Alpha Variant Coronavirus Outbreak in a Nursing Home Despite High Vaccination Coverage: Molecular, Epidemiological, and Immunological Studies

Kathrin Zürcher,1 Irene A. Abela,2,3 Madlen Stange,4,5 Carole Dupont,1 Catrina Mugglin,6,7 Adrian Egli,2,3 Alexandra Trkola,2 Matthias Egger,1,7,8 and Lukas Fenner1,6

1Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland; 2Institute of Medical Virology, University of Zürich, Zurich, Switzerland; 3Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zurich, Switzerland; 4Clinical Bacteriology and Mycology, University Hospital Basel, Basel, Switzerland; 5Kantonsärztlicher Dienst, Gesundheitsamt, Kanton Solothurn, Switzerland; 6Centre for Infectious Disease Epidemiology and Research, University of Cape Town, Cape Town, South Africa; and 7Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom

**Background.** Vaccination may control the coronavirus disease 2019 (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 the uptake of messenger RNA vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was 82% among residents as of 21 January 2021. After diagnosis of COVID-19 in a vaccinated symptomatic healthcare worker (HCW) on 22 February, we performed outbreak investigations in house A (47 residents; 37 HCWs), using SARS-CoV-2–specific polymerase chain reaction (PCR) testing of nasopharyngeal swab samples. We performed whole-genome sequencing of SARS-CoV-2 and serological analyses.

**Results.** We identified 17 individuals with positive PCR results, 10 residents (5 vaccinated) and 7 HCWs (3 vaccinated). The median age (interquartile range) was 86 (70–90) years among residents and 49 (29–59) years among HCWs. Of the 5 vaccinated residents, 3 had mild disease and 2 had no symptoms, whereas all 5 unvaccinated residents had mild to severe disease, and 2 died. Vaccine effectiveness for the prevention of infection among residents was 73.0% (95% confidence interval, 24.7%–90.1%). The 12 available genomes were all alpha variants. Neutralizing titers were significantly higher in vaccinated individuals on reexposure (>1 week after diagnosis) than in vaccinated, unexposed HCWs (P = .01). Transmission networks indicated 4 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.

**Keywords.** B.1.1.7; COVID-19; nursing home; Outbreak; UK variant; Vaccine.

The coronavirus disease 2019 (COVID-19) pandemic, caused by 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 messenger RNA (mRNA) vaccines against SARS-CoV-2 showed promising results, with vaccine efficacy of >90% against symptomatic and severe disease [3, 4].

The Swiss vaccine campaign started in December 2020 with 2 mRNA vaccines (Pfizer-BioNTech/Moderna) [7, 8]. The campaign prioritized people at increased risk, such as nursing home residents, healthcare workers (HCWs), the elderly (aged ≥75 years), and people with severe chronic diseases, regardless of 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 had received ≥1 dose of an mRNA COVID-19 vaccine, and about 30% were completely vaccinated [10].

Nursing homes are critical institutions in this pandemic owing to their high-risk resident population [11]. Outbreaks associated with SARS-CoV-2 in nursing homes have been described elsewhere [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 the transmission events in detail, using epidemiological, molecular epidemiological, and immunological methods.

**METHODS**

**Study Site**

We conducted the current study at a nursing home in the canton of Solothurn, Switzerland, with a capacity of 93 residents in 2 houses. The nursing home was among the first in the canton...
to start vaccinating its HCWs and residents. The mRNA vaccine from Pfizer-BioNTech (BNT162b2) was used, following the manufacturer’s instructions. The first dose was given on 29 December 2020 and the second on 21 January 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 4 floors providing housing for 47 residents (Supplementary Figure 1). 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 22 February, nasopharyngeal swab samples were taken for SARS-CoV-2 polymerase chain reaction (PCR) testing from all close contacts. Later, on 25 February and on 3, 8, and 13 March, PCR testing of nasopharyngeal swab samples was repeated among all HCWs and residents in house A (Figure 1 and Supplementary Figure 2). There were no cases in house B. To document each resident’s room, we elaborated a floor plan of house A (Supplementary Figure 1 and Supplementary Table 1). We collected data for all COVID-19 case patients, including age, sex, dates of vaccination, symptoms, comorbid conditions, and clinical outcomes. SARS-CoV-2 PCR data (Viollier) included the date and result of PCR testing and the cycle threshold (Ct) value.

