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MAJOR ARTICLE

Clinical effectiveness of SARS-cov-2 booster vaccine against Omicron infection in residents and staff of Long-Term Care Facilities: a prospective cohort study (VIVALDI)

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Background: Successive SARS-CoV-2 variants have caused severe disease in long-term care facility (LTCF) residents. Primary vaccination provides strong short-term protection, but data are limited on duration of protection following booster vaccines, particularly against the Omicron variant. We investigated effectiveness of booster vaccination against infections, hospitalisations and deaths among LTCF residents and staff in England.

Methods: We included residents and staff of LTCFs within the VIVALDI study (ISRCTN 14447421) who underwent routine, asymptomatic testing (December 12 2021-March 31 2022). Cox regression was used to estimate relative hazards of SARS-CoV-2 infection, and associated

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hospitalisation and death at 0-13, 14-48, 49-83, 84-111, 112-139 and 140+ days after dose 3 of SARS-CoV-2 vaccination compared to 2 doses (after 84+ days), stratified by previous SARS-CoV-2 infection and adjusting for age, sex, LTCF capacity and local SARS-CoV-2 incidence.

Results: 14175 residents and 19973 staff were included. In residents without prior SARS-CoV-2 infection, infection risk was reduced 0-111 days after first booster, but no protection was apparent after 112 days. Additional protection following booster vaccination waned, but was still present at 140+ days for COVID-associated hospitalisation (aHR: 0.20, 0.06-0.63) and death (aHR: 0.50, 0.20-1.27). Most residents (64.4%) had received primary course of AstraZeneca, but this did not impact on pre- or post-booster risks. Staff showed a similar pattern of waning booster effectiveness against infection, with few hospitalisations and no deaths.

Conclusions: Our findings suggest that booster vaccination provided sustained protection against severe outcomes following infection with the Omicron variant, but no protection against infection from 4 months onwards. Ongoing surveillance for SARS-CoV-2 in LTCFs is crucial.

Keywords: SARS-CoV-2; COVID-19; Omicron; Vaccine effectiveness; long-term care facilities.

INTRODUCTION

The disproportionate impact of COVID-19 on long-term care facilities (LTCFs) has been extensively documented, both in terms of direct effects of morbidity and mortality, and indirect consequences of reduced access to healthcare, services and social interactions[1]. Likely reasons for this include the closed-setting environment of LTCFs, impaired immune responses due to aging and high levels of comorbidity[2]. As such, LTCF residents and staff were prioritised for vaccination against SARS-CoV-2.

Vaccination programmes in UK LTCFs commenced on 8 December 2020[3, 4], with primary series delivery of homologous prime-boost with either BNT162b2 (Pfizer) or ChAdOx1 (AstraZeneca) using an 8-12 week dose interval. LTCF residents and staff were prioritised for additional booster vaccination (third dose) from 14 September 2021 with a fourth dose for adults aged 75 years and over and older residents in LTCFs from Spring 2022[5] based on evidence that protection against severe disease waned from six months following primary vaccination in older adults[6], and concerns about the impact of new variants.

We previously reported high level of short-term protection against infection and severe clinical outcomes following primary course vaccination in LTCF residents and staff, whilst Alpha and Delta variants were dominant[7]. However, we observed substantial waning of protection against infection in staff and against all outcomes (infection, hospital admission, death) in residents from 84 days (12 weeks) following second dose, which was restored following a booster dose[7]. Substantially increased short term protection against symptomatic disease, hospitalisation and

death was also seen in adults >50 years following a third dose booster vaccination during high prevalence of Delta variant, with limited waning of protection after 70 days [8]. Data on booster vaccination effectiveness against Omicron in LTCFs are limited, particularly following a primary course of AstraZeneca. However, three vaccine doses have been reported to offer high levels of protection against hospitalisation with the Omicron variant in community-dwelling adults aged 75 years and over, with minimal waning 2-3 months post-vaccination[9].

The aim of this study was to evaluate the effectiveness of third and fourth dose booster vaccination against infection, hospitalisations and death amongst staff and residents of LTCFs in England, from when the Omicron variant became dominant until the end of the asymptomatic testing programme in LTCF residents (December 12 2021 to March 31 2022).

METHODS

Study design and setting

VIVALDI is a prospective cohort study investigating SARS-CoV-2 in residents and staff in LTCFs in England and is described in detail elsewhere[10]. In the analysis period, following national guidelines, residents were undergoing monthly routine polymerase chain reaction (PCR) testing while staff were undergoing weekly testing using a combination of PCR and lateral flow devices (LFD). We did not require PCR confirmation of positive LFD results in our analyses. Residents with a positive PCR test were not routinely re-tested for 90 days unless they developed new COVID-19 symptoms[11], however, staff resumed asymptomatic LFD testing upon return to work following infection[12].

