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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 August 16th, 2021, by a short-term prediction model and a stochastic dynamic transmission model. Our previous reports are available via simid.be and the covid-en-wetenschap blog.

## Preliminary conclusions

- The short-term prediction model depicts a further increase in new hospitalizations and ICU load, driven by the current trends in positivity ratio. The model predicts between 78 and 136 new hospital admissions and between 242 and 282 patients in ICU on August 28.
- A further increase in hospital admissions is predicted in all regions (Brussels, Flanders and Wallonia), with a doubling of the number of new hospitalizations from August 16 to August 28 in both Brussels and Wallonia, and an increase of 70% in Flanders.
- Social mixing and thus risk behaviour still drives the projected burden of disease. An increase of +50% of the behaviour we estimate for August 2021, shows hospital admission levels in line with the projections using the "September 2020" behaviour which would result in a high pressure on hospital capacity. If the increase in risk behaviour is only +30% of the August 2021 situation, we project on average only half of the daily hospital admissions and ICU load.

# 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.

## 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 and median age of confirmed patients. 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 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, which are likely given the increase in vaccine-induced immunity leading to a decrease in symptom severity, especially for older age groups. Also changes in the testing policy (e.g. changes in testing during a holiday period) can influence the relationship between the positivity ratio and hospital admissions.
- 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.
- 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.

## Model results

The prediction model captures the observed number of hospitalizations well (see Figure 1 and 2). The model predicts an increase in new hospitalizations in the short term. The prediction model predicts between 78 and 136 new hospital admissions on August 28th, 2021. Based on the model output, there is a high probability that the daily number of hospital admissions will exceed the threshold of 75 hospitalisations per day as from August 25th. The ICU-related model predicts between 242 and 282 patients in ICU on August 28th, thereby hitting the national 15% level of ICU beds.

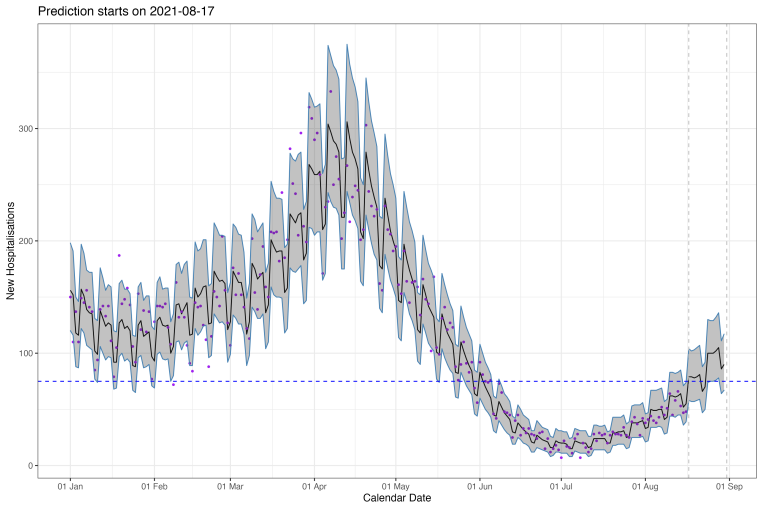



**Figure 1: Short-term prediction model for the hospital admissions (national level)**. The dots represent the reported number of hospital admissions and the grey band shows the prediction interval.

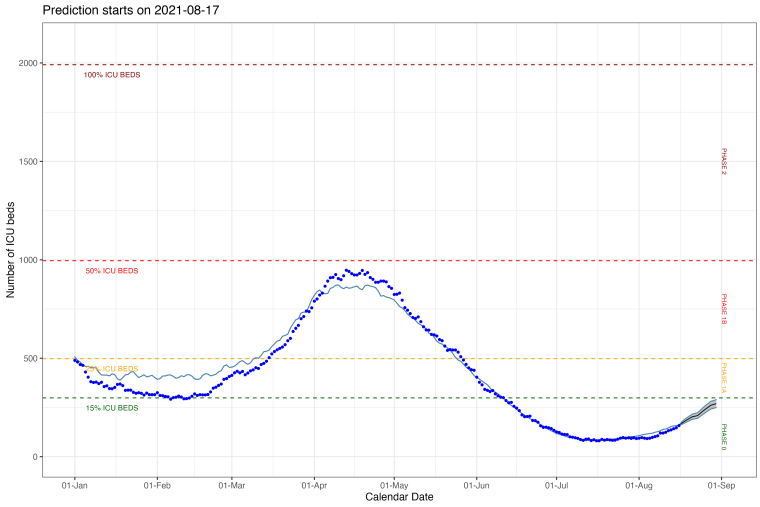



**Figure 2: Short-term prediction model for the ICU load (national level)**. The dots represent the reported ICU load and the very narrow grey band shows the prediction interval.

