Genomic surveillance of SARS-CoV-2 in Belgium

Report of the National Reference Laboratory (UZ Leuven & KU Leuven)

Situation update – 25th of January 2022
(report 2022_65)
Modified version (27/01/2022): minor changes highlighted in italics

Executive summary

81,367 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID; compared to last week's report, 1,151 sequences have been added.

1,919 sequences of positive SARS-CoV-2 samples collected in the context of baseline surveillance between 10/01 and 23/1/2022 have at this stage been analyzed. For those samples, Omicron (BA.1 and BA.2) represented 96.5% (94.4% and 2.1% respectively) of the strains analyzed. Furthermore, 3.3% of samples were characterized as Delta. A first BA.3 family cluster has been detected in Belgium.

Authors (National Reference Laboratory – UZ Leuven and KU Leuven):
Lize Cuypers, Guy Baele, Piet Maes, Simon Dellicour, Louis Nevejan, Tom Wenseleers, Bram Slechten, Johan Van Weyenbergh, Els Keyaerts, Joren Raymenants, Barney Potter, Sunita Janssenswillen, Elke Wollants, Marc Van Ranst, Emmanuel André.

With the collaboration of the laboratories of UCL, ULB, UMons, UNamur, ULiège, UGent, UZA/UAntwerpen, Jessa ZH, AZ Delta, AZ Klina, IPG, AZ St Lucas Gent, OLVZ Aalst, Briant network, ZNA, AZ St Jan Brugge, UZ Brussel, LHUB-ULB, and UZ Leuven/KU Leuven; and Sciensano HealthData.

Previous reports can be downloaded using the following link:
https://www.uzleuven.be/nl/laboratoriumgeneeskunde/genomic-surveillance-sars-cov-2-belgium

Table of contents

1. Monitoring of VOCs in Belgium

Although the B.1.1.529 (BA.1) Omicron- Variant of Concern was first identified on the 24th of November 2021 in Belgium, it has become the dominant lineage in Belgium a month after the first case was detected. This viral population replacement has happened at a very rapid pace (Figure 1). This replacement has also been observed among people hospitalized with COVID-19, as the BA.1 sublineage of Omicron is now responsible for the majority of new hospital admissions for severe & critical COVID-19 disease (Figure 3). Currently, through data from Sciensano, we are aware of 194 hospitalized patients with a BA.1 infection, *of which vaccination status is currently being verified.* The Omicron sublineage BA.2 received Variant Under Investigation (VUI) status last week by the UK Health Security Agency (UKHSA); in Belgium this variant was first discovered in Belgium on *December* 26, 202*1*. One patient was identified with sublineage BA.3 last week on January 16, 2022.

