Alpha variant coronavirus outbreak in a nursing home despite high vaccination coverage: molecular, epidemiological and immunological studies

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Summary:

A SARS-CoV-2 outbreak investigation in a nursing home identified 17 individuals with positive PCR tests, despite 82% mRNA vaccination coverage. Transmission networks constructed based on epidemiological, phylogenetic and immunological data indicated four transmissions from vaccinated to other individuals, and 12 transmission events from unvaccinated individuals.

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ABSTRACT

Background: Vaccination may control the COVID-19 pandemic, including in nursing homes where many high-risk people live. We conducted extensive outbreak investigations.

Methods: We studied an outbreak at a nursing home in Switzerland where vaccination uptake of mRNA vaccines against SARS-CoV-2 was 82% among residents as of Jan 21/2021. After a vaccinated symptomatic HCW was diagnosed with COVID-19 on Feb 22, we did an outbreak investigations in house A (47 residents, 37 HCWs) using SARS-CoV-2-specific PCR in nasopharyngeal swabs. We performed whole-genome sequencing of SARS-CoV-2 and serological analyses.

Results: We identified 17 individuals with positive PCR tests; ten residents (five vaccinated) and seven HCWs (three vaccinated). Median age among residents was 86 years (interquartile range [IQR] 70-90) and 49 years (IQR 29-59) among HCWs. Among the five vaccinated residents, 60% had mild disease and had 40% no symptoms, whereas all five unvaccinated residents had mild to severe disease and two died. The vaccine effectiveness for the prevention of infection among the residents was 73.0% (95% CI 24.7-90.1). The 12 available genomes were all alpha variants. Neutralizing titers were significantly higher in vaccinated individuals upon re-exposure (>1 week after diagnosis) than in vaccinated, unexposed HCWs (p=0.012). Transmission networks indicated four likely or possible transmissions from vaccinated to other individuals, and 12 transmission events from unvaccinated individuals.

Conclusions: COVID-19 outbreaks can occur in nursing homes, including transmission from vaccinated persons to others. Outbreaks might occur silently, underlining the need for continued testing and basic infection control measures in these high-risk settings.

Key words: COVID-19, outbreak, UK variant, B.1.1.7, vaccine, nursing home

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global public health threat (1). A large proportion of the global population remains susceptible to COVID-19 (2). By the end of May 2021, safety and efficacy data had been published for several vaccines (3-6). Clinical trials of mRNA vaccines against SARS-CoV-2 showed promising results with vaccine efficacy of over 90% against symptomatic and severe disease (3, 4).

The Swiss vaccine campaign started in December 2020 with two mRNA vaccines (Pfizer-BioNTech/Moderna) (7, 8). The vaccine campaign prioritized people at increased risk, such as nursing home residents, healthcare workers (HCWs), the elderly (age 75 years or older), and people with severe chronic diseases regardless of their age. Since May 2021, mRNA vaccines have been accessible to the entire Swiss population (9). At the beginning of July, almost 50% of the total Swiss population have received at least one dose of an mRNA COVID-19 vaccine, and about 30% were completely vaccinated (10).

Nursing homes are critical institutions in this pandemic due to their high-risk resident population (11). Outbreaks associated with SARS-CoV-2 in nursing homes have been previously described (12, 13). After a case in a nursing home in Switzerland with high mRNA vaccination coverage in February 2021, we conducted extensive outbreak investigations to explore in detail the transmission events using epidemiological, molecular epidemiological, and immunological methods.

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METHODS

Study site

We conducted this study at a nursing home in the canton of Solothurn, Switzerland, with a capacity of 93 residents in two houses. The nursing home was one of the first in the canton to start vaccinating their HCWs and residents. The mRNA vaccine from Pfizer/BioNTech (BNT162b2) was used, following the manufacturer's instructions. The first dose was given on Dec 29, 2021 and the second on the Jan 21, 2021, to all residents and HCWs willing to be vaccinated. We present an outbreak in February 2021 in house A that did not spread to house B. House A consists of four floors providing housing for 47 residents (Figure S1). A total of 37 HCWs worked in house A during the outbreak.

Data collection

Epidemiological investigations

We collected detailed histories of contacts between HCWs and residents, between residents, and between HCWs. On the day after the first case on February 22, nasopharyngeal swabs were taken for SARS-CoV-2 polymerase chain reaction (PCR) testing from all close contacts. Later, on Feb 25, Mar 3, Mar 8, and Mar 13, PCR testing in nasopharyngeal swabs were repeated among all HCWs and residents in house A (Figure 1 and Figure S2). There was no case in house B. To document each resident's room, we elaborated a floor plan of house A (Figure S1, Table S1). We collected data of all COVID-19 cases, including age, sex, dates of vaccination, symptoms, co-morbidities, and clinical outcomes. SARS-CoV-2 PCR data (Viollier AG, Allschwil, Switzerland) included the date of PCR and result, and the cycle threshold value (ct).

