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Short communication

Appropriateness and preferential use of different seasonal influenza vaccines: A pilot study on the opinion of vaccinating physicians in Italy

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ABSTRACT

In Italy, several types of influenza vaccine are on the market. Available evidence suggests that no single vaccine type is universally appropriate; rather, different types may be more appropriate for different population strata. However, while the concept of appropriateness/preferential use of single vaccines is usually adopted at the central level, little is known about the attitudes of physicians on the matter. A pilot survey of Italian physicians ($N = 372$) revealed that most (about 90%) were aware that the available vaccines were different, and that particular vaccines were more appropriate for specific groups. The availability of explicit guidelines on which vaccine to administer to a given population group was deemed desirable by 93.2% of respondents. The results were consistent with the 2018 Italian and UK normative documents, which indicate adjuvanted vaccines as the most appropriate choice for the elderly, and quadrivalent formulations for the younger age-classes. Public health policy implications are discussed.

1. Introduction

Both in Italy and worldwide, influenza is a serious public health problem and a major source of direct and indirect costs. Annual vaccination is a cornerstone public health measure which significantly reduces the risk of illness, complications, hospitalization and death, and their associated costs [1,2]. In this regard, the 2017–19 Italian National Immunization Plan [2] set the objective of reaching 75% vaccination coverage (VC) as the minimum goal for the elderly and other risk groups, and 95% coverage as the optimal target. Moreover, a circular on the prevention and control of influenza and on the recommendations to be followed is issued by the Italian Ministry of Health each year [3]; this circular is distributed to all regional public health authorities, and provides detailed information on all relevant aspects of seasonal influenza immunization, including available vaccine types. However, until recently, the indication for single vaccine types has been rather generic and essentially based on the summary of product characteristics. For instance, in the 2017/18 season, the elderly could receive any available vaccine, including trivalent split or subunit, quadrivalent split, MF59®-adjuvanted and intradermal vaccines [3].

In Italy, most vaccines are administered by primary care physicians [general practitioners (GPs) and pediatricians], who are offered incentives to increase the VC among their patients [4,5]. Nevertheless, the latest available data suggest that the VC achieved is far from the established goals, being 52.7% in the elderly [6] and 20.3% among at-risk subjects aged 18–64 years [7]. Moreover, the various Italian regions display both highly different VC rates and inhomogeneous use of the above-mentioned vaccine types [4].

Following a thorough evaluation of available clinical and pharmacoeconomic evidence and regional policies (e.g. some regional health authorities explicitly recommend which vaccine to use in a given target group [4]), we previously investigated the appropriateness of using different influenza vaccine types [5]. We defined appropriate vaccine use from the perspectives of efficacy/effectiveness (based on evidence), efficiency (cost-effectiveness) and consistency with the ethical principles and preferences of the individuals involved [8]. This approach was equity-based and suggested that different population groups might benefit more from the use of a more appropriate vaccine formulation. However, given that GPs and pediatricians administer the vast majority of vaccine doses, their views on the concept of appropriateness are highly relevant. Our previous survey [9] revealed that, in the 2014/15 season, more than 50% of GPs did not have the possibility to choose

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among different vaccine types. The aim of the present pilot study was to investigate some aspects of the knowledge, attitudes and practices concerning the use of available influenza vaccines in Italy in a sample of vaccinating GPs and pediatricians.

2. Methods

An *ad hoc* questionnaire was created by the University of Florence and the University of Genoa. This tool consisted of two parts and included 24 items. The first part ($N = 6$ items on the categorical scale) covered demographic (profession and Region) data, general awareness of the national and, when present, regional influenza circulars, attitudes toward broadening the current offer of free vaccination and continuous medical education (CME) on influenza vaccination in the past 12 months. The second main part consisted of eighteen 5-point (1: completely disagree; 2: disagree; 3: neutral; 4: agree; 5: completely agree) Likert-type items covering four domains: physicians' attitudes towards the current vaccination offer, vaccine appropriateness, national/regional guidelines and organizational aspects of the influenza vaccination campaign.

