

Increasing influenza vaccination coverage in recommended population groups in Europe

Expert Rev. Vaccines 8(4), 425–433 (2009)

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The clinical and economic burden of seasonal influenza is frequently underestimated. The cornerstone of controlling and preventing influenza is vaccination. National and international guidelines aim to implement immunization programs and targeted vaccination-coverage rates, which should help to enhance the vaccine uptake, especially in the at-risk population. This review purposes to highlight the vaccination guidelines and the actual vaccination situation in four target groups (the elderly, people with underlying chronic conditions, healthcare workers and children) from a European point of view.

KEYWORDS: coverage • influenza • recommendation • risk group • vaccination

Influenza continues to be a considerable health problem all over the world [1,2]. The WHO assesses that each year there are 3–5 million cases of severe influenza, resulting in 250,000–500,000 deaths worldwide [101].

The control of influenza is currently based on the surveillance, treatment and prevention of the illness. The primary and single most effective method to reduce the burden of disease is annual vaccination. Vaccines are a safe and effective method of preventing severe outcomes of influenza [101]. In particular, elderly people and adults with chronic conditions are at a higher risk for severe complications due to influenza, and may even die. The WHO estimates that vaccination can reduce influenza-related morbidity and mortality by 60% and up to 80%, respectively [101]. Nevertheless, the effectiveness of the vaccine is based not only on the similarity between the virus in the vaccine and in circulation, but also on the age and immunocompetence of the individual. Owing to vaccination, related health costs can be reduced, making influenza vaccination a cost-effective method with regards to influenza-related direct and indirect costs [3].

The focus of the vaccination strategies is more on the at-risk population than the whole population [101]. In May 2003, the World Health Assembly (WHA) released recommendations for the usage of influenza vaccines, which are mainly

targeted at the older population and individuals with underlying diseases [4]. To tie in with the developments introduced by the program of Community Action in the field of Public Health (2003–2008), the European Parliament implemented a further program of Community Action on Health (2008–2013) [5,6]. These guidelines can be identified in national regulations, although there are some distinctions between countries. Nevertheless, all European countries are obligated to achieve the goal of 75% vaccination coverage by 2010/2011 in the aged population [6]. Practically all European member states have influenza immunization guidelines for individuals considered as being at risk. However, there are large discrepancies in the definition of ‘risk’ and, consequently, vaccination coverage rates differ considerably. Aside from the traditional risk groups (the elderly and chronically ill patients), some other groups are regarded at higher than average risk of severe disease: pregnant women, children under the age of 2–5 years, individuals living with those at high risk, healthcare and other care workers, people working in military and veterinary services, and poultry workers [7,8].

This review aims to highlight the European divergences in vaccination coverage rates with regards to the actual recommendations on a national level. Four target groups (the elderly,

people with underlying medical conditions, healthcare workers and children) including current vaccination guidelines were discussed in detail. Data on national vaccination policies in the EU and European Economic Area member states were obtained from the cross-sectional electronic-based survey conducted by the National Seasonal Influenza Vaccination Survey (VENICE) [8].

Vaccine delivery & costs of vaccination

Influenza vaccine distribution numbers provide a beneficial indirect measure of vaccine usage, although sales data have limitations in terms of vaccine coverage assessment in at-risk groups [9]. After the implementation of new recommendations on influenza vaccination, numbers of vaccine doses distributed indicated an increasing trend in both developed and developing countries [10]. Recent data reveal a range of 16,588 (in 2004/2005) to 20,009 (in 2006/2007) doses supplied per 100,000 habitants across all European member states. However, great variations between member states were visible [11].

The socio-economic consequences of the influenza illness include basically direct and indirect costs. Direct costs are acquisition costs, fees or charges with hospitalization and physician visit accounting predominantly for these costs [12]. In 2005, the average European price for the influenza vaccine and the administration fees was estimated to add up to €8.50 and €8.17, respectively [13]. Nevertheless, indirect costs, namely reduced or lost productivity due to work or school absenteeism, answer for the most important costs of illness [14–16]. On average, missed work days due to influenza are presumed to be 1.3–4.9 days [17,18]. The influence of intangible costs (including quality of life or impairment of function) on the socio-economic impact is difficult to quantify.

