

SARS-CoV-2 variants and vaccination in Belgium

Modelling results by the SIMID consortium

This document contains model estimates of hospital admissions and symptomatic infections by a stochastic dynamic transmission model using observational data up to January 3rd, 2022. This analysis focuses on potential developments according to the emergence of the Omicron VOC in Belgium. All previous reports are available via simid.be and the [covid-en-wetenschap](https://www.covid-en-wetenschap.nl/) blog.

Preliminary conclusions

- We explored the impact of the Omicron VOC for Belgium with a country-level stochastic transmission model that incorporates infection- and vaccine-induced immunity levels in the population given the ongoing COVID-19 pandemic. By combining estimates of the predicted penetration of Omicron based on S-gene-target failure data for Belgium with current estimated transmission dynamics in Belgium, the model projects increasing numbers of infections and hospitalisations by the Omicron VOC in the coming weeks, with hospital admissions likely exceeding those observed during the fourth wave.
- All projections are based on currently available information, which may need to be adapted as more information on Omicron becomes available in the coming days and weeks.
- Due to incomplete information on social contact behaviour during the latest holiday period, current transmission dynamics are estimated based on social contact data from early December 2021. Although hospital admissions and overall transmission dynamics are captured well, the interpretation and extrapolation of risk behaviour per contact is complicated. As such, there is insufficient information that is representative for the non-holiday period of January-February 2022 while Omicron is dominant in the context of Belgium. That is, large scale transmission of the Omicron VOC during a non-holiday period has not been observed for Belgium and therefore the projected scenarios are particularly subject to structural uncertainty and sensitive to the imposed assumptions concerning future risk behavior.
- Exploring two scenarios of social contact behaviour in January with relatively high and low protection of current vaccines against infection and severe disease by Omicron, we project high levels of hospital admissions for Q1 of 2022. Although the relative risk of hospital admission per infection is estimated from international data to be lower for Omicron than for Delta, the expected high incidence of infections penetrating all age groups, could still cause a large burden on the healthcare system, both in primary care and in hospitals, especially given the relatively high burden (i.e. hospital load) we were facing at the time of emergence of Omicron.
- We estimated the increase in transmissibility of Omicron relative to Delta based on S-gene-target failure (SGTF) data from Belgium between 30% and 80%, depending on the assumptions for vaccine-related protection against Omicron. In addition, the latest model calibration resulted in a much faster transition to the pre-symptomatic infectious stage after infection with Omicron, relative to Delta. This aligns with a shorter serial interval for Omicron, as reported by Kim et al. (2021, preprint) among others, hence the transmission advantage of Omicron in our projections is not only based on immune escape and increased infectiousness.

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”), another VOC from May 2021 (i.e. B.1.617.2 or “Delta”) and a third VOC from November 2021 (i.e. B.1.529 or “Omicron”). 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.

Model input and assumptions

1. **Gradually accumulating naturally-acquired immunity** in the population is accounted for, as well as immunity induced by vaccination. Immunity after infection is assumed to last till the end of the simulations, except for the Omicron VOC. Recovered individuals without any vaccine-induced protection are exposed to 3% of the force of infection by Omicron compared to fully susceptible individuals. This is based on the reported risk ratio of reinfection for Omicron of 3.3 (95% CI: 2.8 to 3.8) by UK Health Security Agency (Technical briefing 32).
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. For the Omicron VOC, we also use S-gene target failure (SGTF) data to estimate and extrapolate the proportion of Omicron infections among all SARS-CoV-2 infections, relying on a logistic regression model fit we derived from https://github.com/tomwenseleers/newcovid_belgium.
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 35% (95% credible interval (CrI): 29%-40%) 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. **Omicron VOC:** The impact of the Omicron VOC is modelled by the introduction of a third VOC from the end of November 2021 onward. We estimated an increase in transmissibility relative to the Delta variant based on S-gene-target failure (SGTF) data for Belgium between 30% and 80%, depending on the assumptions for vaccine-related protection against Omicron (see below). Estimates of the hazard ratio for hospitalization for Omicron relative to Delta are still uncertain and such estimates may depend on the health structure context (e.g. the population age distribution in the study population, background immunity level in the study population, etc.), hence, a direct generalisation and synthesis of such estimates to the Belgian context is difficult and potentially not trustworthy. Therefore, we included scenarios based on hazard ratios of 25% (best case scenario, according to estimates from Pasteur Institute, 27 December 2021 report) and 50% (worst case scenario, according to estimates from UK Health Security Agency Technical briefing update 31 December 2021). To account for an adjusted serial interval for Omicron, as reported by Kim et al. (2021, preprint), the duration of the latent period for Omicron is estimated in the calibration process. This results in a much faster transition to the pre-symptomatic infectious stage after infection with Omicron, relative to Delta.
6. Our model results contain stochastic variation in the transmission process and parameter uncertainty based on 25 model parameter configurations. The calibration procedure relies on likelihood-based MCMC sampling resulting in 25 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 (400 iterations) with 10 realizations per iteration, periodicity of 10 iterations and leading to 25 different chains based on 25 initial starting configurations.

