

Scenarios for infections and new admissions caused by the Omicron variant Report by the Expert Group for Mathematic Modelling, 17 December 2021



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1. Introduction

This report presents projections for the number of infections and new hospital admissions following the spread of the more transmissible Omicron variant. As we have only little experience with the Omicron variant, we find it important to stress that many questions currently remain unanswered and that our current knowledge is subject to uncertainty. This applies, in particular, to the effect of vaccines on the risk of infection and severe illness, as well as the importance of waning vaccine effectiveness over time. Considerable uncertainty also remains with respect to the transmissibility and the severity of the Omicron variant compared with the Delta variant. The projections presented in this report should therefore be considered as possible scenarios for the development based on a series of assumptions about the Omicron variant. In addition to the considerable uncertainties that are inherent in the model, changes in the population's behaviour may have a decisive impact on the projections and thereby on the development of transmission and hospital admission patterns.

The projections made in this report should be read in light of the rapid spread of the Omicron variant and the latest measures introduced by the Danish government as from 8 December 2021. The projections are described through eight sensitivity scenarios with different combinations of degree of waning immunity (due to waning vaccine effectiveness over time) and transmissibility and admission risk for the Omicron variant relative to the Delta variant. Each sensitivity scenario estimates the development of case numbers and new hospital admissions until 1 January 2022 assuming that no further restrictions are introduced.

The pop10 model was used in the model calculations. pop10 is a further developed version of the pop9 model described in "*Expert Report of 20 September 2021 - Scenarios for the evolution of transmission, new admissions and breakthrough infections with COVID-19*" and subsequently published memos. The update from pop9 to pop10 is described in detail in Appendix 2.

2. Summary

The Omicron variant is still characterised by considerable uncertainties. Therefore, the projected case numbers and numbers of daily new hospital admissions should be considered possible rather than exact scenarios describing the development in weeks to come.

The emergence of the Omicron variant is estimated to cause a surge in case numbers and daily new hospital admissions as we approach 1 January 2022.

The current daily growth rate of the Omicron variant varies across the five Danish regions from 0.22 (North Denmark Region) to 0.38 (Zealand Region), corresponding to a doubling time of 1.8 to 3.2 days, calculated based on data from 16 December 2021. The growth rate is highest in the Zealand Region and lowest in the Central Denmark Region.



The presented scenarios partly take the transmission-reducing measures introduced by the Danish Government on 8 December 2021 into account. The measures presented on 17 December 2021 are not included in the models. Specifically, the following elements are implemented in the model:

- that 10% of the workforce work from home as from 8 December
- that primary schools close as from 15 December
- that an adaptive, transmission-reducing behaviour occurs in the population at high incidences. We assume that adaptive behaviour may reduce the activity corresponding to half of the reduction achieved by introducing the January 2021 lock-down.
- that other societal activities remain unchanged in the period covered by the projections, and that no further restrictions are introduced
- that booster vaccination is being accelerated in the vaccination programme, allowing
 3.5 million citizens to receive booster vaccination by the end of 2021.

The report presents eight sensitivity scenarios based on different combinations of waning immunity following vaccination (a moderate and high level of waning immunity for the Omicron variant relative to the Delta variant) and differences in the relative transmissibility between the Omicron and the Delta variants (the Omicron variant being 1.5 or 2 times more transmissible). In all sensitivity scenarios, the maximal vaccine effectiveness against transmission with the Omicron variant is assumed to be 70% of the maximal protection for the Delta variant. For new admissions, two sensitivity scenarios were also prepared with different admission risks. In one scenario, the Omicron variant has the same risk as the Delta variant; in another, the admission risk of the Omicron variant was assumed to be half that of the Delta variant. In the following, we describe the results of the susceptibility scenarios:

- The estimated daily case number ranges from 9,000 to 45,000 as per 24 December, depending on the degree of waning immunity for the Omicron variant and depending on the relative transmission rate.
- The daily number of new admissions is estimated to fall in the 130-250 range by 24 December, depending on the degree of waning immunity for the Omicron variant and provided that the Omicron variant carries the same admission risk as the Delta variant.
- The daily number of new admissions is estimated to fall in the 120-190 range by 24 December, depending on the degree of waning immunity for the Omicron variant and provided that the Omicron variant carries half the admission risk of the Delta variant.
- It appears from the model calculations that the admitted patients will primarily be vaccinated persons above 50 years of age. This applies to both the scenario with a moderate and a high degree of waning immunity.
- Please note that the model carries an approx. one week time lag from a person tests positive to the person can be admitted to hospital. This means that new admissions triggered by the case numbers on 24 December will not be observed until 1 January 2022, see Figures 3 and 4.



Please note that the restrictions presented by the Danish Government on 17 December are not implemented in the model. Additional measures to reduce transmission may impact the development of case numbers after approx. seven days, whereas up to two weeks need to pass for the effect to be reflected in the number of new hospital admissions.

