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COVID-19 vaccination significantly reduces morbidity and absenteeism among healthcare personnel: A prospective multicenter study



Helena C. Maltezou^{a,*}, Periklis Panagopoulos^b, Flora Sourri^c, Theodoros V. Giannouchos^d, Vasilios Raftopoulos^e, Maria N. Gamaletsou^f, Amalia Karapanou^g, Dimitra-Maria Koukou^h, Athanasia Koutsidouⁱ, Emmanuela Peskelidou^j, Konstantina Papanastasiou^k, Kyriakos Souliotis^{1,m}, Athanasia Louridaⁿ, Nikolaos V. Sipsas^f, Dimitrios Hatzigeorgiou^o

^a Directorate of Research, Studies and Documentation, National Public Health Organization, Athens, Greece

^c Department of Infection Control, 251 Hellenic Air Force General Hospital, Athens, Greece

^e Department of HIV Surveillance, National Public Health Organization, Athens, Greece

^f Pathophysiology Department, Medical School, National and Kapodistrian University of Athens, Greece

^g Infection Control Committee, Laiko General Hospital, Athens, Greece

^h First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece

¹Infection Control Committee, Alexandroupolis University Hospital, Alexandroupolis, Greece

^j COVID-19 Intensive Care Unit, 424 General Military Hospital of Thessaloniki, Thessaloniki, Greece

^k Operating Rooms, 424 General Military Hospital of Thessaloniki, Thessaloniki, Greece

¹Faculty of Social and Political Sciences, University of Peloponnese, Corinth, Greece

^m Health Policy Institute, Athens, Greece

^o Medical Directorate, Hellenic National Defence General Staff, Athens, Greece

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ABSTRACT

Aim: Healthcare personnel (HCP) are prioritized for coronavirus disease 2019 (COVID-19) vaccination to protect them and non-disruptive provision of healthcare services. We assessed the impact of the Pfizer-BioNTech vaccine on morbidity and absenteeism among HCP.

Methods: We studied 7445 HCP in five tertiary-care hospitals in Greece from November 15, 2020 through April 18, 2021.

Results: A total of 910 episodes of absenteeism and 9695 days of absence were recorded during the entire study period. Starting from January 4, 2021, 4823/7445 HCP (64.8%) were fully or partially vaccinated. Overall, 535 episodes of absenteeism occurred from January 4, 2021 through April 18, 2021, including 309 (57.76%) episodes among 2622 unvaccinated HCP and 226 (42.24%) episodes among 4823 vaccinated HCP (11.8 versus 4.7 episodes of absenteeism per 100 HCP, respectively; p-value < 0.001). The mean duration of absenteeism was 11.9 days among unvaccinated HCP compared with 6.9 days among vaccinated HCP (p-value < 0.001). Unvaccinated HCP more frequently developed acute respiratory infection, influenza-like illness, and COVID-19 (p-values < 0.001 for all comparisons). Vaccine effectiveness for fully vaccinated HCP was estimated at 94.16% [confidence interval (CI): 88.50%-98.05%) against COVID-19, 83.62% (CI: 73.36%-90.38%) against SARS-CoV-2 infection (asymptomatic or COVID-19), and 66.42% (CI: 56.86%-74.15%) against absenteeism.

Conclusion: The COVID-19 pandemic had a considerable impact on healthcare workforce. The Pfizer-BioNTech vaccine significantly reduced morbidity, COVID-19, absenteeism and duration of absenteeism among HCP during a period of high SARS-CoV-2 circulation in the community. It is expected that HCP vaccination will protect them and healthcare services and contain healthcare costs.

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^b Second Department of Internal Medicine, Medical School, Democritus University of Thrace, Alexandroupolis, Greece

^d Department of Health Services Policy and Management, Arnold School of Public Health, University of South Carolina, Columbia, SC, United States

ⁿ Infection Control Committee, Aghia Sofia Children's Hospital, Athens, Greece

^{*} Corresponding author at: Directorate of Research, Studies and Documentation,

National Public Health Organization, 3-5 Agrafon Street, Athens 15123 Greece. *E-mail addresses:* helen-maltezou@ath.forthnet.gr, maltezou.helena@gmail.com (H.C. Maltezou).

1. Introduction

As the first and a half year of the coronavirus disease 2019 (COVID-19) pandemic evolved, healthcare facilities in many counties faced an unprecedented burden of COVID-19-associated morbidity [1–4]. From the very beginning of the COVID-19 pandemic, healthcare personnel (HCP) were recognized as a high-risk group for occupational exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), development of COVID-19 and, in several occasions, a fatal outcome [5,6]. A review of 594 sources reported a total of 152,888 infections and 1413 fatalities among HCP during the first pandemic wave globally [5]. In addition, increased rates of absenteeism were noted among HCP, either because of infection or for post-exposure isolation purposes (healthy absenteeism) [7,8]. HCP have been prioritized for COVID-19 vaccination by the World Health Organization and other public health authorities [9]. The rationale for prioritizing HCP for COVID-19 vaccination relies on the need to protect them but also to protect the essential healthcare services from outbreaks and absenteeism particularly during periods of high demand [9]. To the best of our knowledge, there are no published data on COVID-19 vaccine effectiveness (VE) against absenteeism among HCP. The aim of this study was to estimate the impact of the Pfizer-BioNTech messenger RNA (mRNA) COVID-19 vaccine on morbidity and absenteeism in HCP in hospitals in Greece.