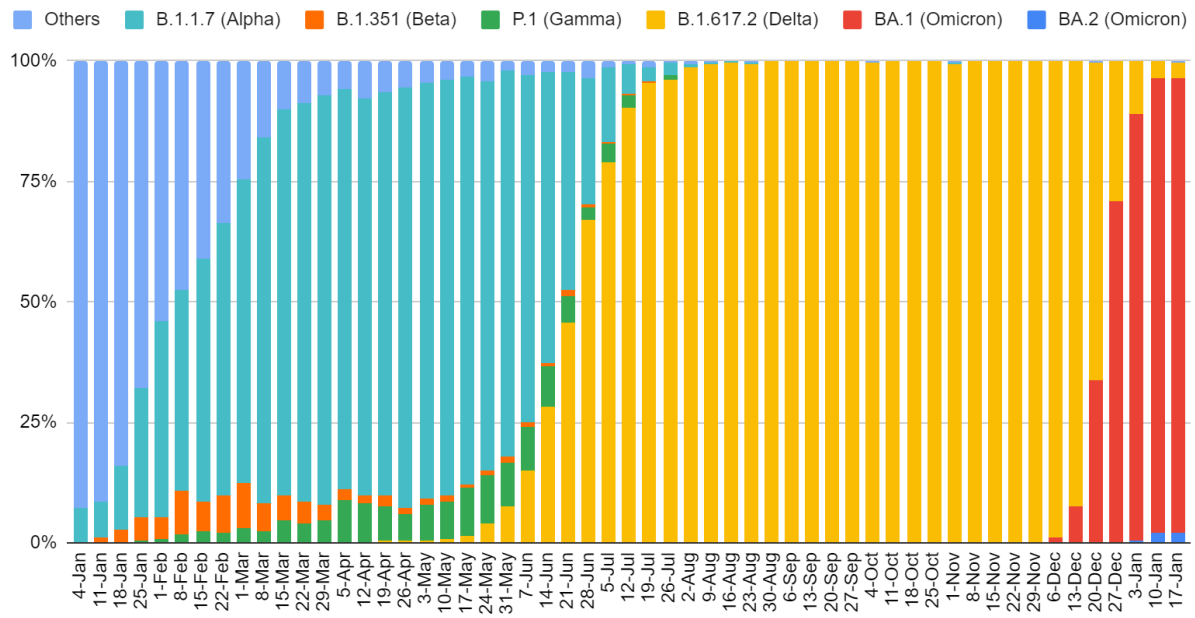

Figure 1: *Weekly evolution of the frequency of variants of concern reported by the* ***baseline surveillance*** *network using a whole genome sequencing (WGS) approach.*

2. Disease severity associated with Omicron infections

We looked at the severity of disease among 216 patients admitted with a new COVID-19 infection in UZ Leuven University Hospitals between 13 December 2021 and 16 January 2022. A genotyping result was available at this stage for the majority of the patients.

During the last period evaluated (Weeks 2&3 2022), Omicron was identified among 83% (10/12) of the patients for which a lineage was yet available and that were classified with severe or critical disease or who have evolved towards a fatal outcome.

While the situation during the previous weeks were in line with a milder severity of Omicron compared to Delta (Figure 4), the more recent hospital admissions rather highlight the intense circulation of Omicron in the community, inevitably resulting in an increase of severe Omicron-related infections. Due to the limited numbers, we cannot yet assess the severity of BA.2 and BA.3.