If rising case numbers trigger behavioural changes in the population, this is expected to reduce transmission. Thus, the model takes activity reductions at high incidences into account. Compared with the activity level on 7 December, the model assumes that adaptive behaviour may reduce activity by up to 25%. It will, however, require considerable behavioural changes to curb transmission of the Omicron variant. If the present daily growth rate for the Omicron variant is, e.g., 0.3 (a daily 35% increase), then stopping the growth in the case number would require halving the societal activity that causes transmission (relative to the activity level observed before 7 December).

3. Background - The Omicron variant

Virus variant B.1.1.529 was first reported on 24 November 2021 based on samples from South Africa, after which it spread globally. On 26 November, the virus variant was categorised as a Variant of Concern and the WHO coined the variant Omicron¹ The variant is characterised by a very high number of mutations in the spike protein (approx. 35 compared with the original Wuhan variant) compared with the up to 10-15 mutations of the Delta variant. Some of these mutations have raised concerns of increased transmissibility and reduced vaccination effectiveness². Early observations from South Africa have also indicated that the Omicron variant carries a higher risk of re-infection than the two previously dominating variants in South Africa (Alpha and Beta)³. In Denmark, the Omicron variant was initially detected on 28 November 2021, but it has subsequently been detected in samples from 22 November, after which it spread to all regions.

Test Center Danmark has developed a variant PCR, which detects the Omicron variant with a high specificity (99.99% validated by WGS). This means that positive PCR tests are quickly be classified by variant type without awaiting results from whole-genome sequencing⁴. The model calculations estimating the evolution of the Omicron variant are based on variant-PCR test results.

International model calculations and studies of vaccine effectiveness

¹ <u>Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern (who.int)</u>

² https://www.ssi.dk/aktuelt/nyheder/2021/ny-variant-vaekker-bekymring-i-danmark-og-resten-af-eu

³ Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern (who.int)

⁴ <u>https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern</u>



Early estimates of the daily growth rate for the Omicron variant were calculated to fall in the 0.26-0.35 range, corresponding to a doubling time of 1.98-2.66 days in Scotland⁵ and ⁶. respectively; countries that are comparable to Denmark with respect to vaccination uptake and booster vaccination programmes. England has also prepared model calculations estimating the expected development⁷. England's "Plan B measures" comprise milder restrictions than those implemented in Denmark. If Plan B is implemented in England, 1,000-6,000 new daily admissions are estimated by 1 January 2022. Taking the population size in Denmark into account⁸. Norway has approximately the same population and case numbers as Denmark, but their official admission rate is only around one third of the rate observed in Denmark. Therefore, the Norwegian model calculations may be recalculated to approx. 21-93 new admissions with the Omicron variant as per 1 January in Denmark. It is assessed that the model calculations for Denmark presented herein roughly follow the pattern of the calculated development of case numbers and new admissions in England and Norway. It should be noted, though, that the models employed in the three countries have important differences in their assumptions and parameters, and that each country has established different scenarios for social activity. Even so, the models from England, Norway and herein report comparable growth rates.

On the current data basis, it is still too early to estimate vaccine effectiveness against the Omicron variant in Denmark. Preliminary international studies have shown a rapidly waning immunity against Omicron infection 15 weeks after patients receive the second dose of the Pfizer vaccine, compared with the effectiveness against Delta infection. After patients receive the third dose, the effectiveness against symptom-producing infection with the Omicron variant is increased to the level observed after the second dose. It remains unknown if immunity recedes following administration of the third vaccination dose⁹. These results are in concordance with studies calculating vaccine effectiveness based on how effectively vaccine-inducing antibodies neutralise the Omicron and the Delta variant in a wide range of recent laboratory studies¹⁰.

4. Model parameters and assumptions

Updating the model

⁵ <u>Coronavirus (COVID-19): Omicron in Scotland - evidence paper - gov.scot (www.gov.scot)</u>

⁶ <u>SARS-CoV-2 variants of concern and variants under investigation (publishing.service.gov.uk)</u>

⁷ <u>Consequences of Omicron (cmmid.github.io)</u>

^{8 &}lt;u>https://www.fhi.no/contentassets/c9e459cd7cc24991810a0d28d7803bd0/vedlegg/risikovurdering-2021-12-13.pdf</u>

⁹ Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern (khub.net) ; News room | Discovery – Discovery

¹⁰ <u>https://www.medrxiv.org/content/10.1101/2021.12.08.21267417v1</u>

MEDRXIV-2021-267417v2-Sigal.pdf (secureservercdn.net);

Estimates of reduced vaccine effectiveness against hospitalization, infection, transmission and symptomatic disease of a new SARS-CoV-2 variant, Omicron (B.1.1.529), using neutralizing antibody titers | medRxiv ; https://www.medrxiv.org/content/10.1101/2021.12.09.21267556v1



Division into age groups

- pop9 has been updated to comprise ten age groups rather than nine. Therefore, the name of the model has changed to pop10 (population model with 10 age groups). This was achieved by dividing the two age groups 0-9 years and 10-19 years into three age groups: 0-4-year-olds, 5-11-year-olds and 12-19-year-olds. This was done to better capture the increasing transmission among school children aged 5-11 years who have only just initiated their vaccination course.
- In pop10, the under-reporting estimates by age group are updated to reflect the latest distribution of tests between age groups and vaccinated/unvaccinated people, see Appendix 2.