Recommended groups in Europe

In 2000, the first recommendation for the use of inactivated influenza vaccines was realized by the WHO [19]. In recent years, many countries have adopted formal national recommendations on influenza immunization policies for specific target groups. However, the definition of risk groups can be complex. The European Centre of Disease Prevention and Control (ECDC) defined risk groups as 'persons at higher than average risk of adverse outcomes should they be infected with seasonal influenza for whom vaccinating with seasonal influenza vaccination is considered effective on the basis of reducing the risk of specified adverse outcomes' [20]. Distinctions between different risk groups can be determined as follows: individuals with an augmented risk of acquiring influenza because they are more susceptible (non-immune); persons with a higher risk of adverse events such as severe disease or death if infected (older people, chronic illness sufferers, pregnant women and very young children); and individuals at a higher risk of transmitting influenza to others at high risk (healthcare workers and nursing-home staff) [20].

In the EU, most countries (except Austria, Bulgaria, Estonia, Finland, Germany, Norway, Slovakia and Poland) subsidize vaccine and administration costs. Older people (generally above 65 years of age) and chronically ill patients receive free vaccination

in almost half of all EU member states. In a third of the countries, the vaccine is reimbursed in some occupational groups (including healthcare workers). Only three countries offer the vaccine at no cost for all children (Romania, Slovakia and Spain) [21].

Older age groups

The risk for serious complications and possibly even death is strongly enhanced in older individuals. With aging, the response to influenza antigens is negatively influenced by the lost capability to maintain memory helper T cells [22,23]. Hence, the decreased function in the immune system (immunosenescence), as well as the higher incidence of underlying chronic diseases with age, affect the susceptibility for influenza infection [24–26]. However, considering that many influenza cases are vaccine preventable, the high burden of influenza in older people is not warranted [27].

In most countries, this risk group is generally defined as people aged 65 years and above. However, there are some exceptions (e.g., Germany, Hungary, Iceland and Greece define it as ≥ 60 years). In a small number of countries, including the USA and Poland, the age cut-off is set to 50 years of age. In total, 23 countries in Europe have implemented an age-based vaccine recommendation; nevertheless, in only 45% of the European member states is the vaccine and its administration free [8,28]. FIGURE 1 presents the actual recommended age groups of the elderly patients in 29 European countries [8].

The coverage rates in the older population were shown to differ widely between countries (2–82%) [8]. This result indicates that only a few countries met the WHO target of 50% in 2006/2007, while the others remained below this [7]. A cross-sectional population-based telephone survey conducted in the UK, Germany, France, Italy and Spain revealed that coverage rates of the elderly did not indicate an increasing trend during six consecutive seasons (2001/2002 to 2006/2007) [29]. On the other hand, data from the USA exhibit a vaccination coverage of 72.1% (for the 2006/2007 season) [30]. This high coverage may be attributed to the fact of very strong guidelines, meaning a lower age cut-off than most European countries (except Poland) [102].

There is now strong evidence in the published literature, that vaccine uptake in this high-risk group should be maintained and even improved. A study performed by Nichol *et al.* examined the effectiveness of the influenza vaccine in elderly patients over a long time period. The survey resulted in a significant reduction in the risk of hospitalization and of death among community-dwelling old individuals [31]. Nevertheless, controversy persists on vaccine usefulness in those individuals. Evidence exists of moderate effectiveness if elders living in the community are vaccinated [32]. Whether observational studies may have overestimated the effectiveness in community-dwelling elderly or how vaccine uptake rates could be affected by them remains ambiguous.

There is support that lowering the age cut-off to 50 years in Europe would be a cost-effective approach [13,33]. These assumptions can be underlined by the enormous indirect costs accrued owing to absenteeism and lost productivity in the age group of 50–64-year-olds if they become infected [17]. Furthermore, the highest rate of influenza-related clinical complications and

physician visits were found in healthy, hence working, adults [34]. In a recent placebo-controlled study by Ciszewski *et al.*, it was shown that influenza vaccination improved the clinical outcome of coronary artery disease (CAD) patients (30–80-year-olds) and diminished the occurrence of coronary ischemic events [35]. Gurfinkel *et al.* even proposed a reduction in mortality and ischemic events in vaccinated CAD patients compared with controls [36]. Given that cardiovascular events are not only in the older population a leading cause of morbidity and mortality in developing countries, advocating a lower age cut-off would be favorable. However, in the light of diverse age structures across Europe, age-based immunization guidelines are reasonable to differ from nation to nation. If conclusive nationwide immunization programs are implemented, a significant reduction in influenza-related mortality rates can be achieved, as was shown among the elderly Dutch population [37,38].

