Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Postvaccination infections among staff of a tertiary care hospital after vaccination with severe acute respiratory syndrome coronavirus 2 vector and mRNA-based vaccines

Sophie Brunner-Ziegler, Tibor Spath, Gabriela Kornek, Franz König, Bernhard Parschalk, Maximilian Schnetzinger, Robert Paul Straßl, Rebeka Savic, Andrea Foit, Helene Resch, Florian Thalhammer

1) Department of Medicine II, Division of Angiology, Medical University of Vienna, Vienna, Austria
2) Department of Hospital Epidemiology and Infection Control, Medical University of Vienna, Vienna, Austria
3) Medical Directorate, Vienna General Hospital, Vienna, Austria
4) Centre for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Vienna, Austria
5) Department of Ear, Nose and Throat Diseases, Medical University of Vienna, Vienna, Austria
6) Department of Anaesthesia, Critical Care and Pain Medicine, Medical University of Vienna, Vienna, Austria
7) Division of Clinical Virology, Medical University of Vienna, Vienna, Austria
8) Department of Urology, Medical University of Vienna, Vienna, Austria

Abstract

Objectives: The identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigen or RNA in respiratory specimens 14 days after administration of all recommended doses of authorized coronavirus disease 2019 (COVID-19) vaccines is defined as breakthrough infection. In the present investigation, mRNA and vector-based SARS-CoV-2 vaccines were analysed with respect to post-vaccination infections in vaccinated hospital employees.

Methods: A total of 8553 staff members were vaccinated with BNT162b2 (47%) or ChAdOx1-S (53%) between January and May 2021. In a retrospective observational cohort study, incidence of SARS-CoV-2 postvaccination infections was analysed in relation to demographic data, viral load, virus variants, vaccine brand and vaccination status at time of positive PCR test (fully vaccinated: 14 days after second dose; partially vaccinated: >21 days after first, but <14 days after second dose; insufficiently vaccinated: <22 days since first dose).

Results: Within the follow-up period, ending on 31 July 2021, person-time at risk-adjusted monthly rates for SARS-CoV-2 postvaccination infections were 0.18% (BNT162b2) and 0.57% (ChAdOx1-S) for insufficiently vaccinated, 0.34% (BNT162b2) and 0.32% (ChAdOx1-S) for partially vaccinated and 0.06% (BNT162b2) and 0.04% (ChAdOx1-S) for fully vaccinated participants. The two vaccine types did not differ with respect to hazard ratios for any of the respective postvaccination infection types. No cases of COVID-19-related hospitalizations or deaths were reported. Genotyping of positive PCR specimens revealed 42 variants of concern: B.1.1.7 (Alpha variant; n = 34), B.1.351 (Beta variant; n = 2), B.1.617.2 (Delta variant; n = 6).

Conclusions: BNT162b2 and ChAdOx1-S are both effective in preventing breakthrough infections; however, it seems important, that all recommended vaccine doses are administered. Sophie Brunner-Ziegler, Clin Microbiol Infect 2022;28:596
© 2021 The Author(s). Published by Elsevier Ltd on behalf of European Society of Clinical Microbiology and Infectious Diseases. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Introduction

According to the US CDC definition, the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigen or
RNA in a respiratory specimen collected from a person at least 14 days after completing all recommended doses of authorized coronavirus disease 2019 (COVID-19) vaccine series is defined as breakthrough infection [1] and described to occur at a prevalence of around 1:10 000 in fully vaccinated persons [1–4].

Data on virological characteristics and potential ongoing transmission risks, especially of mildly symptomatic or asymptomatic SARS-CoV-2 postvaccination infections, remains limited, as observational studies have predominantly focused on end points such as critical illness, hospitalization requirement and death [3–8], most of them without addressing variation by specific vaccines.

Most notably, information on respiratory SARS-CoV-2 RNA detection after vaccination in temporal relation to the individual vaccination date is scarce. As a consequence, the comparison between the diverging definitions of immunization of “14 days after the second vaccination” (CDC) versus “21 days after the first vaccine dose administration” is missing.