At a regional level, the model predicts further increases in all regions (Brussels, Flanders and Wallonia). The prediction model predicts, on August 28th, 2021, between 12 and 44 new hospital admissions in Brussels, between 13 and 79 in Flanders and between 12 and 76 in Wallonia. The ICU-related model predicts between 59 and 80 patients in ICU in Brussels, between 86 and 133 in Flanders and between 65 and 104 in Wallonia, on August 28th. In Brussels, there is a high probability that the ICU capacity exceeds the 25% level of the available ICU beds on August 28th.

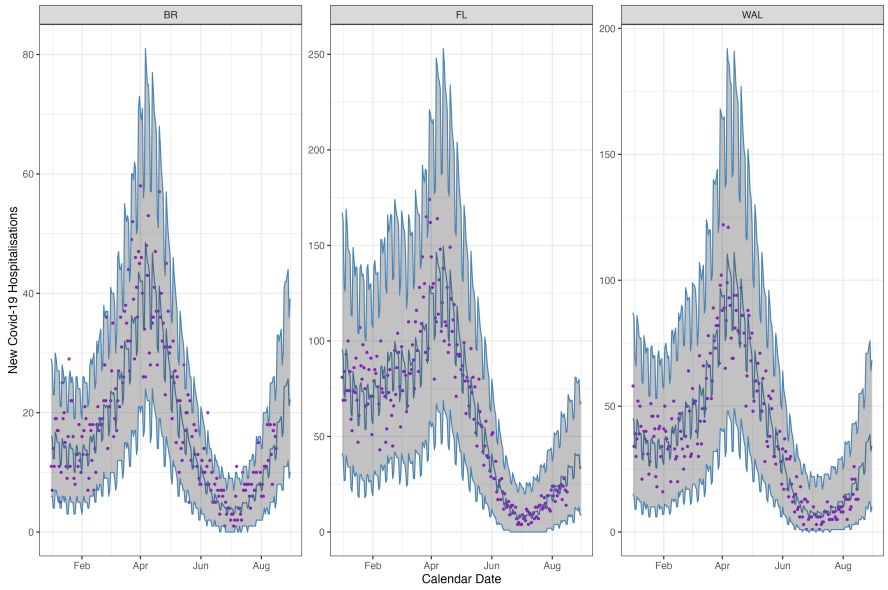



**Figure 3: Short-term prediction model for the hospital admissions (regional level)**. The dots represent the reported number of hospital admissions and the grey band shows the prediction interval. Left panel: Brussels, Middle panel: Flanders, Right panel: Wallonia.

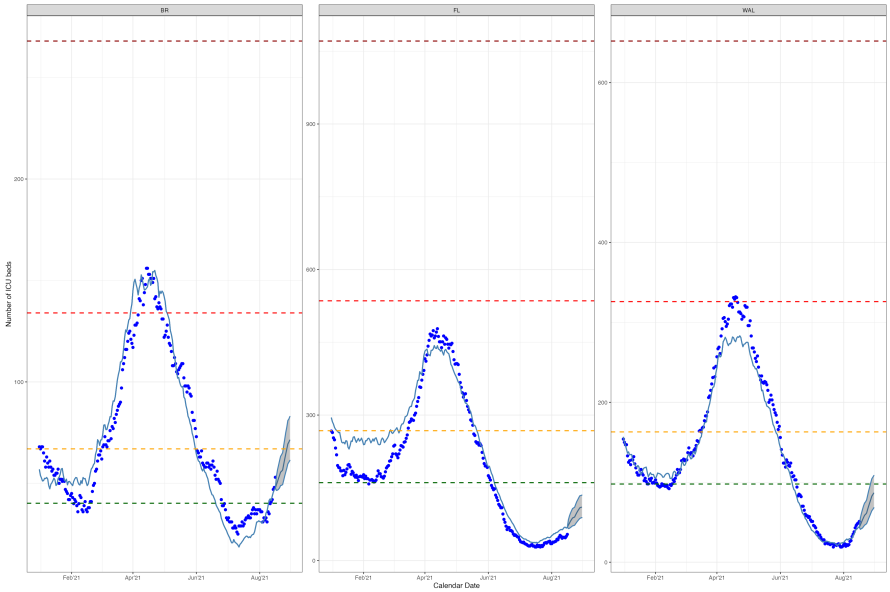



**Figure 4: Short-term prediction model for the ICU load (regional level)**. The dots represent the reported ICU load and the very narrow grey band shows the prediction interval. Left panel: Brussels, Middle panel: Flanders, Right panel: Wallonia.

