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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 by a stochastic dynamic transmission model using observational data up to February 4th, 2022. This analysis focuses on potential developments according to the spread of the Omicron VOC in Belgium. All previous reports are available via simid.be and the covid-en-wetenschap blog.

Preliminary conclusions

- We explored the impact of the Omicron Variant of Concern (VOC) for Belgium with a country-level stochastic transmission model that incorporates infection- and vaccine-induced immunity levels in the population. By combining data from the baseline genomics surveillance of SARS-COV-2 with estimated transmission dynamics for Belgium, the model projects decreasing numbers of infections and hospitalisations by the Omicron VOC in the coming weeks.
- Exploring different scenarios of increased transmission rates with relatively high and low protection of current vaccines against infection and severe disease by Omicron, we project a limited resurgence of hospital admissions. The rise in transmission potential could be due to adapted social contact behaviour, increased infectiousness of an Omicron sub-strain (e.g., BA.2), or both.
- Given our focus on severe disease and hospital admissions, we assume no waning of vaccine-induced immunity after booster vaccination doses over the time span considered in this note. The incidence of breakthrough-infections in the scenarios could still cause a burden on primary care. This should be revisited when new information becomes available.
- 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 national model does not account for local differences in immunity and clustered social contact networks. General trends are captured well, though local outbreaks are underestimated and herd immunity effects are overestimated in sub-populations with immunity levels below the national level, and the reverse may be true in sub-populations with higher than average immunity.

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 experience an Omicron infection risk of 3% of the Omicron force of infection as compared to fully susceptible individuals, thereby allowing for reinfections. This is based on the reported risk ratio of reinfection for Omicron of 3.3 (95% CI: 2.8 to 3.8) by the UK Health Security Agency (Technical briefing 32).

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:** 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 et al., 2021).

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 the baseline genomic surveillance of SARS-CoV-2 data for Belgium between 80% and 140%, depending on the assumptions for vaccine-related protection against Omicron (see below). A differential hazard ratio for hospitalization for Omicron relative to Delta has been pivotal though 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.). According to recent literature (Peralta-Santos et al., 2022), and previous results, we restricted our analysis to the scenario based on a ratio of 25%. To account for an adjusted serial interval for Omicron, as reported by Kim et al. (2021), 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 (200 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 40th conducted on January 9-15th 2022), 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 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. We combine the following options:

    - **Increased transmission**: We explore the effect of an increased risk in contracting SARS-COV-2 as a result of increased social contact or risk behaviour, a more virulent sub-strain of Omicron, or combined. In particular, we look at an increase of +100% and +200% of current dynamics. Translating this to pre-pandemic behaviour is not possible (yet).
    - **Timing**: We explore the effect of an increased transmission from mid-February, the 1st of March or the 1st of May.

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 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:** 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-based vaccines, and boosted individuals are allocated into a separate set of "mRNA booster" health compartments. Waning of vaccine-induced immunity does not apply after booster doses which can be deemed reasonable when focusing on severe disease and hospital admissions with relatively short-term forecasts, 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 up to February 4th, 2022. The default uptake by age is presented in Figure S1. For the model projections, we assume an increase in uptake for the 10-19-year-old population until 80% and 60% uptake for the 5-9-year-old children. The time between 2 mRNA doses is assumed to be 3 weeks.
- Booster doses are assumed to be provided to 75% of the individuals that had 2 doses and in a timely manner, i.e., by March 1st. For most age groups, this threshold has been already reached. For the 20-39-year old population, this means an increase up to ±60% of the target population. Concerning children and adolescents up to 19-years of age, we assume no additional booster doses than those already reported. The age- and dose-specific uptake is presented in Figure S1.
- 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).

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%	67%
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%

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.

Table 2: Vaccine efficacy scenarios for adeno-based and mRNA-based vaccines against the Omicron variant 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%

