Seasonal influenza is widely regarded as a continuing threat to public health, with vaccination remaining the principal measure of prophylaxis. In 2003, the World Health Organization issued targets for influenza vaccine coverage in the elderly of at least 50% by 2006 and 75% by 2010, endorsed by the European Parliament in two resolutions in 2005 and 2006. However, a number of European public health systems lack mechanisms to assess progress in influenza vaccine uptake. The European Vaccine Manufacturers group (EVM) undertook a Europe-wide survey of vaccine distribution over the last five seasons (between 2003 and 2008) to provide baseline data from which vaccination trends may be extrapolated. The survey data showed that the dose distribution level per capita in the 27 EU countries increased from 17% in 2003-4 to 20% in 2006-7; this growth was not maintained in the season 2007-8. Even without information on which age or risk groups received the vaccine, an immunisation rate of approximately 20% of the whole population falls short of the public health goal by more than half: an estimated 49% of the total population fall into risk groups recommended to receive the influenza vaccine in Europe. These data provide the only systematic review of vaccine dose distribution across Europe from a uniform source. Although they represent an important baseline parameter, age- and risk-group related vaccine uptake data with sufficient detail are needed to assist public health policy decision making, immunisation planning and monitoring. In light of this situation, and to support the improvement of policy decision making, immunisation planning and monitoring, vaccination rates across the EU, EVM aims to provide dose distribution data for each influenza season to assist Member States in the implementation of local immunisation policies.

Introduction

Annual influenza epidemics continue to pose a substantial threat to public health. In Europe, estimates suggest that influenza is responsible for between 40,000 excess deaths in a moderate season and up to 220,000 during a severe epidemic [1]. Despite the recent focus on pandemics and accompanying extensive coverage in the media, seasonal influenza is responsible for many more deaths than those caused by influenza pandemics [1]. Consequently, the World Health Organization (WHO) and the Member States of the European Union (EU) recommend annual influenza vaccination for those at high risk of complications. A survey conducted in 2006 by the European Centre for Disease Prevention and Control (ECDC) among EU and European Economic Area (EEA) countries found that in the 23 Member States that responded, immunisation was recommended for the two largest groups targeted by WHO: the elderly above a nationally defined age limit (often 65 years but in some cases 60 or 50 years) and those over the age of six months with chronic illnesses such as heart or lung disease [1,2].

In 2003, the 56th World Health Assembly (WHA) recognised that influenza epidemics “cause fatal complications in up to one million people each year” and “that many of these deaths could be prevented through increased use, particularly in people at high risk, of existing vaccines, which are safe and highly effective”. The WHA urged its member states to increase immunisation against seasonal influenza, and set a coverage target of at least 50% of the elderly by 2006, rising to 75% by 2010 [3]. In October 2005 and June 2006 the European Parliament adopted resolutions calling on the Member States to increase influenza vaccination in line with the WHO recommendations [4,5]. With these guidelines in place, Ryan et al. estimated that risk groups recommended for vaccination against influenza every year accounted for up to 49% of the population of the 25 EU countries in 2006, or 223 million people [6].

Despite these guidelines and targets, no Europe-wide systematic data are available to monitor vaccine uptake. Monitoring is conducted in only some Member States. Furthermore, there is no system to allow performance comparisons across the EU. Consequently, following a request from the European Commission, the European Vaccine Manufacturers group (EVM) surveyed suppliers in the region to provide baseline data on influenza vaccine distribution in the EU. These data represent a valuable indirect measure of vaccine use, and as such can be utilised by public health policy makers in conjunction with information on local vaccination recommendations, implementation measures and reimbursement criteria to assess gaps in provision and improve coverage where necessary.

Methods

In 2008, EVM issued a standardised, retrospective survey to its member companies (Baxter, Crucell, GlaxoSmithKline Biologicals, Novartis Vaccines, Sanofi Pasteur, Sanofi Pasteur MSD, Solvay, and Wyeth) and the Australian company CSL Biotherapies, who collectively supply nearly all of the influenza vaccines distributed in Europe, with the exception of Hungary and Romania, which each have a national producer. The survey was designed to assess the total number of doses supplied to each of the 27 EU Member States during the last five influenza seasons. The supply period was defined by influenza seasons rather than calendar years to reflect immunisation practise: in temperate zones influenza occurs in...
epidemics during the winter and each influenza season consequently straddles the end of one calendar year and the beginning of the next. In the United Kingdom (UK), the study utilised data provided by the local national vaccine industry group (UVIG), which were collected by a similar methodology.

Data were collected covering the five influenza seasons from 2003-4 to 2007-8, which represent the period since the establishment of the WHA targets for influenza vaccine coverage in the elderly. To ensure full compliance with competition law, the manufacturers submitted dose distribution information to a single, independent collection point, where the data were aggregated and anonymised before further analysis was undertaken by the survey group. To determine the level of dose distribution per unit of population, the Eurostat database was accessed to ascertain the number of inhabitants of each of the 27 EU countries on the first of January each year during the survey period (1/1/2003; 1/1/2004; 1/1/2005; 1/1/2006; and 1/1/2007).

Results

The five-year dataset generated by the survey provides a comprehensive picture of influenza vaccine distribution and supply trends in the EU.

Dose distribution: macro-analysis

Throughout the study period, the total number of doses distributed across the region showed a general growth trend, rising from 81.1 million at the lowest point in 2004-5 to a peak of 98.6 million in 2006-7 (Figure 1). However, this overall trend was non-uniform with a slight drop in supply between the first and second year of the surveyed period, and a similar decrease in the last two years of the study (2006-7 to 2007-8).

