Long-term scenarios for the number of new hospitalizations during the Belgian COVID-19 epidemic

RESTORE consortium
Report version 8.0

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Summary

- This report describes the combined impact of different social distancing scenarios, the 501Y.V1 variant and the ongoing vaccination campaign in Belgium and illustrates the importance of epidemic control in the period up to August 1, 2021.
- Changing social distancing behaviour as a result of lifting measures too soon might, in spite of the ongoing vaccination campaign, still lead to a substantial fourth hospitalization wave. However, postponing behavioural changes that increase viral transmission allows the vaccination campaign to offset the transmission risk and associated disease burden.
- Vaccination and seasonality (currently not modelled) are expected to have a positive impact on the incidence of new hospitalisations in the coming period. However, recent evidence from the UK and Denmark indicated that the 501Y.V1 variant is associated with a higher per-case probability of severe and lethal disease. The SIMID and UNamur models explicitly account for a VOC-related increase in transmission and per-case probability of hospitalization, while the UGent model implicitly captures the overall increase.

Introduction

After an initial outbreak of *Severe Acute Respiratory Syndrome coronavirus 2* (SARS-CoV-2) in Wuhan, China, the epidemic has evolved in 2020 into a global pandemic. The prevention of COVID-19 outbreaks has been depending on the successful implementation of non-pharmaceutical interventions, such as social distancing, testing, contact tracing and quarantine. Recently, vaccines have become available and enable many new deconfinement strategies, which can be evaluated via data-driven models to assist in the policy making process. Within this RESTORE consortium, multiple mathematical models have been applied to perform scenario analyses tailored to the Belgian setting, for example, the stochastic compartmental model of Abrams et al. (2021), the deterministic metapopulation model of Alleman et al. (2020), the deterministic compartmental model, explicitly accounting for the nursing home population, by Franco (2020), the individual-based model by Clesse (2020) and a time-series model by Barbe, Blotwijk, and Cools (2020).

All these models have been independently created for the same purpose: to understand and study the spread of SARS-CoV-2 in Belgium. However, modeling the transmission of an infectious disease implies a detailed investigation and understanding of human behaviour, which is not trivial to translate into a set of mathematical equations. As a consequence, each of the mathematical models relies on different assumptions and modelling techniques. By combining the different scenario analyses into an ensemble, we investigate structural model uncertainty. This is standard practise when it comes to model-based decision support, e.g. the Intergovernmental Panel on Climate Change (IPCC) considers the outcomes of more than 10 different models for supporting its reports on climate change (Gerstengarbe et al. 2015). Moreover, an ensemble can be used to mutually validate the projections over time. This report contains different long-term scenarios for the spread of SARS-CoV-2 in Belgium with the purpose of informing upcoming mitigation/relaxation policies.

Methods

Long-term forecasting models

All models used in this report (SIMID, UGent and UNamur) are compartmental models and capture the dynamics of the epidemic by dividing the population into different compartments. By default, it contains susceptible (S), infectious (I) and removed (R) compartments, which is

called an SIR model (Kermack and McKendrick 1927). The models used here differ in the way the compartments are further subdivided to capture the details of COVID-19 disease dynamics, making each model subject to different assumptions (Table 1). The models are based on disease mechanics, hence called mechanistic models, and are well-fit to study long-term scenarios. Since the spread of SARS-CoV-2 is mainly driven by social contact behaviour, data on social contact behaviour at different locations, e.g., home, school, workplace, public transport and during leisure activities are used to translate government policies into tangible scenarios (Willem et al. 2012; Willem et al., 2020b).

More details on the specific properties, assumptions and limitations of each model can be found in the Supplementary materials.

The 501Y.V1 variant

The scenarios in this report consider the introduction of a new variant of concern (VOC), i.e. 501Y.V1 or VOC-202012/01 (lineage B.1.1.7), in the Belgian population from January 1, 2021 onward. Other new VOCs such as the 501Y.V2 or 501Y.V3 variants, are not accounted for explicitly, given their relatively low circulation and properties somewhat similar to that of 501Y.V1. The most recent data indicate that 501Y.V1 is more transmissible than the original strain, with an increase of about 40% compared to the original strain (hereafter referred to as wild-type strain) (Wenseleers 2021). Recent evidence suggests that also the probability of hospitalization and death is higher for 501Y.V1 (Nicholas G. Davies et al. 2021; Horby et al. 2021). The models of SIMID and UNamur account for this increase explicitly, while the model of UGent estimates the overall burden of disease.

Vaccination campaign

All scenarios account for the national vaccination campaign in place. To implement the accomplished vaccinations, we used data provided by Sciensano. For the remaining vaccination campaign, we considered scenarios of 40.000 and 60.000 available first doses per day, with maximum uptake capped at 80% for all age groups. As an extension to Report 7, we now incorporated leaky vaccine models (as compared to an all-or-nothing formulation previously), accounting for the possibility that vaccinated people can acquire protection against severe disease and/or hospitalization but still transmit the virus. We assumed that vaccinated people are fully protected 28 days after first vaccination, with at that moment 70% efficiency in avoiding transmission and 90% efficiency in avoiding hospitalisation. We focus on the uptake of the first dose, since we do not account for waning immunity, vaccine type, nor the differential effect upon receiving a second vaccine dose.