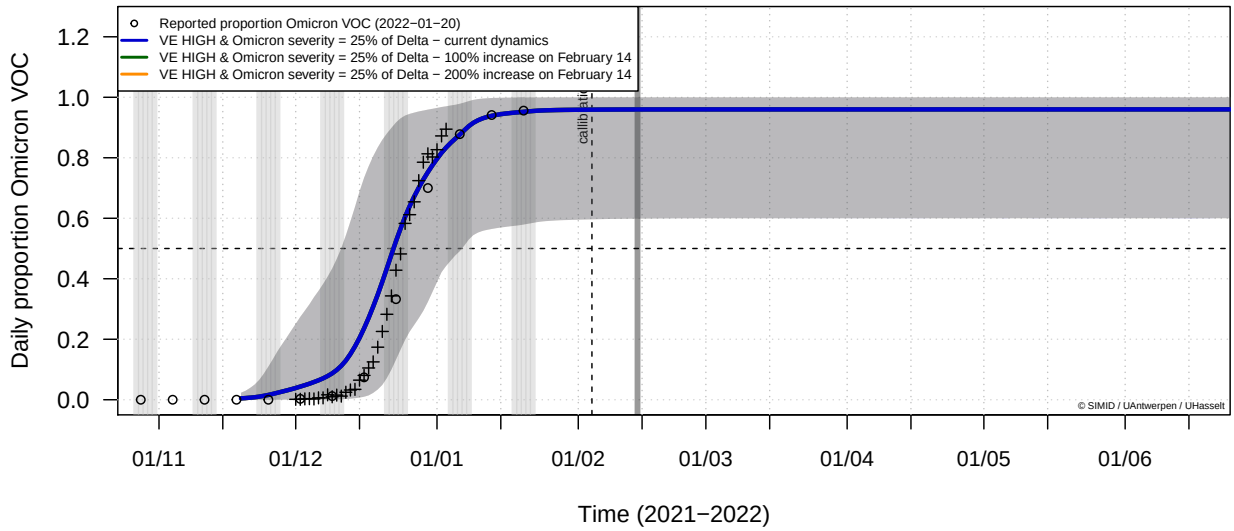


Figure 1: Model projections concerning the daily proportion of Omicron VOC in Belgium. Circles represent the baseline genomic surveillance of SARS-CoV-2 in Belgium reported by the National Reference Laboratory (UZ Leuven & KU Leuven) and the crosses represent the S-gene-target-failure data for Belgium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

- The daily age distribution of hospitalized patients is derived from the individual hospital survey **up to January 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.

- **In this technical note it is challenging to properly calibrate the model and define scenarios for the following reasons: (1) The Omicron VOC has only recently become completely dominant so the observed hospital admissions in January (to which the model is calibrated) might still partly be the result of Delta infections; (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 not able to distinguish the hospital admissions due to Omicron infections that occurred during the Christmas holidays (note also that recent data on serology in unvaccinated persons are not available as an additional source for calibration); (3) Due to reporting delay, we have limited age-specific data on hospital admissions caused by infections acquired in a**

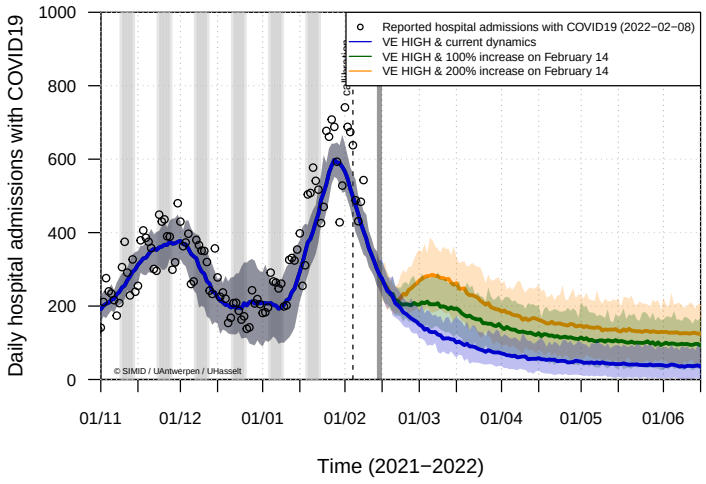
non-holiday period (with associated non-holiday contact behaviour), which hampers establishing the relationship between age-specific contacts, infections and hospital admissions that is representative for the period for which projections are made in this technical note; (4) Policy makers made important 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. (5) The ratio of admissions with COVID-19 over admissions for COVID-19 drastically changed in January 2022, and we have no reference period to inform our model on this for the longer run.

- 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 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.

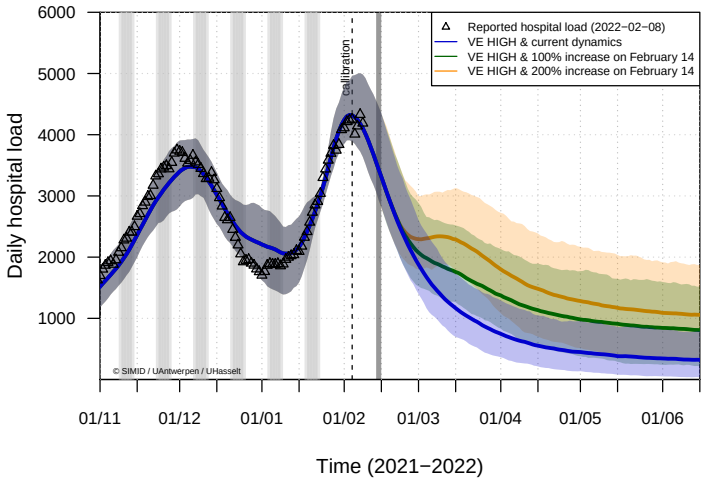
Model results

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.

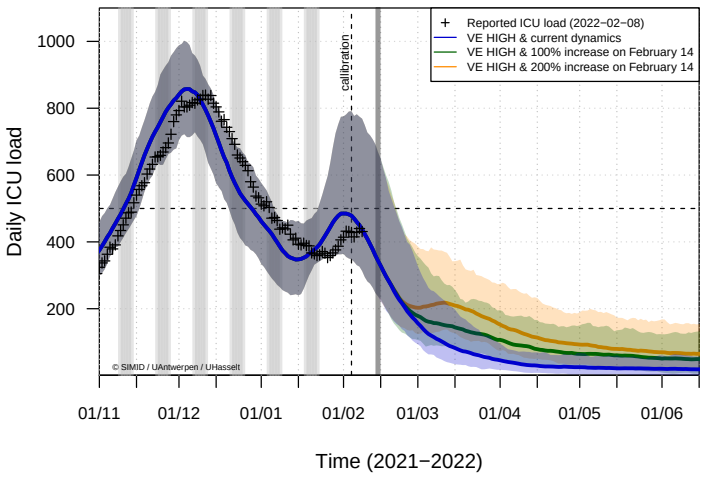
Scenario analysis: HIGH vaccine efficacy with increased transmission from mid February 2022.