7. 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.
8. 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 (and its impact on the daily number of confirmed COVID-19 cases). The reported hospital admissions are complemented 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 COVID-19 related hospital load, we include these new patients in our parameter fitting procedure.
9. The model is calibrated using social contact data of the Belgian CoMiX survey. For each survey wave (with the latest included wave, the 37th conducted on December 7-13th 2021), 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.
10. We evaluate different **scenarios** to explore the combination of Omicron-related severity of disease, vaccine effectiveness and social contact patterns. None of the scenarios include the introduction of infected cases as a result of international travel. We start with the latest model calibration and the projected vaccine uptake scheme as presented in Figures S1. This projection is based on the transmission dynamics estimated for late December 2021 including estimated age-specific features for the upcoming Omicron VOC. In addition, we also explore a linear change in social contact behaviour over 7 days from the 8th of January onward towards the risk behaviour we estimated for November 2021 using the transmission and severity assumptions for Omicron. This scenario is more representative for a non-holiday period with less inter-generational mixing compared to such behavior late December 2021, though it is likely to lack age-specific aspects for Omicron. These approximations are necessary since we currently have no observations on hospital admissions caused by infections acquired during a non-holiday period (with associated contact behaviour) while Omicron is the dominant VOC in Belgium.
11. **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 and booster doses 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 (see Table 1).

- 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 of vaccine-induced immunity is included in the transmission model.** We assume that on average 50% of the vaccine-induced protection will be lost after 6 months. This corresponds with a transition rate of 1/180 days towards the waning immunity compartments.
- **Third doses (boosters) are included in the transmission model.** We assume that all booster doses are mRNA-type vaccines, and boosted individuals will be located in a separate set of “mRNA booster” health compartments. Waning of vaccine-induced immunity does not apply after booster doses which can be deemed reasonable for providing a short-term forecast, though should be revisited provided information becomes available.

12. Vaccine uptake

- The vaccine-type and age-specific uptake in the model of first, second and booster doses over time at the national level is based on the reported data by Sciensano, derived from Epistat on January 3rd, 2022. The default uptake by age is presented in Figure S1. For the model projections, we extrapolate the uptake rate of 1st and 2nd mRNA vaccines of the last 2 weeks for +12y, until 90% coverage is reached at the national level. If the reported uptake is more than 90%, we use the reported uptake. For the projected uptake, the time between 2 mRNA doses is assumed to be 3 weeks.
- Booster doses are assumed to be provided to 90% of the individuals that had 2 doses and in a timely manner, i.e. by February 1st. The age- and dose-specific uptake of the default is presented in Figure S1. We included this high coverage in a short time frame so the projection can be used as reference for the burden of disease, which is assumed to be higher if this target is not reached. If the burden of disease would be under control with these vaccine uptake assumptions, there might be room for delayed or reduced vaccine uptake. In the same spirit, the vaccine coverage of the 1st dose for 5-11-year-olds is assumed to reach 60% by February 1st.
- 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).
- Vaccine uptake for 12-19-year-olds 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 90% of the 10-19-year-old population potentially take up vaccines. A similar approach is used when the target group is for example the 5-11-year-olds.

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). We assume waning of vaccine-induced immunity for 2nd dose of on average 50% after 6 months.

Clinical outcome	Vaccine type	Alpha variant	Delta variant
Infection (Bernal, 2021)	Adeno: 1st dose	49%	30%
Infection (Bernal, 2021)	Adeno: 2nd dose	74%	76%
Infection (Bernal, 2021)	mRNA: 1st dose	48%	36%
Infection (Bernal, 2021)	mRNA: 2nd dose (and booster)	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 (and booster)	95%	96%
Transmission (Harris, 2021)	mRNA and Adeno (and booster)	45%	45%

Table 2: Vaccine efficacy scenarios for adeno-based and mRNA-based vaccines against the Omicron variant by clinical outcome, derived from Barnard et al (2021).

