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SARS-CoV-2 variants and vaccination in Belgium

Modelling results by the SIMID consortium

This document contains model estimates of COVID-19 related burden of disease in Belgium based on a stochastic dynamic transmission model using observational data up to August 23rd, 2022. This analysis focuses on the potential impact of the vaccination campaign starting in September 2022 in Belgium. All previous reports are available via simid.be and the covid-en-wetenschap blog.

Study highlights

- We explored the potential impact of and increasing transmission in September 2022 as a result of resuming societal activities and seasonality. In addition we explore the potential impact of a vaccination campaign starting on September 12, 2022 in different target groups.
- Our scenario analysis shows a new wave in October-November as a result of resuming societal activities and seasonality. However, a booster vaccine campaign with an Omicron dedicated booster and coverage of at least 50% of the oldest population (65 years and older) with already one booster shows a substantial impact on the size thereof. More specifically, including vaccination in the scenario analysis results in a wave moderate in size, near the level of the latest Omicron wave in June. Projections with subsequent vaccination campaign targeting the 18 years and older population show the lowest hospital admission rates in December 2022. While we focus on hospital admissions, high infection rates could lead to significant absenteeism and pressure on primary care.
- While the timing and height of the project peaks are subject to our model assumptions, the main value of this work lies in the relative comparison between different strategies and the overall risk assessment.
- A growing body of evidence shows that individuals who have been infected and/or vaccinated (with or without a booster) lose their protection over time. This implies that infections and therefore hospital admissions could reach a long-term equilibrium, of which the level depends on the waning rates. An equilibrium can be disturbed when a change in contacts and/or transmission dynamics occurs due to (non-)pharmaceutical interventions or seasonality.
- We are making the implicit assumption that Omicron BA.5 will remain dominant throughout the entire simulation period. Nonetheless, other (newly emerging) VOCs may have different transmission probabilities and different probabilities to cause disease, hospitalization or death, and different vaccine effectiveness characteristics against each of these manifestations.
- Our dynamic transmission model has been extended to accommodate a new dedicated booster campaign (fourth or fifth dose) in order to restore a higher protection after waning of natural or vaccine-induced immunity. The assumptions on waning immunity in this report are in accordance to the scenarios as outlined by the ECDC European Covid-19 Scenario Hub (`https://covid19scenariohub.eu/scenarios.html`). More specifically, compared to previous reports, we assume a slower reduction of vaccine effectiveness versus infection over a longer period (8 months on average) and ending at a lower level (i.e., 60% reduction in immunity).

Dynamic Transmission Model

The stochastic model as described by Abrams et al. (2021) has been adapted to include vaccination and the emergence of a VOC from December 2020 (i.e., B.1.1.7 or "Alpha"), a second VOC from May 2021 (i.e., B.1.617.2 or "Delta"), a third VOC from November 2021 (i.e., "Omicron" BA.1 and BA.2) and another VOC from March 2022 (i.e., "Omicron" BA.4 and BA.5). 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.

Model input and assumptions

1. **Gradually accumulating naturally-acquired immunity** in the population has been accounted for, as well as immunity induced by vaccination. Immunity after infection and vaccine-induced immunity obtained after two vaccine doses is assumed to wane over 8 months to reduced protection levels as shown in Table 1).

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

3. **Alpha VOC:** We aggregated the proportion of Alpha, Beta and Gamma VOCs in the population to account for the replacement of the wild-type variant in 2021 by more infectious VOCs for which increased transmissibility and severity are assumed to be equal. The additional transmissibility of the aggregated VOC, which we will denote in this report by the dominant Alpha VOC, was estimated by the model at 32% (95% credible interval (CrI): 26%-40%) relative to the wild-type variant. The model assumed no differential hospital admission probability with respect to the Alpha VOC. Upon infection, the model allowed for a VOC-specific differential hospital length-of-stay and risk of ICU admission.

4. **Delta VOC:** The impact of the Delta VOC has been modelled by the introduction of a second VOC from May 2021 onward with an average increase in transmissibility of 93% (95% CrI: 69%-123%) relative to the Alpha variant. This increase was estimated based on the baseline genomic surveillance data. We assumed 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 upper limit of a 95% confidence interval for the mean ranging up to 4.36, see PHE, Sheikh et al., 2021).

5. **Omicron VOC BA.1 and BA.2:** The impact of the emerging Omicron VOC is modelled by the introduction of a third VOC in the transmission model from the end of November 2021 onward. To account for an adjusted serial interval for Omicron, as reported by Kim et al. (2021), the duration of the latent period for Omicron has been part of the calibration process based on the baseline genomic surveillance of SARS-CoV-2 data for Belgium. This resulted in an increase of 44% (95% CrI: 15%-90%) in transmissibility relative to the Delta variant in combination with an almost instant transition from the exposed to the pre-symptomatic infectious stage after infection with Omicron. In addition, a differential hazard ratio for hospitalization for Omicron relative to Delta has been pivotal. We adopted age-specific hazard ratios for hospital attendance with Omicron compared to Delta from a cohort study in the UK (Nyberg et al., 2022) for our 10-year age bins: (1, 0.89, 0.67, 0.57, 0.54, 0.42, 0.32, 0.42, 0.49 and 0.49). The calibration period covers both the emergence of Omicron sub-lineages BA.1 and BA.2 that became dominant in Belgium on February 28th, 2022. Differences in transmission for BA.2 are absorbed in the wave-specific q-parameters for February-March 2022.

6. **Omicron VOC BA.4 and BA.5:** The impact of the emerging Omicron BA.4 and BA.5 in Belgium has been modelled by the introduction of a fourth VOC in the transmission model from the end of March 2022 onward. We adopted all VOC-specific parameters from the initial Omicron strains except the transmissibility, for which we estimated a relative increase of 57% (95% CrI: 31%-81%). Also the probability to be admitted to ICU given severe disease has been adjusted to meet the reported ICU load.

7. Our model results contain stochastic variation in the transmission process and parameter uncertainty based on multiple model parameter estimations. The calibration procedure relies on likelihood-based MCMC sampling resulting in 100 posterior samples of the joint distribution, each of which can be used to generate stochastic realizations within each scenario under study. 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 (100 iterations) with 10 realizations

per iteration, periodicity of 10 iterations and leading to 100 different chains based on 100 initial starting configurations.

8. 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.

9. Hospital admission data has been the main source of information to inform and calibrate the model given the frequent changes in the Belgian SARS-CoV-2 testing policy and the availability of self-tests for which positive test results are not necessarily confirmed by PCR. The reported hospital admissions are complemented with the number of new positive cases identified in the Belgian hospitals in the last 24h, i.e., patients that have been admitted for another pathology though testing positive for SARS-CoV-2. Given that these infected cases contribute to the COVID-19 related hospital load, we include these new patients in our parameter fitting procedure. The total number of admissions (i.e., SARS-CoV-2 positive individuals that are hospitalized with and for COVID-19) are referred to as "admissions with COVID-19". Projections in terms of "admissions for COVID-19" are based on an estimated proportion of the hospital admissions with COVID-19.

10. The model has been calibrated using social contact data of 47 waves of the Belgian CoMiX survey, with the latest wave conducted between June 28-July 4, 2022. For each survey wave, we estimated age-specific q-parameters (i.e., proportionality factors) to translate social contact patterns into transmission rates. As such, the reported social contact rates are used as a proxy for effective contacts enabling disease transmission and the estimated proportionality factors account for other factors that influence this relation. The latter capture, among other things, age-specific susceptibility and risk behavior during social contacts.

11. We evaluated different **scenarios** to explore adjusted social contact patterns. None of the scenarios included the introduction of more infected cases as a result of increased international travel. All scenarios accounted for a dominance of the latest VOC and the continuous process of rising and waning immunity after infection and vaccination. We started from the latest model calibration and the reported vaccine uptake scheme as presented in Figures S7 and included the following assumptions:

    - **For reference only, we extrapolate the transmission dynamics we estimated for July and August 2022 during the full period September-December 2022**. This scenario intentionally did not take into account school-reopening, restarting activities and seasonality. This scenario represents an underestimation of social contacts and transmission over autumn.
    - **We assumed an increased transmission due to school-reopening, restarting activities and seasonality progressively during the month of September, based on the reported social contact data and estimated transmission during June 2022.** Hence this scenario assumes that behaviour and transmission will be progressively back to the level before summer holidays in 2022. Note that this behaviour is still far away from pre-pandemic behaviour.

12. In addition, the *increased transmission* scenario is presented with different vaccination campaigns, which are the following ones:

    - **Vaccination campaign for individuals aged 65 years and older**, starting on September 12, 2022 and ending on September 30, 2022. The model only vaccinates individuals who are in a waning state, on average 8 months after the previous booster, the other ones being vaccinated after this period.
    - In addition to the vaccination campaign for individuals aged 65 years and older, we explore **booster vaccination for 50-64 year old individuals** starting on October 1st, 2022 and ending on October 31, 2022.
    - In addition to the two vaccination campaigns for 65+ years olds and 50-64 years olds, a **third vaccination campaign for 18-49 year old individuals** starting on November 1st, 2022 and ending on December 31, 2022.

    All of those vaccination campaigns are assumed to be performed with an Omicron dedicated booster reproducing the protection vs. Omicron BA.4 and BA.5 infections similarly to the protection of the previous booster vs. Delta. The uptake is assumed to be either 50% uptake or 100% of the first booster dose uptake. As a supplement, we provide the same vaccination campaigns but with the initial booster (not Omicron dedicated) and initial effectiveness.