Scenarios

We calibrated the models with Belgian incidence data until April 12, 2021 and computed scenarios differing in release date (May 1st or June 1st) and in available first doses per day (40.000 or 60.000). On the release dates, we assumed that contact behaviour will be similar to the one prevailing in September 2020. In all scenarios, schools are closed from March 29th until April 18th, 2021. 40.000 daily first dose vaccinations was chosen as an extension of the current vaccination rate, while 60.000 daily first dose vaccinations was chosen as a plausible future vaccination rate.

Scenario 1 Release date May 1st, 40.000 first doses per day.

Scenario 2 Release date May 1st, 60.000 first doses per day.

Scenario 3 Release date June 1st, 40.000 first doses per day.

Scenario 4 Release date June 1st, 60.000 first doses per day.

Since hospital data currently suggest that the proportion of hospitalised people admitted to ICU has increased, as a consequence of the 501Y.V1 variant becoming dominant, we now assumed 30% of the hospital load as ICU load, instead of the 20% used in previous reports.

Results

Figure 1 shows the ensemble model projection made for RESTORE Report 7 on March 12, 2021 with the new hospitalization data. The models account for the vaccination campaign and for the 501Y.V1 variant under prolongation of the measures effective on March 12, 2021. Subscenario (a) represents a 501Y.V1 strain with a 30% transmissibility increase and subscenario (b) represents a 501Y.V1 strain with a 50% more transmissibility of the 501Y.V1 variant. Although the (mis)matches between the model projections and the data are partly driven by behavioural changes in March, and by differences between the projected and actual vaccine uptake, the scenarios indicate an evolution of the pandemic in-between the (a) and (b) scenario's, which is consistent with a 501Y.V1 variant that is roughly 40% more transmissible.

As can be seen in Figure 2 and Figure 3, a switch to the social contact behaviour from September 2020 as early as May 1st (scenario 1 and 2) might induce a fourth wave flirting with the countries maximum ICU-capacity. Although the timing of the predicted peaks (end May or end June) differs among the different models, the general trend indicates that a resurgence of the epidemic is likely. Postponing the deconfinement date until June 1st (scenario 3 and 4) clearly shows the added value of the ongoing vaccination campaign in lowering the peak size (and final size) of a potential fourth wave. However, when releasing measures on June 1, 2021, caution is still warranted, we thus advice policymakers to release measures later rather than sooner and in a step-by-step manner.

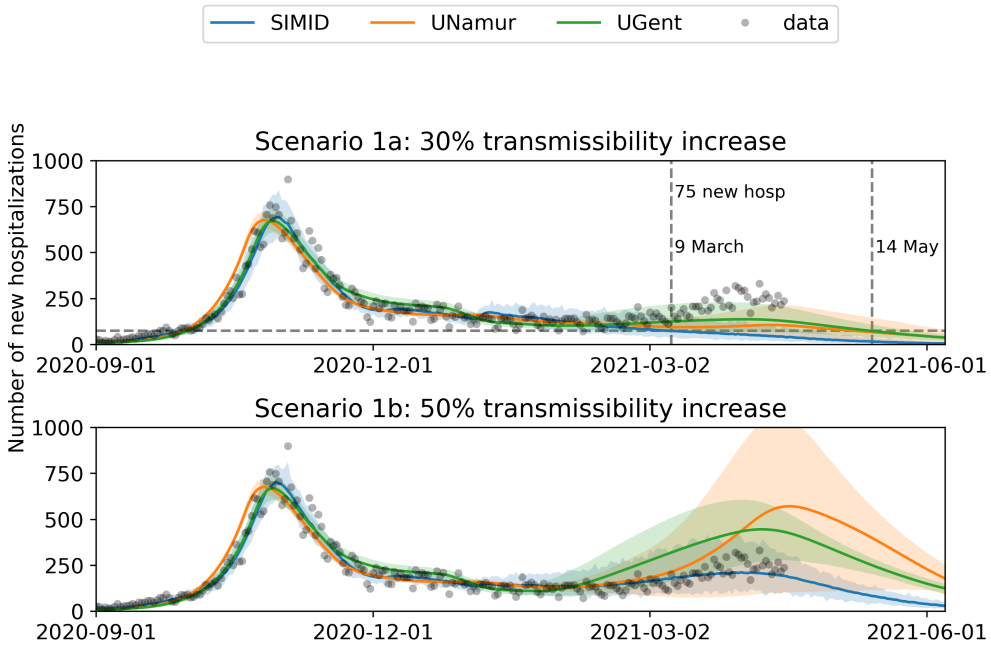

Figure 1: Model trajectories for the number of new hospitalizations for the different scenarios: mean value with 95% credible interval. Models were calibrated on February 1, 2021 and new data are shown up to April 15th, 2021.

