




BRIEF REPORT**Long-term effects of SARS-CoV-2 vaccination in the nursing home setting**

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Abstract

Background: SARS-CoV-2 vaccination has significantly reduced infection, hospitalization, and lethality rates among nursing home (NH) residents, but durability of vaccine effects remains unknown.

This study investigated the long-term impact of BNT162b2 SARS-CoV-2 vaccine on breakthrough infection rates in the NHs of Florence, Italy.

Methods: Participants included residents living in Florence NHs as of April 1st, 2021, who had completed the primary SARS-CoV2 vaccination course by February 15th, 2021. Weekly rates of breakthrough infection were calculated between April 1st and October 31st 2021, with 7-day incidence defined as the number of new confirmed SARS-CoV-2-positive residents over the vaccinated resident census. Hospital admissions and deaths were recorded from local administrative and clinical sources. Patients admitted to NHs after April 1st were excluded to avoid confounding effect of different vaccination timing.

Results: Among 2271 vaccinated residents (mean age 86.6, 74% female), we recorded 105 cases of breakthrough infections. Rates of breakthrough infection remained very low in the 6 months after vaccination, but started to rise over the following months, peaking at 0.94%, and then became stable around 0.2%–0.3%. Over the study period, infection rates remained low as compared to the incidence of SARS-CoV-2 infection during pre-vaccination period. Overall hospitalization and lethality rates were 8%.

Conclusions: Among vaccinated NH residents, rates of breakthrough SARS-CoV-2 infection, hospitalization and lethality remained low up to 9 months following primary vaccination course. A mild resurgence of SARS-CoV-2

Giulia Rivasi and Matteo Bulgaresi contributed equally to this study.

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infection, after 6 months from vaccination, suggests a decline of vaccine effectiveness in preventing transmission.

KEYWORDS

breakthrough infection, COVID-19, nursing home residents, older adults, vaccine

INTRODUCTION

The BNT162b2 mRNA vaccine has proven effective in preventing new SARS-CoV-2 infections and severe COVID-19 disease, with protective effect becoming evident from 2 weeks after the first dose.¹ What remains unclear, however, is how long the vaccine provides protection against COVID-19 and against SARS-CoV-2 transmission.

A recent update to the preliminary efficacy report of the BNT162b2 described a gradual decline of vaccine efficacy in disease prevention over the 6 months following vaccination, with an average 6% reduction of efficacy, every 2 months.² Moreover, available data indicate that the immune response to the BNT162b2 vaccine declines over time after vaccination in all individuals, reaching lower antibody levels among older in comparison with younger adults.^{3–5} These findings raise a concern that, in the upcoming months, a large proportion of vaccinated individuals could lose their protection against SARS-CoV-2 infection, potentially increasing the risk for new epidemic waves. Indeed, recent reports confirm that BNT162b2 effectiveness against infection decreases over time and describe an increase of SARS-CoV-2 cases in fully vaccinated persons (i.e., breakthrough infections), in parallel with the circulation of SARS-CoV-2 variant strains.^{4,6–8}

The issue is even more relevant to nursing home (NH) residents, a vulnerable population characterized by higher risk for severe COVID-19 outcomes^{9–11} and blunted immune response to the BNT162b2 vaccine.^{12,13} Studies have clearly demonstrated that SARS-CoV-2 vaccination had a positive impact on the epidemic course, hospital admissions and death risk among NH residents^{11,14–16} although a decline of effectiveness against SARS-CoV-2 infection has been observed in this population after Delta variant diffusion.⁷ Understanding the long-term effectiveness of vaccination is a necessary prerequisite to develop appropriate preventive healthcare strategies, particularly in subgroups at higher risk of COVID-19-related adverse outcomes such as NH residents.

The present study investigated the long-term impact of BNT162b2 SARS-CoV-2 vaccine on breakthrough infection rates in residents of Florence NHs (Tuscany, Italy).

Key points

- Among vaccinated nursing home residents in Florence, Italy, rates of breakthrough SARS-CoV-2 infection, hospitalization, and lethality remained low up to 9 months following primary vaccination course.
- A mild resurgence of SARS-CoV-2 infection occurred 6 months after the second dose, including a limited number of severe cases.
- Lethality rate remained stable at lower levels as compared to the pre-vaccination period.

