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

RESTORE consortium
Report version 6.1

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Introduction

After an initial outbreak of the novel *Severe Acute Respiratory Syndrome coronavirus 2* (SARS-CoV-2) in early 2020 in Wuhan, China, the epidemic has evolved into a global pandemic. Despite the recent availability of effective vaccines, preventing new COVID-19 outbreaks during the coming months will depend on the successful implementation of non-pharmaceutical interventions, such as social distancing, testing, contact tracing and quarantine. Well-informed models can assist policymakers in the decision-making process. Within this RESTORE consortium multiple mathematical models have been developed to perform scenario analyses specifically tailored to the Belgian setting, for example, the individual-based model of Willem et al. (2020a), the stochastic compartmental model of Abrams et al. (2020), the deterministic metapopulation model of Alleman et al. (2020), the deterministic compartmental model, explicitly accounting for the nursing home population, by Franco (2020) and a time-series model by Barbe, Blotwijk, and Cools (2020).

All of the abovementioned models were 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 extremely difficult to translate into a set of mathematical equations. As a consequence, each of the aforementioned mathematical models relies on different assumptions and modelling techniques. By combining the different scenario analyses into an ensemble, we account for the structural model uncertainty. This is standard practise when it comes to model-based decision support, e.g. the IPCC considers the outcomes of more than 10 different models for supporting its reports on climate change (Gerstengarbe et al. 2015). Moreover, the ensemble can be used to mutually validate the projections over the course of time. This report contains different long-term scenarios for the spread of SARS-CoV-2 in Belgium from five predictive models with the purpose of informing upcoming SARS-CoV-2 mitigation policies.

Methods

Long-term forecasting models

Three of the models used in this report (SIMID, UGent and UNamur) are compartmental models. These models capture the dynamics of the epidemic by dividing the population into different compartments. In its most basic form: susceptible (S), infectious (I) and removed (R), which is called an SIR model (Kermack and McKendrick 1927). The models 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). Closely related is the ULB model of Clesse, which simulates similar COVID-19 disease dynamics but uses an age-homogeneous individual-based approach. This model is more fit to study the effects of individual and household choices. The aforementioned models are primarily 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).

Opposed is the VUB model of Barbe, Blotwijk, and Cools (2020), which is solely data-driven. It infers the rate at which SARS-CoV-2 spreads directly by estimating the effective reproduction number (R_e) with a moving-window approach. The measured data up to one week in the past are used for the calibration and the model prediction is validated on the most recent data. The disease spread is somewhat similar to what can be expected in the compartmental models. Since the trans-

mission rate is estimated from the hospitalization data without a disentanglement of social contact behaviour and transmissibility, the model cannot be used to simulate different scenarios. However, the model is useful to make a reliable extrapolation of the current epidemiological situation. More details on the specific properties, assumptions and limitations of each model can be found in the Supplementary materials.

Scenarios

This report contains the updated scenarios of report 6.0, with new data added and the potential release date shifted from January 18th to March 1st. We also recalibrated the models with the new data until January 11th. In all scenarios, schools re-open on January 4th, 2021 (except high schools and universities). Schools are closed from December 21st, 2020 until January 3rd, 2021, from February 15th, 2021 until February 21st, 2021 and from April 5th, 2021 until April 18th, 2021.

Scenario 1 Contact behaviour similar to the current epidemic trend.

Scenario 2a Contact behaviour similar to September 2020, starting on March 1st, 2021.

Scenario 2b Contact behaviour similar to September 2020, except for work-related contacts, starting on March 1st, 2021. Work-related contacts are kept similar to December.

Scenario 2c Contact behaviour similar to September 2020, except for leisure-related contacts, starting on March 1st, 2021. Leisure-related contacts are kept similar to December.

We also updated the scenarios illustrating the impact of increased contacts during Christmas and New Year with the new data.

Important remark: At the moment these scenarios do not take into account the starting vaccination program (and the implied vaccine induced immunity) as well as the presence of new Variants Of Concern (VOC), which could progressively influence the predictions in a positive or negative way. The uncertainty concerning the rate of transmission and infectiousness of the new VOC is currently too high to provide accurate forecasts accommodating these effects on the epidemic curves.

