- technical note - not peer reviewed -

SARS-CoV-2 variants and vaccination in Belgium [v2021-03-25]

Modelling results by the SIMID consortium (www.simid.be)

This document contains our latest results on the short-term prediction modelling of hospital and ICU admissions, and scenario analyses based on dynamic transmission modelling.

Preliminary conclusions

- The age-specific vaccination uptake and the higher transmissibility and severity of variants of concern (VOC), primarily VOC-202012/1 or lineage B.1.1.7, have caused a change in the relation between confirmed COVID-19 cases, daily number of new hospitalizations, ICU load and number of COVID-19 related deaths (see e.g. Davies et al. 2021, Patone et al. 2021).
- Model scenarios informed by epidemiological data until March 22nd, 2021 and social contact data until March 9th 2021, show an increase up to 330 new hospital admissions per day, on average, by the end of April. The projected hospital load corresponds with >4000 occupied hospital beds at the peak, on average, by May 2021. However, these projections show a large uncertainty interval and should be interpreted with care.
- Model scenarios assuming an instant decrease in transmission from the 29th of March onwards, show a sharp drop in hospital admissions early April and a reduced hospital load. The magnitude of the reduction depends on contact behavior and adherence to the measures.

Short-term modelling

***Summary*:** The short-term prediction model for both the number of new hospitalizations and ICU load that was used previously, had to be adapted for the presence of the VOC in order to explain the observed trends in the data.

Model assumptions to predict new hospitalizations

- The short-term prediction model is based on a statistical regression model, called a distributed lag non-linear model (Gasparrini et al. 2017).
- The model compares the trend in the number of new hospital admissions at province level with a set of early-warning predictors. They are early-warning in the sense that the observed value of the predictors on a given day *d*, is related to the number of new hospitalizations some days later (*d+x*).
- The selected predictors for new hospitalizations are the positivity ratio of the COVID-19 tests and the mobility. There is a small delay (between 4 to 7 days) between the trend of the positivity ratio and the number of hospitalizations, such that we can predict the number of new hospitalizations ahead in time. This delay is linked to the time between symptom onset and hospitalization (Faes et al. 2020). The mobility is based on mobile network data, and is highly correlated with the intervention measures taken.
- To allow for a prediction over a period of 2 weeks, the positivity ratio is further informed with the number of patients with respiratory symptoms that visit the GP (COVID-19 barometer data, https://covid19.healthdata.be/) and data on absenteeism at work,

which are both associated with new hospitalizations in 10 to 14 days. This is similar to the mean time between symptom onset and hospitalizations for the working ages.

- The rate of hospitalization is also allowed to change based on the proportion of VOC in the population.
- There are strong indications from individual (networks of) hospitals that transfer to intensive care, conditional on hospital admission, is changing. More precisely, it seems both transfer to ICU and length of stay in ICU have increased since the beginning of March 2021. However, we have no reliable national data on age distributions of admitted patients to hospitals and ICU, after 20 February 2021, due to a delay in reporting of the hospital stay (Van Goethem et al. 2020). At the time of analysis, there was no data available to us on hospitalized patients regarding the variant that infected them, nor of their vaccination status.

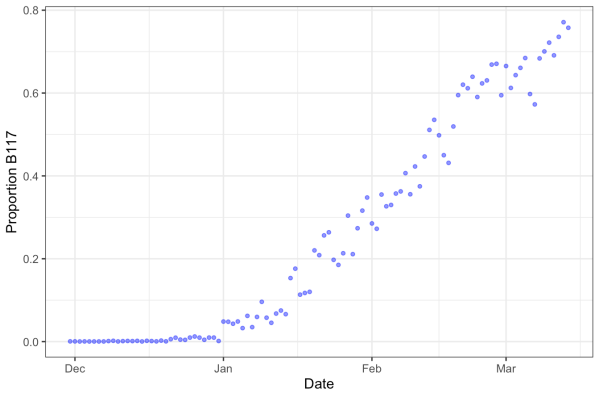

Figure 1: Proportion of VOC B.1.1.7 SARS-CoV infections in Belgium (source: GitHub Tom Wenseleers)