Chronically ill patients

The influenza vaccination policies across the EU include persons with chronic cardiovascular diseases, respiratory diseases and hematological or metabolic disorders. Some countries expand the category to patients with renal or liver diseases, immunological disorders and HIV, as shown in TABLE 1 [8,20]. It is known from the literature that complications arising from influenza are more severe and frequent in adults with chronic conditions including pneumonia, respiratory disease, cardiac disease or cerebrovascular disease [39]. Mortality rates are estimated to range from ten to 377 per 100,000 influenza cases, depending on the number of high-risk conditions [40].

Coverage of people under the age of 65 years with chronic illnesses continued to be much lower than the vaccination levels achieved in elderly adults. Jimenez-Garcia *et al.* identified a coverage level of 57% in Spanish diabetic adults [41]. Furthermore, rates between 30 and 59% were found in a telephone-based survey conducted among chronically ill patients below 65 years of age in five European countries, and the VENICE survey estimated vaccine uptake in clinical risk groups (regardless of age) at 20–75% in seven countries [7,29].

Clearly, it is more complex to implement a targeted risk-group strategy than an age-based approach. This may indicate a possible reason for the low vaccination-coverage rates in younger individuals at risk [42,43]. Furthermore, no WHO targets have been set for the vaccination-coverage level in these patients and, on the other hand, health-promotion campaigns for influenza immunization are recently focusing on this at-risk group. However, epidemiological scientific data, which supports the fact that vaccination reduces the risk of adverse effects in these

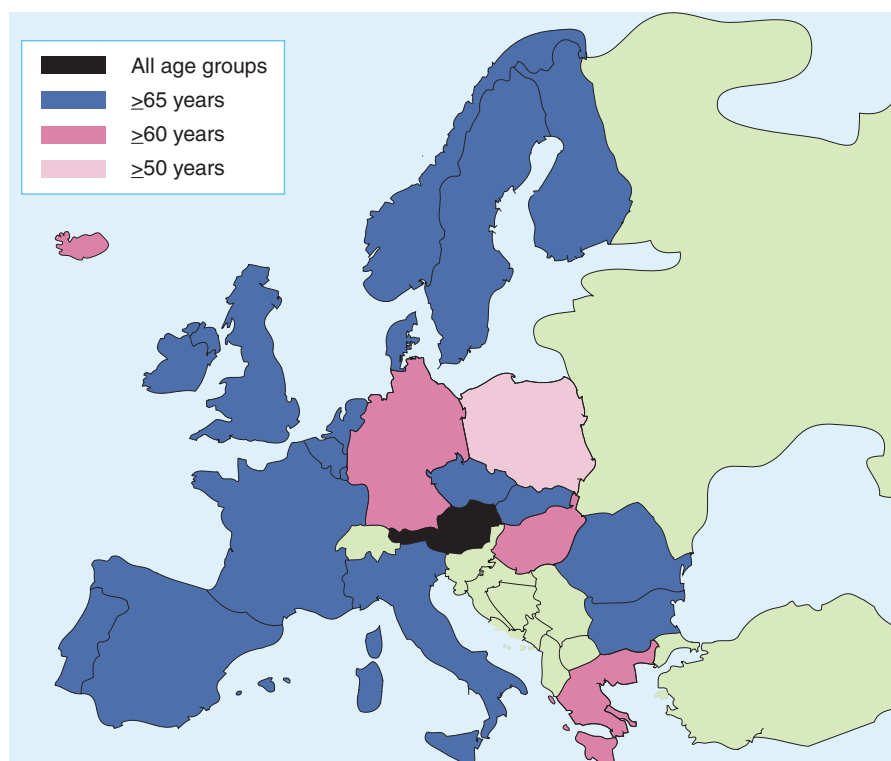


Figure 1. Vaccination recommendations for the elderly population in Europe (29 member states).

individuals, are not ample [44]. Nevertheless, some studies demonstrated raising vaccination coverage, especially in patients with diabetes [29,45].

