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SARS-CoV-2 variants and vaccination in Belgium

Modelling results by the SIMID consortium

This document contains model estimates of hospital and ICU admissions and load using observational data up to May 1st, 2021, by a short term prediction model and a stochastic dynamic transmission model. Our previous reports from February 25th and April 15th, 2021, are available via simid.be and the covid-en-wetenschap website.

Preliminary conclusions

- The age-specific vaccination uptake and the higher transmissibility and severity of variants of concern (VOC), primarily VOC-202012/1 or lineage B.1.1.7, have caused a change in the relation between confirmed COVID-19 cases, daily number of new hospitalizations, hospital load, ICU load and number of COVID-19 related deaths (see e.g. Davies et al. 2021, Patone et al. 2021).
- The short term prediction model depicts a further decrease in new hospitalizations and ICU load, driven by the current decrease in positivity ratio and the observed mobility patterns. The model predicts between 63 and 116 new hospital admissions and between 441 and 468 patients in ICU on May 19th.
- Dynamic stochastic modelling of the underlying mechanisms informed by empirical social contact data up to April 18th, 2021, shows also decreasing trends that reach on average 100 hospital admissions and an ICU load of 500 beds by the end of May. However, these projections show large credible intervals and should be interpreted with care.
- Model scenarios assuming a shift in behavior (and transmission) on 19-24 April, 2021, in line with the situation of 1-24 March, 2021, show a plateau in hospital admissions in May-June 2021.
- Model scenarios assuming also a substantial change in behavior in May 2021, show a resurgence of the hospital admissions and associated occupancy in ICU and non-ICU. This is more pronounced when this behavioural change occurs from the 1st of May, instead of from the 15th of May onwards.

Short-term modelling

Summary: The short-term prediction model for both the number of new hospitalizations and ICU load has been adapted for the presence of the VOC in order to explain the observed trends in the data.

Model assumptions to predict new hospitalizations

- The short-term prediction model is based on a statistical regression model, called a distributed lag non-linear model (Gasparrini et al. 2017).
- The model compares the trend in the number of new hospital admissions at province level with a set of early-warning predictors. They are early-warning in the sense that the observed value of the predictors on a given day d, is related to the number of new hospitalizations some days later $(d + x)$.
- The selected predictors for new hospitalizations are the positivity ratio of the COVID-19 tests and the mobility. There is a small delay (between 4 to 7 days) between the trend of the positivity ratio and the number of hospitalizations, such that we can predict the number of new hospitalizations ahead in time. This delay is linked to the time between symptom onset and hospitalization (Faes et al. 2020). The mobility is based on mobile network data, and is highly correlated with the intervention measures taken.
- To allow for a prediction over a period of 2 weeks, the positivity ratio is further informed by the number of patients with respiratory symptoms who visit a GP (COVID-19 barometer data, https://covid19.healthdata.be/) and data on absenteeism at work, which are both associated with new hospitalizations within 10 to 14 days. This is similar to the mean time between symptom onset and hospitalizations for the working ages.
- The rate of hospitalization is also allowed to change based on the proportion of VOC in the population.

Model assumptions to predict ICU load

We use the bi-monthly distribution of hospital and ICU length of stay and the proportion of hospitalized patients going to ICU, based on the clinical hospital survey (Van Goetem et al. 2020). These probabilities are combined with the observed and predicted number of new hospitalizations to calculate the number of patients in ICU. The short-term prediction model for ICU load has also been adapted to the VOC situation, allowing for a higher proportion of hospitalized patients that need ICU care (i.e. an increase of hospitalized patients going to ICU from 22.7% to 27.1%, based on the clinical hospital survey and surge capacity study). As there is only limited information on the proportion of patients requiring ICU care, these estimates need to be interpreted with caution.

Major limitations (and future work)

- This statistical regression-based prediction model is suited only for short term predictions ($\sim$ 10 days) in time, and depends on the available information on the day of model calibration.
- This method is sensitive to changes in the relation between the positivity ratio and daily incidence of hospitalizations, which are likely given the increase in vaccine-induced immunity leading to a decrease in symptom severity for older age groups.
- The model is not age-structured, as the daily new hospital admission data are only available at the aggregate level, without specification of age, variant type or vaccination status. Given these data constraints, important age-specific differences are ignored in the short term prediction model.
- Recent changes in length of stay in hospital and intensive care can influence estimation of hospital load and ICU load.
- Due to limited information on currently hospitalized patients, there is large uncertainty on the proportion of patients needing intensive care and their length of stay in hospital.

Model results

The prediction model that allows for a change in the rate of hospitalizations due to infections with the VOC captures the observed number of hospitalizations well. The model predicts a further decrease in new hospitalizations. The prediction model predicts between 63 and 116 new hospital admissions on May 19th. The ICU-related model predicts between 441 and 468 patients in ICU on May 19th.

