



Seasonal influenza vaccine dose distribution in 195 countries (2004–2013): Little progress in estimated global vaccination coverage



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ABSTRACT

Seasonal influenza is an important disease which results in 250,000–500,000 annual deaths worldwide. Global targets for vaccination coverage rates (VCRs) in high-risk groups are at least 75% in adults ≥ 65 years and increased coverage in other risk groups. The International Federation of Pharmaceutical Manufacturers and Associations Influenza Vaccine Supply (IFPMA IVS) International Task Force developed a survey methodology in 2008, to assess the global distribution of influenza vaccine doses as a proxy for VCRs. This paper updates the previous survey results on absolute numbers of influenza vaccine doses distributed between 2004 and 2013 inclusive, and dose distribution rates per 1000 population, and provides a qualitative assessment of the principal enablers and barriers to seasonal influenza vaccination. The two main findings from the quantitative portion of the survey are the continued negative trend for dose distribution in the EURO region and the perpetuation of appreciable differences in scale of dose distribution between WHO regions, with no observed convergence in the rates of doses distributed per 1000 population over time. The main findings from the qualitative portion of the survey were that actively managing the vaccination program in real-time and ensuring political commitment to vaccination are important enablers of vaccination, whereas insufficient access to vaccination and lack of political commitment to seasonal influenza vaccination programs are likely contributing to vaccination target failures. In all regions of the world, seasonal influenza vaccination is underutilized as a public health tool. The survey provides evidence of lost opportunity to protect populations against potentially serious influenza-associated disease. We call on the national and international public health communities to re-evaluate their political commitment to the prevention of the annual influenza disease burden and to develop a systematic approach to improve vaccine distribution equitably.

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1. Introduction

Seasonal influenza is an important disease which results in 250,000–500,000 annual deaths worldwide [1], of which about 28,000–111,500 are in children < 5 years of age, predominantly in developing countries [2]. Adults aged 65 years or older, pregnant women, and people of any age with underlying medical

conditions, are at high risk of severe disease or complications [1]. Licensed influenza vaccines are safe and efficacious and are recommended by the World Health Organization (WHO) in priority for pregnant women, children aged between 6 and 59 months, the elderly, individuals with specific underlying medical conditions, and health-care workers [2]. Some countries are progressively expanding the recommended population, with the USA having moved to routine vaccination of any individual > 6 months of age since 2010 [3]. Global targets for vaccination coverage rates (VCRs) in high-risk groups are at least 75% in adults ≥ 65 years and increased coverage in other risk groups [4]. Europe has set similar targets [5]. In the US a 90% target has been set for adults ≥ 65 years and 70% for persons ≥ 18 years, by 2020 [6].

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Globally, there are very limited data on influenza VCRs. Regionally, some seasonal influenza VCR data is available from PAHO (Pan-American Health Organization) for states in AMRO (region of the WHO's Americas Regional Office) [7], and in Europe, data is available for some states from the Vaccine European New Integrated Collaboration Effort (VENICE) [8]. The International Federation of Pharmaceutical Manufacturers and Associations Influenza Vaccine Supply (IFPMA IVS) International Task Force developed a survey methodology, in 2008, to assess the global distribution of influenza vaccine doses [9]. Dose distribution can serve as a proxy for VCRs where coverage data is lacking. The IFPMA IVS cumulated data on the distribution of vaccine doses from 2004 to 2011, in up to 157 countries [9–11]. Previous global vaccine dose distribution surveys suggested that VCRs were substantially below target in all regions [10,11]. Three out of six WHO regions together accounted for about 47% of the global population but only about 4% of the IFPMA IVS doses distributed [10,11]. Overall, global distribution of IFPMA IVS member vaccine doses increased by approximately 87% between 2004 and 2011, but only by approximately 12% between 2008 and 2011. Furthermore, dose distribution decreased in EURO (region of the WHO's European Regional Office) and EMRO (region of the WHO's Eastern Mediterranean Office) between 2009 and 2011. The only countries to ever report achieving seasonal influenza VCR targets in the elderly are the UK and the Netherlands [12,13], and no country has reported target VCRs in other risk groups [14,15], or in health care workers [16].

The aim of this paper is to update the results of the previous surveys, to show the evolution in the number of influenza vaccine doses distributed between 2004 and 2013 inclusive, in absolute numbers and in number of doses distributed per 1000 population, and to provide a qualitative assessment of the principal enablers and barriers to seasonal influenza vaccination, as directly experienced by countries with a significant rate of change in dose distribution.

2. Methods

2.1. Quantitative vaccine dose distribution survey

The methodology used to survey dose distribution has been previously described in Palache et al., 2011 [10]. Briefly, member companies of the IFPMA IVS (Abbott Biologicals, Adimmune Corporation, Biken, bioCSL, Janssen-Crucell, Denka Seiken, Glaxo-SmithKline Biologicals, Green Cross Corporation, Hualan Biological, Kaketsuken, Kitasato Daiichi Sankyo Vaccine, MedImmune, Novartis Vaccines, and Diagnostics, Protein Sciences Corporation, Saint-Petersburg Scientific Research Institute of Vaccines and Sera, Sanofi Pasteur, Sinovac and Takeda), which manufacture and supply the vast majority of the world's seasonal influenza vaccines, agreed to provide information on the supply of seasonal trivalent influenza vaccine doses to all WHO Member States during 2012 and 2013. To ensure compliance with anti-trust regulations, the survey results were confidentially collected and aggregated by the IFPMA Secretariat. The resulting anonymized database was then combined with the results of the previous IFPMA IVS surveys (2004–2011) [9–11].

