European decision-maker perspective with regard to influenza prevention policies

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Keywords

Vaccination • Public Health policy • European Union • Epidemiological monitoring

Summary

Influenza is a public health priority in Europe. The impact of influenza pandemics on public health is very high, but seasonal influenza also constitutes an important burden in terms of hospitalisation and excess deaths. Influenza vaccination is a fundamental pillar of disease prevention. In the absence of a clear decision-making process for vaccination policies, EU institutions have, in recent years, fostered collaboration among Member States. Such collaboration was closer during the 2009 pandemic, which constituted a clear cross-border threat to EU citizens' health. The EU institutions have been supporting national vaccination programmes by providing evidence of the effectiveness and safety of influenza vaccination. Decision 1082/2013 was a major step toward EU collaboration, in that it highlighted the role of pandemic vaccination in the field of preparedness and emergency response, in which concerted action is clearly valuable.

Introduction

Influenza prevention is a public health priority worldwide. In Europe, seasonal influenza causes between 4 and 50 million symptomatic cases each year and the death toll associated with influenza is estimated at between 15,000 and 70,000 every influenza season, in terms of excess deaths [1]. The impact of influenza is even greater in the case of pandemics, when large population age-groups – if not the entire population – are immunologically naïve toward the pandemic viral strain. During the 2009 H1N1 pandemic, 2,900 deaths directly related to influenza were reported by the European Union (EU) Member States during the first 12 months [2], but the increase in mortality rates related to the pandemic virus is estimated to be larger. In addition, the high number of cases occurring in a short period of time places a heavy load on the healthcare system during the influenza season.

Preventive measures to limit the spread of influenza include both individual and public health interventions. Frequent hand-washing and correct respiratory hygiene have proved to be effective in preventing respiratory illnesses, including influenza [3, 4]. However, influenza vaccination is still the main tool for preventing the spread of influenza spread and limiting the burden on public health. In the US, routine annual influenza vaccination is recommended for all persons aged ≥ 6 months who do not have contraindications [5]. Recommendations are more limited in the EU, and vary widely among Member States [6].

This paper presents an overview of the European approach to influenza prevention and describes the point of view of European decision-makers regarding both seasonal and pandemic prevention policies.

The EU decision-making process with regard to vaccination policies

In the EU, responsibility for immunisation programmes, including immunisation schedules, their mandatory or voluntary character and their financing, lies with the individual Member States. As clearly stated in art. 168 of the Lisbon Treaty, harmonisation of national laws and regulations in the field of human health promotion is excluded. On the other hand, the same article reads "The Union shall encourage cooperation between the Member States […] and, if necessary, lend support to their action. It shall in particular encourage cooperation between the Member States to improve the complementarity of their health services in cross-border areas" [7]. Definitively, even though decisions on vaccination issues are taken essentially at the national level, there may nevertheless be some room for action at the European level in terms of support and cooperation between national and EU decision-makers.

During the last few years, for the first time since the foundation of the EU, some pieces of legislation have been delivered by EU institutions in the specific area of vaccination programmes. Specifically, in 2011 and 2014, two Council Conclusions were delivered during the Employment, Social Policy, Health and Consumer Affairs Council meeting under, the Hungarian and Italian Presidencies, respectively. These two Council Conclusions both move in the direction of fostering the ef-