# 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, mortality data and social contact data from the Belgian CoMix survey. All model projections account for an increasing vaccine uptake and 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 **introduction of VOCs in the Belgian population** is accounted for using data from the baseline genomic surveillance of SARS-CoV-2 in Belgium by the National Reference Laboratory.

3. **Alpha VOC:** For the first part of 2021, 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 Alpha VOC, is estimated by the model at 33% (95% credible interval (CrI): 28%-41%) relative to the wild-type variant. Note that this should be viewed as an average increase in transmissibility due to the combined emergence of the aforementioned VOCs rather than an increase in transmissibility completely attributable to the emergence of a single dominant VOC. The model allows for a differential hospital admission probability with respect to the upcoming VOC since January 2021. Therefore, we adopted the age-specific adjusted odds ratio derived from a logistic regression approach for hospital admission by Funk et al. (Eurosurveillance, 2021). As such, we used the ratios for the Alpha variant corresponding with 1.3, 2.3, 1.7 and 1.2 for age groups 0-19y, 20-39y, 40-59y,60-79y and +80y, respectively.

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: 70%-90%) relative to the Alpha variant. This increase is estimated based on the baseline genomic surveillance data (see Figures 5). 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), hence we use a conservative hazard ratio estimate of 2.

5. Our model results contain stochastic variation in the transmission process and parameter uncertainty based on 20 model parameter configurations. The calibration procedure relies on likelihood-based MCMC sampling resulting in 20 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 (300 iterations) with 10 realizations per iteration, periodicity of 10 iterations and leading to 20 different chains based on 20 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. The model is calibrated using social contact data up to the 27th wave of the Belgian CoMix survey conducted from July 20–26, 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 behaviour during social contacts.

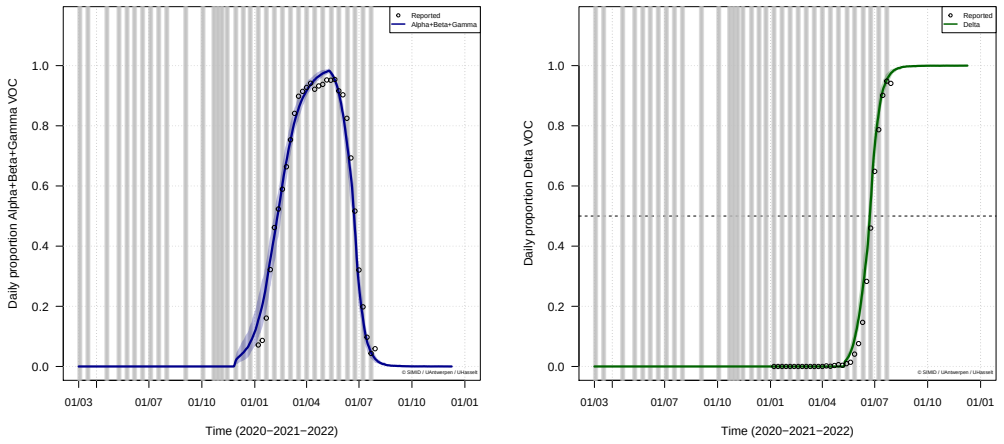



**Figure 5: Reported baseline genomic surveillance data for Belgium and the proportion of the different VOC in the stochastic dynamics model over time.**

8. 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 adaptive behaviour and measures that were previously in place. The scenarios are not intended as justification to return to or re-introduce a specific set of measures and circumstances from the past. All scenarios start from the social mixing and transmission behaviour we estimated up to August 16th and have a simulation horizon up until December 2021. None of the scenarios include the effect of the introduction of infected cases as a result of international travel.