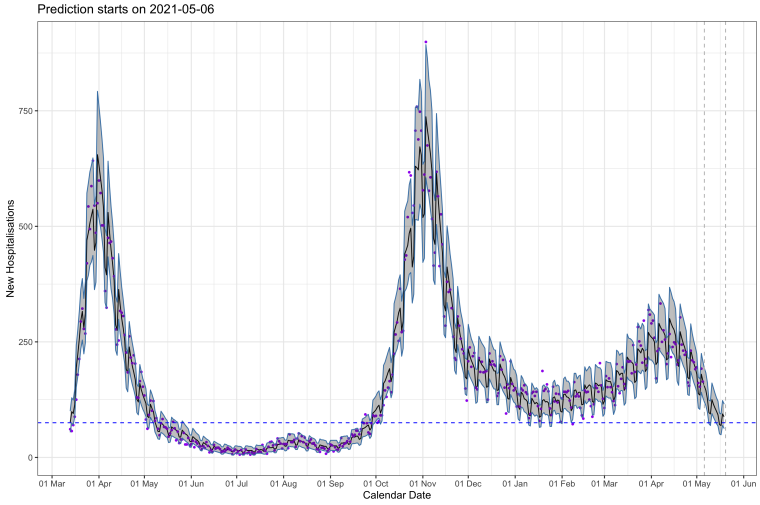

Figure 1: Short term prediction model with VOC adjustments for the hospital admissions. The dots represent the reported number of hospital admissions and the grey band shows the prediction interval.

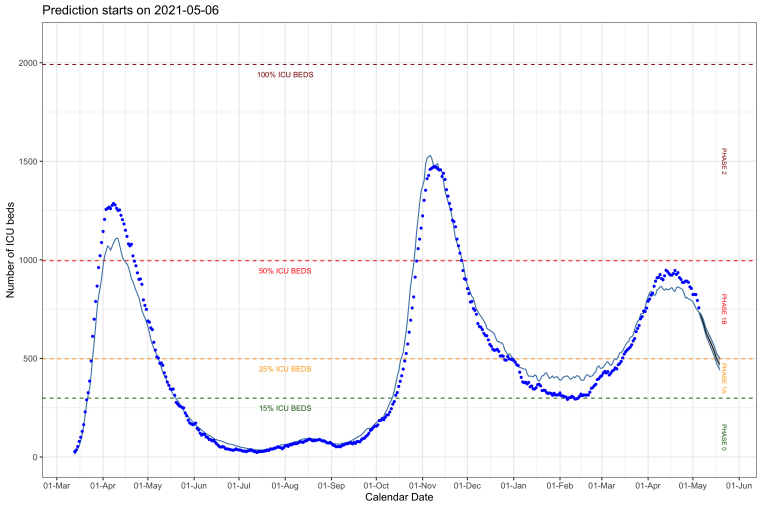

Figure 2: Short term prediction model with VOC adjustments for the ICU load. The dots represent the reported ICU load and the grey band shows the prediction interval.

Dynamic Transmission Model

Summary: The stochastic model as reported by Abrams et al. (2021) has been adapted to include vaccination and the emergence of the VOC B.1.1.7. The model is calibrated on early sero-prevalence data, genomic surveillance S gene dropout data, hospital admission data until May 1st, 2021, and social contact data up to the 20th wave of the Belgian CoMix survey conducted from April 14-20, 2021. Model projections account for the increasing vaccine uptake and the projected hospital admissions are translated into hospital and ICU load using the methodology of the short term prediction model described above.

Model input and assumptions

1. **Gradually accumulating naturally-acquired immunity** in the population is accounted for, as well as immunity induced by vaccination. Vaccine-induced immunity is assumed to last till the end of the simulations.

2. The impact of the introduction of VOC B.1.1.7 in the Belgian population is accounted for using separate data analyses on the gradual penetration of the VOC (i.e. VOC B.1.1.7, Wenseleers 2021) and its **additional transmissibility** is estimated by the model while fitting from January 1, 2021 onward at 30.0% (95% credible interval: 27.9%-33.4%) relative to the old variant.

3. The model was calibrated allowing for a **differential hospital admission probability with respect to the VOC**. The relative increase in the probability of being admitted to hospital was estimated at 36.5% (95% credible interval: 35.3%-40.1%).

4. Our model results contain stochastic variation in the transmission process and parameter uncertainty based on 100 model parameter configurations. The calibration procedure relies on likelihood-based MCMC sampling resulting in 100 posterior samples of the joint distribution, each of which is used to generate a single stochastic realization within each social mixing and/or vaccine uptake scenario.

5. This model is **fully age-structured** but does not simulate the physical interactions of subgroups like nursing home residents and nursing home personnel or healthcare workers in general. Vaccine uptake for health care workers is therefore implemented at the level of the ages of the target group.

6. We designed four **social mixing scenarios** to explore the impact of behavioral changes in the coming weeks and months by re-using estimated transmission dynamics from previous stages in the Belgian COVID-19 epidemic. This approach aims to re-capture social contact and risk behaviour that originates from measures that were previously in place, rather than the translation of measures into behaviour via ad-hoc adjustments of social contact patterns. The scenarios are not intended as justification to return to or reintroduce a specific set of measures and circumstances from the past.

    - **Scenario A:** We assume no changes in social mixing behavior compared to the estimated dynamics up to April 18th, until the end of the simulation.
    - **Scenario B:** We assume a linear shift in behavior (i.e. transmission dynamics) on April 19-25th, towards the dynamics that were estimated for March 1-24th, 2021. This behavior is assumed to be maintained until the end of the simulation.
    - **Scenario C:** We assume the behavioral shift as in scenario B with an additional increase in transmission starting on May 1st, which linearly evolves over 7 days towards the dynamics that were estimated for September 1-30th, 2020. This behavior is assumed to be maintained until the end of the simulation.
    - **Scenario D:** We assume the same behavioral changes as in scenario B, with an additional increase in transmission starting on May 15th, which linearly evolves over 7 days towards the dynamics that were estimated for September 1-30th, 2020. This behavior is assumed to be maintained until the end of the simulation. So scenario D is similar to scenario C, but the assumed change in transmission is imposed at May 15th instead of May 1st.