Results

Scenario analyses

From Figures 1 and 2 it is clear that all models agree both qualitatively and quantitatively on the further evolution of the number of new hospitalisations and the total hospital load if we extrapolate the current contact behaviour (Scenario 1), and hence assume that the current measures remain in place. Compared to report 6.0, the new simulation results suggest that for Scenario 1, we should already have reached 75 hospitalisations per day by January 10th according to the SIMID model, but it is important to stress that these simulations do not incorporate the potential increase of contacts during the Christmas period (which are considered in Figure 3) and returning travellers. Hence, the stabilizing number of new hospitalizations we are currently observing is not in line with the expected decline in new hospitalizations based on contact behaviour prior to the holiday period. This finding implicitly shows the impact of travel importation and to a lesser extent the holiday period (as the trend deviates from the predicted trajectory as of January 4, 2021 onwards). According to the UNamur model the hospitalization threshold will be reached by March 11th, while the UGent model anticipates it to occur somewhere halfway between January 10 and March 11.

For what concerns the scenarios that assume less stringent contact behaviour from March 1st (Figures 1 and 2), the resurgence has shifted according to the shift in release date, as compared to report 6.0. As in report 6.0, there is a considerable discrepancy between the different model projections, though they agree qualitatively in the sense that they all indicate a substantial resurgence of the epidemic from April 2021 onwards for Scenarios 2a and 2b. Moreover, they all indicate that the resurgence is most pronounced under Scenario 2a. The discrepancy between the presented model projections can be explained by the build up of immunity which is different for the different models and by the different level of circulation at the time of relaxation (with the SIMID model being at the lowest level at that time implying a slower resurgence upon relaxation).
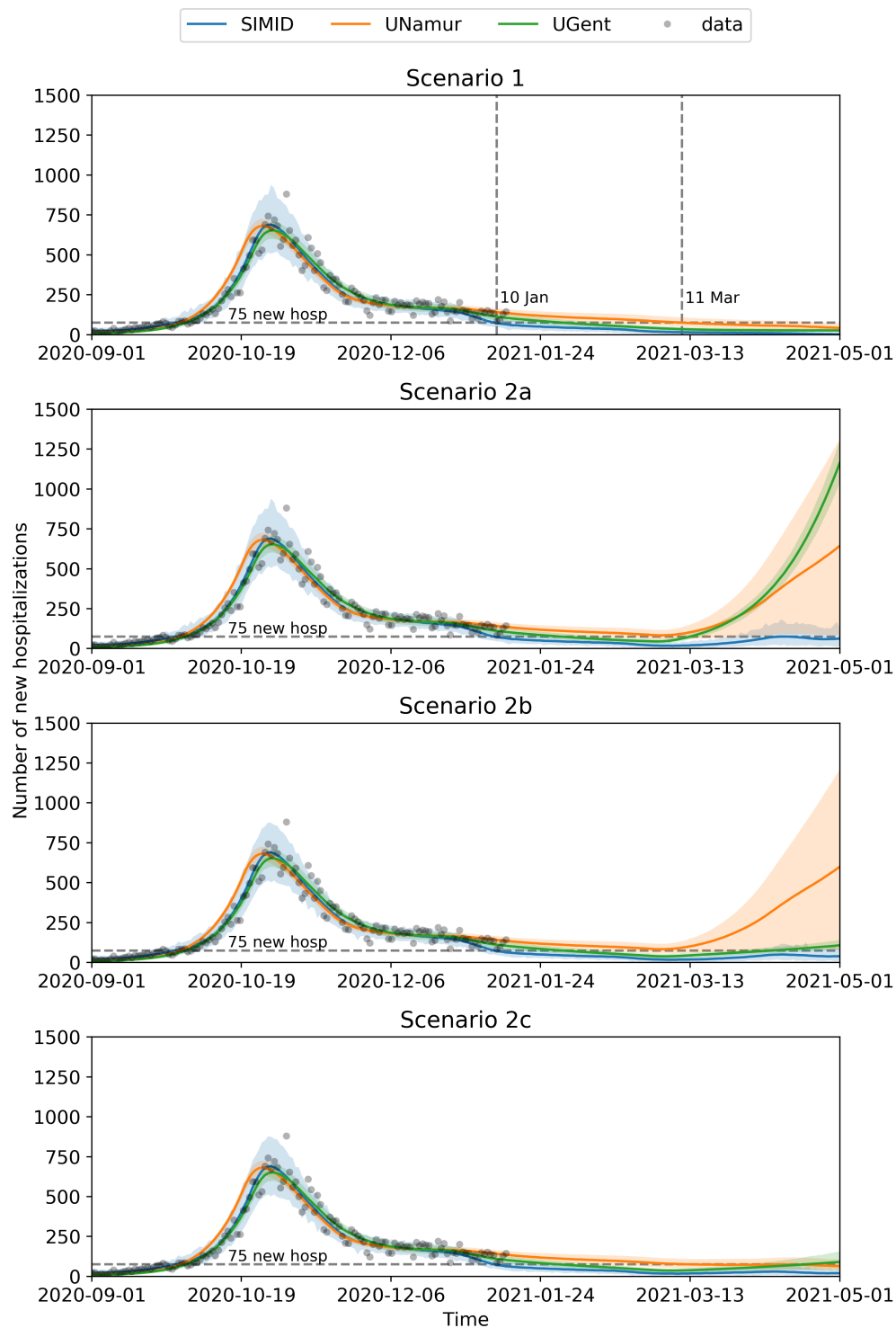
New hospitalisations

