technical note - not peer reviewed - v20230824

SARS-CoV-2 variants and vaccination in Belgium

Modelling results by the SIMID consortium

This document contains model estimates of the COVID-19 related burden of disease in Belgium based on a stochastic dynamic transmission model using observational data up to June 27th, 2023 (last day of hospital surge data in Belgium). This analysis focuses on the potential impact of the vaccination campaign starting in September 2023 in Belgium. All previous reports are available via simid.be and the covid-en-wetenschap blog.
This study was possible thanks to the creation of a new Belgian modeling consortium between UHasselt, UNamur and Sciensano funded by the Cabinet of the Minister of Social Affairs and Health.

Study highlights

- We explore the potential impact of a vaccination campaign starting on September 15, 2023 with an XBB.1.5 booster and with different theoretical uptakes, in addition to the potential impact of increased transmission from September 2023 onward as a result of resuming societal activities after the summer break and seasonality effects (e.g., as a result of a shift from outdoor to indoor contacts).

- Our scenario analysis shows a considerable benefit from the vaccination campaign during November–December 2023. Regarding a possible wave in September–October due to the restart of activities, the benefit increases with an earlier start of the vaccination campaign. The benefit of a campaign targeting the same audience as the flu vaccine is almost double the benefit of a campaign targeting half of that audience. An additional 15% increase in vaccinated people has limited impact.

- Modification of contact rates and seasonality is simulated in the future according to last years collected data and estimated parameters in order to reproduce potential changes in transmission. Therefore, the timing and height of the projected peaks are subject to the model assumptions and are not intended to be predictive. The main value of this work lies in the relative comparison between different strategies and the overall risk assessment.

- We make the implicit assumption that Omicron XBB.1.5 and the close variants currently circulating will remain dominant throughout the simulation period. Nonetheless, other (newly emerging) VOCs may have different transmission probabilities and different probabilities of causing disease, hospitalization, or death, and different vaccine effectiveness characteristics against each of these manifestations. In particular, the still unknown particularities of the very recent EG.5 variant are not taken into account.

- Our dynamic transmission model has been largely extended since the latest technical note to incorporate new features such as the consideration of new omicron variants (BQ.1 and XBB.1.5), immune evasion from variants since Omicron and the consideration of boosters targeting specific variants avoiding this immune evasion. The assumptions on waning immunity and the different scenarios are in accordance with the specifications of the ECDC European Covid-19 Scenario Hub Round 5 (`https://covid19scenariohub.eu/scenarios.html`).

Dynamic Transmission Model

The stochastic model as described by Abrams et al. (2021) is calibrated on early sero-prevalence data, genomic surveillance data, hospital admission data, mortality data and social contact data from the Belgian CoMix survey. The model has been adapted to include multiple features as e.g. vaccination and variants. Most of those improvements and assumptions used are described in the latest Technical note: SARS-CoV-2 variants and vaccination in Belgium (v2022-08-31) as well as in Willem et al. (preprint 2023). We limit descriptions of inputs and assumptions below to new or different features only.

New model inputs and assumptions

1. 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 as well as from the GISAID database. Omicron main subvariants are regrouped as BA.1/BA.2, BA.4/BA.5, BQ.1/BQ.2.75/XBB, XBB.1.5/XBB.1.9/ABB.1.16/EG.1.

2. All Omicron subvariants are modelled using an increase in transmissibility as well as an immune evasion vs. protection against infection and severe forms coming from a previous infection (with a previous variant) or vaccination with an older vaccine. Protections from infection with the current variant or vaccine hat targets the current variant do not allow immune evasion.

3. 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 testing. The reported hospital admissions are complemented by the number of new positive cases identified in Belgian hospitals in the last 24 hours, i.e., patients who have been admitted for another pathology but who tested 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 who are hospitalized with and for COVID-19) are referred to as "admissions with COVID-19". The projections in terms of "admissions for COVID-19" are based on an estimated proportion of hospital admissions with COVID-19. Hospital surge data after June 27th, 2023 are not available due to a shift to sentinel surveillance.

4. The model has been calibrated using social contact data from 47 waves of the Belgian CoMiX survey, with the last wave conducted between June 28 and July 4, 2022. The contact patterns from September 1, 2022 are estimated using the corresponding contact data of the previous year during the same period. For each survey wave, we estimated age-specific q-parameters (i.e., proportionality factors) to translate social contact patterns into transmission rates. As such, reported social contact rates are used as a proxy for effective contacts that enable disease transmission, and estimated proportionality factors account for other factors that influence this relationship. The latter capture, among other things, age-specific susceptibility and risk behavior during social contacts.

