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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 October 08th, 2021, by a stochastic dynamic transmission model. All previous reports are available via simid.be and the covid-en-wetenschap blog.

UPDATE: We included additional scenarios with respect to increased risk behaviour and the reported hospital data on November 18th, 2021, to Figures 1-4. The text and conclusions are not adjusted to the new information.

Preliminary conclusions

- Social mixing and thus risk behavior still drive the projected burden of disease. An increase of +20% of the risk behavior we estimated for late September 2021 would result in a limited increase of the hospital load at the national level. It seems quite certain that the relaxations of September and October will lead to some increase in transmission. Whether the expected increase in transmission is of the specific magnitude we projected for the coming period is impossible to predict at this point in time, but it is presented here as a plausible scenario.
- The regional analysis for the Brussels Capital Region is not conclusive. The regional variability in hospital admissions is hard to capture and the model input does not allow to describe the trends in confirmed cases and the corresponding reproduction number (Rt) from August–September 2021. More recent age-specific, and preferably regional, data on hospital admissions and sero-prevalence could improve the estimation of local transmission to project new hospital admissions.
- The regional analysis for the Flemish region shows a stable hospital admission trend with ongoing transmission dynamics and a moderate increase in hospital admissions when a 20% increase in risk behaviour is assumed. The latter amplifies the regional increasing trends in Rt for September 2021, which end up in almost three times the current hospital admissions. This scenario shows large model uncertainty, which should be considered with the projected average.
- For the Walloon region, we observe a mismatch between Rt based on model output and Rt based on observations for August, 2021, hence the regional hospital forecast requires great caution. Assuming a prolongation of current Rt trends, hospital admissions are likely to remain stable or even decrease. A 20% increase in risk behaviour would lead in a resurgence of hospital admissions. This increase is relatively less compared to the forecasts for Flanders, due to the relative stable trend in confirmed cases and Rt for September 2021 in the Walloon region.
- The analyses are not spatially explicit, hence, the included disease transmission does not accommodate for (social) interactions/mobility within and between Belgian regions nor between the region under study and other countries. Circulation of SARS-CoV-2 in other regions has the potential to boost local community transmission, and requires outcomes to be handled with care. Analyses for Belgium are conducted independent of regional analyses and based on averages. As such, the combination of regional analyses is likely to differ from the national forecasts.
- Main updated modelling features: (1) contrary to previous analyses, the current analyses are calibrated to hospital admissions for both COVID-19 and non-COVID-19 (i.e. 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; (4) the hospital hazard ratio was re-estimated for infections with the VOC.

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 hospital 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. 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 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 36% (95% credible interval (CrI): 29%-42%) 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 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 (1000 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. **New since this report, is that 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 hospital load related to COVID-19, we include these new patients in our analysis and all figures. 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.

8. The model is calibrated using social contact data up to the 30th wave of the Belgian CoMix survey conducted from August 29th till September 7th, 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 two **social mixing scenarios** to explore the impact of behavioral changes by re-using estimated transmission dynamics from previous stages in the Belgian COVID-19 epidemic. All scenarios start from the social mixing and transmission behavior we estimated 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. All behavioral changes are introduced linearly over 7 days.

    - **Scenario A:** We assume no changes in risk behavior.
    - **Scenario B:** We assume a behavioral shift on October 1st, 2021, in line with an increased risk of +20% with respect to the latest estimations for the transmission dynamics. This behavior is assumed to be maintained until the end of the simulation.
    - **Additional Scenario:** We assume a behavioral shift on October 1st, 2021, in line with an increased risk of +30% with respect to the latest estimations for the transmission dynamics. This behavior is assumed to be maintained until the end of the simulation.
    - **Additional Scenario:** We assume a behavioral shift on October 1st, 2021, in line with an increased risk of +40% with respect to the latest estimations for the transmission dynamics. This behavior is assumed to be maintained until the end of the simulation.
    - **Additional Scenario:** We assume a behavioral shift on October 1st, 2021, in line with an increased risk of +60% with respect to the latest estimations for the transmission dynamics. This behavior is assumed to be maintained until the end of the simulation.

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.

- **Booster doses** are not included at this stage. This might encounter the absence of 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 national and regional level are based on the reported uptake by Sciensano, derived from Epistat on October 1st, 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 5.
- 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 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 old potentially take up vaccines.

Region-specific models

- The transmission model we developed for Belgium has been re-calibrated for the Flemish, Walloon and Brussels Capital Region using regional population details and reported hospital admissions. The time-specific age distribution of hospital admissions for Belgium are adopted for the regional models. The number of initial cases in 2020 and the introductions of Alpha and Delta VOC cases are down-scaled in relation to the regional population size. The temporal transmission dynamics (so called age-specific "q-parameters") are re-calibrated from March 2020 onward.
- The age-specific vaccine uptake per region is based on the reported uptake by Sciensano, derived from Epistat on October 1st, 2021. The uptake of the first dose for ages 20-99y is kept fixed, but we account for the administration of the second doses of the mRNA vaccine. Target vaccine uptake levels for persons aged 12-18y are assumed in line with the reported uptake for the 20-30y age group. The uptakes by age group are presented in Figures 6, 7 and 8.