    - **Scenario A:** We assume no changes in risk behaviour after August 16th.
    - **Scenario B:** We assume a behavioral shift on September 1st, 2021, in line with an increased risk of +50% with respect to the estimates for August 2021. This behavior is assumed to be maintained until the end of the simulation.
    - **Scenario C:** We assume a behavioral shift on September 1st, 2021, in line with an increased risk of +30% with respect to the estimates for August 2021. This behavior is assumed to be maintained until the end of the simulation.
    - **Scenario D:** We assume a behavioral shift on September 1st, 2021, in line with the dynamics we estimated for September 2020. This behavior is assumed to be maintained until the end of the simulation.

9. **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 have a lower risk of 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.
    - **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 in the same way using the (higher)

estimates reported in Table 1. 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 given the relatively short time horizon considered after complete vaccination schedule deliveries in the simulation. Therefore, potential differences in effectiveness over time of the different vaccine schedules is not explored in the current 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 | against Alpha variant | against 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% |

10. **Vaccine uptake**

- The vaccine-type and age-specific uptake in the model of first and second doses over time are based on the reported uptake by Sciensano, derived from Epistat on August 11th, 2021. For the model projections, we extrapolate the uptake rate of mRNA vaccines of the last 2 weeks, until a 80% coverage is reached. If the reported uptake is more than 80%, we use the reported uptake. For the projected uptake, the time between 2 mRNA doses is assumed to be 5 weeks. The uptake by age group is presented in Figure 7.
- We do not account explicitly for the 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 dying upon hospitalization).
- 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 (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 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. 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 of hospitalizations. 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 the Delta VOC making the implicit assumption that this 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, are not age-specific but do capture the population-level behaviour.

- We attribute the growth advantage of the VOCs completely to transmissibility, and as such, ignore the potential effect of immune escape.

- 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 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 new symptomatic cases over time.

- This model does not explicitly account for importation by returning travelers which could have a large impact on the evolution of the epidemic. Further work related to this is ongoing. Importantly, an implicit attribution of such cases to local transmission is used instead. Therefore results need to be interpreted with caution.

- We present our modelling results by the mean and pointwise 95% credible interval based on 20 model realizations, which capture stochastic effects and parametric uncertainty. The interplay between these two actors and the presentation of modelling uncertainty is subject of future research.

## Model results and discussion

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

- The dynamic transmission model uses the age-specific hospital admissions over time as main data source for the calibration process. As such, the comparison with the Rt based on the reported cases is used as validation. Figure 6 shows a plateau in the Rt for August 2021 based on the reported cases on the national level, which is captured in the stochastic model. The constant growth of infections, leads to the projected plateau in hospital admissions in the second half of August 2021. The short-term prediction model shows an increase in hospital admissions up to September 1st, which is not observed in the dynamic model. This discrepancy between the two models could be caused by the absence of a change point in behaviour at the beginning of August 2021.Current projections show a decrease in Rt from the end of July 2021, caused by a depletion of susceptible individuals, the increase of vaccine immune-induced immunity, no influx of infected cases and no change in behaviour.

- The quantitative outcomes of the mixing scenarios are highly dependent of the situation on September 1st. If the dynamic model underestimates the transmission in August, the projected peaks are likely an underestimation, and vice versa.

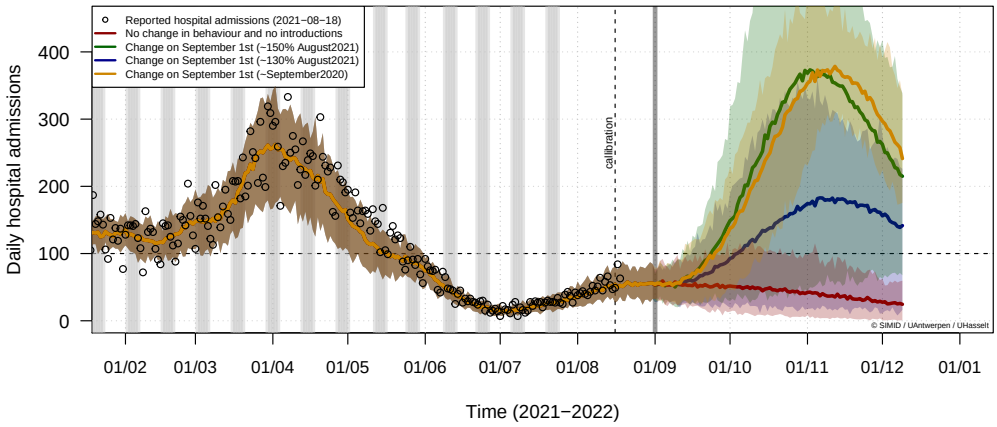
- Qualitatively, we found that the estimated risk behaviour for September 2020 does not cause the same increase in hospital admissions when this behaviour is conducted in September 2021. This is the result of the population immunity, though challenged by the increased transmissibility and severity of the Delta VOC.