If two comorbid conditions are existent (old persons and high-risk), influenza-related death rates are over 100-times greater than in healthy adults [46]. A Spanish study showed that vaccination against influenza was beneficial for old people with cardiac disease and reduced the adjusted risk of winter mortality by 37% during four influenza seasons. The authors estimated that one death could be prevented for every 122 seasonal vaccinations [47]. However, the impact of the influenza vaccine to decrease the all-cause mortality is disputed.

Healthcare workers

In 2003, the WHA recommended vaccination of healthcare workers [4]. In Europe, most countries recommend the immunization of healthcare professionals without a minimum coverage rate for this population [8]. Occupational settings for which the seasonal vaccine is recommended is visible in FIGURE 2 [8]. Staff in the healthcare sector should be vaccinated not only for occupational health reasons (protecting the workers) but also for protecting patients against severe complications of influenza infection. There is strong trial-based evidence that immunization of care-home staff reduced the mortality in at-risk groups [48,49]. Furthermore, absenteeism from work and working days lost can be diminished by vaccination [50,51].

Surprisingly, healthcare workers do not appear to have a strong inclination to get vaccinated. A number of European studies documented low vaccination-coverage levels in this group [7,29,52].

Table 1. Vaccination recommendations for patients with underlying medical conditions (29 member states).

Country	Chronic pulmonary disease*	Cardiovascular disease [†]	Renal disease	Hepatic disease	Hematological or metabolic disorders [‡]	Immunologic disorders	HIV/AIDS
Austria	x	x	x	NA	x	x	NA
Belgium	x	x	x	x	x	x	x
Bulgaria	x	x	x	x	x	x	x
Cyprus	x	x	x	x	x	x	x
Czech Republic	x	x	x		x		
Denmark	x	x			x	x	x
Estonia	x	x	x	x	x	x	x
Finland	x	x	x	x	x	x	x
France	x	x	x		x	x	x
Germany	x	x	x	x	x	x	x
Greece	x	x	x		x	x	x
Hungary	x	x	x		x	x	x
Iceland	x	x	x	x	x	x	x
Ireland	x	x	x	x	x	x	x
Italy	x	x	x		x	x	x
Latvia	x	x	x		x	x	x
Lithuania	x	x	x		x	x	x
Luxembourg	x	x	x		x	x	x
Malta	x	x	x	x	x	x	x
The Netherlands	x	x	x	NA	x	x	x
Norway	x	x	x		x	x	x
Poland	x	x	x	x	x	x	x
Portugal	x	x	x	x	x	x	x
Romania	x	x	x		x	x	x
Slovakia	x	x	x	x	x	x	x
Slovenia	x	x	x		x	x	x
Spain	x	x	x	x	x	x	x
Sweden	x	x					
UK	x	x	x	x	x	x	x

*Including asthma.
[†]Except hypertension.
[‡]Including diabetes mellitus.
 NA: Not available.
 Taken from [8].

Nevertheless, a large number of healthcare workers are encouraged to get vaccinated for the sake of self-protection and not to protect the patients [53,54]. Lack of knowledge is one explanation for the low coverage in healthcare workers [55]. Ridda *et al.* showed that restricted access to vaccination guidelines and other

information among employees working in a hospital resulted in a lower likelihood of recommending elders vaccination [56]. The absence of awareness toward influenza vaccination among medical employees may have a negative impact on vaccination rates, given the key role of vaccination recommendation from medical

professionals [29,37,57]. Nevertheless, not only education of healthcare workers may help to fill knowledge gaps to improve the immunization practices [58]. Healthcare workers indicated concerns about side effects, vaccine shortage and infrequent patient visits, as well as the fear of needles, as reasons against vaccination [54]. Interestingly, coverage rates indicated often differ between areas and types of hospital employment [51,59,60].

Hence, to overcome the barriers and increase the vaccine uptake among healthcare professionals, vaccination campaigns should be implemented in consideration of specific needs at each healthcare sector. With the help of multicomponent programs, including intensive promotional activities, adequate vaccination coverage rates are achievable, at least in nursing staff [61].