Major limitations

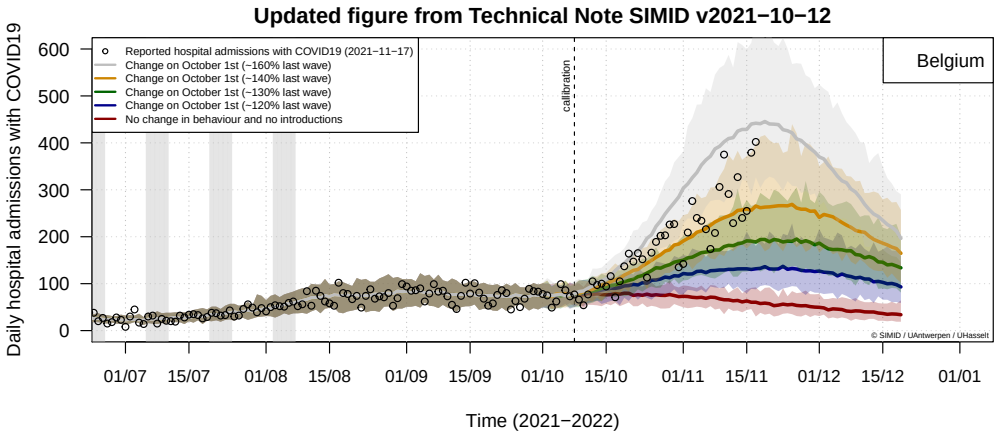
- **This transmission model is suited for scenario analyses to investigate possible future paths, it is not a prediction model.**
- The model is calibrated on hospitalizations and informed by the Belgian CoMix social contact data survey. These empirical social contact data inform mainly the frequency 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. 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 **up to August 17th, 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 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, 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 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.** Importantly, an implicit attribution of such cases to local transmission is used instead. Therefore, results need to be interpreted with caution.
- **The regional modeling exercises are based on applying a stochastic age-discretized compartmental model to the regional incidence data as mentioned above. However, the models are not spatially explicit, hence, disease transmission does not accommodate (social) interactions/mobility between Belgian regions nor between the region under study and other countries. Consequently, all (regional) infections are assumed to result from local transmission.**
- 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

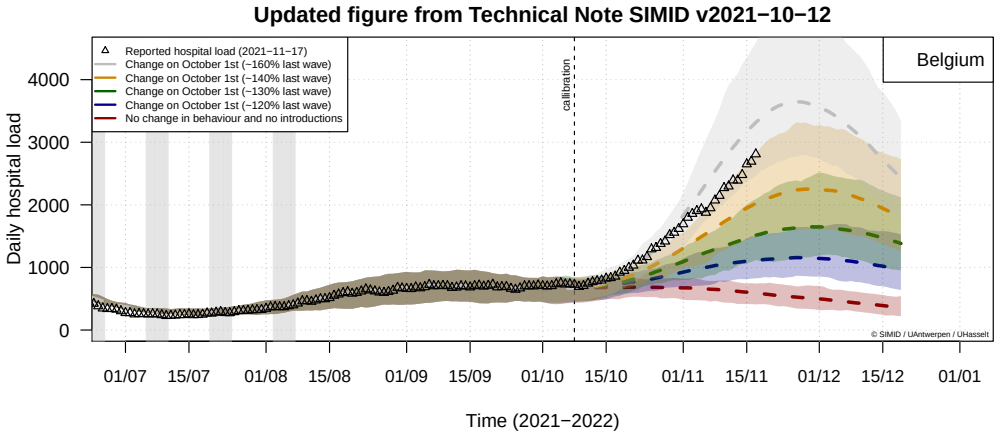
The following figures depict the results of our scenario analyses with respect to social mixing. All projections show a large 95% credible interval and should therefore be interpreted with great caution. The main conclusions are listed at the start of this document. Some additional observations are listed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

- Social mixing behaviour still drives the projected hospital admissions. An increase of +20% in behavior that we estimate for September 2021 on the national level (Scenario B) shows an increase in hospital admissions and ICU load.
- The decreasing trend in the effective reproduction number (Rt) that we observed for August-September 2021 at the national level could be the result of a mix of an increase in local transmission and a decrease of introductions due to international travel.
- The parameter estimation and model calibration are mainly driven by hospital admission data. Both 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.

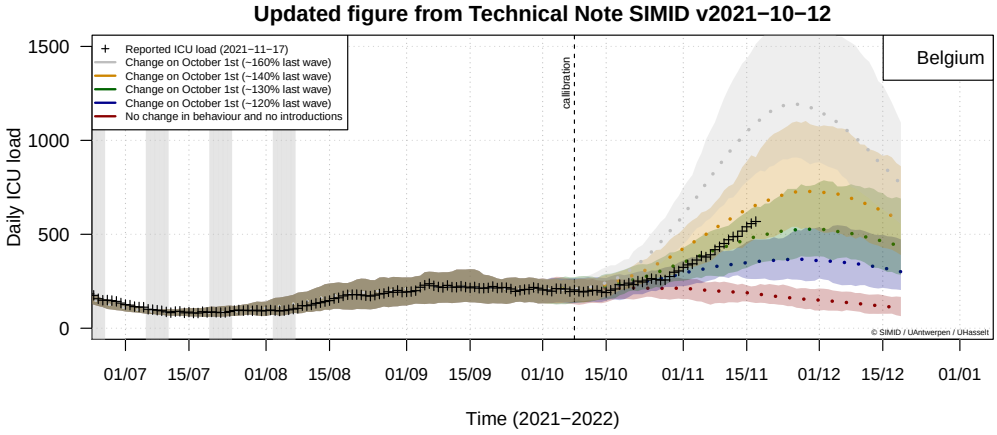
Scenario analysis for Belgium.