5. The vaccine-type and age-specific uptake in the model of first, second and additional booster doses over time at the national level are based on the reported data by Sciensano, derived from Epistat up to August 16, 2023. Uptake by age is presented in Figure S1.

6. We evaluated a **scenario** to explore changes in social contacts and transmission. This scenario does not include the introduction of more infected cases as a result of increased international travel and 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 the Supplement section.

7. The baseline scenario included the following assumptions: Social contact data are estimated from July 1, 2023 as similar to the social contact data of the last known CoMiX survey corresponding to the same period of the previous year, with a smoothing procedure of 15 days. Age-specific q-parameters (i.e., proportionality factors) are estimated using the relative changes between May 2022 and the corresponding period last year applied to the estimated parameters of May 2023. Therefore, similar seasonal variations are considered but applied to the estimated proportionality factors of May 2023 in order to preserve the characteristics of the current variant.

8. In addition, this scenario is presented with different vaccination campaigns:

   - **Vaccination campaign for individuals aged 65 years and older, 50% of flu**, starting on September 15, 2023 and ending on November 15, 2023. Only individuals who are in a waning state, on average 8 months after the previous booster, are vaccinated. The number of vaccinated individuals is equal to 50% of the individuals vaccinated against the flu, as estimated by ECDC from WHO and OECD data (28.8% of 65-69, 31% of 70-79 and 29% of 80+).
   - **Vaccination campaign for people 65 years and older, 100% of flu**, similar to the previous scenario with an uptake equal to the one observed for the flu vaccine (57.6% of 65-69, 62% of 70-79 and 58% of 80+).
   - **Vaccination campaign for individuals aged 65 years and older, 100% of flu + 15%**, similarly to the previous scenario with an uptake equal to the flu vaccine + 15% of the population (72.6% of 65-69, 77% of 70-79 and 73% of 80+).

   All of these vaccination campaigns are assumed to be performed with an XBB.1.5 dedicated booster. The vaccine uptakes by age are presented in Figures S1, S2 and S3.

9. **Vaccine protection:** The levels of protection against infection and severe forms of disease for different VOCs are presented in Table 1. Omicron variants (BA.1/BA.2, BA.4/BA.5, BQ.1/BQ.2.75/XBB, XBB.1.5/XBB.1.9/ABB.1.16/EG.1) have additional reductions in vaccine effectiveness and protection as compared to infections with previous variants, which are estimated by the model (immune evasion concerning new infections). New bivalent boosters or booster targeting a specific variant (mRNA) avoid those reductions vs. current and previous variants (as well as protection from previous infections with the current variant). We assume a transition rate (exponential process) of $\frac{log(2)}{180} \sim 1/260$ days (corresponding to a median time of 6 months) toward the waning immunity compartments with reduced vaccine efficacy levels based on the literature (for protection versus alpha and delta variants) and instructions from the ECDC "European Covid-19 Scenario Hub" (for protection versus Omicron-like variants) using the pessimistic scenario assumptions from Round 5 which are:

   - Protection against infection: 6 months median time to transition to 40% of the initial immunity,
   - Protection against severe outcomes: 6 months median time to transition to 80% of the initial 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 $\sim$ 260 days of waning after infection or vaccination. Other assumptions and references are provided below. Due to the nature of the model using recovered R compartments after infection without a possibility of direct reinfection, the immediate protection after infection corresponds to an artificial 100% protection until individuals enter a waning state. Protections with * are subject to an additional immune evasion for each Omicron subvariant as estimated by the model.

Vaccine type	**Waning rate**	**Alpha**		**Delta**		**Omicron**	
		Infection[1]	**Hospital**[1]	**Infection**[2]	**Hospital**[3]	**Infection**[2]	**Hospital**[4]
Adeno: 1st dose	-	49%	76%	43%	76%[5]	18%*	65%[6]
Adeno: 2nd dose		74%	86%	83%	95%	49*%	81%[6]
mRNA: 1st dose	-	48%	83%	72%	79%[5]	32%*	65%[5]
mRNA: 2nd dose		94%	95%	91%	99%	66%*	81%
Natural or hybrid immunity		100%[7]	100%[7]	100%[7]	100%[7]	100%[7]	100%[7]
Waned immunity after 2nd dose or natural immunity	$\frac{log(2)}{180}$	63%[6]	92[6]%	63%[6]	92%[6]	26%*[6]	65%[6]
Booster (mRNA)		94%[5]	95%[5]	95%	99%[6]	67%*	90%
Waned immunity after booster or hybrid immunity	$\frac{log(2)}{180}$	89%[6]	92%[6]	89%[6]	92%[6]	27%*[6]	72%[6]

[1](Bernal,2021); [2](Andrews,2022b); [3](Andrews,2022a); [4](CDC report,2022); [5](Assumed equal to protection from 2 mRNA doses); [6](ECDC Scenario Hub); [7](Compartments without possibility of infection);

