technical note - not peer reviewed - v20211116 (update)

SARS-CoV-2 variants and vaccination in Belgium

Modelling results by the SIMID consortium

This document contains model estimates of hospital admissions and ICU load using observational data up to November 16th, 2021, by a short-term prediction model and stochastic dynamic transmission model. All previous reports are available via simid.be and the covid-en-wetenschap blog.

UPDATE: We added the latest hospital data on November 25th, 2021, to Figures 5 and 7, together with an extra figure on Rt(hospital). The text and conclusions are not adjusted to the new information.

Preliminary conclusions

- The short-term prediction model forecasts between 298 and 543 new hospital admissions on November 26th, 2021. The ICU-related prediction model shows over 740 patients in ICU on November 26th. If the same speed of growth continues, there is a chance that 1000 ICU beds for COVID-19 patients are needed by the beginning of December.
- The stochastic transmission model for Belgium shows that if the transmission dynamics, captured by the effective reproduction number Rt, remains stable until November 21st 2021 and subsequently decreases, a peak ICU load around 750 beds could be reached by the beginning of December 2021. If Rt remains at a stable level until December 2021, the peak ICU load will be even higher and it will take longer to gradually decrease to a level below 500 ICU beds.
- If the speed at which new infections occur slows down in the second half of November 2021, implying a decreasing Rt value, an ICU load up to 650 beds could be expected based on the stochastic model projections. A stronger reduction in Rt, would lead to a more rapid decline in ICU load after the 650 bed peak, to less than 500 beds by the second week of December.
- Infections as a result of social interactions drive the projected hospital burden. Whether an hypothesized decrease or increase in transmission rates (translated into a change in Rt) is of the specific magnitude we assumed for the coming period, is impossible to estimate at this point in time. However, we present a range of plausible scenarios for Rt evolution, similar to the scenarios we formulated in our previous reports according to a percentage change in social contact behaviour/transmission rates.
- Updated transmission modelling features since October 2021: (1) the parameters are calibrated to hospital admissions with COVID-19 (hospitalised for COVID-19 and hospitalised for other pathologies than COVID-19, but with a positive SARS-CoV-2 test in the last 24h); (2) the most recently observed CoMiX social contact data are included; (3) vaccine-induced protection against transmission was specified; and (4) the hospital hazard ratio was re-estimated for infections with the VOC.

Short-term modelling

Summary: The short-term prediction model for both the number of new hospitalizations and ICU load has been adapted to provide estimates at a regional level, and to take into account differences in vaccination coverage.

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 provide an 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, mobility, median age of confirmed patients and vaccination ratio. 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). Mobility information is based on mobile network data, with predictions as from September 2021 based on the connection between mobility and the intervention measures in the past $1\frac{1}{2}$ year (due to unavailability of the aforementioned mobility data from September 2021 onward).
- 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.healthdate/) and data on absenteeism at work, which are both associated with the number of new hospitalizations within the next 10 to 14 days. This is similar to the mean time between symptom onset and hospitalizations for the working ages.
- The rate of hospitalization changed as a function of the proportion of the Delta VOC which, based on 889 sequences of positive SARS-CoV-2 samples collected as part of the baseline surveillance between 2nd and 15th August, accounts for about 99% of all infections (Genomic surveillance of SARS-CoV-2 in Belgium - report 2021-41).

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 Delta VOC, allowing for a higher proportion of hospitalized patients that need ICU care.

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 relationship between the positivity ratio and daily incidence of hospitalizations.
- 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. This information is only taken into account at the aggregate (provincial) level. Given these data constraints, important age-specific differences are ignored in the short-term prediction model.
- Changes in treatment practices and associated length of stay in hospital and intensive care can influence estimation of hospital load and ICU load.

- Due to a delay in information on currently hospitalized patients, there is large uncertainty on the proportion of patients needing intensive care and their length of stay in hospital.
- The number of new hospitalizations and corresponding ICU load do only take into account the hospital admissions due to COVID-19, and do not account for patients that have been admitted for another pathology, but are COVID-19 positive.
- The ICU length of stay and the proportion of hospitalized patients going to ICU is assumed the same for all patients within the same province, although there are clear indications that the proportion of hospitalized patients going to ICU is lower and length of stay in hospital is shorter for vaccinated individuals. As it is not reported how many of the new hospitalized patients are vaccinated, this is currently not taken into account.