13. **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 levels of protection against infection for different VOCs are presented in Table 1.
- **Hospital admissions:** vaccinated individuals who acquire infection are at lower risk of hospital admission with COVID-19. The level of protection against severe disease, which we assume to be in line with hospital admissions, is presented in Table 1.
- **Transmission:** We do not account for a reduced transmission potential due to vaccination. As such, vaccinated individuals (with or without a booster in the model) who acquire infection have not a lower risk of transmitting the disease.
- **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 top of the protection against infection. Protection induced by the second and booster vaccine doses is assumed to be achieved fully (i.e., depending on the maximal vaccine effectiveness as reported in Table 1) 7 days after administration. We consider differences between mRNA and adenovirus-based vaccines in how they induce immunity and in terms of protection (see Table 1).
- The reported Johnson & Johnson (JnJ; Ad26.COV2.S) and Curevac (CV07050101) vaccines are accounted for in the model as (being similar to) the AstraZeneca vaccine (ChAdOx1). The number of administered vaccine doses is too low to outweigh the increase in computational burden and complexity of the model when adding an additional subdivision in the model.
- **Waning of vaccine-induced immunity after 2 doses is included in the transmission model as a separate set of health-related compartments.** We assume a transition rate of 1/240 days towards the waning immunity compartments with reduced vaccine efficacy levels based on the literature and instructions from the "European Covid-19 Scenario Hub", developed and run by the ECDC (see Table 1). This implies that vaccine-induced immunity after the primary schedule wanes until people receive a booster dose (see next bullet).
- **First booster doses are included in the transmission model as a separate set of health-related compartments.** We assume that all booster doses are mRNA-based vaccines with an increase in protection before waning as specified in Table 1. These boosters follow the same process of waning immunity as second doses. People with a second booster before September 2022 are assumed to be back to the booster dose compartment with initial protection followed by a new waning process.
- **Waning immunity after combined protection of vaccination (with or without a booster) and infection, irrespective of the sequence of these events, is included in the model.** We assume full protection for on average 240 days for each possible combination of infection and base vaccination, after which protection is assumed to wane at the same rate as protection from a single booster dose wanes (see Table 1).
- **Booster doses from September 2022 onward with the Omicron dedicated vaccine are included in the transmission model as a separate set of health-related compartments.** We assume that all extra booster doses are mRNA-based vaccines with potentially different protection before waning as specified in Table 1. Those boosters follow the same process of waning immunity.

Table 1: Immunity levels against infection and hospital admissions by vaccine dose, type, VOC and previous infection state. The table also shows the waning rate and protection plateau after e.g. 240 days of waning after infection, which provides a temporary protection of 100%. Other assumptions and references are provided below.

Vaccine type	**Waning rate**	**Alpha**		**Delta**		**Omicron**	
		Infection[1]	**Hospital**[2]	**Infection**[3]	**Hospital**[4]	**Infection**[3]	**Hospital**[5]
Adeno: 1st dose	-	49%	76%	43%	76%[6]	18%	65%[7]
Adeno: 2nd dose		74%	86%	83%	95%	49%	81%[7]
mRNA: 1st dose	-	48%	83%	72%	79%[6]	32%	65%[6]
mRNA: 2nd dose		94%	95%	91%	99%	66%	81%
Waned immunity after 2nd dose	1/240d	38%[3]	52%[4]	36%	54%	26%	44%
Booster (mRNA)		94%[8]	95%[8]	95%	99%[8]	67%	90%
Waned immunity after booster	1/240d	37%[9]	52%[11]	38%	54%[11]	27%	50%[11]
Waned immunity after infection	1/240d	40%[9]	55%[10]	40%[9]	55%[10]	40%[9]	55%[10]
Omicron dedicated booster						95%[12]	90%[12]
Waned immunity after Omicron dedicated booster	1/240d					36%[12]	50%[12]

[1](Bernal,2021); [2](Stowe,2021); [3](ECDC Scenario Hub); [4](ECDC Scenario Hub); [5](CDC report,2022); [6](Assumed equal to 80% of 2 doses); [7](Assumed equal to mRNA); [8](Assumed equal to protection from 2 mRNA doses); [9](ECDC Scenario Hub); [10](ECDC Scenario Hub); [11](ECDC Scenario Hub); [12](ECDC Scenario Hub);

14. **Vaccine uptake**

    - The vaccine-type and age-specific uptake in the model of first, second and additional booster doses over time at the national level is based on the reported data by Sciensano, derived from Epistat up to August 28th, 2022. The uptake by age is presented in Figure S7.
    - 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).

Major limitations

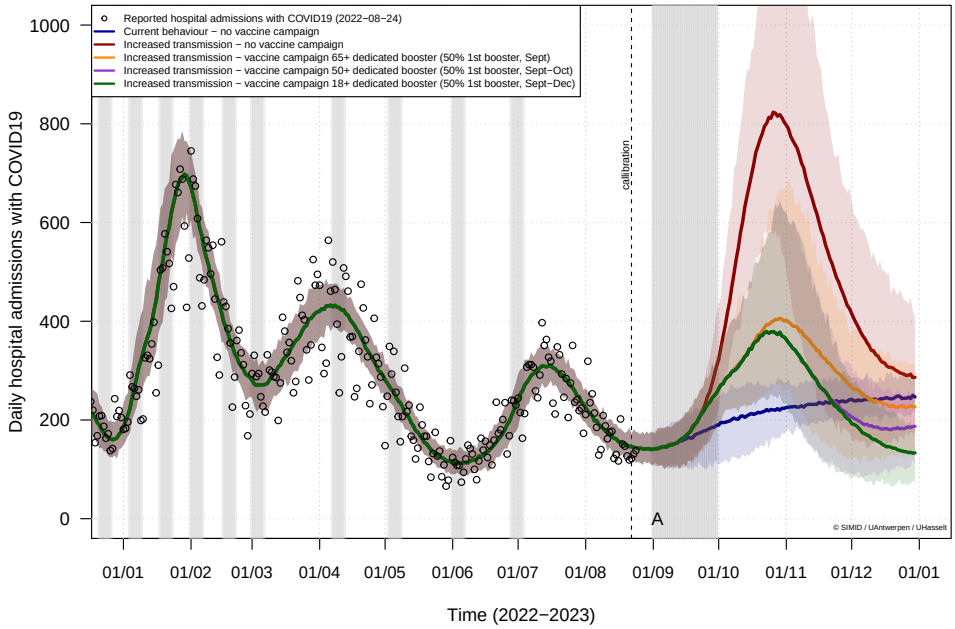
- **This transmission model is suited for scenario analyses to investigate possible future or counterfactual (retrospective) paths, it is not a prediction model.**
- The model is calibrated on hospitalizations and informed by social contact data from the Belgian CoMix survey. These empirical social contact data inform mainly the frequency and age structure of person-to-person social interactions, but are less informative with regard to the adherence to guidelines and restrictions. The fact that the model is primarily calibrated on hospitalization data, and given the time lag between incurring infection and being admitted to hospital, makes this model less sensitive to rapidly changing dynamics. Another issue is that empirical data on social contact patterns is always lagging behind.
- We are making the implicit assumption that the current VOC will remain the dominant strain throughout the entire simulation period. Nonetheless, other (newly emerging) VOCs may have different transmission probabilities and probabilities to cause disease, hospitalization or death, and different vaccine effectiveness characteristics against each of these manifestations.
- The transmission model does not evaluate (severe) outpatient cases, which affect pressure exerted on primary care. Also, the model does not include parameter uncertainty with respect to vaccine effectiveness yet.
- The incremental transmissibility induced by the emergence of different VOCs, which we include in the model, is considered to be age-invariant.

- We attributed the growth advantage of the VOCs mainly to transmissibility, and as such, ignored the potential effect of immune escape after infection on the speed of penetration. Immune escape of vaccine-induced immunity has been considered with the VOC-specific vaccine efficacy values. For Omicrion, we assumed a reduced serial interval, which increases the transmission potential.
- The reduced serial interval for Omicron has been fully attributed to a reduction in the latent, or exposed, period. A potential reduction in the infectious period is not captured by the model at this stage.
- 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 stepwise process.
- This model does not explicitly account for importation of cases by returning travelers which could have impact on the evolution of the epidemic.
- We present our modelling results by the mean and point-wise 95% credible interval based on 100 model realizations, which capture stochastic effects and parametric uncertainty. The interplay between these two sources of uncertainty is subject of future research.
- The national model does not account for local differences in immunity and assumes random mixing in the population. As such, local outbreaks and herd immunity effects in sub-populations with immunity levels below or above the national level, respectively, are underestimated. Given that there are more and more differences (end of holiday period, vaccination campaign) between the different regions, this will likely result in discrepancies between model scenarios and future observations.