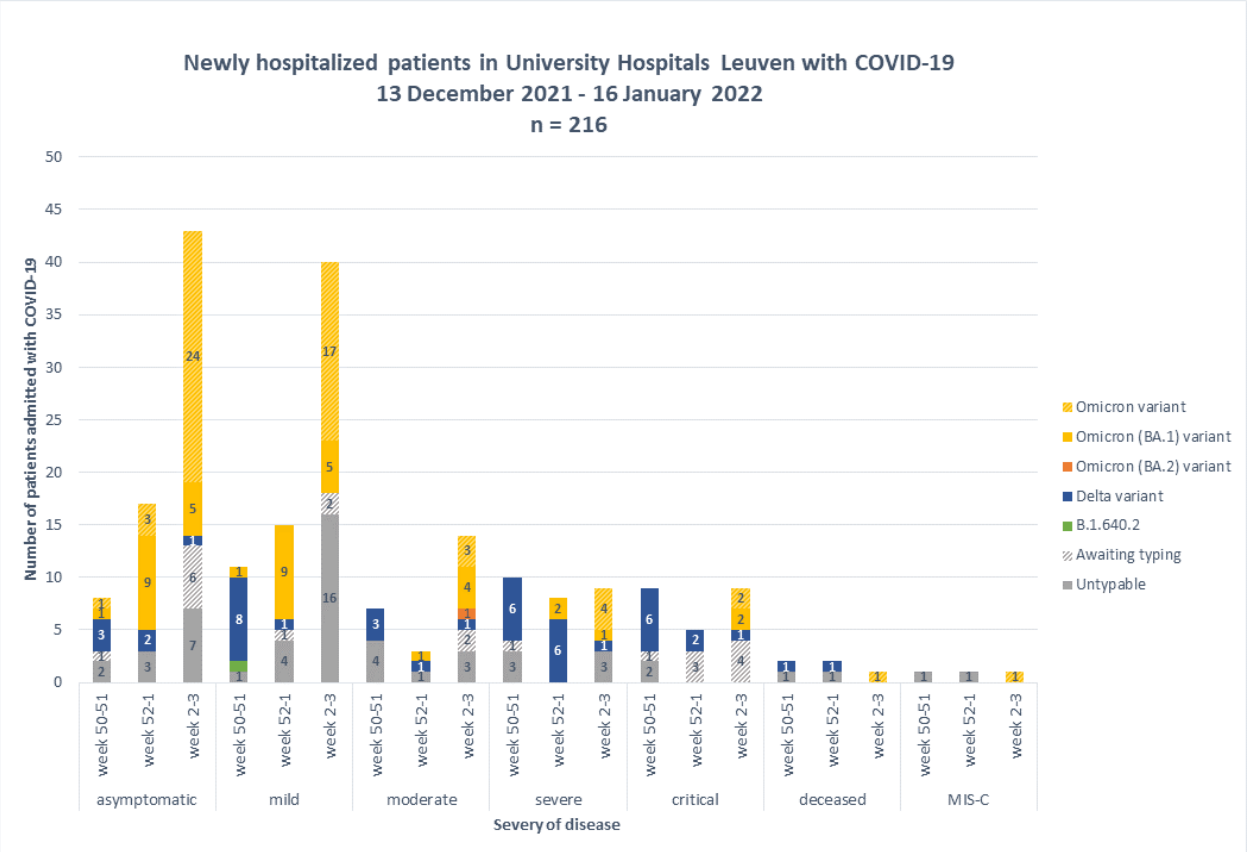

Figure 2: *Severity of disease among 143 patients admitted with COVID-19 to UZ Leuven University Hospitals (13 December 2021 to 16 January 2022).*

3. Epidemiological evolution in Denmark and the United Kingdom with regard to BA.2

Initial analysis of data from Denmark shows no differences in hospitalisations for BA.2 compared to BA.1. Analyses regarding infectiousness and vaccine efficiency etc. are ongoing. It is expected that vaccines also have an effect against severe illness upon BA.2 infection (source).

