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# Effectiveness of BNT162b2 mRNA Coronavirus Disease 2019 (COVID-19) Vaccine Against Acquisition of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Among Healthcare Workers in Long-Term Care Facilities: A Prospective Cohort Study

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***Background.*** We assessed vaccine effectiveness (VE) of BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) acquisition among healthcare workers (HCWs) of long-term care facilities (LTCFs).

***Methods.*** This prospective study, in the framework of the "Senior Shield" program in Israel, included routine weekly nasopharyngeal SARS-CoV-2 RT-PCR testing from all LTCF HCWs since July 2020. All residents and 75% of HCWs were immunized between December 2020 and January 2021. The analysis was limited to HCWs adhering to routine testing. Fully vaccinated (14+ days after second dose; n = 6960) and unvaccinated (n = 2202) HCWs were simultaneously followed until SARS-CoV-2 acquisition or end of follow-up, 11 April 2021. Hazard ratios (HRs) for vaccination versus no vaccination were calculated (Cox proportional hazards regression models, adjusting for sociodemographics and residential-area COVID-19 incidence). VE was calculated as (1–HR) × 100. RT-PCR cycle threshold (Ct) values were compared between vaccinated and unvaccinated HCWs.

***Results.*** At >14 days post–second dose, 40 vaccinated HCWs acquired SARS-CoV-2 (median follow-up, 66 days; cumulative incidence, 0.6%) versus 84 unvaccinated HCWs (median follow-up, 43 days; cumulative incidence, 5.1%) (HR, .11; 95% CI, .07–.17; unadjusted VE, 89%; 95% CI, 83–93%). Adjusted VE >7 and >14 days post–second dose were similar. The median PCR Ct targeting the *ORF1ab* gene among 20 vaccinated and 40 unvaccinated HCWs was 32.0 versus 26.7, respectively (*P* value = .008).

***Conclusions.*** VE following 2 doses of BNT162b2 against SARS-CoV-2 acquisition in LTCF HCWs was high. The lower viral loads among SARS-CoV-2–positive HCWs suggest further reduction in transmission.

**Keywords.** effectiveness; BNT162b2 vaccine; SARS-CoV-2 infection; healthcare workers; long-term care facilities.

The BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine was the first vaccine to receive emergency use authorization, with 95% efficacy against COVID-19 in the Phase III clinical trial [1, 2].

On 19 December 2020, Israel launched a national vaccination campaign using the BNT162b2 vaccine, initially prioritizing healthcare workers (HCWs) and individuals aged 60 years and older. Gradually, COVID-19 immunization was expanded to all individuals aged 16 years or older. By 11 April 2021, nearly 53% of individuals aged16 years or older were immunized with 2 doses. The respective figure was 85% for those aged 60 years or older [3].

Real-life observational studies from Israel have demonstrated effectiveness of 95% or higher against COVID-19 after immunization with 2 doses [4, 5], consistent with studies in other countries [6, 7]. However, vaccine effectiveness (VE) against disease does not necessarily predict the full potential impact of a vaccine, since it does not measure its ability to reduce transmission, an important factor in public health policy. Asymptomatically infected individuals are important in the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), contributing to the evolution of the pandemic [8]. Estimating SARS-CoV-2 acquisition (encompassing both symptomatic and asymptomatic infections) is problematic, mainly due to differences in demographics and other personal characteristics, incentives to be tested, and risk-associated behavior between vaccinated and unvaccinated individuals, resulting in potential

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confounding and selection bias [9]. Thus, the effectiveness of the BNT162b2 vaccine on SARS-CoV-2 transmission and the resulting indirect (herd) protection has not yet been fully elucidated.

Healthcare workers are at risk for SARS-CoV-2 infection [10], and they might transmit the virus to their patients, often a high-risk population for severe COVID-19. Therefore, determining the risk of SARS-CoV-2 acquisition is of utmost importance among HCWs. It was shown that BNT162b2 administered to HCWs was inversely associated with SARS-CoV-2 infection risk [11–20]. The VE of 2 doses was assessed in 4 studies, ranging from 85% to 97%, and mostly did not determine VE against asymptomatic infections separately [11, 16, 17, 19, 20], except for one showing lower VE against asymptomatic SARS-CoV-2 infection than symptomatic infection [21].