The study population comprised sentinel GPs and pediatricians taking part in the Inter-University Center for Research on Influenza and other Transmissible Infections (CIRI-IT) (www.cirinet.it), Genoa (Italy). Until the 2016–2017 influenza season, CIRI-IT was one of the two reference centers of the Italian influenza sentinel surveillance system (InfluNet), monitoring about 2% of the population in 9 Italian Regions.

The survey was conducted in an online modality; potential participants received an invitation by email in March 2018, and a reminder was sent two weeks after the first invitation.

A descriptive analysis of the available data was undertaken. For this purpose, categorical data were expressed as proportions with 95% confidence intervals (CIs), while single-item Likert scores were expressed as medians with interquartile ranges (IQRs) and modes. The internal consistency of the Likert items was measured by means of Cronbach's α. All analyses were performed by means of the R stats package, version 3.1.2 [10].

The Ethics Committee of the Liguria Region (Genoa, Italy) was notified before the start of the study. However, formal ethical approval for this anonymous survey (which involved physicians participating in the national surveillance network) was not necessary, since its nature was non-medical and non-interventional and no sensitive data or personal information were collected.

3. Results

A total of 560 invitations were sent out, and 372 answers were received (a response rate of 66.4%). The median time of survey completion was 6.6 min (IQR: 5.1–9.8 min). Most participants [83.0% (95% CI: 78.8–86.7%)] were GPs, the remaining 17.0% (95% CI: 13.3–21.2%) being pediatricians.

A total of 84.4% (95% CI: 80.3–87.9%) of physicians believed that the current free-of-charge vaccine recommendation (over-65-year-olds, subjects at risk and in key professions) should be broadened. Fig. 1 shows the population groups to whom free vaccination should be extended, according to the respondents. Notably, the most popular answer (38.5%) was the entire Italian population.

Most physicians [91.7% (95% CI: 88.4–94.3%)] were aware that the Italian Ministry of Health issues an annual circular on the prevention and control of influenza. However, only 28.1% (95% CI: 23.6–33.1%) declared that the ministerial circular was somehow amended and/or updated by their regional authorities in order to fit in with local circumstances.

Regarding CME on influenza vaccination, it emerged that, in the previous year, most [71.0%; (95% CI: 66.0–75.6%)] physicians had not taken part in any CME activity. Among those who had, the most popular modalities were: attending a conference/congress [45.3% (95% CI: 35.6–55.2%)], seminar/lecture [28.3% (95% CI: 20.0–37.9%)] and distance learning courses [10.4% (95% CI: 5.3–17.8%)].

In the main part of the survey, the α value was 0.76; internal consistency can therefore be judged acceptable. The main results are reported in Table 1. Briefly, most physicians [93.5% (95% CI: 90.1–95.8%)] believed that influenza vaccination is essential in order to improve the welfare of their region. Indeed, less than a third of participants considered the current VC to be sufficient.

Most physicians disagreed that the available influenza vaccines were the same; for instance, about 90% believed some vaccine types to be more appropriate for some population groups. Most participants [93.2% (95% CI: 90.2–95.6%)] agreed that there was a need to establish explicit guidelines on the appropriateness of the use of different vaccine types; at least three-quarters thought that the availability of such guidelines would reduce the burden of disease and the off-label use of different vaccines, while increas-