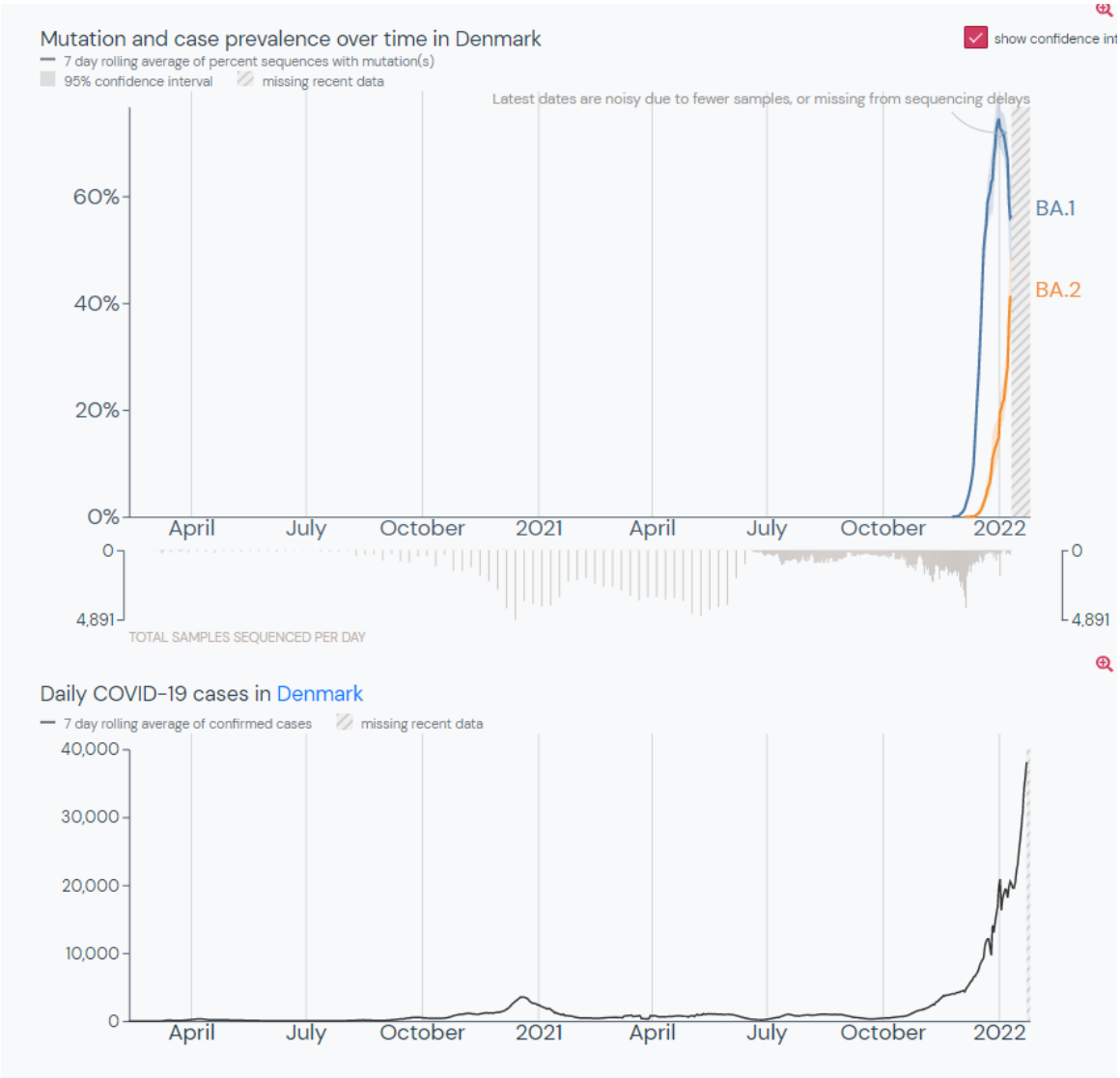

***Figure 3**: Epidemiological evolution in Denmark. BA.2 is now becoming dominant, but the impact of this new variant on the dynamic is yet unclear. Anecdotal reports suggest some patients can be infected with BA.2 shortly after having been infected with BA.1 (source)*

Overall, the original Omicron lineage, BA.1, remains dominant in the UK and the proportion of BA.2 cases is currently low. To date, there have been 426 cases of Omicron BA.2 confirmed by Whole Genome Sequencing (WGS), with the earliest dated 6 December 2021. The areas with the largest number of confirmed cases are London (146) and the South East (97).

Early analyses suggest an increased growth rate compared to BA.1, however, growth rates have a low level of certainty early in the emergence of a variant and further analysis is needed. (source)