Why does this paper matter?

The mild resurgence of SARS-CoV-2 infection suggests a decline of vaccine effectiveness in preventing viral transmission over time.

METHODS

At the beginning of the SARS-CoV-2 vaccination campaign, Tuscany Health System (Tuscany, Italy) prioritized NH residents and healthcare workers to receive the BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 mRNA vaccine. All SARS-CoV-2-naïve NH residents received two doses of vaccine, 21 days apart, between December 27th 2020 and January 17th 2021 (first dose) and between January 21st and February 15th 2021 (second dose), while a single dose was administered, over the same period of time, to residents with a documented history of SARS-CoV-2 infection. Henceforth, both vaccination schemes are referred to as “primary vaccination course.” At the same time, the BNT162b2 vaccine was administered also to all health staff members providing consent. This primary vaccination course, together with strict prevention measures, was associated with a sharp decline in SARS-CoV-2 new cases among NH residents over the following 2 months, with infection rate falling to zero by March 2021, as described in a previous paper.¹⁵

In the present study, we enrolled residents living in Florence NHs as of April 1st 2021, and we calculated the weekly breakthrough infection rates for 7 months, until

October 31st 2021, when administration of BNT162b2 booster doses began. The 7-day incidence of breakthrough infections was calculated as the number of new confirmed SARS-CoV-2-positive residents over the vaccinated resident census. In addition, COVID-19 symptoms, hospital admissions and deaths were recorded. SARS-CoV2 related lethality and hospitalization rate, before and after July 31st 2021, were compared with chi-square.

Information on SARS-CoV2 diagnosis, infection-related symptoms, hospitalization, and lethality was collected from administrative data of the local Health District and from the daily reports of a multidisciplinary team providing “hospital-at-nursing-home” care (GIROT, Gruppo Intervento Rapido Ospedale Territorio)¹⁷ to NH residents affected by COVID-19.

Transmission control strategies, including use of personal protective equipment, were maintained throughout the study period; NH residents and health staff members were screened for SARS-CoV-2 infection every 2 weeks. SARS-CoV-2-positive residents were isolated in dedicated areas and received standardized on-site care by the GIROT team, as detailed elsewhere.¹⁷

As the vaccine campaign was completed, SARS-CoV-2 vaccination became a prerequisite for NH admission. However, patients admitted after April 1st 2021, were excluded from the analysis to avoid confounding effects of a different vaccination timing.

Ethical approval for this research was obtained from the Local Ethic Committee (protocol number 2157).

RESULTS

Among the 2271 vaccinated residents living in Florence NHs as of April 1st 2021 (mean age 86.6 years, 74% female), a total of 105 cases of SARS-CoV-2 breakthrough infections were confirmed during the study period. Baseline characteristics of the study sample and of SARS-CoV2-positive vaccinated residents are reported in Table 1.

Until the end of July, that is, approximately 6 months after complete vaccination, only few cases were observed, with the exception of a 0.4% incidence peak reported in mid-April. Cases of breakthrough infections started to rise over the following months, when weekly infection rates stabilized around 0.2–0.3%, with a pick at 0.94% at the beginning of September 2021 (Figure S1). Throughout the study period, incidence of breakthrough infections remained low as compared to the pre-vaccination period, that is, before the vaccine campaign (Figure 1).

Among vaccinated residents testing positive for SARS-CoV-2 infection, the majority was asymptomatic or mildly symptomatic (83%, Table 1). During the entire

TABLE 1 Characteristics of the study sample

Vaccinated NH residents (n = 2271)	
Mean age (years)	86.6
Female residents	74%
Behavioral symptoms of dementia	6%
Severe disability	76%
Vaccinated SARS-CoV2-positive residents (n = 105)	
Mean age (years)	86.7
Female residents	90%
Severe disability (<2 BADL preserved)	73%
Dementia	
Mild/moderate	23%
Severe	63%
Behavioral symptoms of dementia	21%
Walking capacity	
Preserved (with/without assistance or walking aid)	13%
In wheelchair	51%
Bedridden	35%
Hypertension	49%
Cardiac disease	24%
Atrial fibrillation	19%
Diabetes	22%
Previous stroke	13%
COPD	14%
Chronic kidney disease	20%
COVID-19 symptoms severity	
Absent/minimal	58%
Mild/moderate	25%
Severe	17%

Abbreviations: BADL, Basic Activities of Daily Living; COPD, chronic obstructive pulmonary disease.

study period, 8 residents (8%) were admitted to the hospital and 8 residents (8%) died due to severe COVID-19 disease. Infection lethality was 5% up to 6 months after the primary vaccination course and 8% during the following 3 months. Hospital admission rate was 10% up to 6 months after the primary vaccination cycle and 7% afterwards ($p = 0.82$) (Figure 2).

