

COVID-19 vaccine effectiveness among the staff of the Bologna Health Trust, Italy, December 2020 – April 2021

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Abstract. *Background and aim:* Randomized controlled trials have shown that mRNA vaccines are highly effective in preventing SARS-CoV2 infection. We conducted a study to assess the real-world effectiveness of mRNA vaccines (Pfizer-BioNTech or Moderna) in preventing all and symptomatic SARS-CoV2 infections and COVID-19 related hospitalizations in the staff of the Bologna Health Trust (HT), Italy *Methods:* We followed up retrospectively 9839 staff of the Bologna HT from December 27, 2020 to April 3, 2021 and calculated the effectiveness in partially and fully vaccinated subjects by applying a multivariable Cox proportional hazard model. *Results:* Vaccine effectiveness in preventing SARS-CoV2 infections is 85.5% (95%CI: 75.9-91.3) in the partially vaccinated and 84.8% (95%CI: 73.2-91.4) in the fully vaccinated. In preventing symptomatic infection effectiveness is 81.7% (95%CI: 62.7-91.0) in the partially and 87.1% (95%CI: 69.3-94.6) in the fully vaccinated. There were no COVID-19-related hospitalizations in the partially or fully vaccinated vs 15 hospitalization in the unvaccinated cohort. *Conclusions:* Our results confirm the effectiveness of mRNA vaccines in a real-world setting in Northern Italy.

Key words: COVID-19, vaccine effectiveness, health care workers

Introduction

By the end of May 2021, the coronavirus disease (COVID-19) has caused about 170 million cases and 3,5 million deaths worldwide (1). Control measures such as the use of masks, contact tracing and isolation, testing, physical distancing including lockdown have helped to limit the transmission (2, 3), however they need to be rigorously applied and are very strenuous in the long run (4). Many efforts have been made to develop vaccines against SARS-CoV-2 to return to normal life. Among the early vaccines that were available, BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna), two mRNA vaccines, have been shown to be highly effective in preventing SARS-CoV-2 infections in randomized

controlled trials (5, 6). After authorization by European and Italian regulatory agencies, they were immediately used in vaccination campaigns and as in other countries (7-10), also in Italy health care personnel was considered one of the first target groups of these campaigns. To date the evidence of their effectiveness in real-world settings is growing (11) but is still limited especially in a context of emerging virus variants. Based on surveillance data we conducted a retrospective cohort study with the aim of assessing the effectiveness of mRNA vaccines in preventing asymptomatic, symptomatic SARS-CoV-2 infections and related hospitalization in the staff of the Bologna Health Trust (HT), Emilia Romagna Region (Northern Italy) from December 27, 2020 to April 30, 2021.

Methods

Our study population consisted of all the staff of the Bologna HT. At the beginning, the vaccination campaign, that started on December 27, 2020, targeted all the staff of the HT and not only health care workers. To identify the study population, we used the local staff database which provided demographic and work-related information of each worker.

The outcomes of interest were: SARS-CoV-2 infections (i.e. subjects with a positive PCR SARS-CoV-2 test), symptomatic SARS-CoV-2 infections, COVID-19 related-hospitalizations and COVID-19 related hospitalizations in Intensive care unit (ICU). We identified the subjects that became cases during the follow up by linking the staff database with the local COVID-19 surveillance registry. This registry contains all COVID-19 cases occurred since the beginning of the epidemic and includes social, clinical and epidemiological information collected during the interview with all the cases notified by reference laboratories. This registry includes also information on hospitalizations and on other outcomes of the disease (e.g. recovery or death) as it is continuously fed by data from the hospitals and the peripheral necroscopy services. In this phase of the epidemic, subjects were undergoing SARS-CoV-2 testing in case of symptoms such as fever, cough, asthenia or dyspnoea, in case of contact with a case or because of screening activities.

To retrieve the vaccination status, we used the vaccination archive, which includes type of vaccine and dates of the administration by subject from the beginning of the campaign. Recommended administration was two doses of Pfizer-BioNTech or Moderna 21 or 28 days apart, respectively.

We excluded subjects with a previously documented SARS-CoV-2 infection and subjects vaccinated with non-mRNA vaccines. Individuals with zero follow-up days after vaccination were also excluded.

Case date was defined as either the date of the onset of symptoms or of the test results whichever occurred earlier. Person-time began December 27 and ended April 30 or on the case date if it occurred earlier and was categorized as:

1. unvaccinated,
2. before dose 1 effect (day 0 through day 14 after dose 1),
3. partially vaccinated (>14 days after dose 1 through day 7 after dose 2),
4. fully vaccinated (>7 days after dose 2).

Participants that did not become a case moved from one category to another according to the dose received.