Behavioural changes in the population

- The model takes the recently approved school lock-downs as from 15 December into account and assumes that 10% of the workforce will work from home as from 8 December.
- pop10 introduces local reductions in transmission during high and increasing incidences, much like was done in the popIBM¹¹. The transmission-reducing measures were implemented in the model so that a gradual reduction in activity follows when the regional 7-day incidences exceed 280 infected per 100,000 inhabitants. The activity reduction rises gradually to 20% of that seen during the January lock-down in Denmark at an incidence of 2,100 cases per 100,000 inhabitants. At incidences exceeding 2,100 cases per 100,000 inhabitants, an activity reduction corresponding to 50% of the January 2021 lock-down is assumed. See Appendix 2 for details on the effect as a function of time in the model.

Inclusion of two virus variants

- The model was extended to include two additional tracks to describe the spreading of the Omicron variant. Thus, infection is now divided into four tracks describing vaccinated and unvaccinated citizens who become infected with the Delta variant and the Omicron variant, see Appendix 2.
- Structurally, the two variants are treated identically, except for the fact that it is possible for the Omicron variant to re-infect persons who have previously become infected with the Delta variant, whereas it is not possible to become re-infected with the Delta variant after having become infected with the Omicron variant.

Receding immunity to infection and admission to hospital

¹¹ <u>https://covid19.ssi.dk/-/media/arkiv/subsites/covid19/modelberegninger/notat-fra-ekspertgruppen-for-matematisk-modellering_30112021.pdf?la=da</u>



- pop10 was updated to take waning immunity and the effect of revaccination into account. The calculations assume that protection against infection with SARS-CoV-2 wane exponentially once people are fully vaccinated. Thus, protection against the Delta variant is reduced by 20-35%¹² of the full effect after six months (see Figure B.2.3 in Appendix 2).
- The third vaccination dose is assumed to return protection to its maximum level followed by a protection that wanes more slowly, so that the protection is reduced by approx. 15% after six months. Furthermore, the model assumes that immunity against admission does not wane. Waning immunity is described in more detail in Appendix 2.
- The Omicron variant is assumed to have a maximal vaccine effectiveness against infection of 70% of the maximal protection for the Delta variant with the vaccines used in Denmark. Furthermore, it is assumed that immunity against infection wanes more rapidly for the Omicron variant compared with the Delta variant, see Appendix 2. The sensitivity scenarios include a moderate scenario for waning immunity in which immunity wanes by a downward scaling parameter of 2.5 for the Omicron variant compared with the Delta variant, see Appendix 2.

Assumptions about the prevalence of the Omicron variant

- At the start of the simulation (5 December), the prevalence of the Omicron variant was introduced according to the observed distribution in age groups, vaccination status and regions.
- It was assumed that the Omicron variant has a higher natural transmission rate (and therefore is more infectious). This higher transmission rate is studied as a sensitivity scenario with relative (natural) transmission rates between 1.5 and 2 compared with the Delta variant. This comes in addition to the increased susceptibility among the vaccinated people in connection with the increased waning immunity. It is assumed that the course of the infection is identical for the Omicron variant and the Delta variant. This means that the variants have, e.g., the same latency period and the same delay between infection and admission.
- Uncertainty exists with respect to the severity of the Omicron variant, i.e. the risk of admission following infection with the Omicron variant. The figures presenting new admissions include a scenario in which the Omicron variant has the same admission risk as the Delta variant and another in which the Omicron admission risk is 50% of the admission risk of the Delta variant. In the scenario in which the Omicron variant has half the admission risk of the Delta variant, the number of new admissions due to infection with the Omicron variant is half as high as when the Omicron variant is attributed the same admission risks as the Delta variant.

¹²https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1027920/S1 386 SPI-M potential winter trajectories Imperial College.pdf



Updating the vaccination programme

- As per 12 December 2021, vaccination coverage was estimated to be 83.7% of those invited (including the 5-11-year-olds). It is assumed that vaccination coverage increases in the course of the simulated period and that the target groups (except the 5-11-year-olds) who have not achieved 90% coverage will be administered the same weekly number of doses as in Week 49, until the overall coverage reaches 90%, see Appendix 2.
- Vaccination of children aged 5-11 years is included, and it is assumed that the same number of weekly doses is given as in Week 49 until the coverage in this group reaches 57.3%. This coverage was estimated based on the coverage among the 12-year-olds and it takes a lower propensity to accept vaccination among the 5-9-year-olds into account, see Appendix 2.
- Revaccination is also included in the model's vaccination programme. Revaccination coverage is based on the observed coverage. Revaccination delayis estimated based on the past 14 days, but was adjusted based on the updated guidelines recommending a 4.5- and 5.5-month interval, respectively, between vaccination completion and revaccination. Thus, the objective of reaching a total of 3.5 million revaccinations before the end of 2021 is included in the model, but uncertainties with respect to revaccination coverage in the older age groups entail a risk that the model includes more revaccinated people in the younger age groups. If more people in the older age groups above 40 years of age receive revaccination, the effect on admissions may be higher than calculated by the model, see Appendix 2.