Children

Currently, only a few countries recommend the influenza vaccine to healthy children; whereas, children aged 6 months or older with diabetes, cardiac or renal diseases, an immunocompromised or HIV-positive status or those receiving chronic aspirin therapy should receive the vaccine [62]. At this time, six countries propose to immunize healthy children as presented in FIGURE 3 [8]. Data on vaccination coverage in children are limited, which makes the implementation of specific recommendations difficult [63]. Most data on child vaccination derive from outside Europe.

However, the highest attack rate during community outbreaks of influenza can be found among school-aged children. Commonly, the virus gets transmitted to adults, other children or family members [64]. Children bear a considerable risk for complications due to influenza, leading to an increased need for healthcare resources. Hospitalization rates due to influenza-associated cardiopulmonary conditions may exceed 288 per 10,000 previously healthy children. On the contrary, influenza-related mortality rates are low compared with the elderly target group (0.2–0.8 per 100,000) [65]. Prevention relies on vaccination to reduce the risk of disease transmission to family members, but also to extend the protection to unvaccinated individuals [66–68].

According to the ECDC, data of vaccination-coverage rates of children are urgently required [69]. However, only a few European studies were conducted to estimate children's coverage levels. The Spanish National Health Survey identified the coverage at 7.0 and 6.5% among 6–23-month-old and 2–15-year-old healthy Spanish children, respectively [70]. A community-based survey conducted in eleven European countries estimated the immunization levels of children below the age of 15 years during three influenza seasons. In 2007/2008,

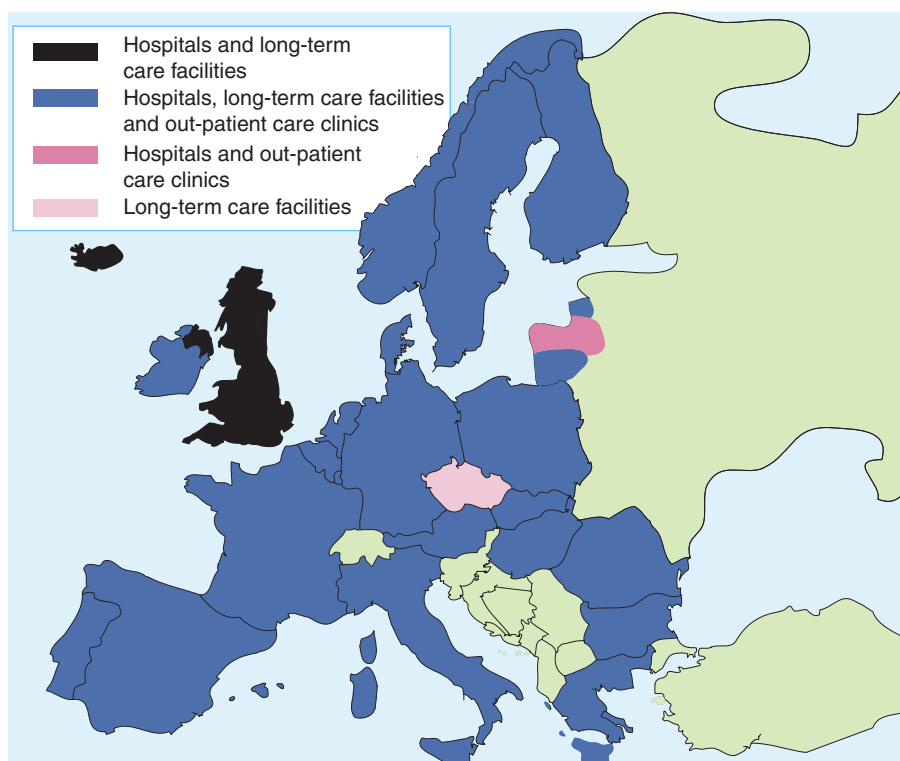


Figure 2. Vaccination recommendations for healthcare workers in Europe (26 member states).

The UK recommends the vaccine for health- and social-care staff directly involved in patient care.

the coverage ranged between 4.2% in Ireland and 19.3% in Germany (UNPUBLISHED DATA) [71]. If children are regarded as an at-risk population, these coverage levels are very low and efforts should be made to enhance these levels.