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Serological analyses

The humoral immune response during the outbreak and immunogenicity of mRNA vaccine was assessed by ABCORA, a bead-based multiplex immunoassay using the Luminex technology to measure specific IgG, IgA, and IgM responses to SARS-CoV-2 subunits of the Spike protein (RBD, S1, S2), and Nucleocapsid (N) protein (14). Positive reactivity for each antigen-antibody class combination is reported as signal-over-cut-off (SOC) (14). Infection and vaccination both give rise to spike protein antibody responses, whereas N protein antibody responses are only present in infected individuals. IgM and IgA reactivity indicates recent immune stimulation. Serology was performed during the outbreak and at least one week after the first sample to analyze seroconversions (T1: 1-18 days, T2 16-30 days after positive PCR test, Figure S2). Samples were assessed for neutralization activity against the vaccine strain Wuhan-Hu-1 using a SARS-CoV-2 pseudovirus neutralization test through the seroreactivity to S1 and RBD in the ABCORA test and directly in a cell-based neutralization test (14). We present results as 50% serum neutralization titers (NT50) and as neutralization index(14). To reassure all employees who were vaccinated, we offered to measure their serological status at the time of the outbreak. A total of 30 vaccinated HCWs participated.

Genomic analyses

We performed whole-genome sequencing of viral RNA whenever the viral quantity in the nasopharyngeal swab sample allowed it. SARS-CoV-2 genomes were sequenced and assembled (15). Out of 17 samples, twelve high-quality whole genomes were assembled and deposited in GISAID (https://www.gisaid.org, Table S2) (16, 17).

Global sequences and metadata were downloaded from GISAID on May 7 2020 (2,802,328 consensus sequences) to investigate possible community sources of infection. The suspected source of infection was Switzerland and, more precisely, the cantons of Solothurn and neighboring cantons. We included all deposited alpha (B.1.1.7) sequences

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collected between Jan 1, 2021, and Mar 10 2021, in Switzerland (4,346 as of May 7 2021) for phylogenetic inference using the nextstrain analysis pipeline v.3.0.3 and augur v.12.0.0 (18, 19). Viral lineages, according to PANGO nomenclature (20), and potential transmission clusters were determined.

Transmission network

We combined epidemiological, serological and genomic data to create a transmission network. The criteria for defining transmission links as likely or possible were based on 1) date of symptoms, 2) date of PCR tests, 3) contact and behavior of the individuals, 4) genomic analyses, 5) PCR ct values (lower levels show higher viral loads indicating a higher transmission potential), 6) level of neutralizing antibodies (lower levels may indicate a higher transmission potential).

Definitions

Severe disease was defined as a persistent temperature, reduced general condition, developing shortness of breath or pneumonia, and requiring hospitalization or supplemental oxygen. Individuals with severe disease are generally ill for two to four weeks. Mild disease was defined as individuals who become infected and experience mild symptoms for just a few days. We defined an asymptomatic case as a person having no symptoms at any time.

Statistical analysis

We used descriptive statistics to describe the characteristics of the residents and HCWs involved in the outbreak. We calculated the vaccine effectiveness using the “csi” command

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and the corresponding 95% confidence interval (95%CI) using binomial distributions. All analyses were performed in Stata (version 16.0, Stata Corp., College Station, USA).

Ethics statement

The cantonal public health authorities' outbreak investigation and data collection were based on the Communicable Diseases Legislation (Epidemics Act). No separate ethical approval was obtained in line with Swiss law.

RESULTS

The first infection was diagnosed on Feb 22, 2021, in a symptomatic HCW (Figure 1A). On Feb 23, house A residents were quarantined and close contacts of the index case tested with a SARS-CoV-2 PCR; an unvaccinated resident and unvaccinated HCW tested positive. Four rounds of PCR testing followed. The first and second screening round of nasopharyngeal swabs detected five infected persons and the third another three persons. Seventeen persons were diagnosed with SARS-CoV-2; ten (21%) of 47 residents and seven (19%) among 37 HCWs. The outbreak was confined to the second floor of house A, except for one infected resident on the third floor. Figure 1B shows the epidemic curve by date of symptoms onset. The comparison with Figure 1A demonstrates that repetitive screening detected several cases before symptom onset. At the time of the outbreak, vaccination coverage in the nursing home was 82% among residents and 51% among HCWs.

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Characteristics of infected individuals

The median age among the residents was 86 years (interquartile range (IQR) 70-90 years); seven were female (70%). The majority (7, 70%) suffered from at least one co-morbidity, most frequently hypertension. Fifty per cent (5/10) of residents were vaccinated

against SARS-CoV-2 (Table 1 and Table S3). Among the 10 SARS-CoV-2 infected residents, 8 (80%) reported symptoms. The two residents with asymptomatic infections (no symptoms) were vaccinated. Vaccinated residents showed mild disease or were asymptomatic. The five unvaccinated showed mild to severe disease, and two of them died.

The median age among the HCWs was 49 years (interquartile range [IQR] 29-59 years), and all were females. Four (57%) were unvaccinated, and the remaining three (47%) were vaccinated against SARS-CoV-2. The majority of infected HCWs were symptomatic (5, 71%, Table 1).

Vaccine effectiveness among residents

Among the 47 residents in house A, 37 (78.7%) were fully vaccinated against SARS-CoV-2, and 10 (21.3%) were not. Among the vaccinated, 5 (13.5%) were infected with SARS-CoV-2 and among the unvaccinated 5 (50%), for an estimated vaccine effectiveness against infection of 73.0% (95%CI 24.7-90.1). Table S1 and Figure S1 give further details on the residents and their vaccination status.

The vaccine effectiveness was not calculated for the HCWs as the denominator was not the same over the whole period, and some HCWs worked only one day during the outbreak and others several days.