The analysis period is defined from December 12, 2021, when the S-gene target failure (SGTF) marker for Omicron (BA.1) was first detected in the dataset[13], to 31 March 2022, when asymptomatic testing in residents ended[14]. Individuals were eligible for inclusion if they had at least one PCR or LFD result available within the analysis period. We excluded individuals who had not received at least two vaccine doses at the start of the analysis period.

Data extraction and linkage

We retrieved all PCR results and available LFD results from routine symptomatic and asymptomatic testing in LTCFs, and positive PCR results from staff and residents who underwent clinical testing in hospitals through the COVID-19 Datastore[15]. Test results, vaccination, hospitalisation and deaths data were linked to study participants using pseudo-identifiers based on individuals' unique National Health Service (NHS) numbers[7]. COVID-19 hospitalisation was defined as an admission within 14 days of a positive PCR or LFD test for SARS-CoV-2, or admission with positive test on the same or subsequent day. COVID-19 death was defined as within 28 days of positive PCR or LFD test.

As previously[7], we linked SARS-CoV2 serological test results for IgG antibodies to the nucleocapsid protein (Abbott ARCHITECT system (Abbott, Maidenhead, UK)) in a subset of participants who consented to blood sampling specifically for the VIVALDI study[16]. Recruitment to the blood sampling part of the study was managed within LTCFs, and so this subset may not be completely representative of the population as a whole (e.g. those residents less able to consent would be less likely to be recruited). We combined positive PCR and LFD results, COVID-19-related hospital admission records, and positive nucleocapsid antibody results before the analysis period into a binary variable indicating evidence of prior SARS-CoV2 exposure.

Care Quality Commission unique location identification (CQC-ID) were used to link residents to LTCFs. Data on bed capacity were retrieved from Capacity Tracker[17], and requested directly from LTCF managers if unavailable. Seven-day rolling rates of SARS-CoV2 incidence at local authority level[18] were used to represent local infection pressure for each LTCF. A data privacy impact assessment was completed for the VIVALDI study and a privacy notice published[19].

Statistical analysis

We examined individual-level vaccine effectiveness against infection, hospitalisation within 14 days and death within 28 days of positive test. Analyses were separately conducted for residents aged 65 years and older and for staff between 18 and 75 years. Individuals were eligible for inclusion if they had complete data on sex and age, had received at least 2 vaccine-doses 84 days (≥12 weeks) before analysis start date, had at least one PCR or LFD test result recorded within the analysis period and were linked to a LTCF with data on total number of staff and residents. Individuals with third vaccine dose recorded prior to start of official rollout on September 14 2021 were excluded.

We used Cox regression models to derive adjusted hazard ratios (HRs) for the risk of each outcome of interest. Vaccination status was included as a time-varying covariable. The reference category was 2 vaccine doses, with 84 days (≥12 weeks) elapsed from Dose 2. The exposure categories were 0–13, 14–48, 49–83, 84-111, 112-139 and 140 or more days following Dose 3, and any time following Dose 4. Individuals could start in the 2-dose vaccinated state and sequentially transition through 3- and 4-dose vaccinated exposure states. Individuals entered the risk period on 12 December 2021, or date of their first recorded PCR/LFD result within VIVALDI if later. Individuals with positive PCR/LFD result within 30 days prior to 12 December 2021 entered the risk period from the 31st day post-positive test. Individuals exited the risk period at the earliest of: outcome of interest or end of analysis period. For hospitalisation, individuals were additionally censored at 15 days post-positive SARS-CoV-2 test if there was no hospital admission by then, and similarly for mortality after 29 days. Baseline hazard was defined over calendar time. 95% CIs were calculated using robust SEs accounting for dependence of infection events within LTCFs.

The primary analysis was stratified by evidence of SARS-CoV2 infection prior to the risk period. We adjusted for sex (binary variable), age (5-knot restricted cubic spline term), LTCF size expressed as total number of beds (linear term), local SARS-CoV2 incidence expressed as 7-day rolling rate per 100 population. Local incidence was included as a 3-knot restricted cubic spline term with separate coefficients for each calendar month. We also evaluated effect of AstraZeneca vs Pfizer primary vaccination course (as recorded for Dose 2) on each outcome. This effect was estimated separately before and after initial booster dose (Dose 3) and tested jointly using a multivariate Wald test.

We also conducted descriptive analysis of the incidence of new and repeat SARS-CoV-2 infections in LTCF staff and residents from October 2020 onwards (when regular testing had been implemented) to evaluate whether the Omicron variant was associated with a rise in reinfections. Repeat infections were considered to be any positive PCR/LFD test recorded over 30 days after previous positive test. Participants were considered to be under follow-up from first recorded PCR/LFD test until 90 days following their last recorded test.

All statistical analyses were conducted using STATA 17.0.