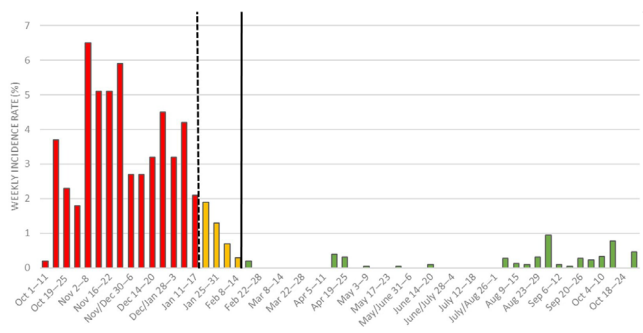


FIGURE 1 Weekly incidence rates of SARS-CoV-2 new cases in nursing homes of the Florence Health District during the pre- and post-vaccination period (October 1st, 2020–October 31st, 2021). The date on the x axis indicates the first day of the monitoring week. Vertical lines indicate administration of the first (dashed line) and second (solid line) vaccine dose

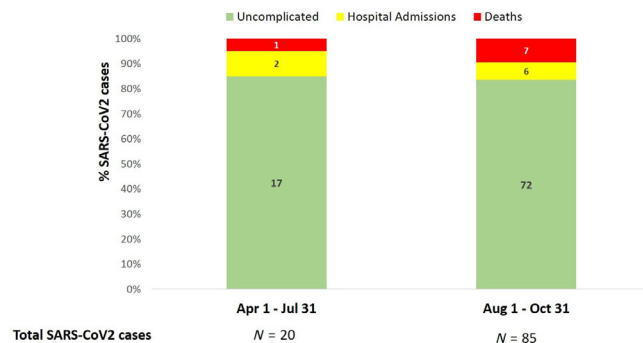


FIGURE 2 Deaths and hospital admissions in SARS-CoV-2 infected residents up to 6 months after the primary vaccination course (April 1–July 31) and during the subsequent 3 months (August 1–October 31). Absolute numbers are reported in the figure and percentages on the y axis

DISCUSSION

Among fully vaccinated residents living in NHs of Florence (Italy), breakthrough infections were rare and incidence rates remained close to zero in the 6 months following complete BNT162b2 vaccination. A trend toward an increase of case rates was observed in subsequent months, although weekly incidence remained low compared to the pre-vaccination period (Figure 1). Hospitalization and lethality remained stable up to 9 months following primary vaccination course (Figure 2).

A recent case–control study showed that the effectiveness of BNT162b2 vaccine against SARS-CoV-2 transmission peaks in the first month after the second dose, then gradually decreases up to 4 months after vaccination.⁴ These data are consistent with reports from population-based studies, showing a reduction of vaccine effectiveness concomitantly with the emergence of variant strains and a

less stringent application of preventive measures.^{6,8,18} Similarly, in a large sample of U.S. NH residents, vaccine effectiveness was found to decrease from 75% to 53%, as the B.1.617.2 (Delta) variant became predominant in the United States, although it was not possible to differentiate between the independent impact of the Delta variant and the waning of vaccine-induced immunity.⁷

Higher case rates have been described in early vaccinated as compared to late vaccinated individuals, suggesting time-dependent reduction in neutralizing antibodies as a contributing factor to reduced vaccine effectiveness.^{6,18} Indeed, a decrease of humoral response to BNT162b2 vaccine has been observed starting from 2 months after vaccination^{3,5} and the occurrence of breakthrough infections was found to correlate with neutralizing antibody titers, with infected individuals showing lower titers than uninfected controls.¹⁹ Notably, most studies agree that antibody levels over time are lower in older than younger adults.⁵ Moreover, older adults show a greater decrease in neutralizing antibody titer up to approximately 3 months after vaccination.³ Therefore, in older adults, neutralizing antibodies may drop below thresholds of protection earlier than in younger individuals, determining a greater susceptibility to breakthrough infections.