Serological analyses

Of the 17 persons diagnosed with SARS-CoV-2, two persons provided no blood sample. Unvaccinated residents and HCWs showed low SARS-CoV-2 antibody reactivity at the first time point but seroconverted showing IgG responses to N and S antigens at the second time point (Figure 2 and Figure S3). Three of the vaccinated individuals revealed a good immunogenic response to the vaccine (no IgG N response) at the first time point, whereas

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five already showed reactivity to the infection, as reflected by high N-protein antibody levels at the first time point. At the second time point, 7/8 vaccinated individuals also developed an N protein antibody response. They showed increased RBD and S1 antibody responses, reflecting a boosted serological response to the vaccine antigen followed by infection (Figure 2 and Figure S3).

In line with prototypic antibody patterns in COVID-19 (21), we detected no neutralizing activity in unvaccinated individuals shortly after PCR diagnosis. Still, neutralization titers over the following weeks reached solid to high neutralization titers (NT50 >250) (Figure 3) (22). Two of the vaccinated individuals displayed no or very low neutralizing activity (NT50=123). The individual without neutralizing antibody response had cancer of unknown origin without cancer suppressive therapy. Neutralizing titers were significantly higher in vaccinated individuals upon re-exposure (black dots) than in vaccinated HCWs (HCWs, light blue) that had not been involved in the outbreak (p=0.012), highlighting a boost of neutralizing antibody activity following infection (Figure 3). Table S4 provides serological information on the vaccinated HCWs (not part of the outbreak) interested in knowing their serological status.

Molecular epidemiological analyses

Of the 17 nasopharyngeal samples, 12 had sufficient viral RNA for subsequent sequencing. All twelve genomes belonged to lineage Alpha/B.1.1.7 and were closely related. Among the 12 genomes, 9 (75%) were identical (0 single nucleotide polymorphism, SNP), and each of the remaining three had one additional SNP (Figure 4). All genomes clustered mostly with other genomes sequenced from Basel-Country. Genomes 17 (group b) and 16 (group c) had one additional SNP aligned with one and two genomes from the community, respectively.

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Transmission network

Table 2 shows the criteria which we applied to describe the transmission events according to the vaccination status and its directions within the transmission network. The transmission network is shown graphically in Figure 5. Person no. 2 infected seven other persons based on strong epidemiological evidence (test date, symptom onset, outbreak observations); two of these persons were assigned to a different genomic subcluster.

We assessed 15 events within the transmission network (Table 2). Four of these events occurred from a vaccinated to any other person: in three likely transmission events (person no. 7 to 10 and 1 to 14), the HCWs (person no. 10 and 1) had prolonged close contact with the residents; and one transmission event (person no. 6 to 17) happened between two residents sharing the room. The fourth transmission event was judged as possible (person no. 9 to 4), the PCR date and the date of symptom onset are relatively close to each other. However, the date of symptom onset and the ct value indicate that person number 9 infected person number 4 (Table 2). The degree of immunoprotection (neutralization titers) did not seem to affect transmission from a vaccinated person (NT50=308 in person no. 9, NT50=10,527 in person no. 7).

DISCUSSION

We performed an extensive COVID-19 outbreak investigation in a nursing home where willing residents and HCWs had been fully vaccinated with an mRNA vaccine. The second dose was given about five weeks before the outbreak. We identified 17 COVID-19 cases, of whom 8 (47%) were vaccinated. Among ten residents infected with SARS-CoV-2, the vaccinated residents had mild disease or were asymptomatic, whereas two died among the unvaccinated residents. We identified four likely or possible SARS-CoV-2 transmissions from vaccinated to other persons.

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The SARS-CoV-2 vaccines play a central role in controlling the COVID-19 pandemic, but the vaccine coverage to achieve herd immunity is high, about 80%, and likely higher with the more infectious delta variant (23, 24). In this outbreak in a nursing home, overall vaccine coverage was 82% among residents and 51% among HCWs. Most of the transmissions originated from unvaccinated individuals, but about one quarter involved vaccinated residents or HCWs. COVID-19 vaccines so far do not provide sterilizing immunity, and our study illustrates the importance of non-pharmaceutical interventions (NPIs) such as wearing face masks, keeping physical distance from other individuals, and rigorous hand hygiene. We have previously shown that the COVID-19 seroprevalence among nursing staff in Switzerland was higher than HCWs in other institutions (25). Of note, in this study, there were only two likely or possible infections from HCWs to others, one vaccinated and one unvaccinated, indicating that HCWs were skilled in protecting others and themselves.

Immunogenicity of mRNA is expected to be present in 95% (95%CI, 90.0 to 97.9) of vaccinated persons after at least seven days after two doses of the mRNA vaccine (3). A multicentre clinical trial found that the Pfizer-BioNTech mRNA SARS-CoV-2 vaccine was effective in preventing COVID-19 disease overall in 95% (95%CI, 90.0 to 97.9) after two doses (3). The study from Israel, using national surveillance data, estimated vaccine effectiveness at 7 days or later after two doses of the Pfizer-BioNTech mRNA SARS-CoV-2 vaccine at 95.3% (95%CI 94.9-95.7) against SARS-CoV-2 infection (26). We found that vaccine effectiveness for infection was ~70% among residents, with wide confidence intervals, which is lower compared to the clinical trial. It is currently unknown how long protection after two doses of SARS-CoV-2 vaccines will last in the elderly. In general, the vaccine response in the elderly shows lower antibody titers, reduced efficacy and protection may be shorter (27, 28). This has, for example, been reported for vaccines against influenza, herpes zoster, or other infectious diseases (27-30).