Patient consent statement

Patient consent was not obtained for use of data other than for the subset of patients who underwent blood sampling specifically for the VIVALDI study. The legal basis to access data from staff and residents without informed consent was provided by Regulation 3(4) of the Health Service (Control of Patient Information) Regulations 2002 (COPI)[20]. Ethical approval for the study was obtained from South Central-Hampshire B Research Ethics Committee (20/SC/0238).

RESULTS

14175 residents and 19793 staff from 328 LTCFs (Table S1) were included in the analysis (Figure 1). 2700 residents (19.0%) and 2911 staff (14.7%) had recorded evidence of SARS-CoV-2 infection prior to the analysis period (Table 1). 60953 PCR (mean±SD per month, 1.92±2.34) and 27533 LFD (0.76±2.36 per month) tests for residents, and 80505 PCR (1.62±2.02 per month) and 281947 LFD (5.16±6.34 per month) tests for staff were included.

In the subset of 971 residents with at least one nucleocapsid antibody result available prior to the analysis period, antibodies indicating prior SARS-CoV-2 infection were found in 304 (31.3%). Of the 304, only 147 (48%) had other evidence of prior infection (i.e. positive PCR or LFD test, or hospital admission for COVID-19) recorded. Of the 2147 staff with at least one nucleocapsid antibody result available prior to the analysis period, antibodies indicating prior SARS-CoV-2 infection were found in 440 (20.5%). Of the 440, only 132 (30.0%) had other evidence of prior infection recorded. These findings indicate that the true proportion of residents and staff with

prior infections is likely to be substantially higher than that based on the available evidence for each individual participant given that a minority of participants underwent antibody testing.

12430 (87.7%) residents and 12505 (63.2%) staff had received a booster vaccination dose prior to the analysis period, and 13487 (95.1%) residents and 16977 (85.8%) staff by the end. First booster doses were Pfizer in the majority (residents n=13044, 96.7%; staff n=14379, 84.7%), with Moderna used in a small number (residents n=414, 3.1%; staff n=2584, 15.2%). Second boosters (fourth vaccine) had been received by 6.9% of residents and 0.9% of staff by the end of the analysis period.

Infection

In residents without known prior SARS-CoV-2 infection, there was reduced risk of SARS-CoV-2 infection in the periods 0-13 days (HR 0.56, 95% CI 0.36-0.88), 14-48 days (HR 0.33, 0.24-0.46), 49-83 days (0.37, 0.29-0.48) and 84-111 days (0.64, 0.51-0.80) after first booster vaccine dose, relative to 2-dose vaccination (Table 2). However, no protection was apparent at 112-139 days (1.04, 0.71-1.53) or 140+ days (1.17, 0.81-1.67) following booster vaccination. Residents with known infection prior to the analysis period were at reduced risk of new infection relative to those without prior infection (HR 0.50, 0.35-0.72), and within this group further protection following booster vaccination followed a similar pattern to that observed in infection-naïve residents. Infection rates were lower after second booster doses, but HR estimates were wide due to limited follow-up time. Additional adjustment for type of primary course before and after booster dose did not improve model fit (P=0.14).

A protective effect of first booster vaccine dose was also seen in staff, although no protection was apparent by 112-139 days (1.21, 1.03-1.41) (Table 3). However, prior infection was not associated with any reduction in risk of new SARS-CoV-2 infection in this group (HR 1.09, 0.94-1.25) and a similar pattern of protection from infection following first booster dose was observed in this group. Additional adjustment for type of primary course before and after booster dose did not improve model fit (P=0.13).

Hospitalisation

In residents without known prior SARS-CoV-2 infection, the first booster dose reduced risk of hospitalisation within 0-13 days of SARS-CoV-2 infection (HR 0.31, 95% CI 0.06-1.60) that was sustained across 14-48 days (0.23, 95%CI 0.08-0.64), 49-83 days (0.18, 0.08-0.40), 84-111 days (0.23, 0.11-0.47), 112-139 days (0.30, 0.11-0.79) and 140+ days (0.20, 0.06-0.63) from receipt of booster dose. No hospitalisations were observed after second booster doses, but follow-up time was limited. Residents with known infection prior to the analysis period were at reduced risk of hospitalisation relative to those without prior infection, and within this group there were too few hospitalisation events to reliably estimate the effect of booster vaccination. Additional adjustment for primary vaccine course type did not improve model fit (P=0.60). Staff

were at low risk of hospitalisation following SARS-CoV-2 infection, precluding meaningful analysis of the effect of booster vaccination.

Death

In residents without known prior SARS-CoV-2 infection, the first booster reduced risk of death within 28 days of SARS-CoV-2 infection after 0-13 days (HR 0.20, 95%CI 0.03-1.55), 14-48 days (0.17, 0.06-0.48), 49-83 days (0.15, 0.07-0.31) and 84-111 days (0.15, 0.08-0.28), with apparent waning in the level of protection by 112-139 days (0.49, 0.23-1.01) and 140+ days (0.50, 0.20-1.27). Residents with known infection prior to the analysis period were at reduced risk of death relative to those without prior infection, and within this group there were too few deaths to evaluate the impact of booster vaccination. No deaths were observed after second booster doses, but limited follow-up time was available. Additional adjustment for primary vaccine course type did not improve model fit (P=0.99). No deaths within 28 days of a positive SARS-CoV-2 test were observed among staff.