Since the residents of long-term care facilities (LTCFs) are a vulnerable population, a national LTCF protection program, "Senior Shield," was initiated in April 2020 in Israel [22]. In this program, routine, government-funded weekly screening of SARS-CoV-2 infection by reverse transcription–polymerase chain reaction (RT-PCR) testing of nasopharyngeal swabs from all LTCF HCWs has been implemented since July 2020. Starting on 22 December 2020, BNT162b2 vaccine was offered to all LTCF HCWs and residents. This task was completed by the end of January 2021, after having enrolled all institutions in Israel. Among HCWs, approximately 75% were vaccinated and 16% were known convalescent. Weekly nasopharyngeal testing of SARS-CoV-2 detection has been ongoing without interruption. We took advantage of the active weekly surveillance of PCR testing, with the primary objective to assess the effectiveness of the BNT162b2 vaccine in preventing the acquisition of SARS-CoV-2 in fully vaccinated HCWs.

Since SARS-CoV-2–neutralizing antibody titers were shown to be highest after 7 and 14 days following immunization with the second BNT162b2 dose [23] and following evidence from previous studies [2, 4, 5], we hypothesized that the risk of SARS-CoV-2 infection 7 or 14 days following immunization will be lower among vaccinated compared with unvaccinated HCWs.

## METHODS

### Study Design and Population

A prospective cohort study was conducted among HCWs aged 16–65 years who took part in the "Senior Shield" program [22, 24]. Since July 2020, all HCWs of all LTCFs in Israel have been required to undergo weekly screening for the detection of asymptomatic SARS-CoV-2 infection via nasopharyngeal RT-PCR testing. Those found positive were provided with the recommended care and requested to be quarantined for 10–14 days. All HCWs and residents at the LTCFs with confirmed cases were repeatedly screened by RT-PCR until all 3 consecutive negative results. The program was active in 1078 LCTFs, both public and private institutions, with 46 024 HCWs (Supplementary Material 1).

Inclusion criteria for the primary analysis were as follows:

1. Adherence to routine screening for SARS-CoV-2 infection by RT-PCR testing—specifically, HCWs who had 12 or more out of the 20 of the planned screening tests for the period September 2020 through January 2021. The rationale by utilizing this criterion was that we considered adherence to testing as a health behavior, a main confounder in VE studies, and to better identify current/active HCWs.
2. Working in LCTFs that vaccinated 75% or more of their employees collectively during 3 consecutive days.
3. Being RT-PCR negative for SARS-CoV-2 infection by the date of immunization with the second vaccine dose.

Unvaccinated HCWs at baseline, who were vaccinated later, were censored upon receiving their first vaccination dose in the primary analysis. Excluded from the primary analysis were HCWs working at institutions that did not have a collective immunization period, partially vaccinated HCWs at baseline (ie, received 1 vaccine dose), and those who had an RT-PCR–confirmed SARS-CoV-2 infection before immunization, or between immunization with the second dose until day 7 or 14 days post-immunization.

A secondary approach was implemented in which data on all vaccinated HCWs were analyzed, regardless of whether they worked at an institution with a collective immunization period, to increase the generalizability of the study findings and reduce potential selection bias. In this analysis, HCWs (n = 1130) who were initially unvaccinated but received the vaccine later contributed follow-up time to both the vaccinated and unvaccinated groups.

### Definition of the Study Variables

Data were obtained through the Senior Shield program on demographics, results of the RT-PCR tests, and COVID-19 immunization.

#### *Follow-up*

The follow-up starting dates were more than 7 and more than 14 days postvaccination with the second BNT162b2 dose. Since, for each LTCF, vaccination was done within 3 consecutive days, the second of the 3 consecutive days was defined at the "index" day for unvaccinated HCWs and events were counted after 7 and after 14 days following this date. By this, we created a matched (common) calendar baseline for the vaccinated and unvaccinated groups at the institution level (mostly calendar weeks 4–5 in 2021), which was important due to substantial changes in COVID-19 incidence during the study period. Both groups were followed until the earliest of the following events: acquisition of SARS-CoV-2 infection or end of follow-up on 11

April 2021. For the unvaccinated individuals who opted to be vaccinated after the index date, the follow-up ended on the date of the first dose administration. We also tested an alternative approach, in which vaccinated and unvaccinated HCWs were not matched by baseline calendar time and were followed until the earliest of the above-mentioned events. The follow-up start date for the unvaccinated group in this analysis was determined as the average date of vaccination with the second vaccine dose, which was 30 January 2021.