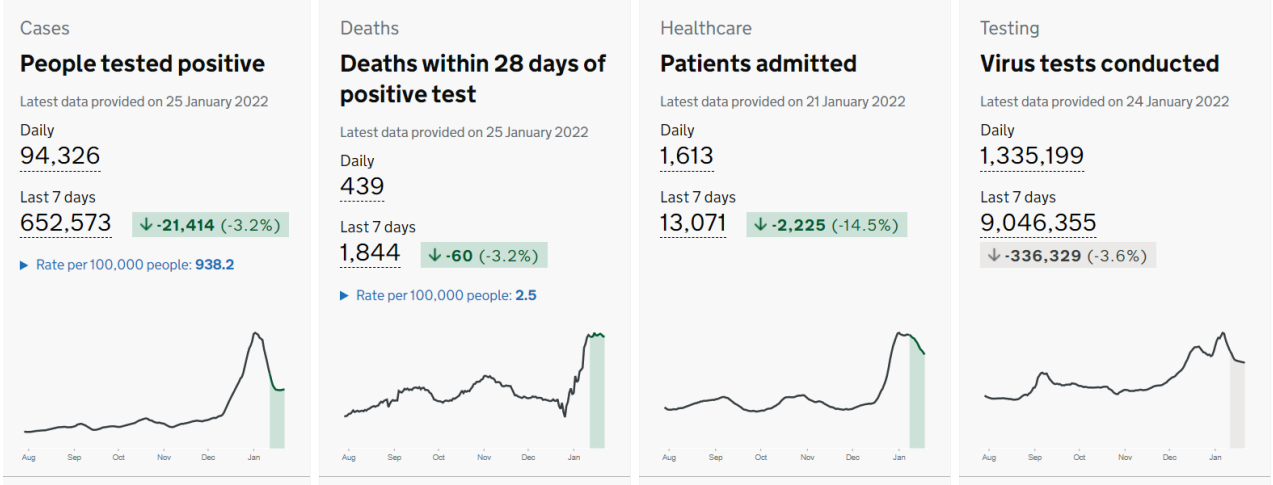

***Figure 4**: Epidemiological evolution in the United Kingdom. The decrease in the number of cases has stopped, but BA.2 cannot be incriminated, as this sub-lineage remains limited at this stage. This recent evolution may therefore be associated with a recent change in disease control restrictions* (Source)

4. Clinical study initiated on Omicron-based vaccine candidate (Pfizer & BioNTech)

Pfizer and BioNTech today (January 25th, 2022) announced the initiation of a clinical study to evaluate the safety, tolerability and immunogenicity of an Omicron-based vaccine candidate in healthy adults 18 through 55 years of age. The study will have three cohorts examining different regimens of the current Pfizer-BioNTech COVID-19 vaccine or an Omicron-based vaccine. The study will draw upon some participants from the companies' Phase 3 COVID-19 booster study and is part of their ongoing efforts to address Omicron and determine the potential need for variant-based vaccines.

The study will evaluate up to 1,420 participants across the three cohorts:

- Cohort #1 (n = 615): Received two doses of the current Pfizer-BioNTech COVID-19 vaccine 90-180 days prior to enrollment; in the study, participants will receive one or two doses of the Omicron-based vaccine
- Cohort #2 (n = 600): Received three doses of the current Pfizer-BioNTech COVID-19 vaccine 90-180 days prior to enrollment; in the study, participants will receive one dose of the current Pfizer-BioNTech COVID-19 vaccine or the Omicron-based vaccine
- Cohort #3 (n=205): Vaccine-naïve participants will receive three doses of the Omicron-based vaccine

Pfizer said it expects initial findings from the study, which will enroll to be available during the first half of 2022. The study will not be large enough that it would be expected to necessarily give data on how strategies compare in terms of how many people are infected or develop COVID symptoms.

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-study-evaluate-omicron-based

https://www.statnews.com/2022/01/25/pfizer-biontech-begin-trial-omicron-based-vaccine/

5. SARS-CoV-2 breakthrough infections elicit potent, broad and durable neutralizing antibody responses (Walls et al., 2022, Cell)

Infections among vaccinated individuals lead to milder COVID-19 symptoms relative to unvaccinated subjects. A few days ago (January 20th, 2022), an accepted manuscript appeared in Cell in which Walls et al. demonstrate that breakthrough infections induce serum binding and neutralizing antibody responses that are markedly more potent, durable and resilient to spike mutations observed in variants than those in subjects who received only two doses of vaccine. To understand whether the sequence of infection and/or vaccination as well as repeated exposures alter the specificity, magnitude, and breadth of antibody responses, Walls et al. followed and compared serum antibodies in individuals who were vaccinated, previously infected and then vaccinated, or vaccinated and then infected predominantly with the SARS-CoV-2 Delta variant.

Walls et al. show that breakthrough cases, subjects who were vaccinated after infection and individuals vaccinated three times have serum neutralizing activity of similar magnitude and breadth, indicating that an increased number of exposures to SARS-CoV-2 antigen(s) enhance the quality of antibody responses. Neutralization of SARS-CoV was, however, moderate underscoring the importance of developing vaccines that elicit broad immunity against sarbecovirus for pandemic preparedness.