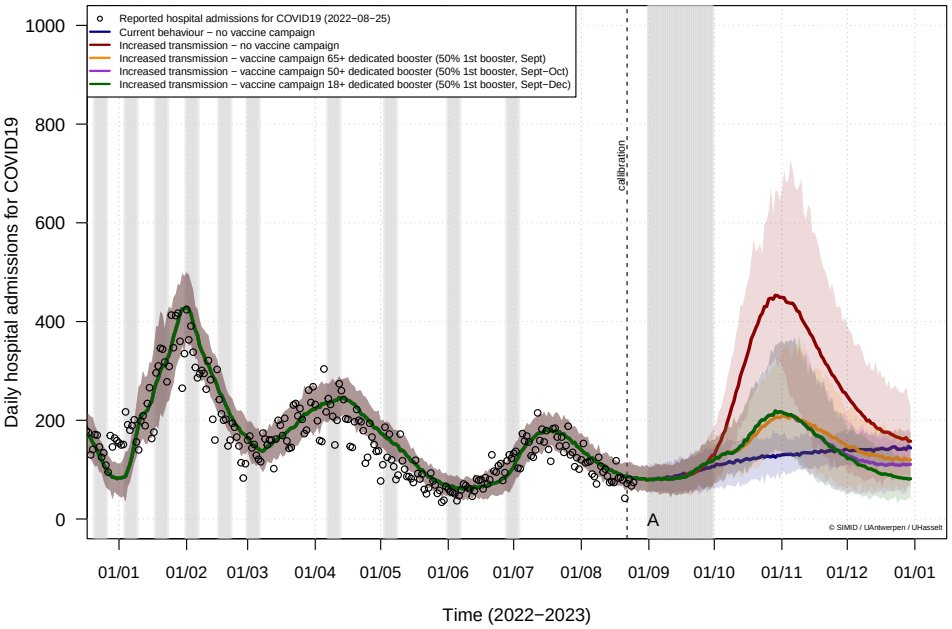
Model results

The following figures depict the results of the scenario analysis specified by changed transmission assumptions. All projections show large point-wise 95% credible intervals and should therefore be interpreted with great caution. The main conclusions are listed at the start of this document.

Potential impact of the vaccination campaign using an Omicron dedicated booster with uptake up to 50% of the 1st booster uptake.

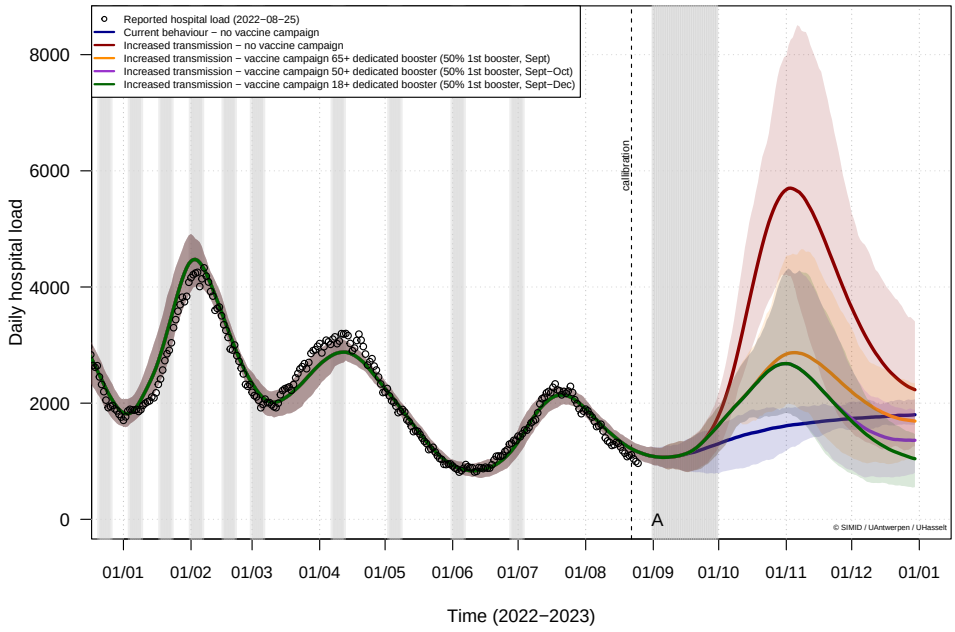


(a) Daily hospital admissions with COVID-19

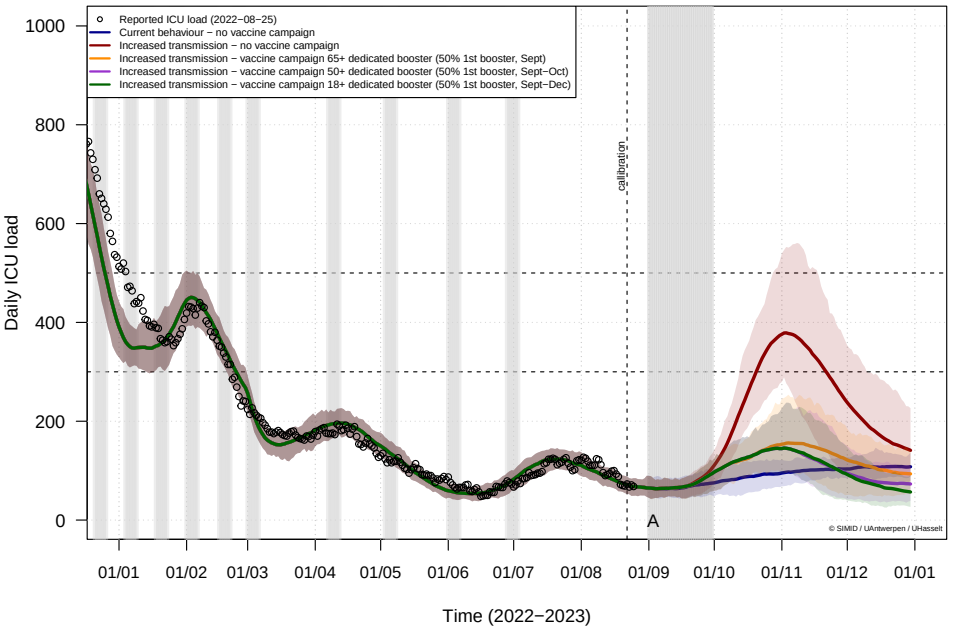


(b) Daily hospital admissions for COVID-19

Figure 1: Model projections for hospital admissions with and for COVID-19 in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

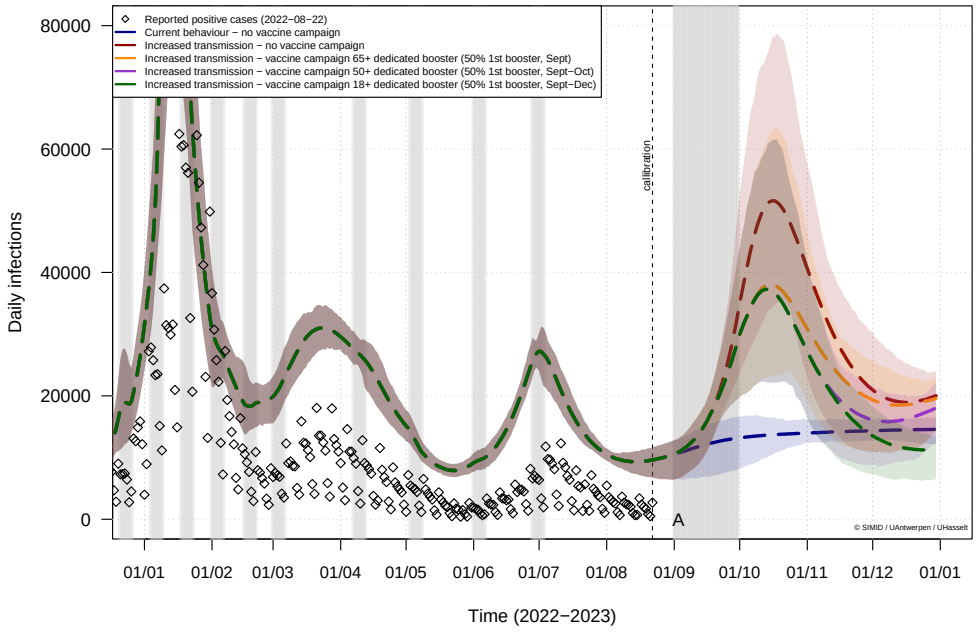


(a) Daily hospital load for COVID-19

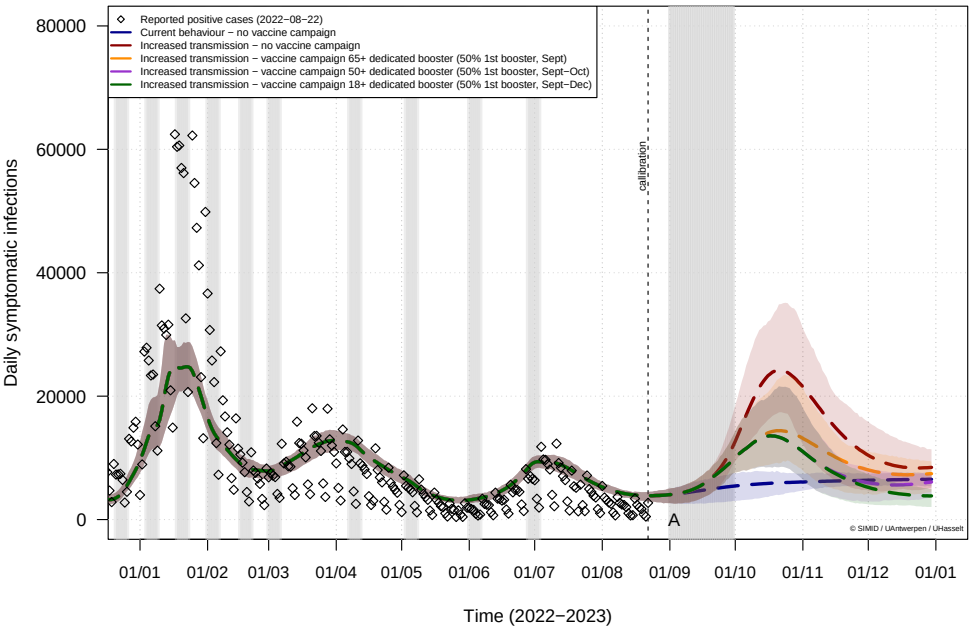


(b) Daily ICU load for COVID-19

Figure 2: Model projections for COVID-19 hospital and ICU load in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.