Model results

The prediction model captures the observed number of hospitalizations well (see Figure 1 and 2). The model predicts a further increase in new hospitalizations in the short term. The prediction model predicts between 298 and 552 new hospital admissions on November 26th, 2021. The ICU-related model predicts over 740 patients in ICU on November 26th, 2021. If the same speed of growth continues, there is a chance that 1000 ICU beds for COVID-19 patients are needed by the beginning of December 2021.

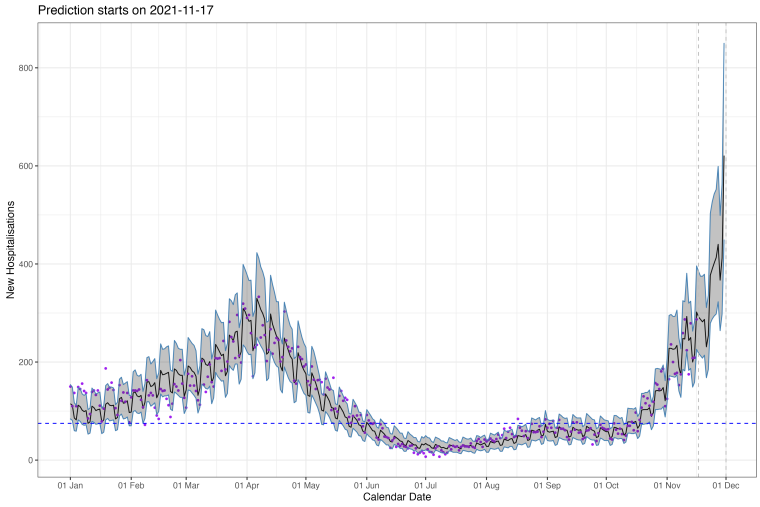


Figure 1: Short-term prediction model for the hospital admissions (national level). The dots represent the reported number of hospital admissions and the grey band shows the prediction interval.

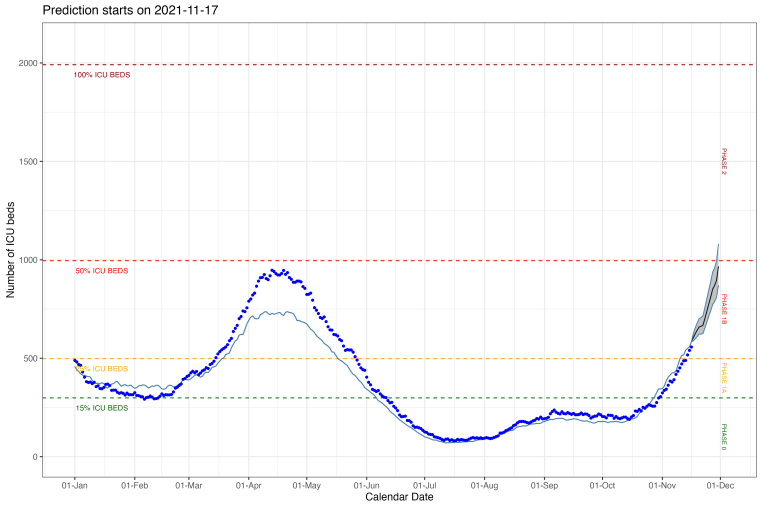


Figure 2: Short-term prediction model for the ICU load (national level). The dots represent the reported ICU load and the very narrow grey band shows the prediction interval.

At a regional level, the model predicts further increases in all regions (Brussels, Flanders and Wallonia). The prediction model predicts, on November 26th, 2021, around 15 (range 5-32) new hospital admissions in Brussels, around 320 (range 216-456) in Flanders and around 76 (range 46-114) in Wallonia. The ICU-related model predicts around 63 (range 56-71) patients in ICU in Brussels, around 556 (range 454-683) in Flanders and around 190 (range 161-225) in Wallonia, on November 26th. In Flanders, there is a high probability that the ICU capacity of 50% level of the available ICU beds is exceeded by the end of November.