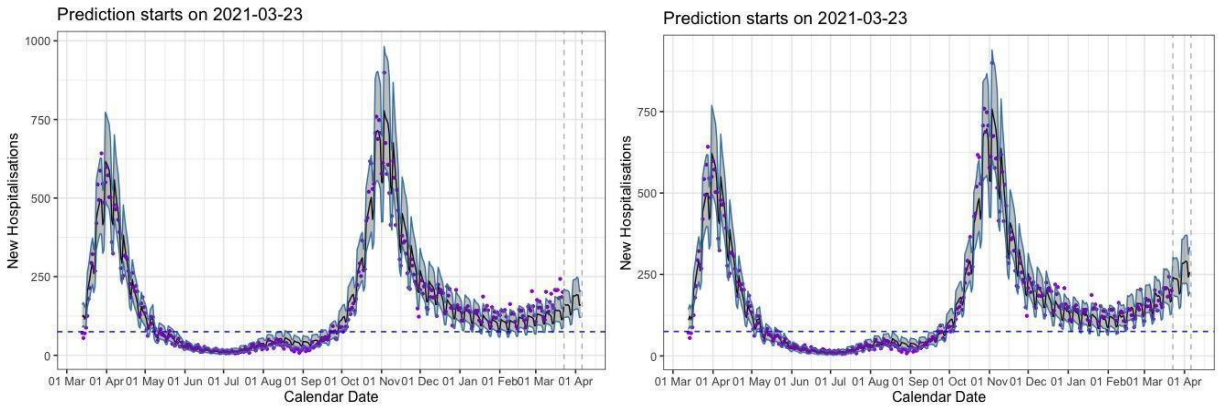

Figure 2: Short-term prediction model without VOC (left) and with VOC (right) adjustments. Dots are the reported number of new hospitalizations; grey bands are predictions.

Model results

The prediction model that does not take into account the VOC is underestimating the observed number of hospitalizations, while the model that allows for a change in the rate of hospitalizations due to infections with the VOC captures the observed number of hospitalizations. The prediction model accounting for the VOC predicts between 222 and 368 new hospital admissions on April 3rd.

Model assumptions to predict ICU load

- We use the bi-monthly distribution of hospital and ICU length of stay and proportion of hospitalized patients going to ICU.
- These probabilities are combined with the observed and predicted new hospitalizations to calculate the number of patients in ICU.
- The short-term prediction model of hospital load had to be adapted for ICU load as well, allowing for a higher proportion of hospitalized patients that need ICU care (an increase of 30% is assumed).

Model results

In case we do not allow for a change in hospitalization rate and changed flow to ICU due to the VOC, we are unable to capture the steep increase in ICU beds observed since the beginning of March. The model accounting for VOC predicts between 649 and 811 patients in ICU on April 5th.

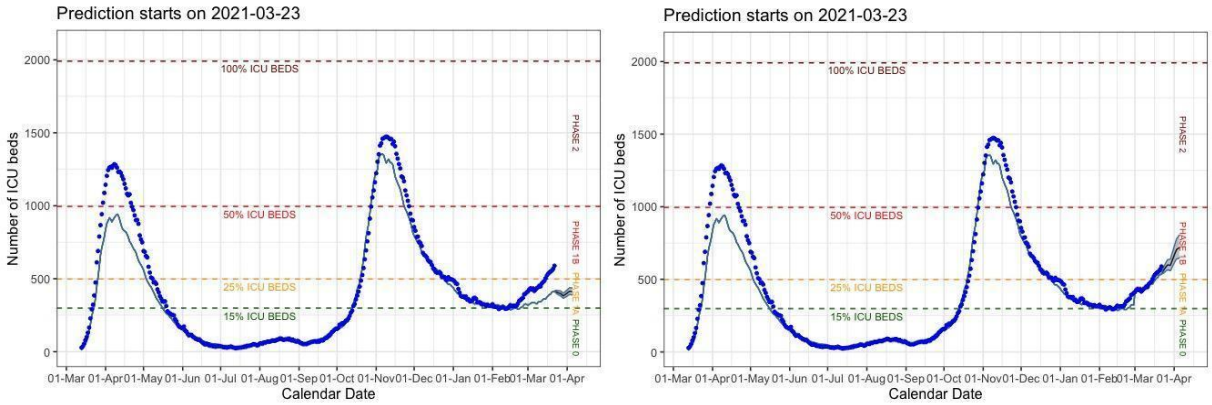

Figure 3: Short term prediction of ICU load (left: no increased proportion of hospitalized patients to ICU, right: 30% increase in proportion of hospitalized patients to ICU)

Dynamic Transmission Model

Summary**:** The stochastic model (https://doi.org/10.1016/j.epidem.2021.100449) has been adapted to include vaccination and the emergence of the VOC B.1.1.7. The model is calibrated on early sero-prevalence data, hospital admission data until March 22nd and social contact data from the 17th wave of the CoMix survey conducted from 3 to 9 March, 2021. Model projections account for the increasing vaccine uptake and the projected hospital admissions are translated into hospital and ICU load using the methodology of the short-term prediction model described above.

