

## HEALTHCARE STUDENTS AND INFLUENZA VACCINATION: A MULTI-CENTER CROSS-SECTIONAL STUDY

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### ARTICLE INFO

#### Article history:

Received 07 January 2020

Revised 03 February 2020

Accepted 29 February 2020

#### Keywords:

seasonal influenza, influenza vaccination, university students, survey, cross-sectional study, healthcare students.

### ABSTRACT

Vaccination coverage rates in healthcare workers in Italy are among the lowest in Europe, and only 10-15% of hospital staff members are immunized against seasonal influenza. The goal of this study was to analyze the attitude and awareness factors of influenza vaccination compliance among Italian future healthcare professionals.

A multi-center cross-sectional study was performed using an online, self-reported and anonymous questionnaire, given to students attending different Healthcare degree programs in 14 Italian Universities. A total of 3,123 questionnaires were collected. More than 90% of students >23 years old were not vaccinated against seasonal influenza during the past years. Students vaccinated over the previous seasons, those that were usually recommended influenza vaccination based on their clinical evaluation or in accordance with the ministerial guidelines, and those that were recommended vaccination by other healthcare workers in the past years, demonstrated a greater acceptance of influenza vaccination. Campaigns promoting influenza vaccination among healthcare workers should consider students attending healthcare courses as a priority group, not only for their training activities in healthcare facilities, but also for their future and potential active role in the healthcare system.

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### 1. Introduction

Vaccinations are recognized as a safe and effective resource to reduce the burden of infectious diseases as well as their morbidity, mortality and healthcare costs (1).

However, vaccine hesitancy and refusal have become an emerging public health problem, as many European countries are facing increasing difficulties in achieving and maintaining the target vaccination rates (2). In Italy, in order to maintain optimal vaccine coverage rates that are needed to ensure vaccination effectiveness, formal recommendations are published by the Ministry of Health through the National Immunization Prevention Plan (NIPP) 2017-2019 (3).

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DOI: 10.3269/1970-5492.2020.15.6

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The NIPP is a document on immunization policies that lists all vaccines offered free of charge to the general population, to high-risk individuals and to certain professional groups (3 - 5).

Among the various professional groups, healthcare workers (HCWs) play a crucial role as they are at a high risk of contracting infectious diseases. Particular attention should therefore be directed towards HCWs in the recommendations by the Ministry of Health regarding vaccination status (6).

Despite this, vaccination coverage rates of Italian HCWs are among the lowest in Europe, fluctuating between 10% and 40%, remaining below the 75% threshold recommended by international Healthcare Authorities (7-9). The perception of risks related to the influenza virus and to its vaccination among Italian healthcare professionals was previously investigated among pharmacists, general practitioners and other healthcare professionals (10-13). Moreover, healthcare facilities, particularly when affiliated with a University, are also populated by students of healthcare courses, which include medical students, nursing students, medical residents (14).

Students of healthcare professions play a crucial role in transmitting diseases to patients and, if adequately trained, could improve their awareness and education on vaccination topics (15, 16).

The goal of this study was to analyze the factors that led university students of healthcare professions to join last year's influenza vaccination campaign, as well as their attitudes and awareness of this vaccine.

## 2. Material and methods

This multi-center cross-sectional study was developed by the Committee of Medical Residents of the Italian Society of Hygiene and Preventive Medicine. The validated questionnaire, available in the literature, included 20 multiple-choice questions with only one possible answer, was self-reported by all participants with the goal of assessing the knowledge and opinions of Medical residents (17).

The students included in this study were enrolled regardless of their age and year of study. Recruitment was voluntary-based and informed consent was obtained electronically from all participants. The questionnaire was given online, self-reported and anonymous. The collected data was stored in a computerized database. All members of the research group, if willing and available to participate to the study, were responsible for recruiting students at their own universities. The study was presented to students during the hygiene and preventive medicine lectures.

The reasoning of the study and procedure to participate were explained to the students, who were then provided with a Quick Response (QR) code, which redirected them to the online questionnaire.

