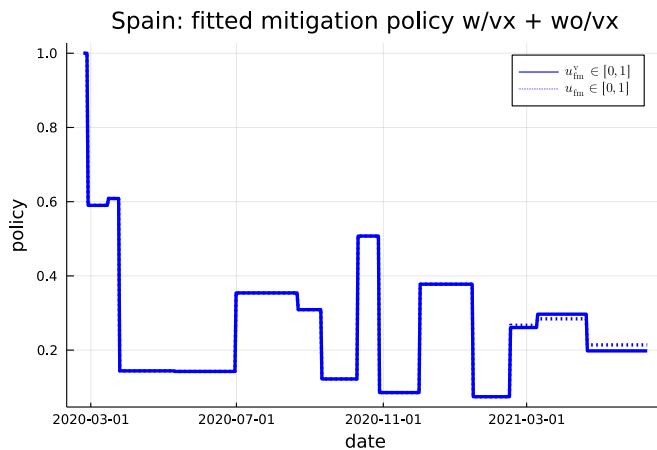
The resulting equivalent mitigation policy for Spain *with* vaccination,  $u_{fm}^v$ , vs. *without* vaccination,  $u_{fm}$ , is displayed in Figure 8.

The resulting equivalent mitigation policy for Norway *with* vaccination,  $u_{fm}^v$ , vs. *without* vaccination,  $u_{fm}$ , is displayed in Figure 9.

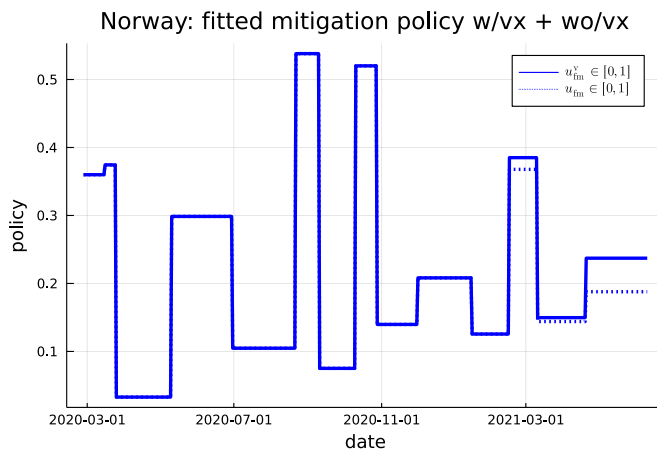
For all countries, the model fit to the cumulative number of confirmed cases (Lie, 2021b) is just as good whether



**Figure 7.** SEICUR model extended with vaccination model, simulation with fitted mitigation policy  $u_{fm}^v$  as in Figure 6. Vaccine is administered according to Figure 2.



**Figure 8.** Fitted equivalent mitigation policy  $u_{fm}^v$  for Spain based on SEICUR model extended with semi-crude vaccination model, compared to fitted equivalent mitigation policy  $u_{fm}$  based on the pure SEICUR model ((Lie, 2021b)). Vaccine is administered according to Figure 2.



**Figure 9.** Fitted equivalent mitigation policy  $u_{fm}^v$  for Norway based on SEICUR model extended with semi-crude vaccination model, compared to fitted equivalent mitigation policy  $u_{fm}$  based on the pure SEICUR model ((Lie, 2021b)). Vaccine is administered according to Figure 2.

the SEICUR model is extended with the vaccination model — leading to equivalent mitigation policy  $u_{fm}^v$ , or whether vaccination is baked into  $u_{fm}$ .

The number of certified infected per capita (and thus: recovered) is highest in Spain, a little lower in Italy, e.g., Figure 4, and quite low in Norway. It is not clear whether the various countries choose to vaccinate people who have recovered. As Figs. 6–9 illustrate, the mitigation policy with vaccination ( $u_{fm}^v$ ) is less restrictive for Norway and (partially for) Italy compared to the case when there is no vaccination ( $u_{fm}$ ). For Spain, the situation is less clear. In conclusion, vaccination allows for relaxing the mitigation policy.

### 3.4 Quenching COVID-19: the importance of vaccination

When a certain fraction of the population has either recovered from COVID-19, or has been vaccinated, herd immunity is reached and infection will die out. An interesting question is whether the current reduction in infection in North America, Europe, and a few other countries is due to rapid vaccination roll-out. This question is not trivial to assess: there was a similar reduction in infection in May–June 2020, so it is possible that the reduction in infection is (partially) due to a seasonal variation in infection rate constants.

It seems like vaccination has dramatically reduced the death rates from COVID-19; this will reduce the strain on the health care system. But it is still possible that there will be growths in infection during the fall of 2021, both due to seasonal variations and due to new mutations.

## 4 Conclusions

In this paper, the SEICUR model discussed in (Lie, 2021b) has been extended in several directions. First the model is extended with migration terms. Comparing the effect of migration solely between Italy and Spain, the model indicates that the number of people per day moving between the countries must be relatively high before a significant change in infection is observed. However, this is based on the assumption that the migrants are “average spreaders”. Some tourists engaging in nightlife activities will most likely be “super spreaders”, so to get a more accurate description, it would probably be necessary to distinguish between super spreaders and regular spreaders.

Second, the SEICUR model is extended to handle demographic variations due to age dependence in rate constants. This is particularly important when considering the risk of serious illness and death. Because this paper has not considered confirmed death rates, simulations have not been carried out and the presentation is mainly included for illustration/future studies.

Thirdly, the SEICUR model is extended with a description of vaccination, with 3 models of the effect of vaccination. The “semi-crude” model has been added to the SEICUR model, and an equivalent mitigation policy has

been fitted to the data when the vaccination model is included. The results indicate that vaccination has most effect on the equivalent mitigation policy in countries with a low level of confirmed infections (e.g., Norway), and less effect in countries with a higher number of confirmed infected (e.g., Spain). This may be due to vaccinating people who have already recovered, or to the relative reduction in the number of susceptibles due to vaccination.

Realistic COVID-19 models need to include migration/network description between the various compartments, and for the case that demographics influence the degree of illness, age distribution models and other types of models distributed in co-morbidity should be used. In the models studied here, an equivalent mitigation policy has been assumed. For more realistic models, it is recommended to improve the effect of genetics, seasonal variations, etc. in the infection rate expression.

The spreading of the Delta mutation in the second and third quarters of 2021 would probably have necessitated using different model parameters (frequency factors, etc.), and would have complicated the total model. Also, hesitance against vaccination in various populations would need to be taken into consideration.

The SEICUR model with the extension of the vaccination model holds the potential for computing some “optimal” transition between mitigation and vaccination using feedback control theory (e.g., Model Predictive Control). Essentially, the “fitted” mitigation policy  $u_{fm}$  is the control variable, and one could specify a cost function for future infection, and then compute how an “optimal” future mitigation policy should be in order to tackle the infection. Some important caveats are that (i) the current model does not describe seasonal variations in infection rate constant, thus relatively short future horizons should be used, (ii) the “fitted” mitigation policy is not directly related to concrete policies (“social distancing”, “mask use”), etc. In summary, MPC is more useful if the mitigation model is extended to hold real mitigation policies  $u$  instead of “fitted” mitigation policy  $u_{fm}$  — it is non-trivial to figure out quantitative real policies from  $u_{fm}$  — beyond “we need a stricter policy” or “we can relax the policy”.

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