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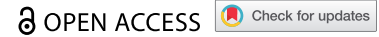


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RESEARCH PAPER



Two years of on-site influenza vaccination strategy in an Italian university hospital: main results and lessons learned

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ABSTRACT

Although the vaccination of healthcare workers (HCWs) is considered essential for preventing influenza circulation in the hospital setting, vaccination coverage (VC) in this group remains low. Among the reasons cited by HCWs is a lack of time to attend the vaccination clinic. For the 2018/2019 influenza season, active (on-site) influenza vaccination was offered directly in 44 operative units (OUs) of the Bari Policlinico hospital (50 OUs, 3,397 HCWs). At the same time, the hospital granted the HCW access to the vaccination clinic during October and December 2018. VC achieved among HCWs of Bari Policlinico during the 2018/2019 influenza season was then analyzed, and the results compared with those of the 2017/18 season. During the 2018/19 season, VC was 20.4% (n = 798) and thus higher than the 14.2% of the 2017/18 season (+6.2%). The highest VC was among physicians (33.4%), followed by other HCWs (23.8%), auxiliary staff (8.6%), and nurses (7.2%). Overall, 284 (36.5%) HCWs were vaccinated at on-site sessions. Multivariate analysis showed that vaccination uptake was associated with male gender and with work in OU where vaccination was actively offered. On the other hand, being a nurse or auxiliary staff member and working in the surgical area were deterrents. Although VC remained unsatisfactory, active on-site vaccination proved to be an important strategy to improve vaccination compliance, increasing 44% compared to the previous season. Nonetheless, mandatory vaccination directed by public health institutions may be the only way to reach a minimum level of coverage.

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Introduction

The vaccination of Healthcare Workers (HCWs) is an effective measure of individual and collective disease protection. It protects both HCWs from the occupational infectious disease and patients from the risk of infection in the nosocomial environment. High vaccination coverage (VC) among HCWs avoids absenteeism and guarantees the quality of the health services offered.¹

Because HCWs care for people at high risk of influenza-related complications (such as patients with chronic disease, cancer, or immunodeficiency), they must be vaccinated annually. Indeed, high VC among HCWs has been shown to reduce the rates of influenza morbidity and mortality among their patients.²

In Italy, the vaccination of HCWs is required by Legislative Decree 9 April 2008 n. 81³. Official recommendations for the immunization of HCWs are also part of the National Immunization Plan⁴ and the annual influenza prevention guidelines provided by the Italian Ministry of Health. In both, HCWs are among the risk categories for which influenza vaccination is strongly recommended.^{5,6} Italy also recommends the active offer of influenza vaccine to HCWs every year during the influenza season (from October to December), with the vaccination strategy managed by the hospital director and occupational physician.

Despite these official recommendations, VC in Italy as reported in the literature, ranges from 10% to 35% far below the optimum level.^{6–8} The causes of poor vaccine compliance by HCWs have been investigated in many studies, which identified vaccine hesitancy as associated with a lack of or inadequate awareness campaigns, insufficient health education regarding vaccine effectiveness and adverse reactions, a perception of not being in a risk category, not having been previously vaccinated against influenza, lack of influenza experience, lack of access to vaccination facilities, and socio-demographic variables.^{9–14} However, one of the most important determinants of non-compliance by HCWs is not attending the vaccination clinic.^{9–14}

Among the policies recommended by international public health organizations to improve VC among HCWs is on-site influenza vaccination (as described by the CDC), a proven and cost-effective strategy that increases employee productivity, reduces overall absenteeism, and prevents direct healthcare costs.² This strategy requires that “vaccination staff” are directly present within the hospital’s operational units (OUs) according to a defined schedule, intending to cover as many departments as possible.²

At Bari Policlinico General University-Hospital (Apulia, South Italy, ~4,000,000 inhabitants), a plan to increase vaccine compliance in HCWs and ensure high influenza VC in the

nosocomial environment was put in place by the Hygiene and Occupational Medicine departments during the 2018/19 influenza season. Initially tested during the 2017/18 influenza season, the plan included on-site vaccination in some OUs. Thus, our study aims to investigate influenza VC among the HCWs of Bari Policlinico General University Hospital. Specifically, we compared the effect of the on-site strategy implemented by the Hygiene department during the 2018/19 influenza season with the results obtained during the previous influenza season and published in a previous report.¹⁵

Material and methods

The study design was cross-sectional and was carried out in two influenza campaigns.