#### *Effectiveness Endpoints—Acquisition of SARS-CoV-2 Infection*

A dichotomous variable (yes or no) was defined based on RT-PCR test results. The primary endpoint was the acquisition of SARS-CoV-2 infection more than 14 days after the second dose administration. To determine acquisition, we included only HCWs who had 3 or more RT-PCR tests during February 2021, 3 or more RT-PCR tests during March 2021, and 1 or more RT-PCR test during April 2021. By this, we created a homogenous cohort in terms of adherence to RT-PCR screening, eliminating the potential effect of immunization on testing. Healthcare workers who tested positive between the first and the second dose administration and up to day 14 after the second dose administration were excluded from the primary analysis. RT-PCR screening policy for SARS-CoV-2 detection in the framework of the Senior Shield program was unchanged throughout the study. A secondary endpoint was SARS-CoV-2 acquisition more than 7 days after the second dose administration.

#### *Independent Variable*

COVID-19 vaccination status (a dichotomous variable) was an independent variable. Fully vaccinated HCWs were defined as those with more than 14 days after 2 doses of BNT162b2 vaccine given 3 weeks apart (±4 days). Healthcare workers who did not receive any dose were classified as unvaccinated. Additional independent variables were considered as covariates (see below).

#### *Covariates*

The following variables were considered as confounders: age (years), gender, population group (general Jewish population, ultraorthodox Jewish population, or Arab population), residential socioeconomic status (SES) [25], and residential area incidence rates of COVID-19. The residential area incidence rates (per 10 000) were categorized by as low (<15), intermediate (15–24), and high (25–457). We also assessed the level of vaccination uptake among all employees per each institution.

#### *Cycle Threshold of SARS-CoV-2 RT-PCR Testing*

Cycle threshold (Ct) of RT-PCR results can be used as a surrogate of viral load, and inversely correlates with COVID-19 severity [26]. Increased Ct values of SARS-CoV-2 RT-PCR results were shown among vaccinated compared with unvaccinated HCWs [21]. Accordingly, we explored differences in Ct values between vaccinated and unvaccinated HCWs. Nasopharyngeal swabs were collected on a weekly basis using a standardized protocol. The majority of samples were tested at MyHeritage laboratory (Petach Tikva, Israel), which daily processed between 10 000 and 20 000 samples. The detection of SARS-CoV-2 at MyHeritage laboratory was based on a single assay that detects the *Orf1ab* gene, the Beijing Genomics Institute Beijing Genomics Institute, BGI SARS-CoV-2 RT-PCR testing kit [27]. The laboratories did not have information on the vaccination status of the HCWs or other background information.

### Data Analysis

Baseline characteristics of the study groups were described using means and standard deviations for continuous variables and counts and percentages for categorical variables.

Curves of cumulative incidence of SARS-CoV-2 infection among vaccinated and unvaccinated groups were created using Kaplan-Meier survival analysis and compared with the log-rank test. Cox proportional hazards regression models [28] with follow-up time (days) as the time scale were constructed to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for SARS-CoV-2 acquisition. The "facilities" were included in the analysis as strata (ie, the variable "facility" was treated as a "matching" variable). Independent variables were COVID-19 vaccination, gender, age, residential SES, and the cumulative incidence of SARS-CoV-2 infection by residential area. We repeated the analysis while including the variable "level of vaccine uptake" in the model, to assess potential indirect (herd) protection. The variables "population group" and "residential SES" were significantly correlated (lower residential SES among Arabs than Jews; Spearman's rank correlation coefficient, −0.59; $P < .0001$); therefore, only residential SES was included in the multivariable model.

We calculated HRs for vaccination compared with no vaccination. Vaccine effectiveness was calculated as $(1 - \text{HR}) \times 100$, and it was calculated from both more than 14 days and more than 7 days after the second vaccine dose until the end of the follow-up. The proportional hazards assumption was tested using the Schoenfeld residuals, with no violations found.

Sensitivity analysis was undertaken, in which the analyses were repeated following our secondary approach that included all vaccinated HCWs, regardless of whether their institution had a collective vaccination period. We did not have the exact reasons for nonadherence or low adherence of HCWs to RT-PCR testing, but mostly it was attributed to logistic reasons. Thus, we reanalyzed the data while considering various levels of adherence to testing to explore a possible impact of potential selection bias.

Differences in the median Ct values from RT-PCR testing between fully vaccinated and unvaccinated HCWs were assessed using the Mann-Whitney *U* test. Two-sided *P* values less

than .05 were considered statistically significant. Analyses were performed using R software, version 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria).

### Ethics

The study protocol was approved by the institutional review board of the Soroka University Medical Center, Beer-Sheva, Israel.