- Social mixing and thus risk behaviour still drives the projected hospital admissions. An increase of +50% of the behaviour we estimate for August 2021 (Scenario B), is in line with the projections with "September 2020" behaviour. If the increase in risk behaviour is only +30% (Scenario C), we project on average only half of the daily hospital admissions and ICU load. It goes without saying that an increase larger than +50%, e.g. pre-pandemic contact behaviour, would result in even more hospitalisations (admissions and load; ICU and non-ICU).

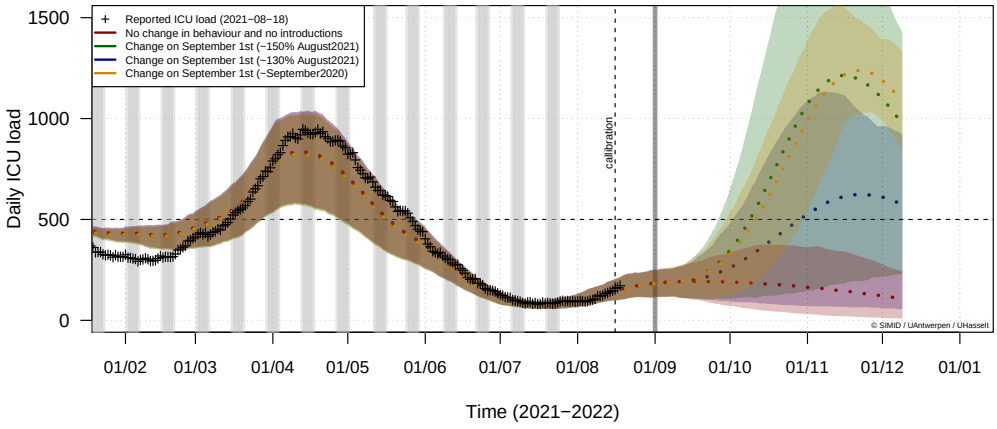
- The relative constant Rt we observe for August 2021 at the national level could be the result of a mix between an upward and a downward trend for different sub-national regions. This may lead to an unexpected increase in cases (cfr. the "New York effect"). A sudden change on the national level caused by regional increases cannot be captured with the current model but requires model calibration with regional data (not shown).

- The model does not account for regional differences in immunity. As such, herd immunity effects in regions with immunity levels above the national level are underestimated.

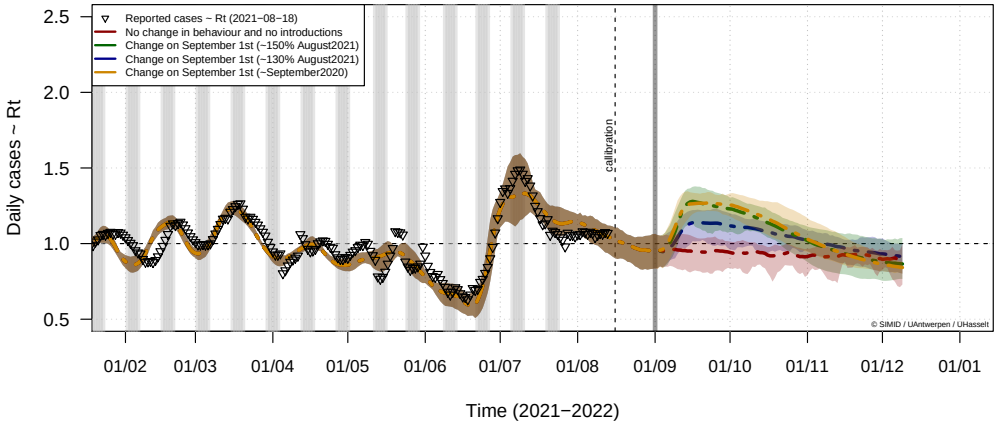
**Social mixing: Compare changes in social contact behavior from September 1st, 2021.**




**(a)** Daily hospital admissions




**(b)** ICU occupancy




**(c)** Reproduction number over time (Rt)

**Figure 6: Model projections on daily hospital admissions, ICU occupancy and reproduction number for different assumptions on social contact behavior from September 1st, 2021.** The results are summarised by the mean (line) and 95% point-wise credible intervals (shaded area) of 20 model runs.