    All scenarios account for the Belgian summer holidays with an instant shift in behavior/transmission on July 1st, 2021. From that moment in time, we apply the behavior we estimated in our model for July 2020 (based on the Belgian CoMix waves 5 and 6).

7. **Vaccine protection**

- **Infection:** we use a "leaky" vaccination approach. For example, vaccination with 75% effectiveness, implies that the likelihood to acquire infection for a vaccinated individual is 75% less compared to a non-vaccinated individual of the same age. The vaccines are assumed to protect against the VOC to the same extent as to the (originally dominant) wild type virus.
- **Hospital admissions:** vaccinated individuals who acquire infection have a lower risk for COVID-19 related hospital admission. Pending more evidence, we assume an overall reduction of 95% as shown in different vaccine trials (Creech et al 2021).
- **Severe non-hospitalized cases** are currently not separately modelled, hence the impact of vaccination on non-hospitalized severe cases, seen in primary care is not separately shown.
- **Vaccine-induced immunity** against infection is implemented as a step function with a switch from 0% to 75% protection against infection 21 days after the first dose. Vaccine-induced protection against hospital admission is implemented in the same way using the (higher) estimates reported above. For the purpose of this document, we do not consider differences between mRNA and adenovirus-based vaccines in how they induce immunity and protection.
- **Waning immunity** is not included at this stage given the relatively short time horizon considered after complete vaccination schedule deliveries in the simulation. Therefore, potential differences in effectiveness over time of full and partially delivered vaccine schedules is not explored in the current analyses.

8. **Vaccine uptake**

- We apply an **age-specific uptake scheme** targeting the most vulnerable population first based on reported first dose uptake by Sciensano on May 1st and non-confirmed estimates on the available doses until July 31st (see Table 1). Vaccine uptake is uncertain as it is subject to variable supply schemes and potentially changing age-specific vaccine acceptance in the population.
- We do not account for waning immunity, differences between vaccine types, nor the effect of a second dose, hence we focus on the uptake of the first (or single) dose.
- Given the delay in registration in Vaccinnet+, we discard 10 days of the reported uptake. For the remaining simulation period, we attribute the available doses by decreasing age group with maximum uptake capped at 80% for the age groups under 70 years of age and 90% for those aged 70 years and older (Beutels 2021). To account for the uptake we currently observe in all age groups, due to risk group vaccination and reserve lists, we included an age-specific baseline uptake per day based on the average of the last 7 observations.
- We do not account explicitly for the risk-group vaccination anymore, though the vaccine uptake does increase for all ages in May 2021.
- As sensitivity analysis 1, we include an uptake scenario in which 30% of the planned uptake for May-July is not realised, and in which the maximum uptake for the age groups under the age of 70y is capped at 60% (instead of 80%). Possible explanations are shortages of doses, unforeseen adverse event signals requiring to stop certain vaccine deliveries, capacity constraints and/or vaccine refusals. Details are presented at the end of this report.

Table 1: Cumulative uptake of at least one dose as % of the Belgian population by age group and the total number of individuals. The shaded rows are based on reported uptake by Sciensano, the others are based on assumptions (see text).

Date	20-39y	40-49y	50-59y	60-69y	70-79y	80-89y	+90y	Total (individuals)	+65y
31/1/21	2%	2%	3%	2%	4%	13%	24%	310,821	7%
28/2/21	5%	6%	6%	4%	4%	14%	26%	523,151	8%
31/3/21	10%	11%	12%	13%	23%	52%	77%	1,404,497	30%
14/4/21	11%	12%	14%	25%	55%	83%	84%	2,124,714	54%
30/4/21	12%	13%	19%	55%	90%	90%	90%	3,020,187	79%
31/5/21	14%	64%	80%	80%	90%	90%	90%	5,145,001	87%
30/6/21	80%	80%	80%	80%	90%	90%	90%	7,384,596	87%
31/7/21	80%	80%	80%	80%	90%	90%	90%	7,439,479	87%

Major limitations (and future work)

- **This transmission model is suited for scenario analyses to investigate possible future paths, it is not a prediction model.**
- The model is calibrated on hospitalizations up to May 1st 2021, and is informed by the 20th wave of the Belgian CoMix social contact data survey. These empirical social contact data inform mainly the frequency and age structure of person-to-person social interactions, but are less informative with regards to the adherence to restrictions. The fact that the model is primarily calibrated on hospitalizations, and given the time lag between incurring infection and being admitted to hospital, makes this model less sensitive for rapidly changing dynamics. Another issue is that empirical data on social contact patterns to inform the model is also lagging.
- The (weekly) age distribution of hospitalized patients is derived from the individual hospital survey in which patients are only included at hospital discharge. This implies a considerable delay in the availability of up to date information concerning the age distribution. In a transition phase in which the weekly age distribution changes drastically, e.g. due to the depletion of susceptible persons in older age groups as a result of vaccination, this delay could have a considerable impact on future trajectories.
- We are using data on the penetration of VOC B.1.1.7, making the implicit assumption that this will remain the dominant strain throughout the simulations. Nonetheless, other VOC may take over from B.1.1.7, with different probabilities of transmission, disease, hospitalization, death, and different vaccine effectiveness characteristics against each of these manifestations.
- The transmission model does not evaluate the prevented (severe) outpatient cases, which affect pressure exerted on primary care. The model does not include parameter uncertainty on vaccine uptake and effectiveness yet, and assumes no waning of vaccine-induced and naturally acquired immunity. The model is fitted to mortality data by age for the first wave, but this has not been possible yet for the second wave.
- The VOC-related incremental transmissibility and probability to be hospitalised is not age-specific in our dynamic model but captures the population-level behaviour.
- Vaccine-induced immunity is implemented by a step function. As such, it is assumed that there is no gradual build-up of immunity in vaccinated persons. We assume a similar vaccine related protection for VOC and non-VOC.
- We present our modelling results by the mean and 95% credible interval of 100 model realizations, which capture stochastic effects and parametric uncertainty. The interplay between these two actors and the presentation of modelling uncertainty is the subject of future research.