## RESULTS

Among 46 024 HCWs, 15 535 were adherent to routine screening for SARS-CoV-2 infection by RT-PCR testing; of these, 9162 (n = 6960 vaccinated and n = 2202 unvaccinated) worked in LTCFs in which employees were vaccinated within 3 consecutive days, and included in the main (calendar-matched) analysis (Figure 1). The mean age of the study sample was 46.2 years and most (79.5%) participants were females. The vaccinated group was older and included more males and individuals who lived in towns/communities of high SES rank and low COVID-19 incidence rates than the unvaccinated group. Vaccinated and unvaccinated HCWs were distributed across all levels of vaccine uptake, although slightly more unvaccinated HCWs worked in institutions with lower uptake (Table 1). Accordingly, we adjusted for these variables in multivariable models.

### Vaccine Effectiveness

Among the vaccinated group, 40 HCWs acquired SARS-CoV-2 infection more than 14 days post–second dose (median follow-up, 66 days; cumulative incidence, 0.6%). Among the unvaccinated group, 84 HCWs acquired SARS-CoV-2 (median follow-up, 43 days; cumulative incidence, 5.1%) (Figure 2). A significantly lower risk of acquisition of SARS-CoV-2 was found among vaccinated compared with unvaccinated HCWs (HR, .11; 95% CI, .07–.17), yielding an unadjusted VE of 89% (95% CI, 83–93%). A multivariable Cox proportional hazards regression model that controlled