The Bari Policlinico General University-Hospital is the largest hospital in southern Italy. It consists of 50 OUs and 1,000 beds and a healthcare staff of 3,397 people, including 1,423 (41.9%) in the service area, 1,005 (29.6%) in the surgical area, and 969 (28.5%) in the medical area.¹⁶

During the 2017/18 season, the Hygiene Department, in collaboration with the Occupational Medicine Department, tested an on-site vaccination strategy in eight OUs (Cardiology, Hematology, Physical Medicine and Rehabilitation, Infectious Diseases, Internal Medicine, Neonatology, Pediatric Oncohematology, Medical Oncology) with patients at high risk of complications related to influenza. Furthermore, from October to December 2017, an ad hoc clinic was set up in the Hygiene Department. The clinic was open for ten hours daily, from Monday to Friday, and could be visited without an appointment. Thus, a two-pronged strategy was designed, with vaccination offered on site (directly in the department) and in the vaccination clinic.

During the 2018/19 influenza season, this strategy was replicated but the on-site strategy targeted 44 of the 50 (88.0%) OUs, for a total of 3,044 HCWs; the six OUs excluded from the on-site strategy were those with an absence of beds and assistance activities (Hygiene, Occupational Medicine, Forensic Medicine, Pathology, Pathological Anatomy).

For both influenza seasons, the head of each OU received specific instructions explaining the vaccination strategy, which was also communicated on the hospital's website and intranet system. Shortly before the vaccination campaign, specific posters were placed in the OUs to announce the vaccination schedule. The on-site clinic in each OU was staffed by Public Health physicians, experts in vaccinology, and residents from the Graduate School of Public Health.

For the 2018/19 influenza season, the following variables were recorded for each vaccinated HCW, using a specific form:

- Surname and name
- Age
- Sex
- Professional category (physician, nurse, other)
- OU
- Specialty (Surgical/Medical/Services)
- Site of vaccination (on-site/Hygiene department)

Informed consent was also obtained at the time of vaccination. Data and informed consent were collected by Public Health physicians. During the 2018/19 influenza season, vaccinated HCWs received a dose of cell-based quadrivalent vaccine (Flucelvax),¹⁷ administered intramuscularly in the deltoid. These vaccinated individuals were followed-up for two weeks in order to detect any adverse effects; anyone suffering an adverse reaction was instructed to notify the Hygiene Department. Adverse reactions reported by HCWs were documented by the Pharmacovigilance Service of the Policlinico Bari General Hospital and entered into the database of the Hygiene department.

The VC in each OU was calculated using the official list of HCWs provided by the hospital director; this list includes the HCW's name, surname, professional category, and OU.

The data were stored according to privacy law. Compiled forms were put in a database created with an Excel spreadsheet and the data were analyzed using STATA MP16 software. Continuous variables were expressed as the mean±standard deviation and range, and categorical variables as proportions. VC (%) was calculated based on the proportion of HCWs vaccinated from the total number of HCWs of Bari Policlinico (in each OU).

The analysis was based on comparing of the overall results of the 2018/19 season with those of the 2017/18 season, already published.¹⁵ The focus was a determination of the results of the on-site strategy for the 2018/19 season. Student's t test was used to compare continuous variables between influenza seasons and the chi-squared test to compare proportions. To assess the determinants of performed influenza vaccination (YES/NO), a multivariate logistic regression model was built, considering vaccination as the outcome and analyzing the determinants sex (male vs. female), age (years), working in an OU targeted by on-site vaccination (YES/NO), specialty, and job tasks. The adjusted odds ratio (aOR) and 95% confidence interval (CI) were calculated. The Hosmer-Lemeshow test was used to evaluate the goodness-of-fit of the multivariate logistic regression model. For all tests, a *p*-value < .05 was considered to indicate statistical significance.