forts of EU Member States to strengthen vaccination programmes, thus underlining the great importance and societal value of immunisation [8, 9]. More importantly, in December 2009, a few months after the declaration of the H1N1 pandemic, a recommendation on seasonal influenza vaccination was issued by the Council of the EU [10]. In this recommendation, EU Member States "are encouraged to adopt and implement […] action plans or policies […] aimed at improving seasonal influenza vaccination coverage, with the aim of reaching, as early as possible and preferably by the 2014-2015 winter season, a vaccination coverage rate of 75% for 'older age-groups' and, if possible, for other risk groups […]. Member States are also encouraged to improve vaccination coverage among healthcare workers". Moreover, Member States should draw up specific action plans aimed at monitoring influenza vaccine coverage and investigating the reasons for low adherence to vaccination. Even though Council recommendations are not binding on the Member States, this recommendation on influenza vaccination is nevertheless the first of its kind in the field of vaccines, and demonstrates the great interest of European decision-makers in influenza prevention. Indeed, the seasonal influenza coverage rates reported by EU Member States are widely variable and mostly suboptimal. There is no statutory system for collecting and monitoring adherence to influenza vaccination in the EU. For this reason, a network of experts (VENICE consortium, Vaccine European New Integrated Collaboration Effort) [11] supported by a grant from the European Centre for Disease Prevention and Control (ECDC) started a regular survey in 2006 to collect, among other data, information on influenza vaccine coverage. The results of the VENICE influenza surveys are publicly available at the VENICE website [11]. Two major issues arise from the analysis of vaccine coverage data. Firstly, only in the Netherlands and some parts of the United Kingdom is the target of 75% of vaccination coverage among elderly people reached. Moreover, data are available from 23 Member States only, and not from all influenza seasons. On the other hand, comparison of the available data on vaccination coverage in the general population in 2008-2009 (seasonal) and in 2009-2010 (pandemic), reveals some evidence that, during a pandemic, vaccination levels are very similar to those reached during a normal influenza season. It would appear that the same people who receive seasonal influenza vaccines are reached during pandemic vaccination programmes. Therefore, pandemic influenza vaccination is better implemented where a well-functioning seasonal influenza vaccination programme is already in place. This evidence supports the need to strengthen seasonal influenza vaccination programmes as part of preparedness plans for future pandemics. Pandemic influenza preparedness plans are a clear area of intervention for EU institutions, since an influenza pandemic is a typical cross-border threat [7]. Therefore, in addition to the clear benefits yielded by a strong seasonal influenza vaccination programme, this is a good reason for the EU to support Member States in improving their programmes.

How EU can support national influenza programmes

The EU decision-maker has limited power to influence national vaccination policies. On the other hand, influenza prevention is perceived as a priority at the EU level because of the potential pandemic threat and its subsequent cross-border issues. As a consequence, the role of the EU – also fostered by the 2009 Council Recommendation – has been to support national vaccination programmes by providing evidence of the effectiveness and safety of influenza vaccination. The perceived low effectiveness of influenza vaccines and the fear of alleged adverse events are considered the main obstacles to improving vaccination adherence. Providing national vaccination programme managers with reliable data on post-marketing evaluation of influenza vaccines may constitute an evident added value. To this end, the ECDC has funded the I-MOVE project [12]. Since the 2008-9 influenza season, I-MOVE has provided estimates of vaccine effectiveness that are usually available a few months after the end of the season. Thanks to a standardised protocol and a fairly large number of participating study sites, these estimates have good geographical representativeness [13]. In addition, only as a result of European collaboration can the study population reach a size large enough to yield robust estimates.

As expected, influenza vaccine effectiveness is strongly dependent on the quality of matching between vaccine strains and circulating virus strains. This was particularly evident during the 2009 pandemic, when the only circulating strain was the pandemic one and vaccine effectiveness was particularly high, reaching 78.4% (95% CI 54.4-89.8) in patients aged < 65 years [14]. Definitively, vaccine effectiveness estimates obtained from such collaborative studies can provide good-quality evidence to support communication. A real perception of the effectiveness of influenza vaccines is a prerequisite to communicating the real benefits of influenza vaccination to the public. Indeed, suboptimal effectiveness – during some seasons it may be even lower than 50% – may be negatively perceived at the individual level, even though the impact of the vaccination programme on public health may be considerable in terms of the lowered global burden of disease.