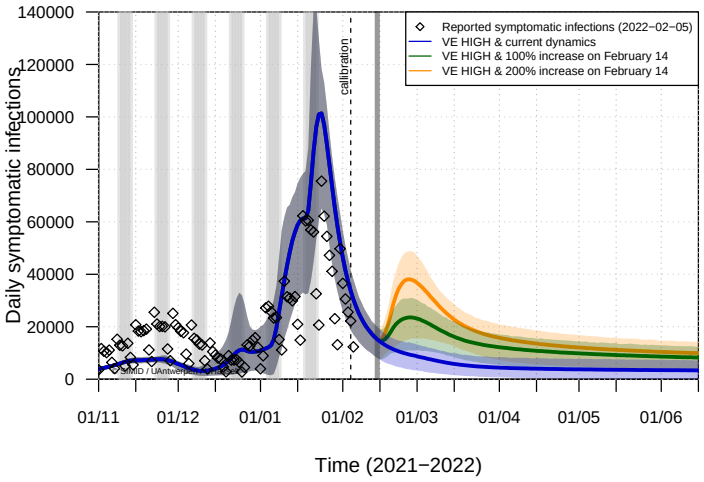
(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



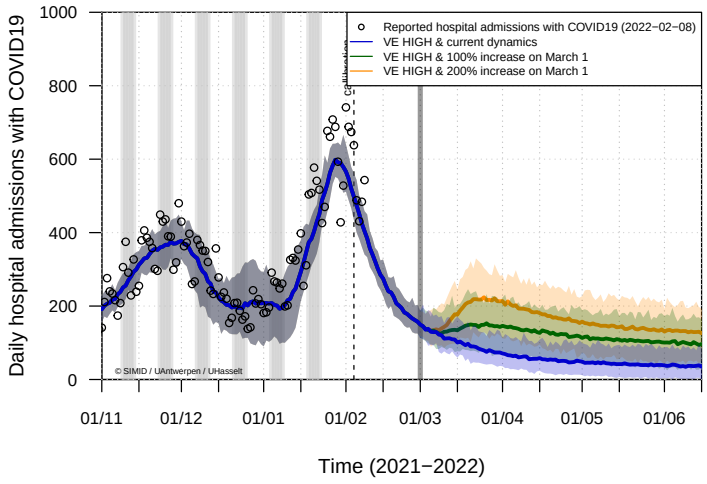
(c) Daily ICU load



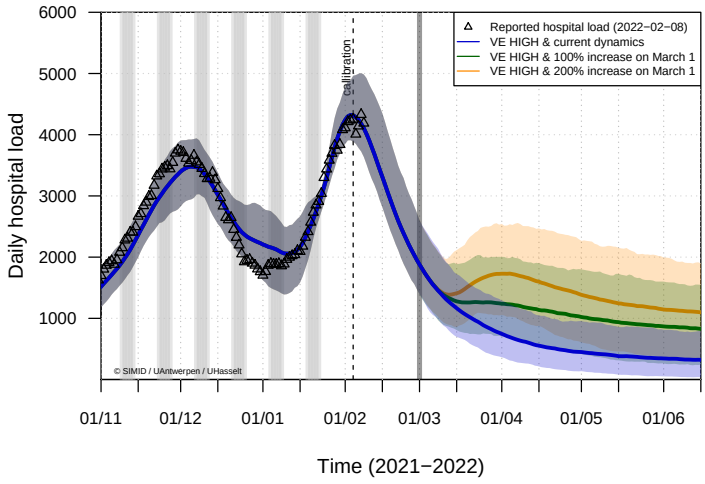
(d) Daily number of simulated symptomatic and overall confirmed cases

Figure 2: Model projections for Belgium for different clinical outcomes, assuming HIGH vaccine efficacy and changes in transmission dynamics mid February 2022. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

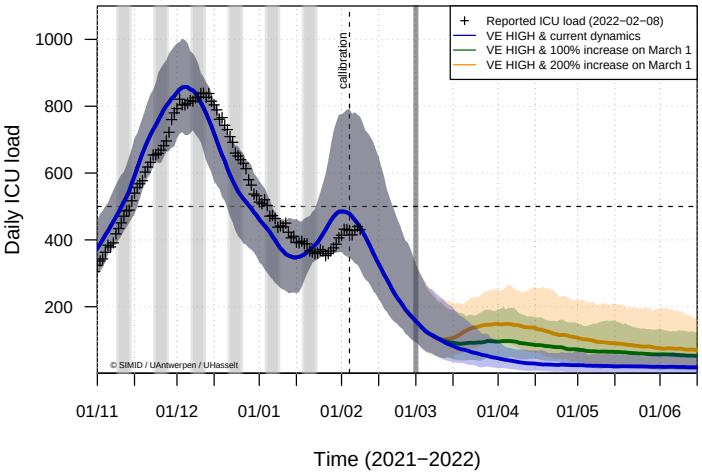
Scenario analysis: HIGH vaccine efficacy with increased transmission from March 1st, 2022.