Figure 1: Long-term model trajectories for the number of new hospitalizations for the different scenarios: mean value with 95% uncertainty interval. The mean value does not represent the most likely evolution as every possibility within the prediction interval could occur. Models were calibrated on January 11, 2020 and new data are shown up to January 13, 2020.
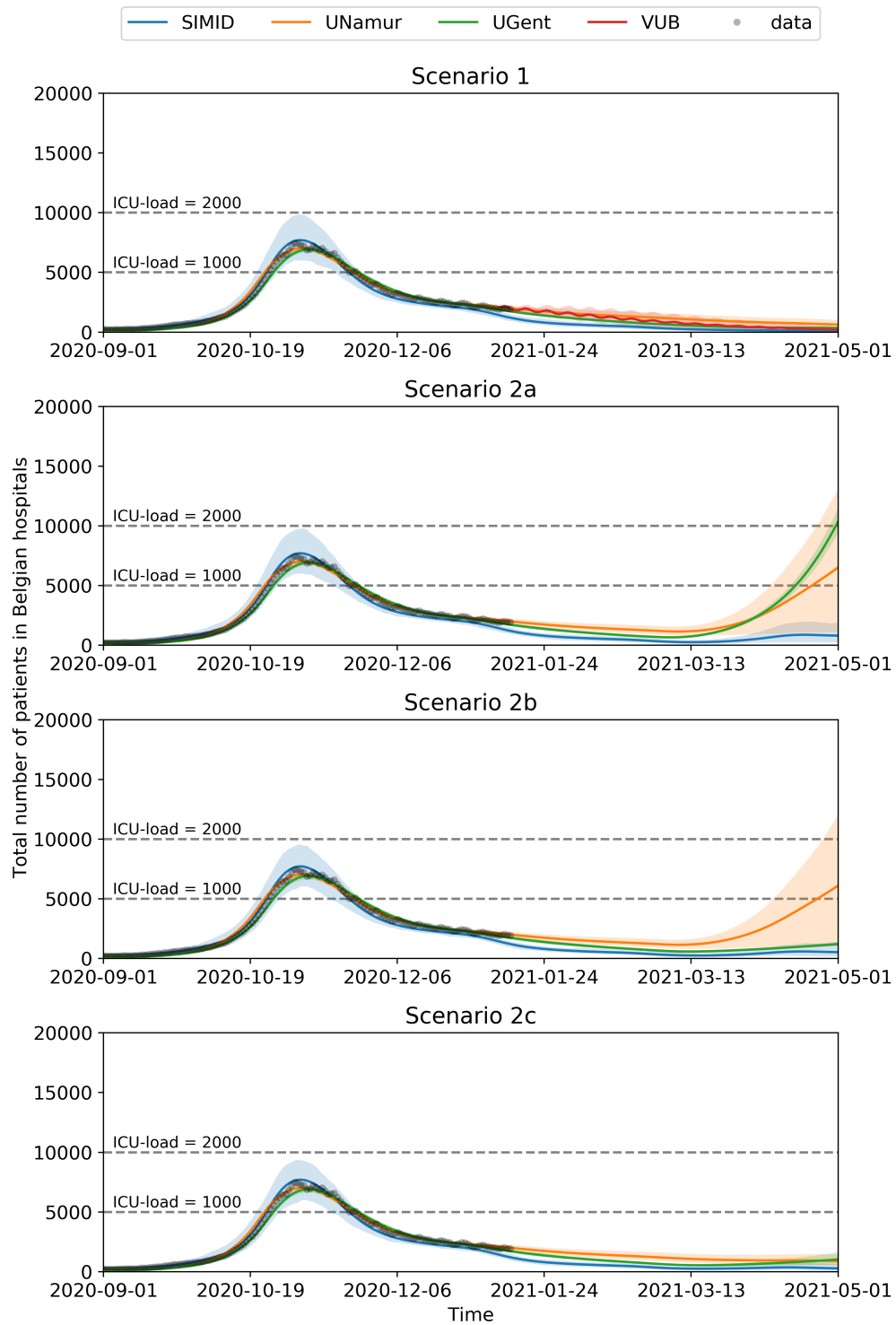
Hospital load