The model updates in pop10 are described in further detail in Appendix 2.

5. Reservations

Various considerable uncertainties are associated with how the prevalence of the Omicron variant will develop in the Danish society. This is so because the Omicron variant was discovered only 3 weeks ago. Furthermore, sufficient Danish data have been available only for a short period of time. Additionally, data are delayed by the period from the sampling to the variant-PCR result is received. The analyses and projections will therefore be adjusted as further knowledge of the variant becomes available.

Uncertainty in the projections of case numbers and new admissions apply, in particular, to:

- How well fully vaccinated and revaccinated individuals are protected against infection and admission to hospital
- How much more infectious than the Delta variant the Omicron variant is.
- If infection with the Omicron variant carries a larger or more limited risk of running a serious disease course than the Delta variant



- How much higher the Omicron variant's ability is to cause re-infection (new infection in previously infected individuals)
- Furthermore, a different age group mix may be expected during the Christmas holydays, which may cause an increased number of admissions if more elderly people become infected. HOPE data from the Christmas of 2020 showed that the total number of contacts per person remains unchanged in the course of Christmas, but that a higher number of family contacts, as opposed to, e.g., occupational contacts, are observed¹³.

6. Results

Figure 1 presents the estimated development in the transmission of the Omicron variant, by region. Negative binomial regression was performed of the number of daily cases for both the Omicron and the Delta variant. Please note that Figure 1 depicts the development in transmission with the Omicron variant only. The model was adjusted for weekday as a weekly pattern is observed in the number of positives recorded with more positives being recorded early in the week. Furthermore, an adjustment was made for the fact that variant PCR was performed in only part of the PCR-positive specimens (more than 90% in the period leading up to 12 December). Table 1 presents the estimated growth rates and the derived doubling times and daily percentage growth by region based on data in the period from 6 December through 13 December.

The largest prevalence of the Omicron variant is observed in the Capital Region of Denmark and in the Central Denmark Region, why these estimates are more reliable. The estimated growth rates range from 0.22 per day to 0.38 per day, corresponding to doubling times ranging from 1.8 to 3.2 days. It is currently too early to establish any effects of the restrictions communicated on 8 December, which apply to nightlife, restaurants and bars, etc. and to the maximum allowed number of individuals in the standing audience at events; these restrictions, as well as restrictions presented on 17 December, were therefore not included in the model.

¹³ <u>https://github.com/mariefly/HOPE/raw/master/Adf%C3%A6rdsindikatorer_0105.pdf</u>





Figure 1: Expected number of cases with the Omicron variant (dots) provided PCR-variant results are available for all samples. Colours identify regions. The solid lines state the estimate in the regression model adjusted for the share with variant-PCR results and the light areas state 95% confidence intervals.

	Growt	h rate (1	/day)	Doublir	ng time (o	lays)	daily growth (%)			
Region	Estimate	lower	upper	Estimate	lower	upper	Estimate	lower	upper	
Capital Region of Denmark Central Denmark Region	0.30 0.22	0.27 0.18	0.33 0.26	2.30 3.15	2.09 2.71	2.57 3.77	35.1 24.6	31.0 20.2	39.4 29.2	
North Denmark Region	0.24	0.19	0.30	2.83	2.31	3.67	27.7	20.8	35.0	

Table 1: Estimated growth rates with 95% confidence intervals for the period from 6 December through 13 December. The growth rates were transformed into doubling times.



Region Zealand	0.38	0.33	0.43	1.83	1.61	2.13	45.9	38.4	53.8
Region of South Denmark	0.32	0.26	0.37	2.19	1.87	2.64	37.2	30.0	44.8

Figure 2 shows the estimated development in the number of new daily cases based on the above described assumptions, whereas Figures 3 and 4 show daily new admissions from early December 2021 to 1 January 2022. The figures show case numbers and new admissions by the Delta variant (orange) and the Omicron variant (green) for the different sensitivity scenarios. The total case numbers and the number of new hospital admissions are shown in purple. The black dots show the actual daily case numbers and the number of admissions up to 13 December. The case number on 14 December is marked in red, as we currently do not have results from all samples taken on that day. The model runs are calibrated against the weekly figures from 4 October to 5 December 2021.

A number of uncertainties remain that are associated with the vaccine effectiveness against infection with the Delta variant. Here, we assume that the maximal vaccine effectiveness is between 75% and 100% and that the degree of waning immunity declines by 20-35% in the course of six months. These ranges were calibrated against the observed development and the best 10% are presented in the figures in this report as the range in the orange graph. In Figures 2-4, eight sensitivity scenarios were run with different parameters for the Omicron variant, specifically for the relative infection rate and the degree of waning immunity with respect to the Delta variant. In Figure 3, the Omicron variant is assumed to carry the same admission risk as the Delta variant, whereas the Omicron variant is assumed to have only half the admission risk of the Delta variant in Figure 4.