2. Methods

2.1. Study design

This was a prospective, observational study of a cohort of 7445 HCP employed in five tertiary-care hospitals across Greece (range: 1135–1728 employees per hospital). The study period extended from November 15, 2020 through April 18, 2021 (weeks 46/2020 through 15/2021, respectively). During the study period there was high circulation of SARS-CoV-2 in the community but no influenza activity [10,11].

2.2. Management of HCP

In accordance with the national guidelines issued on March 13, 2020, HCP were requested to notify the onset of any symptom or exposure to a COVID-19 case to the Infection Control Committee of each hospital [7]. Following interview of the exposed and/or symptomatic HCP and risk assessment, all exposed or symptomatic HCP and HCP tested positive for SARS-CoV-2 were excluded from work, as described previously [7]. In accordance with the revised guidelines issued on March 23, 2021, asymptomatic, fully vaccinated HCP or HCP with a history of recent (<6 months) SARS-CoV-2 infection, are not excluded from work after exposure to a COVID-19 case, regardless of the level of risk exposure [12].

2.3. COVID-19 vaccination program

Vaccination of HCP against COVID-19 started on January 4, 2021. The Pfizer-BioNTech mRNA vaccine was used.

2.4. Data collection

The Infection Control Committee of each hospital actively surveyed the HCP for absenteeism through communication with the Heads of the Departments/Clinics and the Heads of Nurse Stations. Absenteeism because of adverse events after COVID-19 vaccination was recorded. Absenteeism for non-infectious causes and pregnancy leaves were not considered. Annual leaves were prohibited throughout the study period in order to accommodate healthcare needs in a period of high demand. The authors had no involvement in the management of HCP.

The following data were prospectively collected per episode of absenteeism: age, gender, and profession of the absent employee, history of influenza vaccination, history of COVID-19 vaccination (including number of doses), clinical presentation, asymptomatic SARS-CoV-2 infection, COVID-19, absenteeism due to exposure to SARS-CoV-2, and duration of absenteeism and presenteeism (if any). Data were collected using one excel sheet per week. Upon completion of the follow-up of each week's episodes of absenteeism, the excel sheets were forwarded for data entry in the database.

2.5. Definitions

HCP were defined as persons employed in healthcare facilities. regardless of direct contact with patients or biological specimens. HCP were grouped as follows: physicians (including dentists), nursing personnel (nurses, midwifes, nurse assistants), paramedical personnel (pharmacists, biologists, laboratory technicians, physiotherapists, ambulance personnel, social workers, health visitors), supportive personnel (information systems personnel, engineers, waiters, cleaners, laundry personnel, security personnel, stretcher bearers), and administrative personnel. There were no part-time employees in our cohort. Full COVID-19 vaccination was defined as two vaccine doses administered 21 days apart, regardless of the time elapsed after the second dose. Clinical presentation was grouped as follows: febrile episode, acute respiratory illness (ARI), or influenza-like illness (ILI). Febrile episode was defined as fever only. Fever was defined as a temperature of \geq 38.0 °C twice within 24 h. ARI was defined as the onset of at least one respiratory symptom (e.g. cough, sore throat, dyspnea). ILI was defined as the sudden onset of symptoms and fever, malaise, myalgia or headache, and cough, sore throat or shortness of breath. SARS-CoV-2 infection was defined as a laboratoryconfirmed infection with SARS-CoV-2 by real-time reverse transcriptase polymerase chain reaction (RT-PCR) regardless of symptoms. COVID-19 case was defined as a patient with compatible symptoms and a positive SARS-CoV-2 RT-PCR. Absenteeism was defined as absence of a HCP from work duties due to onset of symptoms or for isolation purposes following exposure to SARS-CoV-2 (quarantine). Presenteeism was defined as working while being ill [13].

