Factors predicting health science students' willingness to be vaccinated against seasonal flu during the next campaign

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Abstract

Introduction. Influenza is an infectious disease with a high burden, for which a safe and efficacy vaccine is available. However, vaccination coverage is generally low, also among Health Care Workers (HCW). Health Professions students are comparable to HCW in terms of workplace exposure.
Aim. The study aim was to identify predictive factors of flu vaccination acceptance among Italian students of Health Professions.
Methods. A cross-sectional study was performed using a validated, on-line, anonymous questionnaire. Data were analyzed performing both univariable and multivariable logistic analysis.
Results. The results showed a statistically significant association between intention to vaccinate next year and: geographical distribution, considering themselves at higher risk due to their profession, having been vaccinated last year, having recommended the vaccination last year, and being willing to recommend it next year and being favorable to mandatory vaccination. In conclusion, identifying an effective vaccination strategy and including students in flu vaccination campaigns might have positive effect on vaccination acceptance.

Key words
• influenza vaccines
• health science students
• mandatory vaccination
• cross-sectional study

INTRODUCTION

Influenza is an infectious disease with a very high burden, both in young and adult people (81.8 DALYs per 100 000 population, according to The European Centre for Disease Control and Prevention, ECDC) [1]. In particular, data from the "Burden of Communicable Disease in Europe" project show, for influenza, a low individual but high population burden. The Center for Disease Control and Prevention (CDC) in Atlanta estimated that in the United States, during the 2017-2018 season, influenza affected about 48.8 million people, 22.7 million people requested health care assistance, 959 000 people were hospitalized and 79 400 died [2]. This complex disease management is clearly associated with high costs for the health system, and for people themselves. In Australia, estimated costs related to health care were around $ 115 million in 2008. In Italy, according to the study conducted by Lai and collaborators, the total cost of the nine influenza seasons from 1999 to 2008 was around 15 billion euro. The seasonal average was over 1.3 billion euro [3].

Despite the availability of safe and effective vaccines to prevent seasonal influenza infection, a significant proportion of eligible population remains unvaccinated. In Italy, the flu vaccination is included in the National Immunization Plan (NIP) and is offered free of charge to certain groups of people that are at a higher risk either for age, professional exposure or for health conditions [4]. In particular, a Ministerial document was issued to identify all professionals who could be

exposed to biological agents or who could be a source of infection for others [5]. Obviously, Health Care Workers (HCWs) are included in this group of at-risk professionals. Starting from 2009, the World Health Organization's Strategic Advisory Group of Experts has identified HCWs as a priority target group for flu vaccination [6]. Indeed, HCWs are routinely exposed to infected patients during their worktime, and, at the same time, they might also be carriers of infection for other patients, co-workers, friends and relatives. There are several preventive measures that can be adopted to minimize spreading infections, such as washing hands and covering mouth and nose when coughing or sneezing, but vaccination remains the most effective measure both for self protection and to protect others. In particular, to significantly reduce morbidity, complications and mortality related to influenza, a high vaccination coverage must be achieved in target population groups: 75% of the target population is considered as the minimum rate, while 95% is the optimal rate of immunization. Nevertheless, flu vaccination coverage in Italy is around 15% among the general population, while in people older than 65 years it is 53% and among HCWs it is approximately 15% [7, 8].

A growing body of evidences had identified patients and health care workers' characteristics associated with flu vaccination refusal, and in this study we focused on university students of Health Professions. In fact, workplaces such as health care facilities, are populated not only by professionals but also by students who attend different wards as part of their clinical training.

The aim of this study was to identify predictive factors of flu vaccination acceptance among Italian students of Health Professions.

MATERIALS AND METHODS
Study design

The "Vaccine and vaccine hesitancy" working group of the Committee of Medical Residents of the Italian Society of Hygiene and Preventive Medicine promoted a multi-centre, cross-sectional study administering a validated questionnaire available in literature [9]. The target population consisted of university students of Health Professions degree courses, without any restrictions in terms of age or year of study. The administration took place in 14 Italian Universities, considering the origin of the working group members who voluntarily decided to participate. In each University a member of the research group was in charge of presenting the study and its aims, and of enrolling the students. The enrolment and explanation of the study took place during a lecture (from October 2017 to September 2018). After explaining the modality to participate, a Quick Response (QR) code, redirecting to the online questionnaire, was provided to the students.