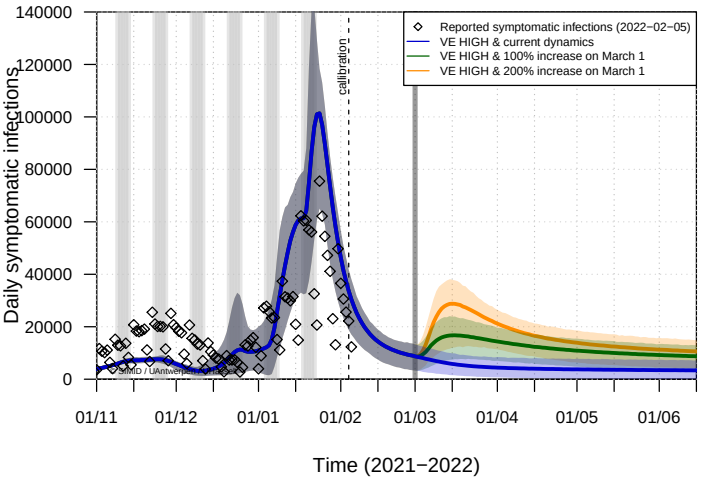
(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



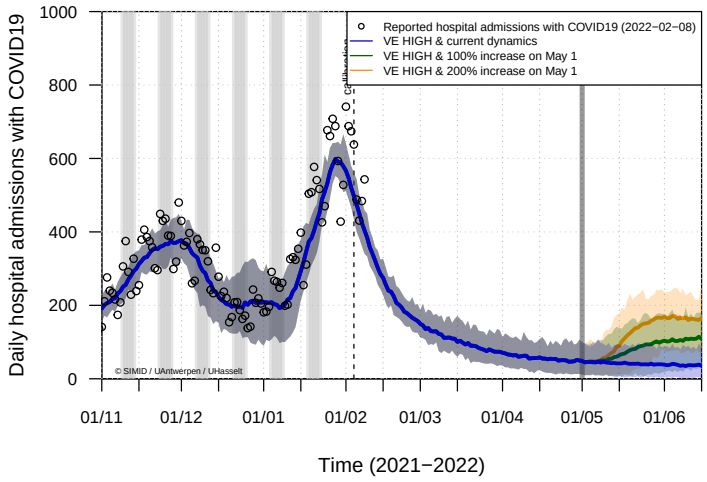
(c) Daily ICU load



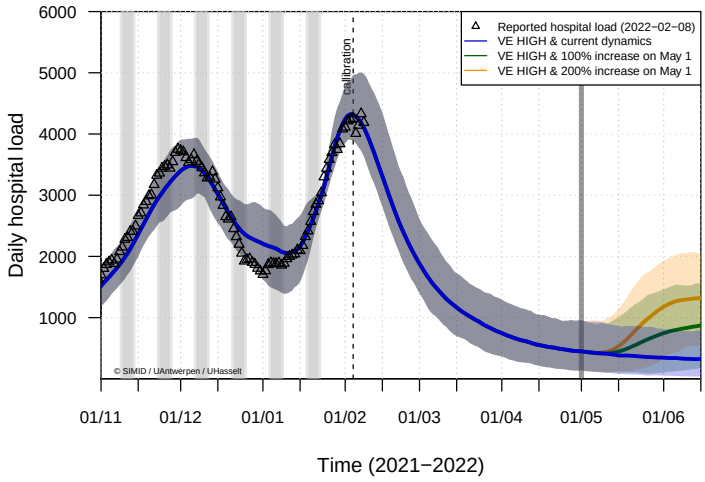
(d) Daily number of simulated symptomatic and overall confirmed cases

Figure 3: Model projections for Belgium for different clinical outcomes, assuming HIGH vaccine efficacy and changes in transmission dynamics from March 1st, 2022. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

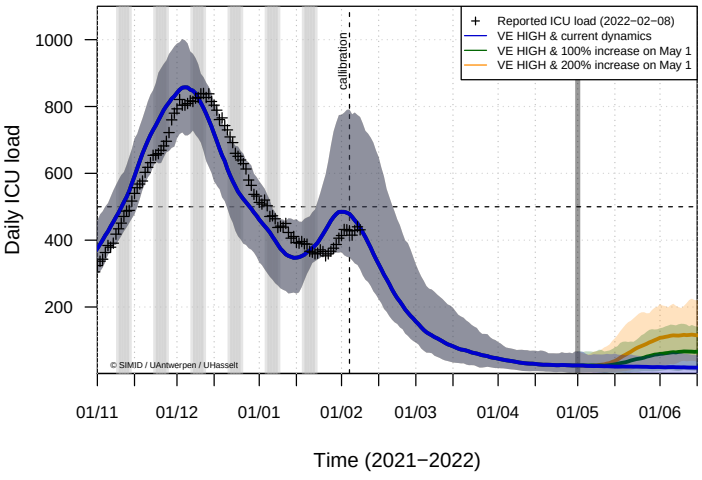
Scenario analysis: HIGH vaccine efficacy with increased transmission from May 1st, 2022.



