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Commentary

Mandatory COVID-19 vaccination for healthcare personnel in the era of new SARS-CoV-2 variants



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From the first weeks of the COVID-19 pandemic it became evident that healthcare personnel (HCP) are at increased risk for infection and many fatalities occurred [1,2]. According to estimates of the World Health Organization (WHO), 80,000 to 180,000 HCP have died from COVID-19 between January 2020 and May 2021 [3]. In this context, HCP were prioritized for COVID-19 vaccination and actually significant protection was conferred to them as early as three weeks after the beginning of vaccination campaigns with mRNA vaccines [4]. Moreover, COVID-19-associated absenteeism incurs costs and additional workforce resources. For instance, absenteeism among 7445 hospital-based HCP amidst the second and the third pandemic wave far exceeded absenteeism recorded during past influenza seasons [4]. In the latter study, full COVID-19 vaccination prevented almost seven out of ten episodes of absenteeism and significantly shortened the duration of absence from work during a period of high healthcare demand [4]. Lastly, genome sequencing reveals that asymptomatic and pre-symptomatic HCP highly contribute to virus spread and onset of outbreaks in healthcare facilities, while transmission events between HCP and from HCP to patients are common [5]. Therefore,

COVID-19 vaccination of HCP also aims to protect the patients as well as healthcare systems from outbreaks and absenteeism.

On April 1, 2021 the Italian Parliament voted the decree-law 44/2021, rendering COVID-19 vaccination mandatory for HCP. Italy was the first European country to approve mandatory vaccination for HCP as a policy against the pandemic [6]. Moreover, despite the intensified vaccination campaigns, as of July 12, 2021, 26.4% of physicians, nurses, and laboratory personnel in Greece were still unvaccinated, with no signs of improvement the last two months (unpublished data). At the same time, marginally more than half of HCP in French hospitals have been fully vaccinated while 66.7% had received at least one vaccine dose [7]. Greece and France also passed laws for mandatory vaccination of HCP on July 23, 2021 (law 4820/2021) and August 5, 2021 (law 1040/2021). In brief, HCP who refused COVID-19 vaccination were excluded from work with salary suspension. Mandatory vaccination concerned all employees in public and private healthcare facilities, regardless of direct patient contact or task, and exemptions were granted based on strict medical criteria only. The French Constitutional Council ruled on the constitutionality of vaccine mandates for HCP, while the Italian and the Greek Councils of State rejected the objections of HCP on the grounds of the need to safeguard the health individually and collectively, providing protection for those attending healthcare facilities [8]. Moreover, in early September 2021 the European Court of Human Rights (ECHR) has rejected requests

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from HCP for interim measures against the new law based on Article 8, explicitly balancing between the principles of “protection of health” and “rights and freedoms of others” and the principle of the “right to respect for private life” [9]. Given the ECHR positioning on this issue, it appears highly unlikely for mandatory COVID-19 vaccination for HCP to be considered a breach of human rights [9].

Upon announcement of the new legislation framework but before the law was put into effect, COVID-19 vaccine uptake rates increased among HCP in French hospitals to 70.1 % for full vaccination and to 81.3 % for at least one dose, while on September 20, 2021, after the sanctions were imposed, vaccination rates were launched at 86.6 % for full vaccination and 92 % for vaccination with at least one dose [7]. Similarly, full vaccination rates among HCP increased to 82.5 % one month after the announcement of the new law in Greece and to 87.9 % for vaccination with at least one dose (unpublished data). In Italy, as of August 2021, 94.4 % of HCP have completed their vaccination [6]. High (>90 %) full vaccination rates were recorded within few months also in Greece and France [7]. Several healthcare facilities in the United States also require HCP to be vaccinated against COVID-19 [10].

The issue of mandatory vaccinations for HCP is not a new one. Mandatory influenza vaccination policies have been implemented extremely successfully in many healthcare facilities in the United States the past two decades, achieving high (>94 %) and sustainable vaccination rates among HCP [11]. Finland was the first European country to switch to a nation-wide mandatory influenza vaccination policy for HCP by compelling healthcare facilities to employ vaccinated HCP only, with excellent results [12]. As high as 99 % vaccination coverage rates were recorded with measles-mumps-rubella, varicella, and hepatitis B vaccine mandates at Vanderbilt University Medical Center [13].