All subjects were enrolled anonymously and on a voluntary basis; informed consent was obtained from all participants. The 21-items on-line questionnaire was created using Google forms ® and all data was deposited in an electronic database protected by password, known only to the data manager. Ethical approval was given by the local Ethical Committee of the University of Perugia (Comitato Universitario di Bioetica), Reference Number 2017-20R.

Sample size

The population of reference for our study consisted of Health Professions students enrolled in 14 Italian Universities. For practical reasons, we assumed the number of new students admitted every year in each Health Professions degree course to remain constant. To calculate the population of reference, the number of new students admitted in every degree programme during the last academic year was multiplied by the duration of that programme in years, and the resulting number of students was 49 643. We then proceeded to calculate the sample size, using the EpiInfo software with a confidence level of 95% and a margin of error of 5%. Not knowing the proportion of vaccine-hesitant students beforehand, since this was one of the aims of the study itself, the expected proportion was set at 50%. This allowed us not only to be more conservative, but also to maximise the required sample size. The resulting sample size consisted of 328 students, but we doubled it to be more conservative. Therefore, we set 764 questionnaires as the minimum number in order for the study to be valid and its results to be accepted.

Statistical analysis

The variable "age" was dichotomized in ≤23 years and >23 years and the answers of the Degree course variable were aggregated into three categories according to the students' field of study: Medicine, Nursing and Other (which includes all the other students of the health professions who completed the questionnaire). According to the geographical area of university, the answers were categorized into: "South and Islands" (Bari, Messina, Naples, Palermo or Salerno), "Centre" (Ancona, L'Aquila, Perugia, Rome or Siena) and "North" (Parma, Pavia, Turin or Udine). The answers to the question "Do you think your level of knowledge about vaccine-preventable diseases and related vaccinations is" were aggregated into two answers, "Good/excellent" and "Insufficient/sufficient/fair". The absolute and relative frequencies were calculated for all qualitative variables; Pearson's Chi-square test (χ^2) was used to analyze categorical variables. A multivariable logistic regression model was used. The dependent variable selected was "For the next season, do you think you are vaccinating against the flu? Yes". Each independent variable in the model is adjusted for all the other independent variables. Results are expressed as adjusted Odds Ratio (aOR) with 95% Confidence Intervals (95% CI). The level of significance chosen for statistical analysis was 0.05. The data was analyzed using statistical software STATA® version 14.

RESULTS

A total of 3137 questionnaires were collected; however, 6 questionnaires were excluded because incorrectly completed. The final sample therefore consisted of 3131 students of Health Professions with an average age of 23.41 years (standard deviation 3.69). 1219 of the student sample was enrolled in medical school

(59.89% male and 40.11% female), 1035 in nursing (74.98% male and 25.02% female) and the remaining 877 in other health professions (71.38% male and 28.62% female). *Table 1* shows the sample description.

Table 2 shows the results of the bivariate analysis; in this section only the statistically significant results are reported. Regarding the question "For the next season, are you planning on vaccinating against the flu?" 32.71% of those aged >23 said that they will get vaccinated against seasonal influenza, compared to 38.21% of those aged ≤23 years; higher percentages of positive answers were found among students enrolled in the Medicine degree course, compared to nursing students or to other degree courses (39.54% *vs* 36.23% *vs* 26.91%); higher percentages of positive answers were also found among students of northern Italian Universities, compared to students of central Italian Universities, southern Italian Universities and Sicily (39.01% *vs* 10.35% *vs* 35.80%). 40.85% of the sample that believes to have a good or excellent level of knowledge about vaccine-preventable diseases will get vaccinated against seasonal influenza next year, compared to 30.42% of the sample that believes to have a low level (insufficient/sufficient/fair) of knowledge about vaccine-preventable diseases. 32.35% of those who have never had a vaccine-preventable disease in the last 5 years, compared to 38.10% of those who had it "at least once" think that they will get vaccinated next year; 34.91% of those who considered themselves to have a higher risk of contracting infectious diseases, compared to 27.41% of those who did not believe it, reported that they will get vaccinated next year. For the question: "Did you get vaccinated against seasonal flu last year?" 96.56% of those who answered "yes" will get the vaccine against seasonal flu next year as well. 44.98% of the subjects that recommended, according to the ministerial indications, vaccination against seasonal flu to patients, family members or general population during the last flu season will also get vaccinated during the next flu season, as opposed to 23.35% of those who did not recommend the vaccination last year. In the same way, 47.94% of the people that, according to the ministerial indications, will recommend vaccina-