Nevertheless, in our sample of NH residents, incidence of breakthrough infections was low and comparable to that previously described for younger adults.¹⁹ Moreover, despite the abovementioned rise in SARS-CoV-2 cases, incidence rates remained considerably lower as compared to the pre-vaccination period.¹⁵ Recent data suggest that individuals with breakthrough infections may be less contagious than unvaccinated persons,¹⁹ which may have contributed to keeping incidence rates low. Moreover, it is important to emphasize that, in the NHs involved in the study, prevention measures were maintained and rigorously applied throughout the study period.

Available literature data from the general population indicate that vaccine effectiveness against severe disease, hospitalization, and death does not decline over time.^{2,4,8} Consistently, in our study sample of NH residents, most breakthrough infections were mild or asymptomatic, as previously observed in healthcare workers.¹⁹ Yet, hospitalization rate (8%) significantly increased as compared to the early post-vaccination period (3%),¹⁵ getting closer to that reported in unvaccinated residents during the second wave (10%).¹⁷ Lethality rate (8%) was significant, but lower than previously reported in unvaccinated residents of the study area (23%)¹⁷ and similar to that observed in the early post-vaccination period (6%).¹⁵ Lethality was consistent with what was recently described in a smaller sample of NH residents during a Spanish post-

vaccination outbreak,²⁰ while hospitalization rate was lower, possibly due to the “hospital-at-nursing home” model of care that has been adopted by the Florence Health District during COVID-19 epidemic.¹⁷

These findings are subject to some limitations. First, humoral response to vaccination was not routinely investigated, thus preventing us to correlate breakthrough infection occurrence with neutralizing titers and to explore the potential role of waning vaccine-induced immunity. Second, variant strains were not systematically assessed in the study sample. Therefore, although Italian epidemiological data show that by July 20th 2021, more than 94% of SARS-CoV-2 molecular swabs detected Delta variants RNA,²¹ we were unable to examine the impact of SARS-CoV-2 variants in NH setting during the post-vaccination period. Even though circulation of SARS-CoV-2 variants had already been documented in the Florence Health District during the early post-vaccination period, we cannot exclude that they may have contributed to the long-term resurgence of infections observed in the present study. Finally, data on vaccination of health staff members were not sufficiently complete to assess its role as a potential confounder.

The strength of our study lies in the constant routine screening for SARS-CoV-2 infection that was carried out every 2 weeks in all NHs of the study area, using antigenic swabs. This allowed for a strict monitoring of incidence rates over an extended period of time.

CONCLUSIONS

Among vaccinated NH residents, rates of breakthrough SARS-CoV-2 infection remained low up to 9 months following primary vaccination course, resulting in a small number of deaths and hospital admissions. A mild resurgence of SARS-CoV-2 infections occurred 6 months after the second dose, including a limited number of severe cases, although lethality rate remained stable at lower levels as compared to the pre-vaccination period.

These findings suggest that vaccinated NH residents might remain at some risk for breakthrough infection in the long term. Therefore, adherence to infection control measures and screening strategies remain crucial for protection of NH residents. Furthermore, our data support the use of booster vaccine doses as a strategy to optimize protective immunity. Ongoing follow-up data are being collected to understand persistence of vaccination effects over a longer period of time.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Conception and design: Giulia Rivasi, Matteo Bulgaresi, Enrico Benvenuti, Enrico Mossello. *Acquisition, analysis and interpretation of data:* all authors. *Drafting the article:* Giulia Rivasi, Matteo Bulgaresi, Chiara Bandinelli, Enrico Benvenuti, Enrico Mossello. *Revising of the article for important intellectual content:* all authors. *Final approval of the version to be published:* all authors.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Figure S1 Weekly incidence rates of SARS-CoV-2 breakthrough infection in nursing homes of Florence during the study period (April 1st, 2021–October 31st, 2021). The date on the x axis indicates the first day of the monitoring week.

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