(a) Daily hospital admissions



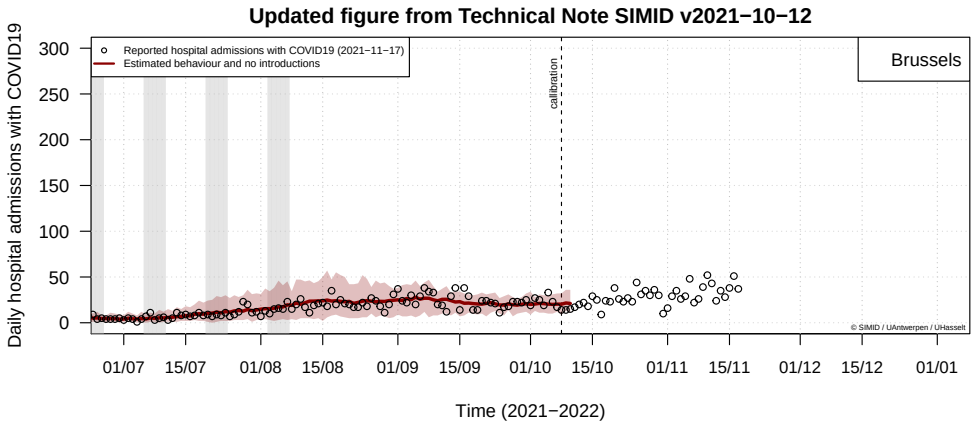
(b) ICU occupancy



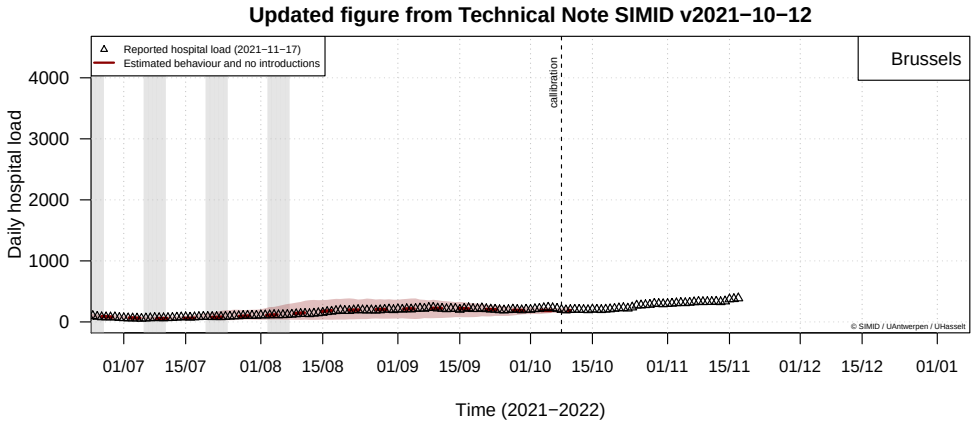
(c) Reproduction number over time (Rt)

Figure 1: Model projections for Belgium on daily hospital admissions, ICU occupancy and reproduction number for different assumptions on social contact behavior from October 1st, 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 18th, 2021.

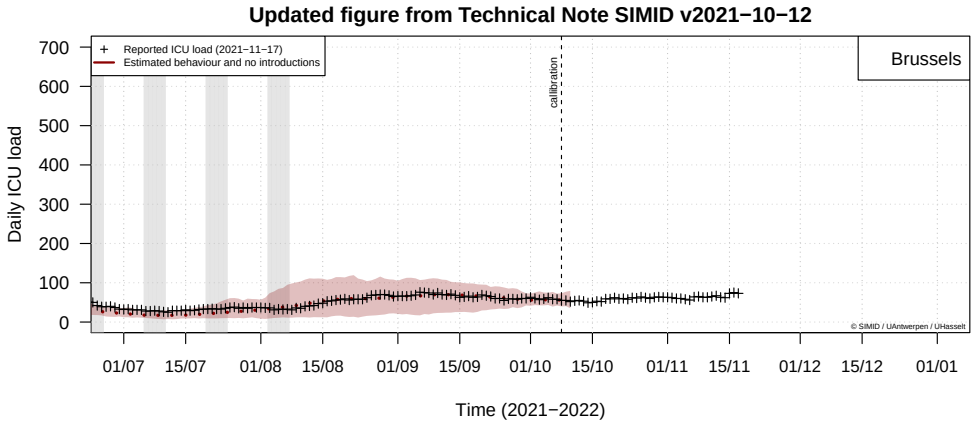
Scenario analysis for the Brussels Capital Region.