For all sensitivity scenarios, a scaling was employed on the maximal vaccine effectiveness against infection for the Omicron variant of 0.7 of the effectiveness of the Delta variant (i.e. the maximal vaccine effectiveness against infection with the Omicron variant is 70% of the maximal vaccine effectiveness against infection with the Delta variant). The left column uses a moderately waning immunity for the Omicron variant compared with the Delta variant. The right column applies a rapidly waning immunity for the Omicron variant.

The top row assumes a relative transmission rate for the Omicron variant compared with the Delta variant of 1.5. The second row has a relative transmission rate of 2. For all sensitivity scenarios, it is observed that the Delta variant will peak and then slowly taper out, meaning that the Delta variant case numbers diminish. Conversely, transmission with the Omicron variant surges in all scenarios, and in some sensitivity scenarios exponential growth is seen. Also, note that within-week variations are present in the number of cases. Specifically, case numbers increase on Monday and Tuesday because people are more socially active during the weekend and then are tested early in the week.

Figure 2 shows that at a relative transmission rate of 1.5, the estimated number of infections falls in the 9,000-20,000 range. At a relative transmission rate of 2, the number of infections is



14,000-45,000 as per 24 December, depending on the degree of waning immunity of the Omicron variant.



Figure 2. Daily simulated number of infections in pop10 for the Delta variant (orange), the Omicron variant (green) and the total number of infections (purple). The observed total number of infections is marked by black dots. (The final dot is coloured red to mark that we do not currently have the results from all samples processed on that day). The figure shows various sensitivity scenarios all of which assume that the maximal vaccine effectiveness of the Omicron variant is 0.7 of the Delta variant. The sensitivity scenarios assume various degrees of waning immunity against infection with the Omicron variant, and a relative transmission rate of 1.5 and 2.

Figure 3 shows a reduction in the number of new admissions with the Delta variant in the course of the simulation period, but an increase in the number of new admissions with the Omicron variant in line with the trend observed for the case numbers. The model operates with a waiting stage where approx. seven days pass from a positive test to admission, which is seen as a delay in time in the increase in new admissions after the increase in case numbers. This means that new admissions triggered by the case numbers on 24 December will not be observed until 1 January 2022, as shown in Figures 3 and 4.

At a relative transmission rate of 1.5, the daily number of new admissions is estimated to fall in the 130-180 range by 24 December. At a relative transmission rate of 2, the daily number of infections is 150-250 as per 24 December, depending on the degree of waning immunity of the Omicron variant. A total estimate across relative transmission rate and degree of waning immunity is thus 130-250 new daily admissions per 24 December if the Omicron variant has the same admission risk as the Delta variant.





Figure 3. Daily simulated new admissions in pop10 for the Delta variant (orange), the Omicron variant (green) and the total number of infections (purple). The observed total number of infections is marked by black dots. The figure shows various sensitivity scenarios all of which assume that the maximal vaccine effectiveness of the Omicron variant is 0.7 of the Delta variant. The sensitivity scenarios range from a moderately waning immunity to a rapidly waning immunity, and from a relative transmission rate of 1.5 to 2. It is assumed that the risk of being admitted to hospital is the same for the Omicron variant and the Delta variant.

In Figure 3, it is assumed that the Omicron variant has the same risk of admission to hospital as the Delta variant. In contrast, if the Omicron variant turns out to have half the admission risk as the Delta variant, the admission figures of the Omicron variant will need to be reduced to half. This is shown in Figure 4 where estimates show that a relative transmission rate of 1.5 may produce 120-160 new admissions as per 24 December 2021, and a relative transmission rate of 2 is estimated to produce 130-190 new admissions as per 24 December 2021. A total estimate across relative transmission rate and degree of waning immunity is thus 120-190 new daily admissions per 24 December if the Omicron variant has half the admission risk as the Delta variant.





Figure 4. Daily simulated new admissions in pop10 for the Delta variant (orange), the Omicron variant (green) and the total number of infections (purple). The observed total number of infections is marked by black dots. The figure shows various sensitivity scenarios all of which assume that the maximal vaccine effectiveness of the Omicron variant is 0.7 of the Delta variant. The sensitivity scenarios range from a moderately waning immunity to a rapidly waning immunity, and from a relative transmission rate of 1.5 to 2. It is assumed that the risk of being admitted to hospital for the Omicron variant is half the risk of being admitted to hospital for the Omicron variant.

New admissions by pop10 age groups

Figure 4 presents the age distribution for new admissions among vaccinated and unvaccinated people, assuming moderately waning immunity and that the Omicron variant has the same admission risk as the Delta variant.