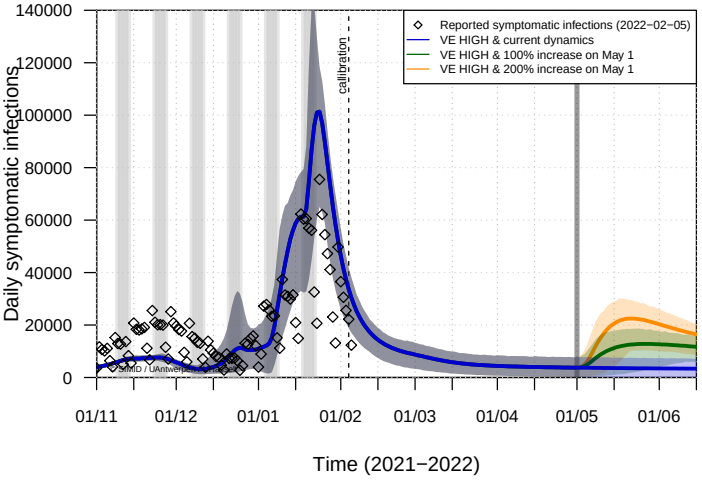
(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



(c) Daily ICU load



(d) Daily number of simulated symptomatic and overall confirmed cases

Figure 4: Model projections for Belgium for different clinical outcomes, assuming HIGH vaccine efficacy and changes in transmission dynamics from May 1st, 2022. 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

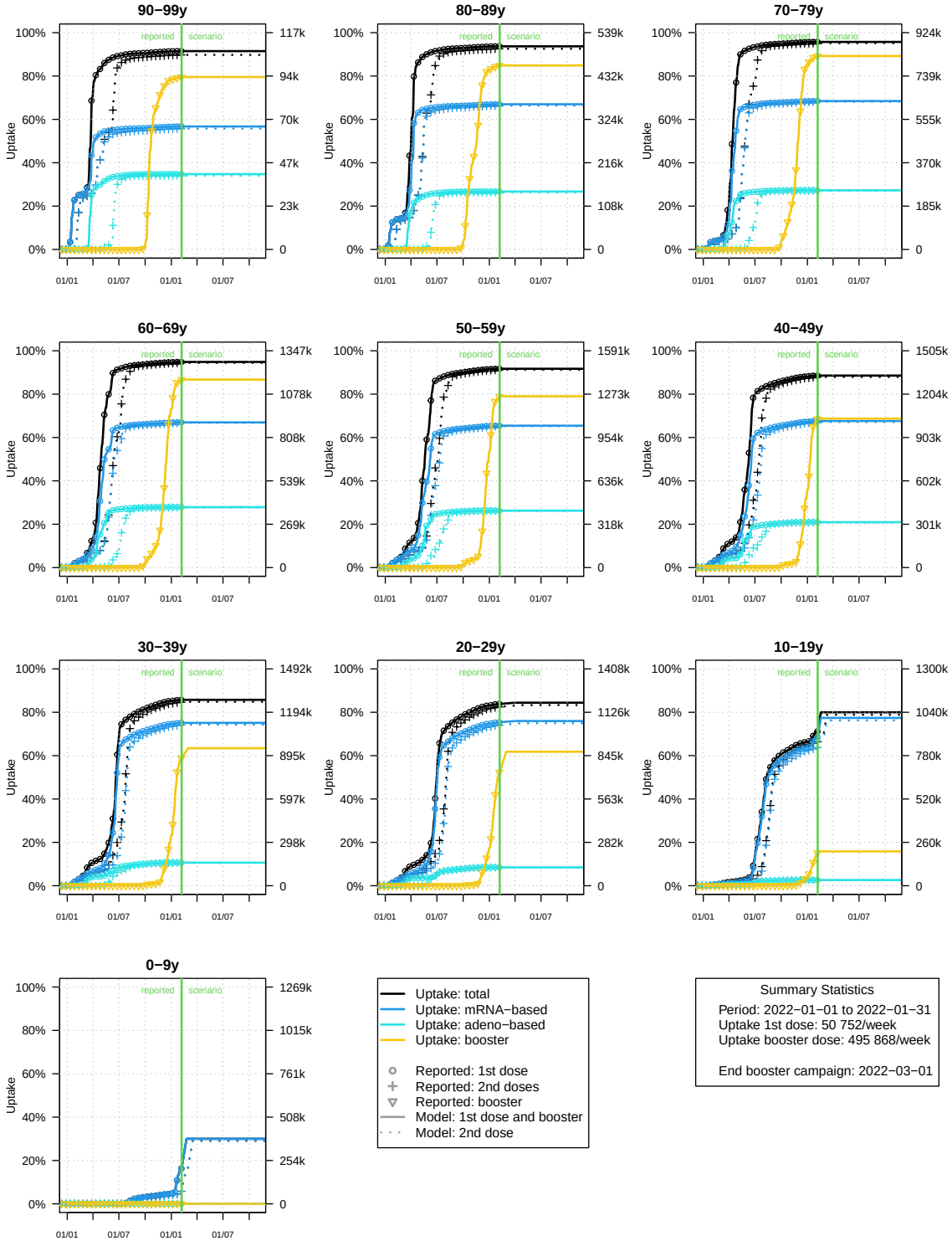
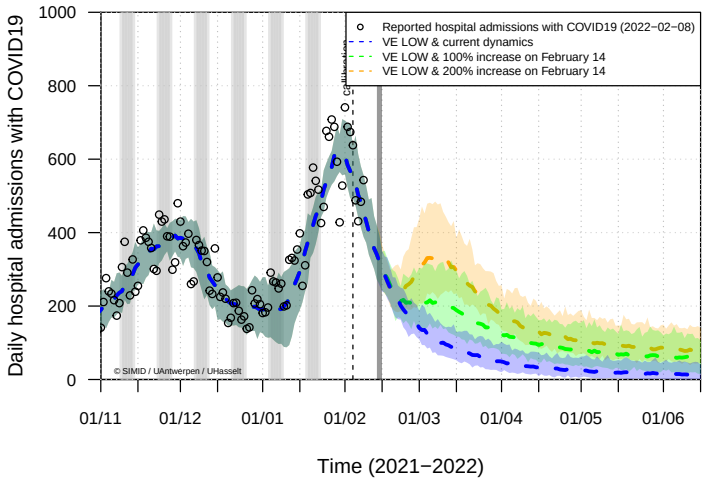
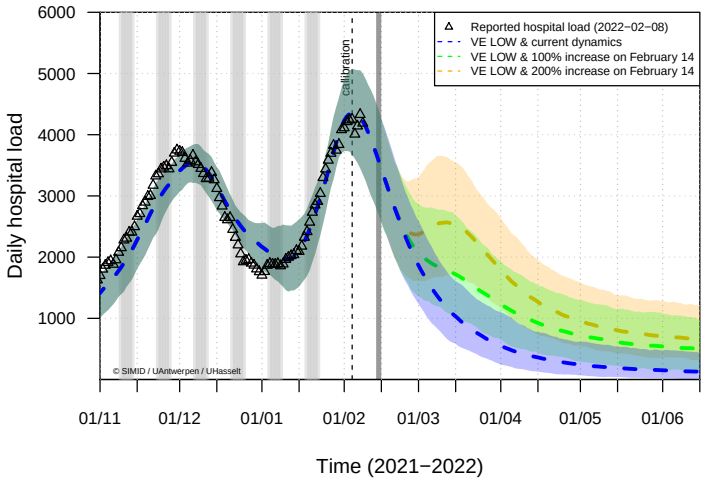