Clinical outcome	Vaccine type	HIGH efficacy assumption	LOW efficacy assumption
Infection	Adeno: 1st dose	23.7%	12.9%
Infection	Adeno: 2nd dose	34.7%	19.0%
Infection	mRNA: 1st dose	34.2%	18.7%
Infection	mRNA: 2nd dose	44.1%	24.1%
Infection	mRNA booster dose	79.2%	44.1%
Severe disease	Adeno: 1st dose	66.3%	49.7%
Severe disease	Adeno: 2nd dose	77.1%	60.0%
Severe disease	mRNA: 1st dose	76.7%	59.6%
Severe disease	mRNA: 2nd dose	83.7%	66.8%
Severe disease	mRNA booster dose	96.9%	83.7%

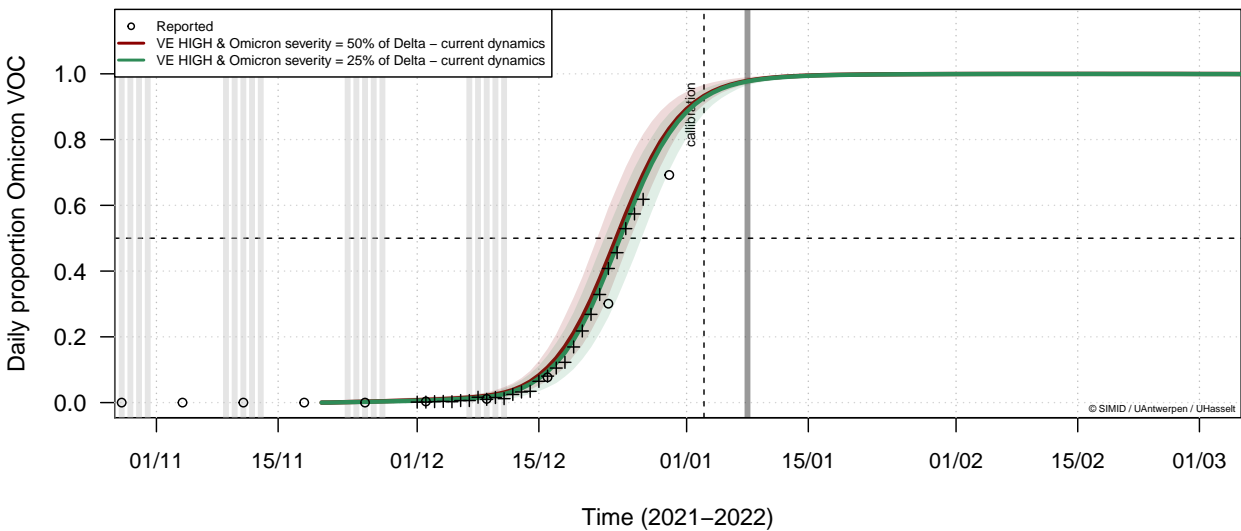


Figure 1: Model projections concerning the daily proportion of Omicron VOC in Belgium. Circles represent the baseline genomic surveillance of SARS-CoV-2 in Belgium reported by the National Reference Laboratory (UZ Leuven & KU Leuven) and the crosses represent the S-gene-target-failure data for Belgium that are Omicron in GISAID database (derived via https://github.com/tomwenseleers/newcovid_belgium on January 3rd, 2022).