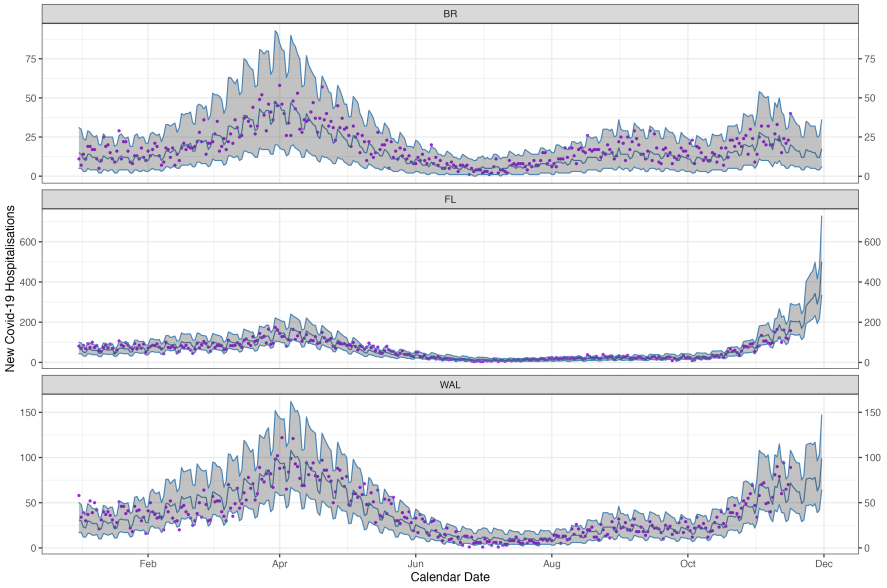


Figure 3: Short-term prediction model for the hospital admissions (regional level). The dots represent the reported number of hospital admissions and the grey band shows the prediction interval. Top panel: Brussels, Middle panel: Flanders, Bottom panel: Wallonia.

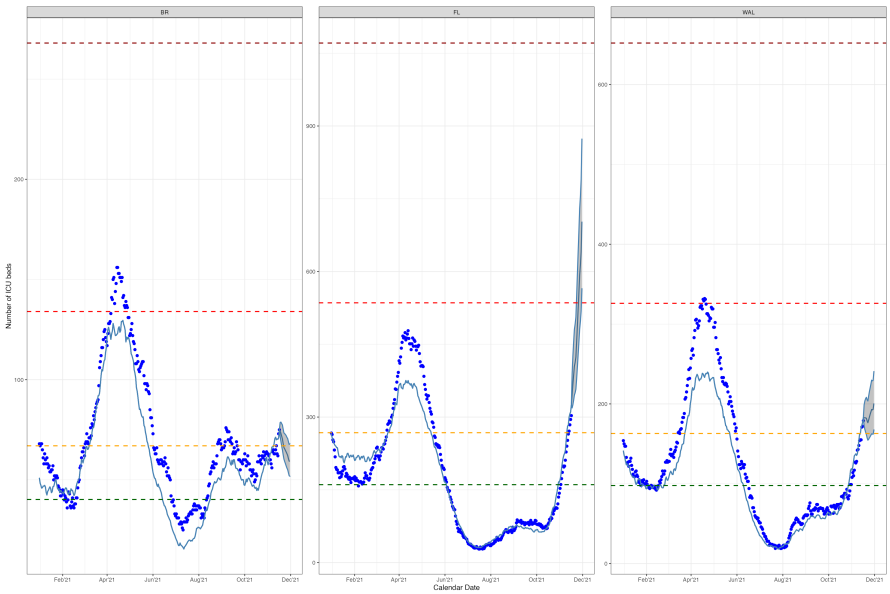


Figure 4: Short-term prediction model for the ICU load (regional level). The dots represent the reported ICU load and the grey band shows the prediction interval. Left panel: Brussels, Middle panel: Flanders, Right panel: Wallonia.

Dynamic Transmission Model

Summary: The stochastic model as described by Abrams et al. (2021) has been adapted to include vaccination and the emergence of one VOC from December 2020 (i.e. B.1.1.7 or "Alpha") and another VOC from May 2021 (i.e. B.1.617.2 or "Delta"). The model is calibrated on early sero-prevalence data, genomic surveillance data, hospital admission data, hospital surge data, mortality data and social contact data from the Belgian CoMiX survey. All model projections account for an increasing vaccine uptake and the ICU load is directly captured within the transmission model.

Model input and assumptions

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

2. The **introduction of VOCs in the Belgian population** is accounted for by using data from the baseline genomic surveillance of SARS-CoV-2 in Belgium at the National Reference Laboratory.