Furthermore, the number of new admissions is stated across the sensitivity scenarios for the relative transmission rate for the Omicron variant compared with the Delta variant. In all scenarios, most admissions are observed among vaccinated citizens and the majority of those admitted are elderly citizens. The scenario with highly waning immunity is qualitatively identical, but the number of persons admitted is higher. Therefore, only the scenario with moderately waning immunity is shown here. The scenario in which the Omicron variant has half the admission risk of the Delta variant will also, qualitatively speaking, be identical, but the admission numbers for the Omicron variant will be approx. half as large, whereas the number of admissions with the Delta variant will remain unchanged.

Compared with previous model reports, a considerably higher share of vaccinated people contributes to new admissions, but considerable uncertainty remains as to the admission risk for (re-) vaccinated citizens who become infected with Omicron.





Figure 5. Daily simulated new admissions in the pop10 by age groups for vaccinated (blue) and unvaccinated (red) individuals in the sensitivity scenario with moderately waning immunity. Sensitivity scenarios range from a relative transmission rate of 1.5 to 2. It is assumed that the risk of being admitted to hospital is the same for the Omicron variant and the Delta variant.



Appendix 1. Graphs from memo of 30 November presenting the observed evolution until 12 December

In the memo of 30 November 2021, various figures presenting the projected evolution were published. In this appendix, we present the same model projections but now including the observed development until 12 December 2021.

In memo of 30 November 2021, pop9/pop10 were not included in the figures as the model was being developed at the time and was therefore unavailable for simulations.

Figure B.1.1 shows that the case numbers since the most recent model memo have continued to follow a steeply increasing trend and have remained in the upper part of the popIBM range. One explanation for this may be that the model does not include increased testing activity after the run, and that waning immunity is not implemented in the popIBM. Furthermore, the Omicron variant was not included in the November model runs.



Figure B.1.1. Daily case numbers ("Smittetal") in popIBM by unvaccinated ("uvaccineret" left column), vaccinated ("Vaccineret" centre column) and total number of infected people ("Total" right column). The black curve shows the weekly observed mean daily case numbers until 21 November 2021, whereas the black dots show the corresponding daily case numbers until 12 December. In popIBM, the vaccine effectiveness against infection is 60-80%, whereas the reduction in transmission risk falls in the 50-80% range for vaccinated individuals.

Figure B.1.2 shows the evolution in new admissions in the modelled scenario from the latter model memo and observed new admissions until 12 December 2021. This figure also shows that new admissions have increased but remain within the range defined by popIBM and popEKF.





Figure B1.2. New admissions ("Nyindlæggelser") in two different models by unvaccinated ("Uvaccineret" left column), vaccinated ("Vaccineret" centre column) and total number of infected people ("Total" right column). The projection from popIBM is shown in orange until 26 December. The projection from popEKF is not subdivided by vaccination status but shown in purple in the right column until 19 December 2021. The black curve shows, week by week, the observed mean daily new admissions until 21 November 2021, whereas the black dots show the corresponding daily numbers until 12 December. In popIBM, the vaccine effectiveness against infection is 60-80%, whereas the reduction in transmission risk falls in the 50-80% range for vaccinated individuals.



Appendix 2. Model updates from pop9 to pop10

- An extra age group was added with corresponding contact matrices. Thus, the model now has a total of 10 age groups.
- Waning immunity was added (B.2.1)
- The model was extended to comprise two virus variants (B.2.2)
- Gradual adaptive behaviour was added in which the overall activity level is reduced corresponding to half of the January 2021 lock-down. At a daily case number of approx. 17,000, this limitation has full effect (B.2.3).
- An overall factor was added to the risk of being admitted to hospital; this factor is updated separately for each region. This test is introduced to compensate for the fact that more infected people will only test positive at admissions, which distorts the admission risk estimate.
- A few changes were made to the under-reporting estimates, partly because new age groups need to be assigned a figure, partly because the model assumes that a difference exists between the behaviour of vaccinated and unvaccinated people. See Table B.2.1.
- Optimisation is based on a 9-week rather than a 7-week period to increase the robustness of the initial conditions. Concurrently, the initialisation method was adjusted to better take any significant curvature of the case numbers into account.
- The maximal vaccine effectiveness for persons below 20 years of age was set to 95% for all runs.
- Optimisation affects the Delta variant only, and a share of the infected people is reassigned at the simulation start on 5 December as infected by the Omicron variant based on the national age distribution.

Age	0-4	5-11	12-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
Unvaccinated	25%	50%	50%	50%	35%	35%	40%	70%	70%	70%
Vaccinated	25%	50%	50%	50%	50%	50%	60%	70%	70%	70%

Table B.2.1: Assumptions in pop10 about the likelihood of testing positive when you have become infected.

B.2.1 Implementation of waning immunity

Persons who have been vaccinated against SARS-CoV-2 achieve protection against becoming infected with the virus and additionally achieve protection against becoming seriously ill (including against admission to hospital) with COVID-19 if they become infected despite their vaccination. The protection against infection and the protection against serious disease will expectedly be waning over time but not necessarily at the same speed. Several studies have



reported a rapidly decreasing protection against infection over time, whereas good vaccine protection against admission with COVID-19 over time was reported^{14,15,16}.