tion against seasonal flu to patients, family members or general population during the next season, will get vaccinated compared to 11.54% of those will be vaccinated but will not recommend the vaccination. 59.22% of those who recommended the vaccination to health workers during the last flu season, compared to 31.50% who did not recommend it, reported that they will get vaccinated next year. 47.44% of those who either participated or collaborated in the organization of vaccination campaigns for health professionals during their internships will get vaccinated against seasonal flu, compared to 34.59% of the sample that has neither participated nor collaborated in the organization of the campaigns. 39.44% of those who have received at least once any requests for clarification on vaccinations, compared to 29.62% of those who have never had any requests for clarification, reported that they will get vaccinated next year. 37.20% of those that are favorable to the possible introduction of mandatory vaccinations for school enrollment said that they will get vaccinated during the next flu season, compared to 11.20% of those that are either contrary or indifferent to this policy. 38.92% of those that are favorable to the possible introduction of mandatory vaccination for health workers said that they will get vaccinated, compared to 6.37% of those that are either contrary or indifferent to it.

Table 3 shows the adjusted odds ratios (aOR). A multivariable logistic regression model was used. The dependent variable used this model was the following "For the next season, are you planning on vaccinating against the flu? Yes". The statistically significant independent variables associated to this statement are: "Geographical area": "Central Italy" and "Northern Italy" (Central Italy aOR 0.62, North aOR 1.27), "Have you ever had a vaccine-preventable disease in the last 5 years? At least once" (aOR 2.46), "Given your future profession and your state of health, do you consider yourself a subject with a higher risk of contracting infectious diseases? Yes" (aOR 1.36), "Did you get vaccinated against seasonal flu last year? Yes" (aOR 69.69), "During the last flu season, did you recommend the vaccination to patients, family members or general pop-

Table 1
Description of the sample. Based on 3131 observations

Variables		Male N (%)	Female N (%)	Total N (%)
Degree Course	Medicine and Surgery	730 (59.89)	489 (40.11)	1219 (38.94)
	Nursing	776 (74.98)	259 (25.02)	1035 (33.05)
	Others*	626 (71.38)	251 (28.62)	877 (28.01)
Did you get vaccinated against seasonal flu last year?	Yes	1908 (68.58)	874 (31.42)	2782 (88.85)
	No	224 (64.18)	125 (35.82)	349 (11.15)
During the next season, do you plan on recommending the flu vaccination to patients, family members or general population?	Yes, according to Ministerial recommendation	1125 (70.14)	479 (29.86)	1604 (51.23)
	Yes, according to clinical evaluation	372 (64.81)	202 (35.19)	574 (18.34)
	No	635 (66.63)	318 (33.37)	953 (30.43)
Age (mean ± SE)		23.24 ± 0.08	23.77 ± 0.12	23.41 ± 3.69

*Other students of health professions.

