Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Vaccine 39 (2021) 6081–6087

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Vaccine complacency and dose distribution inequities limit the benefits of seasonal influenza vaccination, despite a positive trend in use

Abraham Palache [a,*], Steven Rockman [b,c], Beverly Taylor [d], Meral Akcay [e], John K Billington [f], Paula Barbosa [g], on behalf of the IFPMA Influenza Vaccine Supply (IFPMA IVS) task force

[a] Consultant at Abbott, C.J. van Houtenlaan 36, 1381 CP Weesp, the Netherlands
[b] Seqirus Ltd, 63 Poplar Road, Parkville, Victoria 3052, Australia
[c] Department of Immunology and Microbiology, the University of Melbourne, Parkville, Victoria, Australia
[d] Seqirus Vaccines, Renaissance Way, Speke, Liverpool L24 9JW, UK
[e] Sanofi Pasteur, 2 Ave Pont Pasteur, Lyon 69007, France
[f] GSK Vaccines, Av. Fleming 20, 1300 Wavre, Belgium
[g] International Federation of Pharmaceutical Manufacturers and Associations, Ch. des Mines 9, P.O. Box 195, 1211 Geneva 20, Switzerland

ARTICLE INFO

Article history:
Received 11 June 2021
Received in revised form 26 August 2021
Accepted 27 August 2021
Available online 11 September 2021

Keywords:
Seasonal influenza
Vaccination policy
Vaccination coverage rates
Pandemic preparedness
Vaccine recommendations
Monitoring and evaluation

ABSTRACT

Sustainable demand for seasonal influenza vaccines is a component of national security strategies for pandemic preparedness. However, the ongoing COVID-19 pandemic has revealed many weaknesses in the capacity of countries to design and execute sustainable vaccination programs. An influenza pandemic remains a global threat and yet there is no global monitoring system for assessing progress towards influenza vaccination coverage targets. The International Federation of Pharmaceutical Manufacturers and Associations' (IFPMA) Influenza Vaccine Supply International Task Force (IVS) developed a survey method in 2008 to estimate seasonal influenza vaccination coverage rates, which in turn serves as a crude estimate of pandemic preparedness. It provides evidence to guide expanded efforts for pandemic preparedness, specifically for increasing COVID-19 vaccine immunization levels. Furthermore, the results presented herein serve as a proxy for assessing the state of pandemic preparedness at a global and regional level. This paper adds data from 2018 and 2019 to the previous analyses. The current data show an upward or stable global trend in seasonal influenza vaccine dose distributed per 1,000 population with a 7% increase between 2017 and 2018 and 6% increase between 2018 and 2019. However, considerable regional inequities in access to vaccine persist. Three regions, Africa, the Middle-east, and Southeast Asia together account for 50% of the global population but only 6% of distributed seasonal influenza vaccine doses. This is an important finding in the context of the ongoing COVID-19 pandemic, as distribution of influenza vaccine doses in many ways reflects access to COVID-19 vaccines. Moreover, improving seasonal vaccine uptake rates is critical for optimizing the annual benefits by reducing the huge annual influenza-associated societal burdens and by providing protection to vulnerable individuals against serious complications from seasonal influenza infections.

1. Introduction

The World Health Organization's (WHO) Global Action Plan for Influenza Vaccines (GAP) was established in 2006 to increase the production capacity for influenza vaccines, one of several critical actions needed to better prepare for an influenza pandemic [1]. When it ended in November 2016, the GAP had increased seasonal influenza vaccine use and quadrupled the potential production capacity for pandemic influenza vaccine, including through the establishment of local production in low- and middle-income countries (LMICs). Despite improving capacity and accessibility, the report of the third consultation on the GAP concluded that the world was still not ready to adequately respond to an influenza pandemic and that the initial approaches used were unlikely to achieve further progress. Making up for a shortfall of 3.6 billion doses in production capacity would depend on sustainable demand

* Corresponding author.
E-mail addresses: bram.palache@ziggo.nl (A. Palache), Steven.Rockman@Seqirus.com (S. Rockman), Beverly.Taylor@Seqirus.com (B. Taylor), Meral.Akcay@sanofi.com (M. Akcay), john.k.billington@gsk.com (J.K Billington), p.barbosa@ifpma.org (P. Barbosa).

https://doi.org/10.1016/j.vaccine.2021.08.097
0264-410X/

for seasonal vaccines as part of health security strategies in countries.