It was shown that high levels of vaccine coverage among school-children could provide protection against influenza among household contacts and could even reduce mortality rates among older individuals [72]. Weycker *et al.* have produced a stochastic model to estimate the population-wide benefits of routinely vaccinating children aged between 6 months and 18 years. They calculated a 50% reduction of influenza cases if 20% of the study population was vaccinated and a 95% reduction in the incidence among children if 80% vaccination coverage was achieved. As children represent a primary pathway to transmit the infection to the household and the community, the decline of the burden of disease would also be related to the adult population [73].

A study from France revealed that enhanced coverage rates can be obtained by sending free influenza vaccination vouchers to parents of asthmatic children [74]. Also, recall systems to remind individuals to get vaccinated were shown to be effective in improving influenza immunization rates both in children and in adults [75].

To realize higher coverage rates among children, the gain of data that quantify the burden of disease and the cost-effectiveness of vaccinating children in Europe could be the first step towards raising awareness of influenza and influenza vaccination among the government, healthcare providers, physicians and, especially, parents [60].

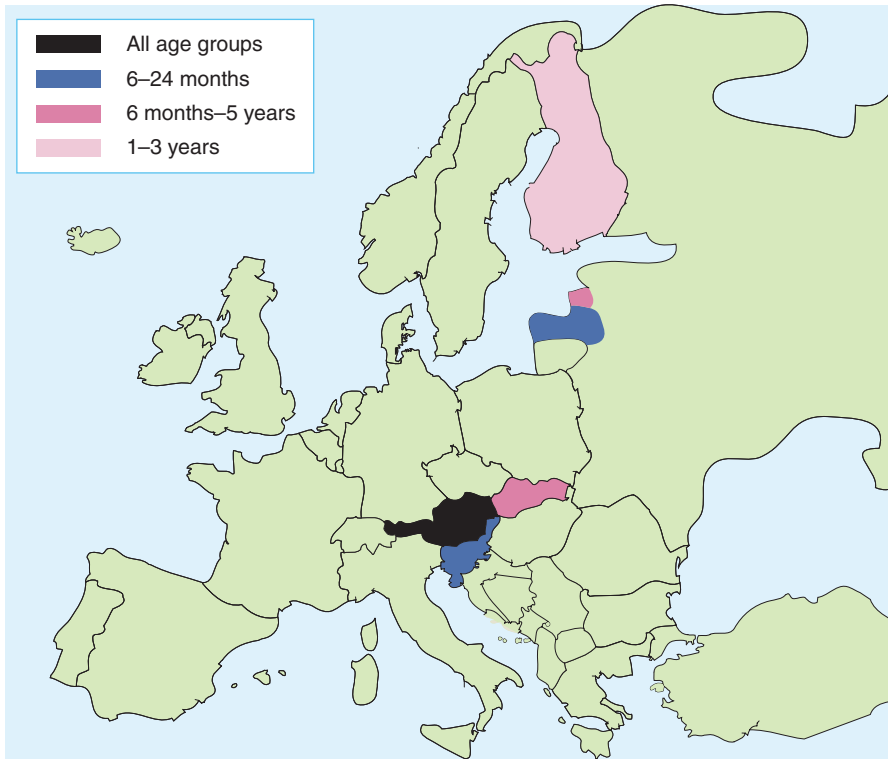


Figure 3. Vaccination recommendations for children in Europe (six member states).

Summary & conclusion

This review disclosed the principal arguments of influenza vaccination in regard to target groups, including the elders, people with underlying chronic diseases, healthcare workers and children in Europe.

The risk of severe complications due to influenza illness is strongly augmented in the elderly population. There is plenty of evidence that vaccination against influenza is an effective approach to prevent older people from the high burden of the disease. The WHO resolution for immunization set the aim for vaccine coverage of 75% by 2010/2011. Coverage of the population with chronic illnesses below 65 years of age persisted in lower vaccination levels than in the elderly. Nevertheless, the literature suggests a reduced risk of severe adverse outcomes if these chronically ill patients get vaccinated. Healthcare workers are known to reveal a very low vaccine-uptake level. Vaccination of healthcare staff should be stronger promoted in order to protect the workers themselves or their patients. Little data in regard to influenza vaccination of children are available. Most studies originate from outside Europe. Children indicate a very high attack rate during influenza outbreaks and vaccination could prevent not only the risk of complications but also the transmission to family members and the community. Accordingly, influenza vaccination coverage rates vary considerably among European countries and target groups.