2.6. Statistical analysis

HCP who had received at least one dose of the COVID-19 vaccine were grouped to the vaccinated group. The primary outcome was the incidence of absenteeism among vaccinated HCP compared with the incidence of absenteeism among unvaccinated HCP. Secondary outcomes were the incidences of ARI, febrile episode, ILI, asymptomatic SARS-CoV-2 infection, COVID-19, postexposure exclusion from work, and duration of absenteeism among vaccinated HCP compared with unvaccinated HCP. There were no missing data or cases lost-to-follow-up in our cohort. Characteristics of HCP with absenteeism and causes of absence are presented using descriptive statistics. Absolute numbers and percentages were used for categorical variables. Means and standard deviation (SD) were used for continuous variables. Comparisons between vaccinated and unvaccinated HCP were performed by using the chi-square test for categorical variables and the two-tailed *t*-test or the Mann-Whitney *U* test for continuous variables depending on their distribution. P-values of <0.05 were considered statistically significant. Absenteeism ratio was estimated as follows: [total number of days of absence/ total number of HCP] [14]. The unadjusted COVID-19-VE against an "outcome" was estimated as follows: [1 - probability of "outcome" in vaccinated HCP/ probability of "outcome" in unvaccinated HCP] \times 100 [15]. Given that vaccination started on January 4, 2021 COVID-19 VE was estimated using data of absenteeism episodes that occurred between this date and April 18, 2021 (weeks 1/2021 and 15/2021, respectively). Finally, we used multivariate regressions to estimate the associations between COVID-19 vaccination and days of absenteeism, COVID-19 and any SARS-CoV-2 infection (COVID-19 or asymptomatic infection) among HCP who were absent from work after January 4, 2021. Since the number of days of absenteeism was expected to be right skewed, we initially conducted a Shapiro-Wilk test to assess the normality of the distribution, which support our hypothesis. We thus conducted a multivariable negative binomial regression (due to overdispersion) to estimate the association between COVID-19 vaccination and days of absenteeism. Similarly, we used two multivariable logistic regression models with two separate outcomes: COVID-19 and any SARS-CoV-2 infection (COVID-19 or asymptomatic infection). The adjusted incidence rate ratio (IRR), 95% confidence interval (CI), and odds ratio (OR) were estimated. All models controlled for HCP age, gender, profession and influenza vaccination status. In addition, we included hospital fixed-effects to control for unobserved hospital level heterogeneity and clustered standard errors at the hospital level. Statistical analyses were conducted using Stata version 17.0, StataCorp, College Station, TX, USA.

2.7. Ethical issues

The study was approved by The Ethics Committees of the participating hospitals (approval numbers: 30/8-1-2021, 2457/4-2-2021, 1/5-2-2021, Y Σ 36/21-12-2020/251). The data were managed in accordance with the European and national laws.

3. Results

Table 1 shows the overall morbidity among the 7445 HCP from November 15, 2020 to April 18, 2021. During the 22-week study period, a total of 910 episodes of absenteeism were recorded among the 7445 HCP, which corresponds to 12.2 episodes per 100 HCP. Table 2 shows the characteristics of HCP with absenteeism. The mean duration of absence was 10.7 (SD: 8.0) days while the total number of days of absence from November 15, 2020 to April 18, 2021 was 9695. The absenteeism ratio was estimated at 1.3 in our cohort throughout the study period. Working while being symptomatic (presenteeism) was recorded in 93 HCP (10.2%) for a mean of 1.3 (SD: 0.6) days before leaving work.

Starting from January 4, 2021, 4823 (64.8%) out of 7445 HCP were fully or partially vaccinated against COVID-19. Fig. 1 depicts the number of episodes of absenteeism per week by HCP vaccination status and the cumulative COVID-vaccine doses administered to HCP. Fig. 2 depicts the total number of days of absence per week by HCP vaccination status and the cumulative COVID-19-vaccine doses administered to HCP. In both figures there are two curves

Table 1

Morbidity in the cohort of 7445 HCP in five hospitals in Greece, November 15, 2020 to April 18, 2021.

Morbidity	N = 7445 (%)
Acute respiratory infection	108 (1.5)
Febrile episode	102 (1.4)
Influenza-like illness	192 (2.6)
Asymptomatic SARS-CoV-2 infection	96 (1.3)
COVID-19	239 (3.2)

HCP: healthcare personnel; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: coronavirus disease 2019.

Table 2

Characteristics of HCP with	absenteeism	in five	hospitals	in Greece,	November	15,
2020 to April 18, 2021.						

Characteristic	N = 910 (%)
Mean age, years (SD)	42.3 (11.0)
Male gender	319 (35.1)
Profession	
physician	172 (18.9)
nursing personnel	411 (45.2)
paramedical personnel	127 (14.0)
supportive personnel	117 (12.9)
administrative personnel	83 (9.1)
Influenza vaccination	367 (40.3)
COVID-19 vaccination	226 (24.8)
one dose	50 (5.5)
two doses	176 (19.3)
Total days of absenteeism	9695
Mean duration of absenteeism, days (SD)	10.7 (8.0)
Presenteeism	93 (10.2)
Mean duration of presenteeism, days (SD)	1.3 (0.6)

HCP: healthcare personnel; SD: standard deviation; COVID-19: coronavirus disease 2019.

(week 46/2020 through week 2/2021 and week 8/2021 through week 15/2021, respectively), which correspond to the second and the third pandemic wave.