3. **Alpha VOC:** We aggregated the proportion of Alpha, Beta and Gamma VOC in the population to account for the replacement of the wild-type variant by more infectious and severe VOCs (for which increased transmissibility and severity is assumed to be equal). The additional transmissibility of the aggregated VOC, which we will denote in this report by the dominant VOC Alpha, is estimated by the model at 35% (95% credible interval (CrI): 29%-40%) relative to the wild-type variant. The model assumes no differential hospital admission probability with respect to the Alpha VOC. Upon infection, the model allows for a VOC-specific differential hospital length-of-stay and risk of ICU admission.

4. **Delta VOC:** The impact of the Delta VOC is modelled by the introduction of a second VOC from May 2021 onward with an average increase in transmissibility of 80% (95% CrI: 65%-99%) relative to the Alpha variant. This increase is estimated based on the baseline genomic surveillance data. We assume a hazard ratio for hospitalization of 2 for the Delta VOC relative to the Alpha VOC. Mean values of 1.8-2.6 have been reported in the UK (with 95% confidence interval up to 4.36, see PHE, Sheikh).

5. Our model results contain stochastic variation in the transmission process and parameter uncertainty based on 40 model parameter configurations. The calibration procedure relies on likelihood-based MCMC sampling resulting in 40 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. The MCMC procedure is, in general, based on the adaptive Metropolis-within-Gibbs algorithm, and parameter configurations are updated starting from previous calibration results based on an additional number of iterations (1000 iterations) with 10 realizations per iteration, periodicity of 10 iterations and leading to 40 different chains based on 40 initial starting configurations.

6. 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.

7. Since the report from October 2021, we complement the reported hospital admissions with the number of new positive cases in the Belgian hospitals in the last 24h that have been admitted for another pathology. Given that these positive cases contribute to the COVID-19 related hospital load, we include these new patients in our analysis and Figure 5. For illustration purposes, we also compare the model trends with the hospital admissions for COVID-19 (Figure 7). Hospital admission data is still the main source of information to inform and calibrate the model given the frequent changes in the Belgian SARS-CoV-2 testing policy (and its impact on the daily number of confirmed COVID-19 cases).

8. The model is calibrated using social contact data up to the 33th wave of the Belgian CoMiX survey conducted from October 12-17th, 2021. For each wave, we estimate age-specific q-parameters (i.e., proportionality factors) to translate social contact data into transmission rates, with estimated social contact rates used as a proxy for effective contacts enabling disease transmission and proportionality factors adjusting for other factors that influence this relation. This captures, among other things, age-specific susceptibility and risk behavior during social contacts.

9. We designed five **social mixing scenarios** to explore the impact of behavioral changes and adjusted transmission dynamics. None of the scenarios include the introduction of infected cases as a result of international travel. All behavioral changes are introduced linearly over 7 days. Note that the proposed scenarios (as described in more detail below) are characterized by a different evolution of the effective reproduction number Rt (based on confirmed cases) over time. This bridges the gap between infections that occur at this moment in time and subsequent hospitalizations somewhat later. Based on these different Rt trends, one can clearly see the extent of uncertainty regarding the future evolution of hospital incidence and load, both in terms of peak size as well as timing.

    - **Scenario A:** We assume a constant decrease in the reproduction number Rt based on new infections from November 1st, 2021 until the start of 2022. In particular, the number of new infections might still increase the coming week, but is assumed to decrease once Rt is below 1.
    - **Scenario B:** We assume a plateau in Rt until November 21st, 2021, and a constant decrease in Rt afterwards.
    - **Scenario C:** We assume a plateau in Rt until December 1st, 2021, and a constant decrease afterwards.
    - **Scenario D:** We assume a fast decrease in Rt from November 21st, 2021.
    - **Scenario E:** We assume an increase in Rt until December 1st, 2021, and a constant decrease afterwards.

10. **Vaccine protection**

    - **Infection:** we use a "leaky" vaccination approach. For example, vaccination with 50% effectiveness, implies that for a vaccinated individual the likelihood to acquire infection is 50% less compared to a non-vaccinated individual of the same age. The level of protection against infection is presented in Table 1.
    - **Hospital admissions:** vaccinated individuals who acquire infection are at lower risk of a COVID-19 related hospital admission. The level of protection against severe disease, which we assume to be in line with hospital admissions, is presented in Table 1.
    - **Transmission:** vaccinated individuals who acquire infection have a lower risk of transmitting the disease. This assumption is based on a study in the UK on the effect of vaccination on household transmission of SARS-CoV-2 (Harris et al., 2021). The level of protection against transmission is presented in Table 1.
    - **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 e.g. 0% to 50% protection against infection 21 days after the first vaccine dose. Vaccine-induced protection against hospital admission is implemented incrementally on the protection against infection. Protection from the 2nd dose is assumed to be present 7 days after administration. We consider differences between mRNA and adenovirus-based vaccines in how they induce immunity and protection.
    - The reported JnJ and Curevac vaccines are accounted for in the model as (being similar to) AstraZeneca. Their numbers of administered vaccine doses are too low to outweigh the increase in computational burden and complexity of the model when adding an additional subdivision in the model.
    - **Waning immunity is not included at this stage.** Therefore, potential differences in effectiveness over time of the different vaccine schedules is not explored in the current analyses.
    - **Third doses (Boosters) are not included at this stage.** This might counterbalance to some extent the absence of explicit waning immunity in the analyses.