To help better prepare for an influenza pandemic, in 2019 the WHO launched its 2019-2030 Global Influenza Strategy [2]. Amongst the 4 objectives of the strategy are the specific actions for countries to "design and implement evidence-based immunization policies and programmes to reduce transmission and disease severity" and for stakeholders to "strengthen national, regional and global planning to enable timely and effective pandemic readiness". The Pandemic Influenza Risk Management (PIRM) guidance, which includes pandemic vaccine production (revised in 2017 [3]), advocates for advanced planning and preparedness to mitigate the impacts of an influenza pandemic. In 2020, the WHO embarked on the development of the Pandemic Influenza Vaccine Response Operational Plan (PIVR OP) [4], based on the outputs of the WHO Pandemic Switch meetings held from 2015 to 2017 [5,6,7] to review the influenza vaccine response during the start of a pandemic. The PIVR-OP is intended to convey how the WHO will operationalize the response to an influenza pandemic. However, as the recent ongoing COVID-19 pandemic has revealed, many weaknesses remain in the capacity of countries to design and execute sustainable vaccination programs. In this regard, Ready2Respond [8], a collaboration between public and private and non-profit sectors, is committed to help low- and middle-income countries use seasonal influenza vaccination programs as a foundation for using vaccines in the event of an emergency such as COVID-19.

The COVID-19 pandemic highlights the consequences of lack of pandemic preparedness, and unfortunately the world remains unprepared for the next influenza pandemic. For example, there is no global monitoring system for influenza vaccination coverage. This is problematic given that ensuring high seasonal influenza vaccination coverage is also an important step towards pandemic preparedness. The International Federation of Pharmaceutical Manufacturers and Associations' (IFPMA) Influenza Vaccine Supply International Task Force (IVS) developed a survey method in 2008 to assess the global distribution of influenza vaccine doses as a proxy for vaccination coverage rates [9], which serves as a crude estimate of this important aspect of pandemic preparedness.

Three regions, Africa (AF), the Middle East (EM), and Southeast Asia (SEA), which account for about 50% of the global population, have consistently only accounted for about 5% of the share of distributed doses. This is an important finding in the context of the ongoing COVID-19 pandemic as distribution of influenza vaccine doses may be a useful proxy for access to COVID-19 vaccines.

This paper adds data from 2018 and 2019 to the previous analyses of seasonal influenza vaccine distribution. These data help to monitor progress toward vaccination coverage and pandemic preparedness goals and provide evidence to guide expanded efforts for pandemic preparedness, specifically for increasing COVID-19 vaccine immunization levels, and to identify weaknesses in current strategies and tactics. Furthermore, the results presented herein serve as a proxy for assessing the state of pandemic preparedness at a global and regional level. They show that much remains to be done to achieve timely and effective pandemic readiness, underscoring the urgency and importance of WHO's and other global efforts underway to better prepare the world for the next pandemic.

2. Methods

The survey methodology was previously described by Palache [9]. Member companies of the IFPMA IVS (Abbott Biologicals, Adimmune Corporation, Biken, Denka Seiken, GC Pharma, GlaxoSmithKline, Hualan Biological, Institute of Ultrapure Biologicals, Kitasato Daiichi Sankyo Vaccine, Saint-Petersburg Scientific Research Institute of Vaccines and Sera, Sanofi Pasteur, Seqirus, Sinovac, and Takeda), who agreed to provide information on the doses of seasonal influenza vaccine supplied to all WHO Member States during 2018 and 2019. 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 (2004–2017). Data were available from a total of 195 countries over the 2004–2019 period.

The manufacturers covered by the survey are based in 13 countries and represent approximately 90% of all influenza vaccine manufacturers globally [10]. Although there has been an increase in the total number of companies producing influenza vaccines in the last decade, the proportion of vaccines covered by the survey has remained relatively constant, declining by only about 5% (from 95% to 90%) since 2013 [11].

