

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Benenson S, Oster Y, Cohen MJ, Nir-Paz R. BNT162b2 mRNA Covid-19 vaccine effectiveness among health care workers. *N Engl J Med*. DOI: [10.1056/NEJMc2101951](https://doi.org/10.1056/NEJMc2101951)

Supplementary Appendix

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Background

B.1.1.7 variant infections in Israel: According to data available in the public domain, the B.1.1.7 (British variant) was introduced in Israel in December 2021 [1, 2]. The variant was estimated to account for 30% to 40% of infections on January 19, 2021 [3]. It has reached 80% of the SARS-CoV-2 isolates by early February 2021 [4].

Methods

Settings

The Hadassah-Hebrew University Medical Center (HHUMC) is a tertiary medical center serving the Jerusalem Urban area in two campuses with 1100 admission beds and 6680 personnel. During the COVID-19 pandemic, only one campus had admission beds for COVID-19 patients. Patients positive for COVID-19 were transferred from one campus to the other. Preparedness in the hospital included building eight new dedicated wards for COVID-19 patients with 150 beds, including 44 intensive care beds.

Laboratory diagnosis of SARS-CoV-2 is done in HHUMC virology laboratory, which can perform more than 5000 RT-PCR tests per day, using in-house tests as well as commercial kits by NeuMoDX, GeneXpert, and others. Some of these tests were done in pools, in order to save time and resources [5].

Since March 2020 HHUMC deployed a screening program (see details below) for all health care workers (HCWs) by PCR from oropharyngeal swabs. There were several rounds of mandatory screening, initiated by a surge in positivity rate of the general population, which allowed us to identify and isolate asymptomatic, pre-symptomatic

and pauci-symptomatic HCWs. In addition, HCWs had free access to voluntary testing, which was open to all and offered a better turnaround time compared to tests that were offered by community health services, and thus promoted the use of such tests widely. HCWs positive test results are also reported to HHUMC, though negative tests are not.

All HCWs' positive SARS-CoV-2 results were immediately reported to HHUMC's Infection Prevention and Control Unit (IPC), which performed a thorough epidemiologic investigation in order to test and quarantine exposed HCWs and reduce the spread of the virus in the hospital [6]. Similar investigation was done in case of positive HCWs that were tested out of the hospital, as well as when a positive patient was detected out of the COVID-19 dedicated wards.

[SARS-CoV-2 testing policies at HHUMC](#)

In the first weeks of the pandemic, the management of HHUMC decided that massive HCWs testing would enable the hospitals to function properly by reducing the need for HCWs quarantine and isolation due to in-hospital exposures. Therefore, a giant lab with high capacity was established and proactive periodic screening program was established, as was published by us [7]. A bi-weekly screening program was applied to all "critical" teams, such as in the Intensive care units, Operation room, Emergency department and COVID-19 dedicated wards. In addition, and due the changes in infection patterns in Israel, all HCWs were instructed to be tested upon returning from vacations and holidays. Another policy decision was to let all HCWs the option to perform PCR whenever they want, in order to create a safe

environment in the hospitals. Other tests included obligatory testing following exposure, as indicated by the IPC, which developed testing protocols to reduce the need for quarantine after low and medium risk exposures (6). Post exposure policy for HCWs not vaccinated, or vaccinated but seven days have not yet passed since the second vaccine, was to perform PCR testing every two or three days until the tenth day from exposure. The post exposure testing policy for vaccinated HCWs (more than seven days since the second vaccine to exposure) was to perform PCR testing on days five and ten from exposure.

Vaccinations

As soon as the first vials of Pfizer and BioNtech BNT162b2 vaccine arrived in Israel, they were deployed to all hospitals for vaccination of HCWs. HHUMC had organized several online lectures and advertisements to encourage all previously uninfected HCWs to get vaccinated.

Data collection

Data regarding COVID-19 positive HCWs was gathered from the IPC unit registry, including date of positive SARS-CoV-2 test. Data regarding the vaccine status of positive HCWs and number of vaccinated personnel every week was obtained from the Human Resources Department. Positive test results, from laboratories outside HHUMC were reported to the IPC unit by the local office of Israeli Ministry of Health (MOH), while negative results were not.