Table 1: Vaccine efficacy for adeno-based and mRNA-based vaccines against the Alpha and Delta variant by clinical outcome derived from Bernal et al. (2021) and Stowe et al. (2021).

Clinical outcome	Vaccine type	Alpha variant	Delta variant
Infection (Bernal, 2021)	Adeno: 1st dose	49%	30%
Infection (Bernal, 2021)	Adeno: 2nd dose	74%	67%
Infection (Bernal, 2021)	mRNA: 1st dose	48%	36%
Infection (Bernal, 2021)	mRNA: 2nd dose	94%	88%
Severe disease (Stowe, 2021)	Adeno: 1st dose	80%	71%
Severe disease (Stowe, 2021)	Adeno: 2nd dose	89%	92%
Severe disease (Stowe, 2021)	mRNA: 1st dose	80%	94%
Severe disease (Stowe, 2021)	mRNA: 2nd dose	95%	96%
Transmission (Harris, 2021)	mRNA and Adeno	45%	45%

11. **Vaccine uptake**

    - The vaccine-type and age-specific uptake in the model of first and second doses over time at the national level is based on the reported uptake by Sciensano, derived from Epistat on November 5th, 2021. For the model projections, we extrapolate the uptake rate of mRNA vaccines of the last 2 weeks, until 85% coverage is reached at the national level. If the reported uptake is more than 85%, we use the reported uptake. For the projected uptake, the time between 2 mRNA doses is assumed to be 3 weeks. The uptake by age group is presented in Figure 6.
    - We do not account explicitly for risk-group vaccination, since the model structure does not allow to model a sub-population with a differential risk and potentially a more severe COVID-19 disease episode once infected (i.e., a higher probability of hospitalization and/or a higher probability of death, if hospitalized).
    - By default, we include vaccine uptake in the population from 12 years of age. For 12-19-year-olds, this is implemented in our 10-year age grouped model structure by applying a proportionate fraction to the 10-19 year age group, i.e. having 80% of 10-19 year olds potentially take up vaccines.

Major limitations

- **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 and informed by 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.
- The daily age distribution of hospitalized patients is derived from the individual hospital survey **up to November 1st, 2021**, 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 of hospitalizations. In a transition phase in which the 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 making the implicit assumption that the Delta VOC will remain the dominant strain throughout the simulations. Nonetheless, other VOCs may take over with different transmission probabilities and probabilities to cause 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.

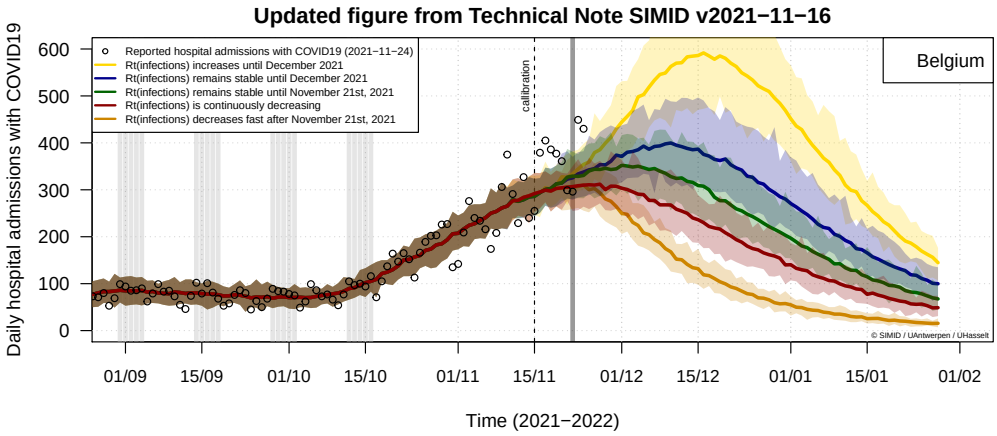
- The incremental transmissibility by the Alpha and Delta VOCs, which we include in the model, is not age-specific.
- We attribute the growth advantage of the VOCs completely to transmissibility, and as such, ignore the potential effect of immune escape on the speed of penetration.
- Vaccine-induced immunity is implemented by a step function. As such, it is assumed that build-up of immunity in vaccinated persons is not a gradual, but a step-wise process.
- We compare 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". Within the model environment, we dispose of perfect information and this allows us to calculate Rt based on all new symptomatic cases over time. The reported Sciensano data on the other hand is affected by changing testing strategies and adherence over time.
- This model does not explicitly account for importation by returning travelers which could have impact on the evolution of the epidemic. Importantly, an implicit attribution of such cases to local transmission is used instead.
- We present our modelling results by the mean and pointwise 95% credible interval based on 40 model realizations, which capture stochastic effects and parametric uncertainty. The interplay between these two sources of uncertainty is subject of future research.