Figure S1: Vaccine uptake by age based on the reported uptake for Belgium and our projection with respect to the uptake of booster doses, in combination with 1st and 2nd doses for 5-11-year-old children.

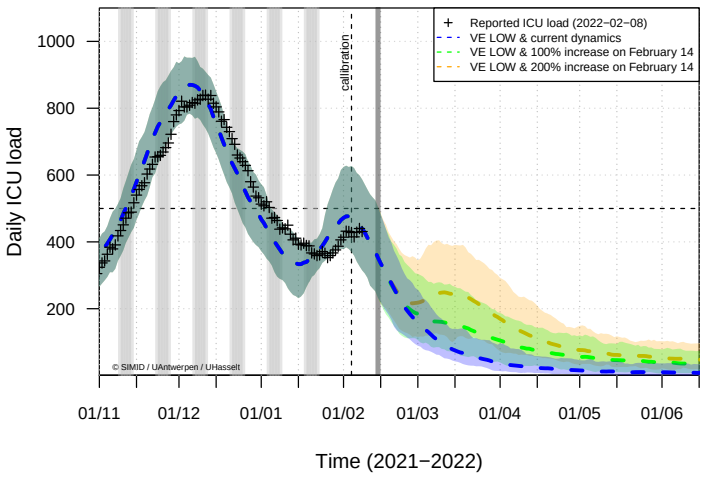
Scenario analysis: LOW vaccine efficacy with increased transmission from mid February 2022.



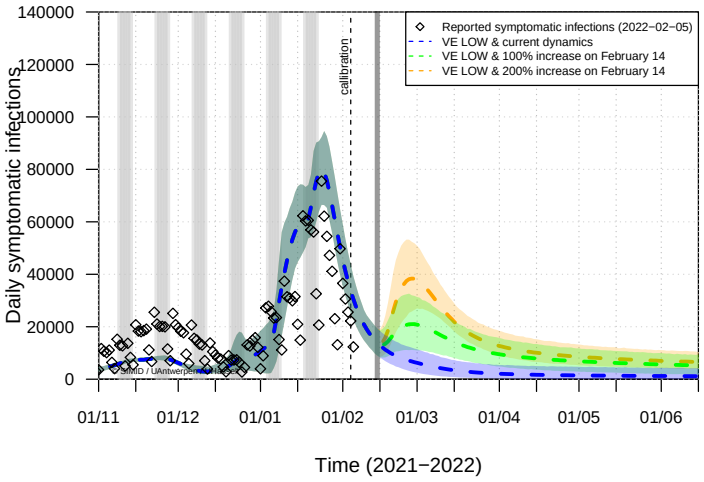
(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



