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Survey of distribution of seasonal influenza vaccine doses in 201 countries (2004–2015): The 2003 World Health Assembly resolution on seasonal influenza vaccination coverage and the 2009 influenza pandemic have had very little impact on improving influenza control and pandemic preparedness

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ABSTRACT

There is no global monitoring system for influenza vaccination coverage, making it difficult to assess progress towards the 2003 World Health Assembly (WHA) vaccination coverage target. In 2008, the IFPMA Influenza Vaccine Supply International Task Force (IVS) developed a survey method to assess the global distribution of influenza vaccine doses as a proxy for vaccination coverage rates. The latest dose distribution data for 2014 and 2015 was used to update previous analyses. Data were confidentially collected and aggregated by the IFPMA Secretariat, and combined with previous IFPMA IVS survey data (2004–2013). Data were available from 201 countries over the 2004–2015 period. A "hurdle" rate was defined as the number of doses required to reach 15.9% of the population in 2008. Overall, the number of distributed doses progressively increased between 2004 and 2011, driven by a 150% increase in AMRO, then plateaued. One percent fewer doses were distributed in 2015 than in 2011. Twenty–three countries were above the hurdle rate in 2015, compared to 15 in 2004, but distribution was highly uneven in and across all WHO regions. Three WHO regions (AMRO, EURO and WPRO) accounted for about 95% of doses distributed. But in EURO and WPRO, distribution rates in 2015 were only marginally higher than in 2004, and in EURO there was an overall downward trend in dose distribution. The vast majority of countries cannot meet the 2003 WHA coverage targets and are inadequately prepared for a global influenza pandemic. With only 5% of influenza vaccine doses being distributed to 50% of the world's population, there is urgency to redress the gross inequities in disease prevention and in pandemic preparedness. The 2003 WHA resolution must be reviewed and revised and a call issued for the renewed commitment of Member States to influenza vaccination coverage targets.

1. Introduction

Influenza is unique amongst vaccine-preventable diseases, in that annual vaccination is necessary for optimal prevention of disease. Antigenic shift occurs less frequently but when it does occur, a global influenza pandemic can ensue. There were three global pandemics in the last century: 1918–1920, 1957–1958, 1968–1969 [1]. The last global pandemic occurred in 2009–2010 [2].

Influenza vaccines have been commercially available since the 1940s [3], but their use has been highly disparate between countries. Seasonal influenza vaccination coverage has remained very modest compared to other routinely administered vaccines. In Europe, one estimate put overall coverage in target groups at less than 45% [4], and some countries have as little as 1% coverage for some target groups [5]. This contrasts with vaccination coverage rates of

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greater than 95% for some routine pediatric vaccines in the EU 28 countries [6].

In 2003, the World Health Assembly (WHA) urged member states with influenza vaccination policies to provide influenza vaccination to high risk groups and to achieve a vaccination coverage rate of 75% in the elderly [7].

Since 2003, the Council of the European Union issued a recommendation for Member States to achieve 75% coverage in the elderly and other risk groups, and to improve the vaccination coverage in health care workers by the 2014–2015 influenza season [8]. In the USA, the 'Healthy People 2020' programme target for influenza vaccination coverage is 70% of all persons ≥6 months of age [9].

There is no global monitoring system for influenza vaccination coverage, making it difficult to assess progress towards the WHA or other vaccination coverage targets. In 2008 the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Influenza Vaccine Supply International Task Force (IVS) developed a survey method to assess the global distribution of influenza vaccine doses as a proxy for vaccination coverage rates [10]. By using a threshold of 159 doses per 1000 population (the "hurdle rate" or number of doses required to vaccinate persons 65 years or older, based on average age distribution in industrialized countries in 2008), the survey classified countries into low and high distributing countries [10].