Serological Analyses

The humoral immune response during the outbreak and immunogenicity of mRNA vaccine was assessed by means of ABCORA, a bead-based multiplex immunoassay using Luminex technology to measure specific immunoglobulin (Ig) G, IgA, and IgM responses to SARS-CoV-2 subunits of the spike protein (receptor binding domain [RBD], spike 1 [S1], spike 2 [S2], and nucleocapsid [N] protein [14]). Positive reactivity for each antigen-antibody class combination is reported as the signal-over-cutoff value [14]. Infection and vaccination both give rise to spike protein antibody responses, whereas N protein antibody responses are present only in infected individuals. IgM and IgA reactivity indicates recent immune stimulation. Serology was performed during the outbreak and ≥ 1 week after the first sample to analyze seroconversions (1–18 days and 16–30 days after the positive PCR result) (Supplementary Figure 2). Samples were assessed for neutralization activity against the vaccine strain Wuhan-Hu-1 using a SARS-CoV-2 pseudovirus neutralization test; activity was assessed 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 the 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.

Figure 1. Epidemic curves based on dates of the first positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) test result (A) and dates of symptom onset (or first positive PCR result in asymptomatic persons) (B). Numbers inside squares represent numbers assigned to the 17 infected persons (residents and healthcare workers [HCWs]).
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]. Of 17 samples, 12 high-quality whole genomes were assembled and deposited in GISAID (https://www.gisaid.org) (Supplementary Table 2) [16, 17].

Global sequences and metadata were downloaded from GISAID on 7 May 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 collected in Switzerland between 1 January and 10 March 2021 (4346 as of 7 May 2021) for phylogenetic inference, using the Nextstrain analysis pipeline (version 3.0.3) and the Augur toolkit (version 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) the date of symptoms, (2) the date of PCR tests, (3) contacts and behavior of the individuals, (4) genomic analyses, (5) PCR Ct values (lower levels show higher viral loads, indicating a higher transmission potential), and (6) level of neutralizing antibodies (lower levels may indicate a higher transmission potential).

**Definitions**

Severe disease was defined as a persistent elevated temperature, reduced general condition, shortness of breath or pneumonia, and requirement for hospitalization or supplemental oxygen. Individuals with severe disease are generally ill for 2–4 weeks. Mild disease was defined as the occurrence of mild symptoms for just a few days. Asymptomatic cases were defined as those with 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, and the corresponding 95% confidence interval (CI) using binomial distributions. All analyses were performed using Stata software (version 16.0; StataCorp).

**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.
antigens at the second time point (Figure 2 and Supplementary Figure 3). Three vaccinated individuals had a good immunogenic response to the vaccine (no IgG N response) at the first time point, whereas 5 already showed reactivity to infection, as reflected by high N protein antibody levels at the first time point. At the second time point, 7 of 8 vaccinated individuals also had 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 Supplementary Figure 3).

In line with prototypic antibody patterns in COVID-19 [14], 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) [21]. 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 on reexposure than in vaccinated HCWs who had not been involved in the outbreak ($P = .01$), highlighting a boost of neutralizing antibody activity after infection (Figure 3). Supplementary Table 4 provides serological information on the vaccinated HCWs (not part of the outbreak) who were interested in knowing their serological status.

### Molecular Epidemiological Analyses

Of the 17 nasopharyngeal samples, 12 had sufficient viral RNA for subsequent sequencing. All 12 genomes belonged to lineage alpha/B.1.1.7 and were closely related. Of the 12 genomes, 9 (75%) were identical (0 single-nucleotide polymorphisms [SNPs]), and each of the remaining 3 had 1 additional SNP (Figure 4). All genomes clustered mostly with other genomes sequenced from Basel-Country (canton). Genomes 17 (group b) and 16 (group c) had 1 additional SNP aligned with 1 and 2 genomes from the community, respectively.
Table 2 shows the criteria we applied to describe the transmission events according to the vaccination status and its direction within the transmission network. The transmission network is shown graphically in Figure 5. Person 2 infected 7 other persons, based on strong epidemiological evidence (test dates, dates of symptom onset, and outbreak observations); 2 of these persons were assigned to a different genomic subcluster.

We assessed 15 events within the transmission network (Table 2). Four of these transmissions were from a vaccinated to another person: in 3 likely transmission events (from person 7 to person 10, and from person 1 to person 14), the HCWs (persons 10 and 1) had prolonged close contact with the residents; 1 transmission event (from person 6 to person...
17) involved 2 residents sharing a room. The fourth transmission event (from person 9 to person 4) was judged as possible; the dates of PCR and of symptom onset were relatively close, but the date of symptom onset and the Ct value indicate that person 9 infected person 4 (Table 2). The degree of immunoprotection (neutralization titers) did not seem to affect transmission from a vaccinated person (NT50, 308 in person 9 and 10 527 in person 7).

![Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) phylogeny of the infected persons in the outbreak compared with selected alpha (B.1.1.7) strains from Switzerland and neighboring countries. A, Phylogeny of B.1.1.7 genomes; including European genomes; vertical blue line represents the outbreak. B, Sequences of the persons involved in the outbreak (person numbers in the hexagons), with 4 subclusters identified, subclusters a–d.](image-url)
| Persons Involved (by No.) | Transmission from vaccinated to vaccinated persons | PCR Test Date | Ct Value | Genomic Subcluster | Date of Symptoms | Symptoms | Epidemiological Relation | Immunological NT50 Interpretation of Transmission |
|--------------------------|--------------------------------------------------|---------------|----------|-------------------|-----------------|---------|-------------------------|-----------------------------------------------|
| 7 → 10                   | 25/2/2021 → 3/3/2021                             | 13 → 28       | a → a    | 21/2/2021 → 2/2/2021 | Cough, shortness of breath, throat pain → shortness of breath, muscle pain | Resident → HCW | 105272 → 2148.6 Likely |
| 6 → 17                   | 25/2/2021 → 8/3/2021                             | 26 → 24       | NA → b   | 26/2/2021 → 10/3/2021| Cough, running nose → shortness of breath, chest pain, headache, throat pain | Resident → resident | 123 → 5081.0 Likely |
| Transmission from vaccinated to unvaccinated person | | | | | | | |
| 1 → 14                   | 22/2/2021 → 3/3/2021                             | 21 → 18       | a → a    | 21/2/2021 → 28/2/2021| Headache, running nose → cough, shortness of breath, weakness | HCW → resident | 50876 → <100 Likely |
| 4 → 9                    | 25/2/2021 → 26/2/2021                            | 13 → 26       | a → NA   | NA → 25/2/2021      | Asymptomatic → shortness of breath, headache, throat pain | HCW → resident | 3075 → <100 Possible |
| 2 → 16                   | 23/2/2021 → 8/3/2021                             | 18 → 39       | NA → c   | 20/2/2020 → NA      | Cough, shortness of breath, fever, confusion → asymptomatic | Resident → HCW | NA → 9602.1 Likely |
| 2 → 7                    | 23/2/2021 → 22/2/2021                            | 18 → 21       | NA → a   | 20/2/2020 → 21/2/2021| Cough, shortness of breath, fever, confusion → headache, running nose | Resident → HCW | NA → 50876 Likely |
| 2 → 8                    | 23/2/2021 → 25/2/2021                            | 18 → 28       | NA → a   | 20/2/2020 → 21/2/2021| Cough, shortness of breath, fever, confusion → shortness of breath, chest pain, throat pain | Resident → resident | NA → 10527.2 Likely |
| 5 → 15                   | 25/2/2021 → 8/3/2021                             | 19 → 24       | NA → c   | 23/2/2021 → NA      | Shortness of breath, fever → asymptomatic | Resident → HCW | <100 → 5081 Likely |
| Transmission from unvaccinated to unvaccinated person | | | | | | | |
| 2 → 5                    | 23/2/2021 → 25/2/2021                            | 18 → 19       | NA → a   | 20/2/2020 → 23/2/2021| Cough, shortness of breath, fever, confusion → shortness of breath, fever | Resident → resident | NA → <100 Likely |
| 2 → 3                    | 23/2/2021 → 25/2/2021                            | 19 → 26       | NA → d   | 20/2/2020 → 25/2/2021| Cough, shortness of breath, fever, confusion → fever, weakness | Resident → resident | NA → <100 Likely |
| 2 → 4                    | 23/2/2021 → 25/2/2021                            | 18 → 26       | NA → a   | 20/2/2020 → 25/2/2021| Cough, shortness of breath, fever, confusion → asymptomatic | Resident → HCW | NA → 3075 Likely |
| 5 → 13                   | 25/2/2021 → 3/3/2021                             | 19 → 28       | a → a    | 23/2/2021 → 2/2/2021 | Shortness of breath, fever → chest pain, muscle pain, running nose | Resident → resident | <100 → 2148.6 Likely |
| 14 → 11                  | 3/3/2021 → 3/3/2021                             | 38 → 18       | a → a    | 5/3/2021 → 28/2/2021 | Throat pain, anosmia, ageusia → cough, shortness of breath, weakness | Resident → HCW | <100 → <100 Possible |
| 14 → 12                  | 3/3/2021 → 3/3/2021                             | 38 → 16       | a → NA   | 5/3/2021 → 50/2/2021 | Throat pain, anosmia, ageusia → cough, shortness of breath, fever, weakness, nausea | Resident → HCW | <100 → <100 Possible |