Major limitations

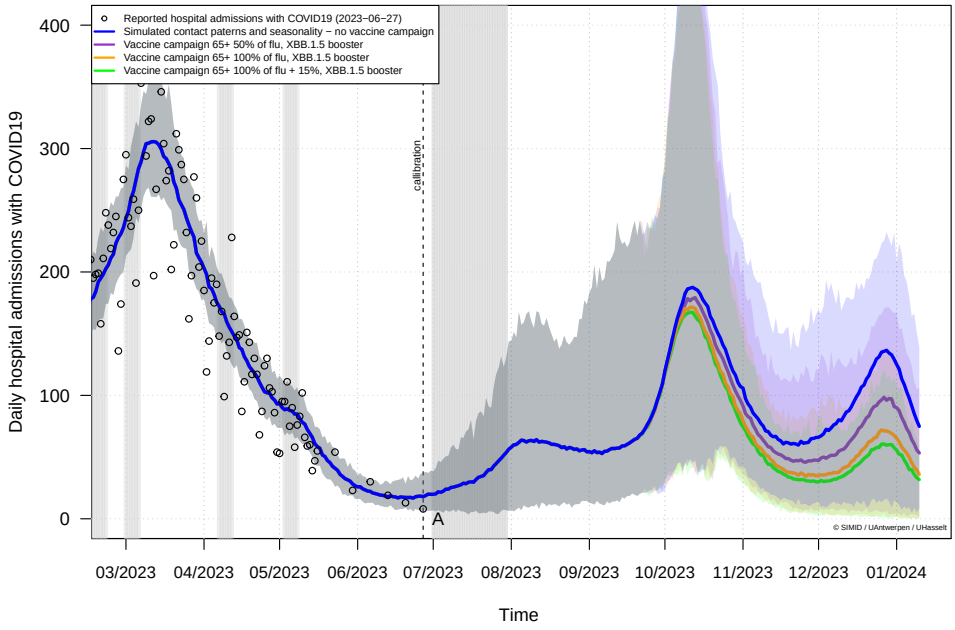
- This transmission model is suited for scenario analyses to investigate possible future or counterfactual (retrospective) paths, it is not a prediction model.
- The model is calibrated on the number of hospitalizations and is informed by social contact data from the Belgian CoMix survey. These empirical social contact data mainly inform the frequency and age structure of person-to-person social interactions, but are less informative with respect to the nature of these contacts and whether they are effective for transmission.
- We make 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 of causing disease, hospitalization, or death, and different vaccine effectiveness characteristics against each of these manifestations.
- The transmission model does not evaluate (severe) outpatient cases that affect the pressure exerted on primary care. Furthermore, the model does not yet include uncertainty about parameters with respect to vaccine effectiveness.
- The incremental transmissibility and immune evasion induced by the emergence of different VOCs, which we include in the model, is considered to be age-invariant.
- This model does not explicitly account for importation of cases by returning travelers, which could have an 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 a 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

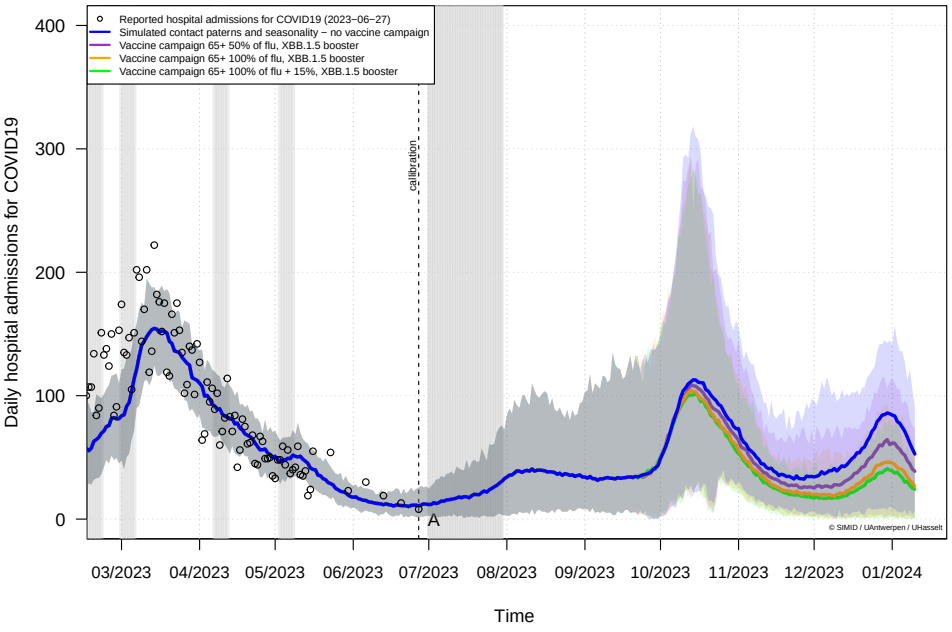
The following figures depict the results of the scenario analysis specified by the changed transmission assumptions. All projections show large point-wise 95% credible intervals and should therefore be interpreted with great caution. The main conclusions are listed in the beginning of this document.