(a) Daily hospital admissions



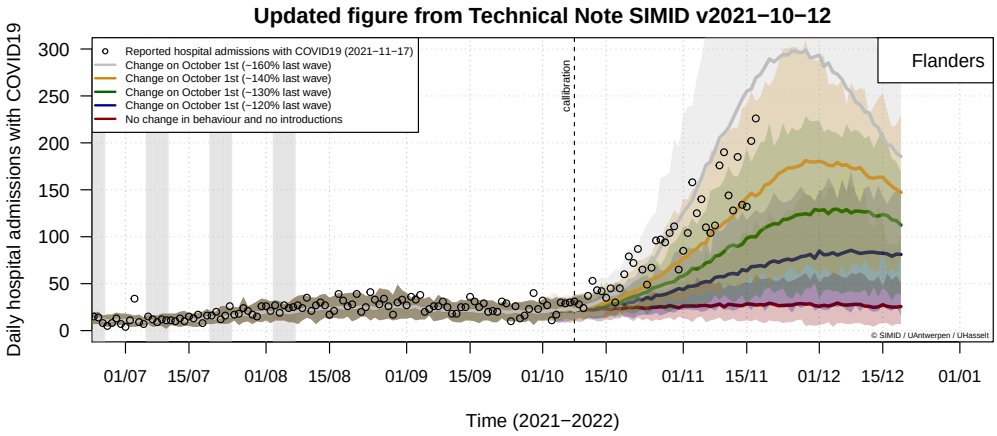
(b) ICU occupancy



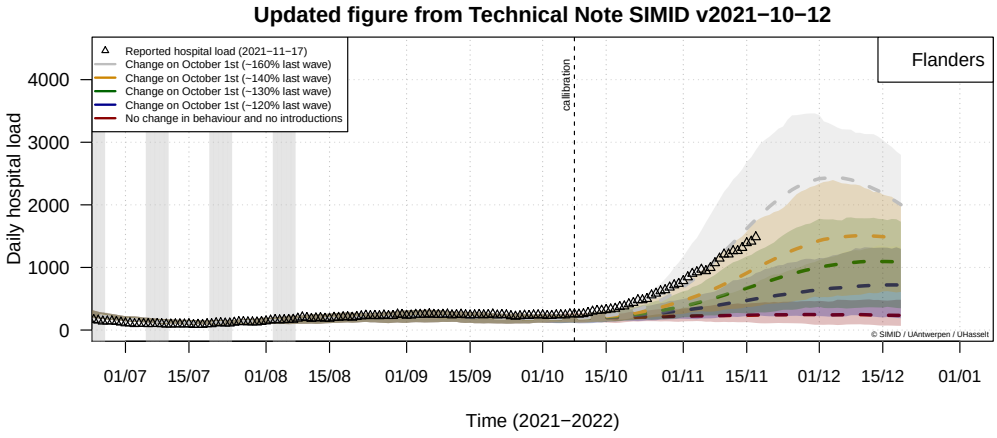
(c) Reproduction number over time (Rt)

Figure 2: Model results for the Brussels Capital Region on daily hospital admissions, ICU load and reproduction number for different assumptions on social contact behavior from October 1st, 2021. The model projections are not conclusive and omitted from the graph. 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 18th, 2021.

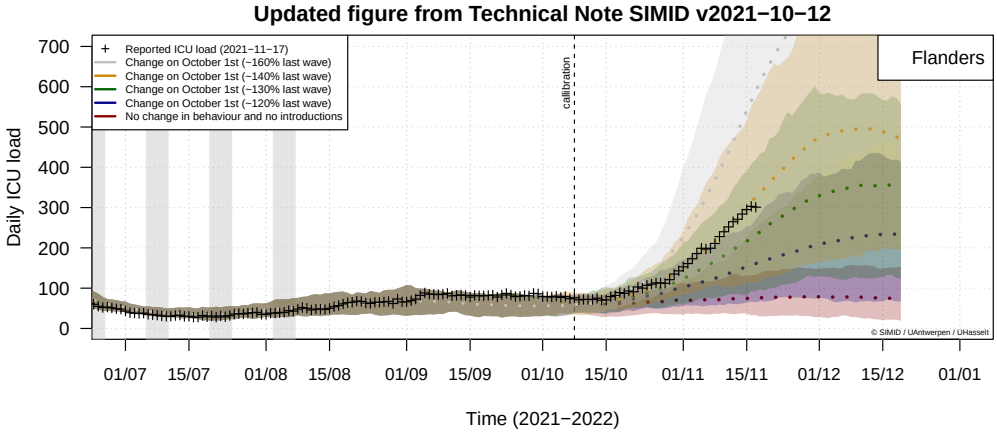
Scenario analysis for the Flemish Region.