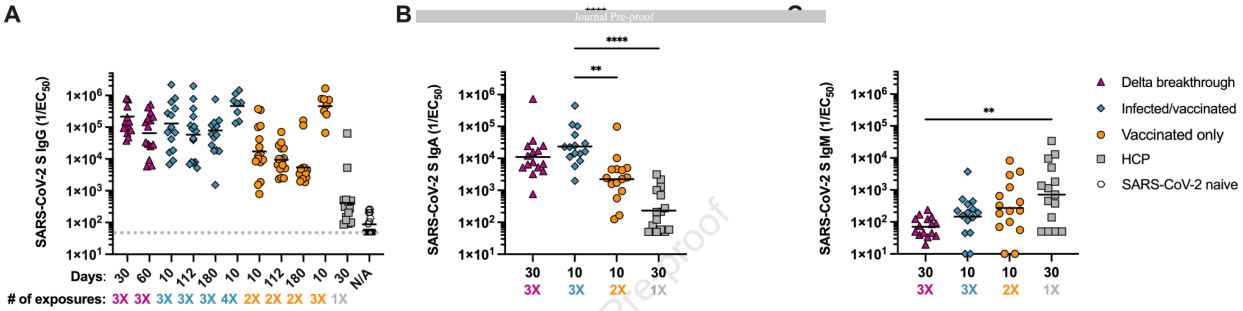

Figure 5: *Serum IgG, IgA, and IgM binding titers were evaluated using ELISAs with the SARS-CoV- 2 Hexapro S antigen (Hsieh et al., 2020). Antibody responses were highest amongst individuals who were exposed to SARS-CoV-2 S three or four times through vaccination or a combination of infection and vaccination. The magnitude of IgG responses for vaccinated individuals who experienced a breakthrough infection was greatest 30 days post-positive PCR test and reduced ~3 fold by day 60. HCP: human convalescent plasma.*

These data suggest that repeated exposures through vaccination, infection or a combination of both induce potent polyclonal serum antibody binding titers. Furthermore, Walls et al. observed a greater durability of binding geometric mean titers (GMTs) over 180 days for the infected/vaccinated relative to the vaccinated-only (two doses) cohorts, which could result from increased number of exposures, different exposure spacing (Parry et al. 2021), or due to actual infection versus vaccination-only.