This data collection was done under an approved protocol by the HHUMC ethics committee (HMO-460-12)

We obtained the Rate of positivity in the Jerusalem population from the official COVID-19 data site of the Israeli MOH [8]. Data on SARS-CoV-2 variants was extracted from the Israeli MOH daily report of 1st February 2021.

Statistics

The at-risk population was all HCWs who did not have any documentations of SARS-CoV-2 positive PCR prior to the time vaccination started. Cases per week were calculated according to the Israeli working week, thus starting from Sunday to Saturday. Rates were calculated on cases per 1000 persons. Similar calculations (cases/1000) were done on data extracted from the Israeli MOH to estimate disease burden at the municipality of Jerusalem.

COVID-19 incidence rate per 1000 at risk HCWs was calculated for each week. The denominator includes HCWs who did not become infected in the previous weeks. The numerator is the sum of all new COVID-19 infections among the HCWs included in the denominator.

Limitations

There are several limitations to our study. First, after the second dose of vaccination there were no mandated PCR screenings for HCWs; therefore we might have underdiagnosed COVID-19 in this population. However, HCWs were still instructed to be tested following every mild symptom, even if supposed to be related to vaccine side effects. Additionally, HCWs were required to be tested following exposure to

previously unknown patients or colleagues. Therefore, we assume that we did not miss many positive cases. We provide additional data regarding COVID-19 rates among HHUMC HCWs who were vaccinated and tested in our institution (supplementary table 2).

Second, Polack et al. have described a mildly reduced immune response to the BNT162b2 vaccine in people older than 60 [9], and most of HHUMC staff are younger than 60 and expected to have an excellent response, which might not reflect the response in different communities. Another limiting factor is the relatively small cohort size which may limit the detection of events with an incidence lower than 0.1 infections/1000/ week.

On the other hand, concerns were raised that vaccinated persons will adhere less to social distancing, masking, and other infection prevention methods, causing a paradoxical rise in infections [10], which was not seen in our study.

Acknowledgements

Ms. Galia Cohen, Ms. Adi Erentroy and Mr. Idan Yahud from the Department of Human Resources, collected the data on the number of workers and the number of those vaccinated at HHUMC.

The HHUMC Infection Prevention and Control team performed all the epidemiological investigations and instructed active surveillance of those exposed to positive SARS-COV-2 patients.

We are grateful for their excellent work that enabled summarizing this data.

Supplementary results

Table S1:

Data regarding positive SARS-CoV-2 healthcare workers during the BNT162b2 vaccination program at the Hadassah Hebrew University Medical Center, according to calendric week

Week	Non-vaccinated HCWs [#]	Vaccinated HCWs ^{&}	Total positive HCW [§]	Non-vaccinated positive HCWs [%]	Vaccinated positive HCWs, according to the weeks since 1 st vaccine dose*								
					1	2	3	4	5	6	7	8	
	N	N (%)	N	N									
13-19 Dec	6252	0	35	35	0	0	0	0	0	0	0	0	0
20-26 Dec	3658	2559 (41.16%)	49	45	4	0	0	0	0	0	0	0	0
27-Dec – 2 Jan	1951	1662 (26.95%)	64	31	25	8	0	0	0	0	0	0	0
3-9 Jan	1055	865 (14.17%)	62	27	8	22	5	0	0	0	0	0	0
10-16 Jan	927	101 (1.67%)	51	14	10	10	16	1	0	0	0	0	0
17-23 Jan	810	103 (1.72%)	37	19	1	3	5	8	1	0	0	0	0
24-30 Jan	784	7 (0.12%)	20	13	2	2	0	2	0	1	0	0	0
31 Jan-6 Feb	771	0	27	17	0	0	2	0	1	1	4	0	0
7-13 Feb	754	0	21	12	0	2	1	0	1	0	1	4	4
Total	NA	5297 (85.79%)	366	213	50	47	29	11	3	2	5	4	4