In order to assess changes in the distribution of seasonal influenza vaccines we used the following parameters, in each year, for all countries, and then categorized data into WHO regions:

- the numbers of countries in which any seasonal influenza vaccine doses were distributed;
- the absolute number of seasonal influenza vaccine doses distributed;
- the number of doses distributed to each country per 1,000 persons
- the annual number of countries globally and in each WHO region with doses distributed $\geq$ 15.9% of the population (the **"hurdle rate"** - defined in a previous survey [9] based on the proportion of the elderly proportion in 2008 [12]).

To adjust for the population size of each country, we used population data from the World Bank [13]. For each of the above parameters, we conducted the following critical analyses over the entire survey period, and over 5-year intervals (2005 – 2009, 2010 – 2014, and 2015 – 2019):

- the compound annual growth rate (CAGR), using Microsoft Excel 365, where:
  CAGR = [(rate per 1,000 in 2019 $-$ rate per 1,000 in 2004)$^{1/16}$ $-$ 1] $\times$ 100;

As in previous IFPMA IVS surveys [9], we also assessed:

- the correlation between the natural log numbers of doses distributed per 1,000 population and natural log of the country Gross National Income (GNI), for countries with any distributed doses globally and in each WHO region, using the regression function in the data analysis add-in for Microsoft Excel 365.

3. Results

Numbers of countries in which any seasonal influenza vaccine doses were distributed – Globally, the number of countries where any doses of seasonal influenza vaccine were distributed increased from 108 in 2004 to 134 in 2019. Note that the total number of countries in the current survey (195) is lower than in the previous survey (200) because of reclassification of Hong Kong, and Macao into a single reporting country (China) and the combination of reports from New Caledonia, French Polynesia, and Wallis and Fatuna with France. The 1.5 % CAGR in the number of countries distributing any doses between 2004 and 2019 remains unchanged from the previous survey (2004–2017). In 2019, 135 countries had some level of dose distribution. The number of countries distributing any doses has remained fairly constant since 2012, except in 2018 when the number of countries dropped by 20 to 115. The

peak year for number of countries distributing any doses was 2011 (140 countries), the year after the 2009–2010 pandemic.

Absolute number of seasonal influenza vaccine doses distributed – The total number of doses distributed in 2004 was approximately 262 million and this had risen to about 531 million in 2019, an overall 103% increase (Supplemental Fig. 1). However, compared to the peak number of doses distributed in 2014 of 534 million doses, the 2019 total represents a 0.3% decline. The overall growth in the number of doses distributed has largely been driven by the increase in absolute number of doses distributed in the Americas (AM) (a 154 million dose difference between 2004 and 2019).

The share of doses distributed to AM has increased from about 41% in 2004 to 49% in 2019, whereas the share for European region (EU) has declined from 34% in 2004 to 27% in 2019. The share from the Western Pacific (WP) has oscillated between an all-time high of 24% in 2004 to a low of 18% in 2019. In 2019, three regions, AF, EM, and SEA, together accounted to 50% of the total population, but only 6% of the share of distributed doses.

Numbers of countries with distributed doses ≥ "hurdle rate" – Globally, the number of countries that achieved the hurdle rate doubled between 2004 and 2019 (from 16 to 31 countries) but the growth in number of countries was not steady, with a year-to-year variation of between 1 and 10. No countries in AF, EM or SEA achieved the hurdle rate in 2019, compared to 18 countries in EU, 9 in AM and 4 in WP.

Numbers of doses distributed in each country per 1,000 persons – The AM and EU regions have consistently had higher distribution rates of seasonal influenza vaccine per 1,000 population than the global rate of 70 doses per 1,000 population (Fig. 1). In 2019, the rate in AM was 259 per 1,000 population, an overall CAGR of 5% between 2004 and 2019. However, the 2019 rate is 20% lower than the peak rate of 322 in 2014. In EU, the 2019 rate of 153 doses per 1,000 population was the highest it has been since the peak of 167 in 2009 (or 8% lower than in the peak year). While the rate in EU is the highest it has been in a decade, it is still 41% lower than the rate in AM, and the EU rate is still marginally below the hurdle threshold. The AM region has consistently surpassed the hurdle rate since 2005 whereas the EU region has only twice exceeded the hurdle rate (in 2008 and 2009). In WP, the rate of 51 per 1,000 population is higher than in recent years, but still below the global rate of 70 per 1,000.