The purpose of the present investigation was to characterize the incidence and distribution of SARS-CoV-2 postvaccination infections in a cohort of approximately 8500 hospital employees of the Austrian General Hospital of Vienna, comparing between mRNA and vector-based vaccine types in temporal relationship to their administration.

Materials and methods

At the General Hospital of Vienna an in-house SARS-CoV-2 vaccination programme, which was voluntary and available for all actively employed (either directly or through a third-party) members who were eligible for vaccination, was launched in January and completed by the end of May 2021. Precondition for the eligibility for vaccination was absence of SARS-CoV-2 infection or COVID-19 disease for at least the past 4 weeks, before administration of the first vaccine dose.

With respect to vaccine types, a total of 8309 (4076 first and 4233 second) doses of COMIRNATY (BNT162b2) COVID-19 mRNA-based vaccines (Pfizer/BioNTech), and 8757 (4524 first and 4233 second) doses of VAXZEVRIA (ChAdOx1-S) COVID-19 viral (chimpanzee adenovirus) vector-based vaccines (AstraZeneca) were administered, according to the summary of product characteristics.

During the entire period, all hospital employees, independent of their vaccination status, were obligated to continue routine testing for SARS-CoV-2 at least once weekly by nasopharyngeal or nasal COVID-19 Antigen Rapid Test Device (Abbott Laboratories, Chicago, IL, USA), according to the test policy of the hospital. Any post-vaccination SARS-CoV-2 antigen detection in a respiratory specimen had to be confirmed by nasopharyngeal PCR testing. All postvaccination SARS-CoV-2 infections were reported to the hospital’s COVID-19-Tracing Team, which was responsible for isolation demands and contact tracing. In the present retrospective observational cohort study, SARS-CoV-2 infection incidence and distribution in vaccinated staff members were analysed in relation to demographic data, vaccine brands and vaccine administration dates. The final cut-off date of follow up to include newly diagnosed postvaccination infections into the present report was 31 July 2021. Vaccination status at the time of positive PCR test result was categorized into three groups and arbitrarily defined as (a) fully vaccinated (≥14 days had elapsed since the second vaccine dose), (b) partially vaccinated (≥21 days had elapsed since the first vaccine dose, but <14 days after the second dose) and (c) insufficiently vaccinated (<22 days had elapsed since the first vaccine dose). According to the CDC definition, the term breakthrough infection was allocated to the first of these groups (confirmed SARS-CoV-2 infection ≥14 days after termination of all recommended vaccine doses).

The study was approved by the ethics committee of the Medical University of Vienna (No.1721/2021) and the medical directorate of the hospital. Due to the retrospective study design the ethics committee provided a waiver of informed consent.

Statistical analysis

We used descriptive statistics and reported counts and proportions for categorical data and measures of distribution as either median (interquartile range (IQR)) or mean ± standard deviation (SD) for continuous data. Chi-square test and independent samples t test and analysis of variance were used for group comparisons. Postvaccination infection rates were standardized by the number of person-days at risk with regard to the three vaccination groups (insufficiently, partially and fully vaccinated participants), by dividing the number of cases by the sum of days at risk. As numbers are quite low, we report the 30 days (i.e. monthly) infection rates. As we had access to aggregated data for uninfected vaccinees only (see section on limitations) we had to make simplifications with regard to the interval between administration of the first and second vaccine doses. Based on the recommendations of the Austrian national vaccination board, we assumed 11 weeks for ChAdOx1-S and 3 weeks for BNT162b2. Simplified Cox regression analysis was performed for comparing ChAdOx1-S against BNT162b2 with respect to hazard ratios for postvaccination infections for the three respective vaccination groups. All statistical analyses were performed using a standard IBM SPSS software package, version 27 (IBM, Armonk, NY, USA).

Results

The vaccination programme took place in winter/spring 2021, with the earliest vaccination on 12 January 2021 and the latest on 27 May 2021. Willingness to participate was extremely high (>95%).

Since the start of SARS-CoV-2 vaccination of 8553 hospital employees, a total of 78 postvaccination infection cases (25 vaccinated with BNT162b2 and 53 vaccinated with ChAdOx1-S) after administration of a minimum of one dose of vaccination had been identified by the end of July 2021.