Waning immunity to infection for individuals

Exponential decay of immunity is assumed starting from maximal immunity. This means that if an individual has maximal protection $VE_{maks} t = t_2$ [66], then the individual will have the time-dependent protection

$$F(t) = VE_{maks} \exp(-\omega_2(t-t_2))\theta(t-t_2)$$

where $\theta(t)$ is the Heavyside step function, ω_2 is a decay parameter for the effect of the second dose, defined as a 20-35% decline after six months¹⁷.

The combination of the Heavyside step function and exponential decay means that until a person is vaccinated, he or she has no immunity against infection, whereas a person achieves maximal protection upon concluded vaccination, after which the protection decays exponentially.

It is assumed that revaccination raises protection to the maximal level achieved by receiving the second vaccination dose. The time at which revaccination takes effect is termed t_3 and the corresponding decay constant ω_3 . Then, the total protection achieved by the vaccinated person is:

$$F(t) = VE_{maks} \left(\exp(-\omega_2(t-t_2)) \theta(t-t_2) \theta(t_3-t) + \exp(-\omega_3(t-t_3)) \theta(t-t_3) \right)$$

No data are available on waning immunity of revaccination, but the effect is expected to decline with time. As the effect will expectedly recede more slowly than that of the previous doses, it is assumed that revaccination declines by approx. 15% in the course of six months, i.e. half the distance between the effect of the second dose and no decline.

¹⁴ Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study - The Lancet

¹⁵ Waning Immunity after the BNT162b2 Vaccine in Israel | NEJM

¹⁶ Effectiveness of Covid-19 Vaccination Against Risk of Symptomatic Infection, Hospitalization, and Death Up to 9 Months: A Swedish Total-Population Cohort Study by Peter Nordström, Marcel Ballin, Anna Nordström :: <u>SSRN</u>

¹⁷https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1027920/S1 386_SPI-M_potential_winter_trajectories_Imperial_College.pdf





Figure B.2.3 shows an example of the protection an individual has over time in the model.

Figure B.2.1: Example of the model description of waning immunity for a person who receives the first vaccine dose after three weeks, the second dose after an additional four weeks and revaccination after an additional 28 weeks. Three weeks after the initial dose, the individual reaches maximal protection and this protection starts declining once the person has concluded vaccination. One week after the person has received revaccination, protection once again reaches the maximal level followed by a more slowly waning immunity. The blue line indicates protection against infection where the coloured areas thus show the model's sample space. The red line indicates protection against admission that does not wane. Please note that VE_{max} is higher against admission than against infection.

Waning immunity to infection in a population

In an individual based model, the above description is sufficient, but a population model needs to take the share of the population that has received booster vaccination into account.

The number of persons who achieve an effect from the second and third doses at the time t are termed $f_2(t)$ and $f_3(t)$, respectively. The total number of people who have concluded vaccination and in whom the vaccination has taken is therefore:

$$F_2(t) = \int_0^t f_2(t_2) dt_2$$

whereas the total number of persons who have received a revaccination dose is:

$$F_3(t) = \int_0^t f_3(t_3) dt_3$$

and the remaining effect of vaccination at the time is:

$$F_2^w(t) = \int_0^t \exp(-\omega_2(t-t_2)) f_2(t_2) dt_2$$

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$$F_3^w(t) = \int_0^t \exp(-\omega_3(t-t_3)) f_3(t_3) dt_3$$

The relative effect of the two vaccines is weighted by the share of vaccinated people who have received revaccination $\frac{F_3(t)}{F_2(t)}$, which yields the total vaccine effectiveness for a population as a function of time:

$$F(t) = V E_{maks} \left(\frac{F_2^w(t)}{F_2(t)} \left(1 - \frac{F_3(t)}{F_2(t)} \right) + \frac{F_3^w(t)}{F_3(t)} \frac{F_3(t)}{F_2(t)} \right)$$

The final terms may be simplified, but it has been stated in full to make it clear where each factor comes from. This vaccine effectiveness is calculated for each age group.

Waning immunity against admission

In the models, we assume that no waning effect exists against hospital admission with COVID-19.

B.2.2. Implementation of the Omicron variant

The model is updated to describe concurrent infection with the Delta variant and the new Omicron variant. As has been the case when new variants emerged in the past, the model comprises four tracks describing the spreading of SARS-CoV-2; two tracks for each variant, one describing vaccinated and another describing unvaccinated people. See Figure B.2.2 for an overview of the updated model structure.



Figure B.2.2. Diagram of the model structure. The model was extended to describe the two virus variants (A: the Delta variant) and (B: the Omicron variant). Structurally, the two variants were introduced in the same manner into the model, apart from the fact that people infected with the Omicron variant may infect persons who have previously become infected with the Delta variant. Please note that there are also considerable differences in the



interaction of each variant with the vaccinated citizens and that the transmission and admission risks vary between variants.