Figure 2: Long-term model trajectories for the hospital load: mean value with 95% uncertainty interval. The dashed lines indicate the number of available ICU beds for COVID-19 patients (1000: normal capacity and 2000: increased capacity).

Christmas and New Year scenario

The potential effect of increasing contacts during the Christmas and New Year period is illustrated in Figure 3. We explored scenarios in which 80% of the total population exhibits behaviour according to the measures implemented; the other 20% of the total population are assumed to meet 4 additional contacts apart from their household members at Christmas, at New Year and at both occasions. A transmission probability of 50% was assumed for these events. The most recent data suggest that the dynamics of the epidemic do not follow the scenario of meeting at both occasions, but a resurgence due to violations on one of these event is still possible.
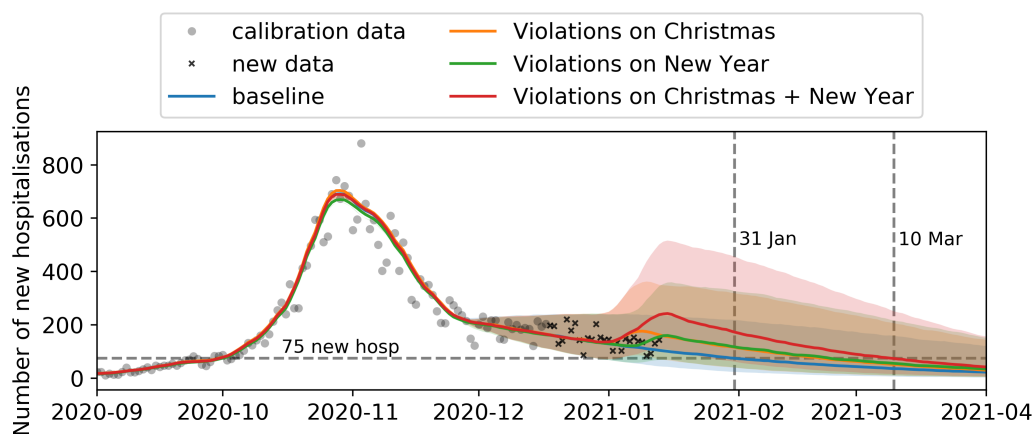

Figure 3: Long-term model trajectories (mean value with 95% uncertainty interval) from ULB model of the number of new hospitalizations if measures were not respected by a part of the population during Christmas and New Year.

Conclusions

In the previous version of the report (v6.0) it was stated that we would reach 75 new hospitalizations between January 10th and January 28th. Under the current social contact behaviour, a stagnation of the decline in new hospitalizations is observed and it is expected that the level of 75 new hospitalizations can only be reached between January 10th and March 11th (Figure 1). Note that this report does not yet fully include the effects of importation of SARS-CoV-2 infections following travel, including subsequent circulation of potentially more infectious VOC such as VOC 202012/01 or lineage B.1.1.7. Furthermore, the beneficial effects of a gradually increasing level of vaccine-induced immunity in the population following ongoing COVID-19 vaccination is not taken into account in this updated report.

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 from social distancing and hygienic measures taken at different locations, e.g., at work and at school.

- All scenarios are hypothetical and we are not able to discern the more plausible scenario given the unpredictable nature of adjusted social behaviour and future measures.

- The models do not take into account the spatial structure of the population.

- We do not account for seasonality or cross-immunity effects as quantitative evidence is scarce.

- Contact tracing, testing and self-isolation are not incorporated, except for the aggregated effect on reducing the number of high-risk contacts.

- We assume no vaccination for now, due to uncertainty on the start date of vaccination and the availability and efficacy of the vaccine. Therefore it is important not to over-interpret the longer term predictions.

- The effects of Christmas and New Year parties are explored for illustrative purposes, but their accuracy is limited.