Incidence density was calculated as the number of cases per 100,000 persons/days. Effectiveness and 95% Confidence Interval (CI) in partially and fully vaccinated was measured using a multivariate Cox proportional hazard model including sex, age group, role, working context and starting week of exposure. Vaccine effectiveness (VE) in preventing all, and only symptomatic infections was calculated as $1 - \text{Hazard ratio (HR)} \times 100$. VE was not calculated for COVID-19-related hospitalizations because of the limited number of events. We replicated the analyses after excluding all non-health care workers.

Results

On December 2020, Bologna HT had a staff of 10999; after excluding subjects with a previous infection (1098), with zero follow-up days (5) and subjects vaccinated with non-mRNA vaccines (57), we included 9839 subjects, 6886 women (70%) and 2953 (30%) men. The majority (73%) were health workers. By April 30, 2021 296 had received only one dose, 7897 two doses, mostly (96%) with Pfizer; there were 443 COVID-19 cases, 214 with symptoms and 17 with a COVID-19-related hospitalization, 4 in ICU. None died during the study period. Table 1 shows the main characteristics of the study population.

The incidence ranged from 14.37 in the fully vaccinated to 70,8 x 100,000 persons/days in the unvaccinated. The adjusted VE in preventing SARS-Cov-2 infection was 85.5% (95%CI: 75.9-91.3) and 84.8% (95%CI: 73.2-91.4) in the partially and the fully vaccinated, respectively. In preventing symptomatic infection VE was 81.7% (95%CI: 62.7-91.0) and 87.1% (95%CI: 69.3-94.6) in the partially and the fully

Table 1. Main characteristics of the study population, Bologna Health Trust

	Cases	Unvaccinated	Partially vaccinated	Fully vaccinated	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
Gender					
F	332 (74.9)	1099 (66.8%)	195 (65.9%)	5592 (70.8%)	6886 (70.0%)
M	111 (25.1)	547 (33.2%)	101 (34.1%)	2305 (29.2%)	2953 (30.0%)
Age class					
18-34	86 (19.4)	332 (20.2%)	69 (23.3%)	1458 (18.5%)	1859 (18.9%)
35-44	94 (21.2)	315 (19.1%)	62 (20.9%)	1462 (18.5%)	1839 (18.7%)
45-54	149 (33.6)	504 (30.6%)	84 (28.4%)	2487 (31.5%)	3075 (31.3%)
55+	114 (25.7)	495 (30.1%)	81 (27.4%)	249 (3.2%)	3066 (31.2%)
Role					
Health worker	311 (70.2)	1061 (64.5%)	198 (66.9%)	5931 (75.1%)	7190 (73.1%)
Technician	90 (20.3)	264 (16%)	45 (15.2%)	1183 (15%)	1492 (15.2%)
Administrative	36 (8.1)	252 (15.3%)	30 (10.1%)	732 (9.3%)	1014 (10.3%)
Other	6 (1.4)	69 (4.2%)	23 (7.8%)	51 (0.6%)	143 (1.5%)
Working context					
Hospital	288 (65.0)	599 (36.4%)	132 (44.6%)	4802 (60.8%)	5533 (56.2%)
Other (i.e. health centres)	155 (35.0)	1047 (63.6%)	164 (55.4%)	3095 (39.2%)	4306 (43.8%)
Total	443 (100)	1646 (100)	296 (100)	7897 (100)	9839 (100)

vaccinated, respectively (Table 2). Similar VE estimates were found when considering only health care workers.

There were no COVID-19 related hospitalizations in partially or fully vaccinated subjects. The vaccine shows also a 37% effectiveness in preventing

infections during the “before dose 1 effect” period in the whole study population. This result is not significant when we consider health care workers only.

There were no COVID-19-related hospitalizations in the partially or fully vaccinated vs 15 hospitalization in the unvaccinated cohort.

Table 2. Incidence and COVID-19 vaccination effectiveness among the staff (all and only health care workers) of the Bologna Local Health Trust, December 27, 2020 - April 30, 2021.

Immunization status	cases	Persons / days	Incidence density per 100.000 persons/days	VE† (95%CI)	P	Adj†VE (95%CI)	P
all							
All infections							
Unvaccinated	259	365,778	70.81	1		1	
Before dose 1 effect	82	119,544	68.59	33.7 (13.0-49.6)	0.003	37.4 (16.7-53.0)	0.001
Partially vaccinated	17	104,880	16.21	84.7 (74.7-90.7)	<0.001	85.5 (75.9-91.3)	<0.001
Fully vaccinated	85	591,499	14.37	80.2 (74.5-84.7)	<0.001	84.8 (73.2-91.4)	<0.001
Symptomatic							
Unvaccinated	133	365,778	36.36	1		1	
Before dose 1 effect	46	119,544	38.48	16.6 (0-43.1)	0.353	20.1 (0-46.5)	0.274
Partially vaccinated	9	104,880	8.58	81.1 (61.9-90.6)	<0.001	81.7 (62.7-91.0)	<0.001