In addition to those results, we can mention that similar projections have been performed for the ECDC European Covid-19 Scenario Hub using a starting date of October 1st, 2023 instead of September 15th, 2023 (as is the case for Belgium) for the vaccination campaign, resulting in a limited benefit regarding a possible wave in September–October. Those results will be available at `https://covid19scenariohub.eu/scenarios.html`.

Potential impact of the vaccination campaign using an XBB.1.5 booster.

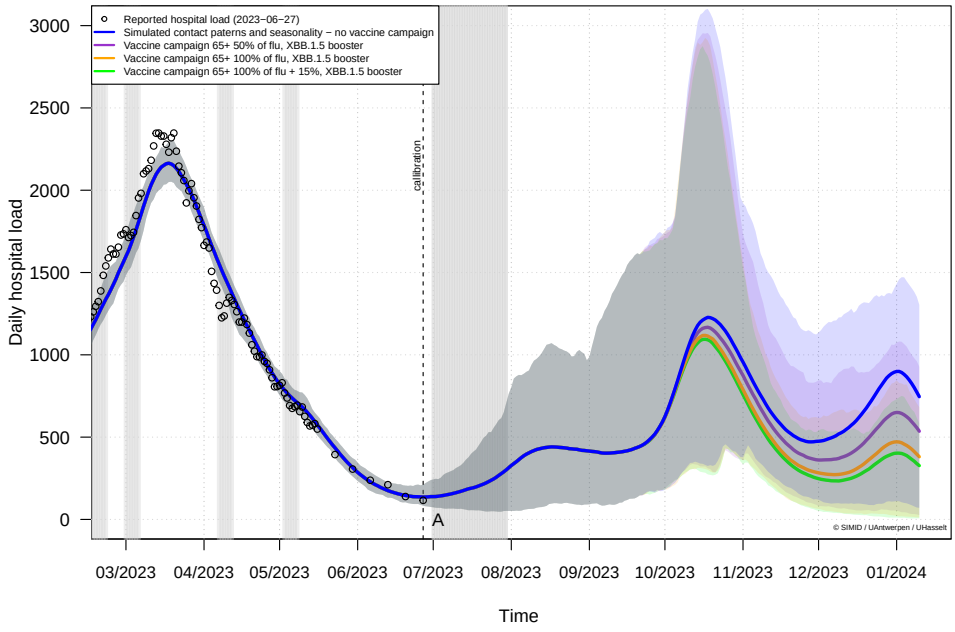


(a) Daily hospital admissions with COVID-19

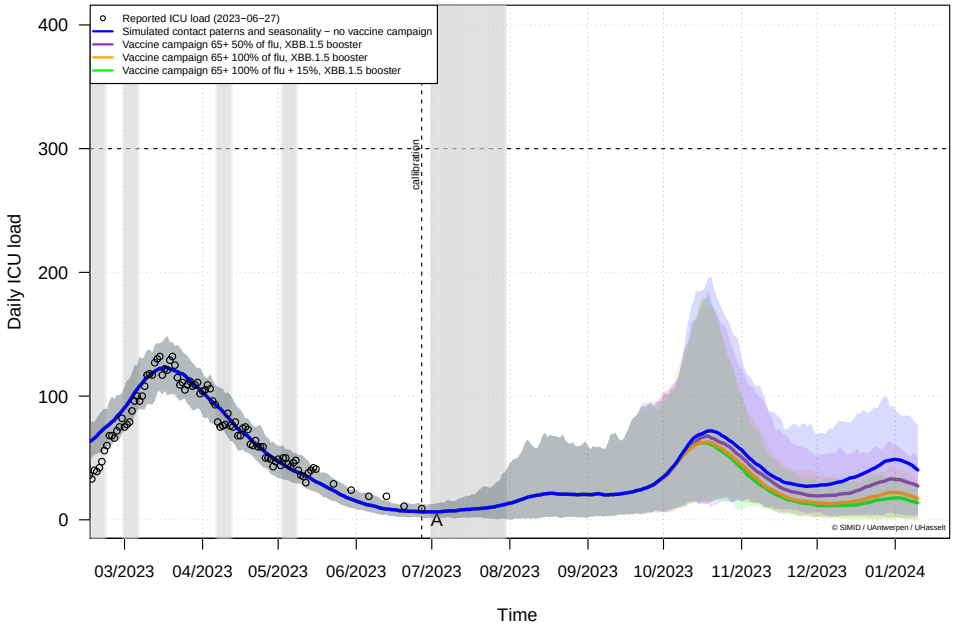


(b) Daily hospital admissions for COVID-19

Figure 1: Model projections for hospital admissions with and for COVID-19 in Belgium when assuming restarting activities and seasonality from September 2023 and different vaccination campaigns. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations based on 50 independent MCMC chains.