Previous quantitative analyses from the IFPMA IVS surveys have found that inequitable dose distribution has persisted across WHO regions since the 2003 WHA resolution [11]. Most notably, SEARO, EMRO and AFRO accounted for less than 5% of the distributed doses but almost half of the global population [12]. In the AMRO, EURO and WPRO regions, where about 95% of the doses were distributed, distribution has been steadily rising in AMRO; peaked in WPRO in 2010 and has remained flat since; and has trended downward in EURO since 2008 [11]. The qualitative analyses conducted so far have revealed that vaccine recommendations alone do not translate into high vaccine coverage rates, and that vaccination coverage rates do not correlate well with countries' income levels [10]. On the other hand, there is some evidence that patient reimbursement and programme communications are associated with higher vaccination coverage [10]. There is also evidence that the active real time management of vaccination programmes and strong political commitment to vaccination are important enablers of vaccination, whilst the lack of access to vaccination and weak government commitments constitute barriers [11].

In this paper, we augment the previous analyses with the latest data on seasonal influenza doses distributed in 2014 and 2015.

2. Methods

The survey methodology was previously described in Palache et al. [10]. Member companies of the IFPMA IVS (Abbott Biologicals, Adimmune Corporation, Biken, Denka Seiken, GlaxoSmithKline Biologicals, Green Cross Corporation, Hualan Biological, Kitasato Daiichi Sankyo Vaccine, MedImmune, Nanotherapeutics, Protein Sciences Corporation, Saint-Petersburg Scientific Research Institute of Vaccines and Sera, Sanofi Pasteur, Seqirus, Sinovac, and Takeda), who manufacture and supply the vast majority of the world's seasonal influenza vaccines, agreed to provide information on the doses of seasonal influenza vaccine supplied to all WHO Member States during 2014 and 2015. The survey results were confidentially collected and aggregated by the IFPMA Secretariat, in compliance with anti-trust regulations. The resulting anonymized database was then combined with the results of the previous IFPMA IVS surveys (2004–2013). Data were available from 201 countries over the 2004–2015 period but data from all countries was not always available in each year.

2.1. Absolute number of doses distributed

Doses distributed by country and by year were both aggregated and categorized into WHO regions.

2.2. Doses distributed per 1000 persons

Doses distributed to each country were then related to a population of 1000, using population data from the United Nations' (UN) statistics database, and analysed by WHO region [13]. To identify countries with sufficient vaccine supply to deliver vaccines to their elderly population (≥65 years), a "hurdle" rate was defined as the number of doses required to reach 15.9% of the population in 2008 (the estimated proportion of elderly in 'more developed countries'), or 159 doses per 1000 persons [10].

2.3. Number of countries above the hurdle rate

The number of countries above the hurdle rate in 2004 was contrasted with the number above in 2015. In addition, an examination was made of regional rates above and below the hurdle rate.

2.4. Compound annual growth rate of doses distributed per 1,000 persons between 2004 and 2015

Compound annual growth rate (CAGR) between 2004 and 2015 was calculated or countries above the hurdle rate in 2004 and in 2015 using Microsoft Excel, where:

$$\text{CAGR} = [(\text{rate per 1000 in } 2015 - \text{rate per } 1000 \text{ in } 2004)^{1/11} - 1] \times 100$$

CAGR was also calculated by region using the annual number of doses distributed per 1000 persons in each region between 2004 and 2015.

2.5. T-test comparisons between dose distribution in 2004 and 2015

Two-sided, paired, *T*-test comparisons were performed between rates of doses distributed/1000 population in 2004 and 2015, by WHO region, using Microsoft Excel.

2.6. Correlation between dose distribution and GNI in a WHO region

Correlation between doses per 1000 population and country gross national income per capita (GNI) [13] in a region, was calculated in Microsoft Excel.

3. Results

3.1. Absolute number of doses distributed

The total number of doses distributed in 2004 was approximately 262 million and this had risen to about 486 million in 2015, an 86% increase (Fig. 1). A maximum number of doses distributed was achieved in 2014, yet 1% fewer doses were distributed in 2015 than in 2011 (Fig. 1).

3.2. Absolute number of doses distributed by WHO region

The overall growth in the number of doses distributed has largely been driven by an increase in AMRO (a 150% increase between 2004 and 2015) (Fig. 2). The share of doses distributed to AMRO has increased, from about 41% in 2004 to 55% in 2015, whereas

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