To calculate the reference population, the number of students admitted to each degree course in the previous academic year was multiplied by the total duration of that course (for practical reasons, the assumption was that the number of students enrolled every year was constant). The total number of students investigated and attending courses was 49,643. The sample size was then calculated using the EpiInfo software, considering a 95% confidence level and a 5% margin of error. The expected proportion of vaccine-hesitant individuals was unknown, but being the goal of the study itself, we set a conservative expected rate at 50% (in order to maximize the required sample size). These calculations led to a sample size of 382 students, but in order to be more conservative, this number was doubled to 764.

Questionnaires were submitted between October 2017 and September 2018 at 14 Italian Universities: Bari, Messina, Naples Vanvitelli, Palermo, Salerno, Ancona, L'Aquila, Perugia, Rome Tor Vergata, Siena, Parma, Pavia, Turin and Udine. Based on the geographical area of the University, the answers were categorized into: "Southern Italy and Islands" (Bari, Messina, Naples, Palermo and Salerno), "Central Italy" (Ancona, L'Aquila, Perugia, Rome and Siena) and "Northern Italy" (Parma, Pavia, Turin and Udine).

The "age" range variable was subsequently set between  $\leq 23$  years and  $> 23$  years, while the "answers" variable of healthcare courses were divided into three categories: Medicine, Nursing and Other (Physiotherapy, health assistant, dietician, dental hygiene, speech therapy, biomedical laboratory technician, neurophysiopathology technician, orthoptics, audiometry, obstetrics, podiatry).

Both absolute and relative frequencies were calculated for all qualitative variables; Pearson's Chi-square test ( $\chi^2$ ) was used to analyze the categorical variables. A multivariate logistic regression model was used. "Seasonal Influenza vaccination during previous season" was selected as the dependent variable. Each independent variable in the model was adjusted for all the other independent variables. Results were expressed as adjusted Odds Ratio (aOR) with 95% Confidence Intervals (95%CI). The level of significance for statistical analysis was set at  $p=0.05$ . The data was analyzed using the statistical software STATA® version 14.

The study was approved by the Bioethics Committee of the University of Perugia, Reference Number 2017-20R. All other local Ethics Committees were notified before beginning the study.

## 3. Results

The sample included 3131 students of Healthcare Professions with an average age of 23.41 years (standard deviation 3.69). 1219 subjects of the student sample were enrolled in medical school (59.89% male), 1035 in nursing (74.98% male) and the remaining 877 in other healthcare professions (71.38% male). The other descriptive characteristics of the sample were reported in Table 1.

n=3,131			
Mean Age and Standard Deviation	23.41 ± 3.69		
		n (%)	
Gender	Female	2132	68.09
	Male	999	31.91
Age	>23 years old	1251	39.96
	≤23 years old	1880	60.04
Healthcare Course	Medicine	1219	38.93
	Nursing	1035	33.06
	Other	877	28.01
University Geographic area	South and Sicily	1044	33.34
	Center	831	26.54
	North	1256	40.11
Self-reported level of knowledge regarding VPDs and related vaccinations	Good / excellent	1349	43.09
	Insufficient/sufficient/fair	1782	56.91
Influenza like illness acquired during previous 5 years	Never	1660	55.41
	At least once	1336	44.59
Self-perceived high risk of contracting VPDs	No	839	26.80
	I don't know	344	10.99
	Yes	1948	62.22
Influenza vaccination during previous season	No	2782	88.85
	Yes	349	11.15
Willingness to accept influenza vaccination during next season	No	2038	65.09
	Yes	1093	34.91
Attitude to recommend influenza vaccination to patients or to family members/general population during previous influenza season	No	1392	44.46
	Yes, based on my clinical evaluation	483	15.43
	Yes, according to the ministerial indications	1256	40.11
Attitude to recommend influenza vaccination to health-care workers during previous influenza season	No	2746	87.70
	Yes	385	12.30
Collaboration in the influenza vaccination campaign for HCWs	Yes	78	2.49
	No	3053	97.51
Previously received request for clarification on influenza vaccination	Yes	1686	53.85
	No	1445	46.15
Opinion on mandatory vaccination for HCWs	Contrary	157	5.01
	Indifferent	240	7.67
	Favorable	2734	87.32