Abbreviations: Ct, cycle threshold; HCW, healthcare worker; NA, not available; NT50, 50% neutralization titer; PCR, polymerase chain reaction.
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 5 weeks before the outbreak. We identified 17 COVID-19 case patients, of whom 8 (47%) were vaccinated. Among 10 residents infected with SARS-CoV-2, the vaccinated residents had mild disease or were asymptomatic, whereas 2 of the unvaccinated residents died. We identified 4 likely or possible SARS-CoV-2 transmissions from vaccinated to other persons.

SARS-CoV-2 vaccines play a central role in controlling the COVID-19 pandemic, but the vaccine coverage needed to achieve herd immunity is about 80%, and likely higher with the more infectious delta variant [22, 23]. In this outbreak in a nursing home, the overall vaccine coverage was 82% among residents and 51% among HCWs. Most 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 nonpharmaceutical interventions, 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 among HCWs in other institutions [24]. Of note, in the current study, there were only 2 likely or possible infections from HCWs to others, 1 vaccinated and 1 unvaccinated HCW, indicating that HCWs were skilled in protecting others and themselves.

Immunogenicity of mRNA is expected to be present in 95% (95% CI, 90.0%–97.9%) of vaccinated persons after ≥7 days after 2 doses of the mRNA vaccine [3]. A multicenter clinical trial found that the Pfizer-BioNTech mRNA SARS-CoV-2 vaccine was effective in preventing COVID-19 disease overall in 95% of vaccinees (95% CI, 90.0%–97.9%) after 2 doses [3]. The study from Israel, using national surveillance data for the Pfizer-BioNTech vaccine, estimated at 95.3% (95% CI, 94.9%–95.7%) the vaccine’s effectiveness against SARS-CoV-2 infection ≥7 days after 2 doses [25]. We found that vaccine effectiveness for infection was approximately 70% among residents, with wide CIs which is lower than in the clinical trial. It is currently unknown how long protection after 2 doses of SARS-CoV-2 vaccines will last in elderly recipients. In general, vaccine response in elderly persons shows lower antibody titers and reduced efficacy, and the duration of protection may be shorter [26, 27]. This has been reported for vaccines against influenza, herpes zoster, and other infectious diseases [26–29].

SARS-CoV-2–infected residents or HCWs who were vaccinated had only mild disease or were asymptomatic. In contrast, among the unvaccinated, 2 residents died and others had severe disease. The study from Israel also showed an estimated
vaccine effectiveness of 97.5% (95% CI, 97.1%–97.8%) against severe disease or COVID-19–related hospitalization and 96.7% (96.0%–97.3%) against COVID-19–related death [25]. A study of the Pfizer-BioNTech mRNA vaccine in older people (aged ≥70 years) from England showed that the effectiveness in preventing symptomatic disease was 70% (95% CI, 59%–78%) 10–13 days after 1 vaccine dose and 89% (85%–93%) 14 days after 2 doses [30]; the same 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 in the same age group.

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 severe symptoms developing in only 3 of 10 vaccinees. Moreover, a majority of vaccinees individuals had neutralizing titers early after infection, which may have helped prevent severe disease. After reexposure, the humoral immune response was boosted, reaching higher neutralizing titers than in fully vaccinated healthy HCWs.

We constructed a transmission network based on biological and epidemiological data. Owing to the relatively low mutation rate of SARS-CoV-2—in contrast to influenza viruses [31], for example—genomic analyses alone will not provide a high-resolution network. Patient 2 transmitted SARS-CoV-2 to 7 persons, indicating a possible superspreader event (with 5 likely and 2 possible transmission events). The 2 possible events belonged to a different genomic subcluster (difference of 1 single mutation), which does not exclude the possibility of a different, unknown source of infection. Of note, we observed 4 SARS-CoV-2 transmission events from vaccinated to vaccinated or unvaccinated persons. There is increasing evidence that outbreaks can occur despite the high level of vaccination among residents [32–36]. The vaccine uptake among HCWs was moderate at the time of the outbreak around 50%, and some infections may have been prevented by higher coverage.