Acknowledgements

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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. 2020)	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 re-susceptibility	no re-susceptibility
	no re-importations	no re-importations
assumptions	asymptomatic individuals 50% less infectious	asymptomatic individuals not infectious
	age-dependent probability of being	age-dependent probability of being
	asymptomatic & developing severe symptoms	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 re-susceptibility	no re-susceptibility
	re-importations from travellers	no re-importations
assumptions	estimated infectiousness per severity	homogeneous hospitalization probability
	age-dependent probability of being	age-dependent probability of being
	asymptomatic & developing severe symptoms	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 subtly in the hospital dynamics and assumptions made. Some of the key differences are: Abrams et al. (2020) 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. (2020) 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. (2020) 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. 2020)

We use a stochastic discrete age-structured compartmental model (Abrams et al. 2020) calibrated on high-level hospitalization data (Sciensano 2020), serial serological survey data (Herzog et al. 2020) and Belgian mortality data (Sciensano 2020). More specifically, the stochastic model predicts (stochastic realisations of) 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. As the model-based long-term predictions rely on changes in social contact behaviour following the exit strategy initiated May 4, 2020, we present such predictions under various scenarios which aim at giving some insights in the future course of the epidemic without being able to assign a probability to each scenario related to the likelihood of a given scenario to become reality. We do account for the current resurgence of COVID-19 in the selection and presentation of plausible scenarios. In this model we are not explicitly accounting for re-importation of the pathogen in the population
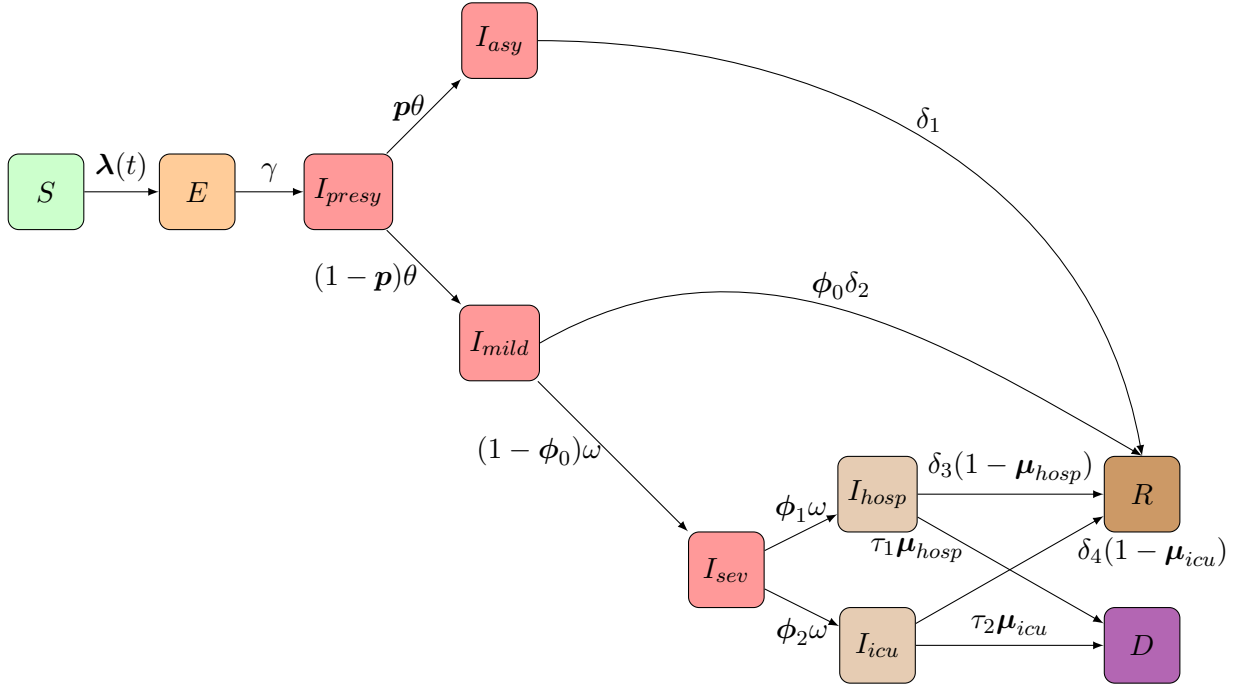

Figure 4: Schematic overview of the flows of individuals in the compartmental model: Following SARS-CoV-2/COVID-19 infection susceptible individuals (S) move to an exposed state (E) and after a latent period individuals further progress to a pre-symptomatic state (I_{presym}) in which they can infect 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 (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 7.