2.1.1. Vaccine dose distribution in absolute numbers between 2004 and 2013

Doses distributed by country and by year were aggregated and then, to facilitate comparisons, were categorized by distribution to WHO region.

2.1.2. Vaccine dose distribution per population size between 2004 and 2013

To assess vaccine dose distribution in relation to each country's population size, the study utilized population data from the UN's (United Nations) statistics database [17]. Doses distributed to each country were expressed per 1000 population for 2004–2013 using the corresponding population figures from the United Nations (UN) statistics database. To facilitate comparisons, countries were then categorized by WHO region. *T*-test analyses were performed between rates of dose distribution/1000 population in 2004 and 2013, and 2008 and 2013, by WHO region.

2.1.3. Rate of change in vaccine dose distribution between 2008 and 2013

To better understand the factors influencing seasonal influenza vaccine dose distribution, countries were categorized into: previously low distribution (<159 doses per 1000 population, in 2008); and, previously high distribution (≥ 159 doses per 1000 population, in 2008). This 'hurdle' rate of 159 doses per 1000 population was previously defined as the number of doses required to vaccinate those aged 65 years or older in industrialized nations [10], and was again utilized to enable comparisons with previous surveys. For each of the two categories of country (low distribution rate and high distribution rate), the 10 countries with the highest increase in dose distribution per 1000 population, and the 10 countries with highest decrease in dose distribution per 1000 population, were singled out for analyses.

2.2. Qualitative vaccine dose distribution survey

Descriptive analysis from selected countries with a change in dose distribution rate of trivalent seasonal influenza vaccine in the last 2 years of the dose distribution survey (2012 and 2013) was collected through phone or e-mail interviews with thought leaders or policy-makers, to determine specific policies and practices associated with positive or negative trends in seasonal influenza vaccination distribution. Questions were designed to assess: national commitments to measure and increase vaccination coverage; implementation of recommendations, funding, and communications; perception of influenza and VCR; country specific barriers or drivers for VCR; and lessons learnt in the delivery of seasonal influenza vaccine.

A convenience sample of thought-leaders from seven countries was selected, based on the trend of change in vaccine dose distribution, and the ability of thought-leaders to inform on enabling policies or barriers to influenza vaccine uptake. The four countries with increasing distribution rates in the last 2 years of the survey invited to participate were: Thailand, Italy, Argentina, and the UK. The three countries with decreasing distribution rates in the last 2 years of the survey invited to participate were: the Netherlands, Switzerland and the Republic of Korea. The selection of countries was restricted to the three regions with the bulk of vaccine doses distribution (AMRO, EURO and WPRO) so that trends in dose distribution in countries from these regions could be further probed.

Persons invited to participate included: a director of a department of infectious, parasitic and immune mediated diseases, at a national public health institute; a director of a national institute of immunization in a ministry of health; the CEO of a consortium between a government and vaccine industry; a Director General at a national ministry of health; the head of a federal commission on vaccination; the head of a national division of vaccine preventable disease control and national immunization program; and a former director of immunization at a national Department of Health.

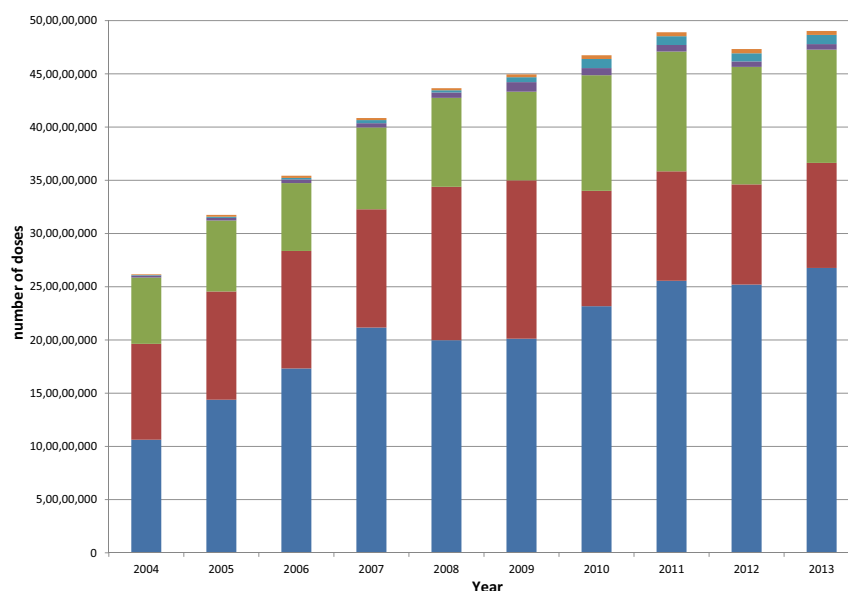


Fig. 1. Seasonal influenza vaccine dose distribution by region.