Reinfections

The appearance and spread of the Omicron variant in late 2021 and early 2022 was associated with a peak in incidence of new SARS-CoV-2 infections that exceeded the previous highest recorded levels in both residents and staff (Figure 2). There was also a substantial rise in the incidence of reinfections detected. In line with our Cox models, residents with prior SARS-CoV-2 infection only displayed moderately lower incidence of new infection than exposure-naïve residents during this period, and in staff the incidence of infection was unrelated to history of previous infection (Figure S1).

Our analysis of the risk of infection in relation to booster vaccination only includes the first observed infection in any given participant within the analysis period. However, we observed two infections within the analysis period, using 30-day cut-off to define new infection episode, in 15 residents (0.11%) and 79 staff (0.40%).

DISCUSSION

We found that SARS-CoV-2 infection and associated hospitalisations and deaths in LTCF residents who had received booster (third dose) vaccination were reduced compared to those who had only received primary vaccine course during the period of Omicron dominance in England. However, no protection against infection was apparent in residents from 112 days following third dose, and there was some waning of protection against hospitalisation and death. Whilst there was some evidence to suggest that infection rates were lower after second booster doses, the follow-up time was limited. Among staff, infections were reduced in those who had received booster vaccination but the rates of hospitalisation and death were too low for analysis. Overall, these findings suggest that booster vaccination provides protection in residents against infection

with the Omicron variant but that this protection wanes, with more moderate waning of protection against associated severe outcomes. Those with prior infection were susceptible to reinfection with Omicron.

Few studies have explored infection and severe outcomes after booster vaccination doses specifically in LTCFs and fewer still have explored this during the period in which the Omicron variant dominated. To the best of our knowledge, this is the only study to evaluate booster effectiveness in residents of LTCFs who have received AstraZeneca vaccine as primary course.

A Canadian study explored the effectiveness of fourth dose vaccination (primarily mRNA-1273), compared to third dose, among residents aged 60 years and older in LTCF and found evidence of improved protection against infection, symptomatic infection, and severe outcomes during the Omicron period[21]. A waning effect was observed after 84 days of third dose, but follow-up time after fourth dose was too limited for analysis[21]. A study conducted in the United States whilst Omicron was dominant estimated that VE against infection was 46.9% in LTCF residents who received a booster dose compared to those who had received 2 dose (primary course) vaccination, where booster vaccination was received 14 or more days prior to a positive test[22].

Our findings are also consistent with studies conducted in Israel which found that a third dose of the BNT162b2 mRNA vaccine compared with receipt of only two doses[23] and a fourth dose of the BN162b2 mRNA vaccine compared with three vaccine doses appeared to be effective in reducing risk of hospitalisation, severe disease and COVID-19 related death[24, 25]. There was evidence of waning effectiveness against infection[24], but sustained protection against severe disease[24, 25]. However, the study exploring third dose vaccine effectiveness was conducted in the general population and excluded healthcare staff and LTCF residents, while the fourth dose studies were conducted in older adults aged 60 years and over but not specifically LTCF residents. These findings may therefore not be generalisable to vulnerable residents of LTCFs.

It might be considered surprising that staff showed a similar pattern of waning protection against SARS-CoV-2 infection following receipt of a booster vaccine dose, but this is consistent with previous work in which we found similar levels and patterns of decline between residents and staff for anti-spike antibody levels following second vaccination dose[26]. However, it is also relevant that booster vaccines within our analysis were based solely on the original Wuhan SARS-CoV-2 strain, and it has been shown that overall anti-spike antibody levels in response to such booster vaccines were not predictive of infection with the Omicron variant[27]. Despite concerns surrounding immunosenescence in older and vulnerable populations, and some uncertainty regarding the exact mechanism of protection given reduced neutralisation against Omicron, it is clear that booster vaccinations did provide substantial protection over the short term in LTCF residents[21, 22].

This study has a number of strengths. Data were collected from a large cohort of LTCF residents and staff across England and linked to routinely collected and high-quality data on testing,

hospitalisations, death and vaccination. The study population underwent regular, asymptomatic testing which enabled the systematic identification of study participants, accurate measurement of person-time at-risk and a comparatively unbiased assessment of vaccine effectiveness compared to studies that rely on symptomatic testing.

A limitation of the study is that it may have underestimated prior infection, as only a subset of participants underwent antibody testing. This will have resulted in an underestimate of the impact of past infection as people without antibody testing, along with those whose antibodies had waned, may have been misclassified as infection-naïve. For both residents and staff, a substantial proportion of those with evidence of prior infection on antibody testing did not have any other evidence of prior infection (i.e. positive PCR or LFD test, or hospital admission for COVID-19) recorded.