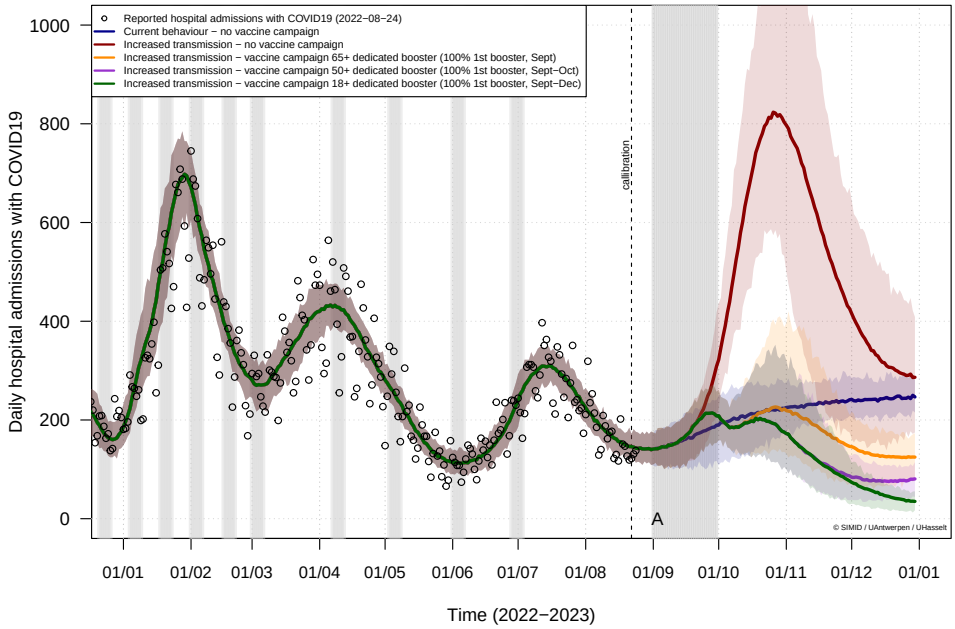
(a) Daily infections



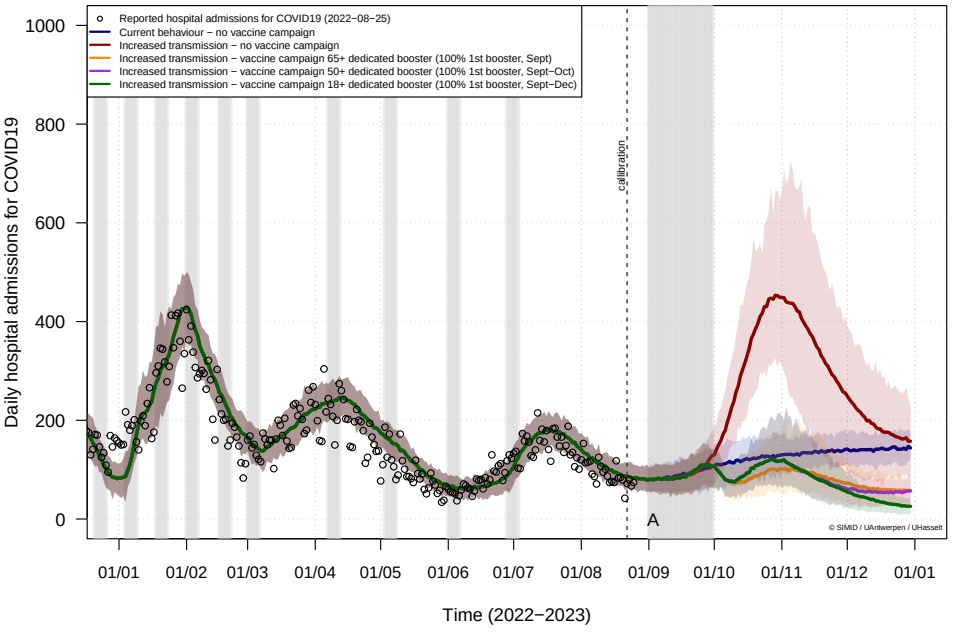
(b) Daily symptomatic infections

Figure 3: Model projections for COVID-19 infections and symptomatic infections in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

Potential impact of the vaccination campaign using an Omicron dedicated booster with uptake up to 100% of the 1st booster uptake.

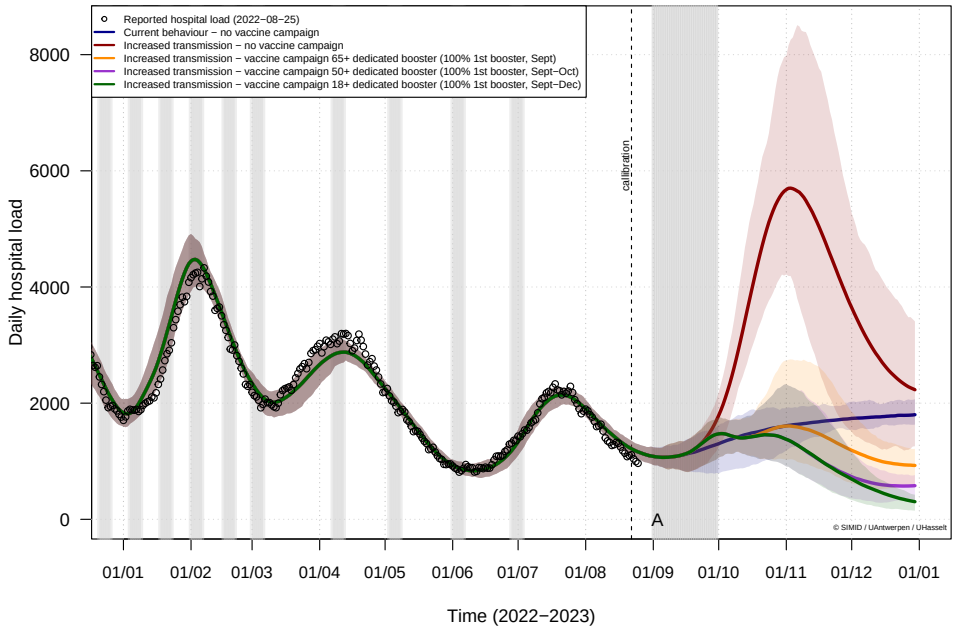


(a) Daily hospital admissions with COVID-19

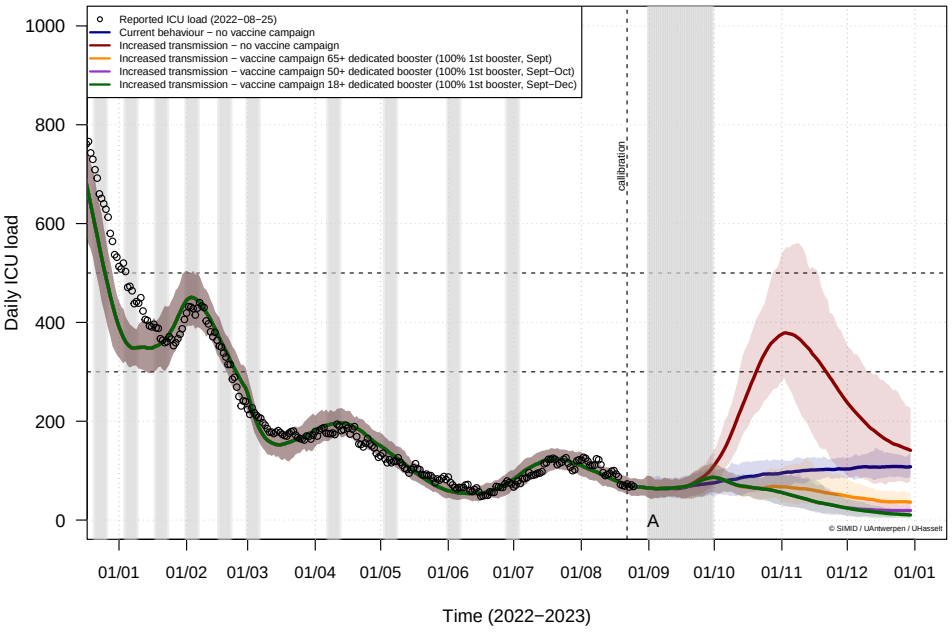


(b) Daily hospital admissions for COVID-19

Figure 4: Model projections for hospital admissions with and for COVID-19 in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

