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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 September 10th, 2021, by a stochastic dynamic transmission model. This analysis is an update of recent modeling work for Belgium and the Brussels Capital Region as described in Technical Note "v20210818" and "v20210823". All previous reports are available via simid.be and the covid-en-wetenschap blog.

UPDATE: We added the reported hospital data on November 18th, 2021, to Figures 1 and 2. The text and conclusions are not adjusted to the new information.

Preliminary conclusions

- Social mixing and thus risk behavior still drives the projected burden of disease. An increase of +50% of the risk behavior we estimated for August 2021 would result in a high pressure on hospital capacity on the national level, which is in line with the projections using the "September 2020" behavior. If the increase in risk behavior is only +30% of the August 2021 situation, we project on average only half of the daily hospital admissions and ICU load.
- A regional analysis for the Brussels Capital Region shows that an increase of +50% of the behavior we estimated for August 2021, could result in a high pressure on hospital capacity.
- When we explore behavioral changes from September 1st, 2021, they lead to different outcomes from the second half of September 2021 onward. In combination with the current variability in reported daily COVID-19 related hospital admissions, we cannot select or rule out any scenario at this moment in time. The transmission model we use is suited for scenario analyses to investigate possible future paths, it is not a prediction model.

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. 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 (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. The model is calibrated using social contact data up to the 28th wave of the Belgian CoMix survey conducted from August 3-9, 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.

8. We designed four **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. This approach aims to re-capture social contact and risk behavior that originates from adaptive behavior 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 behavior we estimated up to September 10th 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 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 transmission dynamics early August 2021, hence, resulting hospital admissions by late 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 early August 2021, in terms of transmission, and late August 2021 in terms of hospital admissions. 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 September 6th, 2021. For the model projections, we extrapolate the uptake rate of mRNA vaccines of the last 2 weeks, until a 80% coverage is reached on the national level. 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 3 weeks. The uptake by age group is presented in Figure 3.
- 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 old, 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 model

1. The transmission model we developed for Belgium has been re-calibrated for the Brussels Capital Region using regional population details and reported hospital admissions up to September 10th, 2021. The time-specific age distribution of hospital admissions for Belgium is adopted for the regional model. 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 September 2020 onward.

2. The age-specific vaccine uptake per region is based on the reported uptake by Sciensano, derived from Epistat on September 6th, 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 in the Brussels Capital Region are assumed to be 55%, in line with the reported uptake for the 20-30y age group on September 6th, 2021. The uptake by age group is presented in Figure 4.

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 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 behavior.

- 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.

- **The regional modeling exercise is based on applying a stochastic age-discretized compartmental model to the regional incidence data as mentioned above. However, the model is not spatially explicit, hence, disease transmission does not accommodate (social) interactions/mobility between Belgian regions nor between the region under study and other countries (see previous bullet). 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 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.

- Qualitatively, we found that the estimated risk behavior for September 2020 on the national level does not cause the same increase in hospital admissions when this behavior would be conducted from September 1th 2021 onward. This is the result of the population immunity, though challenged by the increased transmissibility and severity of the Delta VOC.

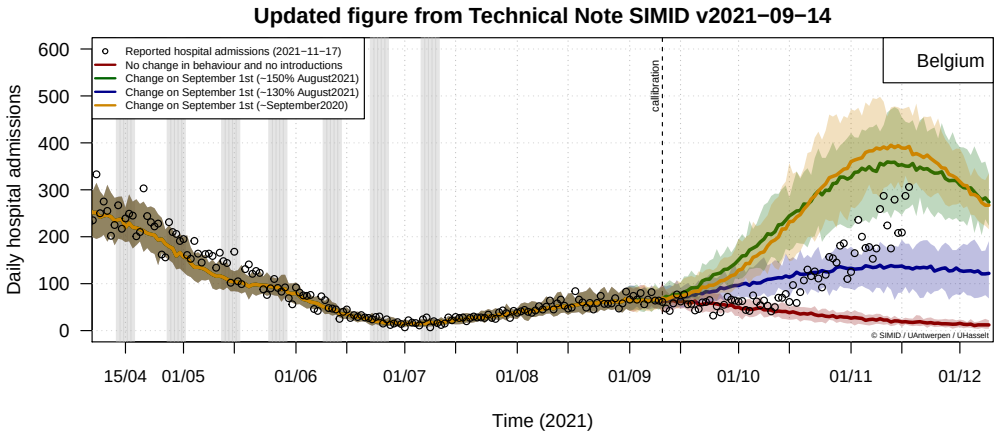
- Social mixing and thus risk behavior still drives the projected hospital admissions. An increase of +50% of the behavior we estimate for August 2021 on the national level (Scenario B), is in line with the projections with "September 2020" behavior. If the increase in risk behavior is only +30% (Scenario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

- The decreasing reproduction number (Rt) that we observe for August-September 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 national model but requires model calibration with regional data.