Model Results

The following figures present the results of our scenario analyses with respect to social mixing and vaccine uptake. All projections show a large credible interval and should be interpreted with great caution.

Scenario A and B: compare continuation of reported social contact behavior on April 14-18 with a switch on April 19-24 (after the Easter holidays) towards the behavior of March 1-24, 2021.

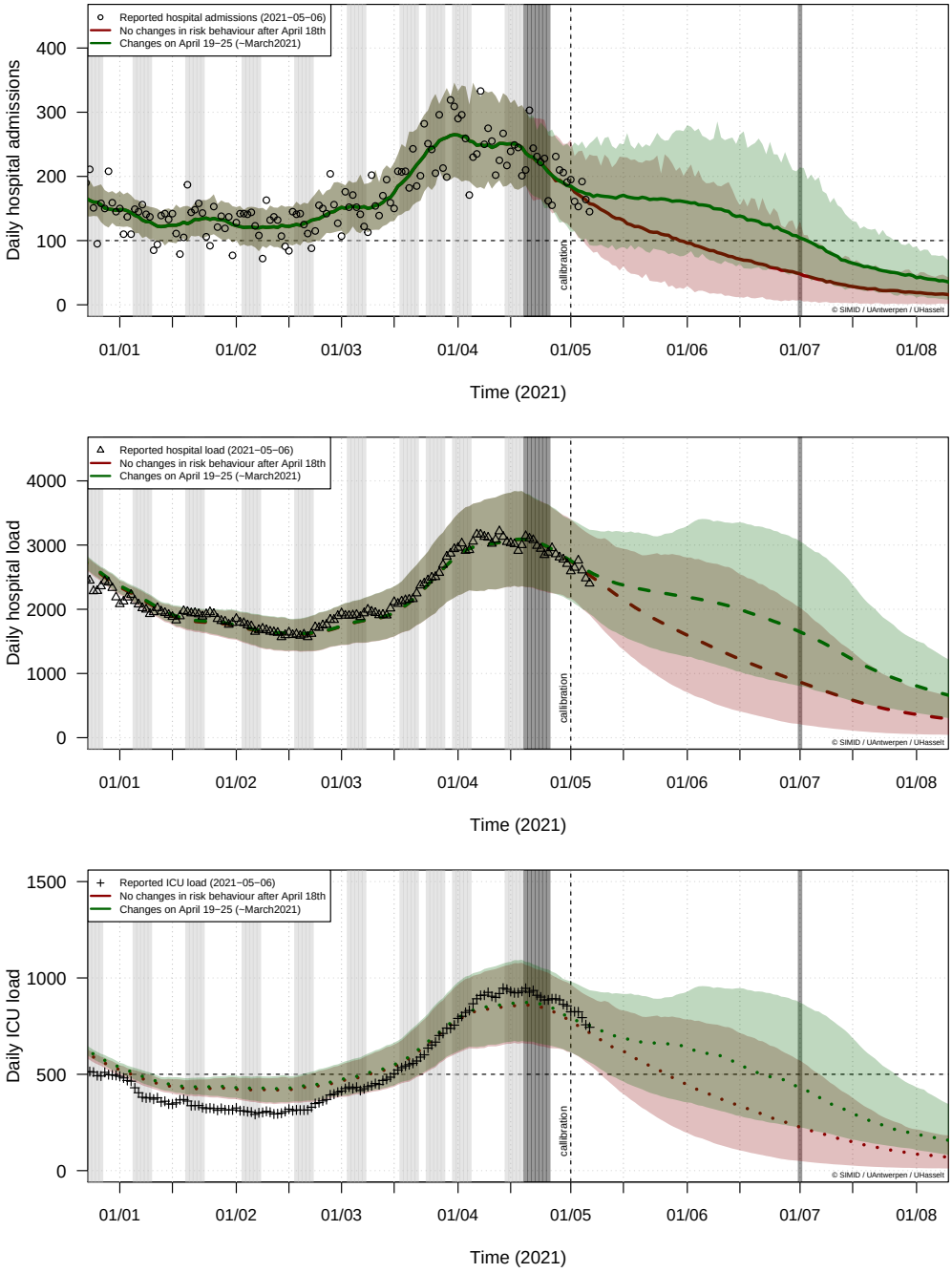

Figure 3: Model projections on daily hospital admissions, daily hospital load and daily ICU occupancy if social contact behavior from early April 2021 is kept constant (Scenario A) or changes on April 19-24, 2021, back to that of 1-24 March 2021 (Scenario B). The results are presented by the mean (line) and point-wise 95% credible interval (shaded area) of 100 model runs.