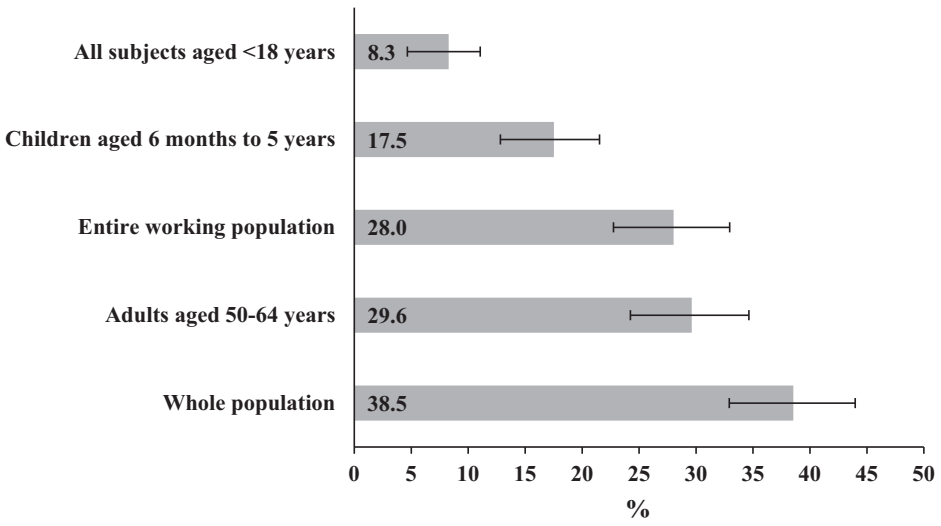

Fig. 1. Population groups to whom the free-of-charge seasonal influenza vaccination offer should be extended, according the study participants.

Table 1
Study participants who agreed/strongly agreed with a given statement, and median and mode scores, by item.

Item	Description	N	% strongly agree/agree (95% CI)	Median (IQR)	Mode
1	Influenza vaccination is essential to increasing the welfare of my Region	372	93.5 (90.1–95.8)	5 (4–5)	5
2	Influenza vaccination coverage rates in my Region are sufficient	371	29.1 (24.5–34.0)	2 (2–4)	2
3	Available influenza vaccines are almost the same, only the brand name changes	369	10.0 (7.2–13.6)	2 (2–3)	2
4	Some influenza vaccines are preferable to others for some population groups	370	91.6 (88.3–94.2)	4 (4–5)	4
5	Some influenza vaccines are more immunogenic and may provide better protection in the elderly	369	88.1 (84.3–91.2)	4 (4–5)	4
6	Adjuvanted influenza vaccines are more appropriate for the elderly, as they enhance immunogenicity	368	88.6 (84.9–91.6)	4 (4–5)	4
7	Quadrivalent influenza vaccines are more appropriate for younger populations, as virus B significantly affects these age-groups	367	67.3 (62.2–72.1)	4 (3–4)	4
8	Given the availability of different influenza vaccines, a physician should have the possibility to choose the most appropriate one for a given patient	368	89.7 (86.1–92.6)	4 (4–5)	4
9	Given the availability of different influenza vaccines, there should be explicit guidelines on which vaccine type to administer to a given population group	369	93.2 (90.2–95.6)	4 (4–5)	4
10	Considering the last Ministerial Circular "Prevention and control of influenza: recommendations for the season 2017–2018", I believe that in future this should explicitly state which vaccine type to administer to a given population group	368	79.9 (75.4–83.9)	4 (4–5)	4
11	The availability of international/national/regional guidelines on which vaccine type to administer to a given population group may reduce the number of cases of influenza and its complications	367	84.2 (80.0–87.8)	4 (4–5)	4
12	The availability of international/national/regional guidelines on which vaccine type to administer to a given population group may increase vaccination coverage	367	73.0 (68.2–77.5)	4 (3–4)	4
13	The availability of international/national/regional guidelines on which vaccine type to administer to a given population group may optimize the physician's work	367	90.2 (86.7–93.0)	4 (4–5)	4
14	The availability of international/national/regional guidelines on which vaccine type to administer to a given population group may reduce the off-label use of single vaccines	367	76.6 (71.9–80.8)	4 (4–5)	4
15	Regional policy on influenza vaccination should consider demographic and epidemiological issues in a given Region	368	91.0 (87.6–93.7)	4 (4–5)	4
16	In the last season, you were provided with a sufficient number of influenza vaccine doses	368	74.7 (70.0–79.1)	4 (3–5)	4
17	In the last season, you had all available vaccine types (TIV, QIV, aTIV, idTIV) you needed	368	45.7 (40.5–50.9)	3 (2–4)	4
18	In the last season, you had a sufficient number of all available vaccine types (TIV, QIV, aTIV, idTIV) you needed	368	50.3 (45.0–55.5)	4 (2–4)	4

ing the overall VC and optimizing the physician's work. Moreover, most physicians [91.0% (95% CI: 87.6–93.7%)] agreed that the guidelines should also consider local circumstances. However, while roughly three quarters [74.7% (95% CI: 70.0–79.1%)] of physicians received a sufficient overall number of vaccine doses, only around half were able to order/manage the type and quantity of the most appropriate vaccine types for their patients (Table 1). A detailed description of single items by Likert level is reported in Appendix, Fig. S1.