Model input and assumptions

1. **Gradually accumulating naturally-acquired immunity** in the population is accounted for, as well as immunity induced by vaccination. Vaccine-induced immunity after a full schedule is assumed to last till the end of the simulations.
2. The impact of the introduction of VOC B.1.1.7 in the Belgian population is accounted for using separate data analyses on the gradual penetration of the VOC (i.e. VOC B.1.1.7, Wenseleers 2021) and its **additional transmissibility** is estimated by the model while fitting from January 1, 2021 onward at approximately **40% relative to the old variant.**

3. The model was calibrated allowing for a differential hospital admission probability with respect to the VOC. The **increase in the probability of being admitted** to hospital was estimated at **36.5% (95% Credible Interval: 35.3%-40.1%).**
4. 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, separately from other groups in the population. Vaccine uptake is therefore implemented at the level of the ages of the target groups.
5. Social mixing and transmission dynamics:
    a. **Scenario A**: We assume no changes in social mixing behavior compared to the estimated dynamics up to March 22nd and schools are closed from April 5th, 2021 until April 18th, 2021.
    b. Scenario B: We assume an instant shift in behavior (i.e., transmission dynamics) on March 29th in line with the estimated dynamics for the week of October 19-25, 2020 during the second Belgian lockdown. This behavior is assumed to be maintained for 3 weeks, and afterwards social contact behavior of early March 2021 is resumed**. This is a purely illustrative scenario on the impact of behavioral changes, which is not intended as a justification for the measures that were in place in that period.**
    c. Scenario C: assumes the behavior shift as in scenario B with an arbitrary increase in the transmission rate of 30%. As such, this scenario is intended to illustrate the impact of a less strict lockdown/lower adherence.
6. Vaccine protection
    a. **Infection**: we use a **"leaky" vaccination approach**. For example, vaccination with **75% effectiveness**, implies that the likelihood to acquire infection for a vaccinated individual is 75% less compared to a non-vaccinated individual of the same age. The vaccines are assumed to protect against the VOC to the same extent as to the (originally dominant) wild type virus.
    b. **Hospital admissions**: vaccinated individuals who acquire infection have a lower risk for COVID-19 related hospital admission. Pending more evidence, we assume an overall reduction of 100% as shown in different vaccine trials (Creech et al 2021).
    c. **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.
    d. **Vaccine-induced immunity** is implemented as a step function with a switch from 0% to 75% protection against infection 21 days after the first dose. Vaccine-induced protection against hospital admission is implemented in the same way. For the purpose of this document, we do not consider differences between mRNA and adenovirus-based vaccines.
    e. **Waning immunity is not included at this stage** given the relative short time horizon after their deployment in the simulation. As such, the second dose is not modelled explicitly in the current analyses.

7. Vaccine uptake
    a. **Age-specific uptake scheme** targeting the most vulnerable population first, based on the reported uptake until 16th March and non-confirmed estimates on the available doses until May 1st (see Table 1). This is a possible scenario of vaccine uptake and could further change depending on the confirmed delivery schemes.
    b. The uptake until 16th of March is based on registrations in VaccinNet via the Sciensano dashboard.
    c. Target group vaccination until February is translated into age categories as follows
        i. Health-care-workers: active population of 20-50y
        ii. Nursing home population: 80-89y

Table 1: Cumulative uptake of at least one dose as % of the Belgian population by age group

	20-49y	**50-59y**	**60-69y**	**70-79y**	**80-89y**	**+90y**
1/2/2021	3%	3%	0%	0%	25%	0%
1/3/2021	6%	6%	0%	0%	25%	0%
1/4/2021	9%	9%	0%	39%	74%	91%
1/5/2021	9%	9%	36%	67%	74%	91%

Major limitations (and future work)

1. This model is suited for scenario analyses to investigate possible future paths, it is not a prediction model.
2. The model is calibrated on hospitalizations up to 22nd March 2021, and is informed by the last available wave of the CoMix social contact data survey dating from the week of 3 March 2021. These empirical social contact data inform mainly the frequency and age structure of physical 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, especially when empirical data on physical contacts to inform the model is lagging.
3. We are using data on the penetration of VOC B.1.1.7, making the implicit assumption that this will remain the dominant strain throughout the simulations. Nonetheless other VOC may take over from B.1.1.7, with different probabilities of transmission, disease, hospitalization, death, and different vaccine effectiveness characteristics against each of these manifestations.
4. The transmission model does not evaluate the prevented (severe) outpatient cases, which affect pressure exerted on primary care. The model does not include parameter uncertainty on vaccine uptake and effectiveness yet, and assumes no waning of vaccine-induced and naturally acquired immunity. The model is fitted to mortality data by age for the first wave, but this has not been done yet for the second wave.
5. We assume a similar vaccine related protection for VOC and non-VOC.
6. Vaccine-induced immunity is implemented by a step function. As such, it is assumed that there is no gradual build-up of immunity in vaccinated persons.
7. We show the model projections from 100 stochastic realizations.