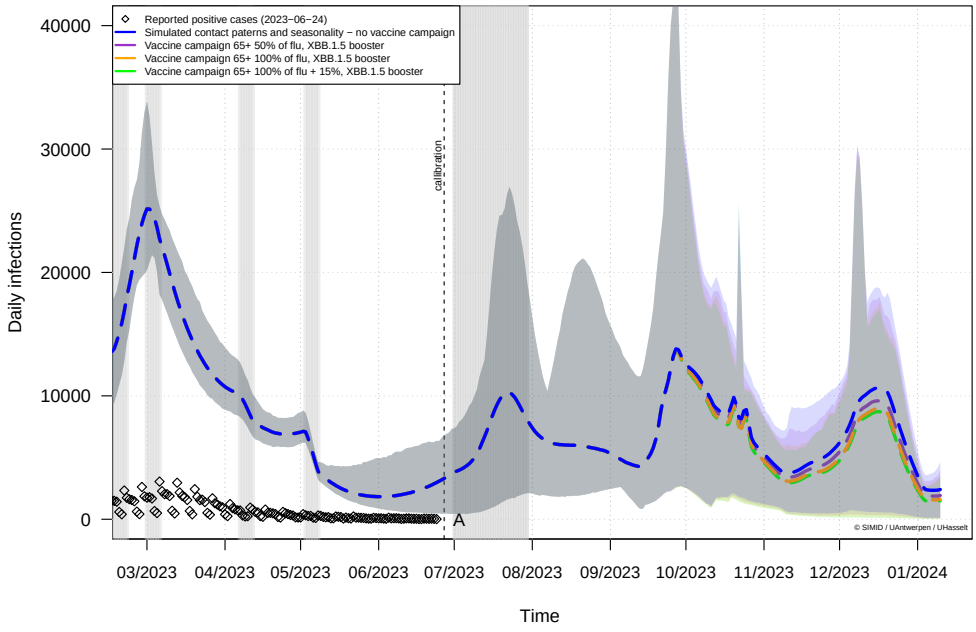


(a) Daily hospital load for COVID-19

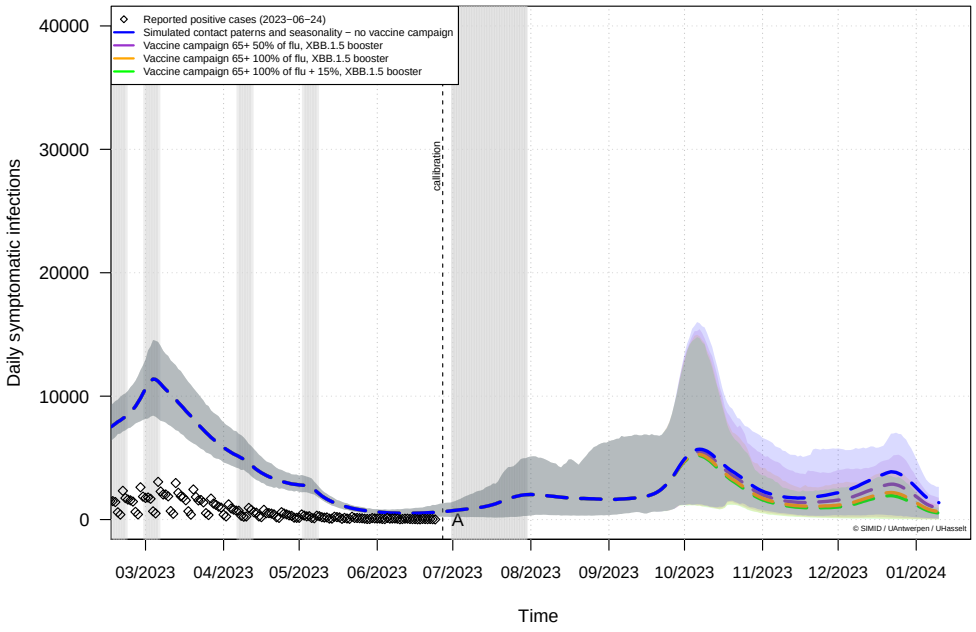


(b) Daily ICU load for COVID-19

Figure 2: Model projections for COVID-19 hospital and ICU load in Belgium when assuming restarting activities and seasonality from September 2023 and different vaccination campaigns. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations based on 50 independent MCMC chains.