Of the 910 episodes of absenteeism recorded from November 15, 2020 to April 18, 2021, 535 episodes (58.79% of all episodes) occurred from January 4, 2021 to April 18, 2021 (weeks 1/2021 and 15/2021, respectively), including 309 episodes (57.76%) that occurred among the 2622 unvaccinated HCP and 226 episodes (42.24%) that occurred among the 4823 vaccinated HCP (11.8 versus 4.7 episodes of absenteeism per 100 HCP, respectively; pvalue < 0.001). Of the 226 vaccinated HCP who developed an episode of absenteeism, 176 (77.88%) were fully vaccinated while 50 (22.12%) had received one vaccine dose. Starting from January 4, 2021, the mean duration of absenteeism was 11.9 (SD: 8.1) days among unvaccinated HCP compared with 6.9 (SD: 5.7) days among vaccinated HCP (p-value < 0.001). Overall, the unvaccinated group had a total of 3683 days of absence from January 4, 2021 to April 18, 2021 while the vaccinated group was absent from work for a total of 1555 days during the same time period. The absenteeism ratio from January 4, 2021 to April 18, 2021 was estimated at 1.4 among the 2622 unvaccinated HCP compared to 0.3 among the 4823 vaccinated HCP. There was no difference in terms of duration of presenteeism between the two groups [mean: 1.3 (SD: 0.7) days and 1.2 (SD: 0.7) days, respectively; p-value = 0.744).

Table 3 shows the morbidity recorded in our cohort from January 4, 2021 to April 18, 2021 per COVID-19 vaccination status. Compared with vaccinated HCP, unvaccinated HCP more frequently developed ARI [44 (1.7%) versus 23 (0.5%) cases; pvalue < 0.001], ILI [65 (2.5%) versus 33 (0.7%) cases; pvalue < 0.001), and COVID-19 [101 (3.9%) versus 23 (0.5%); pvalue < 0.001). There was no significant difference between the two groups in terms of incidence of febrile episode or asymptomatic SARS-CoV-2 infection. The unadjusted COVID-19 VE for fully vaccinated HCP was estimated at 94.16% (CI: 88.50%-98.05%) against COVID-19, 83.62% (CI: 73.36%-90.38%) against SARS-CoV-2 infection (asymptomatic or COVID-19), and 66.42% (CI: 56.86%-74.15%) against absenteeism. The unadjusted COVID-19 VE for vaccinated HCP regardless of number of doses was estimated at 87.62% (CI: 78.78%-93.71%) against COVID-19, 76.27% (CI: 63.41%-84.84%) against SARS-CoV-2 infection (asymptomatic or COVID-19), and 60.24% (CI: 49.78%-68.53%) against absenteeism (full data not shown). Overall, the implementation of the COVID-19 vaccination campaign in the five hospitals was associated with a prevention of 163 COVID-19 cases, 177 cases of any SARS-CoV-2

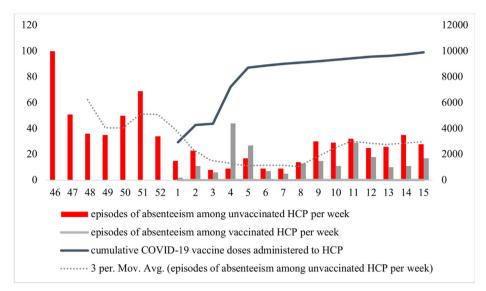


Fig. 1. Number of episodes of absenteeism per week among HCP by COVID- 19 vaccination status and cumulative COVID-19 vaccine doses administered to HCP in five hospitals in Greece, November 15, 2020 to April 18, 2021.

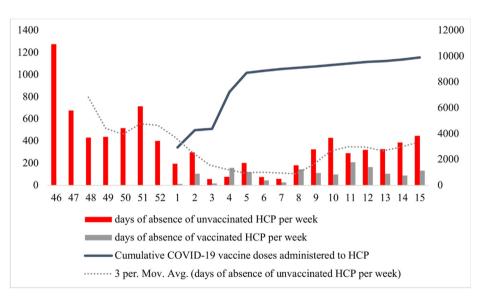


Fig. 2. Number of total days of absence per week among HCP by COVID-19 v vaccination status and cumulative COVID-19 vaccine doses administered to HCP in in five hospitals in Greece, November 15, 2020 to April 18, 2021.

Table 3

Morbidity in the cohort of 7445 HCP by COVID-19 vaccination status in five hospitals in Greece, January 4, 2021 to April 18, 2021.

Morbidity	Vaccinated ^a N = 4823 (64.8%)	Unvaccinated N = 2622 (35.2%)	p-value
Acute respiratory infection Febrile episode Influenza-like illness Asymptomatic SARS-CoV-2 infection	23 (0.5) 51 ^b (1.1) 33 ^b (0.7) 32 (0.7)	44 (1.7) 17 (0.7) 65 (2.5) 25 (1.0)	<0.001 0.076 <0.001 0.170
COVID-19	23 (0.5)	101 (3.9)	<0.001

HCP: healthcare personnel; COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

^a one or two vaccine doses.

^b systemic reaction to vaccination in 43 febrile episodes and 16 cases of influenza-like illness. infection, 342 episodes of absenteeism, and 4551 days of absence from January 4, 2021 to April 18, 2021.