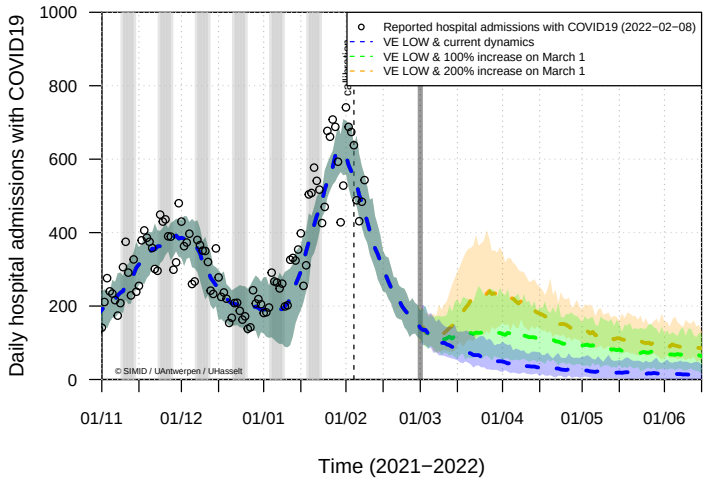
(c) Daily ICU load



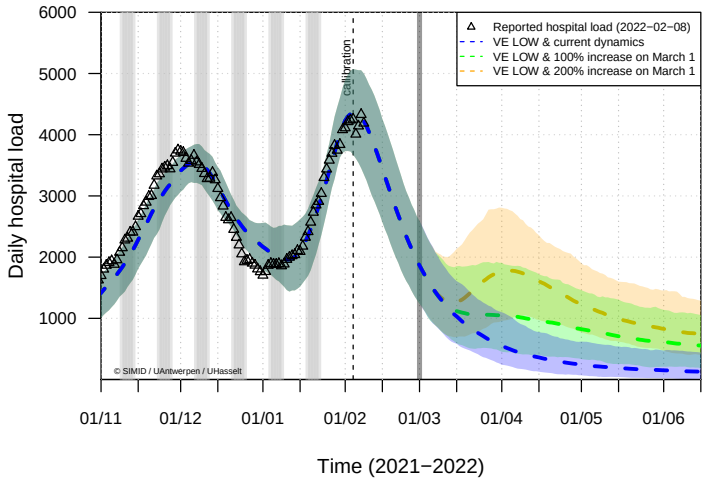
(d) Daily number of simulated symptomatic and overall confirmed cases

Figure S2: Model projections for Belgium for different clinical outcomes, assuming LOW vaccine efficacy and changes in transmission dynamics mid February 2022. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

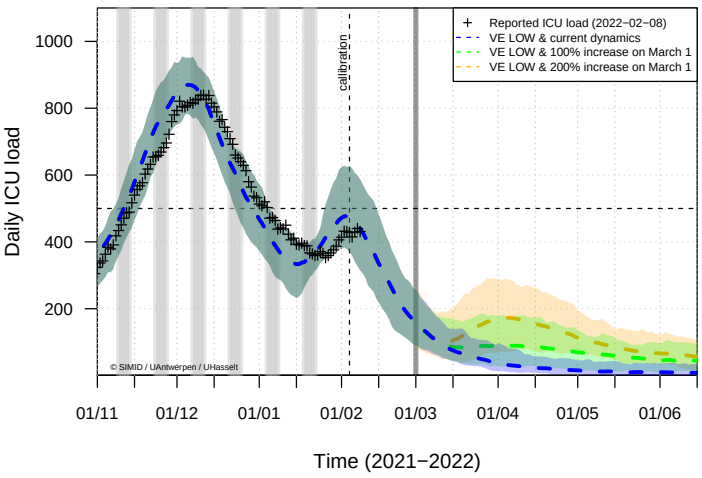
Scenario analysis: LOW vaccine efficacy with increased transmission from March 1st, 2022.



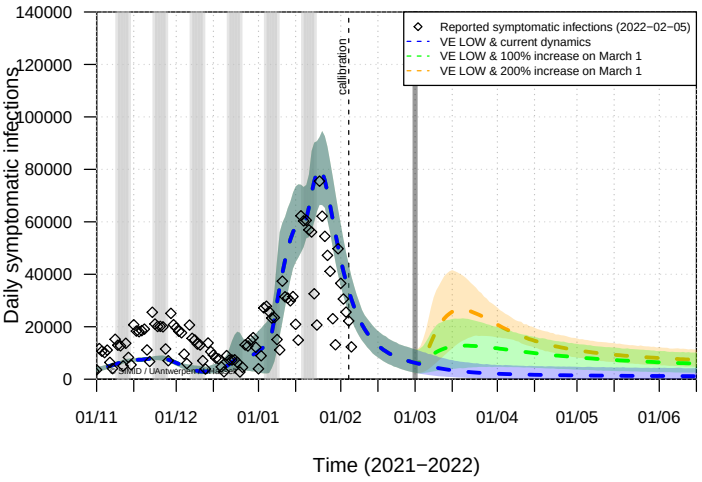
(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