**Table 1. Descriptive analysis of healthcare students enrolled in the study.**

The results of the bivariate analysis were reported in Table 2. With regards to the question “Did you get vaccinated against seasonal influenza last year?” 90.9% of the subjects >23 years old were not vaccinated, compared to 85.7% of those ≤23 years old ( $p < 0.001$ ). Greater vaccination adherence rates were observed among students attending Medical school courses, compared to students attending Nursing or other degree courses (15.0% vs 9.4% vs 7.9%;  $p < 0.001$ ). Students from Southern Italy reported higher vaccination adherence than students from northern and central Italy (13.9% vs 10.4% vs 9.2%;  $p = 0.03$ ).

Good or excellent awareness about VPDs were associated with higher seasonal influenza vaccination coverages (15.3% vs 8.0%;  $p < 0.001$ ). A higher willingness to accept influenza vaccination for the following season was observed among students who were not vaccinated (69.2%) compared to students who were vaccinated (30.8) ( $p < 0.001$ ). Students that recommended influenza vaccination to patients, family members or the general population reported higher vaccination adherence (34.6%) than students that didn't recommend influenza vaccination. In our sample, 23.1% of the students that participated or collaborated in the organization of the vaccination campaign for HCWs during their internship were vaccinated against seasonal flu, compared to 10.8% that did not collaborate in the organization of the vaccination campaigns ( $p < 0.001$ ). Additionally, 12.4% of the sample that was favorable to the possible introduction of the mandatory vaccination for HCWs was vaccinated, compared to 4.8% of those that weren't favorable.

Variables		Influenza vaccination during last season		
		No n (%)	Yes n (%)	p-value
Gender	Female	1908 (89.5)	224 (10.5)	0.096
	Male	874 (87.5)	125 (12.5)	
Age	≤23 years old	1072 (85.7)	179 (14.3)	<0.001
	>23 years old	1710 (90.9)	170 (9.1)	
Healthcare Course	Medicine	1036 (85.0)	183 (15.0)	<0.001
	Nursing	938 (90.6)	97 (9.4)	
	Other	808 (92.1)	69 (7.9)	
University Geographic area	South and Sicily	849 (86.1)	137 (13.9)	0.003
	Centre	807 (90.8)	82 (9.2)	
	North	1126 (89.6)	130 (10.4)	
Self-reported level of knowledge regarding VPDs and related vaccinations	Good / excellent	1143 (84.7)	206 (15.3)	<0.001
	Insufficient/sufficient/fair	1639 (92.0)	143 (8.0)	
Influenza like illness acquired during previous 5 years	Never	1483 (89.3)	177 (10.7)	0.187
	At least once	1173 (87.8)	163 (12.2)	
Self-perceived high risk of contracting VPDs	No	775 (92.4)	64 (7.6)	<0.001
	I don't know	321 (93.3)	23 (6.7)	
	Yes	1686 (86.5)	262 (13.5)	
Willingness to accept influenza vaccination during next season	No	2026 (99.4)	12 (0.6)	<0.001
	Yes	756 (69.2)	337 (30.8)	
Attitude to recommend influenza vaccination to patients or to family members/general population during previous influenza season	No	1335 (95.9)	57 (4.1)	<0.001
	Yes, based on my clinical evaluation	394 (81.6)	89 (18.4)	
	Yes, according to ministerial guidelines	1053 (83.8)	203 (16.2)	
Attitude to recommend influenza vaccination to health-care workers during previous influenza season	No	2537 (92.4)	209 (7.6)	<0.001
	Yes	245 (63.6)	140 (36.4)	
Collaboration in the influenza vaccination campaign for HCWs	Yes	60 (76.9)	18 (23.1)	0.001
	No	2772 (89.2)	331 (10.8)	
Previously received request for clarification on influenza vaccination	Yes	1444 (85.6)	242 (14.4)	<0.001
	No	1338 (92.6)	107 (7.4)	
Opinion on mandatory vaccination for HCWs	Contrary	154 (98.1)	3 (1.9)	<0.001
	Indifferent	233 (97.1)	7 (2.9)	
	Favorable	2395 (87.6)	339 (12.4)	

**Table 2. Univariate analysis of variables associated with influenza vaccination adherence among healthcare students enrolled.**

Finally, table 3 shows the results of the multivariate logistic regression model.