Due to the nature of the data collection for hospitalisation and death records, it was not possible to distinguish between outcomes that occurred in individuals 'with' and 'from' COVID-19.This could potentially have led to underestimation of the protective effect of booster vaccination on these severe outcomes. However, we also note that attribution of a single cause of death is not always clear-cut[28], particularly in the context of an extremely frail population.

Although our analysis focused on the period when the Omicron variant was dominant, we did not have access to sequencing data, so it was not possible to confirm viral sub-lineage or to investigate whether multiple positive PCR tests from the same individual over time were genuine reinfections. It was also not possible to include data on comorbidities which may impact on estimates of vaccine effectiveness.

This study suggests that third dose booster vaccination provides sustained protection against severe outcomes following infection with the Omicron variant in this vulnerable cohort, despite some waning, but protection against infection was not apparent from around 4 months onwards. In England, people aged over 75 years, including LTCF residents, and those who are clinically vulnerable are currently being offered a fourth COVID-19 vaccination dose[5]. Recent studies have shown fourth vaccine doses to be effective against severe illness caused by the Omicron variant when compared with a third dose administered 3-4 months previously in residents of LTCFs and older adults respectively[21, 25] but it is not yet known whether this pattern of waning immunity will continue to be seen. It seems likely that regular vaccination will be required for residents of LTCFs to ensure continued protection against SARS-CoV-2, particularly given the potential for the rapid emergence of new variants which may affect vaccine effectiveness. In this context, our findings underscore the critical need for continued surveillance of vaccine effectiveness against infection and severe outcomes in LTCFs, to inform future decisions on the frequency and timing of vaccination in this vulnerable cohort.

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Potential Conflicts of Interest: LS reports grants from the Department of Health and Social Care during the conduct of the study and is a member of the Social Care Working Group, which reports to the Scientific Advisory Group for Emergencies. AI-S and VB are employed by the Department of Health and Social Care who funded the study. AH reports funding from the COVID Core Studies Programme and is a member of the New and Emerging Respiratory Virus Threats Advisory Group at the Department of Health and Environmental Modelling Group of the Scientific Advisory Group for Emergencies. All other authors declare no competing interests.

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Author contributions: OS conducted statistical analyses and drafted Methods and Results, with MS, TP and AC contributing to coding of data processing and analysis. NLA drafted Introduction and Discussion. MK, HN-L, BA, CF, AI-S, VB, GT, PM, AH, AC and LS are involved in the planning, recruitment and organisation of the Vivaldi cohort study. GT and PM conduct lab work for the study. All authors contributed to the planning an interpretation of this analysis, and contributed to the final manuscript draft.

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FIGURES

Figure 1: Flow chart for inclusion in the analysis of booster vaccine effectiveness.

