BNT162b2 mRNA Covid-19 vaccine effectiveness in the prevention of SARS-CoV-2 infection: a preliminary report

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Summary: BNT162b2 mRNA Covid-19 vaccine showed an high effectiveness in a sample of healthcare workers of Bari Policlinico (especially day 7 after the second vaccine dose). Immunization of healthcare personnel is a priority objective to make the healthcare environment safe.

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Abstract

In the pre-registration trial, data on the efficacy of the BNT162b2 mRNA vaccine against SARS-CoV-2 infection were not collected. The aim of this study was to evaluate vaccine effectiveness (VE) against documented infection. Bari Policlinico University-Hospital healthcare workers (HCWs) who completed the vaccination schedule were matched with HCWs who had refused vaccination. The VE for documented infection was 61.9% (95%CI=19.2–82.0%) 14–20 days after the first dose, 87.9% (95%CI=51.7–97.0%) 21–27 days after the first dose, and 96.0% (95%CI=82.2–99.1) 7 or more days after the second dose. Unvaccinated HCWs remain a concern even in the context of pandemic emergency.

Keywords: COVID-19; documented infection; vaccine effectiveness; healthcare workers

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Abbreviations

CDC: Center for Disease Control and Prevention

GIAVA: Regional Immunization Database

HCW: healthcare worker

VE: vaccine effectiveness

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BACKGROUND

COVID-19 is the infectious disease caused by the novel coronavirus SARS-CoV-2. COVID-19 is now a pandemic, having reached global proportions [1]. At March 15, 2021, the World Health Organization (WHO) has thus far reported ~119,000,000 confirmed cases of COVID-19 globally, including more than 2,600,000 deaths [2]. According to the European Centre for Disease Prevention and Control (ECDC), at March 15, 2021, there have been > 23,000,000 cases and > 560,000 deaths in the EU/EEA [3]. Italy ranks first in Europe in the number of COVID-19-related deaths (100,627; fatality rate: 3.2%) and the second per absolute number of cases (n=3,183,605), including 125,803 cases in healthcare workers (HCWs) [4].

Beginning in December 2020, several vaccines aimed at the prevention of SARS-CoV-2 infection and COVID-19 became available in Europe. A mass vaccination campaign was initiated in Italy and other European countries on December 27, 2020. In Italy, the government opted to prioritize the vaccination of HCWs, a decision in line with the recommendations of the United States Center for Disease Control and Prevention (CDC) [5]. By providing critical care to those who are or might be infected by SARS-CoV-2, HCWs are at high risk of exposure to the virus and thus to the development of COVID-19. Furthermore, vaccinating HCWs safeguards healthcare capacity and can prevent those patients hospitalized for reasons other than COVID-19 from becoming infected. The vaccine available to vaccinate HCWs was the BNT162b2 mRNA COVID-19 vaccine (Comirnaty), the first vaccine to be approved by the European Medicines Agency. This vaccine is indicated for individuals 16 years of age and older and is administered in two-doses delivered at least 21 days apart [6,7].

The pre-licensure trial reported that the vaccine showed 95% efficacy at preventing COVID-19, including severe disease [8]. Aside from transient local and systemic reactions, no safety concerns were identified [8]; however, the trial did not report any information on the vaccine's efficacy in documented Sars-CoV-2 infection.

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Recently, a large observational study [9] investigated the vaccines effectiveness (VE) of the BNT162b2 mRNA vaccine on > 1,000,000 Israeli inhabitants (half vaccinated and half unvaccinated) during the period from December 20, 2020, to February 1, 2021. The authors reported that the vaccine prevented symptomatic illness, with a VE of 94% 7 days after the second dose. The same study investigated VE in preventing documented infection. The results showed that 14–20 days after the first dose, the estimated VE for documented infection was 46% (95%CI: 40–51%); 21–27 days after the first dose it was 60% (95%CI: 53–66%) and in the follow-up period starting 7 days after the second dose it was 92% (95%CI 88–95%). It was therefore concluded that the BNT162b2 mRNA vaccine is effective for a wide range of COVID-19-related outcomes, a finding consistent with that of the initial randomized trial.

The aim of this study was to evaluate VE against SARS-CoV-2 infection in a sample of HCWs immunized with the BNT162b2 mRNA vaccine. Our study was carried out in Apulia (Southern Italy, ~4,000,000 inhabitants), where, from February, 2020 to March 15, 2021, 166,237 confirmed cases of COVID-19 and 4,303 related deaths have been reported [10].

METHODS

Our observational cohort study was conducted at Bari Policlinico General University-Hospital (1,000 beds, 6,000 HCWs), where some 180-hospital bed were reserved for COVID patients and the Emergency Room was charged with the triage and care of COVID-19 patients. December 27, 2020 marked the start of the vaccination campaign for HCWs, with scheduling and follow-up activities coordinated by the Hygiene and Occupational Medicine departments of Bari Policlinico.