Within the study and follow-up period, ending on 31 July 2021, the person-times at risk-adjusted monthly rates for postvaccination infections were 0.18% (BNT162b2) and 0.57% (ChAdOx1-S) for insufficiently vaccinated participants, 0.34% (BNT162b2) and 0.32% (ChAdOx1-S) for partially vaccinated participants and 0.06% (BNT162b2) and 0.04% (ChAdOx1-S) for fully vaccinated participants. There was no difference between the two vaccine brands with respect to hazard ratios for any of the respective post-vaccination infection types. No COVID-19-related need for hospitalization or death was reported.

Information on demographics, vaccine brand, vaccination status and PCR-cycle threshold (CT) values of 78 employees with a positive SARS-CoV-2 test result after at least one vaccination dose is presented in Table 1 and Fig. 1 (postvaccination infection cases did not differ compared with the overall cohort of participants of the vaccination programme with regard to age and gender; data not shown). The chronological distribution of these 78 postvaccination infection cases in relation to first and second vaccination dates and date of positive PCR test result is displayed in Fig. 2. Allocation of breakthrough infections to professional groups showed the highest counts in the nursing personnel (n = 13), followed by the medical and diagnostic service personnel (n = 11) and the medical personnel (n = 8) with a more or less balanced distribution across the remaining
groups. Prevalence of detailed SARS-CoV-2-induced symptoms at time of positive testing, which were recorded by telephone interview through a team of four physicians, is presented in Table 2.

Genotyping of positive PCR specimens revealed variants of concern (VOC) in 42 cases, including B.1.1.7 (n = 34; 24 in the ChAdOx1-S group and ten in the BNT162b2 group), B.1.351 (n = 2; all in the BNT162b2 group) and B.1.617.2 (n = 6; three in the ChAdOx1-S group and three in the BNT162b2 group). In post-vaccination cases, who did receive their second dose, heterologous second doses did not take place and median days between two doses were 21 (IQR 19–34 days) for BNT162b2 vaccine and 77 (IQR 68–87 days) for ChAdOx1-S vaccine. The difference of time between doses was due to recommendations of the Austrian national vaccination board. Fig. 3 illustrates the distribution of post-vaccination infections by vaccination status during the study and follow-up periods. The number of postvaccination SARS-CoV-2 infection cases by duration from first vaccination to positive PCR test result and individual vaccination status is represented in Fig. 4. Curves are displayed separately for the two vaccine types.

Detailed information of clinical characteristics, professional roles, vaccination status and PCR test results of the 18 employees with real breakthrough infections according to the CDC definition (infection ≥14 days after their second vaccine dose) are presented in Table 3.

**Table 3**

| Characteristics of 78 vaccinees with a positive confirmed SARS-CoV-2 test result by vaccination status |
|------------------------------------------------------------------------------------------------|
| Insufficiently vaccinated | Partially vaccinated | Fully vaccinated |
| Total, n | 78 | 23 | 37 | 18 |
| Female, n (%) | 53 (67.9) | 15 (60.9) | 25 (67.6) | 14 (77.8) |
| Age, median (IQR) | 40.5 (19–60) | 36.0 (19–57) | 43.0 (21–60) | 40.0 (24–55) |
| ChAdOx1-S-vaccinated, n (%) | 53 (69.7) | 18 (78.3) | 31 (83.8) | 4 (22.2) |
| BNT162b2-vaccinated, n (%) | 25 (32.1) | 5 (21.7) | 6 (16.2) | 14 (77.8) |
| PCR-CT value of first positive specimen collection, mean ± SD | 24.46 ± 7.10 | 22.55 ± 7.12 | 25.49 ± 7.42 | 24.78 ± 6.37 |

*(Abbreviations: IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.)*

**Fig. 1.** Age and gender distribution of the 78 postvaccination infection cases. The x-axis describes age groups in 5-year intervals. Women are displayed by red, men by black columns.