Table 4 shows the characteristics of HCP with absenteeism from January 4, 2021 to April 18, 2021 by COVID-19 vaccination status and Table 5 summarizes the causes of absenteeism from January 4, 2021 to April 18, 2021 by COVID-19 vaccination status. Compared to vaccinated HCP, unvaccinated HCP were absent from work more frequently because of COVID-19 [101 (32.7%) versus 23 (10.2%) cases; p-value < 0.001]. In contrast, vaccinated HCP were absent from work more frequently because of a febrile episode [51 (22.6%) versus 17 (5.5%) cases; p-value < 0.001] or an asymptomatic SARS-CoV2 infection [32 (14.2%) versus 25 (8.1%) cases; p-value = 0.025]. Finally, exposure to a COVID-19 case was more often recorded as a cause of absence from work in unvaccinated compared with vaccinated HCP [166 (53.7%) versus 87 (38.5%)

Table 4

Characteristics of HCP with absenteeism from January 4, 2021 to April 18, 2021 by status of COVID-19 vaccination.

	Vaccinated*	Unvaccinated	p-value
Characteristic	N = 226 (%)	N = 309 (%)	
Mean age, years (SD)	43.7 (11.0)	41.4 (11.4)	0.008
Male gender	82 (36.3)	103 (33.3)	0.479
Profession			
physician	53 (23.5)	33 (10.7)	< 0.001
nursing personnel	106 (46.9)	146 (47.2)	
paramedical personnel	30 (13.3)	36 (11.7)	
supportive personnel	22 (9.7)	65 (21.0)	
administrative personnel	15 (6.6)	29 (9.4)	
Influenza vaccination	136 (60.2)	80 (25.9)	< 0.001
Total days of absenteeism	1555	3683	
Mean days of absenteeism (SD)	6.9 (5.7)	11.9 (8.1)	< 0.001
Presenteeism	24	26	
Mean days of presenteeism (SD)	1.2 (0.7)	1.3 (0.7)	0.744

HCP: healthcare personnel; SD: standard deviation; COVID-19: coronavirus disease 2019.

^a176 (77.87%) fully vaccinated and 50 (22.12%) with one vaccine dose.

Table 5

Causes of absenteeism and mean days of absence among HCP by COVID-19 vaccination status in five hospitals in Greece, January 4, 2021 to April 18, 2021.

Cause of absence	Vaccinated ^a N = 226 (%) ^b	Unvaccinated N = 309 (%) ^b	p-value
ARI	23 (10.2)	44 (14.2)	0.161
Mean days of absenteeism due to ARI (SD)	8.7 (8.1)	11.6 (7.6)	0.082
Febrile episode	51 ^c (22.6)	17 (5.5)	<0.001
Mean days of absenteeism due to a febrile episode (SD)	2.2 (2.9)	13.9 (7.3)	<0.001
ILI	33 ^c (14.6)	65 (21.0)	0.057
Mean days of absenteeism due to ILI (SD)	7.5 (7.6)	19.9 (10.8)	<0.001
Asymptomatic SARS-CoV-2	32 (14.2)	25 (8.1)	0.025
infection	11.0 (4.1)	12.9 (5.2)	0.143
Mean days of absenteeism due to asymptomatic SARS-CoV-2 infection (SD)			
COVID-19	23 (10.2)	101 (32.7)	< 0.001
Mean days of absenteeism due to COVID-19 (SD)	17.3 (4.9)	20.0 (8.1)	0.179
Exposure to a COVID-19 case	87 (38.5)	166 (53.7)	< 0.001
Mean days of absenteeism due to exposure to a COVID-19 case (SD)	7.3 (3.6)	9.3 (5.9)	0.003

HCP: HCP: healthcare personnel; COVID-19: coronavirus disease 2019; ARI: acute respiratory infection; SD: standard deviation; ILI: influenza-like illness; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

^a 176 (77.87%) fully vaccinated and 50 (22.12%) with one vaccine dose.

^b percentages add over 100% since an episode of absenteeism could be recorded concomitantly by clinical manifestation (acute respiratory infection, febrile episode or influenza-like illness) and as COVID-19.

^c systemic reaction to vaccination in 43 febrile episodes and 16 cases of influenza-like illness.