A HCW requests vaccination by completing an intranet on-line form. The Hygiene Department then contacts the HCW to schedule an appointment for immunization, confirming the date by mail or phone. An appointment for the second dose 21–28 day after the first shot is also made.

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All vaccinations are administered by Public Health physicians who are experts in vaccinology. Two doses of BNT162b2 mRNA vaccine are delivered intramuscularly in the deltoid muscle at least 21 days apart. Vaccination prophylaxis is not mandatory, and the HCW can refuse vaccination. Informed consent is collected at the time of vaccination. All vaccinated HCWs are followed-up for 1 month to assess the development of adverse effects.

Policlinico Bari General Hospital has also adopted a specific procedure for the control and prevention of SARS-CoV-2 infection. In order to protect health personnel, the Bari Policlinico Direction made mandatory the use of personal protective equipment (PPE) for each HCW. Furthermore, all asymptomatic HCWs are screened every 14 days for SARS-CoV-2 infection using molecular test on naso-pharyngeal swabs, obtained as recommended by the WHO [11]. Fast-track access to molecular testing is ensured for HCWs with signs and symptoms of COVID-19 (fever, cough, ageusia, etc.). A commercial real-time PCR assay (Allplex2019-nCoV Assay; Seegene, Seoul, Korea) was used to identify the presence of E gene, RdRP gene and N gene of SARS-CoV-2 virus. Data on infection control and prevention are entered into the computerized GIAVA COVID19 platform, as described below.

The population in this study comprised HCWs who completed the basal vaccination routine (both doses) between December 27, 2020 and January 31, 2021. They were matched with Bari Policlinico HCWs who during the same period did not receive the vaccine, because they refused vaccination (with the exception of those infected during the first days of the vaccination campaign, corresponding to 37 subjects). HCWs with a documented history of SARS-CoV-2 infection before enrollment were excluded from participation in the study (n=447).

The overall vaccination status of HCWs was assessed using the Regional Immunization Database (GIAVA). GIAVA is a computerized vaccination registry containing information on the vaccination history of every Apulian inhabitant; it can also be used to generate an immunization schedule.

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Data on documented cases of SARS-CoV-2 infection were extracted from the surveillance platform GIAVA COVID-19, developed on the basis of the WHO Go.Data outbreak investigation tool [12] and set up to manage the pandemic emergency in Apulia. This platform stores data on COVID-19 patients and their contacts, patient demographics, laboratory and clinical values, the results of SARS-CoV-2 PCR testing, and the follow-up of COVID-19 patients over the course of the disease, with updates of their health status (clinical symptoms, hospitalization, death, recovery).

The final dataset was created as an Excel spreadsheet that included information on sex, age at enrollment, group (vaccinated vs. unvaccinated), and documented infection (YES/NO). An anonymized data analysis was performed using the STATA MP16 software. Continuous variables are reported as the mean±standard deviation and range, and categorical variables as proportions. The Wilcoxon rank sum test was used to compare continuous variables between groups, and the chi-squared test to compare proportions.

The outcome of interest was documented SARS-CoV-2 infection confirmed by a positive PCR test. Survival curves for the vaccinated and unvaccinated groups were plotted using the Kaplan–Meier estimator. A log-rank test was used to compare the two groups. The incidence rate per 1,000 person-days of infection was estimated, including the 95%CIs. The incidence rate ratio (IRR) was also calculated. Three periods were considered: days 14–20 after the first vaccine dose, days 21–27 after the first vaccine dose, and day 7 after the second vaccine dose until the end of follow-up. For each period, a risk ratio for vaccination vs. no vaccination was calculated. VE, defined as one minus the risk ratio, and the 95%CIs were estimated. For all tests, a two-sided p-value< 0.05 was considered to indicate statistical significance.

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RESULTS

The study population comprised 2,034 HCWs: 1,607 (79.0%) in the vaccinated group and 427 (21.0%) in the unvaccinated group. The characteristics of the participants at enrollment are described in Table 1.

The average duration of follow-up was of 60.5±12.9 days, during which time 121 infections were recorded (incidence rate: 0.96 × 1,000 person-days), of which 64 (52.9%; 14 asymptomatics and 50 symptomatics) in unvaccinated group and 54 (47.1%; 17 asymptomatics and 37 symptomatics) in vaccinated group. The incidence rate of infection was higher in the unvaccinated group (2.45 × 1,000 person-days) than in the vaccinated group (0.54 × 1,000 person-days), with an IRR of 0.22 (95%CI: 0.15–0.32; $p < 0.0001$). Figure 1 shows the cumulative incidence curves for documented Sars-CoV-2 infection (log-rank $p < 0.0001$).

The estimated VE for documented infection was 61.9% (95%CI: 19.2–82.0%) during the 14–20 days after the first dose, 87.9% (95%CI: 51.7–97.0%) during the 21–27 days after the first dose, and 96.0% (95%CI: 82.2–99.1) 7 or more days after the second dose.

During the follow-up, there were no serious and/or long-term adverse reactions. The safety of the vaccine is the subject of a report currently in preparation.