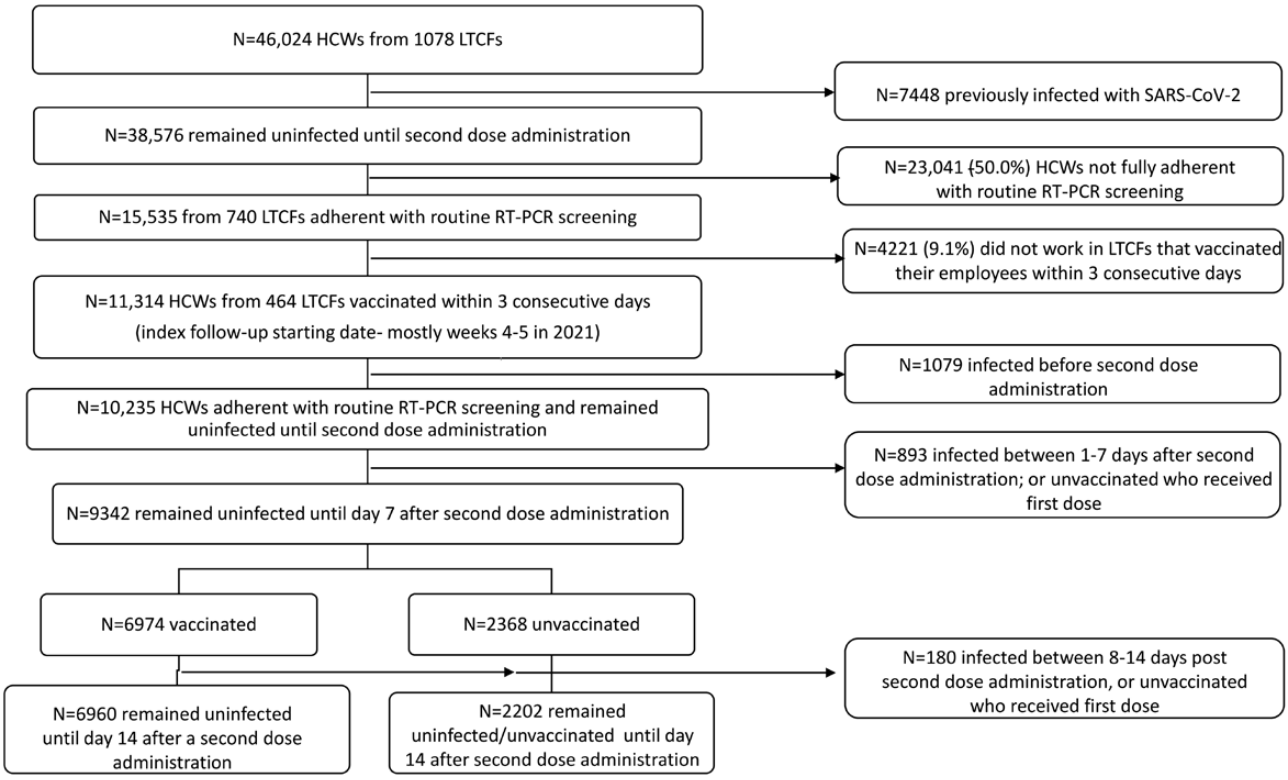


**Figure 1.** Flow chart of selection of the study groups of the primary analysis. A COVID-19 vaccination campaign of HCWs of LTCFs in Israel took place between 22 December 2020 and 29 January 2021. The primary analysis included HCWs who worked in LTCFs that vaccinated ≥75% of their employees during 3 consecutive days. The follow-up starting dates were >7 and >14 days postvaccination with the second BNT162b2 dose. The second of the 3 consecutive vaccination days was defined as the "index" date for starting the follow-up among the unvaccinated HCWs. By this, we created a matched (common) calendar baseline for the vaccinated and unvaccinated groups at the institution level (mostly weeks 4–5 in 2021). Overall, 4221 HCWs (9.1%) did not work in LTCFs that vaccinated ≥75% of their employees within 3 consecutive days, and thus were excluded from the primary analysis. Overall, 6974 vaccinated and 2368 unvaccinated HCWs were included in the primary analysis of vaccine effectiveness against SARS-CoV-2 >7 days post–second dose. The respective numbers were 6960 and 2202 for the effectiveness analysis >14 days post–second dose. Abbreviations: COVID-19, coronavirus disease 2019; HCW, healthcare worker; LTCF, long-term care facility; RT-PCR, reverse transcription–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

**Table 1. Baseline Characteristics of the Study Sample: Primary Analysis**

| | Unvaccinated (n = 2202) | Vaccinated, 2 Doses + 14 Days (n = 6960)[a] | Overall (N = 9162) |
|---|---|---|---|
| Sex, n (%) | | | |
| Female | 1827 (83.0%) | 5456 (78.4%) | 7283 (79.5%) |
| Male | 373 (16.9%) | 1476 (21.2%) | 1849 (20.2%) |
| Missing | 2 (0.1%) | 28 (0.4%) | 30 (0.3%) |
| Age (years) | | | |
| Mean (SD) | 43.1 (11.7) | 47.2 (11.7) | 46.2 (11.8) |
| Median (IQR) | 44.0 (19.0) | 48.0 (19.0) | 47.0 (19.0) |
| (Minimum, maximum) | (16.0, 65.0) | (16.0, 65.0) | (16.0, 65.0) |
| Residential socioeconomic status, n (%) | | | |
| Low | 576 (26.2%) | 1736 (24.9%) | 2312 (25.2%) |
| Intermediate | 682 (31.0%) | 2140 (30.7%) | 2822 (30.8%) |
| High | 605 (27.5%) | 2424 (34.8%) | 3029 (33.1%) |
| Missing | 339 (15.4%) | 660 (9.5%) | 999 (10.9%) |
| Population group, n (%) | | | |
| General Jewish population | 1745 (79.2%) | 5540 (79.6%) | 7285 (79.5%) |
| Ultraorthodox Jewish population | 65 (3.0%) | 107 (1.5%) | 172 (1.9%) |
| Arab population | 392 (17.8%) | 1313 (18.9%) | 1705 (18.6%) |
| Calendar week of starting the follow-up, n (%) | | | |
| 3 | 73 (3.3%) | 384 (5.5%) | 457 (5.0%) |
| 4 | 1227 (55.7%) | 4323 (62.1%) | 5550 (60.6%) |
| 5 | 892 (40.5%) | 2240 (32.2%) | 3132 (32.6%) |
| 6 | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| 7 | 10 (0.5%) | 13 (0.2%) | 23 (0.1%) |
| Residential area incidence of SARS-CoV-2 infection, n (%) | | | |
| Low (<15 per 10 000 persons) | 524 (23.8%) | 2220 (31.9%) | 2744 (29.9%) |
| Intermediate (15–24 per 10 000 persons) | 632 (28.7%) | 2115 (30.4%) | 2747 (30.0%) |
| High (25–457 per 10 000 persons) | 730 (33.2%) | 2024 (29.1%) | 2754 (30.1%) |
| Missing | 316 (14.4%) | 601 (8.6%) | 917 (10.0%) |
| COVID-19 vaccination level per facility | | | |
| 0–59% | 343 (15.6%) | 411 (5.9%) | 754 (8.2%) |
| 60–69% | 532 (24.2%) | 1232 (17.7%) | 1764 (19.3%) |
| 70–79% | 831 (37.7%) | 2702 (38.8%) | 3533 (38.6%) |
| 80–89% | 403 (18.3%) | 2194 (31.5%) | 2597 (28.3%) |
| 90–100% | 20 (0.9%) | 280 (4.0%) | 300 (3.3%) |
| Missing | 73 (3.3%) | 141 (2.0%) | 214 (2.3%) |