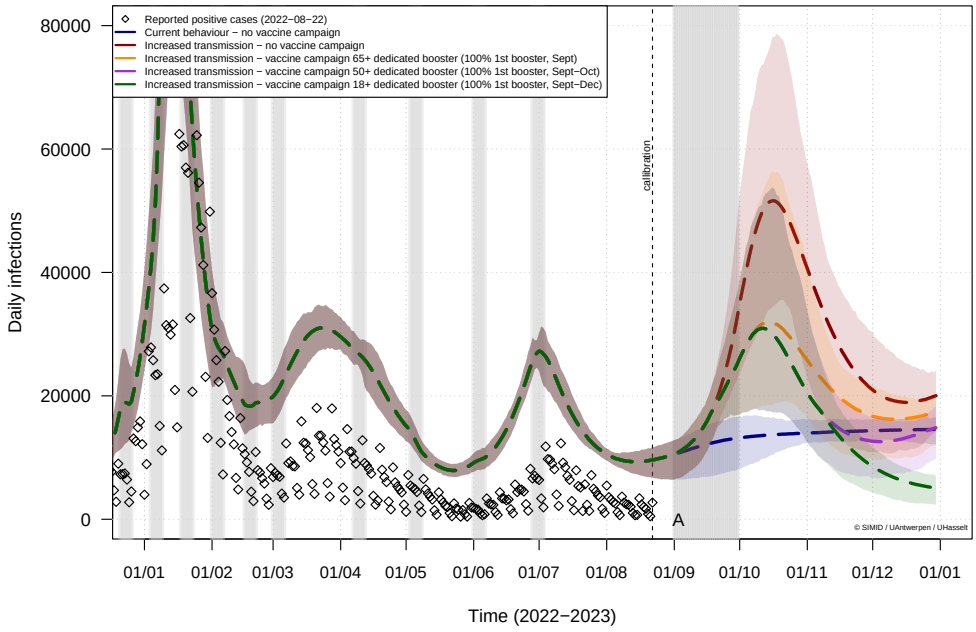


(a) Daily hospital load for COVID-19

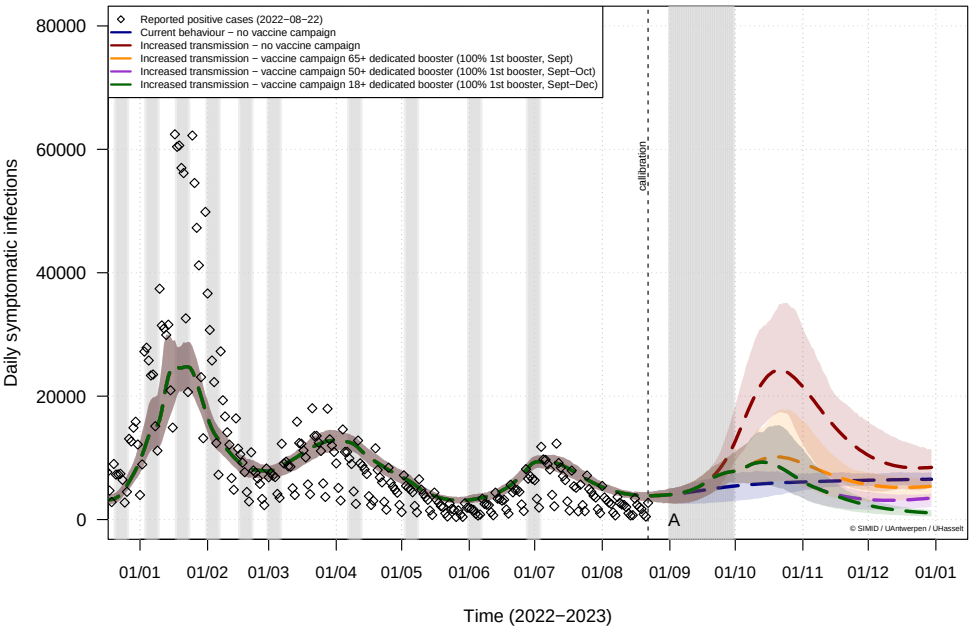


(b) Daily ICU load for COVID-19

Figure 5: Model projections for COVID-19 hospital and ICU load in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.



(a) Daily infections



(b) Daily symptomatic infections

Figure 6: Model projections for COVID-19 infections and symptomatic infections in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

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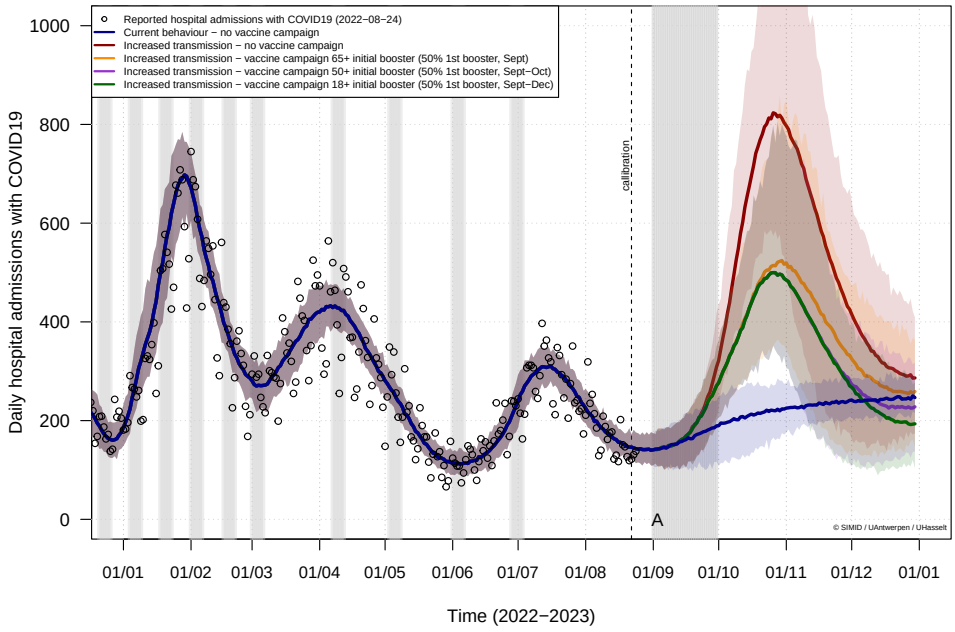
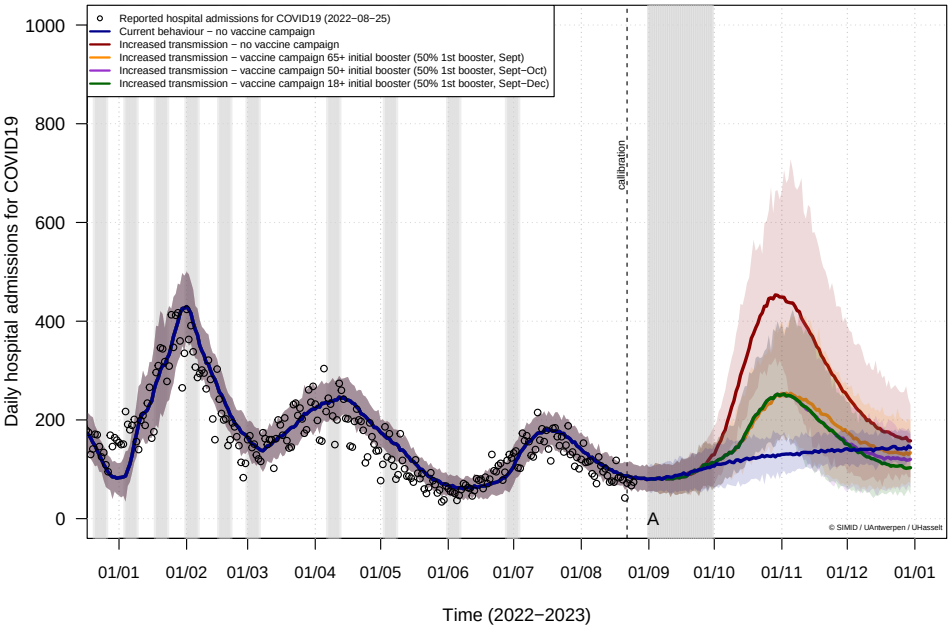
SUPPLEMENT

Potential impact of the vaccination campaign using the initial booster (not Omicron dedicated) with uptake up to 50% of the 1st booster uptake.