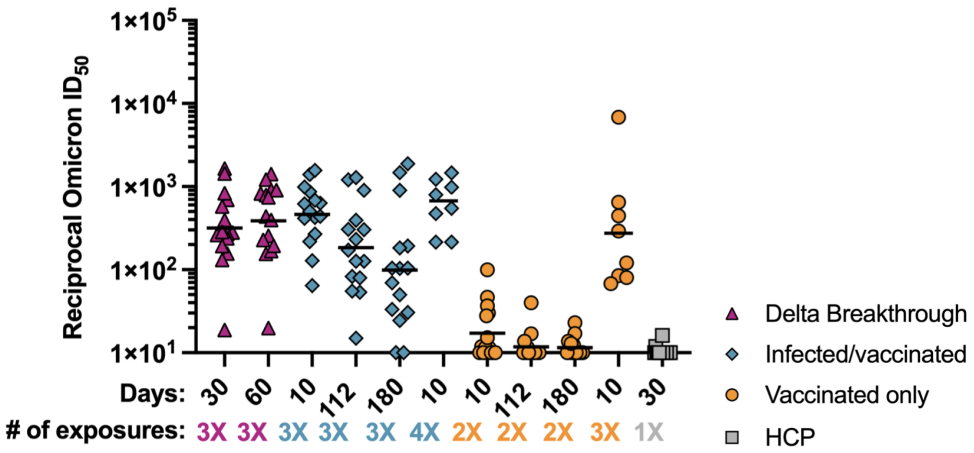

Figure 6: *Evaluation of serum neutralizing activity of breakthrough, infected/vaccinated, or triple vaccinated individuals against Omicron. Breakthrough cases experienced a ~7-8 fold decrease in neutralization potency compared to vesicular stomatitis virus (VSV) pseudotyped with SARS-CoV-2 G614 S. Infected/vaccinated individuals experienced a ~6.6 fold decrease in neutralization capacity after 10 days, 14-fold decrease after 112 days, and an 18-fold decrease after 180 days compared to G614 VSV S. Vaccinated-only (2 doses) subjects experienced ≥11-22-fold reductions of neutralizing GMTs against Omicron versus G614 S VSV, which are likely underestimates due to the limit of detection of the assay. Following a third vaccination, Walls et al. observed enhanced neutralizing activity against Omicron for both infected/vaccinated subjects (1.3-fold GMT rise compared to 10 days post second dose) and vaccinated-only individuals (16-fold GMT rise compared to 10 days post second dose), in agreement with recent data (Garcia-Beltran et al., 2021).*

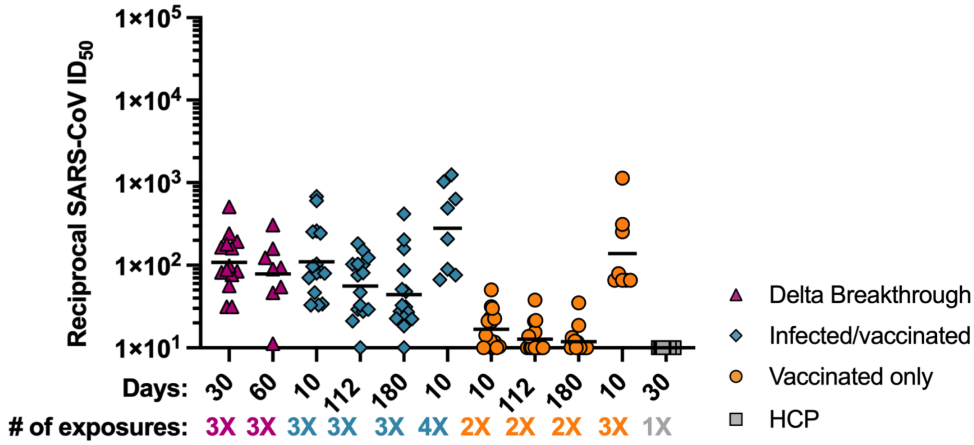

Figure 7: The reduction of serum neutralizing activity against SARS-CoV following up to three SARS-CoV-2 S exposures, along with previous studies (Martinez et al., 2021; Stamatatos et al., 2021; Walls et al., 2021a), suggest that combinations of COVID-19 disease and vaccination would leave the population more vulnerable to infection by a genetically divergent sarbecovirus. However, four exposures to SARS-CoV-2 S, through infection followed by three vaccinations, elicit SARS-CoV serum neutralizing titers with a magnitude that is equivalent to protective levels for SARS-CoV-2 based on clinical trial evaluation of COVID-19 vaccines (Baden et al., 2021; Polack et al., 2020). These findings suggest that repeated exposures may improve elicitation of broadly neutralizing sarbecovirus antibodies, but not broadly reactive betacoronavirus antibodies based on the comparable cross-reactive responses to OC43 and HKU1 S observed for all cohorts. Moreover, a recent study indicated that survivors of SARS-CoV infection

who subsequently received a COVID-19 vaccine had broader sarbecovirus neutralizing antibody responses than subjects only exposed to SARS-CoV-2 virus or vaccine (Tan et al., 2021b). These data lend further support to the ongoing development of several vaccine candidates (Cohen et al., 2021; Martinez et al., 2021; Walls et al., 2021) designed to specifically elicit broad sarbecovirus immunity and could protect against SARS-CoV-2 variants and putative future zoonotic sarbecoviruses.

https://www.sciencedirect.com/science/article/pii/S0092867422000691