(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 from September 2023 and different vaccination campaigns. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 100 stochastic model realisations based on 50 independent MCMC chains.

Contributors to this report (alphabetically)

- Christel Faes (Universiteit Hasselt)
- Lander Willem (Universiteit Antwerpen)
- Maikel Bosschaert (Universiteit Hasselt)
- Nicolas Franco (Université de Namur, Universiteit Hasselt)
- Nicolas Herman (Université de Namur)
- Niel Hens (Universiteit Hasselt, Universiteit Antwerpen)
- Philippe Beutels (Universiteit Antwerpen)
- Steven Abrams (Universiteit Hasselt, Universiteit Antwerpen)
- Toon Braeye (Sciensano)

Acknowledgments

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

Selected references:

- Abrams S, et al. (2021) Modeling the early phase of the Belgian COVID-19 epidemic using a stochastic compartmental model and studying its implied future trajectories. Epidemics. 100449.
- Andrews N et al (2022a) Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines. NEJM. 386:340-50.
- Andrews N et al (2022b) Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. NEJM.
- Bernal J, et al. (2021) Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. NEJM. 385(7).
- CDC Morbidity and Mortality Weekly Report. January 28, 2022. Vol 71. No 4.
- Coletti P, et al. (2020) CoMix: comparing mixing patterns in the Belgian population during and after lockdown. Scientific reports, 10.
- ECDC European Covid-19 Scenario Hub `https://covid19scenariohub.eu`
- Willem L, et al. (2023) Modelling the interplay of vaccination and variants of concern on the age-specific burden of COVID-19 (preprint)
- Stowe J, et al. (2021) Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant.Preprint at The Global Health Network.
- Wenseleers T (2021) Analysis of VOCs for Belgium https://github.com/tomwenseleers/newcovid_belgium