Major limitations

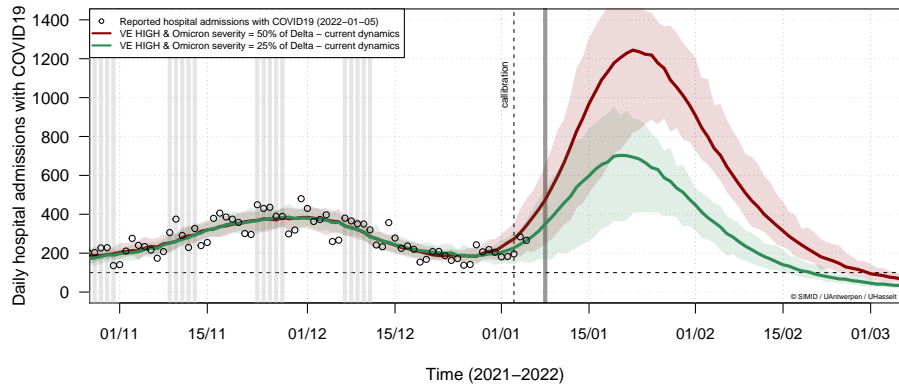
- **This transmission model is suited for scenario analyses to investigate possible future or counterfactual retrospective paths, it is not a prediction model.**
- The model is calibrated on hospitalizations and informed by the Belgian CoMiX social contact data survey. These empirical social contact 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.
- **In this technical note it is particularly difficult to properly calibrate the model and define scenarios for the following reasons: (1) The Omicron VOC has only become completely dominant near the end of the Christmas holiday period and the observed hospital admissions (to which the model is calibrated) during that period were still the result of (mostly) Delta infections and (to a much lesser extent) Omicron infections acquired before and at the start of the holiday period; (2) social contact behaviour is known to be very different during holiday versus non-holiday periods, not only in terms of the number of contacts made, but also in terms of age-specificity (i.e. age structure), and we are currently only starting to observe the impact of infections that occurred during the Christmas holidays on hospital admissions (to which the model is calibrated, note also that recent data on serology in unvaccinated persons are not available as an additional source for calibration); (3) We currently have no observations on hospital admissions caused by infections acquired in a non-holiday period (with associated non-holiday contact behaviour) while Omicron is the dominant VOC in Belgium, which would allow us to establish the relationship between age-specific contacts, infections and hospital admissions that is representative of the period for which projections are made in this technical note; this means that we work with approximate scenarios concerning non-holiday social contact behaviour for January-February 2022 and not a prediction of the most likely outcome (4) policy makers made important changes to the rules of quarantine and isolation from 10th January onwards, which is likely to alter the transmission dynamics over and above that of the previous points.**
- The daily age distribution of hospitalized patients is derived from the individual hospital survey **up to December 31st, 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 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.
- **Hospitalization lengths are considered similar for Omicron VOC to those for Delta VOC due to lack of data on this matter at this point in time. Projections on hospital load might be altered by a modification of hospitalization lengths of stay. Projections concerning ICU are not presented in this note since ICU rates might have completely changed due to Omicron VOC and are still unknown.**
- We are making the implicit assumption that the Omicron VOC will remain the dominant strain throughout the entire simulation period. Nonetheless, other (new emerging) VOCs may have 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.
- The incremental transmissibility by the VOCs, which we include in the model, is not age-specific.

- We attribute the growth advantage of the Alpha and Delta VOCs completely to transmissibility, and as such, ignore the potential effect of immune escape on the speed of penetration. For Omicron, we include immune escape by allowing for reinfections in addition to reduced vaccine-related protection.
- The reduced serial interval for Omicron is fully attributed to a reduction in the latent, or exposed, period. As such, 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 by returning travelers which could have impact on the evolution of the epidemic. Importantly, an implicit attribution of such cases to local transmission is used instead.
- We present our modelling results by the mean and pointwise 95% credible interval based on 25 model realizations, which capture stochastic effects and parametric uncertainty. The interplay between these two sources of uncertainty is subject of future research.
- Social mixing behaviour is assumed to be constant in the forward projections, unless explicitly stated in the scenario definitions. Without increased risk behaviour, the incidence of new infections decreases due to decreasing number of susceptible individuals. Behavioural changes might counter this decreasing force of infection, though this is not studied here thoroughly.
- The model projections are based on the hospital admissions with COVID-19, hence one can interpret them to represent the upper limit for hospital admissions due to COVID-19.
- 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.

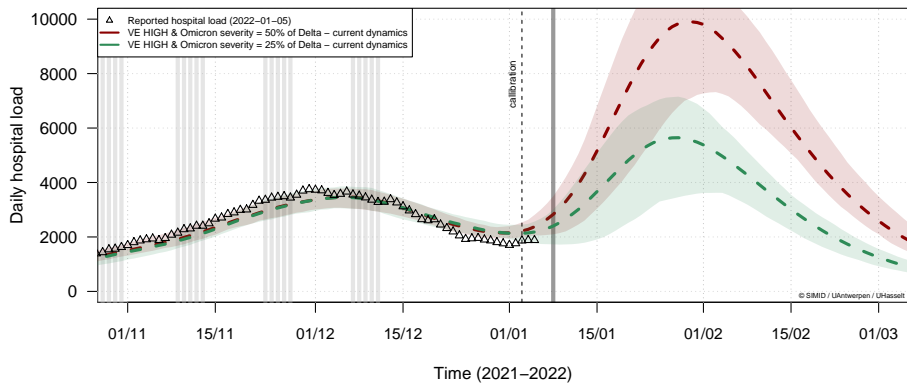
Model results

The following figures depict the results of our scenario analyses with respect to social mixing and vaccine uptake. 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.