The research conducted for this study was carried out in accordance with the Helsinki Declaration. The ethics committee approved the protocol of Apulian Regional Observatory for Epidemiology.

Results

During the 2018/19 influenza season, 798 HCWs received the influenza vaccination (VC: 20.4%), compared to 482 HCWs (VC: 14.2%) during the 2017/18 season. Among the former, 284 (36.5%) were vaccinated on site.

Figure 1 shows the VC per hospital area (medical, surgical, services). In the surgery and service specialties, VC during the 2018/19 influenza season was twice that of the 2017/18 season, whereas VC in the medical area was nearly the same.

The characteristics (sex, age, professional category, chronic diseases) of the vaccinated HCWs during the two seasons are described in Table 1.

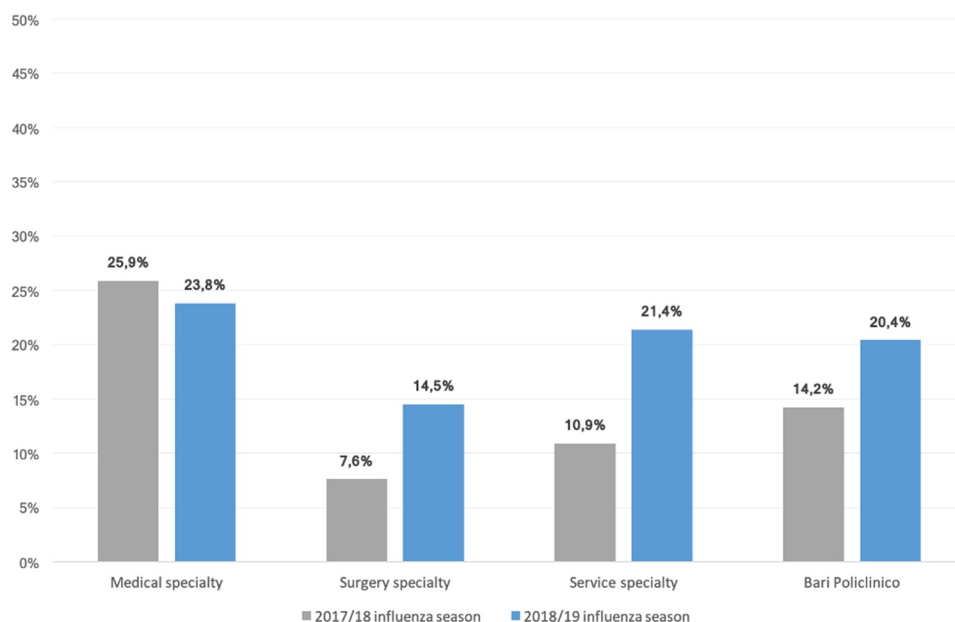


Figure 1. Vaccination coverage (%) of Bari Policlinico healthcare workers (HCWs), per hospital area (medical, surgical, services) for the influenza seasons of 2017/18 and 2018/19.