(a) Daily hospital admissions



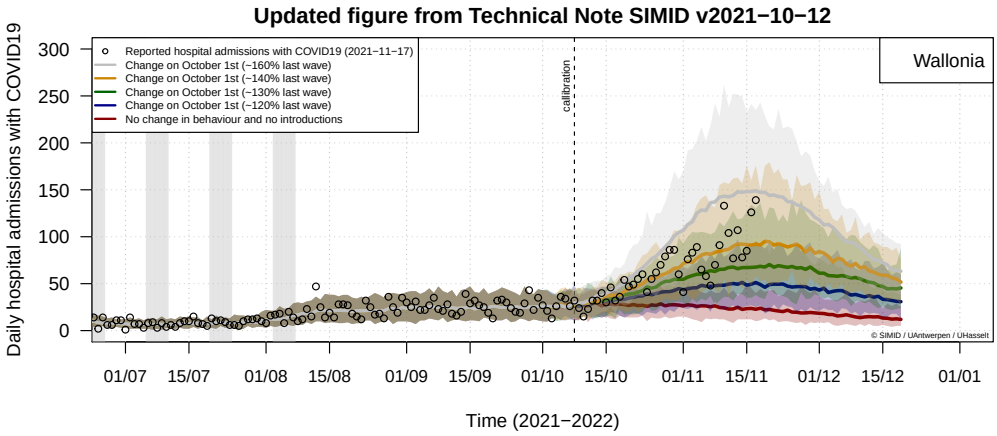
(b) ICU occupancy



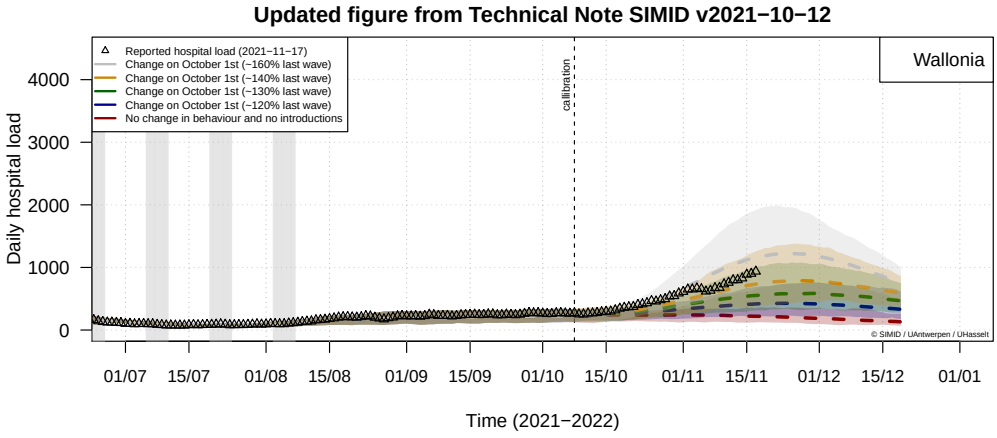
(c) Reproduction number over time (Rt)

Figure 3: Model projections for the Flemish Region on daily hospital admissions, ICU load and reproduction number for different assumptions on social contact behavior from October 1st, 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 18th, 2021.

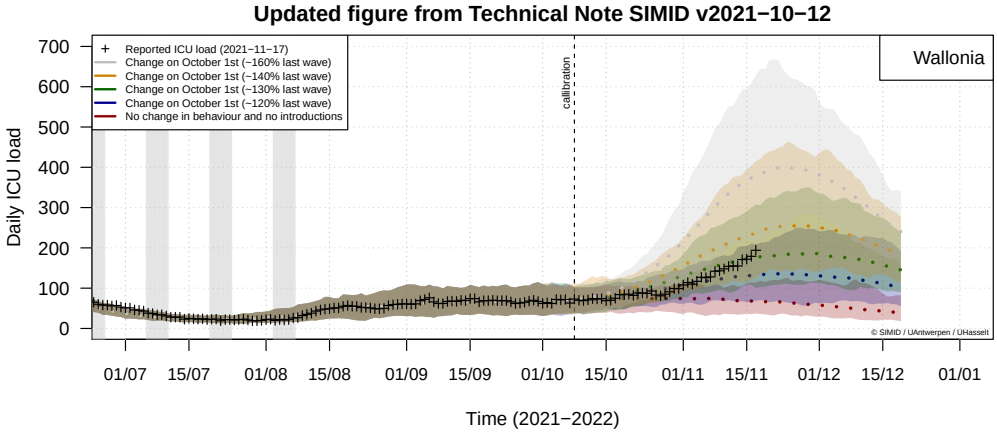
Scenario analysis for the Walloon Region.



(a) Daily hospital admissions



(b) ICU occupancy



(c) Reproduction number over time (Rt)

Figure 4: Model projections for the Walloon Region on daily hospital admissions, ICU load and reproduction number for different assumptions on social contact behavior from October 1st, 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 18th, 2021.

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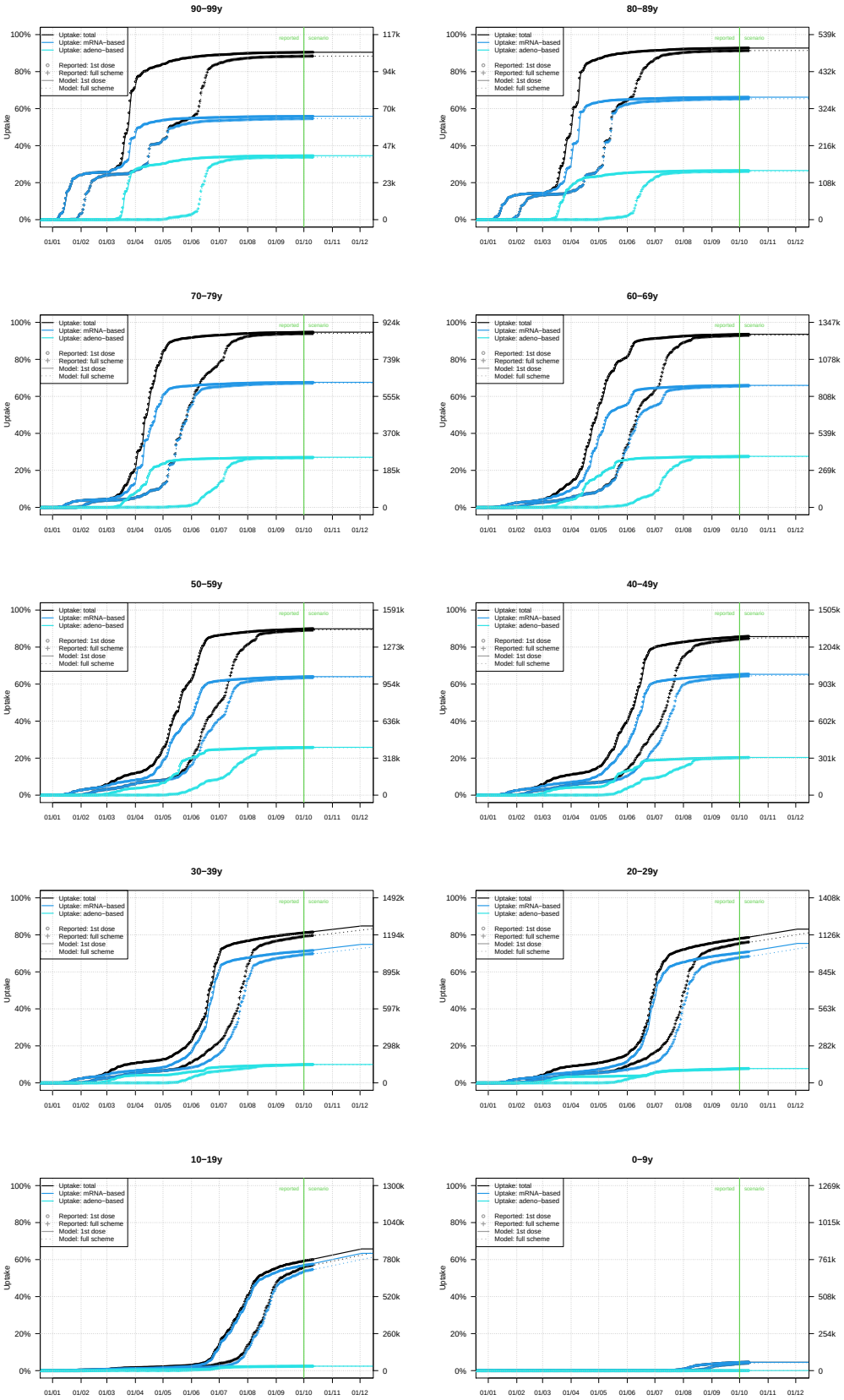