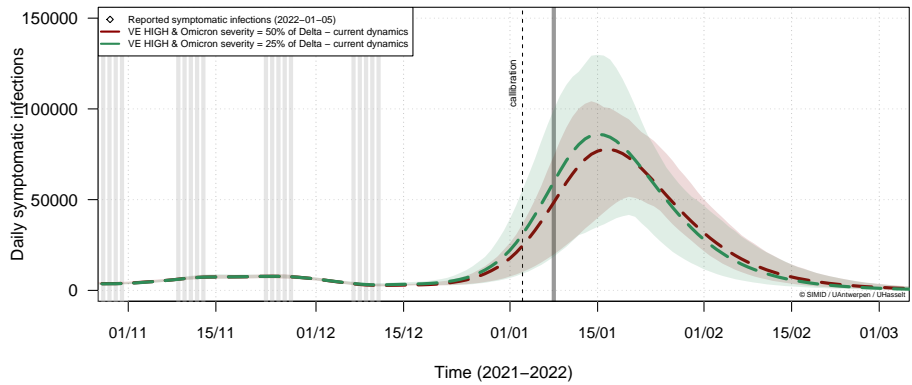
Scenario analysis: using the HIGH vaccine efficacy assumption and current dynamics.



(a) Daily hospital admissions with COVID-19



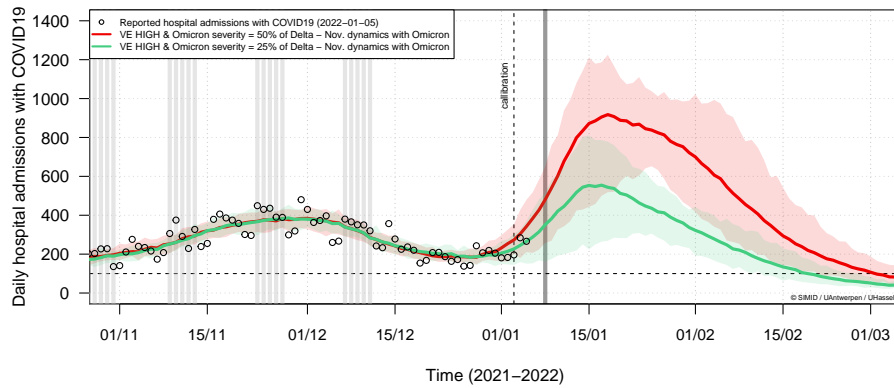
(b) Daily hospital load



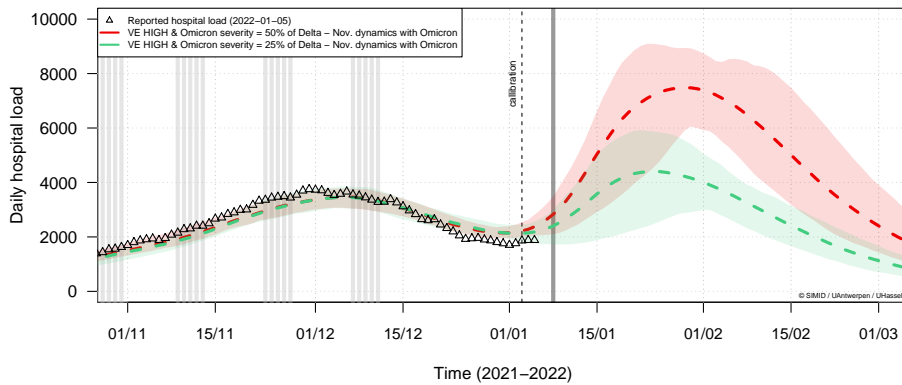
(c) Daily number of new symptomatic infections

Figure 2: Model projections for Belgium on daily hospital admissions, hospital load and symptomatic infections for different assumptions on Omicron VOC severity against hospitalisations. These projections are based on the current dynamics, based on social contact data from December 2021, with Omicron but during a school-holiday. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