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, a mentality parameter Ω is introduced for home interactions, school interactions, work interactions and for the combination of transport, leisure and other interactions. These mentality 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,

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

The model further takes into account the effect of *social inertia* when measures are taken. In reality, social restrictions or relaxations represent a 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,

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

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 seven model parameters (transmission rate, β, compliance model, l and τ, and the four mentality parameters) were calibrated to the daily Belgian hospitalizations between September 1st, 2020 and December 13th, 2020. 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 chain is thinned and the cornerplots (Foreman-Mackey 2016) are examined to analyse correlations between model parameters and unidentifiability issues. All calibrated parameters except the home mentality parameter (Ω_{home}) were identifiable.
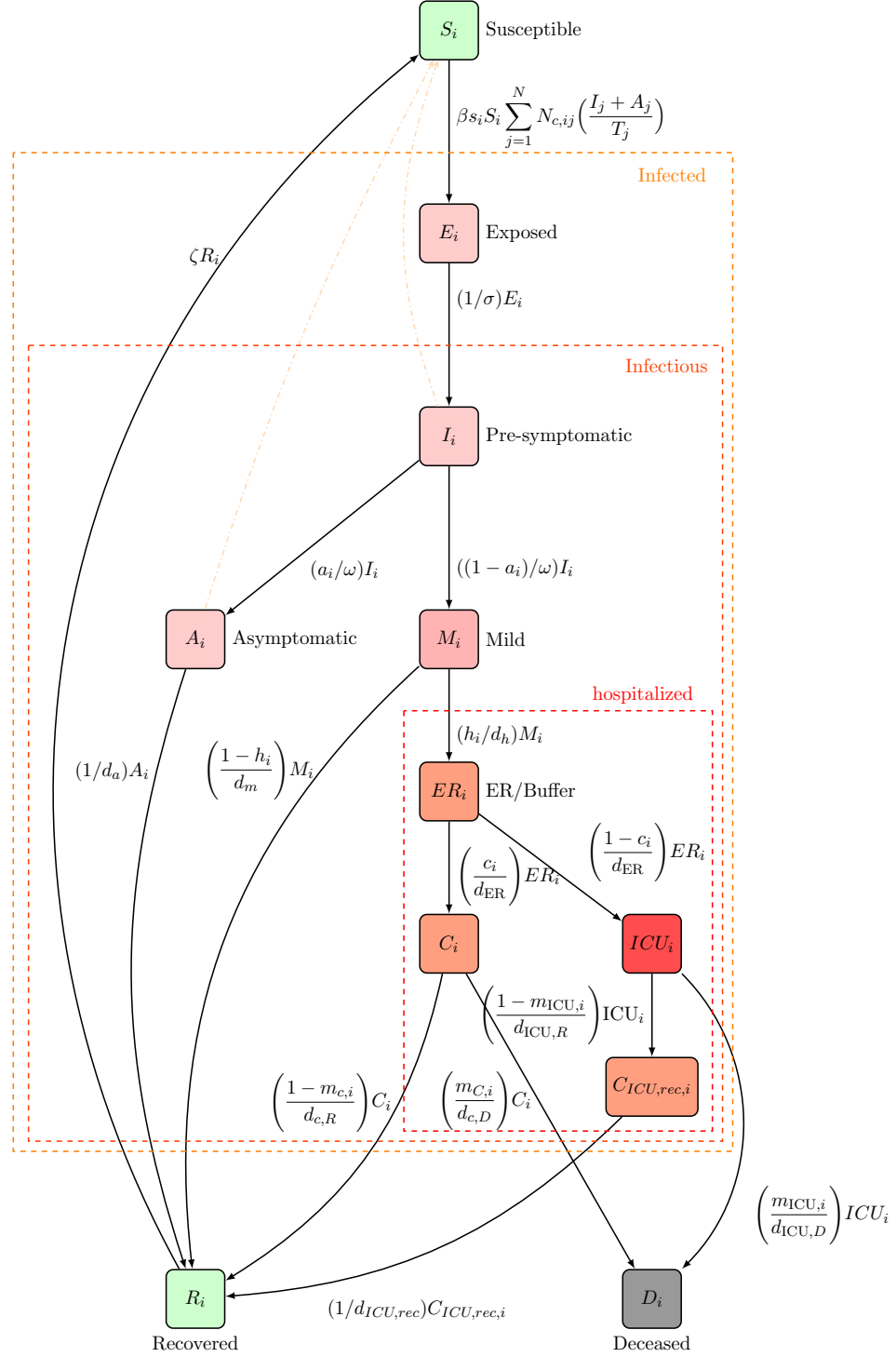
Figure 5: Extended SEIRD dynamics used in this study. Nodes represent model states, edges denote transfers.
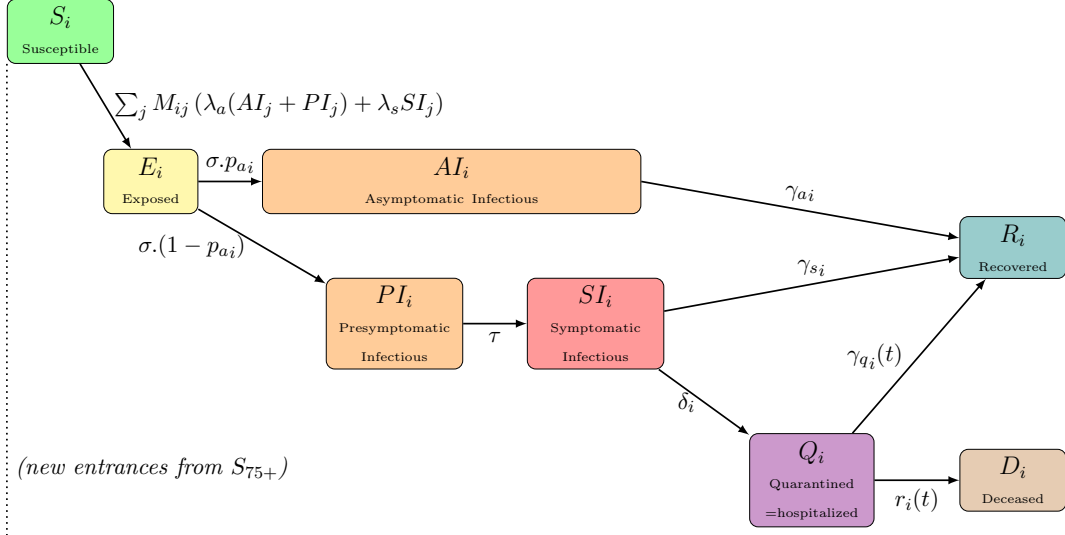
UNamur (Franco 2020)