Scenario C and D: After returning to pre-Easter holidays contact behaviour on April 19-25th, compare a second change in behavior on May 1-7 (Scenario C) or on May 15-21 (Scenario D) towards social contact behaviour estimated for September 2020.

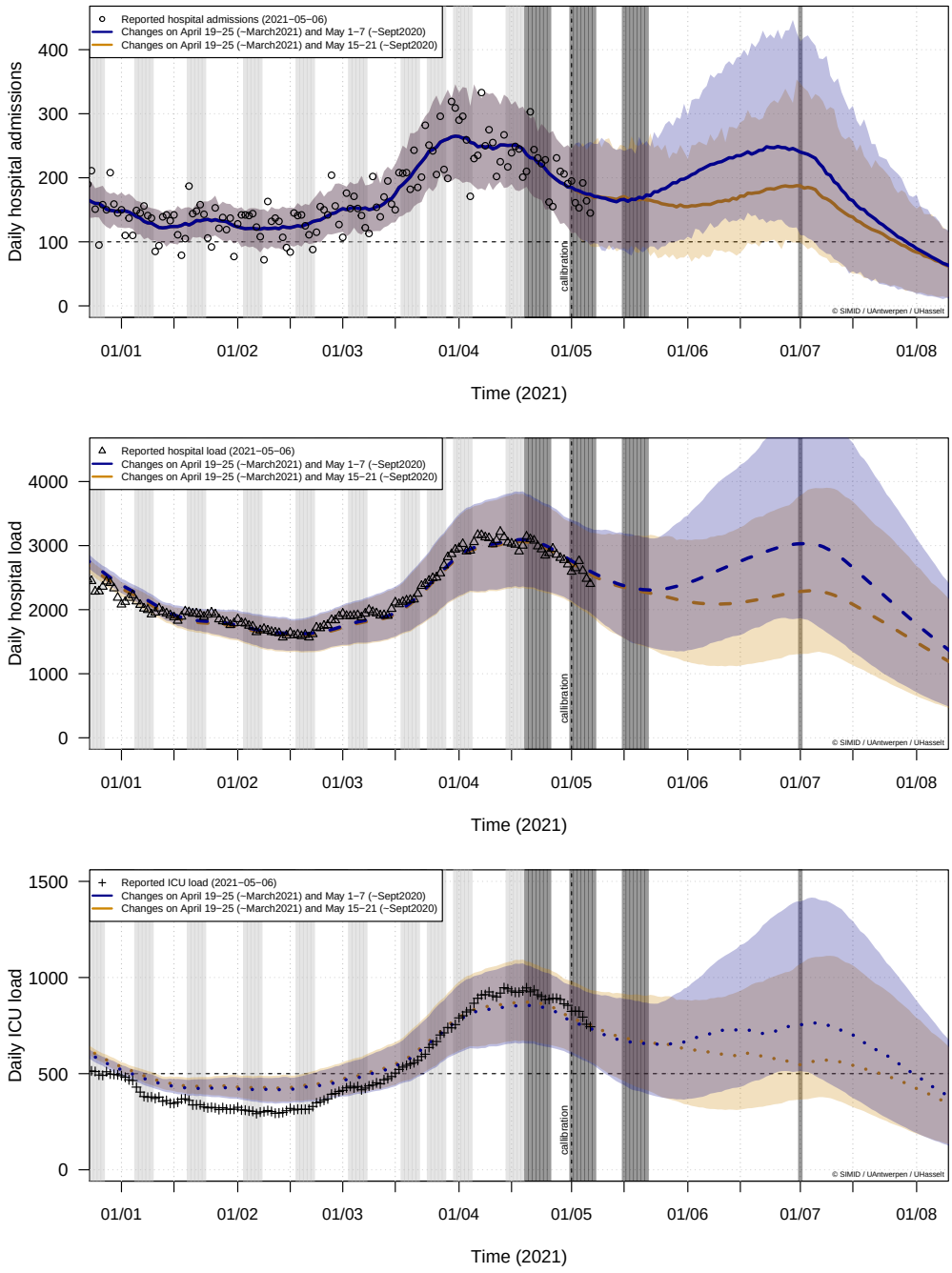

Figure 4: Model projections on daily hospital admissions, hospital load and ICU occupancy if after resuming pre-Easter holidays social contact behavior on April 19-28, it changes again on May 1-7 (Scenario C) or May 15-21 (Scenario D), 2021, in line with the estimated behavior of September 2020. The results are presented by the mean (line) and point-wise 95% credible interval (shaded area) of 100 model runs.

Sensitivity analysis 1: Scenario B with 30% less vaccine uptake from the 1st of May 2021 or the maximum uptake for the age groups below 70 years of age capped at 60%.