In the model, the Omicron variant is different from the Delta variant in two ways:

1) the Omicron variant is assumed only to infect citizens who have passed Delta variant infection, whereas the opposite is not assumed.

2) the Omicron variant is assumed to have a reduced susceptibility to vaccination. This is implemented as a lower maximal VE and as a more quickly waning protection (against infection) for the Omicron variant than for the Delta variant (see Figure B.2.3). Thus, a good, but more short-lived protection against infection with the Omicron variant is assumed among persons who have recently received revaccination.

The more rapidly waning immunity is controlled by a parameter that varies between 2.5 and 3; values that are coined moderately waning immunity and rapidly waning immunity (for the Omicron variant). Figure B.2.3 shows an example using the parameter value 2.5.



Figure B.2.3: Example model description of vaccine protection against infection with the Delta variant (blue curves) and the Omicron variant (green curves). The coloured areas show the sample space of the model.

B.2.3. Implementation of adaptive behaviours in pop10

In pop10, a model for adaptive behaviour was implemented. Thus, when the incidence exceeds 280 cases per 100,000 in a region, the activity level is reduced gradually until an incidence of 2,100 is reached, at which level it is assumed that the activity corresponds to half of the activity recorded during the January 2021 lock-down. The threshold of concern for municipalities is an incidence of 400, which is multiplied by 0.7 to take into account the fact that the region will



have a lower mean incidence than will be the case in the municipalities with the highest incidence.

Compared with the real world, adaptive behaviour kicks in faster in the model as behaviour is based on the current incidence level and not the reported level, which usually carries a few days of delay. Real-world behavioural changes will also to a higher degree be driven by individual events like, e.g., press briefings, whereas these changes are implemented in the model as gradual changes.



Figure B.2.6: Adaptive behaviour in the five regions in the model runs. Rows state the relative transmission rate for Delta and Omicron. Furthermore, moderately waning (red) and rapidly waning (green) VE are shown. In this presentation, 0 corresponds to no adaptive behaviour and 1 to the activity level observed in January 2021. It is assumed that the population as a whole will not reduce the activity level in complete absence of official restrictions; therefore, the upper limit is set to 0.5.

B.2.4. Algorithm for the projection of vaccine rollout

This section describes the algorithm used to project the upcoming vaccine rollout. The algorithm comprises two parts: one is used to project the number of persons who complete their vaccination course over time, and another that is used to project the number of persons who receive revaccination.

The algorithm takes its starting point in the time trend of recorded doses administered in each vaccine target group. To project the number of persons vaccinated, the model bases calculations on a reference week, which is defined as the past week (Week 49). The first part of the algorithm assumes that as many people as initiated their vaccination course in the reference week will initiate their vaccination course in each of the projected weeks.

The projection of vaccines is processed differently for the 5-11-year-olds and for citizens aged more than 12 years of age. For the 12+ year-olds, the model assumes that when the coverage



reaches 90% in a given target group, no more new vaccination courses will be initiated in the target group. Furthermore, when the coverage of the vaccination programme overall reaches 90%, it is assumed that no more vaccination courses will be initiated in any target group.

For the 5-11-year-olds, it is assumed that the vaccination rollout will continue at the same speed as observed in Week 49 until the coverage reaches 57.3%, after which the model assumes that no more vaccination courses will be initiated. This coverage level was selected based on the coverage among the 12-year-olds, which was approx. 66% at the time the algorithm was run. Based on a vaccination willingness study from the Hope Project¹⁸, the vaccine uptake among 5-9-year-olds was adjusted downwards.



Figure B.2.5: Initiation of vaccination courses according to model assumptions. The period leading up to the dotted line was established based on the recorded doses, whereas the period after the dotted line shows the projection produced by the algorithm.

The second part of the algorithm projects the number of persons in each target group who receive revaccination when they are offered the third dose. The algorithm is based on the number of revaccinations administered within the past 14 days. First, the coverage of revaccination is estimated in combination with target groups and age groups. The share of persons who have had the opportunity to receive revaccination and who have received revaccination is used to project the share who will accept their third dose in the period covered by the simulation. The time of revaccination is initially determined based on the waiting-time distribution observed in the previous 14 days for various target groups and age groups. This time point is then adjusted to take into account the recently introduced shorter intervals between

¹⁸ <u>https://psyarxiv.com/8e49j/</u>



concluded vaccination and revaccination and the objective that 3.5 million receive revaccination before end of year 2021.

In the used vaccination rollout, the objective that 3.5 million citizens receive revaccination at the turn of year is thus met. It deserves mention that uncertainties in the estimated revaccination coverage means that more citizens below 40 years of age have advanced their revaccination than expected based on the recommendation of a 5.5-month interval between concluded vaccination and revaccination in this group. This may cause a bias towards lower age groups in the vaccination rollout model used than may be expected given the objective to achieve 3.5 million booster vaccinations by the turn of year.



Figure B.2.6: Share of vaccinated citizens who accept revaccination. The period leading up to the dotted line was established based on the recorded doses, whereas the period after the dotted line shows the projection produced by the algorithm.