8. The state transitions in the dynamic compartmental model are based on exponential rates that correspond with the following average periods:
    a. Latency period: 1.06 day
    b. Infectious period at pre-symptomatic stage: 2.14 days
    c. Time between symptom onset and hospitalization by 10-year age group: [11.45; 10.06; 10.01; 9.09; 7.26; 4.65; 4.63; 3.42; 2.99; 3.32] days
    d. The average time between infection and hospital admission for individuals >50 years of age ranges between 6.19 – 7.85 days.
9. The age-specific vaccine uptake until March 2021 is not fully in line with the reported uptake by Sciensano, and is subject for further research.

Model results

Scenario A: with continued constant social contact behavior (as estimated in early March)

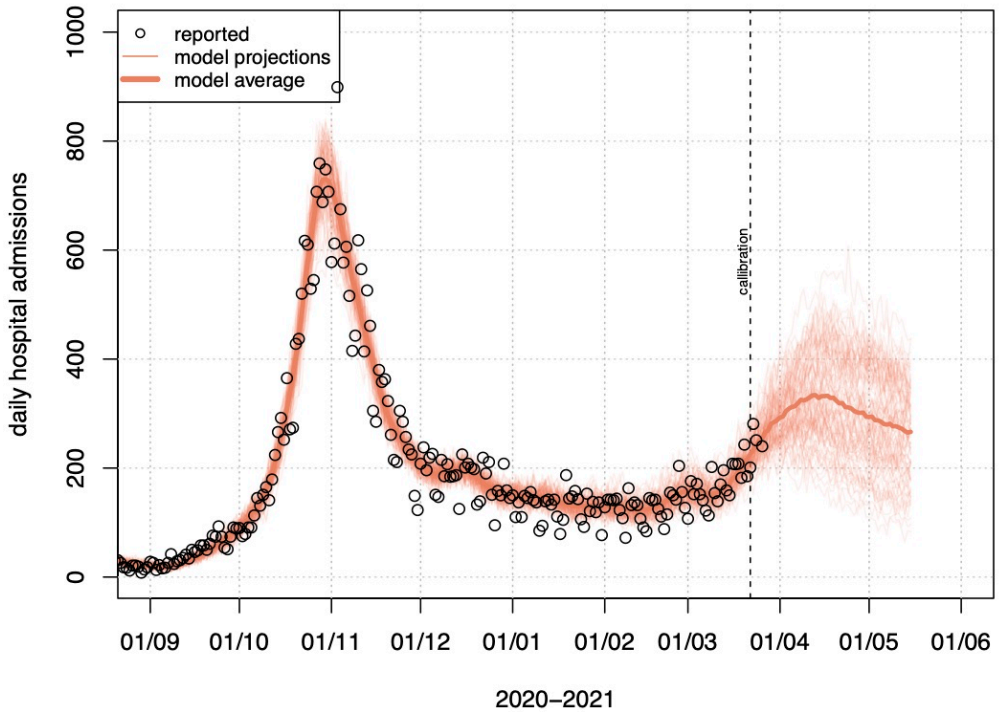

Figure 4: Model projections on daily hospital admissions if social contact behavior from early March 2021 is kept constant and the vaccination campaign continues **(Scenario A).**