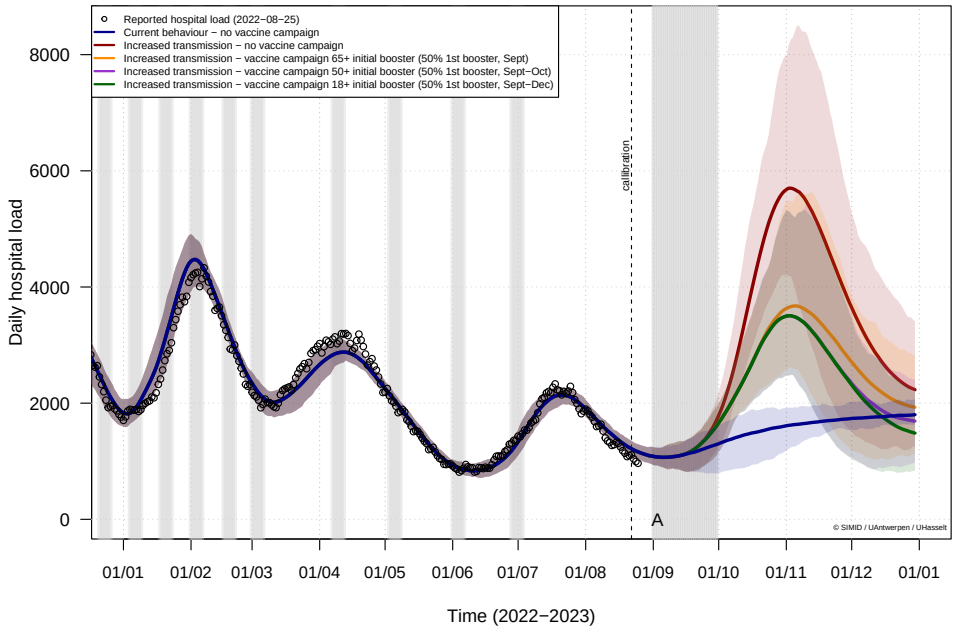


(a) Daily hospital admissions with COVID-19

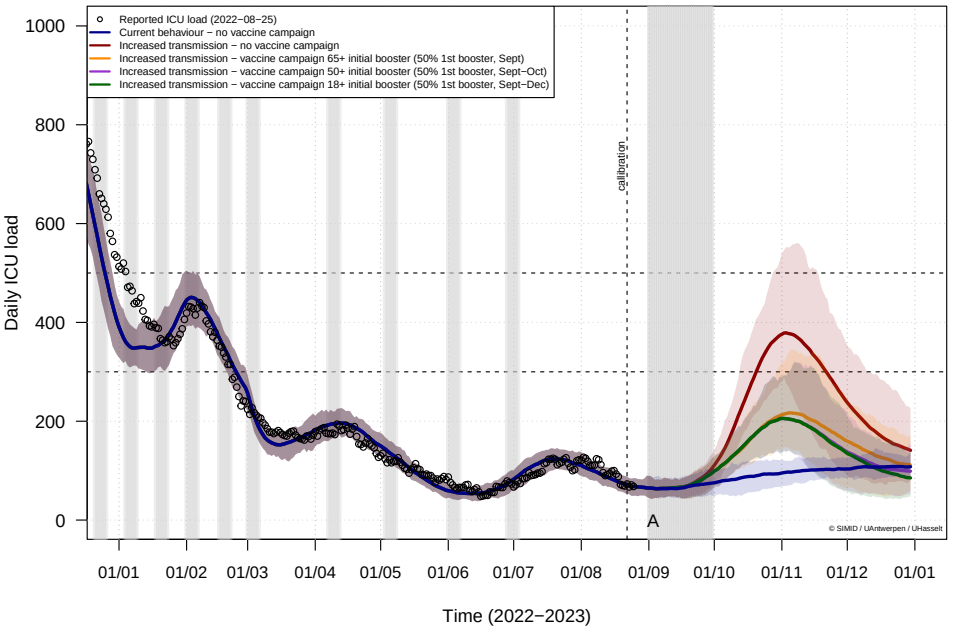


(b) Daily hospital admissions for COVID-19

Figure S1: Model projections for hospital admissions with and for COVID-19 in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

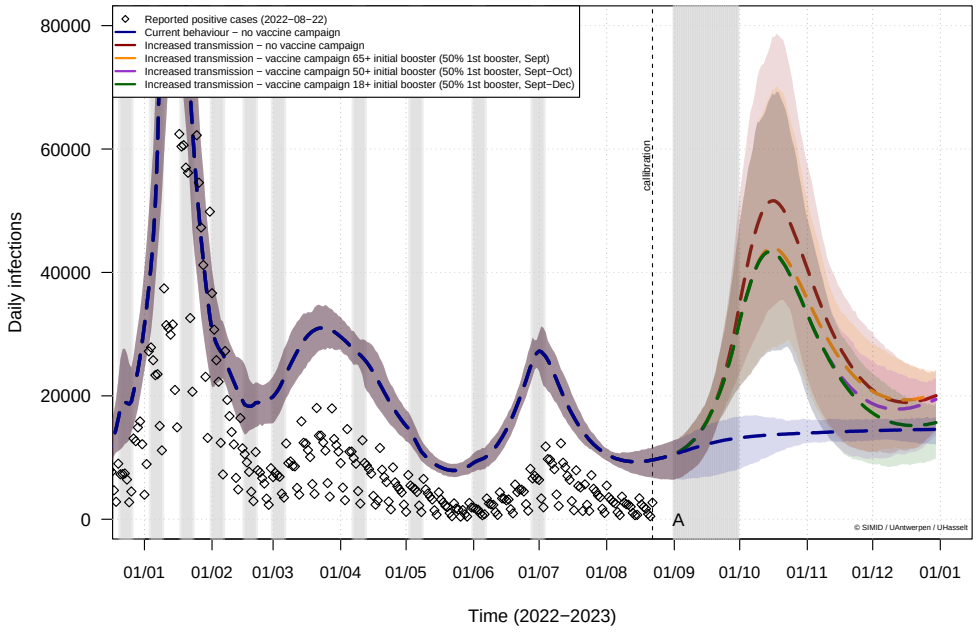


(a) Daily hospital load for COVID-19

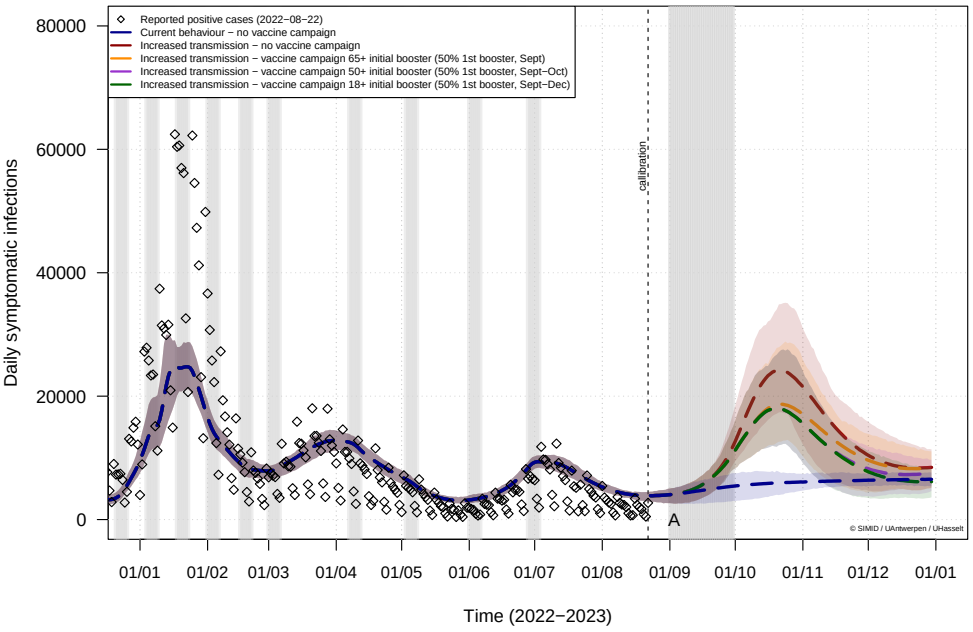


(b) Daily ICU load for COVID-19

Figure S2: Model projections for COVID-19 hospital and ICU load in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.