cases; p-value < 0.001]. In addition, 59 out of 226 (26.1%) episodes of absenteeism among vaccinated HCP were associated with adverse events after COVID-19 vaccination, including 43 out of 51 febrile episodes and 16 out of 33 ILI cases. In terms of duration of absence, unvaccinated HCP who developed a febrile episode were absent from work for a mean of 13.9 (SD: 1.8) days compared with 2.2 (SD: 2.9) days of absence of vaccinated HCP with a febrile episode, unvaccinated HCP who developed ILI were absent for a mean of 19.9 (SD: 10.8) days compared with 7.5 (SD: 7.6) days of vaccinated HCP with ILI, and unvaccinated HCP who were absent because of exposure were excluded for a mean of 9.3 (SD: 5.9) days compared to 7.3 (SD: 3.6) days of vaccinated HCP (p-value < 0.001 for all comparisons). The two groups did not differ in terms of duration of absence because of ARI, COVID-19 or asymptomatic SARS-CoV-2 infection. The three multivariable regression analyses showed that among the 535 HCP who had an episode of absenteeism from work after January 4, 2021, COVID-19 vaccination was associated with fewer days of absenteeism (Adjusted IRR = 0.56, 95% CI = 0.43–0.72, p-value < 0.001), a 77% decreased likelihood in developing COVID-19 (Adjusted OR = 0.23, 95% CI = 0.09–0.55, pvalue = 0.001), and a 59% decreased likelihood in contracting and having any SARS-COV-2 infection (COVID-19 or asymptomatic) (OR = 0.41, 95% CI = 0.21–0.77, p-value = 0.006).

4. Discussion

This is a prospective, observational study of 7445 HCP in five tertiary-care hospitals in Greece that was conducted to evaluate the impact of the Pfizer-BioNTech vaccine on HCP morbidity and absenteeism. Our study clearly showed that vaccination of HCP significantly conferred protection against ARI, ILI, COVID-19, and absenteeism.

The COVID-19 pandemic had a significant impact on healthcare workforce absenteeism [7,8]. During the first pandemic wave, more than 5% of HCP working in Emergency Departments in Spain were on sick leave up to 20% of time [16], while 39% (127/326) of physicians working in a London hospital had at least one sickness episode for a median absence of 7 days between March 16 and April 26, 2020 [17].

Our study found that during a period of high circulation of SARS-CoV-2 in the community but no influenza activity [11], absenteeism among HCP far exceeded the absenteeism recorded during influenza seasons [13,18,19]. In particular, during a 22week period we found an overall absenteeism ratio of 1.3. In contrast, a multi-center study in the United States over three influenza seasons found an absenteeism ratio ranging from 0.58 to 0.62 among HCP vaccinated against seasonal influenza and from 0.66 to 1.03 among unvaccinated HCP, depending on the matching between influenza vaccine strains and circulating strains [14]. In our cohort, the absenteeism ratio in the COVID-vaccinated group was 0.3 which is almost half the absenteeism ratio reported in the influenza-vaccinated group in the United States study during a 12-week period [14]. This is of outmost importance, given that in our previous cost-of-illness analysis we found that absenteeism was the major driver of total costs for the management of exposed or infected HCP during the first pandemic wave in Greece, accounting for 80.4% of all expenditures [20]. In a similar line, 65 symptomatic employees (24.6% of all) were on sick leave for a mean of 19.2 days and 69 new employees were contracted during a COVID-19 outbreak in a long-term care facility in Spain, accounting

for approximately one third of a total of 276,281 Euros spent during a one-month period [21].

In the current study, the COVID-19 VE against absenteeism was estimated at 66.42%. In practice, COVID-19 vaccination prevented almost seven out of ten episodes of absenteeism among HCP but also significantly reduced the length of absence from work. The fact that the national guidelines which recommended no exclusion from work of asymptomatic, full vaccinated HCP after exposure, were issued in late March 2021 most probably accounts for the 66.42% VE against absenteeism. It is expected that the full implementation of the revised guidelines will further reduce the rate of absenteeism among fully vaccinated HCP in the near future. Recent studies show that influenza is also associated with increased HCP absenteeism and economic costs [14,19]. Furthermore, in a study it was shown that absenteeism and increased work hours, because of the need to accommodate healthcare demands and absence of ill staff, have been directly related with the level of ILI in the community [13]. Vaccination of HCP against seasonal influenza also significantly reduced influenza-associated morbidity, incidence and duration of sick absenteeism among HCP and proved to be cost-saving in terms of avoided absenteeism [18.22].

In our cohort, the overall COVID-19 vaccination with the Pfizer-BioNTech vaccine had an effectiveness of 94.16% against COVID-19. Interim estimates of Pfizer-BioNTech and Moderna mRNA vaccines among HCP in 31 United States sites indicated 82% VE of a single dose (95% CIs; 74%-87%) and a 94% VE after the second dose (95% CIs: 87%-97%) against COVID-19 [23]. An Israeli observational study of a cohort of 6710 HCP (mean age: 44.3 years; 66.5% women) in one medical center also showed significant reduction of symptomatic (from 149.8 to 4.7 cases per 100,000 persondays) and asymptomatic SARS-CoV-2 infections (from 67.0 to 11.3 cases per 100,000 person-days) with the use of the Pfizer-BioNTech vaccine [24]. Moreover, asymptomatic SARS-CoV-2 infections accounted for approximately one fourth of SARS-CoV-2 infections diagnosed in our cohort. It should be kept in mind, that although symptomatic cases pose a higher risk of transmission of SARS-CoV-2 infection, asymptomatic and pre-symptomatic cases also contribute to transmission and may prove critical in healthcare settings where high-risk groups receive healthcare [25]. These findings underline the need to strictly adhere to infection control measures. Moreover, approximately one out of ten HCP continued to work for a mean of 1.3 days despite being symptomatic. Beyond the loss of productivity, poorer quality of services and financial losses [13,26], presenteeism of HCP is of concern given that SARS-CoV-2 viral load peaks shortly after the onset of symptoms [27].