SUPPLEMENT

Reported uptake and vaccination scenarios

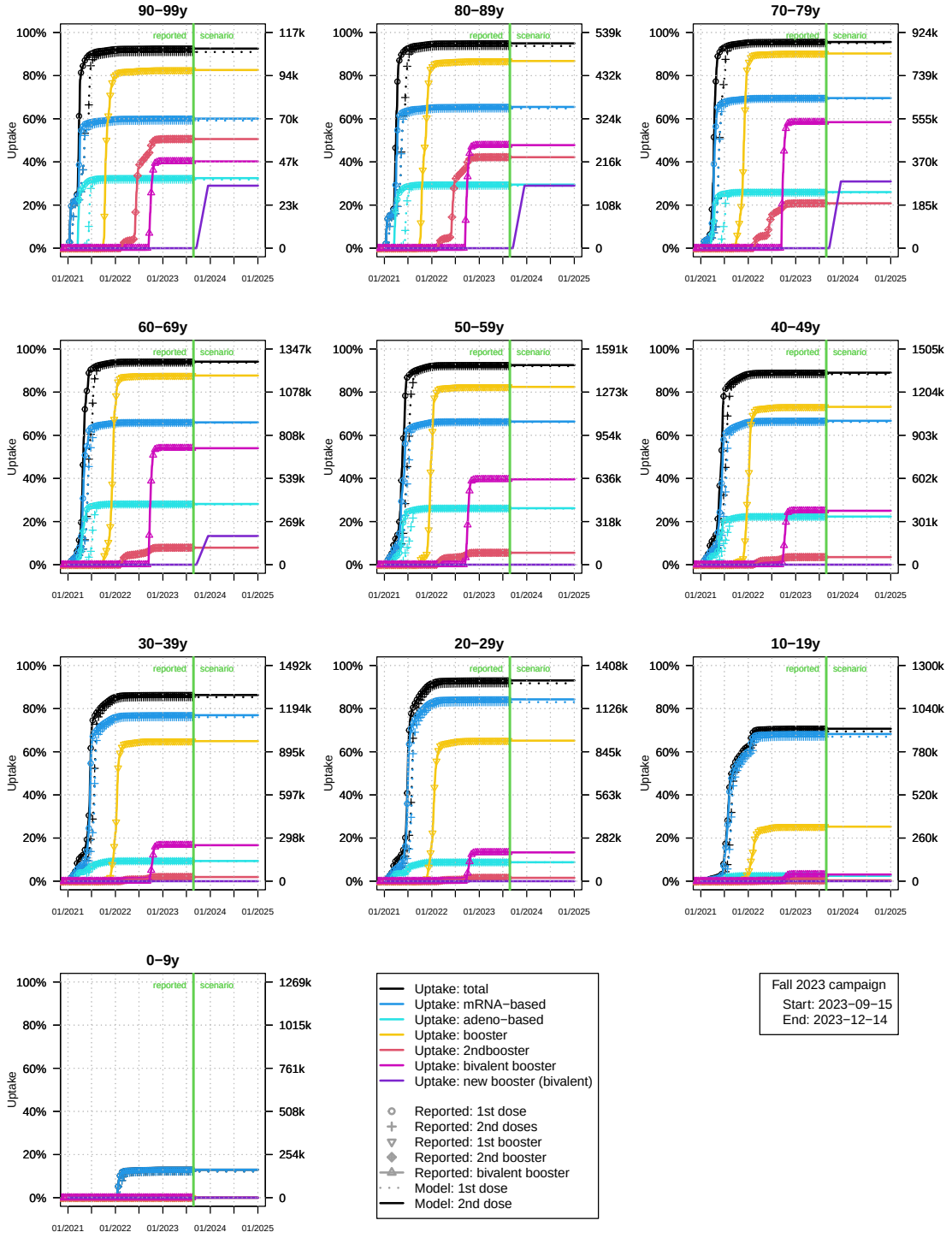


Figure S1: Vaccine uptake by age, vaccine-type and dose based on the reported uptake for Belgium on August 16th, 2023, with scenarios of vaccination campaign up to 50% of the flu uptake.

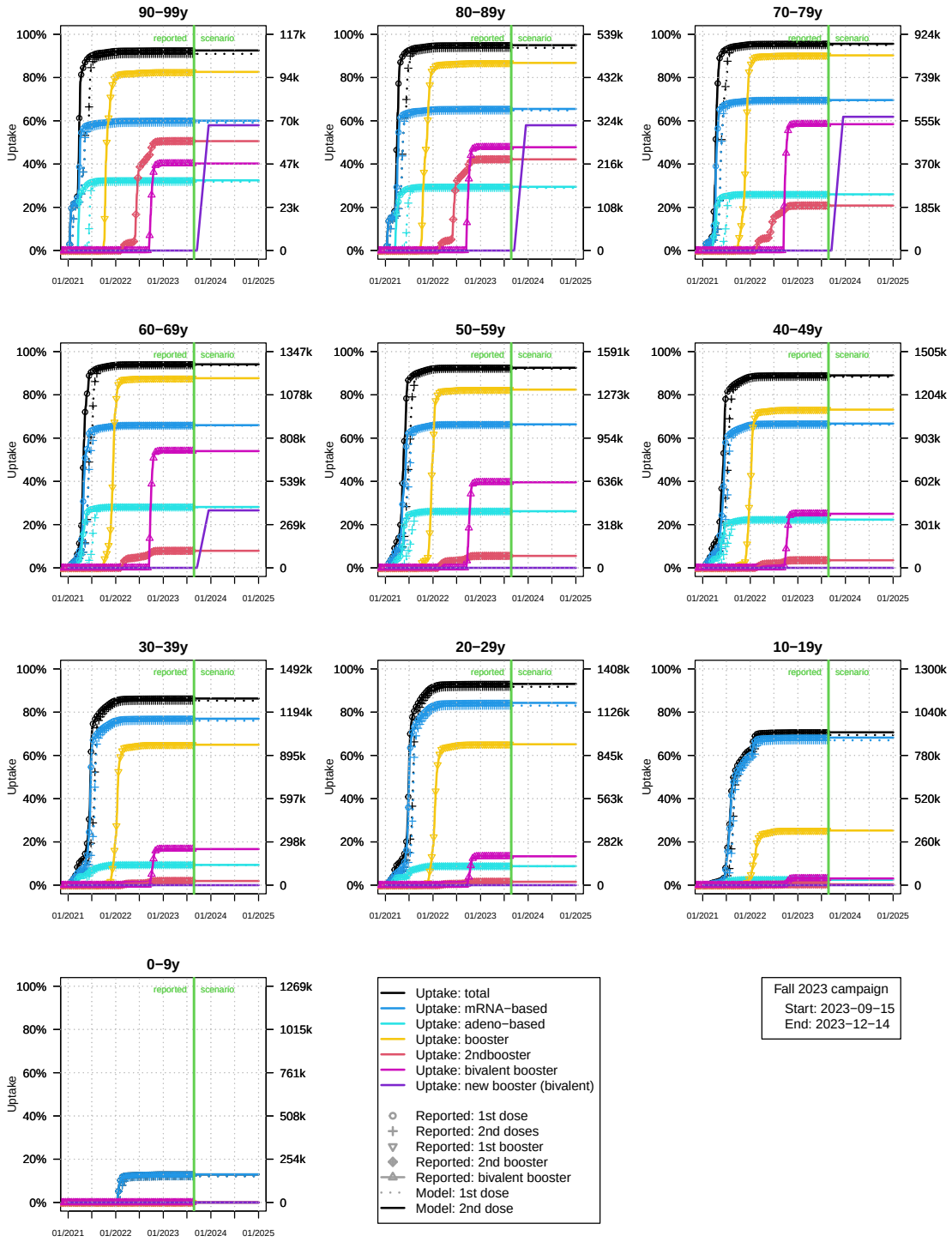


Figure S2: Vaccine uptake by age, vaccine-type and dose based on the reported uptake for Belgium on August 16th, 2023, with scenarios of vaccination campaign up to 100% of the flu uptake.