Figure 5: Included vaccine uptake by age based on the reported uptake for Belgium.

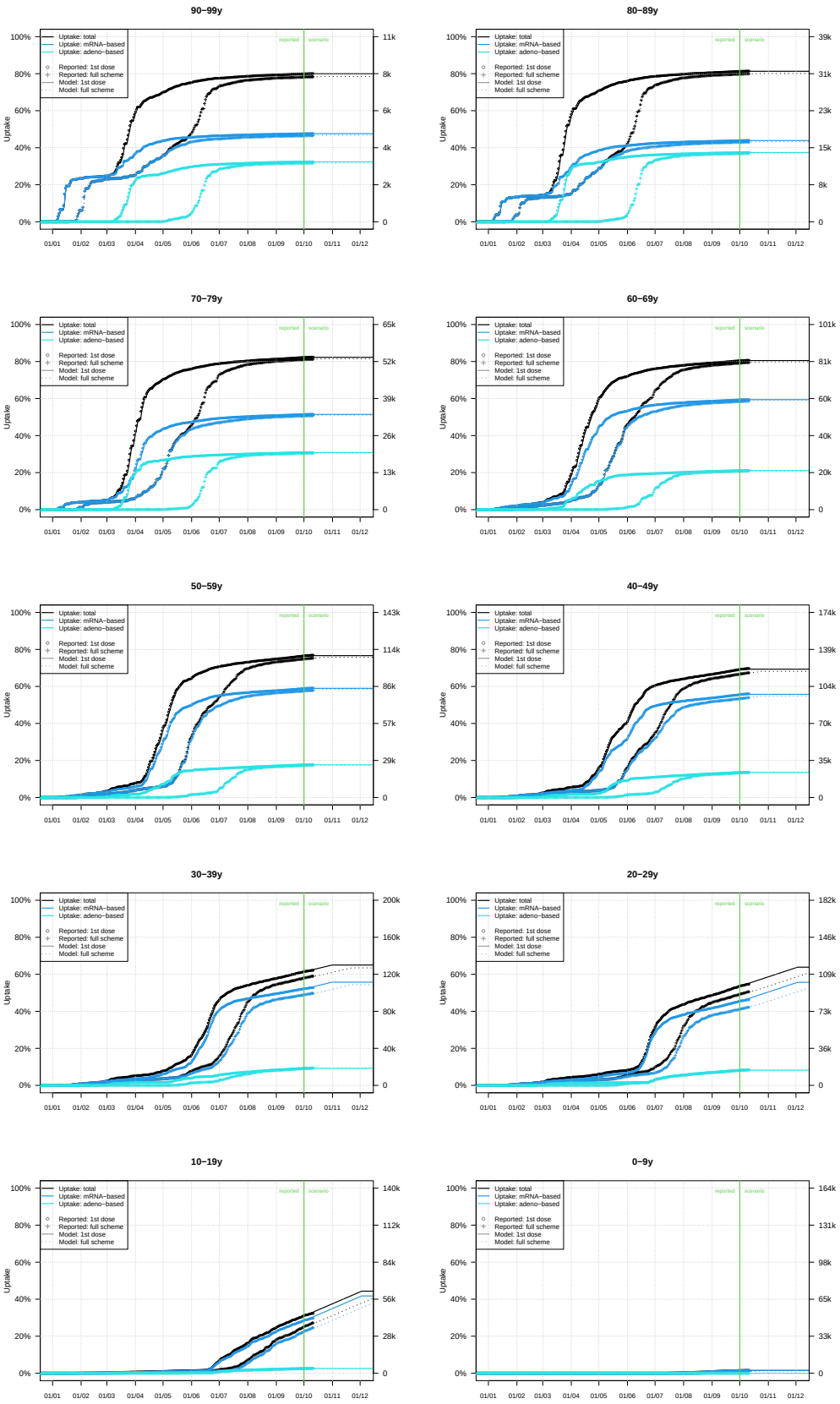


Figure 6: Included vaccine uptake by age based on the reported uptake for the Brussels Capital Region.