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SARS-CoV-2 infected residents or HCWs who were vaccinated had only mild disease or were asymptomatic. In contrast, among the unvaccinated, two residents died and others had severe disease. The study from Isreal also showed an estimated vaccine effectiveness against severe or COVID-19-related hospitalization of 97.5% (95%CI 97.1-97.8) and 96.7% (95%CI 96.0-97.3) against COVID-19-related death (26). A study in older people (70 years and above) from England showed that 10 to 13 days after one dose of the Pfizer-BioNTech mRNA SARS-CoV-2 vaccine, the vaccine effectiveness was 70% (95%CI 59%-78%) in preventing symptomatic disease and 14 days after two doses the vaccine effectiveness was 89% (95%CI 85%-93%). The latter study showed that vaccinated older people with COVID-19 had a 44% lower risk of hospitalization and a 51% lower risk of death than unvaccinated people (31). Our data confirm the efficacy of the vaccine in triggering the humoral immune response in most individuals. The exception was a vaccinated resident with possible immunosuppression due to cancer. This resident showed no protective levels at the time of infection, but seroconverted after infection. Even during an outbreak with the variant of concern Alpha (B.1.1.7), the immunogenicity of the mRNA Pfizer-BioNTech was protective, with only three of ten vaccinated individuals developing severe symptoms. Moreover, a majority of the vaccinated individuals had neutralizing titers early post-infection, a factor that might have reduced severe disease. After re-exposure, the humoral immune response was boosted, reaching higher neutralizing titers than fully vaccinated healthy HCWs.

We constructed a transmission network based on biological and epidemiological data. Due to the relatively low mutation rate of SARS-CoV-2 in contrast to, for example, influenza viruses (32), genomic analyses alone will not provide a high-resolution network. Patient no. 2 transmitted SARS-CoV-2 to seven persons indicating a possible superspreader event (5 likely and 2 possible transmission events). The two possible events belonged to a different genomic subcluster (difference of one single mutation) which does not exclude the possibility of a different, unknown source of infection. Of note, we observed four SARS-CoV-

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2 transmission events from vaccinated to vaccinated and unvaccinated persons. There is increasing evidence that outbreaks can occur despite the high level of vaccination among residents (33-37). The vaccine uptake among HCWs was moderate at the time of the outbreak, and some of the infections might have been prevented by a higher coverage.

This study has several limitations. In five nasal swab samples, viral RNA concentration was too low and could not be sequenced. However, infections with potential immune escape mutations were absent or extremely rare at that time in Switzerland (38). In addition, not all of the infected individuals were willing or were able to provide blood samples. A major strength of this study is the collection of comprehensive data (PCR tests, clinical, genomic, and serological data) and the use of the different data types to construct a transmission network.

In conclusion, despite the high vaccine efficacy of mRNA vaccines and documented immunoprotection after vaccination, COVID-19 outbreaks can occur in high-risk settings such as nursing homes, even when reaching vaccine coverage of over 80% among residents. Such outbreaks might go undetected, and continued testing of any person with even mild symptoms followed by isolation and quarantine in case of infections as well as serial testing of unvaccinated HCWs as per National recommendations is required in the nursing home and other high-risk settings. Furthermore, high vaccination uptake among HCWs and residents is needed, and basic infection control measures, including wearing masks when in close contact. Serological analyses, which can distinguish between infection and vaccination, contribute to understanding transmission. They also provide important information on protective antibody levels post-vaccination in the elderly and other populations.

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AUTHORS CONTRIBUTIONS

Conception and design: ME, LF. Outbreak investigations: KZ, CM, CD, LF. Data collection: CM, IAA, AT, AE, KZ, CD. Data analysis: KZ, CM, IAA, AT, AE, MS. Wrote the first draft of the paper KZ, CD, LF. KZ and LF revised it based on comments from all authors. All authors reviewed and approved the final version of the manuscript.

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COMPETING INTERESTS

IAA reports Promedica Grant 14851M outside of the conduct of the study. AE reports grants or contracts from Swiss National Science Foundation on bacteriology and metagenomics, SPHN/PHRT on sepsis research, PHRT on bacterial infection after stem cell transplantation, and PHRT on bacterial infection after stem cell transplantation and notes that none of the grants are in a direct relationship to this particular publication. AT reports grants or contracts from Swiss National Science Foundation as Co-Pi and collaborator on COVID-19 grants; unrelated to study, Swiss Federal Office of Public Health for COVID-19 diagnostic surveillance; unrelated to study, and Gilead COVID grant initiative as Co-Pi; unrelated to

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study; consulting fees from Roche for COVID diagnostics unrelated to the study and Neuroimmune for COVID therapy unrelated to the study; payment or honoraria for COVID lecture unrelated to the study from Schweizer Lungen Liga; participation on a Data Safety Monitoring Board or Advisory Board for Neurimmune for COVID therapy unrelated to the study; and received materials for COVID-19 diagnostics evaluation unrelated to the study from Roche. All other authors declare that they have no conflicts of interest.

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Figure 1: Epidemic curves based on (A) date of first positive SARS-CoV-2 PCR test result or (B) date of symptoms start/onset of symptoms.

Figure 2: Serological profiling of the SARS-CoV-2 specific humoral responses in the outbreak patients at the nursing home. Assessment of the multiplex SARS-CoV-2 ABCORA on unvaccinated (light and dark red) and vaccinated (grey and black) residents and health care workers. Light red and grey depict the first time point of sampling (T1, 1-18 days after diagnosis), dark red and black the second time point (T2, 16-30 days). Depicted are signal over cut off (SOC) values, all values >1 are positive. RBD, S1, and S2 correspond to subunits of the SARS-CoV-2 spike protein, N to the Nucleocapsid protein.