Discussion

In the cohort of 8553 employees, in whom at least one vaccine dose of BNT162b2 or ChAdOx1-S vaccine had been administered, occurrence of postvaccination infection was substantially higher than previously reported [1–4,9]. This discrepancy suggests that earlier numbers of reported breakthrough cases are probably a substantial undercount of infections among vaccinated people, as vaccinees with infections who are asymptomatic or who experience mild illness might not seek testing proactively.

Even if all infected employees of the present investigation were either asymptomatic or at least suffering from mild to moderate COVID-19-like symptoms and none required hospitalization, available mean PCR-CT values at time of positive testing of 24.46 ± 7.10 suggest relatively high viral load. So far, investigations on the comparison of viral load amounts between BNT162b2 vaccinees with postvaccination infection and non-vaccinated infected persons revealed controversial results, ranging from substantially lower CT values to comparable viral loads among unvaccinated versus
vaccinated people [10,11]. For explanation, authors were discussing a suboptimal protection of SARS-CoV-2 vaccines against VOC [11]. Though we do not have adequate information available if any person of our cohort of postvaccination infection cases caused further transmission of the virus, we observed a rapid increase of CT values within a short period, displaying values > 30 within 48 hours after the first positive test in most cases. In postvaccination infection cases, we found no difference in mean CT values between the two vaccine brands.

Published data on sex distribution of postvaccination infections vary from favouring either women [12] or men [8] to reflecting the entire population [1]. With respect to the present investigation, we interpret the higher percentage of postvaccination infections in women as a consequence of the higher proportion of females

---

**Table 2**

Detailed symptoms of 78 postvaccination SARS-CoV-2 infection cases by vaccine brand and vaccination status

| Occurrence of symptoms, n | BNT162b2 (n = 11) | ChAdOx1-S (n = 39) | Fully vaccinated participants (n = 18) |
|---------------------------|------------------|-------------------|---------------------------------------|
|                           |                  |                   | BNT162b2 (n = 14) | ChAdOx1-S (n = 4) |
| No/indefinite             | 7                | 25                | 5                      | 2                     |
| Fever/shivering           | 2                | 6                 |                        |                       |
| Cough                     | 3                | 4                 |                        |                       |
| Odour and taste disorder  | 1                | 4                 |                        |                       |
| Myalgia                   | 2                | 3                 | 1                      | 0                     |
| Cephalgia/Vertigo         | 5                | 4                 |                        |                       |
| Fatigue/Malaise/Exhaustion| 3                | 3                 |                        |                       |
| Sore throat               | 3                | 4                 | 3                      | 0                     |
| Rhinitis                  | 3                | 7                 | 4                      | 2                     |
| Eye redness               | 0                | 1                 |                        |                       |

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

* At time of first positive test result; some vaccinees reported more than one of the above listed symptoms.
within the hospital staff. In the same way, highest absolute counts of postvaccination infections in health-care staff member groups with direct patient contact rather reflect the higher proportion of those groups within tertiary health-care institutions than an effective higher risk for a postvaccination infection.

Among the 78 cases, the proportion of postvaccination infections attributed to VOC was similar to the reported distribution of VOC throughout the general Austrian population at that time. Accordingly, the latest breakthrough infections were attributed to B.1.617.2 (variant Delta), which was rapidly evolving to become the dominant circulating genotype during the late follow-up period. A recent article reported barely any inhibition of variant Delta in individuals who had received only a single dose of either BNT162b2 or ChAdOx1-S [13]. In the context of the present investigation, the distribution of VOC among partially and fully vaccinated persons is mirroring rather the evolution of variants than the effectiveness of single versus full vaccine doses.