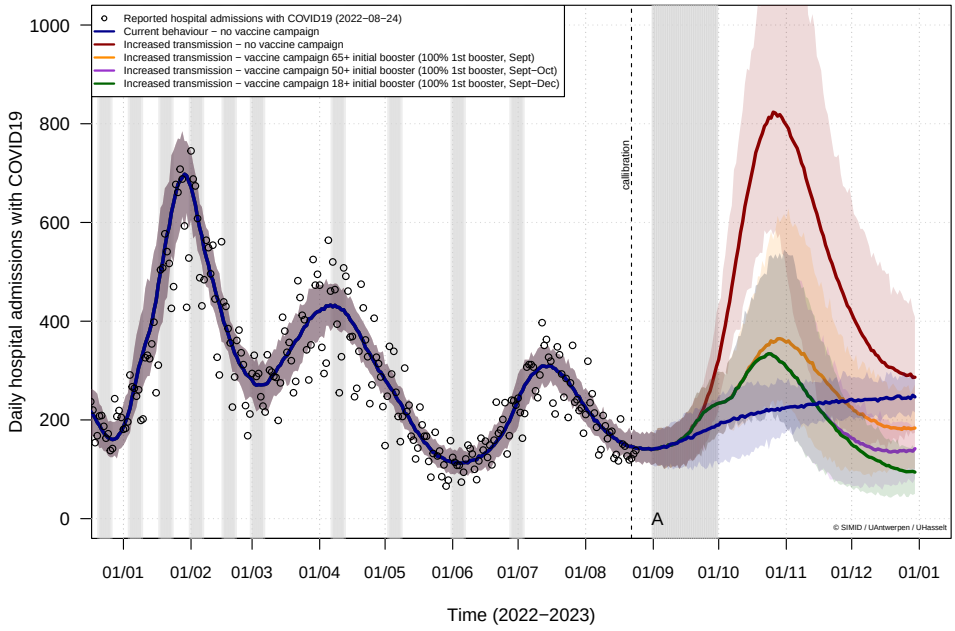
(a) Daily infections



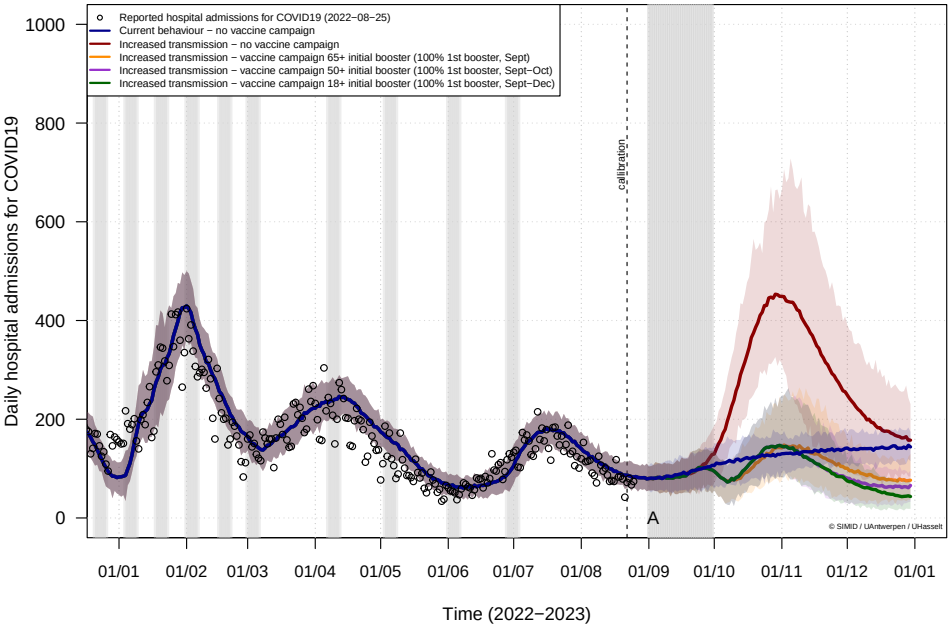
(b) Daily symptomatic infections

Figure S3: Model projections for COVID-19 infections and symptomatic infections in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

Potential impact of the vaccination campaign using the initial booster (not Omicron dedicated) with uptake up to 100% of the 1st booster uptake.

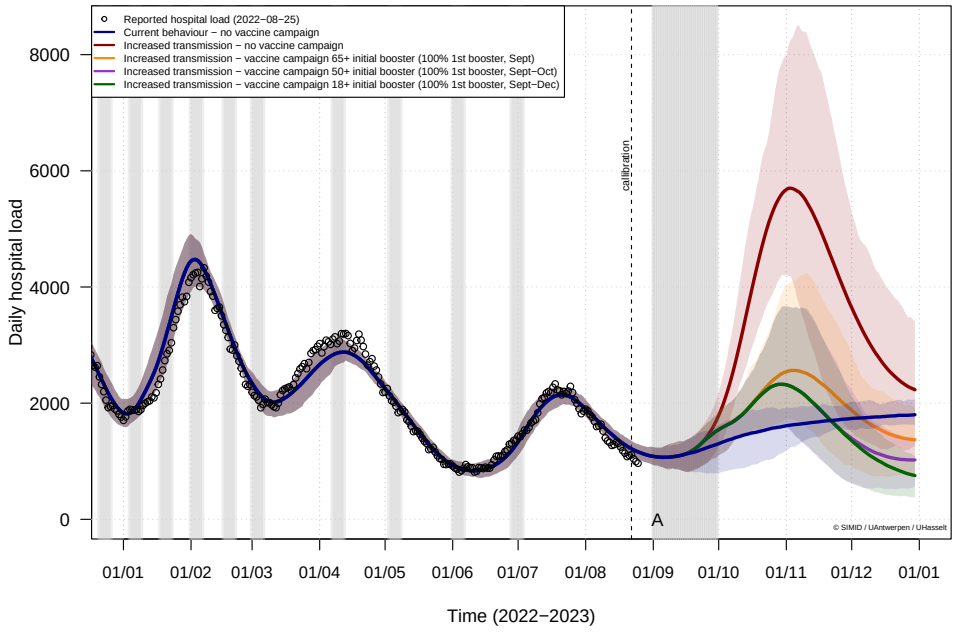


(a) Daily hospital admissions with COVID-19

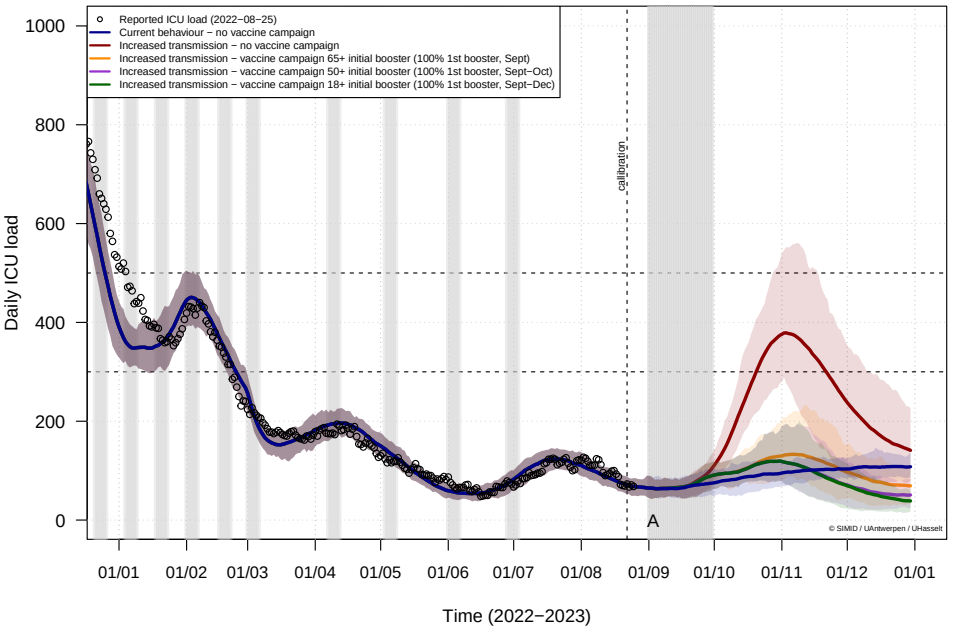


(b) Daily hospital admissions for COVID-19

Figure S4: Model projections for hospital admissions with and for COVID-19 in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

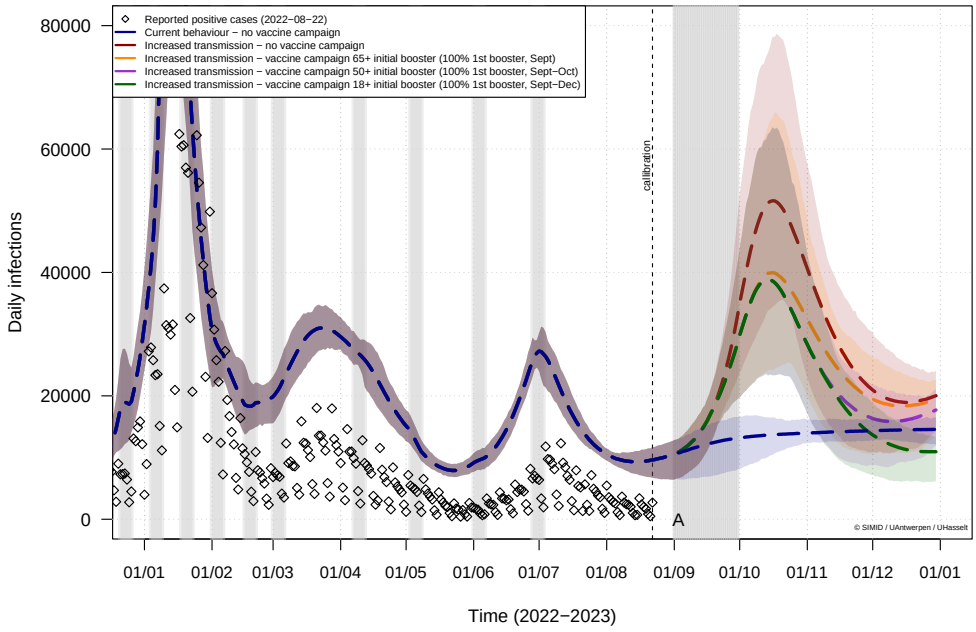


(a) Daily hospital load for COVID-19

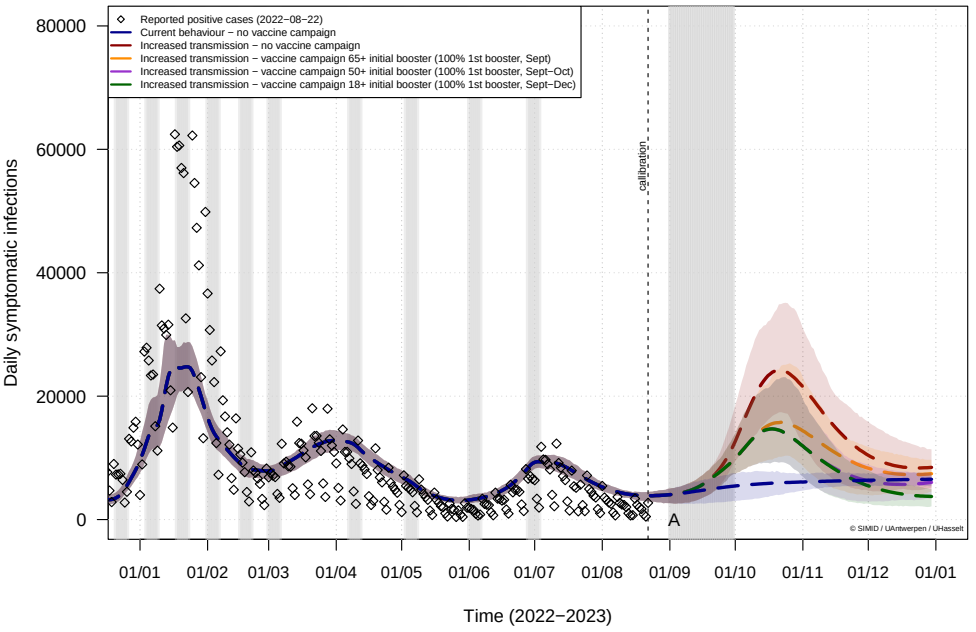


(b) Daily ICU load for COVID-19

Figure S5: Model projections for COVID-19 hospital and ICU load in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.