Figure 3: Neutralization titers assessed in unvaccinated and vaccinated individuals during outbreak as well as health care workers. 50% neutralization titers (NT50) against Wuhan-Hu-1 pseudotype post SARS-CoV-2 infection of unvaccinated (light and dark red) and vaccinated (grey and black) health care workers (open circles) and residents (closed circles at T1 (1-18 days) and T2 (16-30 days) after positive PCR. Vaccinated health care workers (HCW) not involved in the outbreak are shown in light blue. Black line depicts the median. Solid circles indicate residents, open circles HCWs.

Figure 4: SARS-CoV-2 phylogeny of the outbreak patients compared to selected alpha (B.1.1.7) strains from Switzerland and neighboring countries. Panel A shows the phylogeny of B.1.1.7 genomes including European genomes and the blue line indicates the outbreak. Panel B shows the sequences of the patients involved in the outbreak (numbers in the hegaxongs correspond to the patient numbers) and identifies four subclusters (a-d).

Figure 5: Transmission network based on symptom onset, test date, epidemiological data, observations of the nursing home management and their nurses. The different shaded colors of the circles indicate the genomic subclusters: blue is sub-cluster a, green is sub-cluster b, red is sub-cluster c, yellow is sub-cluster d, and no fill for missing. A symptomatic cases indicates a person with any symptom.

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TABLES AND FIGURES

Table 1: Characteristics of residents and HCWs with COVID-19.

	Total	Residents	Health care workers
	n=17 (100%)	n=10 (100%)	n=7 (100%)
Sex			
Female	14 (82%)	7 (70%)	7 (100%)
Male	3 (18%)	3 (30%)	0 (0%)
Median age in years, (IQR)	65 (54-86)	86 (70-90)	49 (29-58)
SARS-CoV-2 vaccine received*	8 (47%)	5 (50%)	3 (43%)
Symptoms			
Any	13 (76%)	8 (80%)	5 (71%)
Shortness of breath	7	5	2
Cough	5	4	1
Throat pain	5	3	2
Fever	4	3	1
Chest pain	4	2	2
Headache	3	1	2
Weakness	3	2	1
Running nose	3	1	2
Muscle pain	1	0	1
Anosmia	1	0	1
Ageusia	1	0	1
Confusion	1	1	0
Nausea	1	0	1
Co-morbidities			
Any	8 (47%)	7 (70%)	1 (14%)
Hypertension	4	3	1

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Lung disease	3	3	0
Cardiovascular disease	2	1	1
Diabetes	2	2	0
Cancer	1	1	0
Metabolic syndrome (adiposities)	1	1	0
Mortality[&]	2 (%)	2(%)	0(%)

*Two doses of mRNA vaccine; [&]Both deaths were in unvaccinated residents.

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Table 2: Transmission events according to the COVID-19 vaccination status.

Patient	Criteria								
	PCR test		Genomics	Epidemiological			Immunology	Interpretation of transmission
No.	Date	Ct value	Subcluster	Date of Symptoms	Symptoms	Relation	50% neutralisation titer (NT50)	
Transmission from vaccinated to vaccinated persons								
7 → 10	25/02/2021 → 03/03/2021	13 → 28	a → a	21/02/2021 → 02/03/2021	cough, shortness of breath, throat pain → shortness of breath, muscle pain	resident → HCW	10527.2 → 2148.6	Likely
6 → 17	25/02/2021 → 08/03/2021	25 → 24	- → b	26/02/2021 → 10/03/2021	cough, running nose → shortness of breath, chest pain, headache, throat pain	resident → resident	123 → 5081.0	Likely
Transmission from vaccinated to unvaccinated perons								
1 → 14	22/02/2021 → 03/03/2021	21 → 18	a → a	21/02/2021 → 28/02/2021	headache, running nose → cough, shortness of breath, weakness	HCW → resident	5087.6 → <100	Likely
4 → 9	25/02/2021 → 26/02/2021	13 → 26	a → -	- → 25/02/2021	Asymptomatic → shortness of breath, headache, throat pain	HCW → resident	307.5 → <100	Possible
Transmission from unvaccinated to vaccinated persons								
2 → 16	23/02/2021 → 08/03/2021	18 → 39	- → c	20/02/2020 → -	cough, shortness of breath, fever, confusion → asymptomatic	resident → HCW	- → 9602.1	Likely
2 → 1	23/02/2021 → 22/02/2021	18 → 21	- → a	20/02/2020 → 21/02/2021	cough, shortness of breath, fever, confusion → headache, running nose	resident → HCW	- → 5087.6	Likely
2 → 7	23/02/2021 → 25/02/2021	18 → 14	- → a	20/02/2020 → 21/02/2021	cough, shortness of breath, fever, confusion → shortness of breath, chest pain, throat pain	resident → resident	- → 10527.2	Likely
2 → 8	23/02/2021 → 25/02/2021	18 → 28	- → -	20/02/2020 → -	cough, shortness of breath, fever, confusion → asymptomatic	resident → resident	- → 508.1	Likely
5 → 15	25/02/2021 → 08/03/2021	19 → 24	- → -	23/02/2021 → -	shortness of breath, fever → asymptomatic	resident → HCW	<100 → 5081	Likely
Transmission from unvaccinated to unvaccinated persons								
2 → 5	23/02/2021 → 25/02/21	18 → 19	- → a	20/02/2020 → 23/02/2021	cough, shortness of breath, fever, confusion → shortness of breath, fever	resident → resident	- → <100	Likely
2 → 3	23/02/2021 → 25/02/2021	18 → 19	- → d	20/02/2020 → 25/02/2021	cough, shortness of breath, fever, confusion → fever, weakness	resident → resident	- → <100	Likely
2 → 4	23/02/2021 → 25/02/2021	18 → 26	- → a	20/02/2020 → -	cough, shortness of breath, fever, confusion → asymptomatic	resident → HCW	- → 307.5	Likely
5 → 13	25/02/2021 → 03/03/2021	19 → 28	a → a	23/02/2021 → 02/03/2021	shortness of breath, fever → chest pain, muscle pain, running nose	resident → resident	<100 → 2148.6	Likely
14 → 11	03/03/2021 → 03/03/2021	38 → 18	a → a	05/03/2021 → 28/02/2021	throat pain, anosmia, ageusia → cough, shortness of breath, weakness	resident → HCW	<100 → <100	Possible
14 → 12	03/03/2021 → 03/03/2021	38 → 16	a → -	05/03/2021 → 05/03/2021	throat pain, anosmia, ageusia → cough, shortness of breath, fever, weakness, nausea	resident → HCW	<100 → <100	Possible