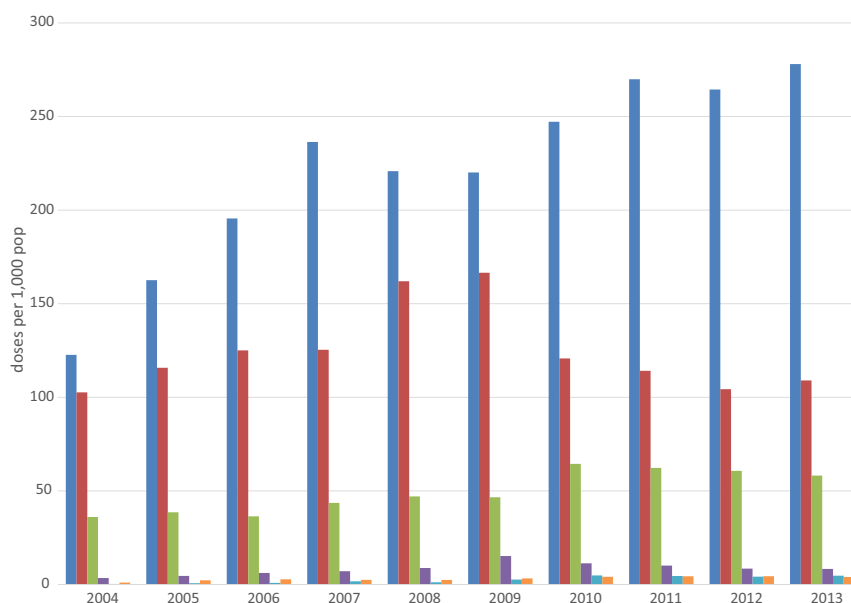


Fig. 2. Seasonal influenza vaccine doses distributed per 1000.

3. Findings

3.1. Quantitative vaccine dose distribution survey results

There has been an 87% increase in the total number of IFPMA IVS doses of seasonal influenza vaccine distributed between 2004 and 2013 (from approximately 262–490 million), with variation by WHO region (Fig. 1). In EURO, the increase in number of doses distributed between 2004 and 2013 was 9.6%, but it decreased by 31.5% between 2008 and 2013.

The number of IFPMA IVS doses distributed per 1000 population in each WHO region is shown in Fig. 2. A country-by-country breakdown is shown for AMRO and EURO in Figs. 3 and 4. Between 2004 and 2013, there was a significant increase in the number of doses distributed per 1000 population in AMRO (T -test, $p=0.01$) and the combined regions of AFRO (region of the WHO's African Regional

Office), AMRO and SEARO (region of the WHO's Southeast Asian Regional Office) (T -test, $p=0.02$), but not in EURO or WPRO (region of the WHO's Western Pacific Regional Office). Between 2008 and 2013, the only significant change in doses distribution was in EURO, where a significant decrease occurred (T -test, $p=0.04$).

Based on the hurdle rate of <159 doses per 1000 population, 166 of the 195 countries were classified as low-distribution in 2008. There were no doses distributed in 52 (31%) countries in either 2008 or 2013 and in the 114 countries with some dose distribution, 66 (58%) had an increase in the number of doses distributed per 1000 population between 2008 and 2013. Out of the 29 countries classified as high-distribution in 2008, only 7 (24%) increased the numbers of doses distributed per 1000 population between 2008 and 2013. High distribution countries with an increase in the number of doses distributed per 1000 population in 2013 were either from the AMRO or WPRO regions. Eighteen out of the

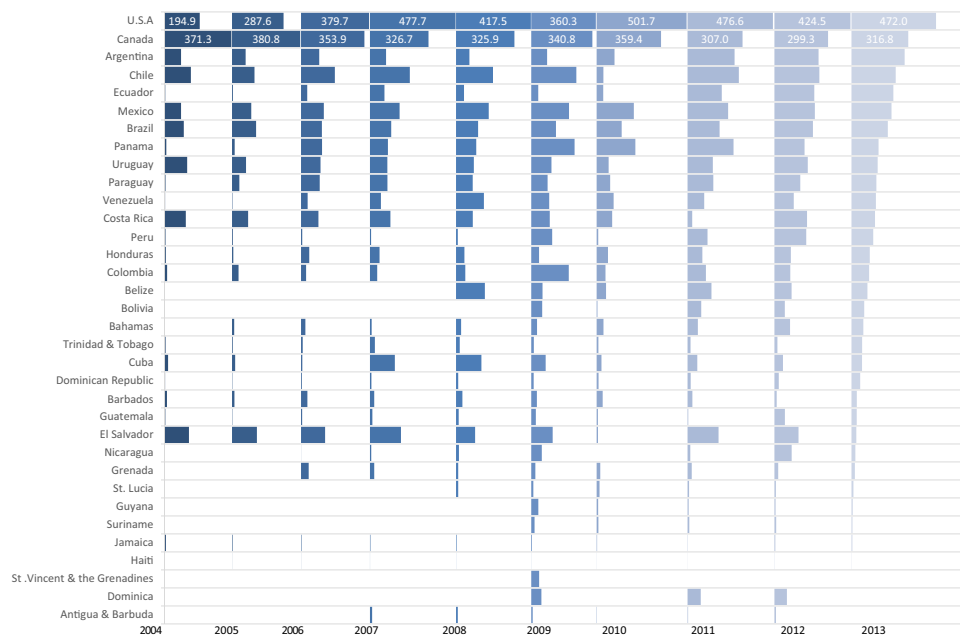


Fig. 3. Influenza vaccine doses distributed per 1000 in AMRO.