Table 2
Bivariate associations. Used Pearson's Chi-square test

Variables		"For the next season, are you planning on vaccinating against the flu?"		
		No (%)	Yes (%)	p-value
Gender	Female	1381 (64.77)	751 (35.23)	0.588
	Male	657 (65.77)	342 (34.23)	
Age	>23 years old	773 (61.79)	478 (38.21)	0.002
	≤23 years old	1265 (67.29)	615 (32.71)	
Degree Course	Medicine and Surgery	737 (60.46)	482 (39.54)	<0.001
	Nursing	660 (63.77)	375 (36.23)	
	Other	641 (73.09)	236 (26.91)	
Geographical area	South and Sicily	633 (64.20)	353 (35.80)	<0.001
	Centre	639 (71.88)	250 (28.12)	
	North	766 (60.99)	490 (39.01)	
You think your level of knowledge about vaccine-preventable diseases and related vaccinations is	Good/excellent	798 (59.15)	551 (40.85)	<0.001
	Insufficient/sufficient/fair	1240 (69.58)	542 (30.42)	
Have you ever had a vaccine-preventable disease in the last 5 years?	Never	1123 (67.65)	537 (32.35)	0.001
	At least once	827 (61.90)	509 (38.10)	
Given your future profession and your state of health, do you consider yourself a subject with a higher risk of contracting infectious diseases?	No	609 (72.59)	230 (27.41)	<0.001
	I don't know	239 (69.48)	105 (30.52)	
	Yes	1190 (61.09)	1093 (34.91)	
Did you get vaccinated against seasonal flu last year?	No	2026 (72.83)	756 (27.17)	<0.001
	Yes	12 (3.44)	337 (96.56)	
During the last flu season did you recommend the vaccination to patients, family members or general population?	No	1067 (76.65)	325 (23.35)	<0.001
	Yes, based on my clinical evaluation	280 (57.97)	203 (42.03)	
	Yes, according to the ministerial indications	691 (55.02)	565 (44.98)	
During the next season, do you plan on recommending the flu vaccination to patients, family members or general population?	No	843 (88.46)	110 (11.54)	<0.001
	Yes, based on my clinical evaluation	360 (62.72)	214 (37.28)	
	Yes, according to the ministerial indications	835 (52.06)	769 (47.94)	
During the last flu vaccination campaign, did you recommend the flu vaccination to any health workers?	No	1881 (68.50)	865 (31.50)	<0.001
	Yes	157 (40.78)	228 (59.22)	
Have you ever participated directly or collaborated in the organization of the vaccination campaigns for health professionals during your internship?	Yes	41 (52.56)	37 (47.44)	0.019
	No	1997 (65.41)	1056 (34.59)	
Have you ever received any requests for clarification on the topic of vaccinations (composition, contraindications, precautions, ...)?	Yes	1021 (60.56)	665 (39.44)	<0.001
	No	1017 (70.38)	428 (29.62)	
What is your opinion about the introduction of mandatory vaccinations for school access?	Contrary	111 (88.80)	14 (11.20)	<0.001
	Indifferent	156 (84.32)	29 (15.68)	
	Favorable	1771 (62.78)	1050 (37.22)	
How would you evaluate the possible introduction of mandatory vaccinations for health workers?	Contrary	147 (93.63)	10 (6.37)	<0.001
	Indifferent	221 (92.08)	19 (7.92)	
	Favorable	1670 (61.08)	1064 (38.92)	

Table 3
Multivariable logistic regression. Adjusted odds ratio are presented. Each independent variable is adjusted for all the other independent variables. Based on 2996 observations