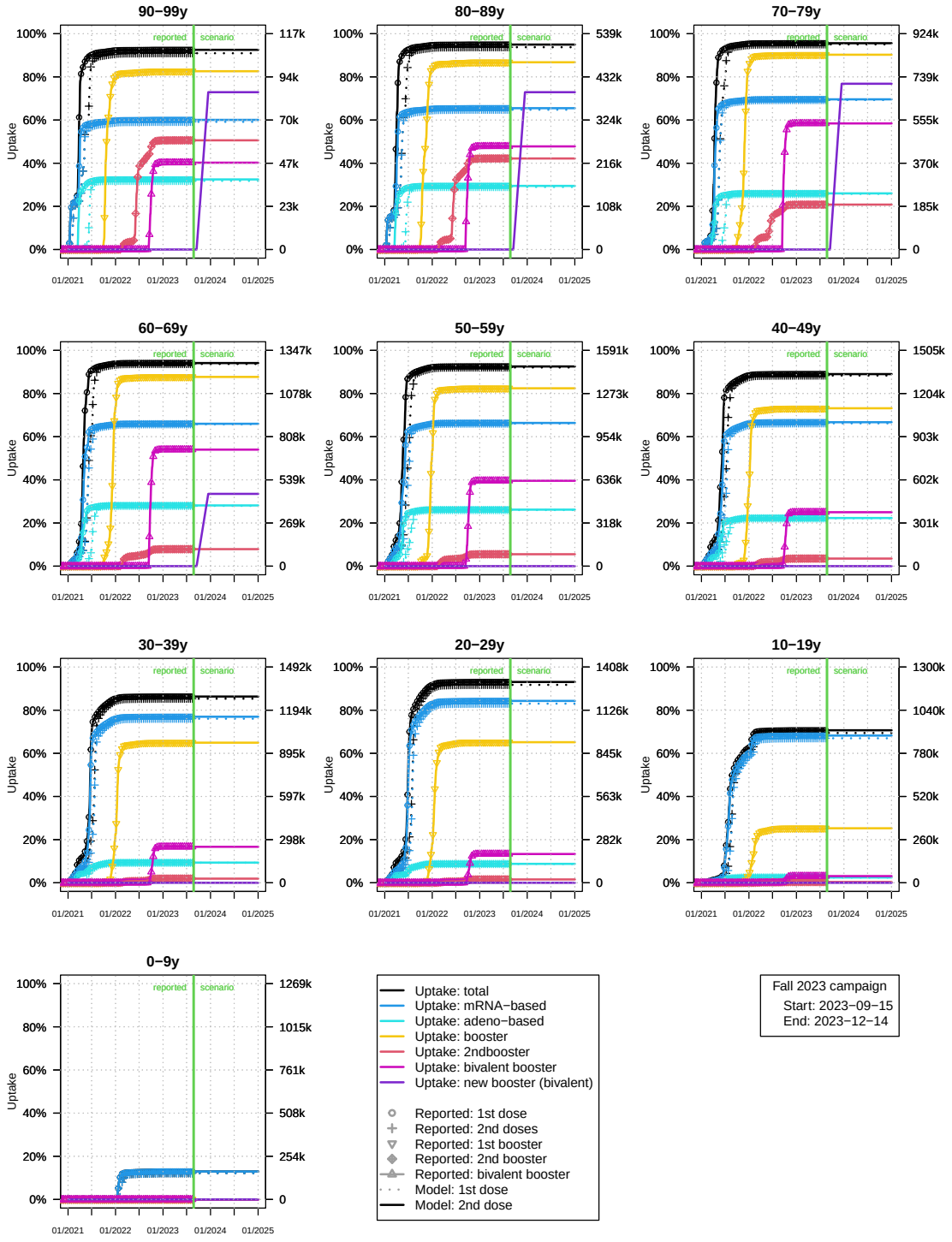


Figure S3: Vaccine uptake by age, vaccine-type and dose based on the reported uptake for Belgium on August 16th, 2023, with scenarios of vaccination campaign up to 100% of the flu uptake plus 15% of the population.