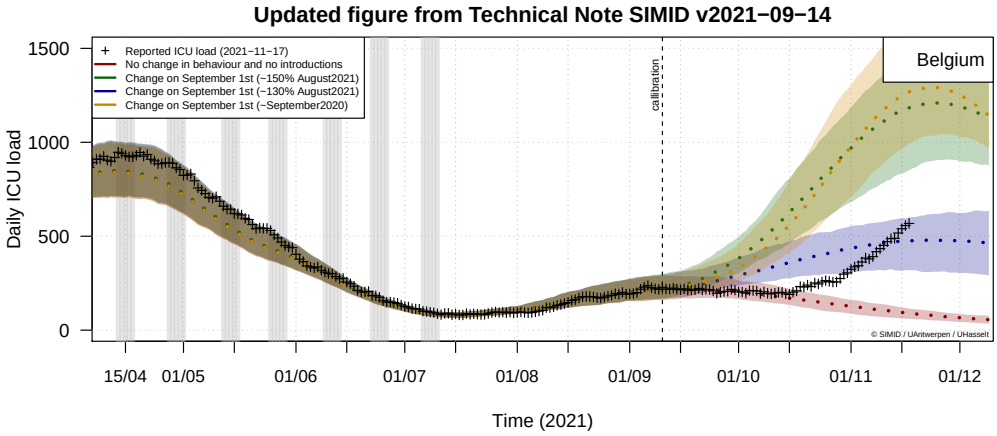
- The national model does not account for regional differences in immunity. As such, herd immunity effects in regions with immunity levels above the national level are underestimated.

- For the Brussels Capital Region, we found that the estimated risk behavior for "September 2020" causes an increase in hospital admissions up to an average of 160 per day. An increase of +50% and +30% of the behavior we estimate for August 2021 (Scenario B and C), lead to substantial hospital admissions and ICU load. Based on the reported hospital admissions up to September 14th, we cannot select or rule out any scenario at this moment in time. This analysis does not account for international mobility that can cause extra introductions of cases leading to increased transmission levels and more hospital admissions.

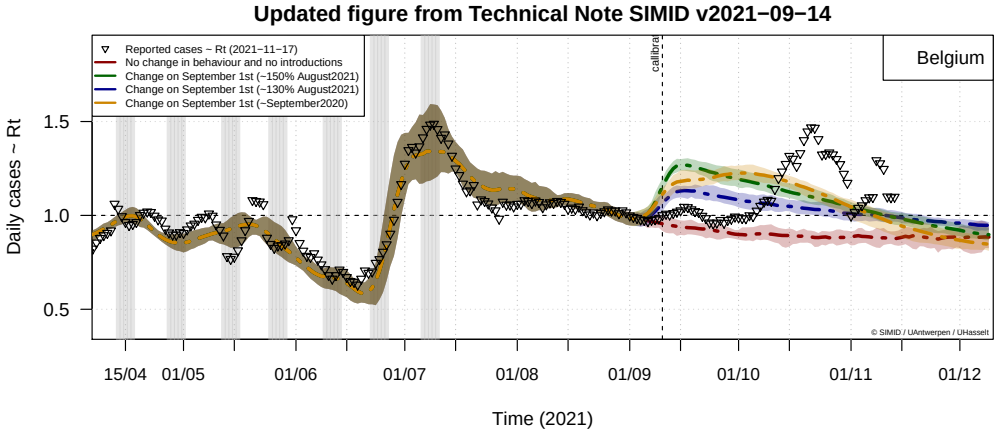
Scenario analysis for Belgium on social contact behavior from September 1st, 2021.