Independent variable		Dependent variable: "For the next season, are you planning on vaccinating against the flu? Yes"		
		aOR	95% CI	p-value
Gender	Female	1		
	Male	1.01	0.82-1.23	0.982
Age	As the unit increases	0.99	0.97-1.02	0.749
Degree Course	Medicine and Surgery	1		
	Nursing	1.15	0.92-1.46	0.224
	Other	1.05	0.81-1.36	0.706
Geographical area	South and Sicily	1		
	Center	0.62	0.48-0.80	<0.001
	North	1.27	1.01-1.61	0.044
You think your level of knowledge about vaccine-preventable diseases and related vaccinations is	Good / excellent	1		
	Insufficient/sufficient/fair	0.96	0.79-1.17	0.671
Have you ever had a vaccine-preventable disease in the last 5 years?	Never	1		
	At least once	1.46	1.21-1.76	<0.001
Given your future profession and your state of health, do you consider yourself a subject with a higher risk of contracting infectious diseases?	No	1		
	I don't know	1.35	0.96-1.90	0.089
	Yes	1.36	1.08-1.70	0.008
Did you get vaccinated against seasonal flu last year?	No	1		
	Yes	69.69	37.57-129.28	<0.001
During the last flu season did you recommend vaccination to patients, family members, general population?	No	1		
	Yes, based on my clinical evaluation	0.90	0.64-1.26	0.530
	Yes, according to the ministerial indications	0.74	0.57-0.97	0.027
During the next season, do you plan to recommend flu vaccination to patients, family members, general population?	No	1		
	Yes, based on my clinical evaluation	4.01	2.81-5.74	<0.001
	Yes, according to the ministerial indications	7.02	5.12-9-62	<0.001
During the last flu vaccination campaign did you recommend the flu vaccination to health workers?	No	1		
	Yes	1.31	0.97-1.78	0.080
Have you ever participated directly or collaborated in the organization of the vaccination campaign for health professionals during your internship?	Yes	1		
	No	0.90	0.50-1.62	0.721
Have you ever received requests for clarification on vaccinations (composition, contraindication, precautions, ...)?	Yes	1		
	No	0.94	0.76-1.16	0.566
What is your opinion about the introduction of mandatory vaccination for school access?	Contrary	1		
	Indifferent	0.83	0.31-2.20	0.708
	Favorable	0.77	0.34-1.76	0.536
How would you evaluate the possible introduction of mandatory vaccination for health workers?	Contrary	1		
	Indifferent	1.01	0.35-2.96	0.985
	Favorable	7.17	2.91-17.69	<0.001

ulation? Yes, according to the ministerial indications" (aOR 0.74), "During the next season, do you plan on recommending the flu vaccination to patients, family members or general population? Yes, based on my clinical evaluation" (aOR 4.01) and "Yes, according to the ministerial indications" (aOR 7.02), "How would you evaluate the possible introduction of mandatory vaccination for healthcare workers? Favorable" (aOR 7.17). Each independent variable is adjusted for all the other independent variables in *Table 3*.

DISCUSSION

Influenza infection can be mild (in more than 50% of the cases) or severe [10], depending on several factors such as seasonal flu virus strain, whether that specific strain was included in the vaccine, immune system conditions, age and co-morbidities [11]. Moreover, according to a WHO estimation, between 5% and 15% of the total population may be affected by flu every year [11]. Flu vaccination is currently the main measure to reduce the burden of influenza. According to the CDC, in the United States, influenza vaccination was able not only to prevent 5.3 million cases of influenza in the period 2016-2017, but it also decreased by 2.6 million the medical visits due to flu and avoided 85 000 influenza-related hospitalizations [12]. A recent systematic review and meta-analysis estimated that the increased occupational risk of pandemic influenza infection among HCWs is approximately 6% [13]. Nonetheless, there are several factors affecting vaccination uptake among HCWs [14]. Most of them are country and context specific, as confirmed by an ECDC study [15]. According to a previous Italian study, one of the factors impacting on flu vaccination uptake among HCWs was whether they would consider themselves at a higher risk of infection [16]. This data was also confirmed in our sample, where considering themselves as a high risk group due to the future profession, was statistically associated to an increased vaccination uptake during the next flu season, both in bivariate (p-value <0.001) and multivariable analysis (aOR = 1.36, 95% CI = 1.08-1.70; p-value = 0.008). At the same time, the social network and peers' influence have a considerable impact on flu vaccination uptake among HCWs [17]. In particular, our study confirmed that having recommended the flu vaccination the previous year and planning on recommending it during the next season to patients, family members or the general population, was statistically associated with an increased vaccination uptake. Moreover, we found a border-line significant association between having recommended the flu vaccination to HCWs and flu vaccination acceptance (p-value = 0.08). Also the social pressure may play an important role [18]. Indeed, the vast majority of our sample agreed with the introduction of the mandatory vaccination law and 87.3% of our sample also agreed with the hypothetical introduction of mandatory vaccination for HCWs. Moreover, being in favor of mandatory vaccination was also associated with flu vaccination acceptance (aOR= 7.17, 95% CI = 2.91-17.69; p-value <0.001). A detailed analysis of the factors associated to being favorable to the mandatory vaccination, will be reported in a companion paper. Recently, Frederick