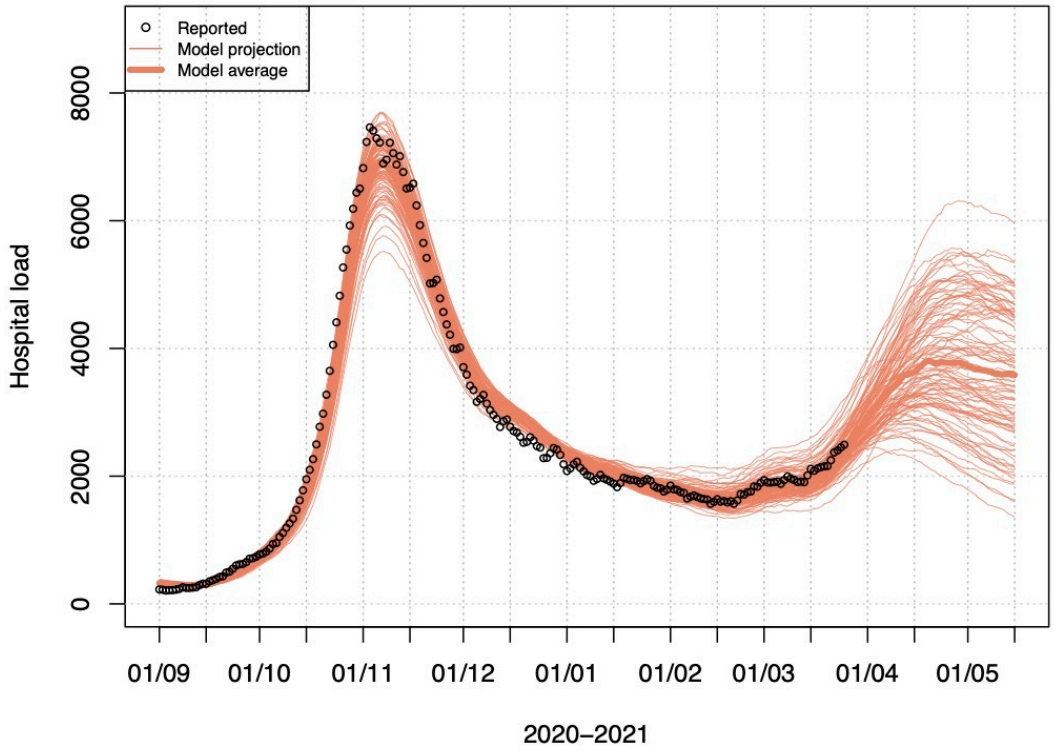

Figure 5: Model projections on hospital load if social contact behavior from early March 2021 is kept constant and the vaccination campaign continues **(Scenario A).**

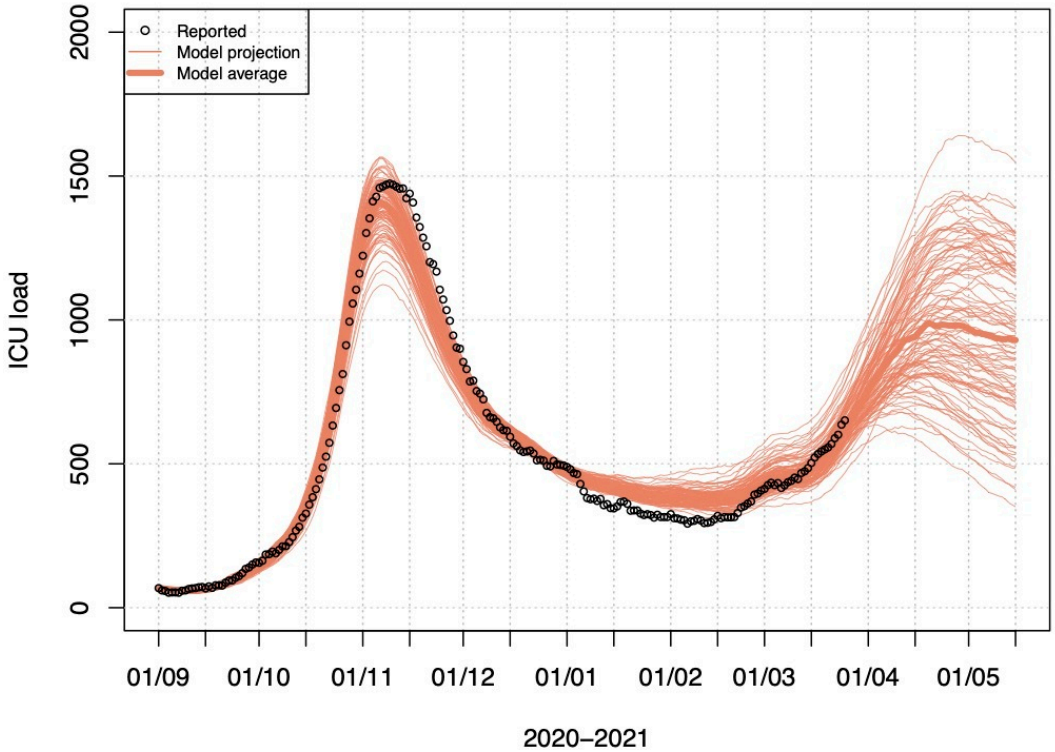

Figure 6: Model projections on ICU load if social contact behavior from early March 2021 is kept constant and the vaccination campaign continues **(Scenario A).**