(a) Daily infections



(b) Daily symptomatic infections

Figure S6: Model projections for COVID-19 infections and symptomatic infections in Belgium when assuming restarting activities and seasonality during September 2022 and successive vaccination campaigns by age group. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations.

Reported uptake and vaccination scenarios

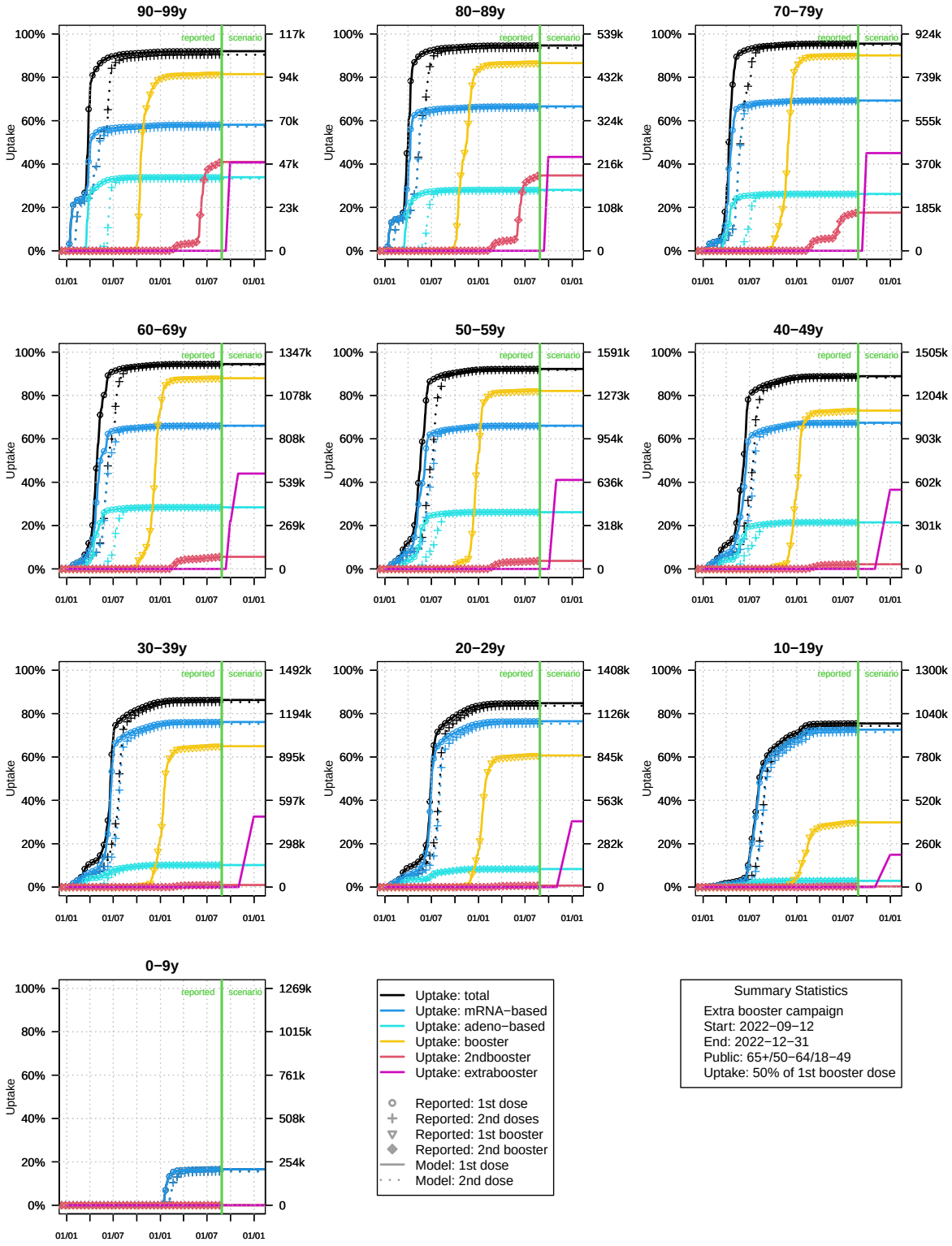


Figure S7: Vaccine uptake by age, vaccine-type and dose based on the reported uptake for Belgium on August 28th, 2022, with scenarios of vaccination campaign up to 50% of the uptake of the first booster dose.

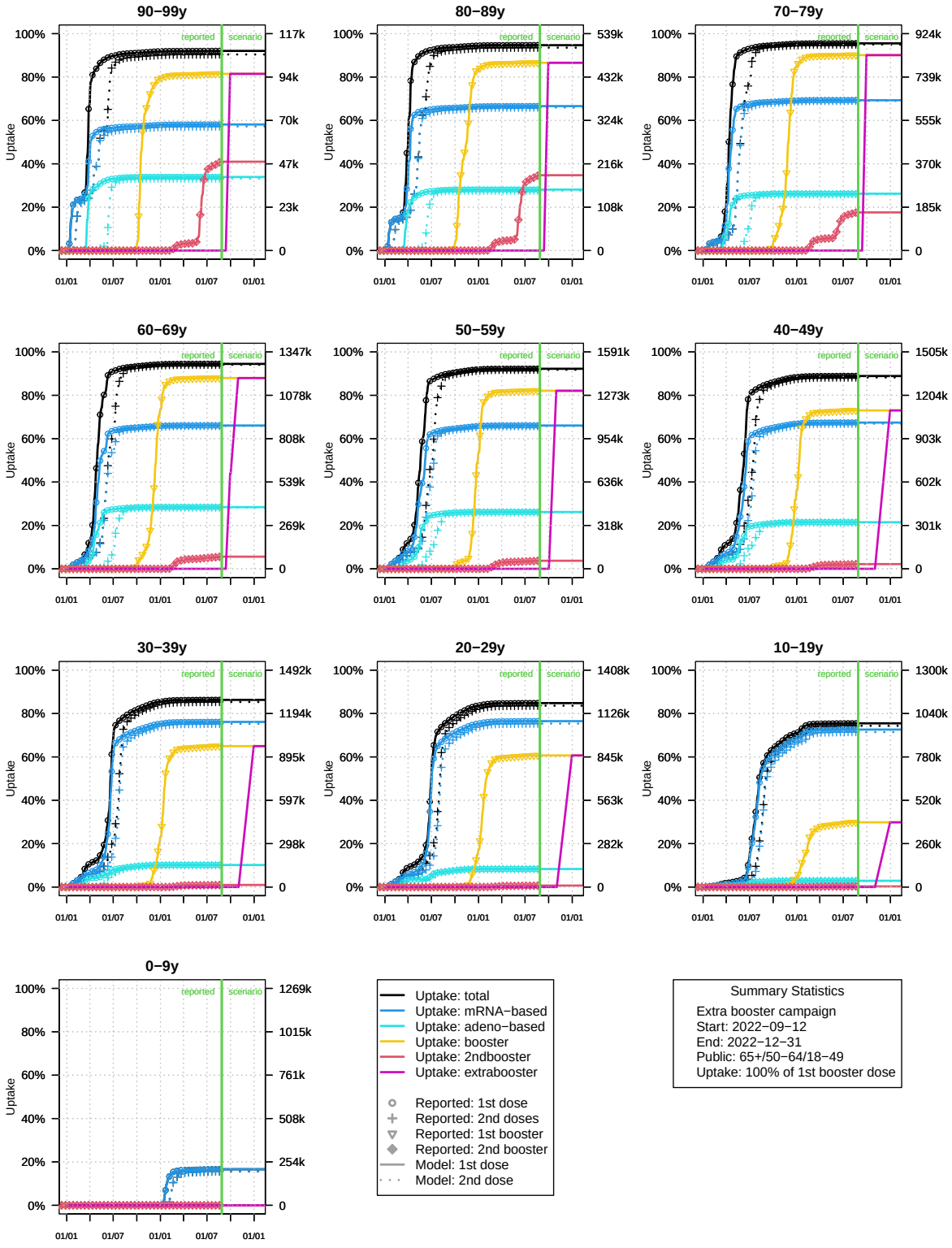


Figure S8: Vaccine uptake by age, vaccine-type and dose based on the reported uptake for Belgium on August 28th, 2022, with scenarios of vaccination campaign up to 100% of the uptake of the first booster dose.