With regards to the dependent variable of seasonal influenza vaccination acceptance during previous season, a significant higher vaccination adherence was observed with willingness to accept influenza vaccination during next influenza season (AdjOR 66.4; 95% CI = 36.1-122.2), attitude to recommend influenza vaccination to patients or to family members/general population according to clinical evaluation (AdjOR 2.8; 95% CI = 1.7-4.7), attitude to recommend influenza vaccination to patients or to family members/general population according to guidelines of the Ministry of Health (AdjOR 2.2; 95% CI = 1.4-3.4), attitude to recommend influenza vaccination to other HCWs (AdjOR 4.1; 95% CI = 2.9-0.9).

Independent variable	Influenza vaccination adherence during last season			
	aOR	95% CI	p-value	
Gender	Female	Ref		
	Male	1.01	0.75-1.36	0.959
Age	≤23 years old	1.01	0.74-1.38	0.945
	>23 years old	Ref		
Healthcare Course	Medicine	Ref		
	Nursing	0.73	0.51-1.03	0.074
	Other	0.94	0.64-1.39	0.751
University Geographic area	South and Sicily	Ref		
	Centre	0.97	0.67-1.40	0.868
	North	0.79	0.56-1.10	0.155
Self-reported level of knowledge regarding VPDs and related vaccinations	Good / excellent	Ref		
	Insufficient/sufficient/fair	0.79	0.59-1.05	0.106
Influenza-like illness acquired during previous 5 years	Never	Ref		
	At least once	1.08	0.82-1.43	0.566
Self-perceived high risk of contracting VPDs	No	Ref		
	I don't know	0.96	0.53-1.72	0.886
	Yes	1.18	0.82-1.69	0.359
Willingness to accept influenza vaccination during next season	No	Ref		
	Yes	66.4	36.13-122.19	<0.001
Attitude to recommend influenza vaccination to patients or to family members/general population during previous influenza season	No	Ref		
	Yes, based on my clinical evaluation	2.80	1.66-4.72	<0.001
	Yes, according to ministerial indications	2.20	1.41-3.43	<0.001
Attitude to recommend influenza vaccination to health-care workers during previous influenza season	No	Ref		
	Yes	4.13	2.95-5.78	<0.001
Collaboration in influenza vaccination campaign for HCWs	Yes	Ref		
	No	1.14	0.55-2.35	0.716
Previously received request for clarification on influenza vaccine	Yes	Ref		
	No	1.09	0.79-1.49	0.605
Opinion on mandatory vaccination for HCWs	Contrary	Ref		
	Indifferent	2.00	0.37-10.77	0.418
	Favorable	1.71	0.42-7.08	0.457

**Table 3. Multivariate logistic regression analysis of variables associated with influenza vaccination adherence among healthcare students enrolled. (AdjOR and CI 95% are listed; each variable was adjusted for other independent variables)**

## 4. Discussion

According to the European Centre for Disease Control and Prevention, each year in Europe 15,000-70,000 deaths are attributed to influenza, and 90% of them occur in elderly subjects with underlying chronic clinical conditions (18).

Since 2000, an influenza surveillance system (InfluNet) coordinated by the National Institute of Health and the Ministry of Health, has been established in Italy as well (19).

In addition, the Ministry of Health developed a community-based hands-on surveillance system (InfluWeb) and a report combining information from different sources (Flunews). These systems describe the characteristics of the seasonal epidemic, and they have shown that in Italy the incidence of influenza is 1 case in 1000 subjects, with 80% of unvaccinated cases (20).