(continued)

Immunization status	cases	Persons / days	Incidence density per 100.000 persons/days	VE† (95%CI)	P	Adj†VE (95%CI)	P
Fully vaccinated	21	591,499	3.55	90.4 (84.6-94.0)	<0.001	87.1 (69.3-94.6)	<0.001
COVID-19 related hospitalizations							
Unvaccinated	15	365,778	4.10	§			
Before dose 1 effect	2	119,544	1.67				
Partially vaccinated	0	104,880	0.00				
Fully vaccinated	0	591,499	0.00				
COVID-19 related hospitalizations in ICU¶							
Unvaccinated	4	365,778	1.09				
Before dose 1 effect	0	119,544	0.00				
Partially vaccinated	0	104,880	0.00				
Fully vaccinated	0	591,499	0.00				
Health care workers							
All infections							
Unvaccinated	167	245,968	67.90	1		1	
Before dose 1 effect	67	89,558	74.81	45.5 (0-45.5)	0.064	25.9 (0-46.2)	0.068
Partially vaccinated	10	78,593	12.72	87.7 (76.4-93.6)	<0.001	87.8 (76.5-93.7)	<0.001
Fully vaccinated	67	450,135	14.88	78.1 (70.5-83.7)	<0.001	84.4 (69.7-92.0)	<0.001
Symptomatic							
Unvaccinated	80	245,968	32.52	1		1	
Before dose 1 effect	38	89,558	42.43	3.2 (0-37.7)	0.884	5.9 (0-40.4)	0.793
Partially vaccinated	6	78,593	7.63	82.7 (59.2-92.6)	<0.001	83.1 (60.0-92.9)	<0.001
Fully vaccinated	13	450,135	2.89	90.8 (83.2-95.0)	<0.001	86.5 (62.9-95.1)	<0.001
COVID-19 related hospitalizations							
Unvaccinated	8	245,968	3.25	§			
Before dose 1 effect	1	89,558	1.12				
Partially vaccinated	0	78,593	0.00				
Fully vaccinated	0	450,135	0.00				
COVID-19 related hospitalizations in ICU¶							
Unvaccinated	2	245,968	0.81				
Before dose 1 effect	0	89,558	0.00				
Partially vaccinated	0	78,593	0.00				
Fully vaccinated	0	450,135	0.00				

†VE Vaccine effectiveness; ‡adjusted for sex, age, starting week of exposure, role, working context; §multivariate analyses was not run because of the few numbers; ¶ICU intensive care unit

Conclusions

This study shows that mRNA vaccines have an effectiveness of about 85-87% in preventing all and only symptomatic SARS-CoV-2 infections. These findings are consistent with previous literature (7-10) on vaccine effectiveness in health care workers even if comparisons between studies is difficult because of differences in variants prevalence, transmission and methods including case ascertainment. For instance, in this study due to the lack of regular screening, the vaccinated staff could more likely relax some prevention methods (12) than in studies where a regular screening is organized (7-10, 13).

Our study confirms also the high effectiveness of just one dose of vaccine after two weeks from the administration and before dose 2 starts its effect as reported by other authors (7-9) and the very high effectiveness in preventing COVID-19-related hospitalizations found in other studies (11). During the follow-up there were no cases hospitalized among partially or fully vaccinated. As reported by other authors (8) we also found a certain effectiveness in preventing infections in the first 14 days, but this effectiveness disappears when we consider symptomatic infections or hospitalizations or only health care workers.

The findings of this study have to be seen in light of some limitations. First, due to the observational nature of the study residual confounding is a possibility. For instance, we did not take completely account of the differences in exposure and health seeking behaviours among the staff. Second, lack of active laboratory surveillance might have resulted in an underestimation of asymptomatic cases. Third, the results are not directly transferrable to the general population. Fourth, due to the limited sample size caution is needed in interpreting the results regarding the rarest outcomes.

Despite these limitations, the present research contributes to the growing body of evidence providing additional data on the effectiveness of mRNA vaccines in a non-controlled setting during a high COVID-19 incidence period that in March reached 630 cases per 100.000 inhabitants per week (14) and a very high prevalence of the UK (93.3%) and the Brazilian (6.8%) variants (15), that are considered more transmissible.

Further work is certainly required to test these results in other populations and with longer follow up.

Our study confirms the effectiveness of both one and two doses of mRNA vaccines in preventing SARS-CoV-2 infections also in a context of emerging new variants. These results underscore the importance of vaccination among health care workers and can be helpful to increase vaccine coverage in the general population.

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