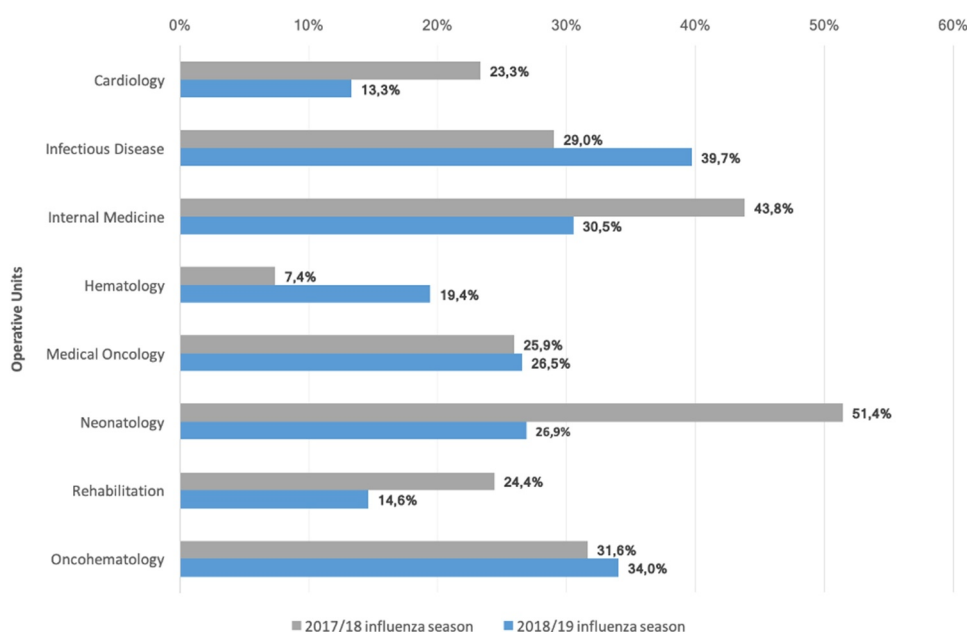


Figure 2. Vaccination coverage (%) in the OUs offering on-site vaccination during both the 2017/2018 and the 2018/19 influenza seasons.

During the 2018/19 influenza season, the lowest VC was among nurses (7.2%), with better coverage in auxiliary staff (8.6%) and other HCWs (23.8%). Physicians had the highest VC (33.4%).

The absence of any serious and/or long-term adverse reactions during the two weeks of follow-up demonstrated the vaccine's safety. The most commonly reported reactions were pain at the injection site and, rarely (<1/100), mild fever (<38°C). All adverse events were resolved without sequelae.

An analysis of on-site vaccination in the OUs during 2017/18 and 2018/19 revealed significant variations in VC (Figure 2).

The multivariate logistic regression model described an association between vaccination (YES/NO) and male sex (aOR = 1.4; 95%CI = 1.2–1.6), employment in the Medical vs.

Surgery area (aOR = 0.6; 95%CI = 0.5–0.7), being a physician (nurse vs. physician: aOR = 0.2; 95%CI = 0.1–0.2; auxiliary staff vs. physician; aOR = 0.2; 95%CI = 0.1–0.2), and working in an OU targeted by the on-site strategy (aOR = 1.4; 95%CI = 1.1–1.8). None of the other determinants were significantly associated with the outcome ($p > .05$; Table 2).

Discussion

Previous studies have shown an increase in VC over time. This is the case at our hospital, where VC increased from 9% during the 2016/17 influenza season (offered only in the vaccination clinic) to 20% during the 2018/19 influenza season. The introduction of on-site strategy doubling the VC for the 2017/18 vs.

Table 1. Characteristics of the vaccinated healthcare workers (HCWs) per influenza season (2017/18 and 2018/19).

HCW characteristics	2017/18 season (n = 482)	2018/19 season (n = 799)	p-value
Age; mean±SD (range)	45.5 ± 13.2 (25.0–70.0)	45.3 ± 11.9 (24.0–69.0)	.789
Female sex; n (%)	254 (50.8)	424 (53.1)	.612
Professional category; n (%)			.167
• Physician	295 (61.3)	563 (70.6)	
• Nurse	48 (10.0)	99 (12.4)	
• Other	139 (28.7)	136 (17.0)	
At least one chronic disease*; n (%)			1.000
• Allergy	237 (49.2)	385 (48.3)	
• Cardiopathy	102 (21.2)	179 (22.4)	
• Endocrinopathy	60 (12.4)	95 (11.9)	
• Respiratory disease	59 (11.8)	89 (11.2)	
• Gastrointestinal disease	14 (2.9)	34 (4.3)	
• Tumor	14 (2.9)	19 (2.4)	
• Nephropathy	7 (1.5)	10 (1.3)	
• Other	2 (0.4)	6 (0.7)	
	26 (5.4)	38 (4.7)	

*Many HCWs had multiple diseases.

Table 2. Analysis of the determinants of immunization (YES/NO) in a multivariate logistic regression model.