The primary analysis included HCWs who were adherent to RT-PCR testing and worked in LTCFs that vaccinated ≥75% of their employees against COVID-19 during 3 consecutive days. Follow-up starting date was determined by the vaccination time in each LTCF (mostly calendar weeks 4–5 [approximately end of January] in 2021) + 14 days, thus yielding a matched/common calendar period for the vaccinated and unvaccinated HCWs at the institution level (Methods section).

Abbreviations: COVID-19, coronavirus disease 2019; HCW, healthcare worker; IQR, interquartile range; LTCF, long-term care facility; RT-PCR, reverse transcription–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

[a]Vaccinated with 2 doses of BNT162b2 COVID-19 vaccine, 3 weeks apart, and remained negative for SARS-CoV-2 until 14 days postvaccination.

for potential confounders showed an adjusted VE of 89% (95% CI, 83–93%) more than 14 days after immunization with the second dose (Table 2). The level of vaccine uptake by the employees in each institution was inversely related to SARS-CoV-2 infection incidence, but it did not affect the VE estimates (Supplementary Table 1).

The results were similar when considering the period of more than 7 days after the second dose (Supplementary Table 2, Supplementary Table 3, and Supplementary Figure 1).

#### Sensitivity Analysis

Sensitivity analysis that included all vaccinated HCWs (n = 11 496) who received 2 vaccine doses and unvaccinated HCWs (n = 3151) (Supplementary Figure 2) showed comparable characteristics between these groups and those who were included in the primary analysis (Supplementary Table 4). During a median follow-up of 65 and 41 days in vaccinated and unvaccinated HCWs, respectively, the cumulative incidence of SARS-CoV-2 infection more than 14 days post–second dose was 1.2% (n = 131 events) and 7.9% (n = 182 events), respectively (Supplementary Figure 3). The adjusted HR for the COVID-19 immunization was .15 (95% CI, .11–.19) (Supplementary Table 5), yielding a VE of 85% (95% CI, 81–89%).

Considering different levels of adherence to routine RT-PCR testing by HCWs showed 85–90% VE against SARS-CoV-2 infection more than 14 days post–second dose (Supplementary Table 6).

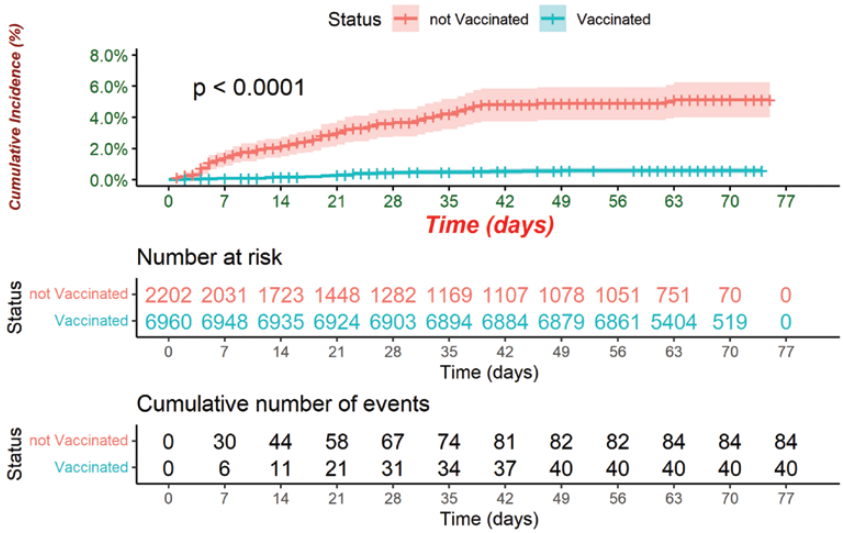


**Figure 2.** Cumulative incidence of RT-PCR–confirmed SARS-CoV-2 infection among healthcare workers 14 days after vaccination with the second dose of BNT162b2 compared with unvaccinated healthcare workers. Results of the primary analysis of calendar-matched groups. *P* value by log-rank test. Shaded lines represent 95% confidence intervals. Abbreviations: RT-PCR, reverse transcription–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

### SARS-CoV-2 RT-PCR Ct Values and BNT162b2 Immunization

Information on Ct values from RT-PCR testing was available for 64 HCWs (20 were vaccinated and 44 were unvaccinated) (Figure 3). The median (interquartile range [IQR]) Ct value was significantly higher among fully vaccinated individuals than unvaccinated ones (32.0 [IQR, 14.5] vs 26.7 [IQR, 8.8]; $P = .008$).