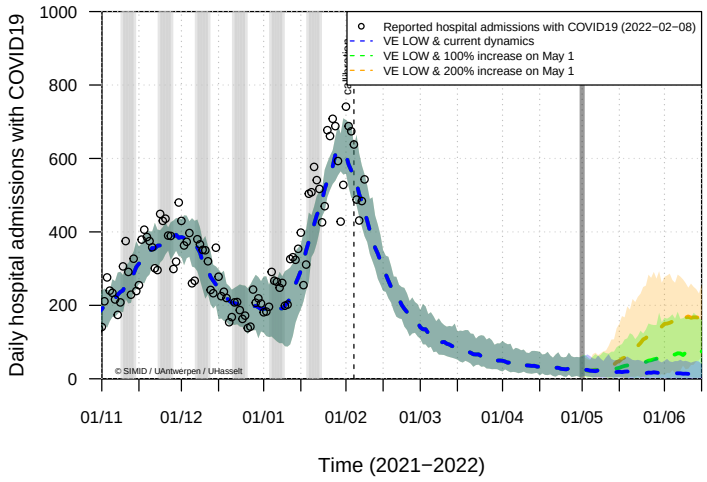
(c) Daily ICU load



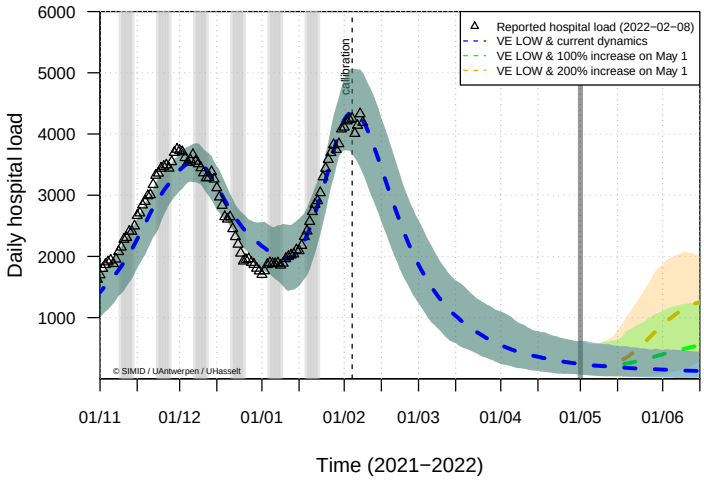
(d) Daily number of simulated symptomatic and overall confirmed cases

Figure S3: Model projections for Belgium for different clinical outcomes, assuming LOW vaccine efficacy and changes in transmission dynamics from March 1st, 2022. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.

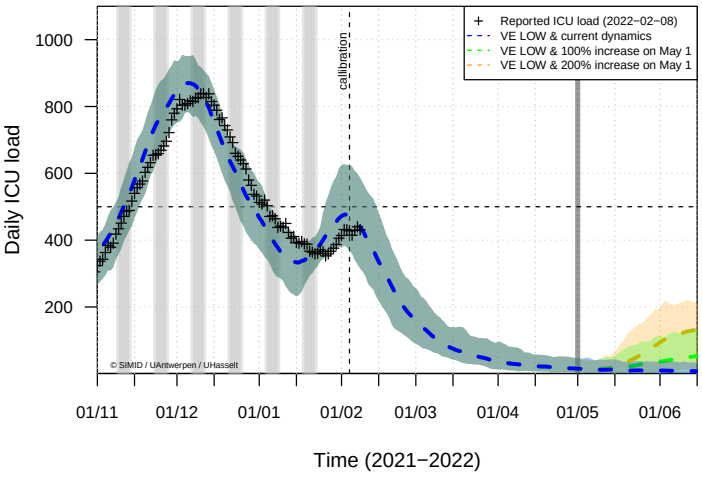
Scenario analysis: LOW vaccine efficacy with increased transmission from May 1st, 2022.



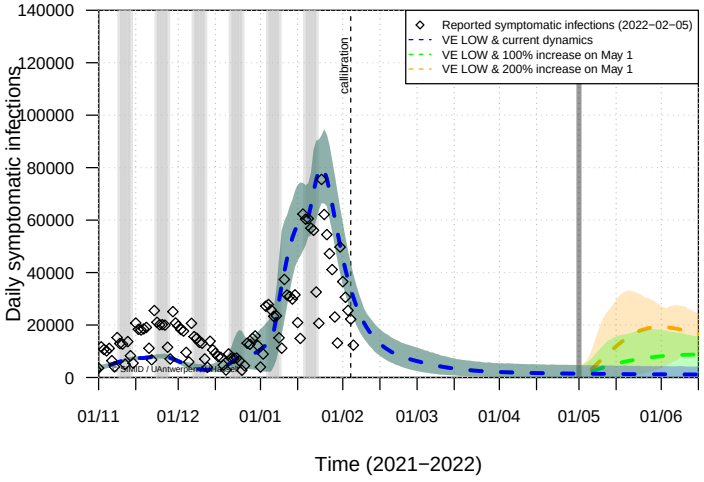
(a) Daily hospital admissions with COVID-19



(b) Daily hospital load



(c) Daily ICU load



(d) Daily number of simulated symptomatic and overall confirmed cases

Figure S4: Model projections for Belgium for different clinical outcomes, assuming LOW vaccine efficacy and changes in transmission dynamics from May 1st, 2022. The results are summarized by the mean (line) and 95% point-wise credible intervals (shaded area) of 25 model runs.