4. Conclusions

The year 2018 has seen several major changes in Europe in the field of influenza vaccination policies. First, in February 2018, the Public Health England (PHE), following conclusions drafted by the Joint Committee on Vaccination and Immunization (JCVI), recommended that GPs and community pharmacists should preferentially use the adjuvanted trivalent and quadrivalent vaccines in adults aged ≥65 and 18–64 years, respectively [11]. Second, the indication for quadrivalent vaccines has been extended to subjects aged ≥6 months (instead of ≥3 years) [12]. Third, the intradermal vaccine has been permanently withdrawn (at least in Italy) from the market [12]. Fourth, in May 2018, the Italian Ministry of Health issued its annual recommendations for the 2018/19 influenza season [12]. For the first time, it was explicitly stated that the adjuvanted vaccine should provide better protection than unadjuvanted trivalent and quadrivalent formulations in the oldest old (≥75 years). By contrast, the unadjuvanted quadrivalent formulation is preferable in other target groups. To keep pace with the above-mentioned changes, we have updated our proposal [5] on the appropriate use of the vaccines available in Italy [13]: adjuvanted trivalent for subjects aged >70 years and quadrivalent for those aged <70 years. The results of the present pilot survey may provide further useful insights into the appropriate use of the influenza vaccines in Italy.

While the theoretical grounds of our concept of appropriateness are well-defined [5,8] and fortified by the recent Italian [12] and UK [11] normative documents, it has been conceived from the point of view of evidence-based Public Health, and without the active engagement of vaccinating physicians. Anecdotally, we discovered (during question-answer sessions/discussions at major congresses) that some physicians were "unsure" when faced with choosing the most appropriate influenza vaccine for their patients; by contrast, these physicians had no doubts when choosing among tens of antibiotics. Indeed, Italian guidelines on the ambulatory treatment of common infections (e.g. community-acquired pneumonia [14]) according to age, severity, etc. have existed for years. In this regard, the above-described Italian recommendations for the 2018/19 season could make a difference, and are seen by the authors as a milestone. These guidelines may not only dispel much of the clinical uncertainty evinced by vaccinating physicians, but also medico-legal implications.

While many studies have investigated the knowledge, attitudes and practices of GPs concerning influenza vaccination in Italy, only Levi et al. [9] have assessed these aspects with specific regard to the different types of vaccine. Moreover, to the best of our knowl-

edge, no studies have focused on the use of available influenza vaccines in specific population groups. In general, our results confirm the most recent recommendations issued by the Italian Ministry of Health [12], in that more explicit guidelines on which vaccine to administer to a given population group were deemed necessary by vaccinating physicians. Indeed, it emerged that only half of the participants were able to order the desired quantity of the most appropriate vaccine. Recommendation by the GP is known to be the main driver of annual influenza VC [15]; the commitment of GPs is therefore crucial to achieving the minimum target of 75% [2]. Interestingly, in our survey, about three-quarters of physicians agreed that the availability of explicit guidelines on the appropriateness of the use of single vaccine types could increase VC.

The main drawback of the present study is that our sample was drawn from among influenza sentinel physicians, who may be more sensitive to the issue of vaccination. However, we believe that this limitation has little impact on the overall conclusions, since: (i) the aim of the study was not to discover how many doses a physician administers (i.e. VC); and (ii) the participants were from eight different regions with different procurement policies (i.e. different public market shares of single vaccines). Moreover, the VC rate among the patients of sentinel physicians is known to be close to regional averages. Furthermore, we had a relatively high response rate, and had no reason to suppose that responders somehow differed from non-responders.

To conclude, in the setting of fiscal federalism, single Italian Regions should provide vaccinating physicians with explicit and unambiguous guidelines on which vaccine to administer to a given population group. To date, it seems that the adjuvanted trivalent vaccine is the most appropriate choice for the elderly, while the unadjuvanted quadrivalent formulation is preferable for younger age-groups. The availability of such guidelines could increase VC and therefore improve the overall welfare of Italian Regions.

Conflict of interest

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

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2018.12.057.

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