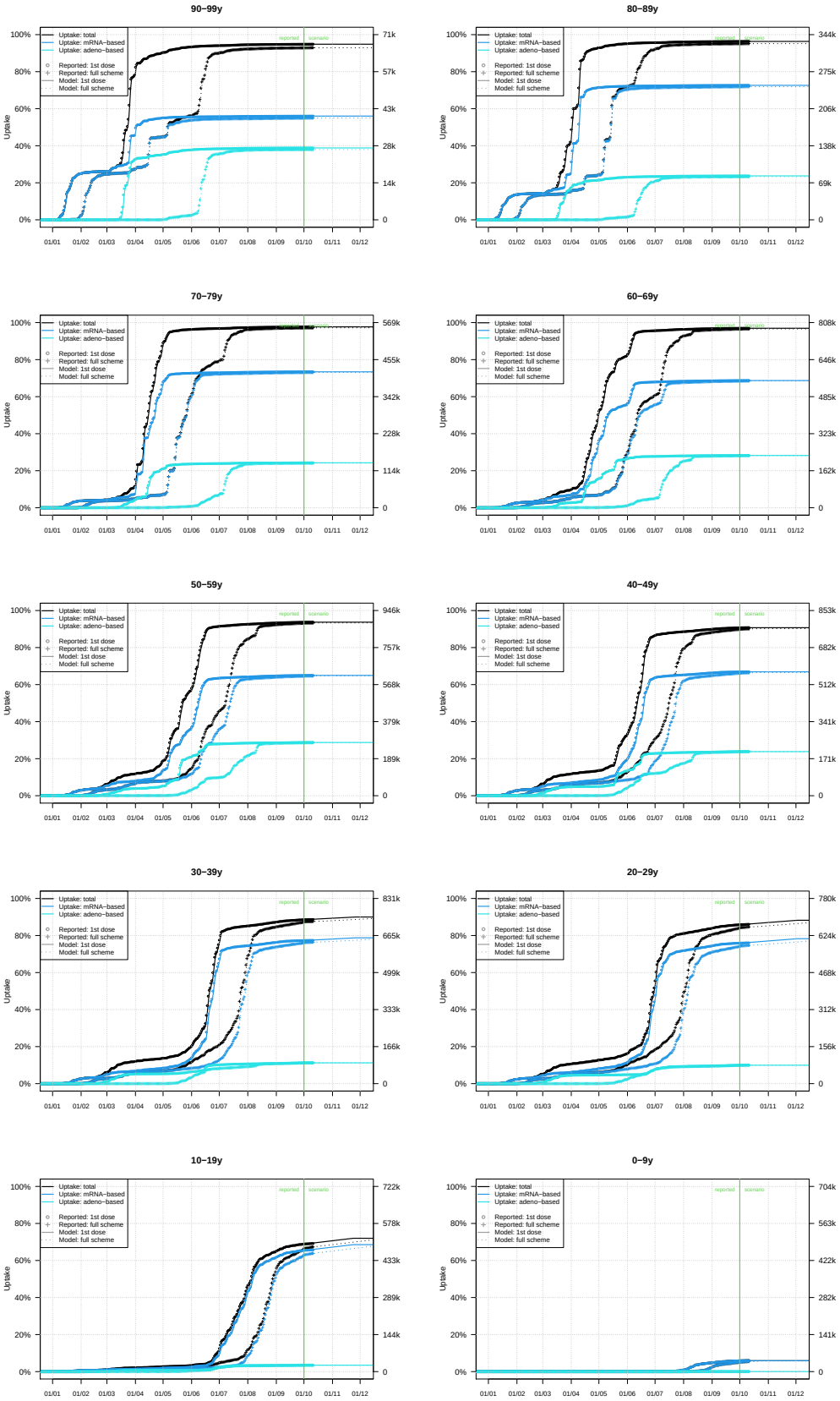


Figure 7: Included vaccine uptake by age based on the reported uptake for the Flemish Region.