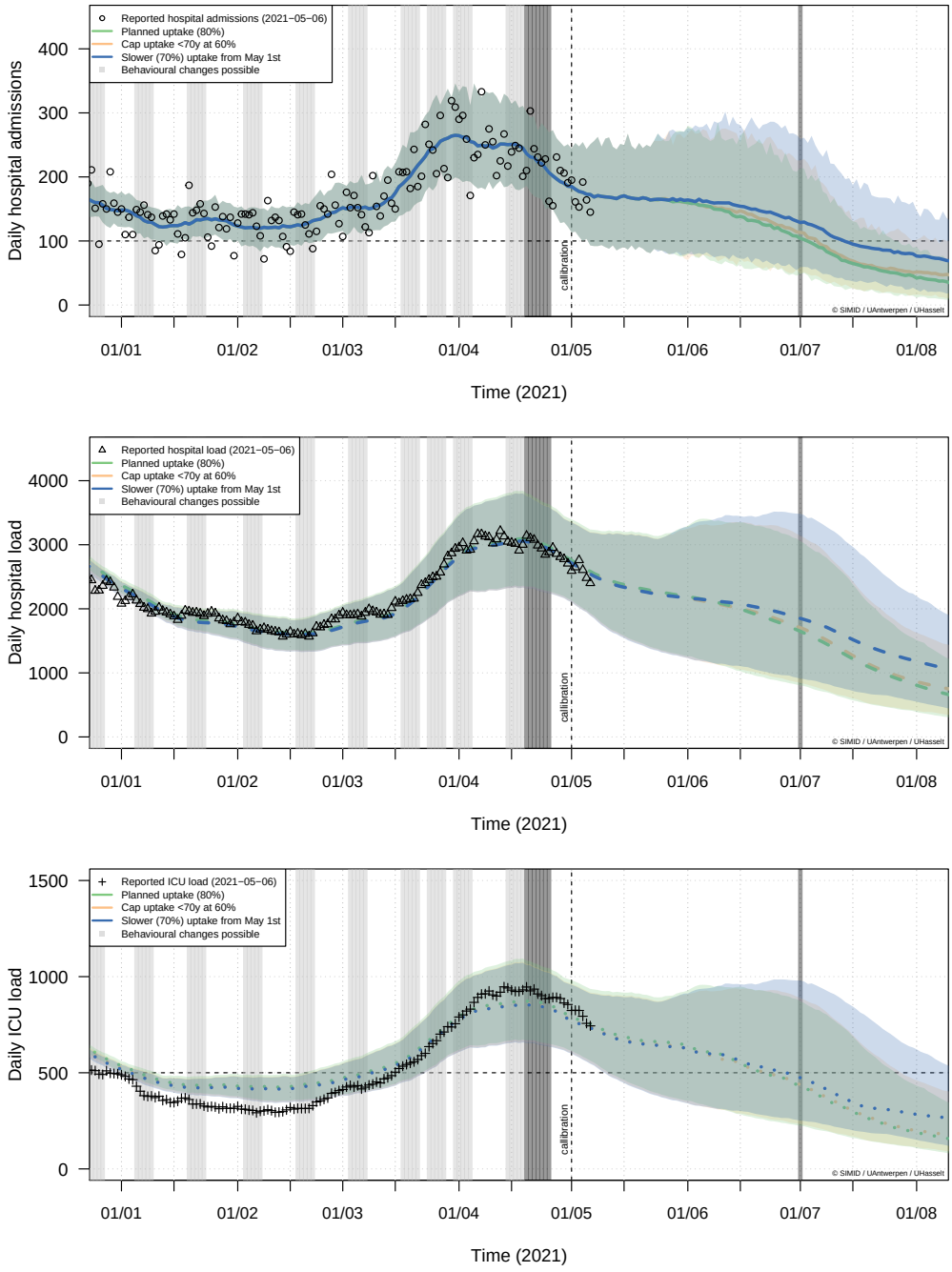

Figure 5: Model projections on daily hospital admissions, daily hospital load and daily ICU occupancy if social contact behavior changes on April 19-24, 2021, back to that of 1-24 March 2021 (Scenario B). The results are presented by the mean (line) and point-wise 95% credible interval (shaded area) of 100 model runs.

Sensitivity analysis 2: Scenario D with 30% less vaccine uptake from the 1st of May 2021 or the maximum uptake for the age groups below 70 years of age capped at 60%.