Scenario B: With instant change in behavior on March 29th for 3 weeks

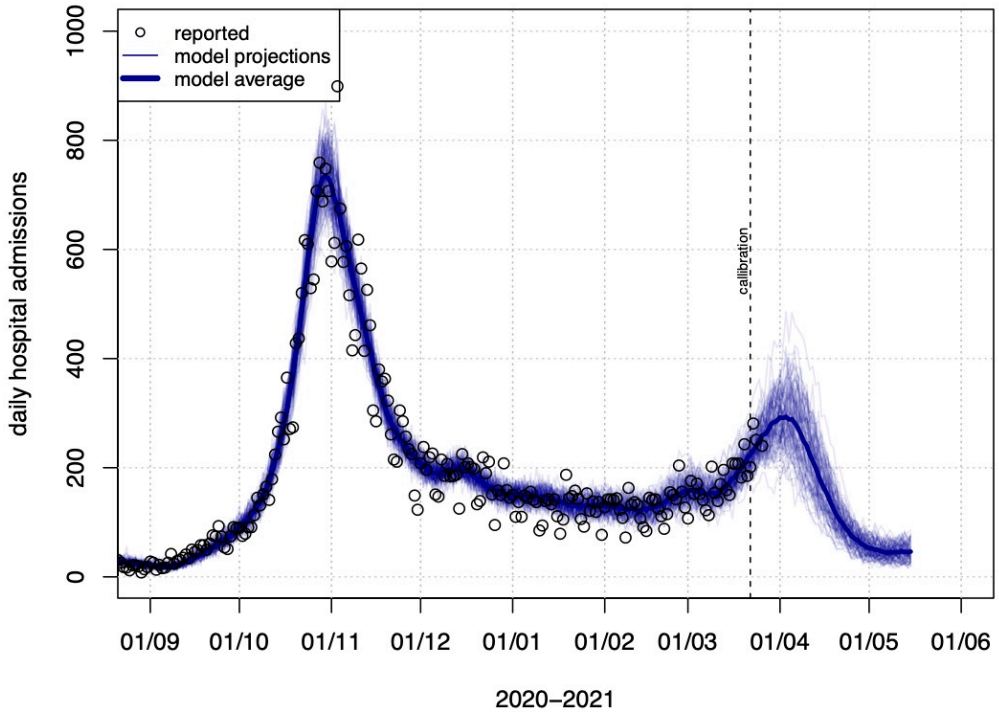

Figure 7: Model projections on daily hospital admissions if social contact behavior changed on March 29th 2021 for 3 weeks and the vaccination campaign continues **(Scenario B).**

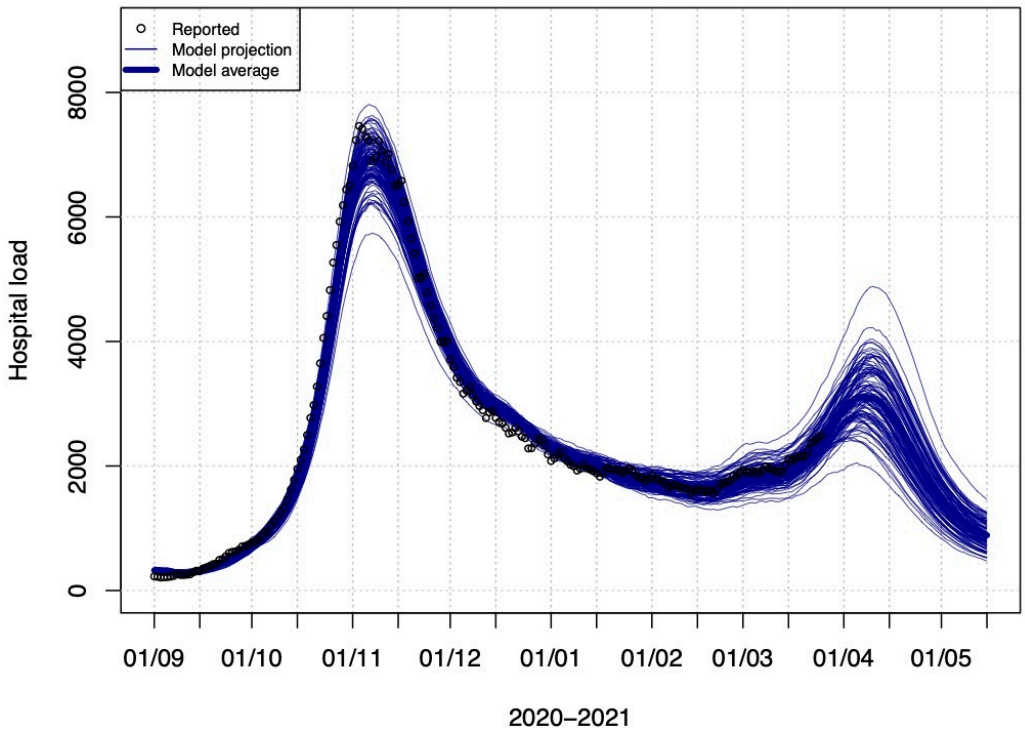

Figure 8: Model projections on hospital load if social contact behavior changed on March 29th 2021 for 3 weeks and the vaccination campaign continues **(Scenario B).**