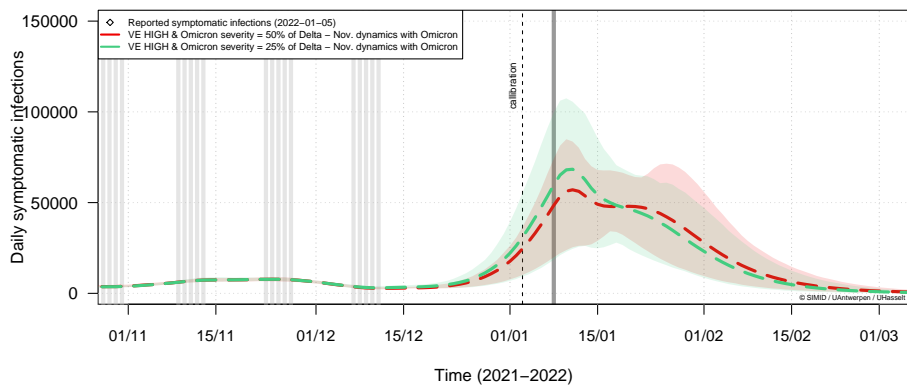
Scenario analysis: using the HIGH vaccine efficacy assumption and November behaviour with Omicron as proxy.



(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



(c) Daily number of new symptomatic infections

Figure 3: Model projections for Belgium of daily hospital admissions, hospital load and symptomatic infections using different assumptions on Omicron VOC severity. These projections are based on a change in social contact behaviour from 8th of January towards the risk behaviour we estimated for November 2021 with general transmission and severity assumptions for Omicron. See "Model input and assumptions 10." for pros and cons. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