## DISCUSSION

In this study among HCWs in LTCFs, BNT162b2 VE against SARS-CoV-2 acquisition was 89% after 14 days postvaccination with the second dose. This finding was consistent after adjustment for confounders, and when considering the period of more than 7 days after second dose. Our results were obtained

**Table 2. Relationships of COVID-19 Immunization and Other Covariates With the Acquisition of SARS-CoV-2 Infection More Than 14 Days After Immunization With the Second Dose of BNT162b2 COVID-19 Vaccine**

| | Unadjusted HR (95% CI) | *P* Value | Adjusted HR[a] (95% CI) | *P* Value |
|---|---|---|---|---|
| COVID-19 vaccination | | <.0001 | | <.0001 |
| Unvaccinated | 1.00 | | 1.00 | |
| Vaccinated (2 doses + 14 days) | .11 (.07, .17) | | .11 (.07, .17) | |
| Age, years | .96 (.95, .98) | <.0001 | .97 (.96, .99) | .0112 |
| Sex | | .460 | | .650 |
| Female | 1.00 | | 1.00 | |
| Male | 1.19 (.74, 1.91) | | 1.10 (.90, 1.74) | |
| Residential area incidence rate of SARS-CoV-2 infection | | | | |
| Low (<15 per 10 000 persons) | 1.00 | | 1.00 | |
| Intermediate (15–24 per 10 000 persons) | 1.33 (.68, 2.61) | .399 | 1.95 (.51, 3.82) | .051 |
| High (25–457 per 10 000 persons) | 3.32 (1.75, 6.31) | .0002 | 3.81 (2.00, 7.24) | <.0001 |
| Residential socioeconomic status[b] | | | | |
| Low | 1.00 | | 1.00 | |
| Intermediate | .67 (.42, 1.07) | .099 | .63 (.41, .96) | .0326 |
| High | .37 (.20, .69) | .0018 | .48 (.27, .84) | .0112 |
| Population group[b] | | | | |
| General Jewish population | 1.00 | | | |
| Ultraorthodox Jewish population | 1.60 (.54, 4.72) | .389 | Not included | |
| Arab population | 2.16 (1.29, 3.63) | .0032 | Not included | |

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Multivariable Cox regression model adjusted for the variables in the table except for "population group," given its high correlation with residential area socioeconomic status.

[b]The variable population group was correlated with residential socioeconomic status (Spearman's rank correlation coefficient, –0.59; *P* value < .0001); therefore, only the variable residential socioeconomic status was included in the model.

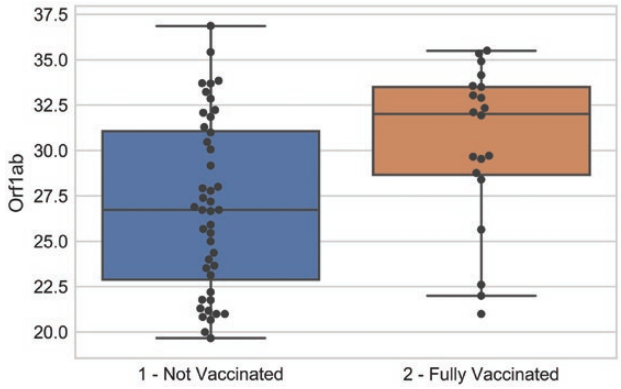


**Figure 3.** Box plots of Ct values from RT-PCR testing targeting the SARS-CoV-2 *ORF1ab* gene among BNT162b2 fully vaccinated and unvaccinated individuals. Fully vaccinated: >14 days after the second dose. Box plots of Ct values (*y*-axis) of SARS-CoV-2–positive RT-PCR results according to COVID-19 vaccination status (*x*-axis) among healthcare workers. The line in the middle of the box represents the median level, the lower bound of the box represents the 25th percentile, the upper bound of the box represents the 75th percentile, the lowest point of the lower whisker represents the minimum, and the highest point of the upper whisker represents the maximum. Each circle represents the Ct value for 1 participant. *P* value = .008 by Mann-Whitney *U* test. Abbreviations: COVID-19, coronavirus disease 2019; Ct, cycle threshold; RT-PCR, reverse transcription–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

in a "well controlled" setting, by assessing comparable groups in terms of utilization of SARS-CoV-2 RT-PCR screening tests and follow-up calendar, during a mass deployment of COVID-19 immunization and substantial changes in the disease incidence in Israel [4, 5, 29].