Hospital incidence

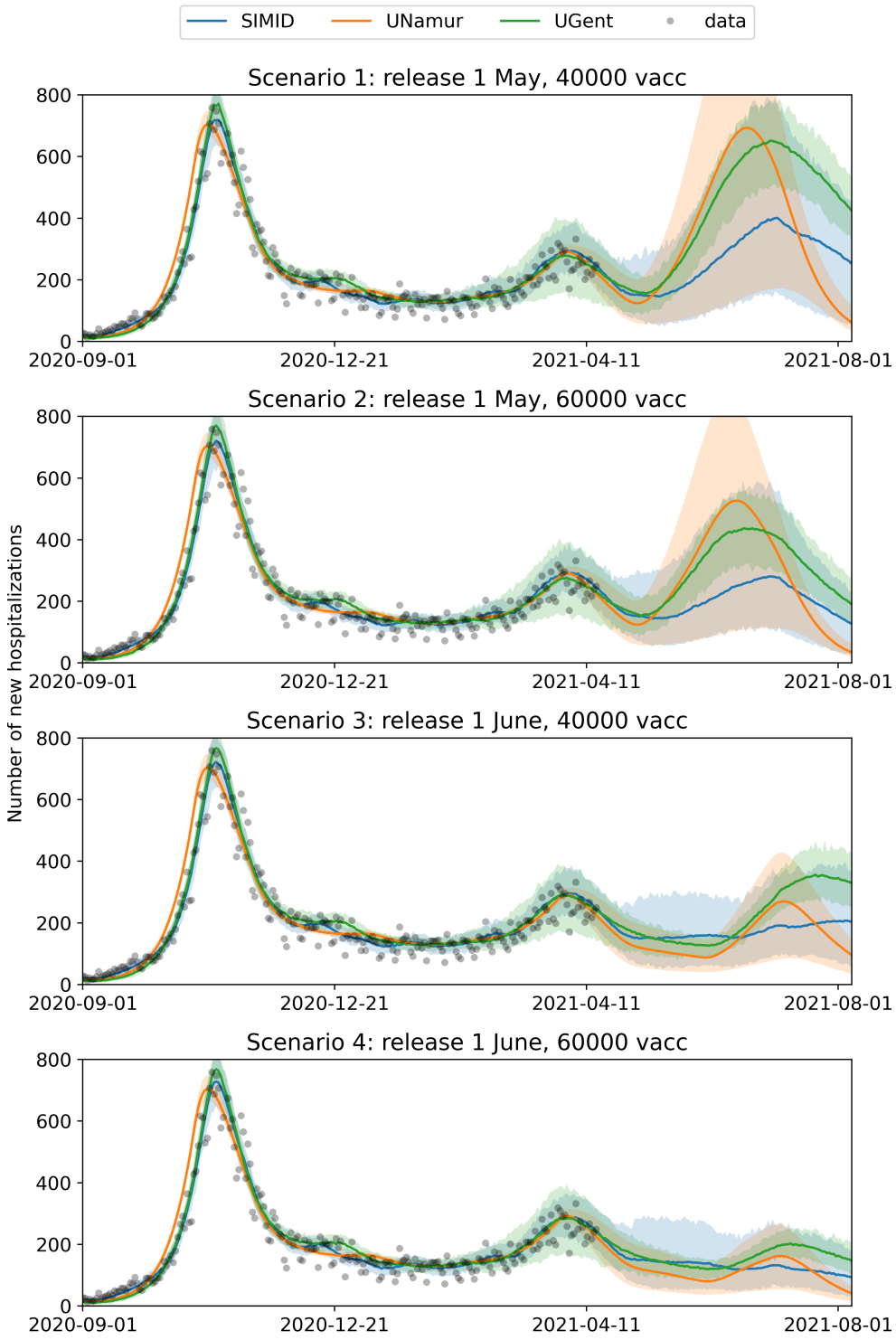

Figure 2: Model trajectories for the number of new hospitalizations for the different scenarios: mean value with 95% credible interval. Models were calibrated on April 12, 2021 and new data are shown up to April 15, 2021.