Model results and discussion

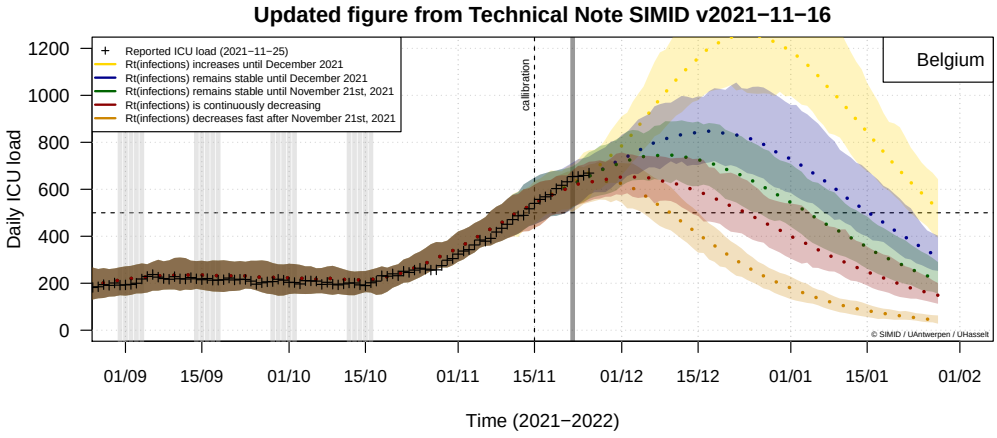
The following figures depict the results of our scenario analyses with respect to social mixing. All projections show a large 95% credible interval and should therefore be interpreted with great caution. The main conclusions are listed at the start of this document. Some additional observations and discussion points are listed hereunder:

- Social mixing behaviour still drives the projected hospital admissions and ICU load.
- The model projections are based on the hospital admissions with COVID-19, hence one can interpret them to represent the upper limit for hospital admissions for COVID-19. This is shown in Figure 7.
- The parameter estimation and model calibration are mainly driven by hospital admission data. The scenarios that are explored, provide plausible results up to the current time point (based on available hospital data) and therefore provide a plausible range of outcomes for the coming period. The scenarios under study aim to translate assumptions with respect to social contact behavior into the hospital burden when accounting for vaccine uptake.
- The national model does not account for local differences in immunity. As such, herd immunity effects in sub-populations with immunity levels above the national level are underestimated.

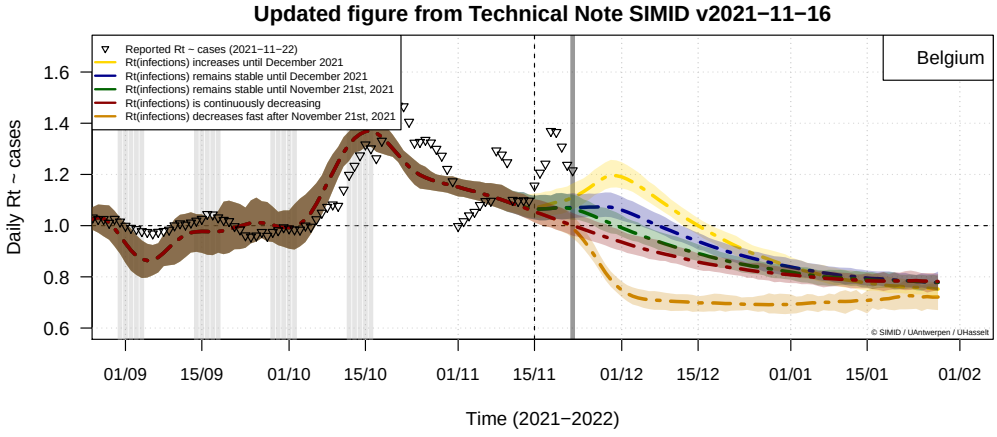
Scenario analysis for Belgium.