Determinant	aOR	95%CI	p-Value
Sex (male vs. female)	1.36	1.15–1.61	.000
Age (years)	1.00	0.99–1.01	.424
Area			
• Surgery vs. medical	0.57	0.46–0.71	.000
• Service vs. medical	0.88	0.69–1.14	.345
Profession			
• Nurse vs. physician	0.17	0.13–0.21	.000
• Auxiliary staff vs. physician	0.20	0.14–0.29	.000
• Other vs. physician	0.78	0.58–1.03	0.084
OU targeted by the on-site strategy (YES/NO)	1.39	1.05–1.84	.021

Goodness-of-fit chi-squared = 858.8; p-value = .926

the 2016/17 season, with a further increase of around 44% in 2018/19 vs. 2017/18 season. Nonetheless, despite the efforts made to implement the two-pronged vaccination strategy, in terms of technical requirements and number of personnel, VC continues to be unsatisfactory and far from the minimum target set by national and regional Public Health institutions.

Clinical departments achieved the highest VCs, without substantial differences between the two seasons. However, compared to the 2017/18 season, VC in the surgery and service areas doubled in the 2018/19 season. All OUs in these areas had been included in the on-site strategy of 2017/18. Consistent with our previous experience and literature reports, physicians were the most compliant with vaccinations, although coverage in this group was also not satisfactory (33%).

Comparing of the OUs targeted by the on-site strategy in both 2017/18 and 2018/19 shows the conflicting results obtained in the same OU. Specifically, in two OUs (Medical Oncology and Oncohematology) the VC achieved during the two seasons was similar, in four (Cardiology, Internal Medicine, Neonatology and Physical Medicine and Rehabilitation) it was worse in 2018/19 than in 2017/18, and in two OUs (Infectious Disease and Hematology) coverage was better in 2018/19 than during 2017/18. While the set-up of our study does not allow for definitive explanations of these discordant values, we can offer several hypotheses.

First, during the 2018/19 season, to increase the number of targeted OUs, the period during which on-site vaccination was possible in each unit was shorter than during the 2017/18 season, due to limited staff availability. On-site vaccination available for only a few hours on a single day could not reach those HCWs, who may, for example, have been engaged in different procedures and were later also unable to be vaccinated in the clinic. An important lesson that emerged from our experience was that increasing VC among HCWs requires many hours of work by highly qualified physicians who are experts in vaccinology. Additional efforts would be challenging as it could increase the number of the staff, vaccinology specialists are in short supply.

A second possible explanation is the end of the “novelty effect” of the on-site strategy, resulting in a lower willingness of OU chiefs to encourage participation by their personnel. Third, the HCW may have been vaccinated in another setting, such as the practice of his or her general practitioner (GP), but information on this eventuality was not collected. Conversely, in those OUs where an increase in VC was achieved, the positive feedback created by the experience of the 2017/18 season may have led to greater compliance during the 2018/19 vaccine offering.

The logistic regression model showed an association between vaccination and working in an OU targeted by the on-site strategy, which suggests that an on-site vaccination clinic is an effective strategy to increase the compliance of HCWs in OUs. A study performed in 2020 study showed that healthcare personnel’ compliance increases when a vaccine is actively offered through “mobile stations.”¹⁸ The regression model also indicated greater compliance by males, physicians, and HCWs working in OUs in the medical area. However, in contrast to reports in the literature there was no association between age and vaccination, although it must also be noted that half of the vaccinated physicians were medical residents, and therefore young, which may have been a source of confounding bias. Our findings are supported by several studies.^{9–14,19} For example, Barbadoro et al. investigated the role of sex in VC and found a lower rate of VC in female HCWs (OR = 0.73 95%CI = 0.61–0.86).²⁰ In a retrospective study published in 2020, Antinolfi et al.²¹ identified male sex, working within the medical care area, and being a physician as the factors predicting influenza vaccine uptake among HCWs.

An important strength of our study was the large target population (~4,000 HCWs), the on-site strategy, which has not been well-evaluated in the literature, the comparison of two influenza seasons, and the topicality of vaccination in HCWs concerning to strategic decision-making by Public Health authorities. In addition, this study included a regression analysis, which could not be performed in our previous one. Nonetheless, a major limitation was our inability to determine and thus further analyze the reasons for vaccine refusal, including whether HCWs not immunized in the hospital had been vaccinated by their GP or had purchased the vaccine from the pharmacy. This lack of information was pertinent to both influenza seasons.