Hospital load

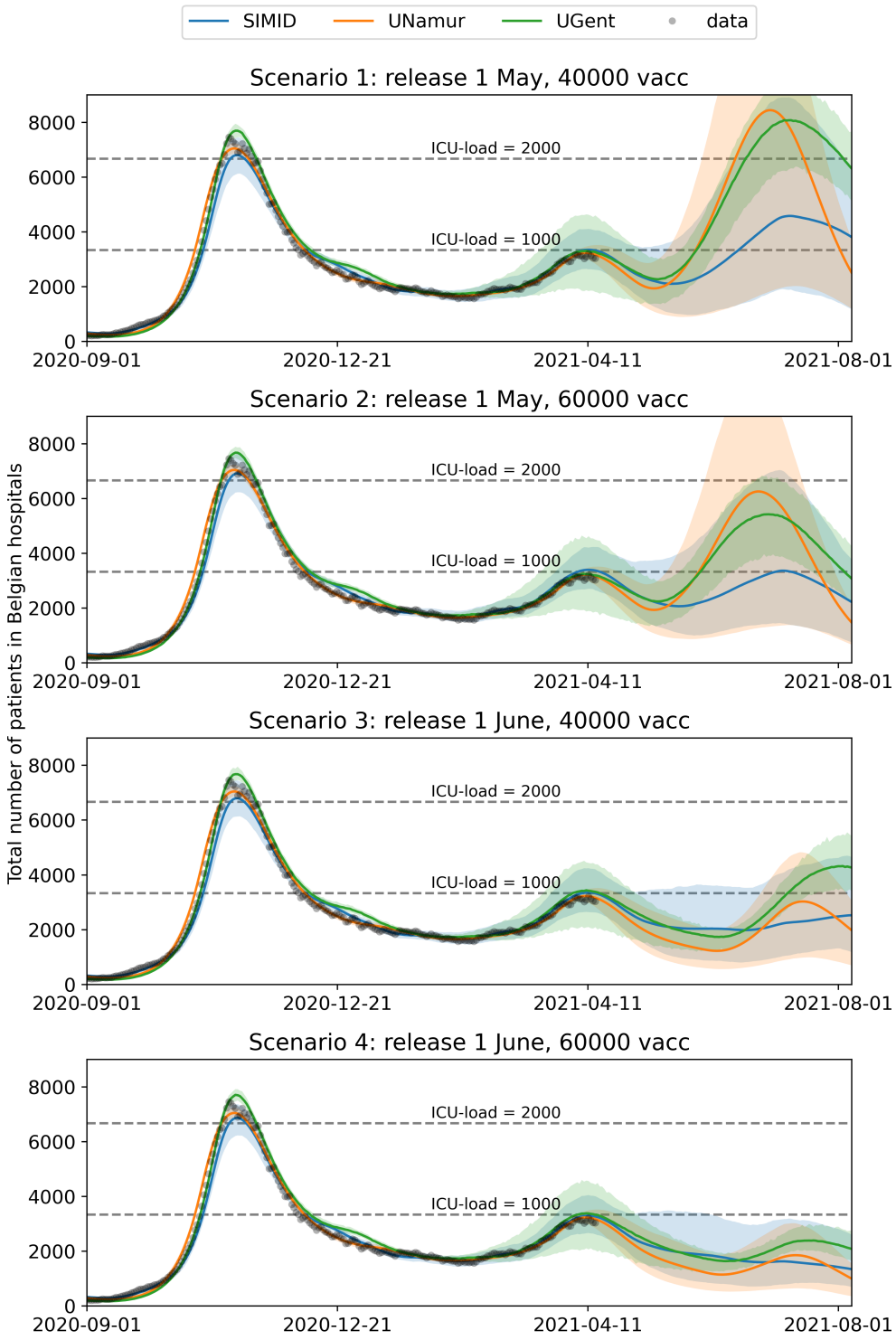

Figure 3: Model trajectories for the hospital load in terms of the mean value with 95% credible interval. The dashed lines indicate the corresponding level of ICU beds for COVID-19 patients when assuming that 30% of the admissions require ICU (1000: normal capacity and 2000: increased capacity).

Limitations

There are several limitations for the models used in this report,

- The different scenarios are expressed in terms of changes in social contact behaviour. These are used as proxies for changes in transmissibility, which result in part from the combination of social distancing and hygienic measures taken at different locations, e.g., at home, at work and at school.
- Scenarios should not to be interpreted as predictions, since we are not able to discern the most plausible scenario given the unpredictable nature of adjusted social behaviour, future measures, the appearance of new strains and uncertainties with regard to vaccine efficacy and supply. These scenarios represent projections based on a constant or previously estimated situation.
- The models do not consider the spatial structure of the population. Although at Ghent University, a spatially explicit model is nearing completion.
- We do not account for seasonality nor cross-immunity, although these effects might influence the transmission dynamics.
- The effects of contact tracing, testing and self-isolation are incorporated indirectly within the estimated transmission potential within the population over time.
- We do not account for other VOCs than the 501Y.V1 variant although the 501Y.V2 variant and the 501Y.V3 variant have been detected in Belgium by February 2021.
- The advantage of prioritising vulnerable people and care personnel is not accounted for in these projections, hence only age-specific vaccination effects are captured.

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Table 1: Main properties, assumptions and limitations of each model. The complete model descriptions can be found in the supplementary materials.

	SIMID (Abrams et al. 2021)	UGent (Alleman et al. 2020)
model type	stochastic, extended SEIRD	deterministic, extended SEIRD
	nation-level	nation-level
	SDEs (exponentially distributed rates)	ODEs
	mechanistic	mechanistic
properties	age-stratified	age-stratified
	asymptomatic cases	asymptomatic cases
	pre-symptomatic infectiousness	pre-symptomatic infectiousness
	no waning immunity	no waning immunity
	no re-importations	no re-importations
assumptions	asymptomatic individuals 50% less infectious	asymptomatic individuals not infectious
	age-dependent probability of being asymptomatic & developing severe symptoms	age-dependent probability of being asymptomatic & developing severe symptoms
	deaths in hospitals only	deaths in hospitals only
	distinction between ICU and non-ICU care	distinction between ICU and non-ICU care, recovery stay after ICU
	UNamur (Franco 2020)	VUB (Barbe, Blotwijk, and Cools 2020)
model type	deterministic, extended SEIQRD	deterministic, extended SIR
	nation-level	nation-level
	ODEs	ODEs
	mechanistic	moving window calibration (gray box)
properties	age-stratified	non-age-stratified
	asymptomatic cases	no asymptomatic cases
	pre-symptomatic infectiousness	no pre-symptomatic infectiousness
	no waning immunity	no waning immunity
	re-importations from travellers	no re-importations
assumptions	estimated infectiousness per severity	homogeneous hospitalization probability
	age-dependent probability of being asymptomatic & developing severe symptoms	age-dependent probability of being asymptomatic & developing severe symptoms
	separated deaths from nursing homes and hospital	deaths in hospitals only
	ULB (Clesse 2020)	
model type	stochastic, extended SEIQRD	
	nation-level	
	individual-based model	
	mechanistic	
properties	non-age-stratified	
	no asymptomatic cases	
	no pre-symptomatic infectiousness	
	no re-susceptibility	
	no re-importations	
	no vaccination	
assumptions	accounts for transmission in households	
	temperature correlation for infectiousness	
	short and long-term hospitalizations	
	shorter stays at hospitals in summer	