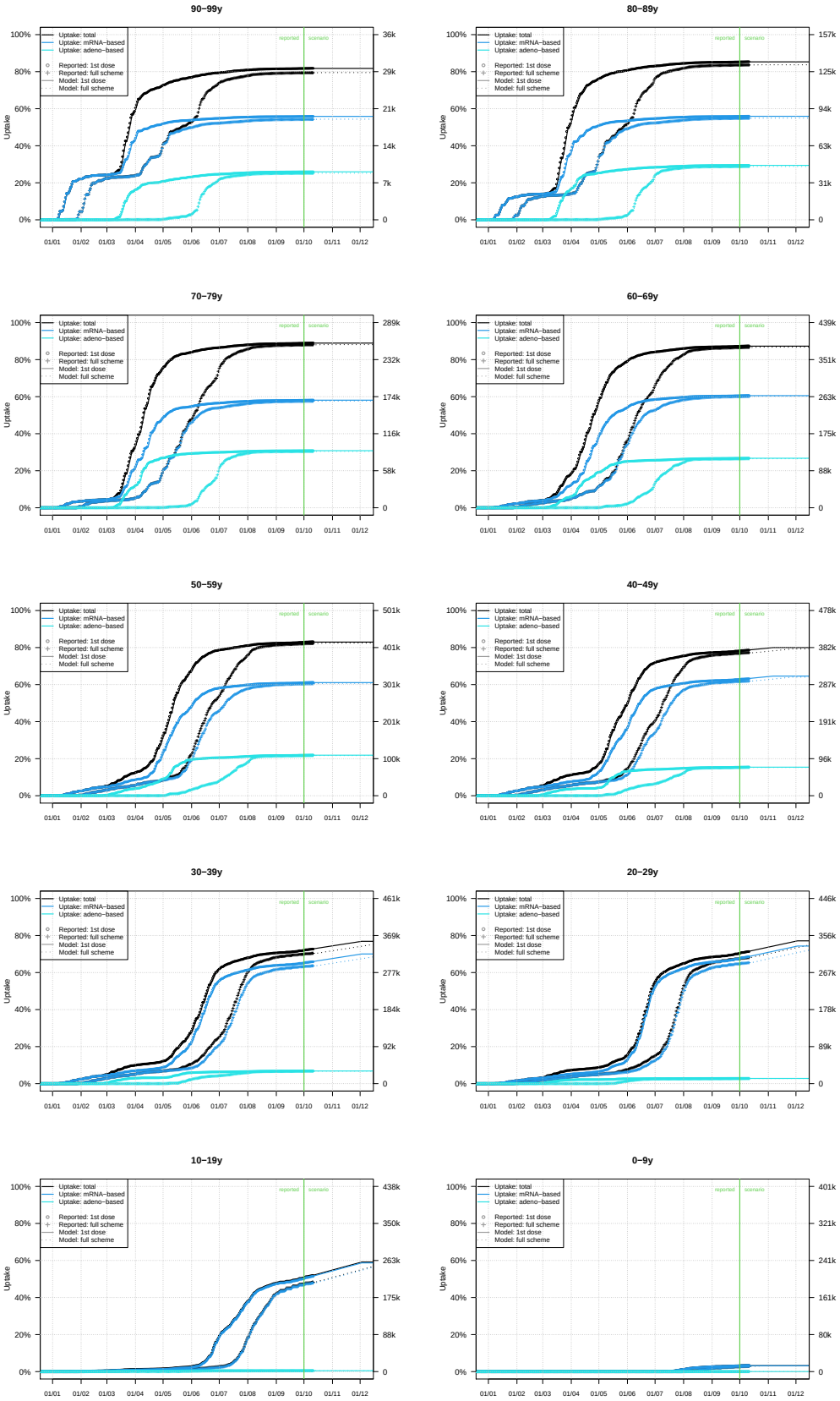


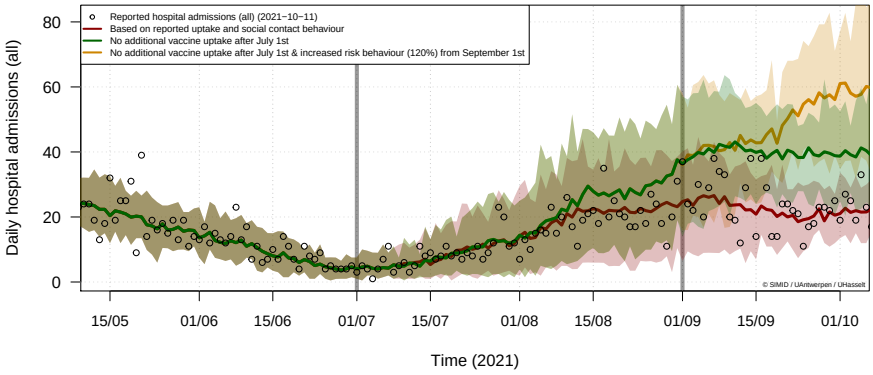
Figure 8: Included vaccine uptake by age based on the reported uptake for the Walloon Region.

SUPPLEMENT: Retrospective analysis for the Brussels Capital Region.

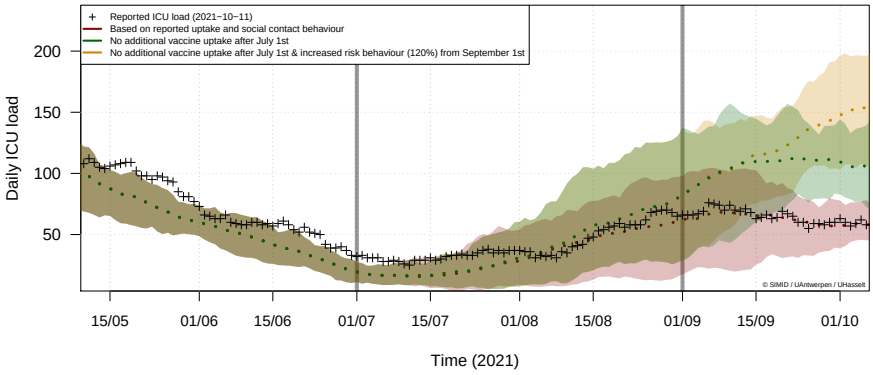
We ran some counterfactual scenarios to explore the impact of vaccine uptake and behavioral changes for the Brussels Capital Region for July–September 2021. All scenarios start from the social mixing and transmission dynamics we estimated based on reported hospital admissions, and have a simulation horizon up until the last observation at moment of writing. None of the scenarios include the effect of the introduction of infected cases.

- We use the estimated risk behaviour over time and included the reported vaccine uptake by age.
- We use the estimated risk behaviour over time but excluded all vaccine uptake from July 1st.
- We assume no vaccine uptake from July 1st and add a behavioral shift on September 1st, 2021. The latter is introduced linearly over 7 days and in line with an increased risk of +20% with respect to the latest regional estimates.

This counterfactual analysis qualitatively explores the benefit of the vaccine uptake over summer in the Brussels Capital Region and a potential burden of disease prevented. Note that this analysis assumes no behavioural changes w.r.t. the absence of vaccine uptake. A retrospective approach is used to exclude uncertainty on future social contact behaviour.



(a) Daily hospital admissions



(b) ICU occupancy

Figure 9: Model results for the Brussels Capital Region on daily hospital admissions and ICU load for different assumptions on vaccine uptake from July 1st, 2021, and social contact behavior from September 1st, 2021. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 40 model runs.