HCWs - healthcare workers; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NA, not applicable

#All HCWs who were not infected by SARS-CoV-2 prior to the relevant week and had not been vaccinated on or prior to that current week

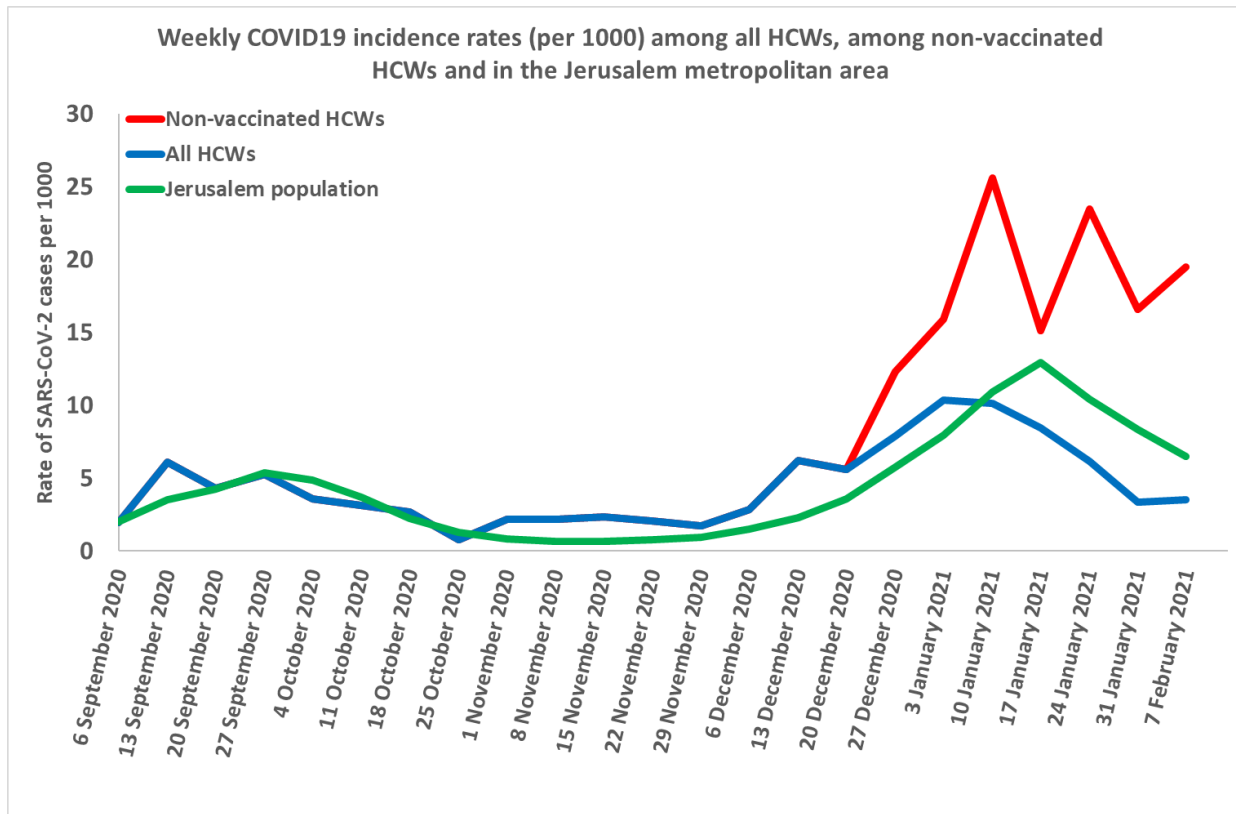
&Number of vaccinated HCWs per week (percent out of 6252 at risk HCWs before the vaccination program)

\$Total number of Sars-CoV-2 found to be positive by PCR in that week. This number includes both vaccinated and non-vaccinated cases.

%The number of non-vaccinated HCWs found to be positive at this specific week.