Supplementary materials

Model comparison

Of the five models, four models (Abrams, Alleman, UNamur and Barbé) assume homogeneous mixing of the entire population. As a non-spatial individual-based model, Clesse is the only exception. Currently, two patch models are under development. These allow to simulate the disease at a smaller spatial resolution (municipalities) and account for the effects of work & leisure mobility. Of the five models, four models (Abrams, Alleman, Franco and Clesse) extended the classical SIRD model structure to an extension of a SEIRD model structure. The addition of an exposed (E) compartment accounts for individuals being infected with the virus who are not yet infectious (latent). The infectious (I) compartment is split to account for the effects of pre-symptomatic, symptomatic and fully asymptomatic transmission, as these have been shown to be important in the spread of SARS-CoV-2 (Ganyani et al. 2020; Gudbjartsson et al. 2020). Opposed is the model of (Barbe, Blotwijk, and Cools 2020), which uses SIRD dynamics. The models of Abrams, Alleman and Franco split every compartment into age layers to account for different COVID-19 severity in individuals of different ages, as COVID-19 shows remarkably higher incidences in older individuals (Faes et al. 2020). These models then differ in the hospital dynamics and assumptions made. Some of the key differences are: Abrams et al. (2021) and Alleman et al. (2020) assume deaths only arise in hospitals, while Franco (2020) accounts for nursing home deaths. Alleman et al. (2020) assume mildly symptomatic individuals self-quarantine while Abrams et al. (2021) and Franco (2020) assume these individuals are still infectious to some degree. The model of Franco (2020) does not explicitly account for intensive care while the models of Abrams et al. (2021) and Alleman et al. (2020) do. Four models use a mechanistic approach (Abrams, Alleman, Franco and Clesse) while one model (Barbé) uses a data-driven approach. A detailed overview of the key differences is provided in Table 1. In what follows, each model is discussed separately in more detail.

SIMID (UHasselt/UAntwerp) (Abrams et al. 2021)

We use a stochastic discrete age-structured compartmental model (Abrams et al. 2021) calibrated on hospitalization and morality data (Sciensano 2020), serial serological survey data (Herzog et al. 2020) and social contact data Coletti et al. 2020; Willem et al., 2020b. The stochastic model projects the daily number of new hospitalizations per age group (i.e., 10 year age groups). The modeling approach depends on assumptions with regard to the transmission process which inevitably implies an underestimation of the level of uncertainty. In this model we are not explicitly accounting for a constant re-introductions in the population.

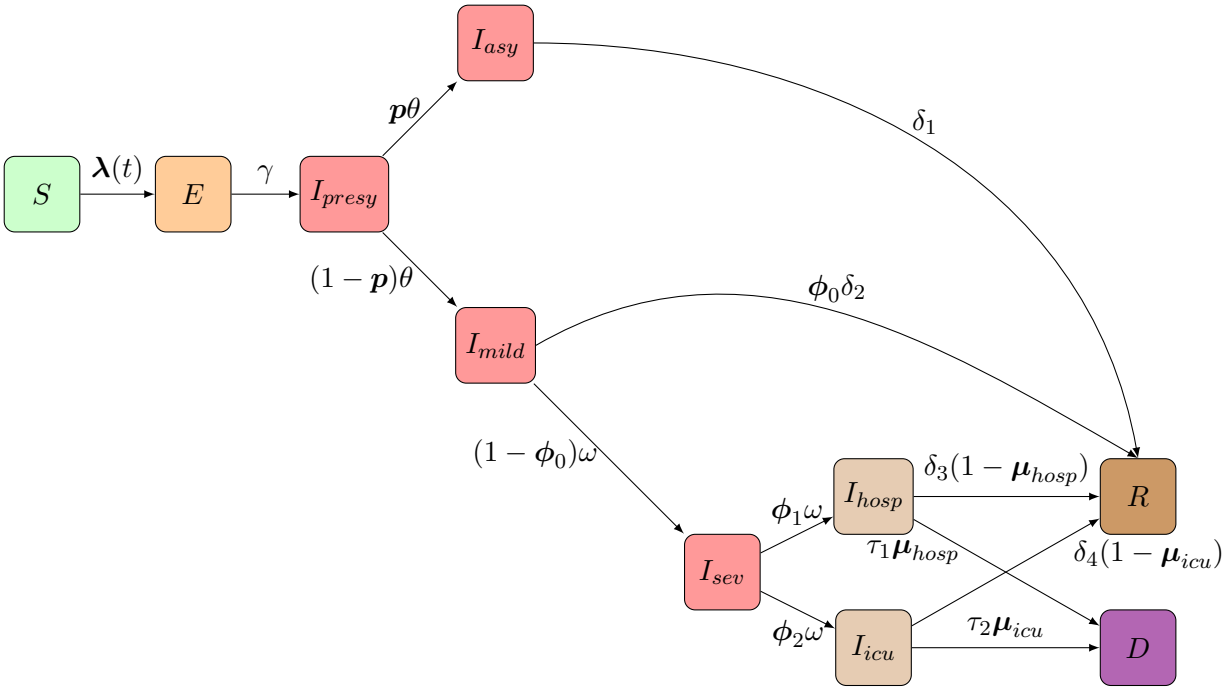

Figure 4: Schematic overview of the main transitions in the compartmental SIMID model. To model the impact of a VOC and vaccination, compartments have been duplicated. In essence, SARS-CoV-2 infected susceptible individuals (S) move to an exposed state (E) and after a latent period individuals further progress to a pre-symptomatic state (I_{presym}) in which they can infect others. Consequently, individuals stay either completely symptom-free (I_{asym}) or develop mild symptoms (I_{mild}). Asymptomatic individuals will recover over time. Upon having mild symptoms, persons either recover (R) or require hospitalization (going from I_{sev} to I_{hosp} or I_{icu}) prior to recovery (R) or death (D).