(a) Daily hospital admissions



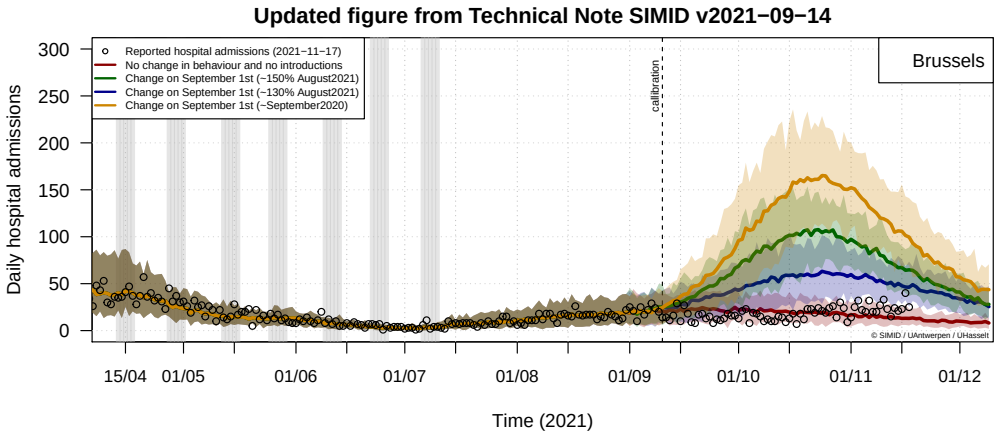
(b) ICU occupancy



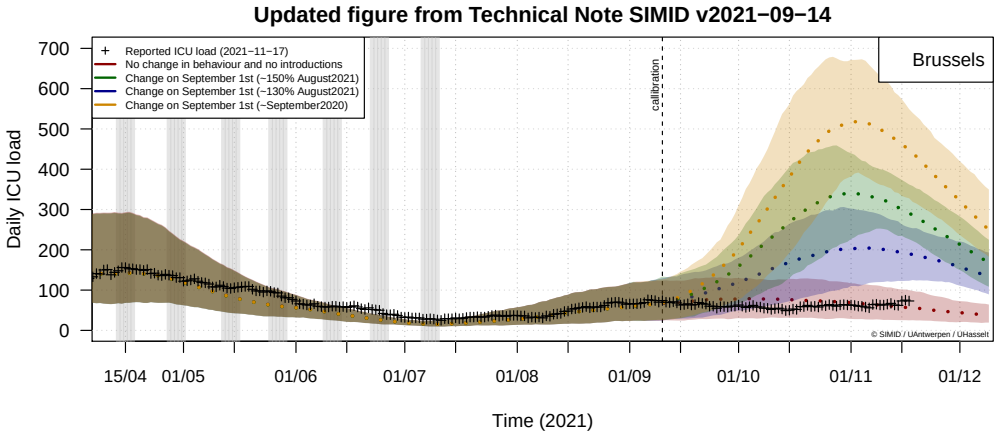
(c) Reproduction number over time (Rt)

Figure 1: Model projections for Belgium on daily hospital admissions, ICU occupancy and reproduction number for different assumptions on social contact behavior from September 1st, 2021. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 20 model runs. UPDATE: We added the reported hospital data on November 18th, 2021.

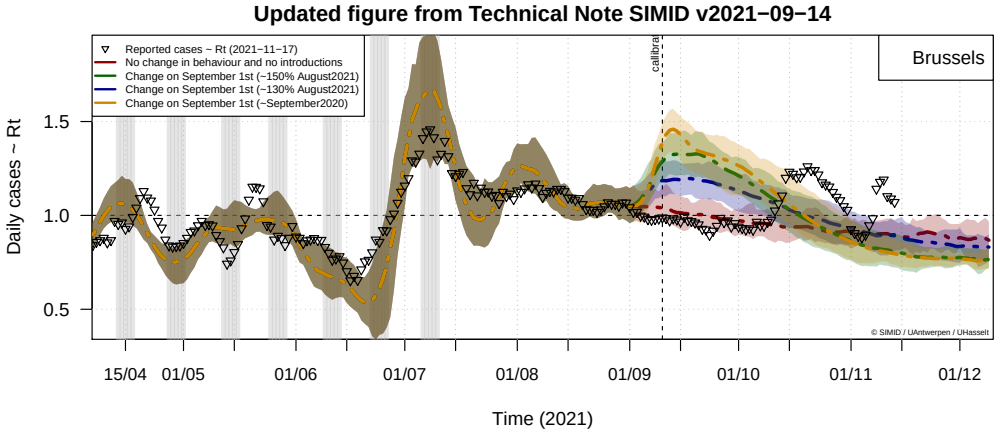
Scenario analysis for the Brussels Capital Region.