Fig. 4. Influenza vaccine doses distributed per 1000 in EURO.

21 high-distribution countries (86%) that had a decrease in numbers of doses distributed per 1000 population between 2008 and 2013 were from the EURO region.

In previous IFPMA IVS surveys [10,11], change in distribution of doses per 1000 population was not correlated with country income. However, in 2013, greater number of doses distributed per 1000 population were moderately correlated with higher Gross National Income in AMRO, WPRO, and SEARO: $r = 0.69, 0.64, \text{ and } 0.65$ respectively.

3.2. Qualitative vaccine dose distribution survey results

A total of 6 thought leaders from five countries accepted to participate in the qualitative survey: individuals from Italy ($n = 1$),

Netherlands ($n = 1$), Thailand ($n = 1$), Republic of Korea ($n = 2$), and the UK ($n = 1$). Italy, Thailand, and the UK participated by telephone interview. The thought leader from the Netherlands responded in writing. The thought leaders from the Republic of Korea responded in writing and participated by telephone interview.

The Netherlands, Italy, and UK had important increases in dose distribution in the 2008/2009 and 2009/2010 influenza seasons, most likely because of the heightened public and provider awareness associated with the 2009 H1N1 pandemic. However, since 2010, the Netherlands and Italy have an overall downward trend in dose distribution, with Italy rebounding slightly between 2012 and 2013. The distribution in the UK suggests a constant upward trend in non-pandemic influenza seasons, since 2004, with the drop in distribution in 2010 most likely to be a data artifact. Thailand and

Table 1
Summary of policies that enable seasonal influenza vaccine uptake, as described in the qualitative assessment interviews.

Policies that enable seasonal influenza vaccination		
Category	Sub-category	Description
Vaccine advocacy and education	For the general public	Media campaigns, including with or without high profile public figures, targeted at educating the public on the risks of the disease and the risks and benefits of vaccination
	For the elderly	Directed at the elderly
	For high risk groups	Directed specifically to high-risk target groups (COPD, heart disease, etc.)
	For vaccinators	Directed at vaccinators such as through reminder letters, expert training, conferences, university lectures
Building public trust		Education on the risk and benefits of seasonal influenza directed at vaccinators
		Education directed at vaccinators on how to raise vaccination coverage
	Monitoring of adverse events following vaccination	Rapid investigation by authorities of reports of adverse events following seasonal influenza vaccination
	Communications to the general public	Rapid and transparent communication on adverse events following seasonal influenza vaccination; communicating on the incidence of disease and the public health impacts
Real-time management of the vaccination program		Monitoring seasonal influenza incidence and the public health and economic impacts
		Communicating to on the impacts of the vaccination program
	Disease surveillance	
	Evaluation of vaccination program impact	
Political commitment	Monitoring vaccination coverage in real time	Communicating in real-time on vaccination coverage/vaccine distribution for the purpose of vaccination performance management
	Taking necessary actions, in real-time, to improve vaccination performance	Using real-time vaccination coverage to identify and correct issues related to vaccination coverage (supply issues, access issues, communication issues, etc.)
	Prioritizing influenza within the health portfolio	Obtaining a political commitment to emphasize the importance of seasonal influenza vaccination
	Increase delivery points	Provide access to vaccine at many/all public or private health care facilities
Improving access to vaccination	Reduce restrictions to access	Eliminate restrictions such as location of residence to access delivery points
	Eliminate/reduce payment for vaccination	Provide vaccination at no out-of-pocket expense to vaccinees
	Re-consider age limits for vaccination of the elderly	Increase vaccination coverage by lowering age of vaccination for the elderly
	Provide monetary incentives to vaccinators	Compensate vaccinators for vaccination

the Republic of Korea have overall upward trends in dose distribution since 2008, but there has been a considerable decline in Korea between 2012 and 2013. Korea's highest rate of distribution were preceding and following the pandemic years (2009 and 2010) declining between 2004 and 2009, although overall rates were high in any given year. In Thailand, the rates of distribution were higher in 2012 and 2013 than in 2009 and 2010. Therefore the impact of the H1N1 pandemic on vaccine doses distribution is likely to be highly contextual. For instance, a downward trend in the Netherlands after the pandemic years, but an overall upward trend in the UK since 2004, can be attributed to differences in the application of policies. An attitude that favors individual choice over public pressure to get vaccinated may explain the differences in trends between these two countries.