UGent (Alleman et al. 2020)

We extend the classical SEIRD model to incorporate more expert knowledge on SARS-CoV-2 (Alleman et al. 2020). The model accounts for pre-symptomatic and asymptomatic transmission, as these have been shown to be important contributors to SARS-CoV-2 spread (Ganyani et al. 2020; Wei et al. 2020; Gudbjartsson et al. 2020). Furthermore, the susceptibility to SARS-CoV-2, the severity of the disease and the susceptibility to an asymptomatic infection depend on the age of the individual (Nicholas G Davies et al. 2020). Our model takes hospitals explicitly in account and distinguishes between regular hospital wards (Cohort) and intensive care units (ICUs). Our model further accounts for a recovery stay of 6 days in Cohort after an ICU stay. From the pooled dataset of two Ghent (Belgium) hospitals, we computed the mortalities, length-of-stays in both hospital wards and the probability of needing intensive care. A flowchart of the model and its compartments is available in Figure 5.

We used age-stratified social contact rates from a study which has been made available using the Socrates tool (Willem et al., 2020b) to model age-specific social mixing. These social contact data are available at home, in the workplace, in schools, on public transport, during leisure activities and during other activities. The *Community mobility data* from Google (2020) are used as the primary weights for the contributions of work (G_{work}), transport ($G_{\text{transport}}$), recreation ($G_{\text{retail \& recreation}}$) and other contacts ($G_{\text{supermarkets}}$). Next, an effectiveness parameter Ω is introduced for home interactions, school interactions, work interactions and for the combination of transport, leisure and other interactions. These effectiveness parameters scale the relative contributions of each interaction matrix under lockdown measures and must be inferred from hospitalization data (Sciensano 2020) under varying social policies. All the above results in the following linear combination of interaction matrices to model social policies,

$$\begin{aligned}\boldsymbol{N}_{\text{c, total}}(t) = \Omega_{\text{home}}\boldsymbol{N}_{\text{c, home}} + \Omega_{\text{schools}}H_{\text{schools}}(t)\boldsymbol{N}_{\text{c, schools}} + \Omega_{\text{work}}G_{\text{work}}(t)\boldsymbol{N}_{\text{c, work}} + \\ \Omega_{\text{rest}}\Big[G_{\text{transport}}(t)\boldsymbol{N}_{\text{c, transport}} + G_{\text{retail \& recreation}}(t)\boldsymbol{N}_{\text{c, leisure}} + G_{\text{supermarkets}}(t)\boldsymbol{N}_{\text{c, others}}\Big],\end{aligned} \tag{1}$$

The model takes into account the effect of *social inertia* when lockdown measures are taken. In reality, lockdown restrictions represent a large change in behaviour which is gradual and cannot be modeled using a step-wise change of the social interaction matrix $\boldsymbol{N_c}$. In our model, we use a delayed ramp to model compliance,

$$\boldsymbol{N_c} = \boldsymbol{N}_{\text{c, old}} + f^k(\boldsymbol{N}_{\text{c, new}} - \boldsymbol{N}_{\text{c, old}}) \tag{2}$$

where,

$$f^k = \begin{cases} 0.0, & \text{if } k \leq \tau \\ \frac{k}{l} - \frac{\tau}{l}, & \text{if } \tau < k \leq \tau + l \\ 1.0, & \text{otherwise} \end{cases}$$

where τ is the number of days before measures start having an effect and l is the number of additional days after the time delay until full compliance is reached. k denotes the number of days since a change in social policy. The nine model parameters (transmission rate, $R_0(\beta, \omega, d_a)$; compliance model, l and τ; and the four effectiveness parameters) were calibrated to the daily Belgian hospitalizations between September 1st, 2020 and Februrary 1st, 2021. First a *particle swarm optimization* (Eberhart and Kennedy 1995) is performed to find the global minimum of the Poisson objective function. Next, the optimal parameter set is used as a starting point for the red-blue Markov-Chain Monte-Carlo method proposed by Goodman and Weare (2010). The chain is run until the length exceeds 50 times the integrated autocorrelation time. Subsequently, the

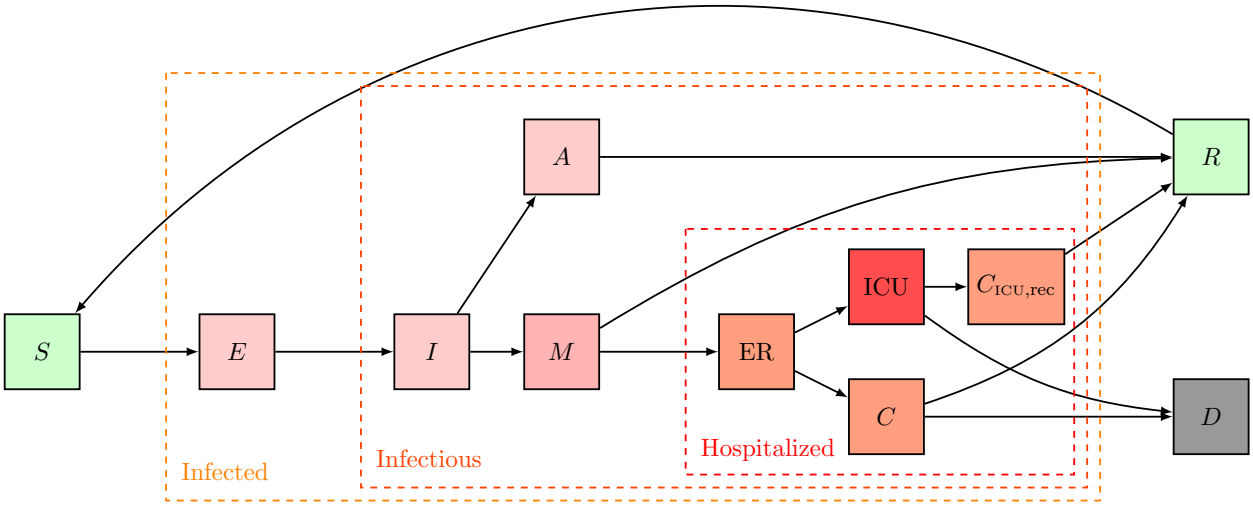

Figure 5: Extended SEIRD dynamics used in this study. Nodes represent model states, edges denote transfers.

chain is thinned and the cornerplots (Foreman-Mackey 2016) are examined to analyse correlations between model parameters and unidentifiability issues. All calibrated parameters were identifiable.