SARS-CoV-2 infections after one or two vaccine doses of mRNA COVID-19 vaccines have occasionally occurred and are almost always asymptomatic or mild [24,28]. A study in two institutions in California where PCR testing in nasal swabs of asymptomatic HCP was intensified after the initiation of COVID-19 vaccinations, found that 2.59% (379/14,604 employees) tested positive [28]. In our cohort, 1.2% of vaccinated HCP developed SARS-CoV-2 infection (asymptomatic or COVID-19). Overall, the mean duration of absence from work per episode was significantly shorter among vaccinated HCP compared with unvaccinated HCP, which indicates milder morbidity after vaccination. This was more pronounced in febrile episodes and in cases of ILI, and it is attributed to the fact that most febrile episodes and half cases of ILI among vaccinated HCP concerned systemic reactions after COVID-19 vaccination.

In our study, one out of three HCP declined COVID-19 vaccination despite on-site vaccination, which is of concern. Mandatory vaccination policies for HCP are increasingly adopted in several countries [29]. An observational cohort study conducted in three university medical centers (2304 outpatient HCP) with mandatory influenza vaccination policies and four Veteran Affairs healthcare systems (1759 outpatient HCP) with no mandatory influenza vaccination policies over three influenza seasons (2012–2013 through 2014–2015) found that mandatory influenza vaccination policies significantly increased vaccine uptake rates while HCP symptomatic absenteeism diminished as rates of influenza vaccine uptake increased [14]. Our findings indicate that the implementation of mandatory COVID-19 vaccination policies for HCP should be explored.

Clear strengths of our study include the active follow-up of a large cohort of HCP, the prospective collection of data about each episode of absenteeism, the multi-site design, and the study of several morbidity and absenteeism outcomes. A limitation is that the dynamics of SARS-CoV-2 transmission may vary by healthcare facility, although we adjusted for unobserved hospital heterogeneity and clustering in our multivariable analyses. In addition, all participating hospitals provided healthcare to a large number of COVID-19 cases during the study period. Another limitation is the observational design of the study however randomization was not feasible due to ethical considerations. Finally, it is possible that COVID-19 VE is underestimated because of the applied definition of full vaccination. Despite, our results are in-line with the growing literature on COVID-19 vaccines globally.

In conclusion, the current study offers insight on the occupational risk of healthcare workforce and important implications for policy makers and healthcare facilities in the context of the ongoing COVID-19 pandemic. It also provides real-life evidence about VE of the Pfizer-BioNTech mRNA COVID-19 vaccine in significantly reducing the risk of ARI, ILI, COVID-19, and absenteeism and the duration of absenteeism among HCP during a period of high virus circulation in the community. Vaccination of HCP against COVID-19 is expected to improve healthcare services and to contain healthcare costs. Efforts are need to raise vaccine uptake rates among HCP. The beneficial impact of COVID-19 vaccination on HCP morbidity and absenteeism might guide vaccination policies to preserve human and financial resources in other work settings.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- World Health Organization. Coronavirus disease (COVID-19) pandemic, available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (last accessed: September 12, 2021).
- [2] Palladino R, Bollon J, Ragazzoni L, Barone-Adesi F. Excess deaths and hospital admissions for COVID-19 due to a late implementation of the lockdown in Italy. Int J Environ Res Public Health 2020;17:5644.
- [3] Flores S, Gavin N, Romney ML, et al. COVID-19: New York City pandemic notes from the first 30 days. Am J Emerg Med 2020;38:1534–5.