When comparing these data against the number of doses that would be required to cover the proportion of the population at risk that is recommended for vaccination in Europe (up to 49.1% for the EU25; ranging from 41.6% in Cyprus to 56.4% in the UK [6]) it became clear that neither the EU Member States collectively (Figure 2) nor any individual country (Figure 3) sustained this level. Throughout the survey period, sufficient doses to immunise the entire at-risk population were available only during one season in a single country: during a substantial increase in supply in Malta in the 2005-6 season (Figure 3). Across the EU as a whole, the dose distribution level *per capita* reached above 20% in a single season during the study period; the level of supply required to immunise all those in at-risk groups was not reached in any of the years (Figure 2).

Dose distribution: by country

The country data show wide variations in distribution between different EU Member States. Not surprisingly, the five largest countries (France, Germany, Italy, Spain and the UK) accounted for the majority of doses distributed in the EU region. Regarding the number of distributed doses, these countries received a consistent share of the total, amounting to approximately 75% in each season (ranging from 74.7% in 2004-5 to 76.6% in 2005-6). Based on the population of these countries, this corresponds to a greater than representative proportion as their aggregate population remained steady during the period, with just over 62% of the total inhabitants of the 27 EU countries.

Disproportionate vaccine distribution is even more evident when the data are analysed in conjunction with the Eurostat database; the supply per unit of population shows wide variance between countries, in some Member States from year to year (Figure 3). Of particular note is the dramatic, albeit unsustained, increase in dose distribution in Malta in 2005-6, during a season of robust policy support targeting at-risk groups. Also noteworthy is the trend towards higher distribution in the EU15 countries versus the newer Member States. However, this is confounded to some degree by the relatively lower supply in some of the Nordic countries.

Discussion

This study provides for the first time a systematic view, drawn from a uniform source, of seasonal influenza vaccine distribution across Europe. While a number of methodological limitations
necessarily exist, these data nonetheless represent an important baseline against which the implementation of immunisation guidelines in the Member States may be assessed.

The survey group performed a number of quality audits, including an assessment against information compiled by national vaccine industry groups. However, a number of methodological limitations remain:

• Although vaccine supply and coverage are likely to be inextricably linked, the survey data represent the total number of doses distributed per country rather than the direct uptake in specific groups recommended for immunisation.

• The data necessarily provide an overestimation of vaccine coverage as a small percentage of doses remain unused and/or are returned each year. This proportion varies from year to year and by country (ranging from approximately 0 to 10%) and can be determined accurately only for those territories with centralised purchasing systems.

• The data for Hungary and Romania include the doses supplied by EVM survey participants, but not those supplied by local Hungarian and Romanian manufacturers.

Notwithstanding, the study reveals a clear variance in vaccine distribution between the 27 EU countries, with a trend towards greater provision in the EU15 Member States. However, it is noteworthy that these generally higher levels of supply per capita are not consistent, and whilst detailed economic analysis is beyond the scope of this paper, distribution levels do not appear to follow a simple direct correlation with economic development status. For instance, during the last three years of the study, Malta consistently achieved the highest levels of supply per capita throughout the EU27, while Cyprus and, in the latter years of the survey, Romania had a performance similar to those of several EU15 countries. Similarly, distribution levels in Denmark and Sweden were below those in many other EU15 Member States, including the five largest (France, Germany, Italy, Spain and the UK). These confounders suggest that a more subtle blend of factors relating to immunisation policy implementation influence overall vaccine supply, rather than a simple linear correlation with income.

At the macro level, the data collected over the 2003-4 to 2007-8 influenza seasons describe a modest growth in the dose distribution level per capita (from approximately 17% to just under 20%). However, while this trend is encouraging, the distribution rates both at the European and Member State level remain substantially below the rates required to immunise the estimated 49% of the population recommended for seasonal influenza vaccination [6].

Given the serious and ongoing threat posed by annual influenza epidemics, improving immunisation coverage remains an important policy objective for WHO and the EU. Achieving this will require concerted efforts at the national level to ensure the effective implementation of existing guidelines. In some countries the current recommendations will need to be adapted to encompass all those who are at risk.

Previous research conducted in 11 European countries identified a number of key factors that would motivate at-risk populations to seek influenza vaccination [7]. Most important was the proactive recommendation by a healthcare professional, followed by information on the disease and the vaccine, and adequate funding to reimburse patients for vaccination or to make it cheaper. Notably, the three countries in which authorities provided low or no funding for seasonal influenza vaccination achieved the lowest coverage levels [7].

Based on a recognition at the national level of the need for robust vaccination policies, combined with long-term commitment to their effective implementation, vaccine production and distribution capacity can expand to meet the challenge of improving coverage.
rates. While increasing capacities is a long-term process requiring significant investment, it is clear from historical data that vaccine distribution can increase dramatically to meet demand: notably, during the period 1994–2003, global distribution of influenza vaccines more than doubled [8].

Conclusion
With influenza continuing to pose a public health challenge, the introduction of robust vaccine monitoring systems represents an important step to assess progress in reaching immunisation goals in Europe, and to inform public health decision making for improving protection across the region. This survey provides for the first time a unique view of vaccine supply throughout the EU. The data demonstrate significant differences in vaccine distribution between European countries. With some variation, the results indicate that immunisation in many countries often does not even reach half of those who are considered by national authorities to be at high risk of complications from influenza infection. However, complementary surveys with age- and risk-group specific information will be needed to focus national health interventions on the specific drivers and hurdles for influenza immunisation. Analysis of the study data in conjunction with local recommendations, reimbursement processes and public health communication campaigns should provide valuable insights into the efficacy of vaccination policies in the Member States. EVM aims to provide systematic supply data on a regular basis which will complement national efforts to assist policy makers in determining the most effective approaches to improving vaccination levels amongst those at risk from seasonal influenza.

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