Abbreviations: Ct, Cycle threshold of the PCR run, HCW, health care worker

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Figure 1

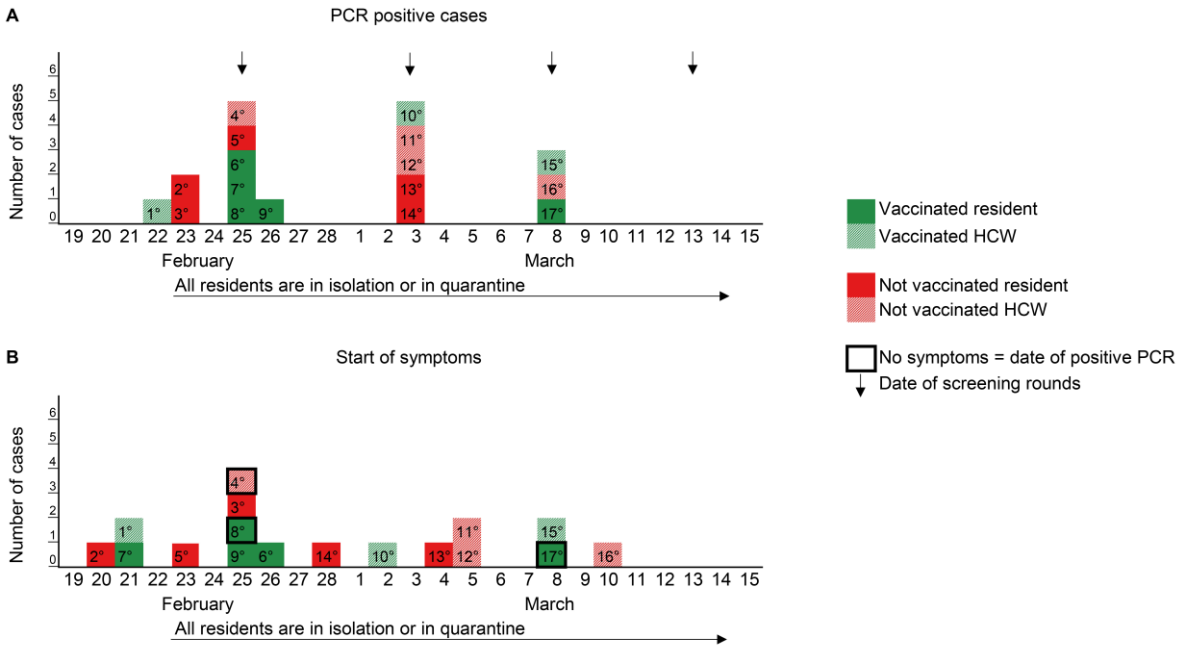

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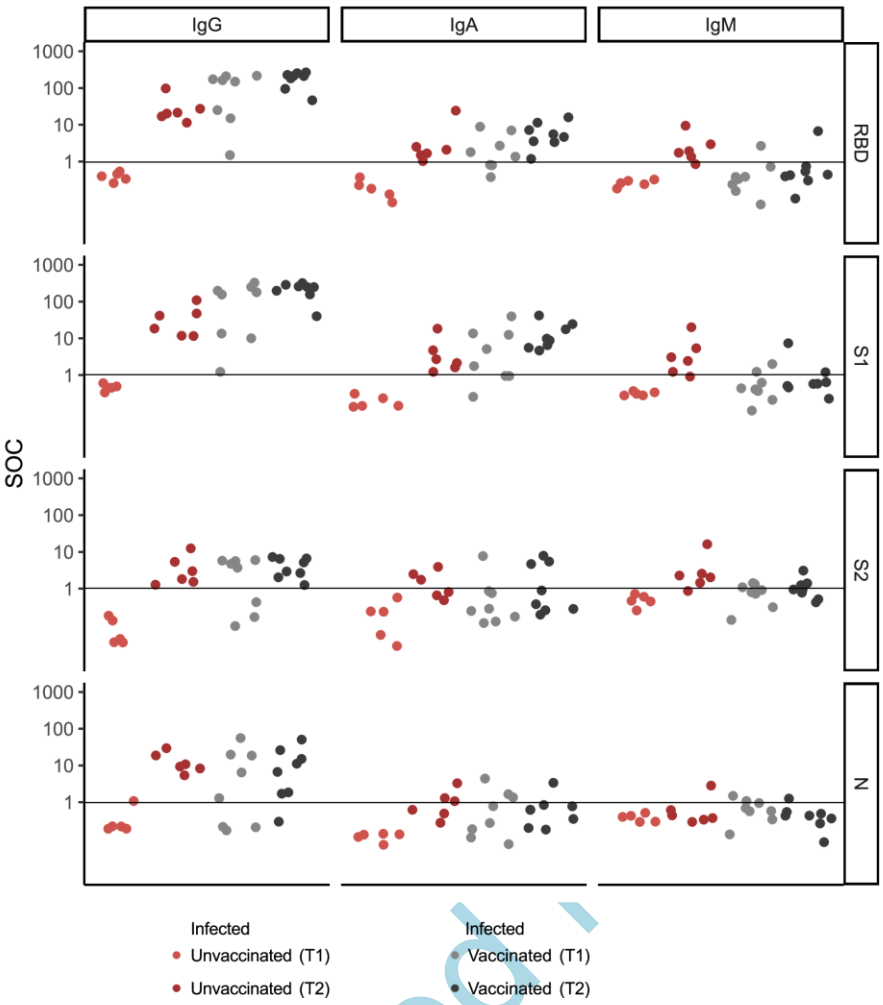
Figure 2