UNamur (Franco 2020)

The model initially developed at UNamur (Franco 2020) is a continuous age-structured compartmental model based on differential equations, calibrated on public Sciensano data on hospitalization, mortality and serology from blood donors.

The Belgian population is divided into 8 compartments in order to take account of the different possible stages of the disease as well as the separation between asymptomatic and symptomatic people with a different infectiousness. Each compartment is divided into 5 age classes with different characteristics concerning the behaviour and evolution of the disease. A schematic view of the structure of the model is presented in Figure 6. The transmission of the coronavirus between all classes is computed using social contact data at different places (home, work, school, leisure) (Willem et al. 2012; Willem et al., 2020b). Except social contact data, all of the 70 parameters of the model are estimated using a Monte Carlo method, hence there is no assumption coming from others studies. Nursing homes are modelled as isolated entities in order to take account of the different spread timing of the coronavirus compared to the general population. Specific parameters for the situation in nursing homes take account of a variable hospitalisation policy based on hospitals load as well as a probability that deaths coming directly from nursing homes are related to the covid-19. There is a specific estimation of potential reimportations coming from travellers during the holiday period. The model is mainly calibrated using hospitalisations and deaths using both incidence and prevalence data (depending on which one is the more appropriate for the considered data) coming from Sciensano's public raw data (Sciensano 2020). The model specifically accounts for the under-reporting in new hospitalizations due to transfers of patients from a non-COVID unit as well as improvement of care methods at the hospital since the first wave. Additional constraints on seroprevalence are coming from Sciensano's serological studies on blood donors as reported in Sciensano epidemiological reports. The only positive PCR tests which are taken into consideration are those coming from nursing homes from an overall test campaign in April-May.

All the technical details as well as estimated parameters can be found in (Franco 2020).