Vaccine safety issues are another potential obstacle to influenza vaccine acceptance. Indeed, vaccines, unlike other drugs and medical interventions, are administered both to healthy subjects and to fragile individuals, such as very young children and elderly people. For this reason, any potential safety issue is usually overestimated and the fear of alleged adverse events following immunisation (AEFI) is the main reason why many people are sceptical towards vaccination. Vaccine safety monitoring is strictly regulated in the EU, with the European Medicine Agency (EMA) playing a crucial role, especially during the pre-marketing phase [15]. On the other hand, monitoring and assessing vaccine safety during the post-marketing phase may present some challenges in the absence of a clear commitment. Responsibility for

post-marketing surveillance is shared between pharmacovigilance authorities and vaccine producers. The basic system of AEFI surveillance is constituted by the statutory pharmacovigilance system – shared with all other drugs – present in all EU Member States and coordinated by the EMA through the Eudravigilance system [16]. This is a routine passive surveillance system, which is good enough to detect clear safety signals, but not sufficiently well designed to support vaccine programme managers who deal with vaccine hesitancy or anti-vaccine lobbies. For this purpose, pre-emptive strategies are needed, and good evidence on alleged adverse events should be rapidly available to vaccine managers.

Post-marketing studies to assess vaccine safety are complex and expensive. EU-wide collaboration in this field is a clear added value, as recently demonstrated after the marketing of A(H1N1) pandemic vaccines. The VAESCO consortium (Vaccine adverse events surveillance and communication) – a consortium of public health institutions sponsored by the ECDC [17] with the purpose of starting a European collaboration in the field of post-marketing vaccine surveillance – assessed the risk of Guillain-Barré syndrome (GBS) by means of a multinational case-control study [18] followed by a prospective self-controlled case series study [19]. The conclusion of both studies was that the risk of GBS was not significantly elevated after influenza A(H1N1) pandemic vaccination; this research was made possible only by EU collaboration, which ensured a population size large enough to achieve the necessary study power [19]. Finally, the valuable role of the EU was clearly shown when an unexpected increase in narcolepsy cases was reported in Finland and Sweden in 2010, after vaccination with Pandemrix® [20]. In that case, too, the EU committed a substantial amount of resources to assessing the narcolepsy signal. The VAESCO consortium conducted an ECDC-sponsored study in six EU Member States, which provided evidence of the association between narcolepsy cases in adolescents and Pandemrix® vaccination [21].

Vaccination as a preparedness measure against cross-border threats

Although the EU institutions cannot make any attempt to harmonise human vaccination practices, they should foster cooperation between Member States with regard to cross-border health threats. The level of cooperation and the limits of EU coordination in this field were recently defined by the Decision of the European Parliament and of the Council N° 1082/2013/EU on serious cross-border threats to health [22]. The Decision, which is binding and is to be implemented at the national level, provides the EU Member States with four benefits: 1) preparedness planning capacity should be reinforced, to ensure that all Member States are adequately prepared in the event of an emerging crisis; 2) risk assessment and management should be improved at the national level, with the support of the EU agencies responsible (ECDC, EMA etc.); 3) a new mechanism for the joint procurement of vaccines and medicines in the event of a health emergency is in place, in order to ensure the provision of emergency vaccine/medications in all Member States; 4) the response at the EU level will be coordinated by the Health Security Committee, which has a solid legal mandate to quickly take decisions in the event of an emergency.

Decision 1082 constitutes a major step toward EU collaboration in the field of infectious disease prevention. In particular, two main principles regarding vaccination are evident: a) vaccines are an important component of emergency preparedness; b) a mechanism for purchasing vaccines through EU joint procurement is in place, which also provides a clear advantage deriving from the economy of scale. In particular, seasonal influenza vaccination should be an important component of pandemic preparedness, since a strong vaccination system for seasonal influenza is clearly necessary in order to achieve good coverage during a pandemic. In addition, the joint procurement mechanism has been specifically set up to support the weaker Member States, which may have difficulty purchasing pandemic vaccines. This demonstrates that the EU decision-maker does acknowledge the strategic role of influenza vaccination in preparing Europe to tackle the pandemic threat.

Conclusions

EU decision-making in the field of influenza prevention, as well as of all other vaccination policies, is not clearly established. Nevertheless, there is quite large room for collaboration, especially in the field of post-marketing vaccine surveillance. In addition, there is a clear added value in the area of emergency preparedness and response, in which common EU policies, and even the joint procurement of vaccines, are ensured in the event of a pandemic.

Acknowledgments

No funding declared for this overview.

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■ Received on January 14, 2016. Accepted on February 22, 2016.

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