Despite a reduced neutralizing response against Delta for both vaccine types after full immunization, Williams et al. reported higher vaccination effectiveness for BNT162b2 than for ChAdOx1-S (88% versus 60%) [14]. Also, Liu et al. argued that an increase in breakthrough infections might occur as a result of an up to 2.5 fold

![Fig. 3. Distribution of postvaccination infections during the study and follow-up period by vaccination status.](image)

![Fig. 4. Postvaccination SARS-CoV-2 infection cases by the interval between initial vaccine dose administration and positive PCR test result according to vaccination status (insufficiently and partially vaccinated versus completely vaccinated). Green columns present insufficiently and partially vaccinated persons; blue columns present fully vaccinated persons. Curves are separately displayed for ChAdOx1 and BNT162b2.](image)
In the present investigation, we report on postvaccination infections in a cohort of tertiary care hospital employees, in whom mRNA and vector-based COVID-19 vaccines were administered in around equal parts. Findings verify that both vaccine types protect against both wild-type and also variant SARS-CoV-2 breakthrough infections at least with respect to severe illness. To ensure maximal possible protection against SARS-CoV-2 infections it seems essentially important, however, that all recommended vaccine doses are administered.

**Transparency declaration**

We declare no conflicting interests. Funding: This study received no funding.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2021.11.023.

**References**

1. CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 vaccine breakthrough infections reported to CDC – United States, January 1–April 30, 2021. MMWR Morb Mortal Wkly Rep 2021;70:792–3.

2. Swift MD, Breeher LE, Tande AJ, Tommasso CP, Hainy CM, Chu H, et al. Effectiveness of messenger RNA coronavirus disease 2019 (COVID-19) vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a cohort of healthcare personnel. Clin Infect Dis 2021;73: e1366–e9.

3. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, 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.

4. Tande AJ, Pollock BD, Shah ND, Farrugia A, Virk A, Swift M, et al. Impact of the COVID-19 vaccine on asymptomatic infection among patients undergoing pre-procedural COVID-19 molecular screening. Clin Infect Dis 2021:ciab229. https://doi.org/10.1093/cid/ciab229.

5. Office for National Statistics. Deaths involving COVID-19 by vaccination status, England: deaths occurring between 2 January and 2 July 2021. Release date: 13 September 2021. London: ONS; 2021.

6. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. C4591001 clinical trial group. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. N Engl J Med 2020;383:2603–15.

7. Baden LR, El Sahly HM, Essink B, Korff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:40–54.

8. Pollett SD, Richard SA, Fries AC, Simons MP, Mende K, Lalani T, et al. The SARS-CoV-2 mRNA vaccine breakthrough infection phenotype includes significant symptoms, live virus shedding, and viral genetic diversity. Clin Infect Dis 2021:ciab543. https://doi.org/10.1093/cid/ciab543. Online ahead of print.

9. Tenforde MW, Dzion SM, Self WH, Talbott HK, Lindell CJ, Steingrub JS, et al. Effectiveness of Pfizer-BioNTech and Moderna vaccines against COVID-19 among hospitalized adults aged ‡65 years – United States, January–March 2021. MMWR Morb Mortal Wkly Rep 2021;70:674–9.

10. Levine-Tiefenbrun M, Yelin I, Katz R, Hertzli E, Golan Z, Schreiber L, et al. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. Nat Med 2021;27:790–2.

11. Ioannou P, Karakonstantis S, Astrinaki E, Saplamidou S, Vitsaxaki E, Hamilos G, et al. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. Nat Med 2021;27:790–2.

12. Teran RA, Walblay KA, Shane EL, Xydis S, Gagner A, et al. Post-vaccination SARS-CoV-2 infections among skilled nursing facility residents and staff members – Chicago, Illinois, December 2020–March 2021. MMWR Morb Mortal Wkly Rep 2021;70:632–8.

13. Planas D, Veyer D, Badaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature 2021;596:276–80.

14. Williams SV, Vusurika A, Ladhani SN, Fernandez Ruiz De Olano E, Hyanger N, Aano F, et al. An outbreak caused by the SARS-CoV-2 Delta (B.1.617.2) variant in a care home after partial vaccination with a single dose of the COVID-19 vaccine Vaxzevria, London, England, April 2021. Euro Surveill 2021;26:2100626.

15. Liu C, Ginn HM, Dejnirattisai W, Supasa P, Wang B, Tukeprakhon A, et al. Reduced neutralization of SARS-CoV-2 B.1.617.2 by vaccine and convalescent serum. Cell 2021;184:4220–4226e15.