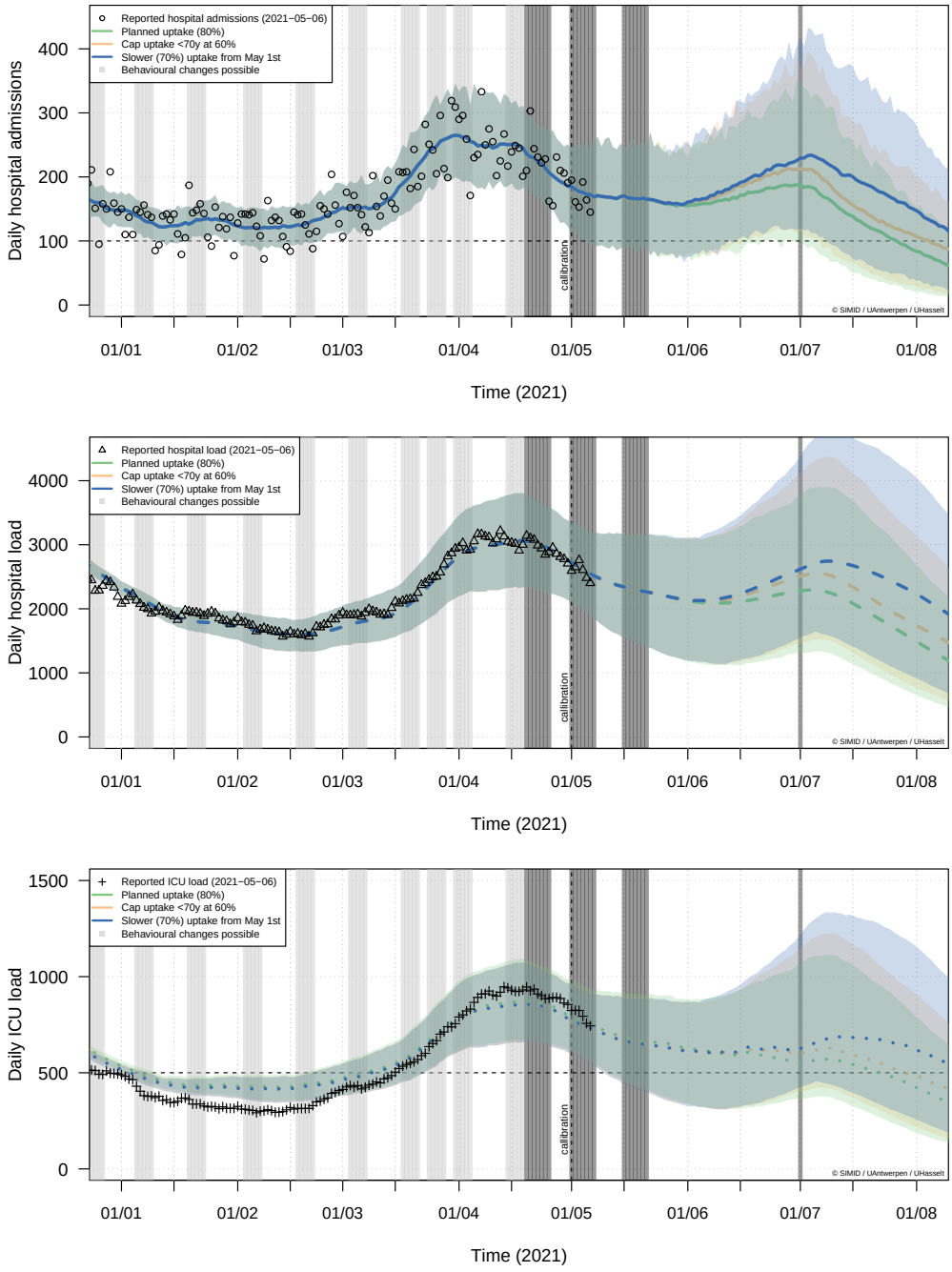

Figure 6: Model projections on daily hospital admissions, hospital load and ICU occupancy if after resuming pre-Easter holidays social contact behavior on April 19-28, it changes again on May 15-21, 2021, in line with the estimated behavior of September 2020 (Scenario D). The results are presented by the mean (line) and point-wise 95% credible interval (shaded area) of 100 model runs.

Contributors

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- Philippe Beutels (Universiteit Antwerpen)
- Steven Abrams (Universiteit Antwerpen en Universiteit Hasselt)

Selected references:

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- Van Goethem N, et al. Rapid establishment of a national surveillance of COVID-19 hospitalizations in Belgium. Arch. Public Health, 78, 121 (2020)
- Wenseleers T (2021) Analysis of VOC for Belgium https://github.com/tomwenseleers/newcovid_belgium

SUPPLEMENTS

This supplement contains more info on vaccine uptake using an alternative scenario to investigate sensitivity. We also show additional figures on the evolution of age-specific hospital admissions. The latter is based on the average observations from all runs per scenario. Finally, we illustrate the reproduction number over time (Rt) in the simulation model with the Rt based on the confirmed cases by Sciensano using the R package "EpiEstim". For the model, we calculate Rt based on the projected new infections over time.

Table 2: Projected cumulative vaccine uptake if 30% of the planned uptake for May-July is not realised. The update is presented in terms of the % of the Belgian population by age group and the total number of individuals who received at least one dose. The shaded rows are based on reported uptake by Sciensano, the other rows are based on adjusted expectations (see text).

Date	20-39y	40-49y	50-59y	60-69y	70-79y	80-89y	+90y	Total (individuals)	+65y
31/1/21	2%	2%	3%	2%	4%	13%	24%	310,821	7%
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14/4/21	11%	12%	14%	25%	55%	83%	84%	2,124,714	54%
30/4/21	12%	13%	19%	54%	90%	90%	90%	3,004,121	79%
31/5/21	14%	21%	80%	80%	90%	90%	90%	4,491,491	87%
30/6/21	37%	80%	80%	80%	90%	90%	90%	6,059,208	87%
31/7/21	80%	80%	80%	80%	90%	90%	90%	7,439,479	87%

Table 3: Projected cumulative vaccine uptake if the maximum uptake for the age groups under the age of 70y is capped at 60% (instead of 80%). The update is presented in terms of the % of the Belgian population by age group and the total number of individuals who received at least one dose. The shaded rows are based on reported uptake by Sciensano, the other rows are based on adjusted expectations (see text).