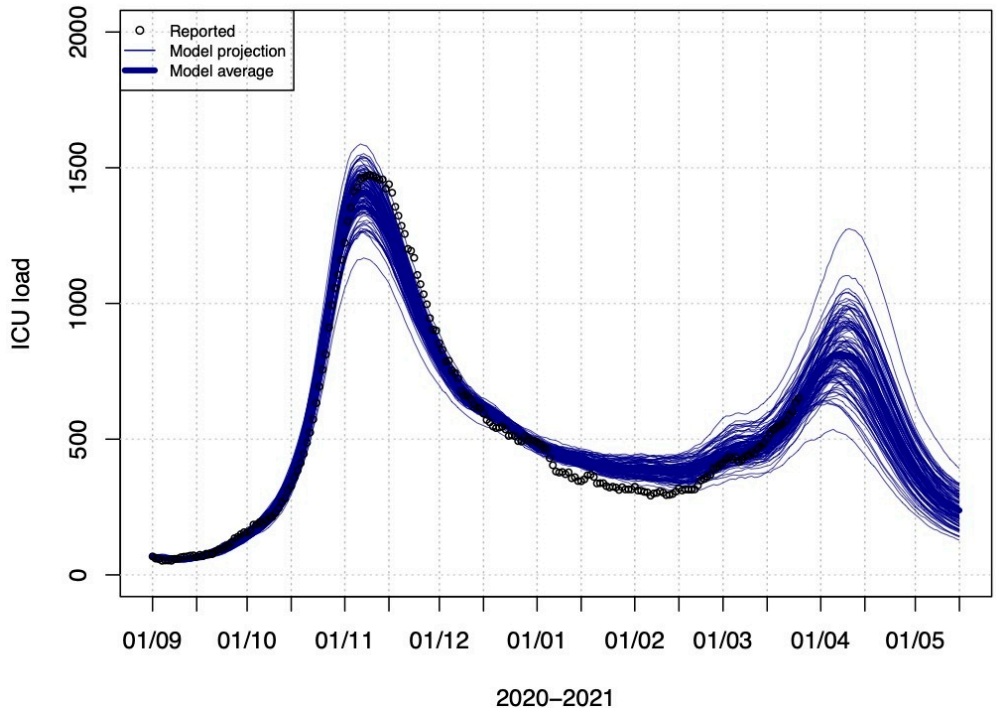

Figure 9: Model projections on ICU load if social contact behavior changed on March 29th and the vaccination campaign continues **(Scenario B).**

Scenario C: With instant change in behavior on March 29th for 3 weeks, but with 30% more transmission compared to scenario B.

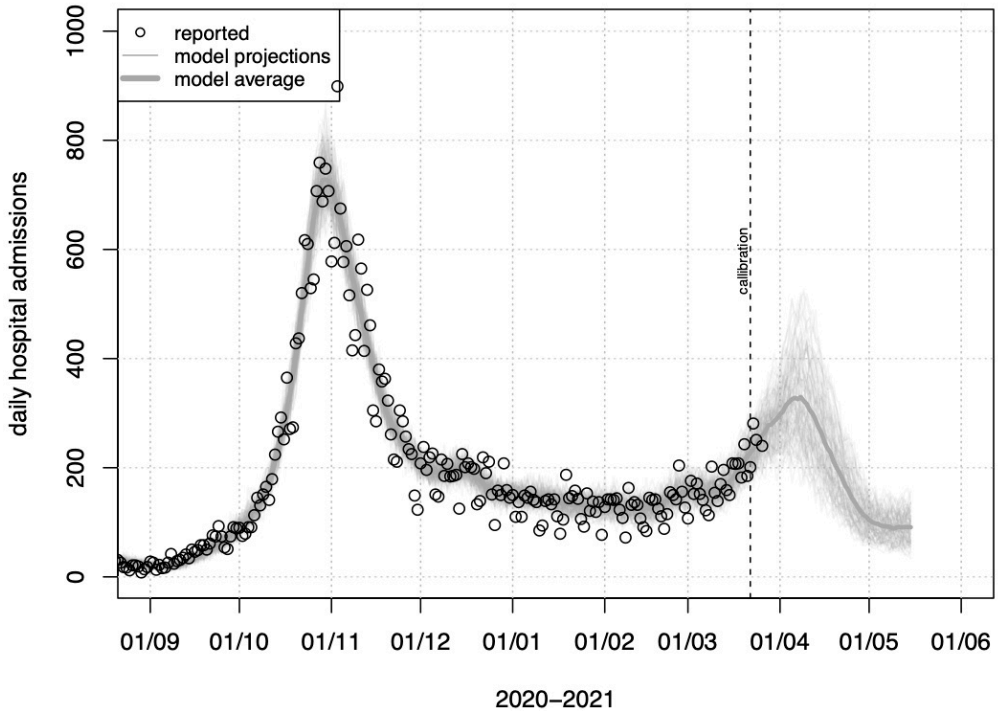

Figure 10: Model projections on daily hospital admissions if social contact behavior changed less on March 29th and the vaccination campaign continues **(Scenario C).**