To the best of our knowledge, few studies have investigated the effects of on-site vaccination on VC in HCWs. Our data are consistent with those of a 2018 Italian study²² conducted at the “Bambino Gesù” Rome Pediatric Hospital, which showed that

an on-site vaccination strategy significantly increased VC among HCWs during two consecutive influenza seasons. The strategies at Turin “Molinetto” Hospital²³ to increase the vaccination of HCWs during the 2018/19 influenza season included informational material, direct educational sessions for HCWs, an extended access time to the Occupational Medicine vaccination clinic, elimination of the appointment requirement, the use of “mobile vaccination units” (MVUs), and the organization of vaccination sessions within departments. At the end of the season, 593 doses were administered (+46% compared to the previous season), 7% of which were administered at MVUs. The authors attributed most of the vaccination increase to the reorganization of the Occupational Medicine Clinic. At the same time the MVUs were useful to HCWs who were not confined to a detached office. An on-site campaign targeting HCWs at a Turkish tertiary children’s hospital during the 2017/18 influenza season showed significantly improved VC among health-care personnel.²⁴ In A survey conducted among 2265 HCWs in the USA during the 2017/18 influenza season, 78.4% reported having been vaccinated against influenza. VC was highest among HCWs in whom vaccination was required by their employer (94.8%) and lowest among those working in settings where vaccination was not required, promoted, or offered on-site (47.6%).²

In this study, despite the two-pronged strategy, 80% of the HCWs of the Policlinico University Hospital opted not to be vaccinated against the flu. These data are in line with those of the cited studies and further demonstrate the difficulties in vaccinating HCWs appropriately. Although the safety of vaccinations is well established^{25,26} and many different vaccination campaign approaches have been implemented, including cooperation between Public Health and Occupational Medicine physicians, specific regulations by Public Health institutions may ultimately be necessary to increase vaccination compliance and to reduce the susceptibility of patients and staff in the hospital and other care settings.^{27–30} In fact, in June 2020, the Apulian Regional Authority approved a Regional Law³¹ (contested in 2018 and blocked by the Italian Government) that makes hepatitis B, measles, mumps, rubella, varicella, diphtheria, tetanus, pertussis, and influenza vaccinations mandatory for HCWs. In the absence of demonstrated natural immunity, the failure of a HCW to agree to these vaccinations can result in his or her being considered unqualified for the job. Apulia is the second Italian region, after Emilia Romagna, to promote this particular strategy.

The 2020/21 influenza season will occur against the continuing SARS-COV-2 pandemic background, which can be expected to have major repercussions on flu VC among HCWs (and the general population). The CDC has warned that vaccination against the flu, while reducing the risk of flu illness and related hospitalization and death, will not protect against COVID-19. Nonetheless, vaccination against the flu during the pandemic is critical to reduce the risk of influenza and lessen the overall impact of respiratory illnesses within the population and therefore the burden on the healthcare system posed by COVID-19.³² While it has been hypothesized that influenza (and anti-pneumococcal) vaccines contribute to direct and indirect protection against Sars-CoV-2,^{33,34} this remains controversial and must be further studied.

During the writing of this manuscript, the 2020/21 influenza vaccination program was activated. The preliminary results suggest a significant increase in vaccination compliance among HCWs, but whether this is due to the pandemic or to mandatory vaccination is thus far unclear. The data will be analyzed in a future publication comparing the 2019/20 and 2020/21 influenza vaccination seasons.

In conclusion, although the on-site strategy seems to improve VC, it is insufficient to achieve immunization targets, even when implemented in synergy with other strategies due to the COVID-19 pandemic, 2020/21 flu season will differ from previous ones. Whether it results in better VC and the better compliance of HCWs than in earlier seasons remains to be determined. The 2020/21 data are also expected to provide insights into the cost-benefits of a massive vaccination campaign with high participation by both the general population and HCWs.

Abbreviations

CDC	Center for Disease Control and Prevention
HCWs	Healthcare workers
OU	Operative unit
VC	Vaccine coverage

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