et al. demonstrated the effectiveness of mandatory flu vaccination policies both to protect HCWs and to improve vaccination coverage. The Authors compared the total number of HCWs days off due to symptomatic flu and the vaccination coverage in 3 hospital where vaccination was mandatory and in 4 hospital where it was not. After the introduction of mandatory flu vaccination for HCWs, in the 3 American hospitals of the study, HCWs' absenteeism was significantly reduced and flu vaccination uptake was higher [19]. Absenteeism due to sick leave plays a major impact on the Healthcare System, not only in terms of disease-related deaths and complications requiring hospital care, but also in terms of economic burden and loss of productivity. As a matter of fact, workers taking days off due to influenza lead to a shortage of staff that could cause not only a disruption of the normal functioning of the facility but also a reduction in hospital elective admissions or outpatient visits. It has been estimated that, in the European Union, seasonal influenza contributes to an economic burden of € 6-14 billion years annually, considering both the direct and indirect costs related to it [20]. This burden could be significantly reduced through an appropriate vaccination programme, whose benefits in terms of public health and monetary savings would definitely overweight the costs associated with its implementation [21]. Study by Colombo *et al.* showed that, regarding influenza vaccination for HCWs, the benefit-cost ratio to the Local Health Unit is € 4.2, meaning that for every € 1 invested there is a return of € 4.2 [22]. However, other policies should be adopted along with mandatory vaccination, in order to increase HCWs uptake [23]. According to the systematic review conducted by Schmid *et al.*, other factors can predict flu vaccination uptake, such as general attitudes on vaccination, having being previously vaccinated, having a personal history of influenza infection and specific vaccination knowledge [18]. In our analysis, both having had a vaccine-preventable disease in the last 5 years and having been vaccinated against flu the previous year were shown to positively affect vaccination uptake. Furthermore, a recent review found a strict association between HCWs vaccination and attitude of HCWs towards recommending the vaccination to their patients [24]. However, it is important to highlight that having good skills in communication and an updated knowledge on this issue are essential for an efficient counselling session with hesitant patients [15, 24, 25]. Moreover, having a positive attitude toward vaccinations (considered as having collaborated in vaccination campaigns and being willing to provide clarifications on the topic of vaccinations) was also associated to an increased vaccination uptake according to the bivariate analysis; however, the multivariable analysis did not confirm these data. This was probably due to the fact that only a small number of students had the possibility to take part in these activities during their university years. At the same time, even if more than half of our sample reported an insufficient/sufficient/fair level of knowledge, this was not statistically significant in the multivariable analysis.

The wide variation in vaccination coverage among HCWs might also be affected by the high variability

of professional profiles included in this group. Previous systematic reviews found a flu vaccination coverage among HCWs ranging between 9-53%, for the following professional profiles: dental students, nurses, ancillary workers and physicians [26-29]. However, even if statistical significant differences were found in our sample in the bivariate analysis, these were not confirmed by the multivariable analysis.

To the best of our knowledge, this is the first study aimed at assessing the factors associated with flu vaccination acceptance among Health Professions students. This was a cross sectional study and for this reason it was not possible to establish any causal relationship between variables. However, we used a validated questionnaire, and even if an information bias may not be completely excluded, we tried to reduce it. Furthermore, we also controlled for potential social desirability bias, through an anonymous on-line administration. Nevertheless, this study has some important strengths, because the questionnaire was on-line and with mandatory answers, so there were no missing data. Moreover, the on-line administration was very inexpensive, easy to fill and allowed to reach a high number of students. Indeed, another important strength is the large sample size achieved. Nevertheless, 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 they facilitated the analysis.