DISCUSSION

The VEs determined in our study are slightly higher than those reported by Dagan N et al. [9], although the value at 7 or more days after the second dose is very similar. However, the sample size of the two studies was very different and our study population consisted solely of HCWs, a group largely excluded by the other study. HCWs are clearly at higher risk of exposure to Sars-CoV-2, which would explain the larger number of infections in our unvaccinated group. Furthermore, since

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even vaccinated HCWs are periodically screened with a PCR test, to reduce the risk of nosocomial outbreaks, the results for this group are highly reliable and the risk of under-reporting is very low. Keehner J et al. [13] evidenced how, in a sample of 36,659 US HCWs, only 8 HCWs tested positive 8 to 14 days after the second vaccination, and 7 tested positive 15 or more days after the second vaccination. Benenson S et al. [14] set up a study conducted in an Israelian nosocomial setting, showing that vaccination of HCWs with the BNT162b2 vaccine resulted in a major reduction of new cases of Covid-19 among those who received two doses of the vaccine. Finally, CDC reported the results of a study looked at the effectiveness of Pfizer-BioNTech and Moderna mRNA vaccines in preventing SARS-CoV-2 infections among 3,950 US HCWs, concluding that risk of infection was reduced by 90% two or more weeks after second dose of vaccine [15]. All these evidences match our results.

Regarding sample characteristics, it is observed that unvaccinated subjects had a higher age compared to vaccinated ones and that physicians seems to be more compliant to vaccination compared to other professional categories; indeed, many experiences reported in scientific literature [16] showed that older age is a determinant of vaccination hesitancy/refusal, while being a physician is a determinant of vaccination compliance.

Further studies are needed to determine the VE of the BNT162b2 mRNA vaccine in different populations and over a longer follow-up period. Thus far, the data are consistent with the absolute effectiveness of the vaccine in the prevention of SARS-CoV-2 infection and in the prevention of COVID-19 disease. These results may influence vaccination willingness among HCWs, as a vaccine that confers disease prevention can be regarded as a form of personal protective equipment. Moreover, a vaccine that prevents infection could dramatically limit circulation of the virus in the hospital setting. Vaccination can therefore be perceived both as a means of self-protection and as an ethical obligation to guarantee the safety of others, especially high-risk hospital patients. Vaccination hesitancy among HCWs has thus far been tolerated, and vaccination has yet to become

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mandatory. However, given the duration and seriousness of the pandemic and the emergence of more aggressive variants of the virus, this policy warrants very serious reconsideration. Indeed, on March 31, 2021, Italian government made mandatory COVID-19 vaccination for HCWs to deal with pandemic emergency.

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Footnote page

No funds were requested or obtained to carry out this study.

The authors have no competing interests to declare.

The manuscript has not been presented at a meeting.

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Table 1. Characteristics of the two study groups at baseline

Variable	Vaccinated (n=1,607)	Unvaccinated (n=427)	Total (n=2,034)	p-value
Age (years); mean±SD (range)	43.2±12.8 (20–70)	49.7±9.9 (23–69)	44.4±12.6 (20–70)	< 0.0001
Female; n (%)	915 (56.9)	261 (61.1)	1.176 (57.8)	0.120
Professional category				
• Physician	417 (25.9)	77 (18.0)	494 (24.3)	0.001
• Other HCWs	1.190 (74.1)	350 (72.0)	1.540 (75.7)	

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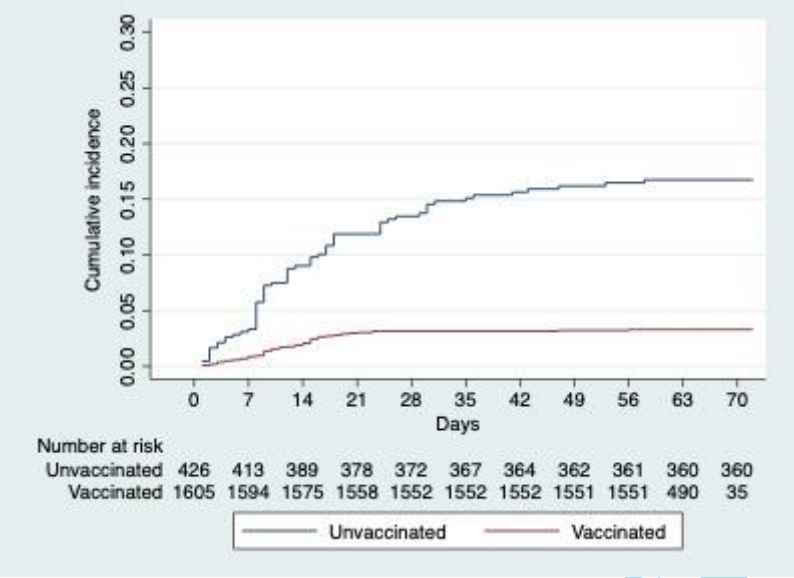
Figure 1



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