The main enabling policies identified in the interviews are shown in Table 1. Enabling factors were categorized thematically and can be summarized as promotion of vaccination, building public trust, actively managing the vaccination program in real-time, ensuring political commitment to vaccination, and enabling better access to vaccination (including limiting or eliminating out-of-pocket expenses).

The main barriers identified are shown in Table 2. They include lack of public demand, lack of public confidence, insufficient access to vaccination, lack of political commitment to seasonal influenza vaccination programs, deficient programs, and lack of education for vaccinators.

The key identified contributors to vaccination target failures were political commitment to seasonal influenza vaccination, which is variable between countries (with some countries still hesitating to implement corrective measures to reach vaccination targets), and poor program performance (such as failure to monitor vaccination coverage and take corrective actions in real time). Political support was linked to real time management where both disease outbreaks and vaccination coverage were being used

to take corrective measures and to demonstrate the impacts of vaccination.

Real-time management of the seasonal influenza vaccination programs (monitoring of vaccination coverage and implementation of corrective actions, and weekly disease surveillance) was cited as critical for achieving vaccination coverage targets. Electronic records of vaccination enable real time analyses of vaccination coverage by age and risk group, which is then communicated directly to vaccination providers.

Both enablers and barriers were consistently identified by countries regardless of their classification as increasing or declining countries.

4. Discussion

The two main quantitative findings from this survey are: a continued negative trend for dose distribution in the EURO region; and, the continued appreciable differences in scale of dose distribution between WHO regions, with no observed convergence in the number of doses distributed per 1000 population over time. The rate of growth in seasonal influenza vaccine dose distribution has dramatically slowed since 2008, with only an approximate 12% increase in number of doses distributed between 2008 and 2013 (436 and 490 million doses respectively) and only 39% of countries (76 out of 196) having increased the number of doses distributed per 1000 population over the same time period. In 2013, only 21 out of 196 countries (11%) had achieved or surpassed the hurdle rate of 159 doses per 1000 population.

This coincides with a concurrent global economic downturn, but the slowed rate of growth in the distribution of vaccine doses is unlikely to be related to economic woes, since we could find no strong correlations between vaccine dose distribution and national wealth (GNI), consistent with previous findings [10,11].

Table 2

Summary of barriers to seasonal influenza vaccine uptake, as described in the qualitative assessment interviews.

Factors identified as obstacles to vaccine uptake		
Category	Sub-category	Description
Lack of public demand	Perception of low risk from influenza Risk groups do not identify as being at high-risk	Influenza not associated with severe consequences (health or financial) Risk groups fail to associate an increased risk from influenza with their underlying conditions
Lack of public confidence	Doubt or lack of evidence of vaccine effectiveness Mistrust of government Negative fallout from H1N1 pandemic	Influenza vaccination is perceived as poorly effective. Data on vaccine effectiveness not available for all countries Public perception that vaccination policies are set for motives other than public health Perception of government over-reaction to the H1N1 pandemic. Fear of rare adverse events associated with pandemic H1N1 vaccines Perception of link between seasonal influenza vaccination and severe adverse events/deaths. Fears generated by media attention on some quality issues with vaccine
Challenges with access to vaccination	Low seasonal influenza vaccination coverage in health care workers Access not facilitated for high risk groups Supply management deficiencies	Low vaccination coverage in health care workers lowers public confidence in vaccine Lack of special vaccine delivery points for high-risk groups may limit access Issues with timely supply of vaccine due to quality issues (vaccine recalls) or other supply management issues
Lack of political commitment	Lack of vaccinator motivation Low priority of influenza	Vaccinators not always adept/motivated to counsel for vaccination Other disease may be given priority over influenza within the health portfolio, especially in tropical settings where other infectious disease are prevalent
Influenza vaccination program deficiencies	Failure to monitor disease and vaccination coverage in real time Vaccination coverage for specific targets not monitored because denominators are unknown Emphasis on individual choice Low cost-effectiveness of targeting small risk groups	Without information of vaccination coverage and disease incidence in real-time, corrective action cannot be taken to limit spread of disease and increase vaccination coverage where needed Without coverage data, impacts of vaccination cannot be assessed and used to inform the program May undermine the public health objectives of high vaccination coverage Some risk groups may be small in number and require disproportionate efforts to access
Educational deficiencies	Insufficient training on vaccination	Vaccination not prominent and sometime marginal in medical training curricula

In addition to the global stagnation in rates of doses distributed, there are important regional disparities. The rates of distribution in EURO and WPRO represent only 39% and 21%, respectively of the rate in AMRO, in 2013. SEARO, EMRO and AFRO show an insignificant distribution. This, in itself, suggests that a major global review of tactics to achieve seasonal influenza vaccination targets is warranted. Important lessons may be learned from the experiences and policies, from countries that have consistently increased vaccine utilization over time, such as the UK. The qualitative survey indicates that real-time management of the vaccination program is critical for demonstrating the impact of the program and in turn generating the political support to sustain and grow the program. This was reported by the UK, but countries other than the UK may also use real-time data for the management of their influenza programs to some degree. This is also a key learning from the management of the H1N1 pandemic in the US [18].