* The numbers indicate weeks since 1st dose of the vaccine for all newly diagnosed vaccinated- HCWs. For example, on the week beginning January 3rd 2021, there were 8 HCWs diagnosed with COVID-19 who were vaccinated in that week; 22 positive HCWs who were vaccinated the previous week; 5 positive HCWs who were vaccinated two weeks prior.

Figure S1

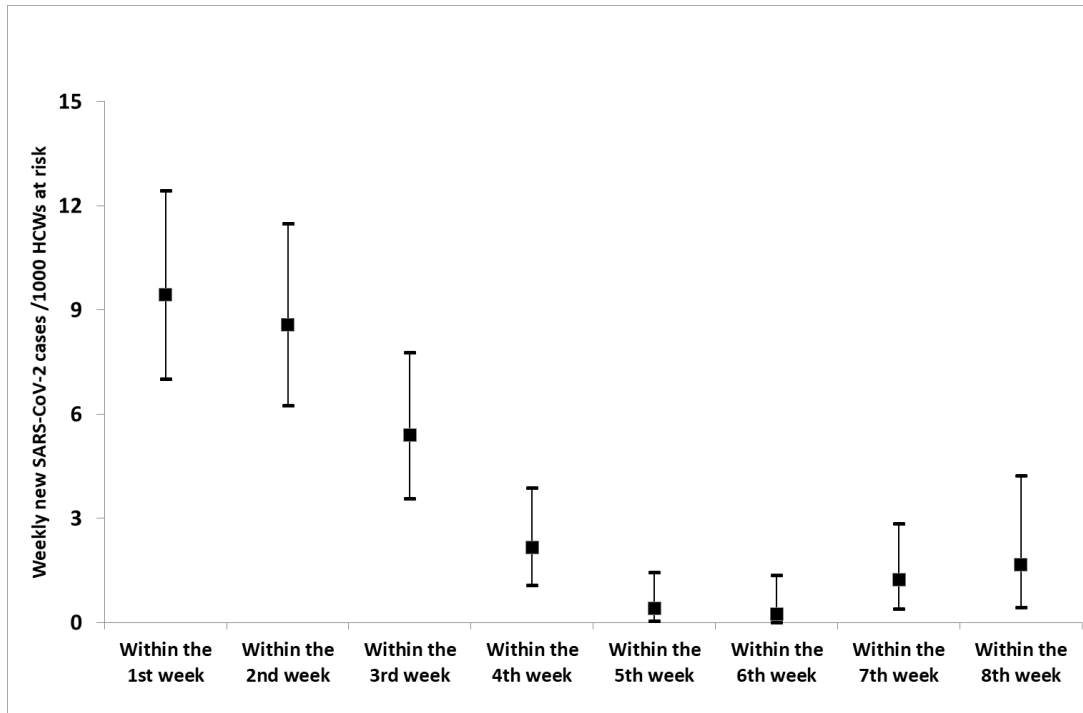


Rates of SARS-CoV-2 cases per 1000 persons at risk, by calendar weeks of diagnosis. The dark Blue line is the overall rate among HCWs at HHUMC. The Red line is the rate among non-vaccinated HCWs, presented from the time 1st vaccination began. The green line is the Jerusalem metropolitan area SARS-CoV-2 incidence rate. In the last two months, the HHUMC rate was higher compared to the community rate in Jerusalem; higher rates in HHUMC have probably resulted from proactive periodic screening of HHUMC HCWs. Clearly, non-vaccination HCWs became infected at the

highest rates as opposed to the vaccinated HCWs. It is not clear why a much higher incidence of SARS-CoV-2 was observed in the non-vaccinated HCWs. Potentially a bias towards riskier behavior and less adherence were involved, which are also patterned by lower tendency to comply with vaccination policy as well as compliance with personal protection practices, have led to this higher incidence.