The health system across Europe is complex and, hence, governmental policies regarding immunization differ from each other. Nevertheless, strong vaccination recommendations are not the only cornerstone for successful vaccine-uptake rates in the population.

Despite universal influenza vaccination for all age groups in Austria, uptake rates remain considerably low [76]. The very high uptake achieved in the UK may be ascribed by financial incentives given to general practitioners and a regular coverage monitoring with feedback to local primary-care trusts [77]. Hence, even the best vaccination guideline is only as good as the program having been implemented by the government.

The surveillance of vaccine coverage is one way to increase the coverage in itself. However, in order to achieve and maintain an adequate immunization level in the population, it is important to conduct routine surveys in order to monitor annual influenza vaccination uptake. Different approaches to conduct surveys are available (medical records, surveys, data from the pharmaceutical industry and sales data), but the selection of the appropriate methodology depends on various factors. Hence, distinct approaches for influenza coverage surveillance make the intercountry comparison challenging [79].

It is difficult to evaluate the impact of advertisement on the decision of getting vaccinated or not. In several countries, specific information resources regarding influenza vaccination have been implemented, including posters or leaflets, as well as mass media campaigns that are supported by different sources [8].

In a number of European countries, the national government fund partial or all of the cost of the influenza vaccine and the administration fees in the at-risk groups, including older individuals, chronically ill patients, occupational groups and children [8]. From the literature, it is known that free supply of the vaccine is a strong driving force for people to get vaccinated [29,54,78,79].

Strong efforts have to be undertaken at national and international levels to enhance coverage rates in all target groups to realize the aims of the WHO in 2010/2011. To achieve this goal, scientific advice, surveillance and international collaboration in the area of vaccination could lead to a step forward in combating against the burden of influenza disease in the future.

Expert commentary

The vaccine uptake across European target groups differs widely and is, in most states, far from the 75% influenza vaccination-coverage target [29]. A high immunization level would not only diminish the mortality and overall disease burden of influenza, but also enhance the manufacturing capacity for producing life-saving vaccines in case of an influenza pandemic. Different approaches have to be taken into consideration to improve vaccine-uptake levels in Europe, including a precise definition of the at-risk groups, the scientific point of view on the impact of vaccination and the demand on studies on driving forces and barriers toward vaccination. If we

are aware of the fact that healthcare professionals play a principal role in advising the at-risk population to get vaccinated, coverage rates could be improved by hospital staff who are more active in recommending the vaccine. Furthermore, information and education campaigns with regards to influenza disease and the vaccines as well as the contribution of healthcare workers in these vaccination campaigns could lead to a positive development of the seasonal influenza vaccination-coverage levels in Europe.

Five-year view

In the next few years, vaccination coverage rates should be strongly enhanced to prevent severe complications and death due to influenza illness mainly in target groups.

When data on the epidemiology of the disease and the vaccines' benefits are available, especially in at-risk groups, such as elderly patients, individuals with chronic medical conditions, healthcare

workers or children, national and international authorities can establish more precise guidelines. The expansion of vaccination policies could include lowering the cut-off age to 50 years and providing financial incentives for all target groups. Routine surveillance of influenza manifestation and monitoring of the effectiveness of influenza vaccination should be performed across all European countries. These could be areas to target for increased vaccine uptake in the at-risk population in Europe.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Key issues

- Annual vaccination is the most cost-effective method to prevent and control influenza spread.
- Vaccination-coverage rates vary considerably between European countries.
- In order to enhance vaccination coverage rates, particularly in the at-risk groups, immunization programs are implemented by national and international authorities.
- The WHO determined a target for the elderly to achieve 75% by 2010/2011.
- No WHO target has been set for the population with chronic illnesses.
- Healthcare workers indicate low vaccine coverage even though their recommendation is the primary motivation for people getting vaccinated.
- The burden of disease in children is still underestimated and data on vaccination coverage rates are urgently required.

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