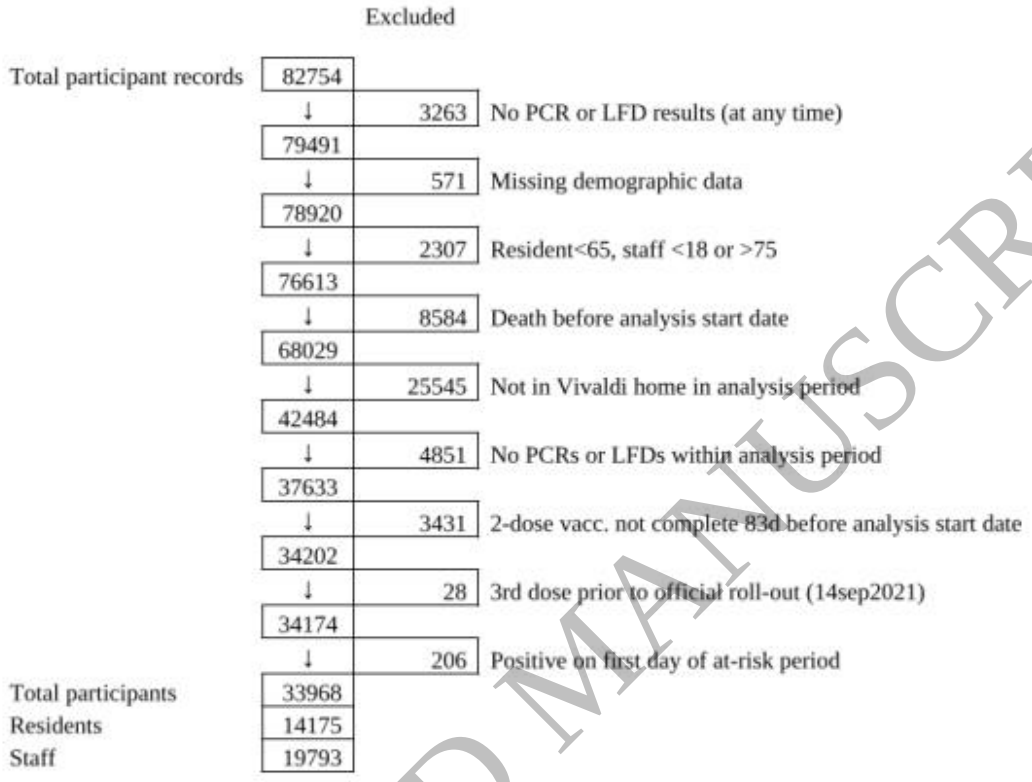
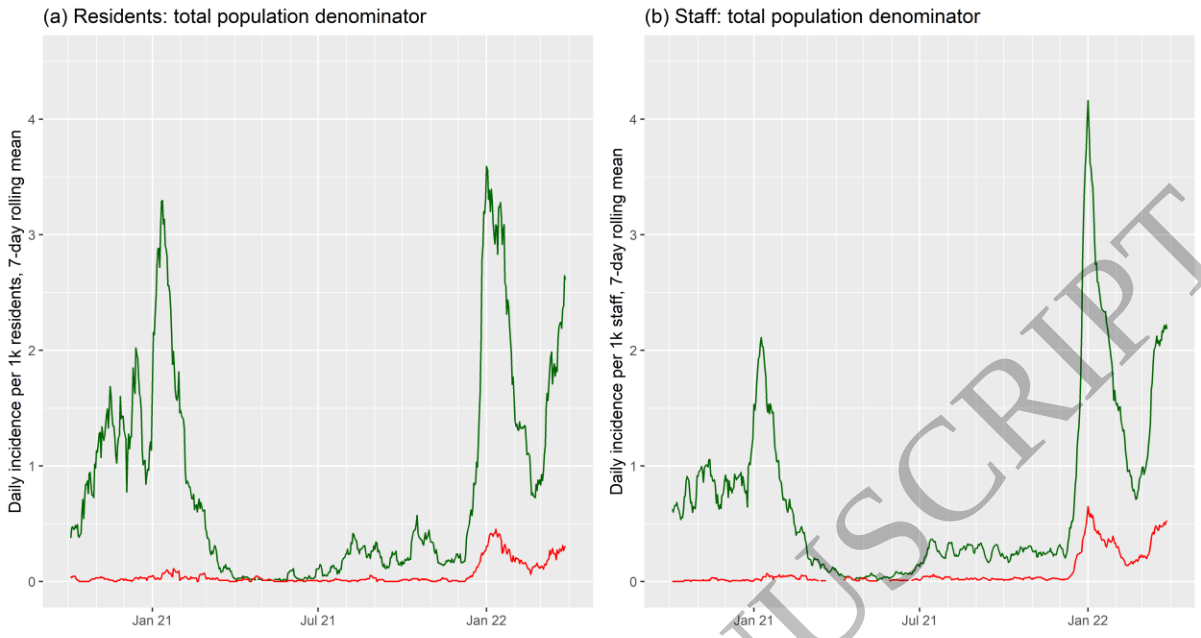


Figure 2: Rolling 7-day average incidence rate of new SARS-CoV-2 infections (green) and repeat SARS-CoV-2 infections (red) among residents (a) and staff (b) of long-term care facilities in the Vivaldi study. Incidence rates are calculated according to the total population under follow-up for residents and staff (and are proportional to total case counts).



TABLES

Table 1 Characteristics of residents and staff included in the analysis of booster vaccine effectiveness.

	Residents	**Staff**	**All participants**
N	14175	19793	33968
Age (IQR, range)	84.4 (76.4-90.4, 65.0-114.2)	50.8 (37.0-59.0, 18.0-75.0)	62.0 (47.0-81.8, 18.0-114.2)
Male sex	4619 (32.6)	4296 (21.7)	8915 (26.2)
Female sex	9556 (67.4)	15497 (78.3)	25053 (73.8)
Prior SARS-CoV-2 exposure			
Pre-analysis PCR positive	1958 (13.8)	2078 (10.5)	4036 (11.9)
Pre-analysis LFD positive	77 (0.5)	670 (3.4)	747 (2.2)
Pre-analysis COVID-19 admission	899 (6.3)	140 (0.7)	1039 (3.1)
Pre-analysis N-antibody results available	971 (6.9)	2147 (10.8)	3118 (9.2)
Pre-analysis N-antibody positive	304 (2.1)	440 (2.2)	744 (2.2)
Total pre-analysis infection	2700 (19.0)	2911 (14.7)	5611 (16.5)
Vaccination			
First dose			
AstraZeneca	8958 (63.2)	10496 (53.0)	19454 (57.3)