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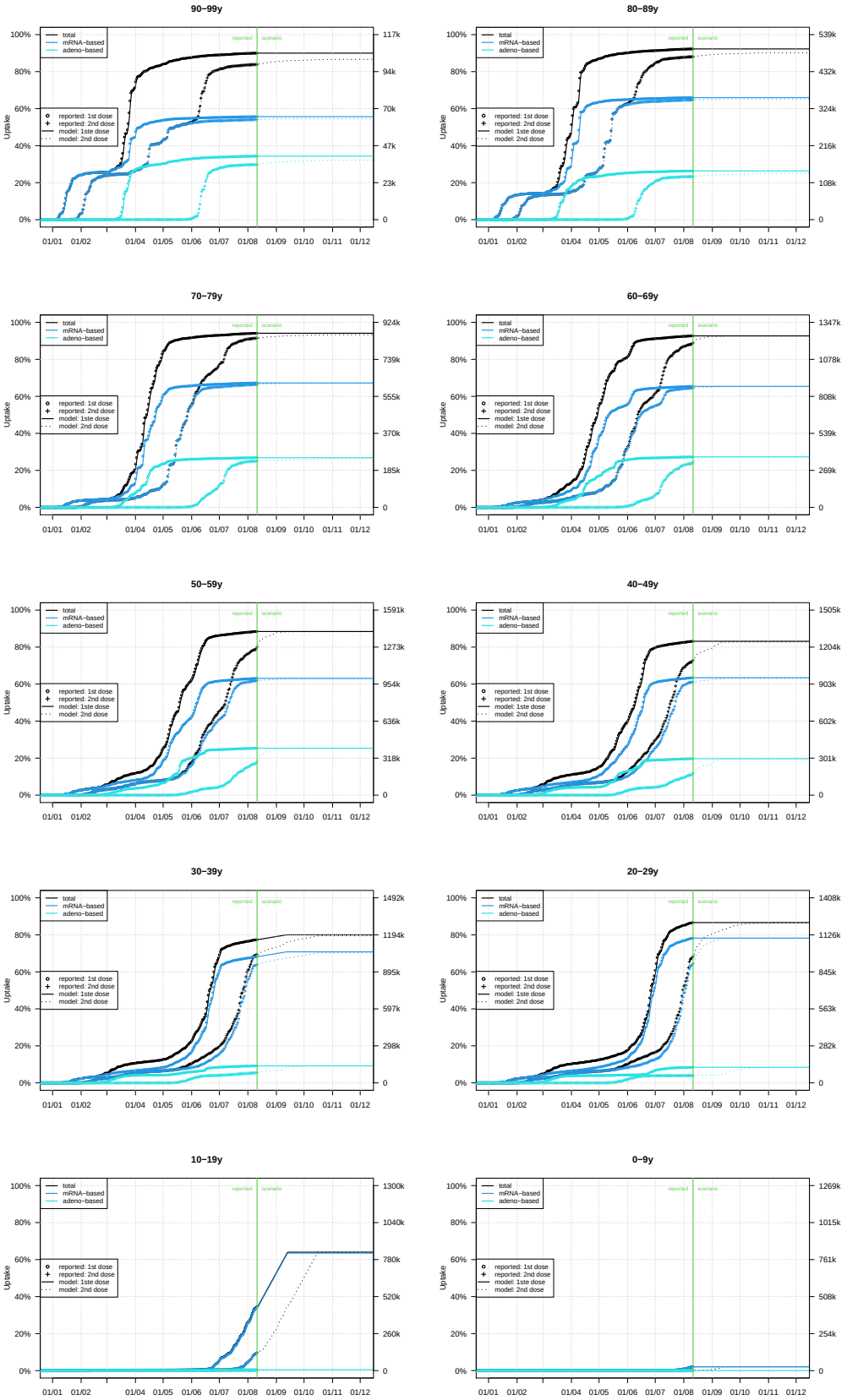


**Figure 7: Vaccine uptake by age based on the reported uptake for Belgium on August 11th, 2021.**