The current study has several limitations. In 5 nasal swab samples, the 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 [37]. In addition, not all of the infected individuals were willing or were able to provide blood samples. A major strength of the study was the collection of comprehensive data (PCR, 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 after reaching vaccine coverage of >80% among residents. Such outbreaks might go undetected; 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, per national recommendations, is required in nursing homes and other high-risk settings. High vaccination uptake among HCWs and residents is also needed, along with basic infection control measures, including wearing masks during close contact. Serological analyses, which can distinguish between infection and vaccination, contribute to our understanding of transmission. They also provide important information on protective antibody levels after vaccination in the elderly and other populations.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. We thank all residents and healthcare workers at the nursing home for their willingness to participate. We are also indebted to the staff at the nursing home for assisting with data collection.

Author contributions. Study conception and design: M. E and L. F. Outbreak investigations: K. Z., C. D., C. M., and L. F. Data collection: K. Z., I. A. A., C. D., C. M., A. E., and A.T. Data analysis: K. Z., I. A. A., M. S., C. M., A. E., and A. T. Writing of the first draft: K. Z., C. D., and L. F. Revision based on comments from all authors: K. Z. and L. F. Review and approval of the final version of the manuscript: all authors.

Financial support. M. E. and K. Z. were supported by special project funding grant 189498 from the Swiss National Science Foundation and the National Institute of Allergy and Infectious Diseases (grant 5U01-A1069924-05).

Potential conflicts of interest. I. A. A reports support from Promedic (grant 14851M), outside the conduct of the study. A. E. reports grants or contracts from SNSF for bacteriology and metagenomics, from Swiss Personalized Health Network (SPHN)/Personalized Health and Related Technologies (PHRT) for sepsis research, and from PHRT for bacterial infection after stem cell transplantation; none of the grants are related to the current publication. A. T. reports the following, all unrelated to the current study: grants or contracts from SNSF (as co–principal investigator and collaborator on coronavirus disease 2019 [COVID-19] grants), the Swiss Federal Office of Public Health (for COVID-19 diagnostic surveillance), and the Gilead COVID grant initiative (as co–principal investigator); consulting fees from Roche for COVID diagnostics and from Neuroimmune for COVID therapy; payment or honoraria from Schweizer Lungen Liga for a COVID lecture unrelated to the study; participation on a COVID therapy data safety monitoring board or advisory board for Neuroimmune; and receipt of materials for COVID-19 diagnostics evaluation from Roche. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382:727–33.

2. So AD, Woo J. Reserving coronavirus disease 2019 vaccines for global access: cross sectional analysis. BMJ 2020; 371:m4750.

3. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020; 383:2603–15.
4. Anderson EJ, Roubahd NG, Widge AT, et al. Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. N Engl J Med 2020; 383:2427–38.
5. London School of Hygiene & Tropical Medicine. COVID-19 vaccine tracker. London, UK: London School of Hygiene & Tropical Medicine, 2020. Available at: https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/. Accessed June 2021.
6. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021; 397:99–111.
7. Swissmedic. Swissmedic grants authorisation for the first COVID-19 vaccine in Switzerland. Bern, Switzerland: Swissmedic, 2020. Available at: https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/covid-19-impfstoff-erstzulassung.html. Accessed June 2021.
8. Swissmedic. Swissmedic grants authorisation for the COVID-19 vaccine from Moderna: second COVID-19 vaccine authorised in Switzerland. Bern, Switzerland: Swissmedic, 2021. Available at: https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/zulassung-covid-19-impfstoff-moderna.html. Accessed June 2021.
9. Federal Office of Public Health. COVID-19 Switzerland. Bern, Switzerland: Federal Office of Public Health, 2021. Available at: https://www.covid19.admin.ch/en/overview. Accessed June 2021.
10. Ritchie H, Ortiz-Ospina E, Belkhiran D, et al. Coronavirus pandemic (COVID-19). Available at: https://ourworldindata.org/coronavirus. Accessed June 2021.
11. Smith PW, Bennett G, Bradley S, et al. SHEA/APIC guideline: infection prevention and control in the long-term care facility, July 2008. Infect Control Hosp Epidemiol 2008; 29:785–814.
12. Burugorri-Pierre C, Lafuente-Lafuente C, Oasi C, et al. Investigation of an outbreak of COVID-19 in a French nursing home with most residents vaccinated. JAMA Network Open 2021; 4:e21252–94.e
13. Cavanaugh A, Fortier S, Lewis P, et al. COVID-19 outbreak associated with a SARS-CoV-2 R1 lineage variant in a skilled nursing facility after vaccination program—Kentucky, March 2021. MMWR Morb Mort Wkly Rep 2021; 70:639–43.
14. Abela IA, Pasin C, Schwarzmüller M, et al. Multifactorial seroprofiling dissects the contribution of pre-existing human coronaviruses responses to SARS-CoV-2 immunity. Nat Commun 2021; 12:6703.
15. Stange M, Mari A, Roloff T, et al. SARS-CoV-2 outbreak in a tri-national urban area is dominated by a B.1 lineage variant linked to a mass gathering event. PLoS Pathog 2021; 17:e1009374.
16. Elbe S, Buckland-Merrett G. Data, disease and diplomacy: GISAID’s innovative contribution to global health. Glob Chall 2017; 1:33–46.
17. Shu Y, McCauley J. GISAID: global initiative on sharing all influenza data—from vision to reality. Euro Surveill 2017; 22:30494.
18. Hadfield J, Megill C, Bell SM, et al. Nextstrain: real-time tracking of pathogen evolution. Bioinformatics 2018; 34:4121–3.
19. Sagulenko P, Fuller V, Neher RA. TreeTime: maximum-likelihood phylodynamic analysis. Virus Evol 2018; 4:vke042.
20. Rambaut A, Holmes EC, O’Toole A, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. Nat Microbiol 2020; 5:1403–7.
21. US Food and Drug Administration. Decision memorandum—neutralization titer. Silver Spring, MD: US Food and Drug Administration, 2020.
22. Gomes MGM, Ferreira MU, Corder RM, et al. Individual variation in susceptibility or exposure to SARS-CoV-2 lowers the herd immunity threshold. J Theor Biol 2022; 540:111063.
23. Anderson RM, Vegvari G, Trusscott J, Collyer BS. Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination. Lancet 2020; 396:1614–6.
24. Zürcher K, Mugglin G, Suter-Riniker F, et al. Seroprevalence of SARS-CoV-2 in healthcare workers from outpatient facilities and retirement or nursing homes in a Swiss canton. Swiss Med Wkly 2021; 151:w30021.
25. Haas EJ, Angulo FJ, McLaughlin JM, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet 2021; 397:1819–29.
26. Weinberger B, Herndler-Brandstetter D, Schwanninger A, Weiskopf D, Grubeck-Loening B. Biology of immune responses to vaccines in elderly persons. Clin Infect Dis 2008; 46:1078–84.
27. Crooke SN, Osvyannikova IG, Poland GA, Kennedy RB. Immunosenescence and human vaccine immune responses. Immun Ageing 2019; 16:25.
28. Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. Vaccine 2006; 24:1159–69.
29. Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med 2005; 352:2271–84.
30. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021; 373:n1088.
31. Lucey M, Macori G, Mullane N, et al. Whole-genome sequencing to track severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in nosocomial outbreaks. Clin Infect Dis 2021; 72:e727–35.
32. Britton A, Jacobs Slifka KM, Edens C, et al. Effectiveness of the Pfizer-BioNTech COVID-19 vaccine among residents of two skilled nursing facilities experiencing COVID-19 outbreaks—Connecticut, December 2020-February 2021. MMWR Morb Mortal Wkly Rep 2021; 70:396–401.
33. White EM, Yang X, Blackman C, Feifer RA, Gravenstein S, Mor V. Incident SARS-CoV-2 infection among mRNA-vaccinated and unvaccinated nursing home residents. N Engl J Med 2021; 385:474–476.
34. Un décès et des contaminations malgré la vaccination. Le Matin. 11 April 2021.
35. “Trotz impfung ansteckend? Nach Leichlingen weitere Corona-Ausbrüche in Altenheimen”. Westdeutscher Rundfunk (WDR). 16 April 2021.
36. Knellwolf B. ”Trotz Impfung im Altenheim angesteckt: warum die Erkenntnis daraus positiv ist”. St. Galler Tagblatt. Tagblatt. 30 March 2021.
37. Goncalves Cabecinhas AR, Roloff T, Stange M, et al. SARS-CoV-2 N501Y introduction and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021; 373:n1088.