CONCLUSION

In conclusion, even if university students are not health professionals yet, they spend part of their time in healthcare facilities for their clinical training, and they will be the health care workers of the future. For these reasons, it is extremely important to invest in their education and to directly involve them in vaccination campaigns. Including students as a target group for flu vaccination campaigns might have a positive effect in increasing flu vaccination acceptance, because it would allow a stronger relationship between peers, it would improve awareness in considering themselves as a high-risk group, and it would increase their knowledge thanks to active training on the field. Engaging healthcare students in flu vaccination campaigns may also help them to care more both for themselves and for their patients. Moreover, identifying an effective vaccination strategy for HCWs can positively affect vaccination coverage and help achieve herd immunity, considering HCWs as a strategic target group.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

REFERENCES

1. Cassini A, Colzani E, Pini A, Mangen MJ, Plass D, McDonald SA, et al. Impact of infectious diseases on population health using incidence-based disability-adjusted life years (DALYs): results from the Burden of Communicable Diseases in Europe study, European Union and European Economic Area countries, 2009 to 2013. Euro surveillance: bulletin Europeen sur les maladies transmissibles [European communicable disease bulletin]. 2018;23(16).
2. Center for Disease Control and Prevention. Estimated influenza illnesses, medical visits, hospitalizations and deaths in the United States. 2017-2018 influenza season. CDC; January 2019. Available from: https://www.cdc.gov/flu/about/burden/estimates.htm.
3. Lai PL, Panatto D, Ansaldi F, Canepa P, Amicizia D, Patria AG, et al. Burden of the 1999-2008 seasonal influenza epidemics in Italy: comparison with the H1N1v (A/California/07/09) pandemic. Hum Vacc. 2011;7(Suppl):217-25.
4. Italia. Ministry of Health. National Immunization Plan 2017-2019. [Piano Nazionale Prevenzione Vaccinale 2017-2019], (2017). Available from: www.salute.gov.it/imgs/C_17_pubblicazioni_2571_allegato.pdf
5. Italia. Ministry of Health. Prevenzione e controllo dell'influenza: raccomandazioni per la stagione 2018-2019, (2018). Available from: www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2018&codLeg=64381&parte=1%20&serie=null
6. World Health Organization. Strategic Advisory Group of Experts on Immunization. Report of the extraordinary meeting on the influenza A (H1N1) 2009 pandemic, 7 July 2009. Wkly Epidemiol Rec. 2009;84(30):301-4.
7. Italia. Ministero della Salute [Ministry of Health]. Influenza, dati coperture vaccinali 2018. [Influenza, data on vaccination coverage 2018]. February 2019. Available from: www.salute.gov.it/portale/influenza/dettaglioContenutiInfluenza.jsp?lingua=italiano&id=679&area=influenza&menu=vuoto.
8. Mereckiene J, Cotter S, Weber JT, Nicoll A, D'Ancona F, Lopalco PL, et al. Influenza A(H1N1)pdm09 vaccination policies and coverage in Europe. Euro surveillance: Bulletin Europeen sur les maladies transmissibles [European Communicable Disease Bulletin]. 2012;17(4).
9. Amodio E, Tramuto F, Maringhini G, Asciutto R, Firenze A, Vitale F, et al. Are medical residents a "core group" for future improvement of influenza vaccination coverage in health-care workers? A study among medical residents at the University Hospital of Palermo (Sicily). Vaccine. 2011;29(45):8113-7.
10. Hayward AC, Fragaszy EB, Bermingham A, Wang L, Copas A, Edmunds WJ, et al. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. Lancet Respir Med. 2014;2(6):445-54.
11. World Health Organization. Influenza (Seasonal) 2018. February 2019. Available from: www.who.int/en/newsroom/fact-sheets/detail/influenza-(seasonal).
12. Center for Disease Control and Prevention. Vaccine effectiveness. How well does the flu vaccine work? 12 ottobre 2018. January 2019. Available from: www.cdc.gov/flu/about/qa/vaccineeffect.htm.
13. Lietz J, Westermann C, Nienhaus A, Schablon A. The

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Occupational risk of Influenza A (H1N1) Infection among healthcare personnel during the 2009 pandemic. A systematic review and meta-analysis of observational studies. PloS One. 2016;11(8):e0162061.