Pfizer BioNTech	5215 (36.8)	9091 (45.9)	14306 (42.1)
Moderna	2 (0.0)	197 (1.0)	199 (0.6)
Second dose			
AstraZeneca	9133 (64.4)	10484 (53.0)	19617 (57.8)
Pfizer BioNTech	5039 (35.5)	9104 (46.0)	14143 (41.6)
Moderna	2 (0.0)	196 (1.0)	198 (0.6)
Second dose to analysis start (days) (IQR, range)			
AstraZeneca	248 (233-258, 84-337)	218 (196-249, 84-305)	241 (207-256, 84-337)
Pfizer BioNTech	263 (252-271, 86-348)	259 (216-276, 84-348)	261 (234-275, 84-348)
Moderna	129 (97-160, 97-160)	123 (104-150, 84-289)	123 (103-150, 84-289)
Booster dose (at start of period)	12430 (87.7)	12505 (63.2)	24935 (73.4)
AstraZeneca	11 (0.1)	9 (0.1)	20 (0.1)
Pfizer BioNTech	12077 (97.2)	11160 (89.2)	23237 (93.2)
Moderna	342 (2.8)	1336 (10.7)	1678 (6.7)
Booster dose (by end of period)	13487 (95.1)	16977 (85.8)	30464 (89.7)
AstraZeneca	29 (0.2)	14 (0.1)	43 (0.1)
Pfizer BioNTech	13044 (96.7)	14379 (84.7)	27423 (90.0)
Moderna	414 (3.1)	2584 (15.2)	2998 (9.8)
Booster interval from dose 2 (IQR, range)	203 (191-217, 25-436)	199 (187-220, 56-436)	201 (189-218, 25-436)
2nd booster dose (by end of period)	985 (6.9)	173 (0.9)	1158 (3.4)
AstraZeneca	5 (0.5)	0 (0.0)	5 (0.4)
Pfizer BioNTech	768 (78.0)	144 (83.2)	912 (78.8)
Moderna	212 (21.5)	29 (16.8)	241 (20.8)
PCR testing (total tests)	60953	80505	141458
Tests per person per month (mean, SE)	1.92 (2.34)	1.62 (2.02)	1.75 (2.17)
LFD testing (total tests)	27533	281995	309528
Tests per person per month (mean, SE)	0.76 (2.36)	5.16 (6.34)	3.32 (5.52)

Table 2 Crude event rates and adjusted hazard ratios against PCR or LFD-positive SARS-CoV2 infections, hospitalisation within 14 days and deaths within 28 days of a positive PCR or LFD test for LTCF residents, by prior SARS-CoV2 exposure, and vaccination status

SARS-CoV-2 infections						
Prior SARS-CoV-2 exposure	**Vaccination status**	**Person-days**	**Infections**	**IR /1000pd**	**HR (95% CI)***	**HR (95% CI)***
Unexposed	D2 84+d	50569	215	4.25	Ref.	
	D3 0-13d	10350	42	4.06	0.56 (0.36-0.88)	

	D3 14-48d	75307	142	1.89	0.33 (0.24-0.46)	
	D3 49-83d	245243	537	2.19	0.37 (0.29-0.48)	
	D3 84-111d	233204	737	3.16	0.64 (0.51-0.80)	
	D3 112-139d	193957	467	2.41	1.04 (0.71-1.53)	
	D3 140+d	142948	430	3.01	1.17 (0.81-1.67)	
	D4 0+d	6991	16	2.29	0.78 (0.37-1.65)	
Exposed	D2 84+d	16788	31	1.85	0.50 (0.35-0.72)	Ref.
	D3 0-13d	3204	4	1.25		0.30 (0.11-0.87)
	D3 14-48d	19271	12	0.62		0.22 (0.12-0.42)
	D3 49-83d	63998	89	1.39		0.45 (0.28-0.72)
	D3 84-111d	60728	112	1.84		0.75 (0.47-1.18)
	D3 112-139d	50557	72	1.42		1.34 (0.79-2.28)
	D3 140+d	39885	70	1.76		1.44 (0.80-2.61)
	D4 0+d	1718	1	0.58		0.35 (0.05-2.58)
SARS-CoV-2 hospitalisations						
Prior SARS-CoV-2 exposure	**Vaccination status**	**Person-days**	**Hosp.**	**IR /1000pd**	**HR (95% CI)***	**HR (95% CI) ***
Unexposed	D2 84+d	53453	15	0.28	Ref.	
	D3 0-13d	10629	2	0.19	0.31 (0.06-1.60)	
	D3 14-48d	77043	7	0.09	0.23 (0.08-0.64)	
	D3 49-83d	251213	21	0.08	0.18 (0.08-0.40)	
	D3 84-111d	243597	23	0.09	0.23 (0.11-0.47)	
	D3 112-139d	201821	13	0.06	0.30 (0.11-0.79)	
	D3 140+d	147979	6	0.04	0.20 (0.06-0.63)	
	D4 0+d	7095	0	0	—	
Exposed	D2 84+d	17229	0	0	—	Ref.
	D3 0-13d	3259	0	0	—	—
	D3 14-48d	19415	0	0	—	—
	D3 49-83d	64986	1	0.02	—	—
	D3 84-111d	62445	1	0.02	—	—
	D3 112-139d	51754	1	0.02	—	
	D3 140+d	40806	0	0	—	
	D4 0+d	1720	0	0	—	—
SARS-CoV-2 mortality						
Prior SARS-CoV-2 exposure	**Vaccination status**	**Person-days**	**Deaths (w. 28d)**	**IR /1000pd**	**HR (95% CI)***	**HR (95% CI) ***
Unexposed	D2 84+d	55824	23	0.41	Ref.	
	D3 0-13d	10640	1	0.09	0.20 (0.03-1.55)	
	D3 14-48d	78127	6	0.08	0.17 (0.06-0.48)	
	D3 49-83d	254082	18	0.07	0.15 (0.07-0.31)	