AMRO continues to dominate the rate of dose distribution (Fig. 2), where growth is driven by countries that initially had very little distribution. However, improving on already high dose distribution rates is particularly challenging as can be seen from the US and Canada, where distribution rates may have plateaued (Fig. 3).

Growth in the dose distribution rate in WPRO rose by 71% between 2004 and 2013, but only by 27% between 2008 and 2013. The scale of distribution in this region pales in comparison with AMRO: 58 versus 278 doses per 1000 population in 2013, respectively.

In EURO (Fig. 4), only 11 of 53 countries (21%) had increased rates of doses distributed between 2008 and 2013, and the distribution rate in 2013 was 35% lower than the peak distribution in 2009. Rates of distribution fell in 38 out of 53 (72%) countries between 2008 and 2013. What's more, EURO was the only region that experienced a decreased rate of distribution during this period, with the drop in rate being statistically significant. Given these findings, and based on the tactics to achieve goals laid out in the EU Council recommendations [19], national and international public health communities

may well need to re-evaluate their political commitment to the prevention of the annual influenza disease burden.

On the whole, the quantitative survey found that in all regions of the world, seasonal influenza vaccination is underutilized as a public health tool. Globally, the WHO's targets for influenza control [20] are not being achieved. There is an important cause for concern, with evidence of slowed expansion of vaccine distribution and, more importantly, evidence of reduced distribution in 42% of countries globally, between 2008 and 2013. In Europe, 72% of countries had lower dose distribution rates in 2013 than in 2008.

The barriers identified by the qualitative survey have known corrective actions which are regularly implemented in countries with successful programs. However, the survey identified that in at least one country the underlying cause of program deficiencies may be a lack of political commitment to seasonal influenza vaccination. Real time management of the vaccination program will help to secure political commitment by demonstrating the impact of the disease and of vaccination.

When policy enablers are implemented independently of each other, they are unlikely to be impactful. The qualitative survey identified cases where some, but not all, enablers were utilized, for instance communication to the public but no real-time monitoring of vaccination coverage.

One of the most important findings from the qualitative survey was an emphasis on active management of the vaccination program. This was identified as the key enabler by countries that practice real-time management and also recognized as a deficiency by countries which do not. The active monitoring of vaccination coverage and the real-time identification of solutions tailored to specific coverage issues were deemed critical for meeting program targets. It is not a coincidence that the UK, which enjoys the highest vaccination coverage amongst European states, manages its program in real-time and attracts the highest of political commitments. Clearly, a combination of active management and political commitment are fundamental to a successful vaccination

program. Furthermore, the often used argument of vaccine effectiveness has not dissuaded political commitment to vaccination in the UK, even though the UK uses the same vaccines as elsewhere in Europe.

There is considerable stagnation in seasonal influenza vaccination coverage and a lack of interest or motivation in specific countries in all WHO regions, and in EURO as a whole. This is in spite of the strong scientific evidence-based consensus about the impact of the disease and the benefits of vaccination [21,22], the unequivocal international recommendations from WHO [2] as well as the recommendations for universal seasonal influenza vaccination in various countries [23].

The surveys highlight a lag in implementing both international and national recommendations by public health authorities in several countries. This may well have resulted in a significant vaccine-preventable burden from influenza disease. In Europe alone, un-prevented influenza has been estimated at 1.6–1.7 million cases annually [15]. A French study estimated the total cost of influenza at more than 1796 million € each year [24]. In the United States, the yearly total costs (direct and indirect) of an influenza epidemic have been calculated at approximately €10,000–17,000 million. In some settings as little as 40% of health care professionals (HCPs) are immunized against influenza [25] even though vaccination could reduce mortality among their patients by up to 44% [26].

In Europe, a lack of public confidence in the reaction to the H1N1 pandemic in 2009, including poor communication to stakeholders, confusion between reported adverse events (narcolepsy) from an adjuvanted pandemic vaccine [27–30] and non-adjuvanted seasonal influenza vaccines, have likely contributed to the contraction of vaccine uptake. A more pragmatic approach to influenza vaccination might, therefore, be considered in Europe. The US, for instance, has opted to recommend influenza vaccination in all age groups since 2010 [3] with a relatively constant number of doses distributed per capita since 2007. To some extent, this policy may also protect from the backlash against influenza vaccination seen in post-H1N1 Europe, as influenza vaccination increasingly becomes part of the social norm.

In addition to the considerable economic and social impacts from an un-prevented burden of disease, consensus groups have also highlighted the risks to pandemic preparedness from poor seasonal influenza vaccine delivery [21,22]. Since the infrastructure for seasonal influenza vaccination is ultimately the usable infrastructure for a response to an influenza pandemic, the surveys also highlight a public health failure to adequately prepare for and manage a next influenza pandemic.