(a) Daily hospital admissions



(b) ICU occupancy



(c) Reproduction number over time (Rt)

Figure 2: Model projections for the Brussels Capital Region on daily hospital admissions, ICU occupancy and reproduction number for different assumptions on social contact behavior from September 1st, 2021. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 20 model runs. UPDATE: We added the reported hospital data on November 18th, 2021.

Contributors to this report (alphabetically)

- Christel Faes (Universiteit Hasselt)
- Lander Willem (Universiteit Antwerpen)
- Niel Hens (Universiteit Hasselt en Universiteit Antwerpen)
- Philippe Beutels (Universiteit Antwerpen)
- Steven Abrams (Universiteit Antwerpen en Universiteit Hasselt)

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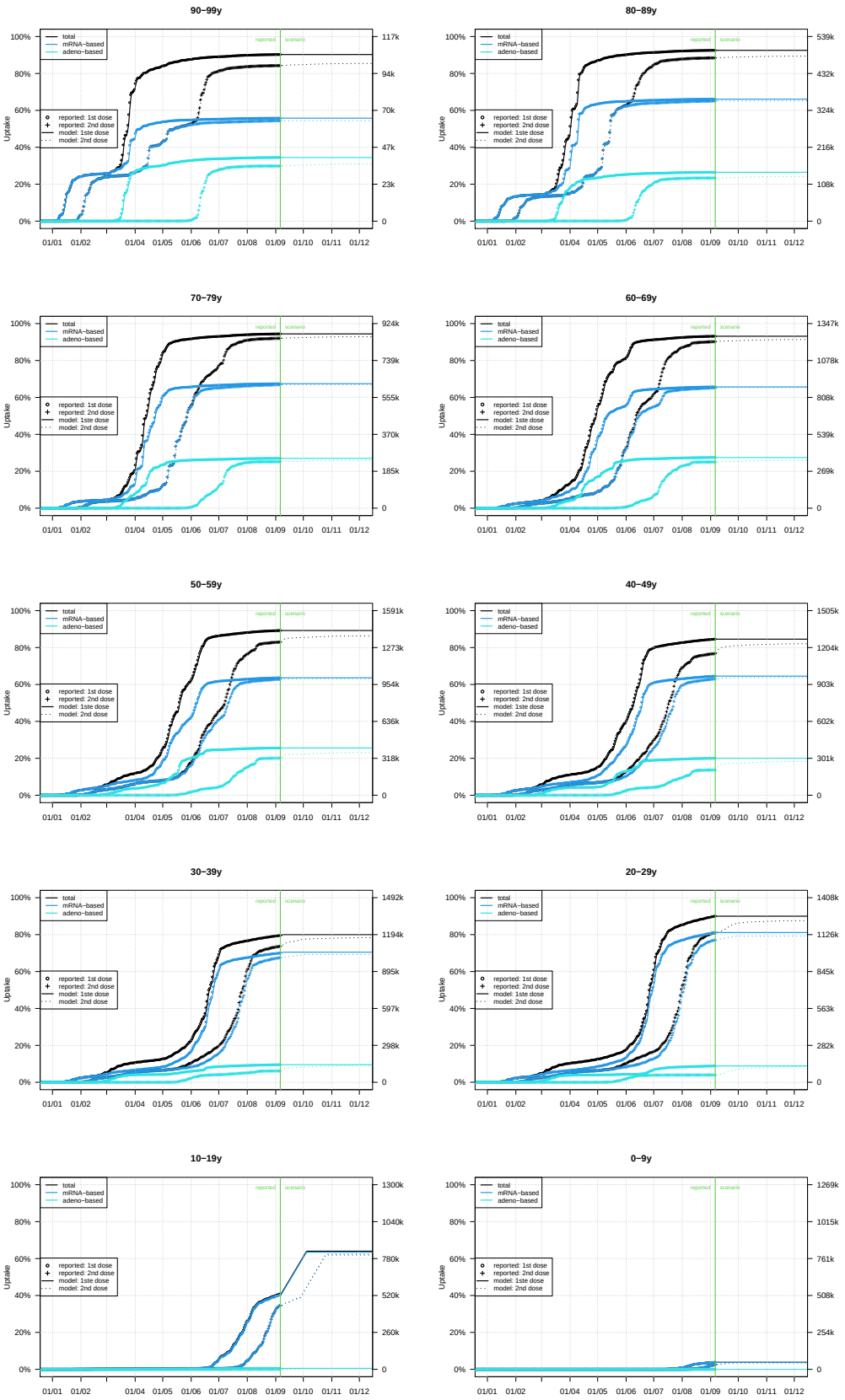

Figure 3: Vaccine uptake by age based on the reported uptake for Belgium on September 6th, 2021.