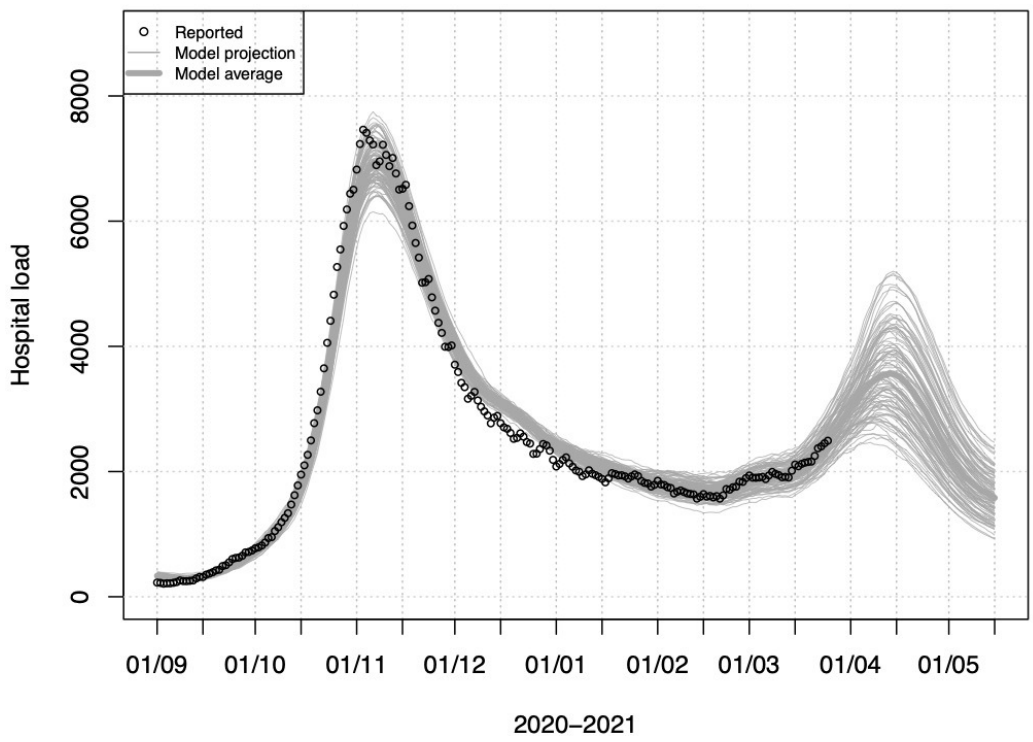

Figure 11: Model projections on hospital load if social contact behavior changed less on March 29th and the vaccination campaign continues **(Scenario C).**

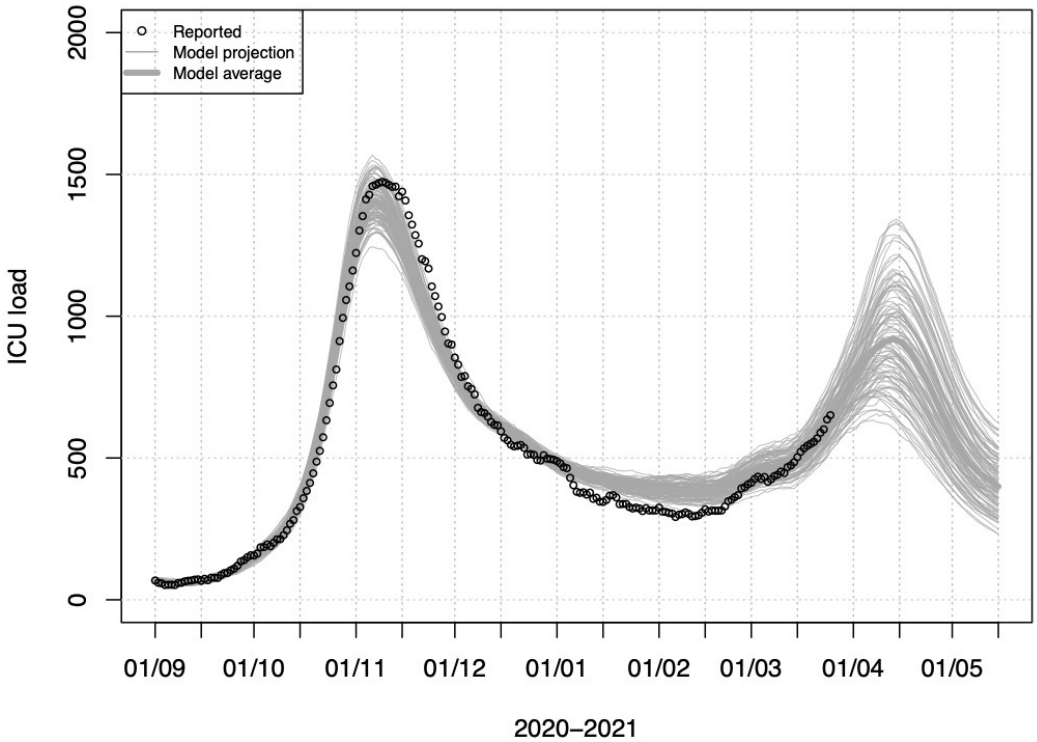

Figure 12: Model projections on ICU load if social contact behavior changed less on March 29th and the vaccination campaign continues **(Scenario C).**

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