14. Dini G, Toletone A, Sticchi L, Orsi A, Bragazzi NL, Durando P. Influenza vaccination in healthcare workers. A comprehensive critical appraisal of the literature. Hum Vaccin Immunother. 2018;14(3):772-89. Epub 2017/08/09.

15. European Centre of Disease Prevention and Control. Let's talk about hesitancy. Stockholm: ECDC; 2016.

16. Durando P, Alicino C, Dini G, Barberis I, Bagnasco AM, Iudici R, et al. Determinants of adherence to seasonal influenza vaccination among healthcare workers from an Italian region: results from a cross-sectional study. BMJ open. 2016;6(5):e010779.

17. Llupia A, Puig J, Mena G, Bayas JM, Trilla A. The social network around influenza vaccination in health care workers: a cross-sectional study. Implementation science: IS. 2016;11(1):152.

18. Schmid P, Rauber D, Betsch C, Lidolt G, Denker ML. Barriers of influenza vaccination intention and behavior. A systematic review of influenza vaccine hesitancy, 2005-2016. PloS One. 2017;12(1):e0170550.

19. Frederick J, Brown AC, Cummings DA, Gaydos CA, Gibert CL, Gorse GJ, et al. Protecting healthcare personnel in outpatient settings. The influence of mandatory versus nonmandatory influenza vaccination policies on workplace absenteeism during multiple respiratory virus seasons. Inf Contr Hosp Epidemiol. 2018;39(4):452-61.

20. Preaud E, Durand L, Macabeo B, Farkas N, Sloesen B, Palache A, et al. Annual public health and economic benefits of seasonal influenza vaccination: a European estimate. BMC Pub Health. 2014;14:813.

21. Imai C, Toizumi M, Hall L, Lambert S, Halton K, Merollini K. A systematic review and meta-analysis of the direct epidemiological and economic effects of seasonal influenza vaccination on healthcare workers. PloS One. 2018;13(6):e0198685.

22. Colombo GL, Ferro A, Vinci M, Zordan M, Serra G. Cost-benefit analysis of influenza vaccination in a public healthcare unit. Therapeutics and clinical risk management. 2006;2(2):219-26.

23. Maltezou HC, Theodoridou K, Ledda C, Rapisarda V, Theodoridou M. Vaccination of healthcare workers: is mandatory vaccination needed? Exp Rev Vaccines. 2018 Dec 1.

24. Di Pietro ML, Poscia A, Teleman AA, Maged D, Ricciardi W. Vaccine hesitancy: parental, professional and public responsibility. Ann Ist Super Sanità. 2017;53(2):157-62.

25. Gianfredi V, Grisci C, Nucci D, Parisi V, Moretti M. Recenti progressi in medicina. [Communication in health]. La comunicazione in sanità. 2018;109(7):374-83.

26. La Torre G, Mannocci A, Ursillo P, Bontempi C, Firenze A, Panico MG, et al. Prevalence of influenza vaccination among nurses and ancillary workers in Italy: systematic review and meta analysis. Hum Vaccines. 2011;7(7):728-33.

27. Leone Roberti Maggiore U, Scala C, Toletone A, Debarbieri N, Perria M, D'Amico B, et al. Susceptibility to vaccine-preventable diseases and vaccination adherence among healthcare workers in Italy: A cross-sectional survey at a regional acute-care university hospital and a systematic review. Hum Vaccines Immunother. 2017;13(2):470-6.

28. Bish A, Yardley L, Nicoll A, Michie S. Factors associated with uptake of vaccination against pandemic influenza: a systematic review. Vaccine. 2011;29(38):6472-84.

29. Gianfredi V, Nucci D, Salvatori T, Orlacchio F, Villarini M, Moretti M, et al. "PErCEIVE in Umbria": evaluation of anti-influenza vaccination's perception among Umbrian pharmacists. J Prev Med Hygiene. 2018;59(1):E14-E9.