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- [5] Bandyopadhyay S, Baticulon RE, Kadhum M, et al. Infection and mortality of healthcare workers worldwide from COVID-19: a systemic review. BMJ Global Health 2020;5:e003097.
- [6] Nguyen LH, Drew DA, Graham MS, et al. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. Lancet Public Health 2020;5:e475–83.
- [7] Maltezou HC, Dedoukou X, Tseroni M, et al. SARS-CoV-2 infection in healthcare personnel with high-risk occupational exposure: evaluation of seven-day exclusion from work policy. Clin Infect Dis 2020;71:3182–7.
- [8] Groenewold MR, Burrer SL, Ahmed F, Uzicanin A, Free H, Luckhaupt SE. Increases in health-related workplace absenteeism among workers in essential critical infrastructure occupations during the COVID-19 pandemic – United States, March-April 2020. MMWR Morb Mortal Wkly Rep 2020;69:853–8.
- [9] World Health Organization. World Health Organization Strategic Advisory Group of Experts on Immunization roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply. Version 1.1 13 November 2020, available at: https://www.who.int/docs/default-source/immunization/ sage/covid/sage-prioritization-roadmap-covid19-vaccines.pdf? Status=Temp&sfvrsn=bf227443_2 (last accessed: September 12, 2021).
- [10] National Public Health Organization. Daily Report of Epidemiological Surveillance of SARS-CoV-2 infection (COVID-19), available at: https:// eody.gov.gr/wp-content/uploads/2021/05/covid-gr-daily-report-20210515. pdf (last accessed: September 12, 2021) [in Greek].
- [11] National Public Health Organization. Weekly Report of Epidemiological Surveillance of Influenza, Week 18/2021 (03-09 May 2021), available at: https://eody.gov.gr/wp-content/uploads/2020/10/18.2021-FLU-WEEK.pdf (last accessed: September 12, 2021) [in Greek].
- [12] National Public Health Organization. Guidelines for isolation of vaccinated HCP and HCP with a history of SARS-CoV-2 infection, available at: https:// eody.gov.gr/odigies-karantinas-emvoliasmenon-anarrosanton/ (last accessed: September 12, 2021) [in Greek].
- [13] Challener DW, Breeher LE, Frain JE, Swift MD, Tosk PK, O' Horo J. Healthcare personnel absenteeism, presenteeism, and staffing challenges during epidemics. Infect Control Hosp Epidemiol 2021;42:388-91.
- [14] Frederick J, Brown AC, Cummings DA, et al. Protecting healthcare personnel in outpatient settings: the influenza of mandatory versus nonmandatory influenza vaccination policies on workplace absenteeism during multiple respiratory virus seasons. Infect Control Hosp Epidemiol 2018;39:452–61.
- [15] Halloran ME, Struchiner CJ, Longini Jr IM. Study designs for evaluating different efficacy and effectiveness aspects of vaccines. Am J Epidemiol 1997;146:789–803.

- [16] Alquezar-Arbe A, Pinera P, Jacob J, et al. Impact of the COVID-19 pandemic on hospital emergency departments: results of a survey of departments in 2020 the Spanish ENCOVUR study. Emergencias 2020;32:320–31.
- [17] Khorasanee R, Grundy T, Isted A, Breeze R. The effects of COVID-19 on sickness of medical staff across departments: a single centre experience. Clin Med (Lond) 2021;21:e150–4.
- [18] Van Buynder PG, Konrad S, Kersteins KF, et al. Healthcare worker influenza immunization vaccinate or mask policy: strategies for cost effective implementation and subsequent reductions in staff absenteeism due to illness. Vaccine 2015;33:1625–8.
- [19] Gianino MM, Politano G, Scarmozzino A, et al. Cost of sickness absenteeism during seasonal influenza outbreaks of medium intensity among health care workers. Int J Environ Res Public Health 2019;16:747.
- [20] Maltezou HC, Giannouchos TV, Pavli A, et al. Costs associated with COVID-19 in healthcare personnel in Greece: a cost-of-illness analysis. J Hosp Infect 2021;114:126–33.
- [21] Romero MM, Avendano Cespedes A, Tabernero Sahuquillo MT, et al. COVID-19 outbreak in long-term care facilities from Spain. Many lessons to learn. PloS One 2020;15:e0241030.
- [22] Imai C, Toizumi M, Hall L, Lambert S, Halton K, Merollini K. A systemic review and meta-analysis of the direct epidemiological and economic effects of seasonal influenza vaccination on healthcare workers. PLoS ONE 2018;13: e0198685.
- [23] Pilishvili T, Fleming-Dutra KE, Farrar JL, et al. Interim estimates of vaccine effectiveness of Pfizer-BioNTech and Moderna COVID-19 vaccines among health care personnel – 33 U.S. sites, January-March 2021. MMWR Morb Mortal Wkly Rep 2021;70:753-8.
- [24] Angel Y, Spitzer A, Henig O, et al. Association between vaccination with BNT162b2 and incidence of symptomatic and asymptomatic SARS-CoV-2 infections among health care workers. JAMA 2021;325:2457–65.
- [25] Wu P, Liu F, Chang Z, et al. Assessing asymptomatic, pre-symptomatic and symptomatic transmission risk of SARS-CoV-2. Clin Infect Dis 2021 Mar 27; ciab271. doi: 10.1093/cid/ciab271. Online ahead of print.
- [26] Poti Homrich PH, Dantas-Filho FF, Martins LL, Marcon ER. Presenteeism among health care workers: literature review. Rev Bras Med Trab 2020;18:97–102.
- [27] To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020;20:565–74.
- [28] Keehner J, Horton LE, Pfeffer MA, et al. SARS-CoV-2 infection after vaccination in health care workers in California. New Engl J Med 2021;384:1774–5.
- [29] Maltezou HC, Theodoridou K, Ledda C, Rapisarda V, Theodoridou M. Vaccination of healthcare workers: is mandatory vaccination needed? Expert Rev Vaccines 2019;18:5–13.