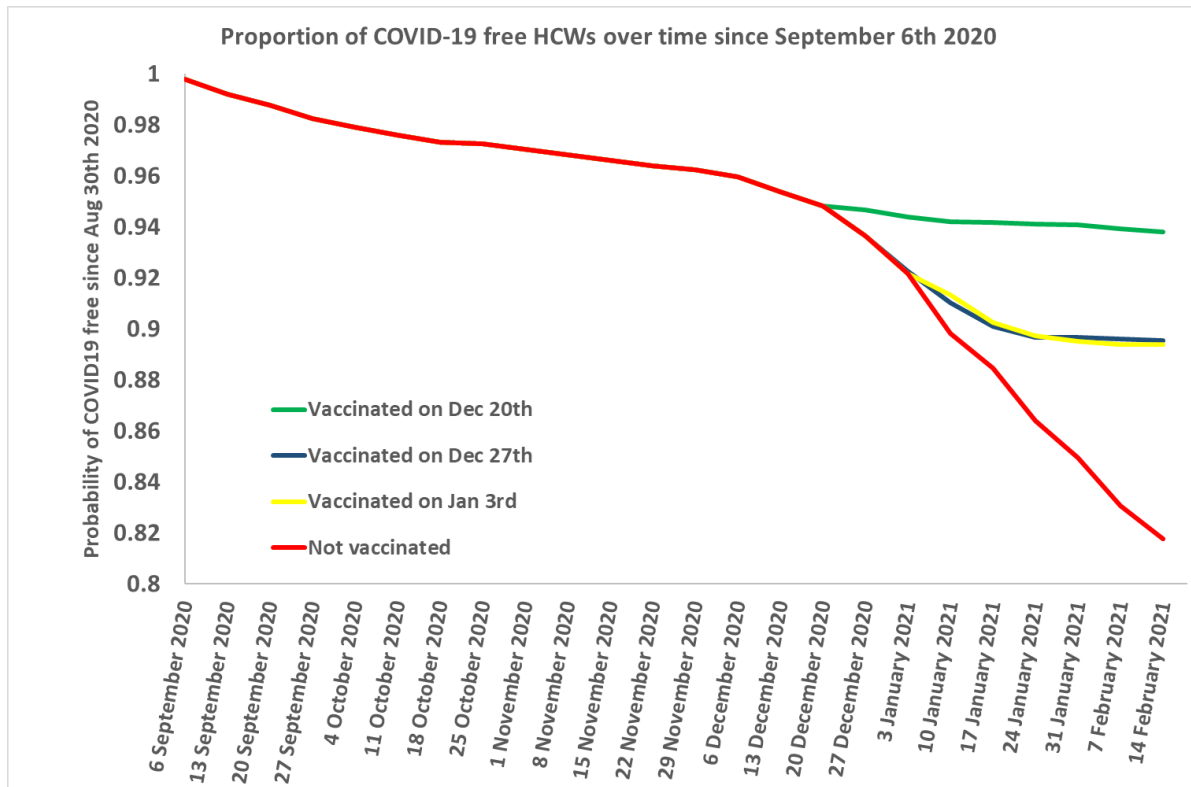
Figure S2

Weekly new SARS-CoV-2 cases /1000 HCWs at risk in relation to time since 1st vaccination



Incidence rates (per 1000 HCWs) and their 95% confidence intervals are presented per week since 1st vaccination. In each week, the denominator includes HCWs who did not become infected in the previous weeks. The numerator is the sum of all new COVID-19 infections among the HCWs included in the denominator. From the third week since vaccination, the rates drop. At week six, there were no new infections.

Figure S3



A cohort of all HCWs at HHUMC, followed since the end of August 2020. COVID-19 infection occurred at an almost steady rate. Vaccination began early during the surge of infections in the Jerusalem area. Clearly, vaccinated HCWs were protected from infection. Apparently, later 1st vaccination resulted in a later protection from getting infected as is seen from the green, blue and yellow lines. Still it is obscure why those vaccinated at the 3rd of January, had the same curve as those vaccinated at the week of December 27th. Those not vaccinated had increased

rate of getting infected (red line). Those vaccinated during the first week had a 0.011 probability of COVID-19 in the 8 weeks after first vaccine dose, compared with those that have not been vaccinated, who had a 0.13 probability of COVID-19 during the same time period.

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