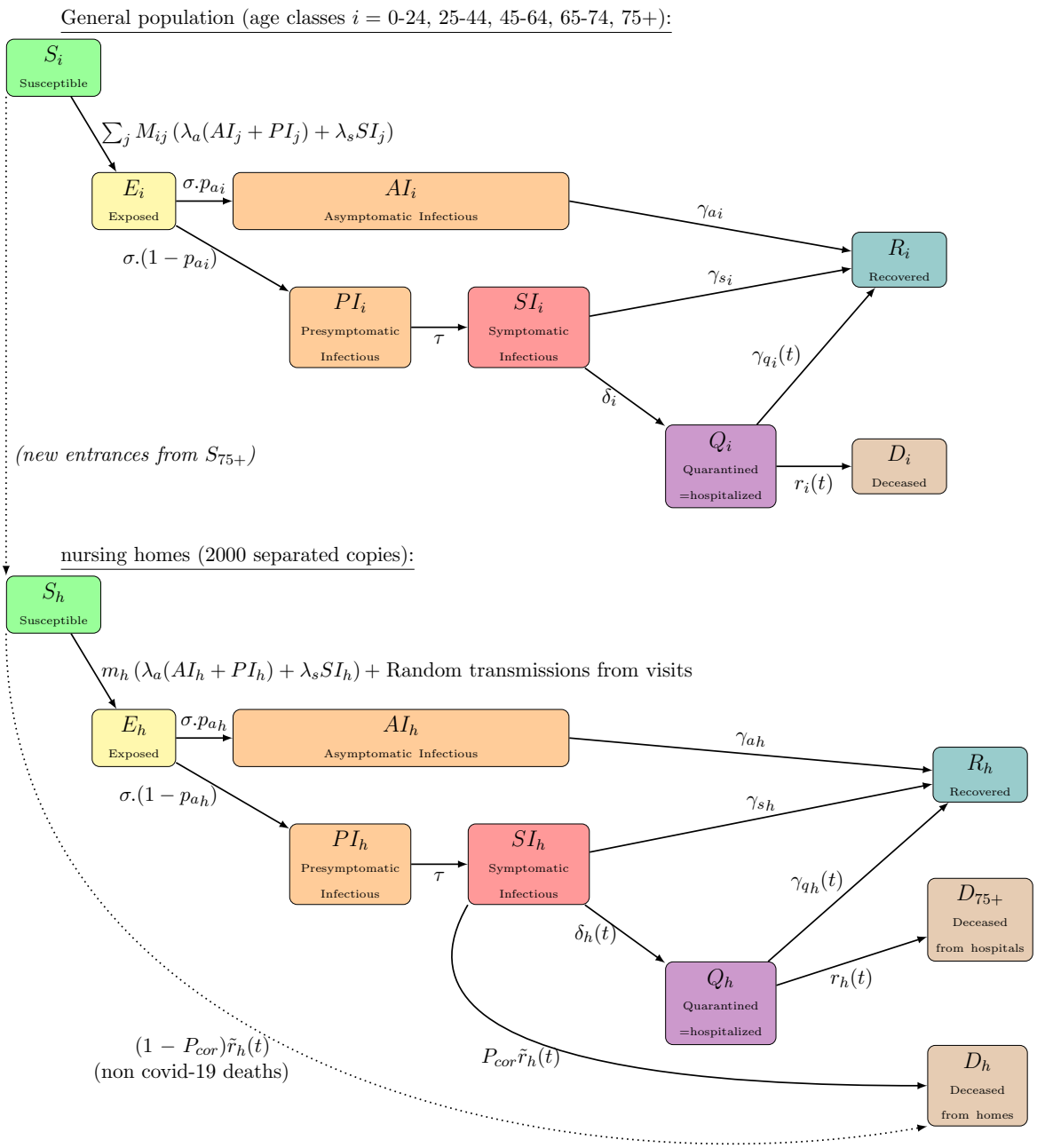

Figure 6: Schematic view of the UNamur compartmental model.

VUB (Barbe, Blotwijk, and Cools 2020)

This analysis applies a time series approach wherein the log-number of events $\log(X_t)$ (with X_t the number of events of interest) is assumed to follow a first order auto-regressive process with a piecewise linear drift driven by a Gaussian cyclo-stationary process. The cyclo-stationarity is a priori set to a weekly periodicity to account for the weekend effect. The model choice is derived from a linearisation of the standard SEIR-model equations. The analysis uses the publicly available national data daily distributed by Sciensano. Projections are obtained by transforming the time series parameters to the parameters of the SEIR model equations proceeded by solving the SEIR differential equations numerically through a standard Runge-Kutta 4/5 numerical scheme. Currently the model applies 23 parameters and 7 knot points.

The model is data-driven which serves as a projection model with limited possibility of scenario simulations. The uncertainty analysis relies on the assumed Gaussian cyclo-stationary noise process. The weekend-effect is modelled non-parametrically by analysis of the periodogram of the model residuals w.r.t $\log(X_t)$. The Fourier coefficient corresponding to a weekly periodicity is used in the residual's spectral density.

ULB (Clesse, 2020)

This individual-based SEIQRD model is calibrated on the daily number of hospitalizations. The model is *not* aged-structured but it implements optional effects such as intra-familial contamination, week-end fluctuations, two populations with different contact behaviours, and a possible correlation between the reproduction number and the averaged daily temperature. Eleven periods, limited by ten time knots, are considered according to the evolution of measures taken by Belgian authorities, and one reproduction number is associated to each of them. Stochasticity is included on the duration of the infecting period as well as on the time between infection and hospitalization. The effect of Christmas and/or New year parties is implemented through an effective one-day variation of the reproduction number corresponding to product of the averaged number of additional contacts, the probability of transmission, and the fraction of the involved population.

A total of 13 calibrated parameters are considered. The parameter means, best-fits and uncertainties are reconstructed through a Markov-Chain-Monte-Carlo method based on the Metroplolis-Hastings algorithm, using the public `MontePython` code. Details on the model and parameter assumptions (fixed, varying...) are available on demand.

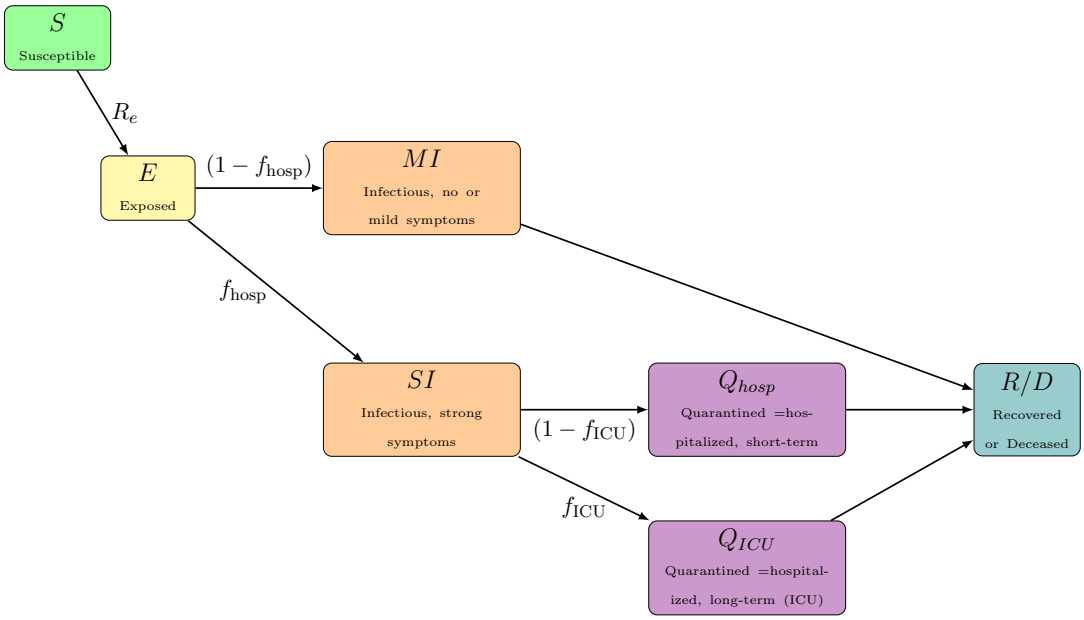

Figure 7: Schematic view of the ULB compartmental model. Each compartment is doubled in order to allow the analysis of two populations with different contact behaviours.