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).

General population (age classes i = 0-24, 25-44, 45-64, 65-74, 75+):

S_i
Susceptible

$\sum_j M_{ij} \left(\lambda_a (AI_j + PI_j) + \lambda_s SI_j \right)$

E_i
Exposed

$\sigma \cdot p_{a_i}$

AI_i
Asymptomatic Infectious

γ_{a_i}

$\sigma \cdot (1 - p_{a_i})$

PI_i
Presymptomatic
Infectious

τ

SI_i
Symptomatic
Infectious

γ_{s_i}

R_i
Recovered

$\gamma_{q_i}(t)$

δ_i

Q_i
Quarantined
=hospitalized

$r_i(t)$

D_i
Deceased

(new entrances from S_{75+})

nursing homes (2000 separated copies):

S_h
Susceptible

$m_h \left(\lambda_a (AI_h + PI_h) + \lambda_s SI_h \right) +$ Random transmissions from visits

E_h
Exposed

$\sigma \cdot p_{a_h}$

AI_h
Asymptomatic Infectious

γ_{a_h}

$\sigma \cdot (1 - p_{a_h})$

PI_h
Presymptomatic
Infectious

τ

SI_h
Symptomatic
Infectious

γ_{s_h}

R_h
Recovered

$\gamma_{q_h}(t)$

$\delta_h(t)$

Q_h
Quarantined
=hospitalized

$r_h(t)$

D_{75+}
Deceased
from hospitals

$(1 - P_{cor}) \tilde{r}_h(t)$
(non covid-19 deaths)
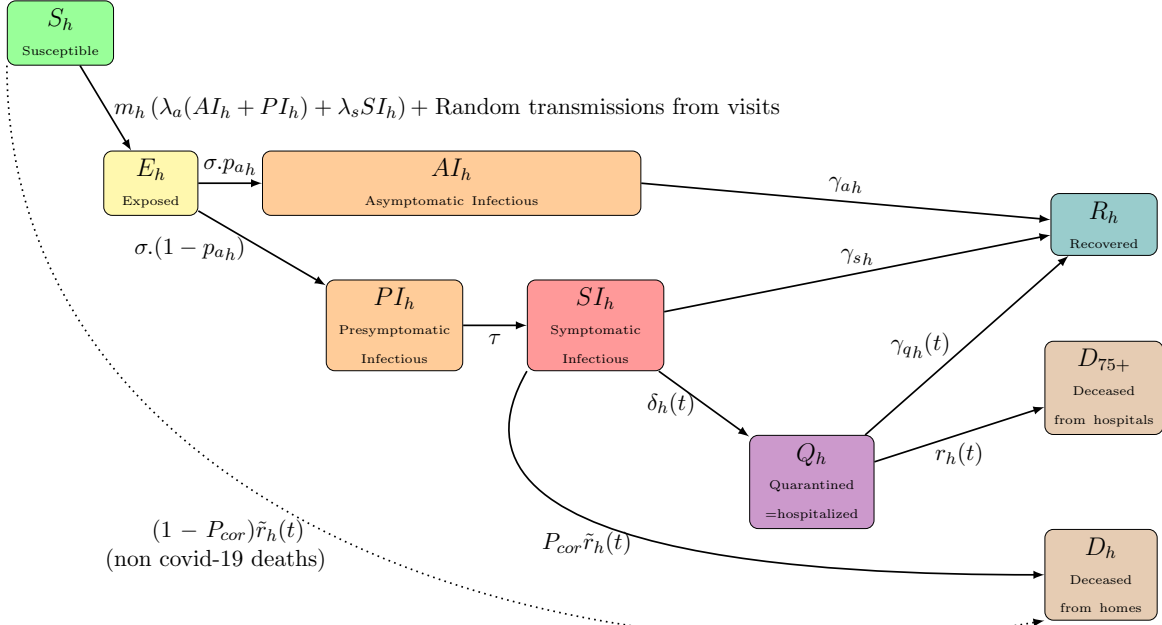
$P_{cor} \tilde{r}_h(t)$

D_h
Deceased
from homes

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. Forecasts 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 prediction 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.
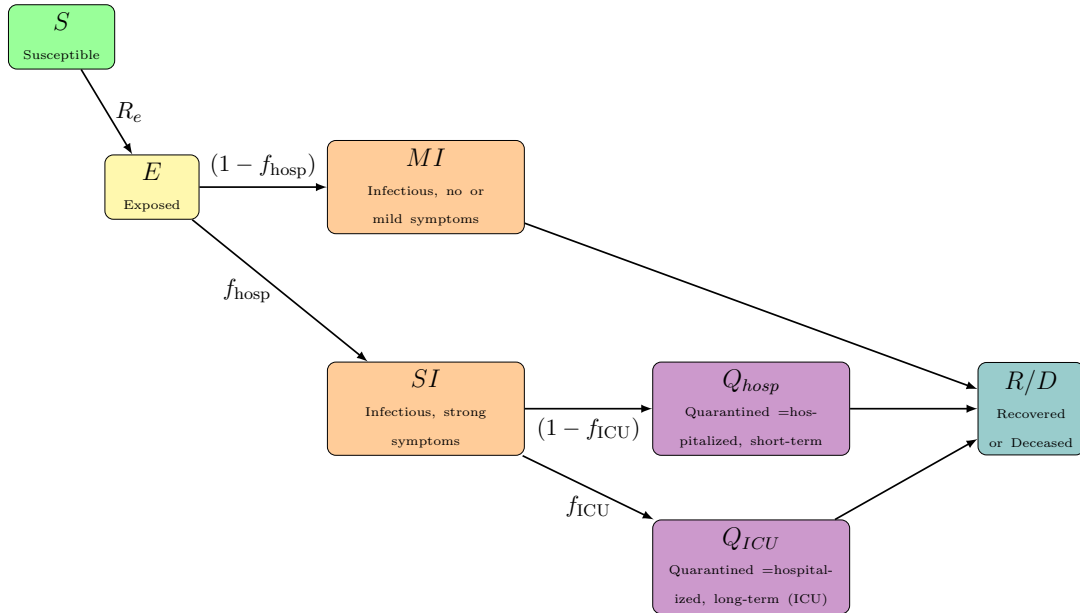

Figure 7: Schematic view of the ULB compartmental model. Each compartment is doubled in order to allow the analysis of two populations with different contact behaviours.