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15 Figure 3

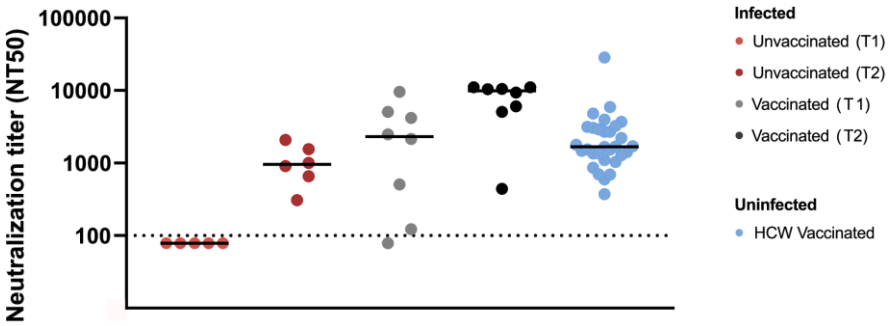

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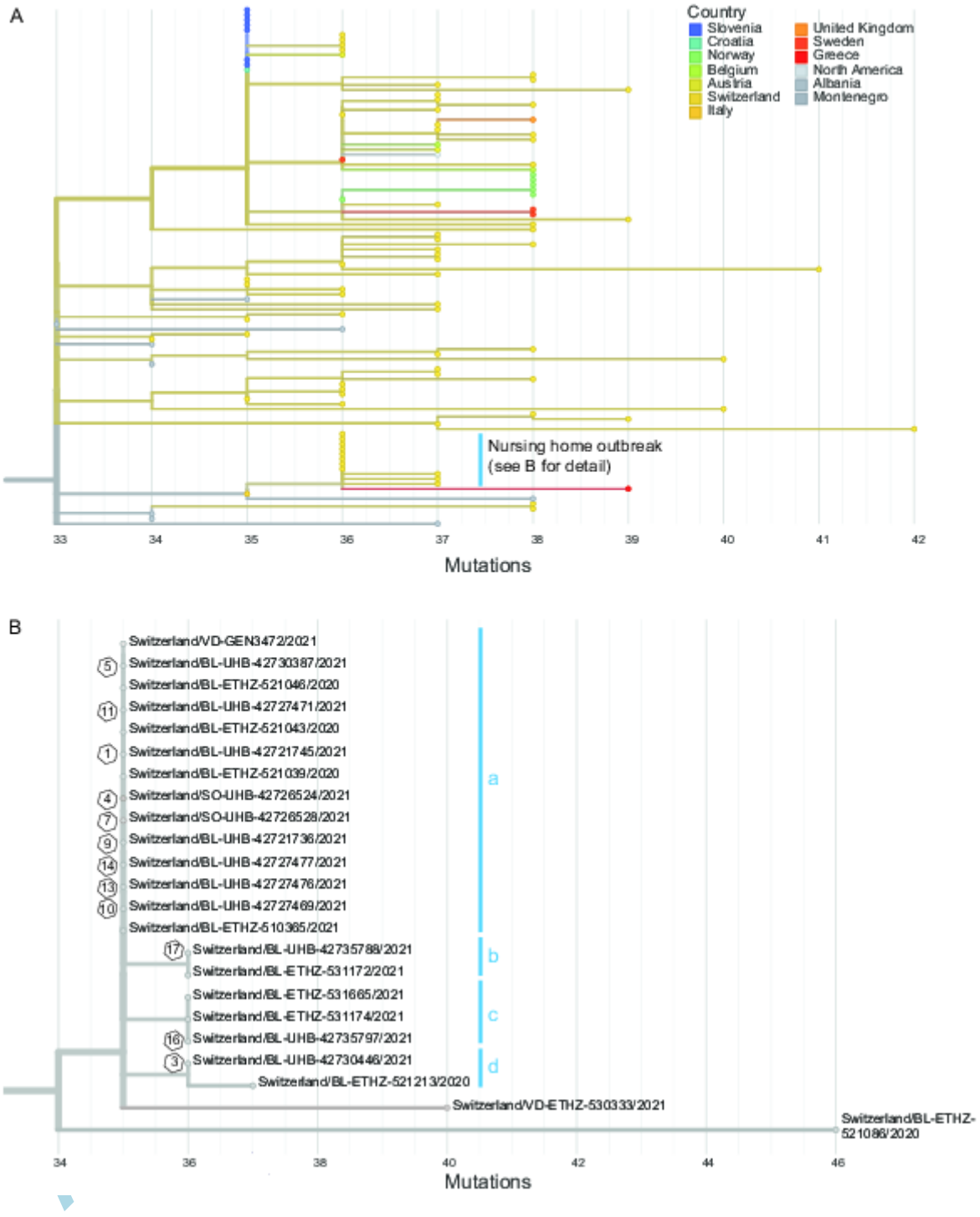
Figure 4