The deployment of COVID-19 vaccines has significantly reduced mortality rates among infected individuals and among the general population. Nonetheless, as we enter the fourth winter season of COVID-19 era, COVID-19 remains the leading cause of death from a single infectious agent globally that can be prevented by vaccination [14]. In our view, public health authorities and other stakeholders should adopt mandatory COVID-19 vaccination policies for HCP in order to achieve high coverage rates. Switch to such a policy is even more imperative in the context of the dominance of the highly transmissible Omicron (B.1.1.529) variant and the continued evolution of viruses part of the Omicron complex [15]. For instance, a recent study of more than 1.5 million SARS-CoV-2 cases showed reduced risk of severe outcomes (hospitalization and death) in patients infected with Omicron variant compared with Delta variant, nevertheless a booster vaccination with mRNA vaccines offered more than 70 % protection against these severe outcomes in patients with Omicron breakthrough infections [16]. Moreover, unvaccinated cancer patients with COVID-19 during the Omicron dominance remain highly susceptible to hospitalization, complications, and fatalities, similarly to infections with Alpha-Delta variants [17]. That said, a history of COVID-19 vaccination is strongly predictive of improved COVID-19-associated outcomes rather than a reduced pathogenicity of Omicron variant [17]. However, patients with comorbidities might have low or no protection after vaccination also. The past months two new Omicron sub-lineages (BA.4 and BA.5) emerged and are becoming the dominant variants in many countries [18,19]. Even through the existing mRNA vaccines target the ancestral Spike, three doses of mRNA vaccines most likely provide sufficient protection against severe outcomes associated with the newly emerging Omicron subvariants, as indicated by a dramatic increase of neutralizing-antibody titers overall, sufficient neutralizing-antibody titers against newly emerging Omicron subvariants, and > 90 % effectiveness against COVID-19 hospitalization and death after the booster dose [18,20,21]. We also found that, in the context of the manda-

tory vaccination policy in Greece, a third (booster) mRNA dose administered from September 2021 onwards significantly reduced the duration of absenteeism among HCP during a 22-week follow-up period dominated by Omicron [22]. Moreover, an Israeli multi-center study that was conducted during Omicron dominance, showed a 19.8 % rate of breakthrough infections in HCP after 3 BNT162b2 mRNA doses (full vaccination plus booster) compared with 6.9 % in HCP who had received a fourth shot in January 2022 [23]. Data from the same country suggest that protection of a fourth mRNA dose against confirmed infection appears short-lived, whereas protection against severe illness does not wane during the study period [24]. Nonetheless, *in vitro* investigations indicate low neutralization efficiency against BA.4 and BA.5 new Omicron sub-variants even at one month after the fourth vaccine dose [25]. More efficient vaccines that will confer more specific protection against infections with new emerging variants are needed.

Beyond direct host protection, findings indicate that compared with unvaccinated infected patients, SARS-CoV-2 viral loads in upper respiratory tract during the first five symptomatic days were significantly lower in fully vaccinated patients with Delta variant breakthrough infections and in boosted patients with Omicron variant breakthrough infections [26]. Therefore, COVID-19 vaccines may reduce the risk of virus transmission and consequently infectiousness. The expected surge of COVID-19 cases in coming weeks can result in a rise in hospitalizations, especially among people at risk of severe disease [17]. After all, vulnerable patients who seek healthcare, especially high-risk populations who cannot elicit good immune responses post-vaccination, expect the highest levels of safety within healthcare facilities and support mandatory vaccinations for HCP to a significant extent [27].

Lastly, COVID-19 and seasonal influenza share the same risk groups and present with similar symptoms. To the extent that seasonal influenza will probably coincide with COVID-19 the next season, the pressure on healthcare systems could far exceed the pressure during the COVID-19 era alone. Ensuring HCP vaccination against both viruses is expected to facilitate decisions about antiviral agents and infection control, to reduce significantly their contribution on COVID-19 and influenza transmission in-hospital, to protect them from severe outcomes, especially those with comorbidities, and to protect the essential healthcare services from HCP absenteeism during the winter season. Yet, given the uncertainties about COVID-19 seasonality, the emergence of new SARS-CoV-2 variants, and the waning of vaccine-induced immunity over time, defining the optimal timing for booster doses is challenging. There is ongoing research for updated vaccines against the new variants, particularly as the next winter season approaches. However, the impact of mandatory vaccination for HCP on their vaccine confidence remains questioning, and may affect acceptance for routine vaccinations and new vaccines as in the general population [28] and challenge trust in government/public health authorities. In this respect, vaccine hesitancy is a key issue that should be addressed early. Uncertainty over the factors that impact COVID-19 outcomes across countries challenges global partners and policy makers to more effective plan for future pandemics [29].

Switch to a mandatory public health policy requires that four criteria are satisfied: first, it should be a public health necessity; second, the policy has to be proven that it is effective, in other words that it works; third, the benefit-risk ratio of the policy should be favorable; and fourth, the policy should be the only solution [30,31]. In our opinion, all four criteria are fulfilled for mandatory vaccination of HCP against COVID-19. In the coming season it is expected that beyond host protection, mandatory HCP vaccination will strengthen the capacity of healthcare systems to respond, through reducing the risk of SARS-CoV-2 transmission and HCP absenteeism.

Data availability

No data was used for the research described in the article.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Elisabeth Botelho-Nevers conduct COVID-19 vaccine trials including Janssen, Pfizer and Moderna, Sanofi-Pasteur COVID-19 vaccines. Elisabeth Botelho-Nevers participated in vaccines scientific advisory boards for Pfizer, Janssen, Sanofi Pasteur: honorarium were paid for her institution. Helena C. Malteizou, Caterina Ledda and Amandine Gagneux-Brunon have no conflict of interest to declare.

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