Healthcare workers are at increased risk for SARS-CoV-2 infection [10, 30, 31]; in addition, HCWs of LTCFs might play a role in the virus transmission within the institution [32–34]. Long-term care facilities have been at the epicenter of COVID-19 outbreaks in many countries, with high mortality among residents [32–34], who are highly vulnerable to severe and fatal disease given their usually advanced age, living environments, dependence on staff, and functional and comorbid conditions. Accordingly, conferring maximal protection against both asymptomatic infection and disease to both HCWs and residents of LTCFs was highly pursued in Israel, resulting in the "Senior Shield" program [22, 24]. The Ministry of Health designated a special taskforce for the deployment of COVID-19 vaccines among LTCF HCWs and residents, resulting in Israel being the first country to complete vaccination of all LTCFs as early as February 2021.

Our estimate of 89% effectiveness of a 2-dose BNT162b2 regimen against SARS-CoV-2 acquisition is consistent with findings of a study from England that reported 85% VE against any SARS-CoV-2 infection among HCWs [11]. Other studies reported a higher effectiveness of more than 95% [16, 17], a discrepancy that might be due to methodological variation.

We found significantly higher Ct values among vaccinated than unvaccinated HCWs. It was proposed that Ct values might represent viral load, and inversely correlate with COVID-19 severity [26] and transmissibility [35, 36]. Other studies from Israel and the United States provided supportive fundings[20, 21, 37].

Our study has limitations. We did not have data on symptoms, since the main goal of the RT-PCR screening was to detect and quarantine positive workers in order to prevent/stop the virus transmission. Thus, we were not able to produce separate VE estimates for asymptomatic or symptomatic infections as was the case in other studies among HCWs. We included working adults aged 65 years or younger; thus, severe comorbidities likely are not an issue in this population. Moreover, most participants were women; thus, direct extrapolation to the general population might be limited. We assessed only short-term protection following vaccination, and therefore could not assess potential waning immunity. Our study was undertaken during a period in which the SARS-CoV-2 Alpha variant (B0.1.1.7) was predominant [4]. Current evidence showed waning immunity about 6 months following vaccination [38, 39] with the second BNT162b2 dose, and reduced 40–50% effectiveness against the Delta variant, although effectiveness against COVID-19 hospitalization was 89% [40]. Most (75%) HCWs in our cohort received the BNT162b2 vaccine and 25% were unvaccinated HCWs. Likely these groups differ in health behaviors. To account for these factors, we included in the primary analysis HCWs adherent to routine screening for SARS-CoV-2 infection, prior to and during COVID-19 vaccine deployment, thus creating homogeneous groups in terms of RT-PCR testing uptake and minimizing the potential effect of immunization on testing.

Information on Ct values was available for approximately 50% of infected HCWs; this was due to differences between the laboratories in reporting format of the RT-PCR test results. The missingness was not related to vaccination status of the HCWs, since the laboratories did not have background information on the HCWs.

Our study has several strengths. We prospectively and systematically collected samples periodically from all our participants, reducing the potential biases in comparing vaccinated with unvaccinated HCWs. Our analytical approach adjusted for potential confounders that might affect both vaccine uptake and COVID-19 incidence—and importantly, matching on calendar time during a period with marked fluctuations in disease incidence. Last, we considered multiple sensitivity analyses showing consistent findings comparable with the main analysis.

#### Conclusions

Vaccination with 2 doses of BNT162b2 vaccine was highly effective in preventing acquisition of SARS-CoV-2 infection in HCWs of LTCFs, thus reducing the potential for transmission of the virus to the community and, in particular, this highly vulnerable population.

## 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

***Author contributions.*** N. M., A. M., and O. B. conceived the study; K. M., D. C., M. M., I. G., and R. D. contributed to the study design; N. M. supervised all aspects of the study; A. M. and O. B. were responsible for data curation and analysis and verified the underlying data and results; K. M., D. C., and R. D. contributed to data analysis; K. M. and R. D. wrote the first draft of the manuscript. All authors critically reviewed the manuscript and contributed to writing and editing and approved the final version.

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***Data availability.*** Data analyzed in this study cannot be made publicly available since legal restrictions apply.

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