The limitations of our quantitative findings include some likely error in the reporting of numbers of doses by each vaccine distributor, but the uniform compilation of data from a standardized global source, representing approximately 79% of the global seasonal influenza vaccine production [31], means that the impact of any error should be minimal. We acknowledge that in a few countries dose distribution may not accurately reflect vaccination coverage. And dose distribution in countries that are supplied primarily by non-IVS members [31] like India and China (with 12 local influenza vaccine manufacturers), may be underrepresented. In EURO, however, all doses are sourced from IFPMA IVS members [32]. In spite of these limitations, the IFPMA IVS dose distribution data reasonably represents vaccine utilization in the WHO regions, and shows temporal evolution.

We also acknowledge that the ‘hurdle’ rate was developed for the purpose of having a single comparator to facilitate comparisons between all countries within and between WHO regions, but may not be representative of the actual number of doses required to vaccinate those aged 65 years or older in developing nations (where populations may be younger on the whole).

For our qualitative findings, we acknowledge that the sampling of countries was minimal and may not be representative. As previously noted, enablers and barriers of vaccination may be contextual and unique to individual countries. However, there was a high degree of concordance in the responses elicited which suggests that a larger sample size may not significantly alter our findings.

5. Recommendation

The IFPMA IVS survey provides important data on the dose distribution trends in the different WHO regions. The current IFPMA IVS dose distribution survey, corroborates the findings of the previous surveys [10,11], and finds that dose distribution in EURO is declining with 72% of countries distributing fewer doses of influenza vaccine in 2013 than in 2008. Globally, in 2013, 89% of countries had not achieved the hurdle rate of 159 doses distributed per 1000 population.

These trends have been monitored since 2004 and highlight a potentially serious public health failure to implement international recommendations and achieve vaccination targets. Given the global scale of these shortcomings, we believe it is time for strong and immediate policy actions to address the slow or absent progress toward meeting the seasonal influenza vaccination coverage targets. We call on the national and international public health communities to re-evaluate their political commitment in prevention of the annual influenza disease burden. Internationally mandated agencies, like WHO, have a critical role to play in ensuring that international disease control targets are set and monitored, but national health agencies and professional associations must assume responsibility for the implementation and success or failures of control programs. In addition, we encourage national departments of health and medical leaders to develop a systematic approach to improve vaccine distribution equitably across regions in order to facilitate a tangible reversal of the negative trend and to increase the probability to meet the VCR targets.

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Conflict of interest statement: B. Palache is a consultant to Abbott Biological. V. Oriol-Mathieu is an employee of Janssen–Crucell. M. Fino is an employee of Protein Sciences Corporation. Abbott biological, Janssen–Crucell and Protein Sciences Corporation are members of the IFPMA IVS. The IFPMA IVS member companies develop, manufacture and supply the majority of the world’s influenza vaccines. Representatives of IFPMA IVS member companies are full-time or contract employees of those companies and may have other financial interests in those companies. M. Xydia-Charmant is an employee of the IFPMA.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.vaccine.2015.08.082>.