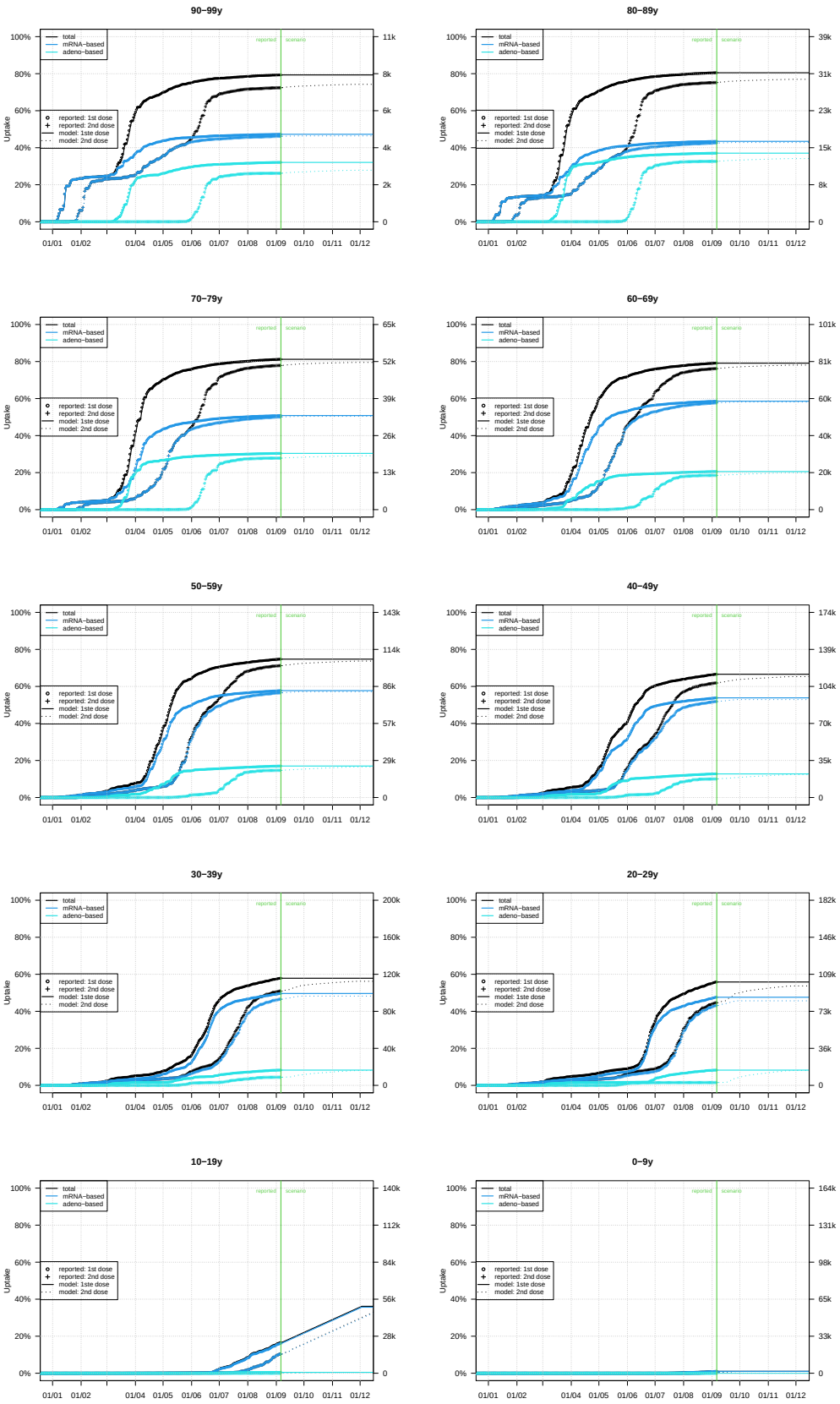

Figure 4: Vaccine uptake by age based on the reported uptake for the Brussels Capital Region on September 6th, 2021.