	D3 84-111d	251293	27	0.11	0.15 (0.08-0.28)	
	D3 112-139d	210572	39	0.19	0.49 (0.23-1.01)	
	D3 140+d	151975	17	0.11	0.50 (0.20-1.27)	
	D4 0+d	7222	0	0	—	
Exposed	D2 84+d	17565	0	0	—	Ref.
	D3 0-13d	3268	0	0		—
	D3 14-48d	19506	1	0.05		—
	D3 49-83d	65357	0	0		—
	D3 84-111d	63674	9	0.14		—
	D3 112-139d	53106	3	0.06		—
	D3 140+d	41562	1	0.02		—
	D4 0+d	1720	0	0		—

*HR values in the two columns are from mathematically identical statistical models, but HRs in right-hand column are expressed relative to 'D2 84+d' vaccine status in individuals with prior SARS-CoV-2 infection.

Table 3 Crude event rates and adjusted hazard ratios against PCR or LFD-positive SARS-CoV2 infections, and crude event rates for hospitalisation within 14 days of a positive PCR or LFD test for LTCF staff, by prior SARS-CoV2 exposure, and vaccination status

SARS-CoV-2 infections						
Prior SARS-CoV-2 exposure	**Vaccination status**	**Person-days**	**Infections**	**IR /1000pd**	**HR (95% CI)***	**HR (95% CI) ***
Unexposed	D2 84+d	240831	909	3.77	Ref.	
	D3 0-13d	50432	142	2.82	0.33 (0.27-0.41)	
	D3 14-48d	220952	434	1.96	0.38 (0.33-0.43)	
	D3 49-83d	354361	731	2.06	0.57 (0.51-0.64)	
	D3 84-111d	297767	800	2.69	0.67 (0.59-0.76)	
	D3 112-139d	190912	442	2.32	1.21 (1.03-1.42)	
	D3 140+d	140821	461	3.27	1.72 (1.48-1.99)	
	D4 0+d	4818	7	1.45	0.77 (0.36-1.65)	
Exposed	D2 84+d	50290	200	3.98	1.09 (0.94-1.25)	Ref.
	D3 0-13d	7822	16	2.05		0.21 (0.12-0.36)
	D3 14-48d	30758	47	1.53		0.28 (0.20-0.39)
	D3 49-83d	58004	141	2.43		0.50 (0.40-0.62)
	D3 84-111d	52154	167	3.2		0.59 (0.47-0.73)
	D3 112-139d	38584	94	2.44		1.15 (0.87-1.53)
	D3 140+d	33867	101	2.98		1.43 (1.13-1.81)
	D4 0+d	479	0	0		—
SARS-CoV-2 hospitalisations						
Prior SARS-CoV-2 exposure	**Vaccination status**	**Person-days**	**Hosp.**	**IR /1000pd**	**HR (95% CI)***	**HR (95% CI) ***

Unexposed	D2 84+d	253522	2	0.01	—	
	D3 0-13d	51485	1	0.02	—	
	D3 14-48d	226901	3	0.01	—	
	D3 49-83d	363558	7	0.02	—	
	D3 84-111d	309364	4	0.01	—	
	D3 112-139d	198028	2	0.01	—	
	D3 140+d	146879	0	0	—	
	D4 0+d	4888	0	0	—	
Exposed	D2 84+d	53279	2	0.04	—	—
	D3 0-13d	7925	0	0		—
	D3 14-48d	31440	1	0.03		—
	D3 49-83d	59781	1	0.02		—
	D3 84-111d	54484	2	0.04		—
	D3 112-139d	40358	1	0.02		—
	D3 140+d	35167	0	0		—
	D4 0+d	479	0	0		—

*HR values in the two columns are from mathematically identical statistical models, but HRs in right-hand column are expressed relative to 'D2 84+d' vaccine status in individuals with prior SARS-CoV-2 infection.