References

- [1] World Health Organization. Influenza seasonal. Fact sheet no 211. Geneva: Media Center; 2014. Available at: <http://www.who.int/mediacentre/factsheets/fs211/en/> [accessed 14.05.15].
- [2] World Health Organization. Vaccines against influenza WHO position paper. *Wkly Epidemiol Rec* 2012;47(87):461–76.
- [3] Fiore AE, Uyeki TM, Broder K, Euler GL, Singleton JA, Iskander JK, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep* 2010;59(RR-8):1–62.
- [4] World Health Assembly. Resolution WHA56.19. Prevention and control of influenza pandemics and annual epidemics; 2003. Available at: http://apps.who.int/gb/archive/pdf_files/WHA56/ea56r19.pdf [accessed 03.03.15].
- [5] The Council of the European Union. Council recommendation of 22 December 2009 on seasonal influenza vaccination; 2009. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:348:0071:0072:EN:PDF> [accessed 15.07.15].
- [6] Office of Disease Prevention Health Promotion. Healthy People 2020. Immunization and Infectious diseases – objectives. IID-12. 7 and IID-12. 12. Washington: Office of Disease Prevention and Health Promotion; 2015. Available at: <https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives> [Accessed 03.03.15].
- [7] Pan American Health Organization. Influenza vaccine. PAHO/WHO Scientific and Technical Material. Influenza vaccine coverage data; 2015. Available at: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=374&Itemid=40962&lang=en [accessed 12.05.15].
- [8] Vaccine European New Integrated Collaboration Effort. VENICE III. Available at: <http://venice.cineca.org/> [accessed 12.05.15].
- [9] The International Federation of Pharmaceutical Manufacturers Associations Influenza Vaccine Supply (IFPMA IVS) Task Force. Influenza vaccine distribution in 141 countries, 2004–2007. In: *ESWI Third European Influenza Conference*. 2008.
- [10] Palache A. Seasonal influenza vaccine provision in 157 countries (2004–2009) and the potential influence of national public health policies. *Vaccine* 2011; 29: 9459–9466.
- [11] Palache A, Oriol-Mathieu V, Abelin A, Music T. Influenza Vaccine Supply Task Force (IFPMA IVS). Seasonal influenza vaccine dose distribution in 157 countries (2004–2011). *Vaccine* 2014;32:6369–76. <http://dx.doi.org/10.1016/j.vaccine.2014.07.012>.
- [12] ECDC. Seasonal influenza vaccination in Europe Overview of vaccination recommendations and coverage rates in the EU Member States for the 2012–13 influenza season. Stockholm: ECDC; 2015.
- [13] US Centers for Disease Control and Prevention. Flu vaccination coverage in the United States, Influenza Season 2013: Sept 18, 2014 <http://www.cdc.gov/flu/fluview/coverage-1314estimates.htm> [Accessed 03.03.15].
- [14] Blank PR, Schwenkglenks M, Szucs TD. Influenza vaccination coverage rates in five European countries during season 2006/07 and trends over six consecutive seasons. *BMC Public Health* 2008;8:272. <http://dx.doi.org/10.1186/1471-2458-8-272>.
- [15] Preaud E, Durand L, Macabeo B, Farkas N, Sloesen B, Palache A, Shupo F, Samson SI. The Vaccines Europe influenza working group. Annual public health and economic benefits of seasonal influenza vaccination: a European estimate. *BMC Public Health* 2014;14:813. <http://dx.doi.org/10.1186/1471-2458-14-813>.
- [16] Blank PR, Szucs TD. Increasing influenza vaccination coverage in recommended population groups in Europe. *Expert Rev Vaccines* 2009;8(4): 425–33.
- [17] United Nations. United Nations Statistics Division. National Accounts Main Aggregates Database; 2014. Available at: <http://unstats.un.org/unsd/snaama/Introduction.asp> [accessed 05.03.15].
- [18] Stroud C, Nadig L, Altevoigt BM. The 2009 H1N1 influenza vaccination campaign: summary of a workshop series. Washington DC: Institute of Medicine. National Academies Press; 2010. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK54191/> [Accessed 24.08.15].
- [19] State of play on implementation of the Council Recommendation of 22 December 2009 on seasonal influenza vaccination (2009/1019/EU). Commission Staff Working Document SWD (2014) 8 final 2014.
- [20] World Health Assembly. Prevention and control of influenza pandemics and annual epidemics. WHA56. 19; 2003. Available at: http://apps.who.int/gb/archive/e/e_wha56.html [accessed 18.05.15].
- [21] Asia-Pacific Alliance for the Control of Influenza. Influenza. Consensus statements. 2014. Available at: <http://www.apaci.asia/influenza/consensus-statements> [accessed 17.05.15].
- [22] Rüttimann RW, Bonvehí PE, Vilar-Compte D, Isturiz RE, Labarca JA, Vidal EI. Influenza among the elderly in the Americas: a consensus statement. *Rev Panam Salud Publica* 2013;33(6):446–52.
- [23] Grohskopf LA, Olsen SJ, Sokolow LZ, Bresee JS, Cox NJ, Broder KR, Karron RA, Walter EB. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP) – United States, 2014–15 Influenza Season. *MMWR* 2014;63(32):691–7.
- [24] The Council of the European Union. Proposal for a Council recommendation on seasonal influenza vaccination. COM (2009) 353 final/2. Brussels: The Council of the European Union; 2009. Available at: http://www.epha.org/IMG/pdf/seasonflu_rec2009_en.pdf [accessed 15.07.15].
- [25] World Medical Association. Influenza immunization campaign. 2015. Available at: <http://www.wma.net/en/20activities/60campaigns/10immunization/index.html> [accessed 02.08.15].
- [26] Pearson ML, Bridges CB, Harper SA. Influenza vaccination of health-care personnel recommendations of the Healthcare Infection Control Practices Advisory Committee (HICPAC) and the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006;55(RR02):1–16.
- [27] Nohynek H, Jokinen J, Partinen M, Vaarala O, Kirjavainen T, Sundman J, et al. AS03 adjuvanted A/H1N1 vaccine associated with an abrupt increase in the incidence of childhood narcolepsy in Finland. *PLoS ONE* 2012;7(3):e33536. <http://dx.doi.org/10.1371/journal.pone.0033536>.
- [28] Miller E, Andrews N, Stellitano L, Stowe J, Winstone AM, Sheeerson J, et al. Risk of narcolepsy357 in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza358 vaccine: retrospective analysis. *BMJ* 2013;346:f794.
- [29] Caille-Brillet AL, Raude J, Lapidus N, De Lamballerie X, Carrat F, Setbon M. Trends in influenza vaccination behaviours – results from the COPANFLU cohort, France, 2006 to 2011. *Euro Surveill* 2013;18(45). pii: 20628.
- [30] Peretti-Watel P, Verger P, Raude J, Constant A, Gautier A, Jestin C, et al. Dramatic change in public attitudes towards vaccination during the 2009 influenza A(H1N1) pandemic in France. *Euro Surveill* 2013;18(44). pii: 20623.
- [31] Partridge J, Kienny MP. Global production capacity of seasonal influenza vaccine in 2011. *Vaccine* 2013;31(5):728–31.
- [32] European Center for Disease Prevention and Control. Influenza vaccination. 2015. Available at: http://ecdc.europa.eu/en/healthtopics/seasonal_influenza_vaccines/Pages/influenza_vaccination.aspx. [accessed 03.03.15].