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SUPPLEMENT

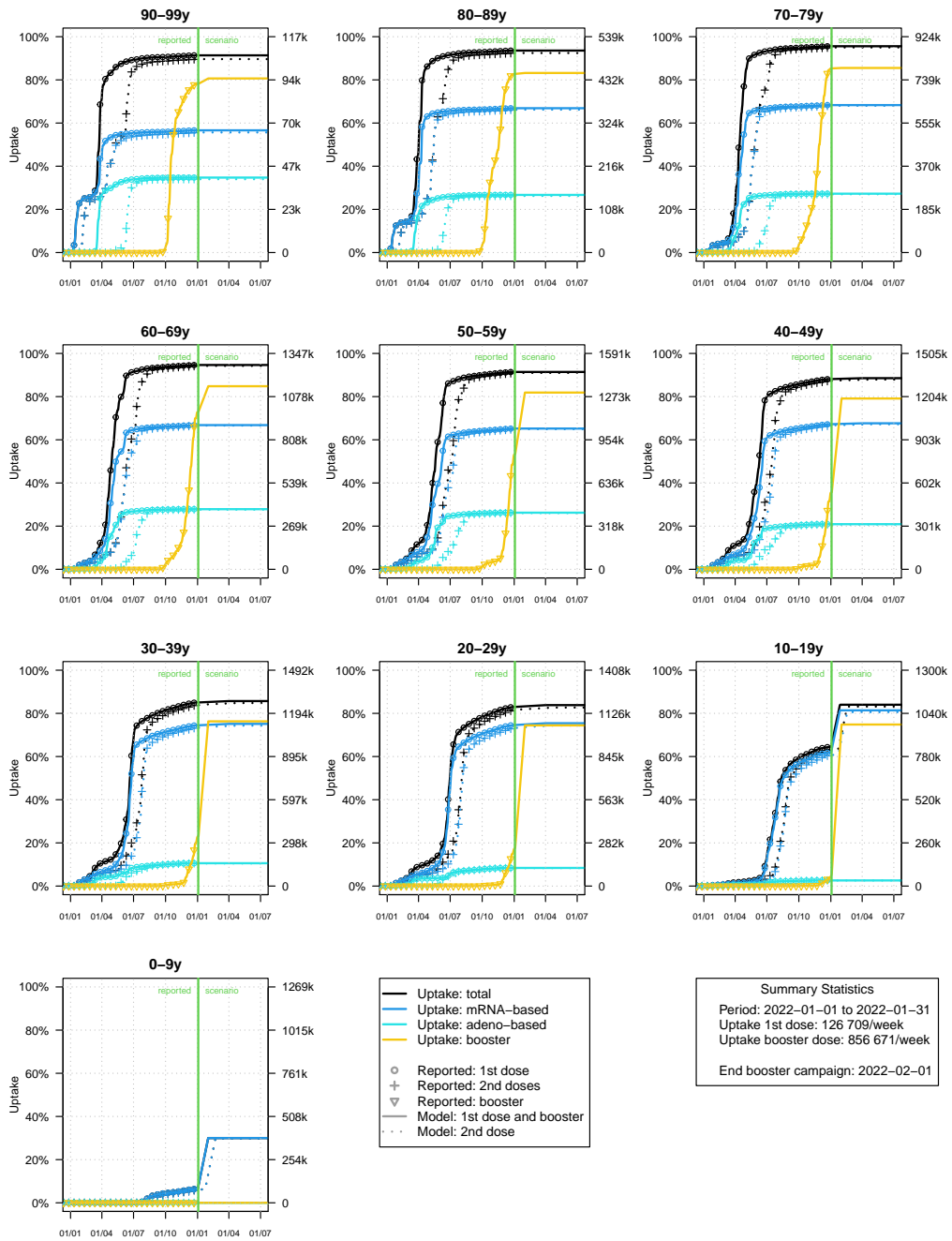
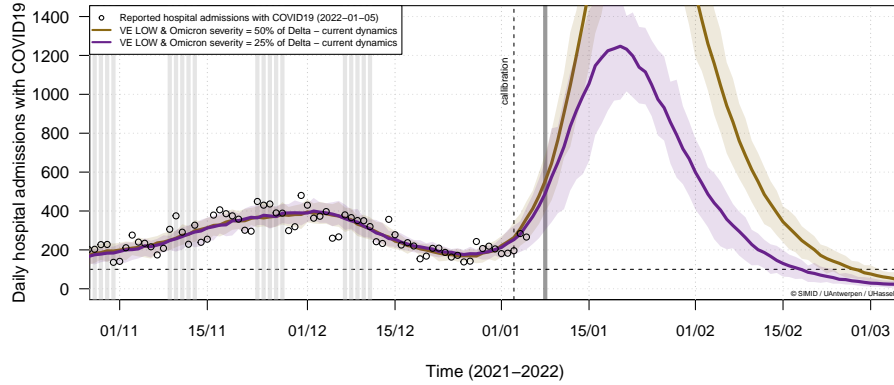
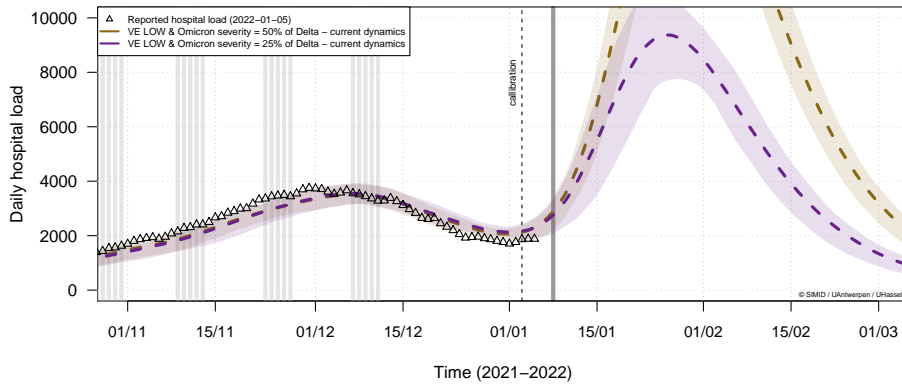


Figure S1: Vaccine uptake by age based on the reported uptake for Belgium and our projection with respect to the uptake of booster doses, in combination with 1st and 2nd doses for 5-11-year-old children.

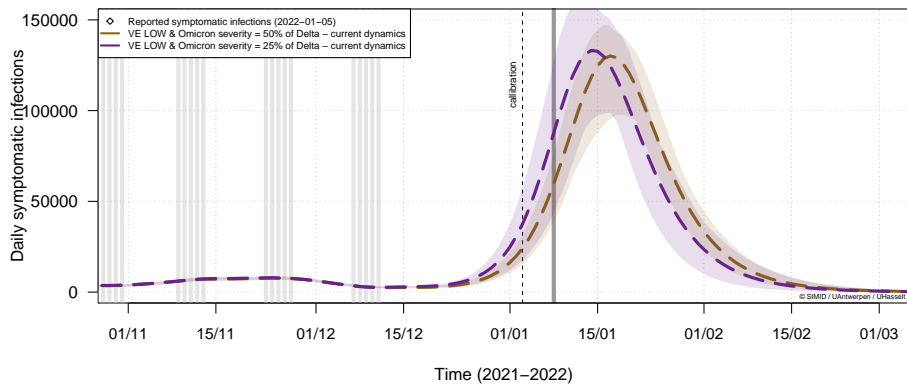
Extra Scenario analysis: using the LOW vaccine efficacy assumption and current behaviour.