A
Country
Slovenia
Croatia
Norway
Belgium
Austria
Switzerland
Italy
United Kingdom
Sweden
Greece
North America
Albania
Montenegro
Nursing home outbreak
(see B for detail)
33
34
35
36
37
38
39
40
41
42
Mutations
B
Switzerland/VD-GEN347/2021
Switzerland/BL-UHB-42730387/2021
Switzerland/BL-ETHZ-521046/2020
Switzerland/BL-UHB-42727471/2021
Switzerland/BL-ETHZ-521043/2020
Switzerland/BL-UHB-42721745/2021
Switzerland/BL-ETHZ-521039/2020
Switzerland/SO-UHB-42726524/2021
Switzerland/SO-UHB-42726528/2021
Switzerland/BL-UHB-42721736/2021
Switzerland/BL-UHB-42727477/2021
Switzerland/BL-UHB-42727476/2021
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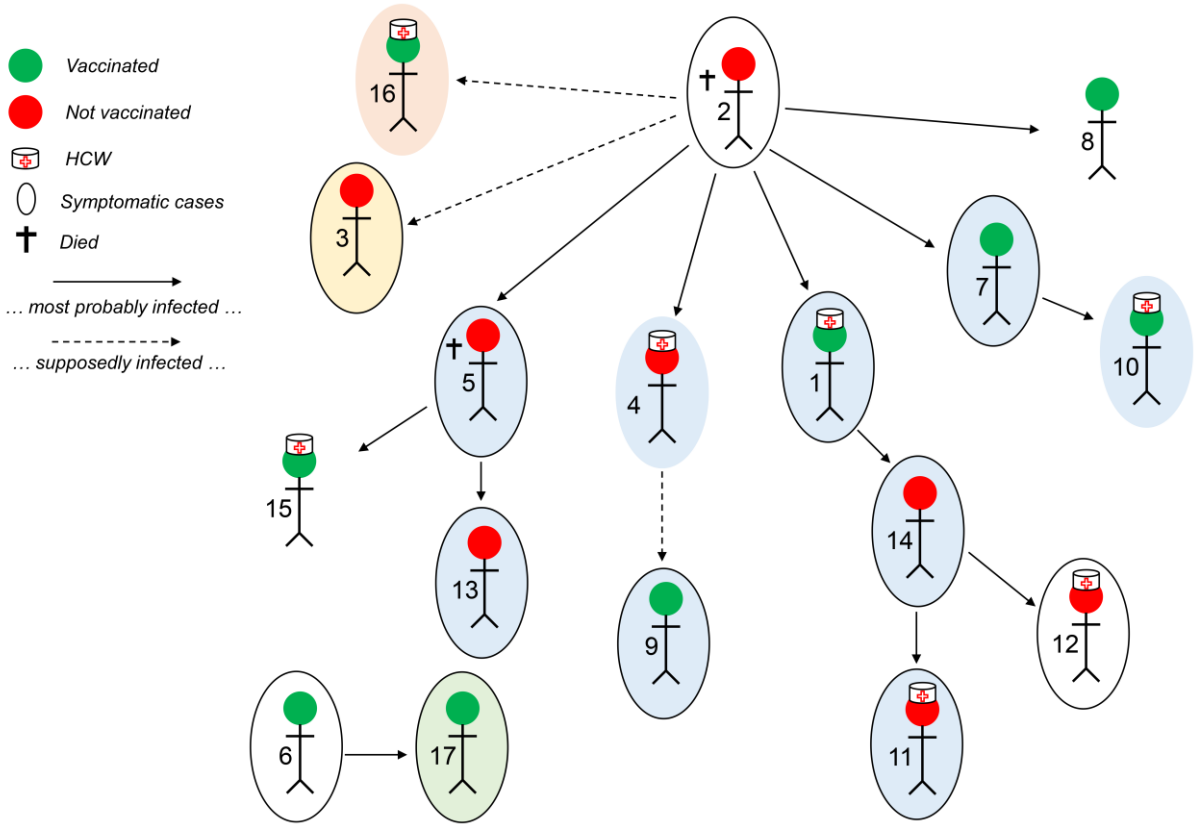
Switzerland/BL-ETHZ-531172/2021
Switzerland/BL-ETHZ-531665/2021
Switzerland/BL-ETHZ-531174/2021
Switzerland/BL-UHB-42735797/2021
Switzerland/BL-UHB-42730446/2021
Switzerland/BL-ETHZ-521213/2020
Switzerland/VD-ETHZ-530333/2021
Switzerland/BL-ETHZ-521086/2020
a
b
c
d
34
36
38
40
42
44
46
Mutations

Figure 5



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