Date	20-39y	40-49y	50-59y	60-69y	70-79y	80-89y	+90y	Total (individuals)	+65y
31/1/21	2%	2%	3%	2%	4%	13%	24%	310,821	7%
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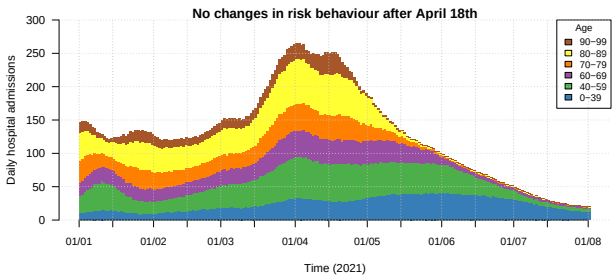
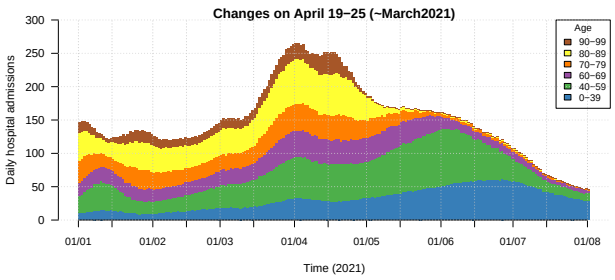
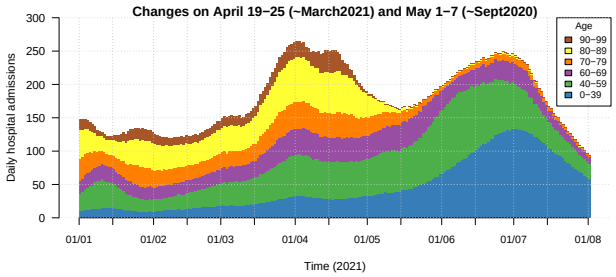
31/5/21	36%	36%	60%	60%	90%	90%	90%	5,145,001	81%
30/6/21	60%	60%	60%	60%	90%	90%	90%	5,971,031	81%
31/7/21	60%	60%	60%	60%	90%	90%	90%	5,971,031	81%



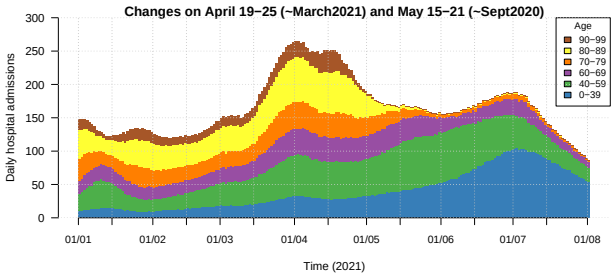
Scenario A



Scenario B

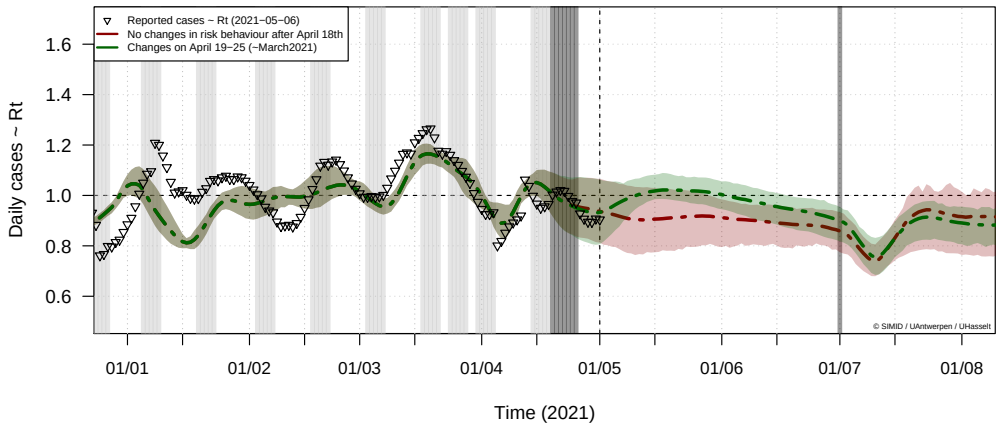


Scenario C

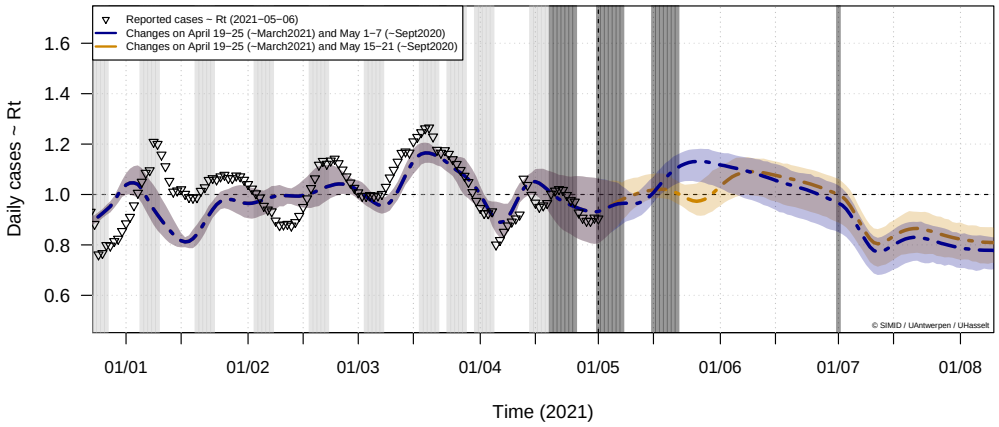


Scenario D

Figure 7: Model projections on age-specific hospital admissions by social mixing scenario presented by the average of 100 model runs.



(a) Scenario A and B.



(b) Scenario C and D.

Figure 8: Estimated reproduction number over time (Rt) based on the confirmed cases by Sciensano and the model results on new infections. The model results are presented by the mean (dotted line) and point-wise 95% credible interval (shaded area) of 100 model runs.