(a) Daily hospital admissions with COVID-19



(b) ICU occupancy



(c) Reproduction number over time (Rt)

Figure 5: Model projections for Belgium on daily hospital admissions, ICU occupancy and reproduction number for different assumptions on transmission dynamics from November 15th, 2021. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 40 model runs.UPDATE: We added the reported hospital data on November 25th, 2021.

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Acknowledgments

Sciensano for financial support in collecting CoMiX data in Belgium and making hospital data publicly available. Lize Cuypers and Emmanuel André for sharing the summary data behind: Genomic surveillance of SARS-CoV-2 in Belgium Report of the National Reference Laboratory (UZ Leuven & KU Leuven). Tom Wenseleers for discussions on VOC. We used computational resources and services provided by the Flemish Supercomputer Centre (VSC), funded by the FWO and the Flemish Government. All members of the SIMID COVID-19 modelling team.

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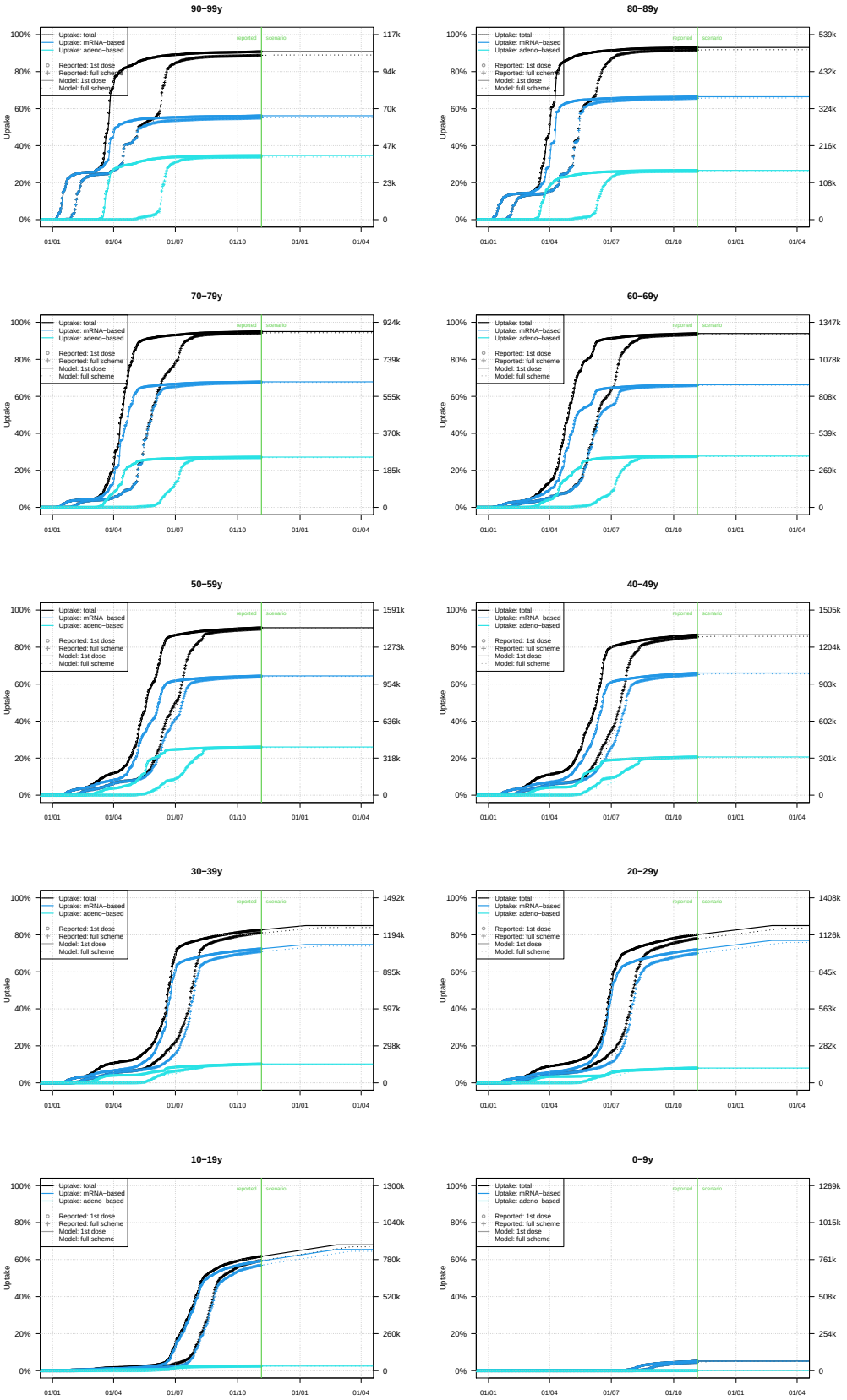