Given the results, significant efforts are needed to increase influenza vaccination coverage. New evidence is showing the potential impact of big data and the use of immunization information systems as valuable tools to collect data regarding vaccination coverage rate, people's reactions to outbreaks, and to improve awareness of ones' own vaccination status (21-26). Although influenza vaccination remains the most efficient tool in preventing influenza infections, and even if its strongly recommended to HCWs, there is still a general lack of awareness regarding the importance of flu vaccination, as well as its role in reducing the burden of influenza (14, 17, 27). However, despite the efforts to increase flu vaccination coverage, influenza vaccination coverage in Italy is still extremely low (28).

The objective of this study was to analyze the factors of influenza vaccination compliance among a large sample of Italian Healthcare university students and their attitude regarding influenza vaccination. Our results proved that only 11.15% of the 3,131 students were vaccinated against seasonal influenza during the previous season. This finding is lower than many of the previous studies focusing on Italian medical and nursing students, which reported higher coverage rates: 35.4% among students of Modena and Reggio Emilia University, 20.9% of students attending the Bari School of Medicine and 12.5% of students from the Florence University (29-31).

Moreover, in our study flu vaccination rates resulted lower than those observed among healthcare students in other countries such as USA (43%) or Australia (53.8%) (32, 33). On the other hand, it is notable that only 34.9% of the sample is planning on being vaccinated during the next flu season, and students who did not received the vaccine this year are significantly more likely to get vaccinated next year (69.2% vs 30.8%).

The data, although not verifiable, strongly suggests the importance of an appropriate training during academic courses focused on vaccinations, also as an occasion to administer influenza vaccines or to increase the students' knowledge and awareness (13, 16).

The results of our multivariate regression model confirmed the association between having received the influenza vaccination during previous season and having the intention to get vaccinated during the next flu season (17, 27).

In addition, being vaccinated against the flu is significantly associated with having recommended the vaccination during the last flu season, not only to patients and family members, but also to other HCWs.

This finding seems to confirm that healthcare trainees or students who were vaccinated against influenza at least once in the previous five seasons are significantly more inclined to get vaccinated and to recommend influenza vaccination (34, 35).

A European study reported that lack of knowledge and risk perception about influenza vaccination during early years of medical studies was associated with lower vaccination rates (36).

Similarly, in our survey 56.9% of students reported little knowledge on VPDs and almost all have never participated in the organization of vaccination campaigns for healthcare professionals during their internships.

Although 62.2% of students belong to a high-risk professional group, only 12.3% recommended influenza vaccination to other HCWs.

In general, students that received information about vaccinations recommended it to patients or family members during the previous (54%) or next (70%) influenza seasons.

Finally, 87.3% were favorable to mandatory vaccinations for healthcare professionals.

The study has some limitations: the information was self-reported and recall bias cannot be excluded. Lastly, the questionnaire was based on multiple-choice items that probably limited the understanding of such a complex phenomenon but facilitated the analysis.

## 5. Conclusions

In conclusion, an active collaboration between academic and public health institutions could contribute to an increase of knowledge and awareness on influenza vaccination among healthcare students.

Nevertheless, knowledge and attitude regarding influenza vaccinations should be consolidated and implemented during study courses. Also, the introduction of mandatory vaccination for HCWs and healthcare students attending clinical wards should be considered in future (37, 38)

Lastly, influenza vaccination campaigns should focus on healthcare students as a priority group, for their future potential active role as public health opinion leaders, in order to promote vaccination adherence and awareness among the general population and other HCWs.

## Acknowledgements

The Authors would like to thank the members of the working group who actively contributed to the project: Enrico Alagna, University of Palermo; Claudia Alessandrini, University of Rome "Tor Vergata"; Paola Cella, University of Parma; Bruno Cosenza, University of Messina; Alessandro Cuda, University of Pavia; Angelo D'Ambrosio, University of Torino; Matteo D'Angelo, University of Udine; Sara De Nitto, University of Bari; Francesca di Gaspare, University of Rome "Tor Vergata"; Giuseppe Ferrucci, University of Salerno; Leandro Gentile, University of Pavia; Francesco Mazzù, University of Messina; Pasquale Stefanizzi, University of Bari; Marina Di Vincenzo, University of Marche; Lucia Kundisova, University of Siena; Gianluca Voglino, University of Torino. Furthermore, the Authors would like to thank all the students who voluntarily participated to the study.

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