(a) Daily hospital admissions with COVID-19



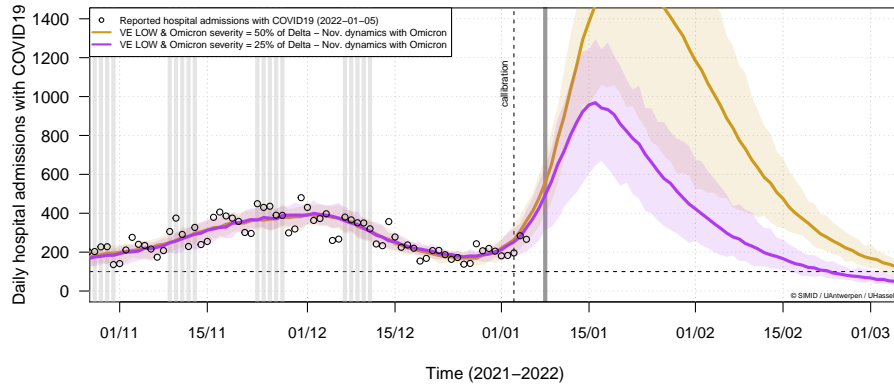
(b) Daily hospital load



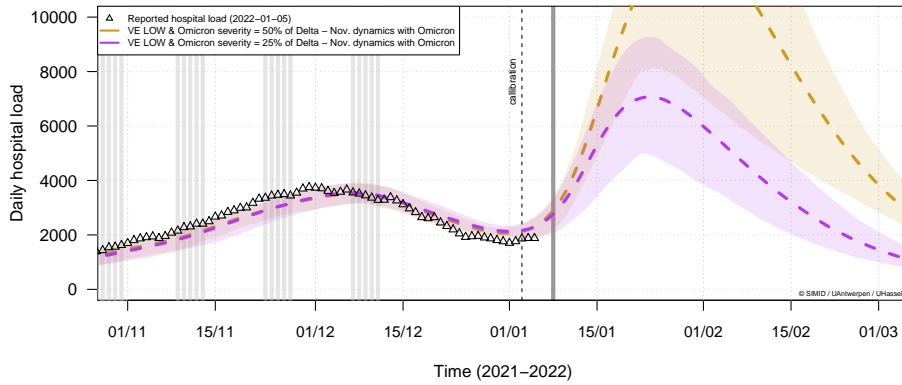
(c) Daily number of new symptomatic infections

Figure S2: Model projections for Belgium on daily hospital admissions, hospital load and symptomatic infections for different assumptions on Omicron VOC severity against hospitalisations. Those projections are based on the current dynamics, based on data from December 2021, with Omicron but during a school-holiday. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

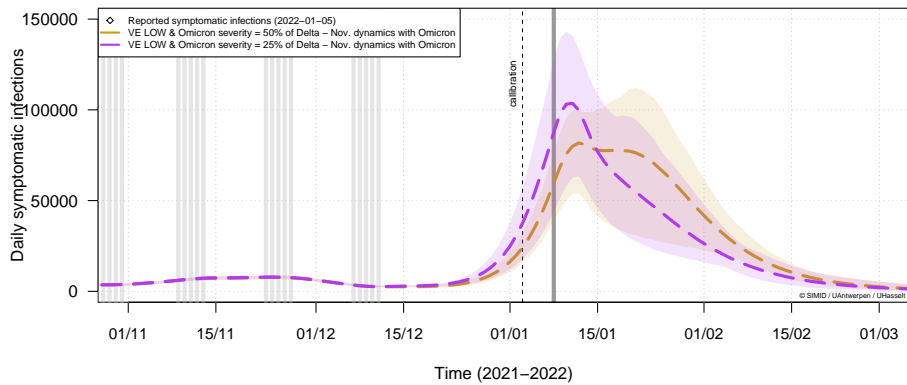
Extra scenario analysis: using the LOW vaccine efficacy assumption and November behaviour with Omicron as proxy.



(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



(c) Daily number of new symptomatic infections

Figure S3: Model projections for Belgium on daily hospital admissions, hospital load and symptomatic infections for different assumptions on Omicron VOC severity against hospitalisations. Those projections are based on a change in social contact behaviour from 8th of January towards the risk behaviour we estimated for November 2021 with general transmission and severity assumptions for Omicron. See "Model input and assumptions 10." for pros and cons. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.