Figure 6: Included vaccine uptake by age based on the reported uptake for Belgium.

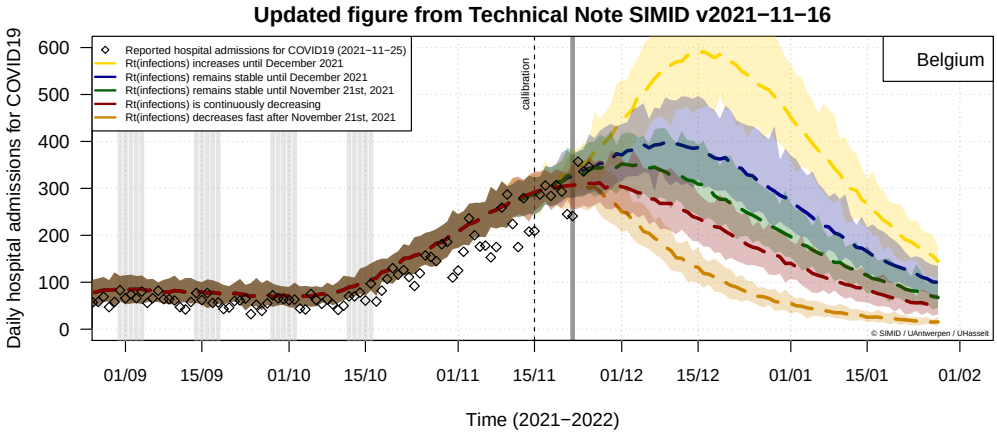

Figure 7: Model projections for Belgium on daily hospital admissions for COVID-19 with different assumptions on transmission dynamics from November 15th, 2021. The model projections account for the hospital admissions with COVID-19, hence one can be interpret them as the upper limit for the admissions for COVID-19. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 40 model runs.UPDATE: We added the reported hospital data on November 25th, 2021.

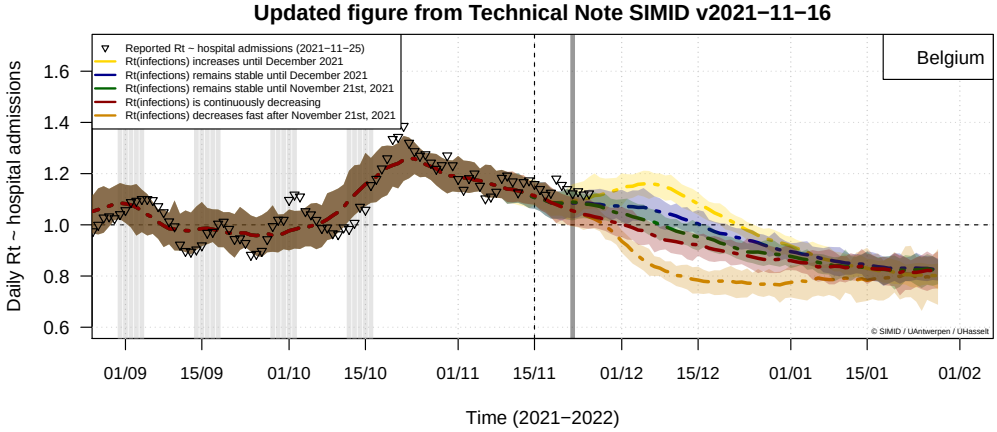

Figure 8: Model projections for Belgium in terms of the daily reproduction number (Rt) based on hospital admissions for COVID-19. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 40 model runs.