However, the overall regional growth rates in dose distribution mask inequities of distribution within each region. The intra-regional ranges are shown in Supplemental Fig. 2. The greatest inequities in distribution can be observed in AF, where a majority of countries (66%) have no distribution, and in WP where 54% have none, and in SEA where the median dose distribution rate is only 2 doses per 1,000 population.

Five-year average numbers of doses distributed –There was little change in the 5-year average number of doses distributed for the last two periods. The 5-year average declined slightly in WP and AM (two regions with high use) and globally (Fig. 2). All three regions where vaccine usage is the lowest (EM, SEA, AF) showed steady increase from period to period, but the averages are very small relative to the other regions.

Percentage of vaccines per population – Fig. 3 shows the percentage of vaccines distributed per population, by WHO region, for

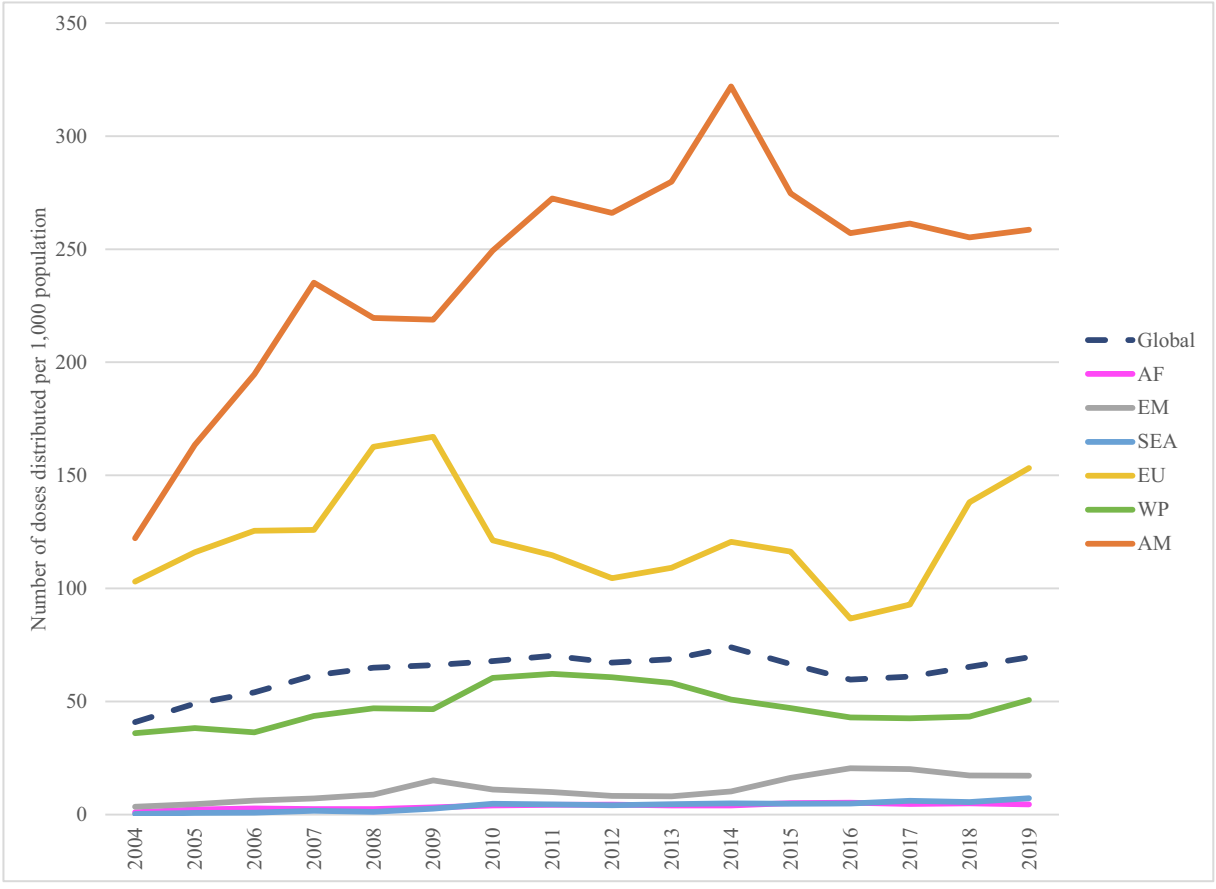

Fig. 1. Number of doses of seasonal influenza vaccine distributed per 1,000 persons by year and WHO region.

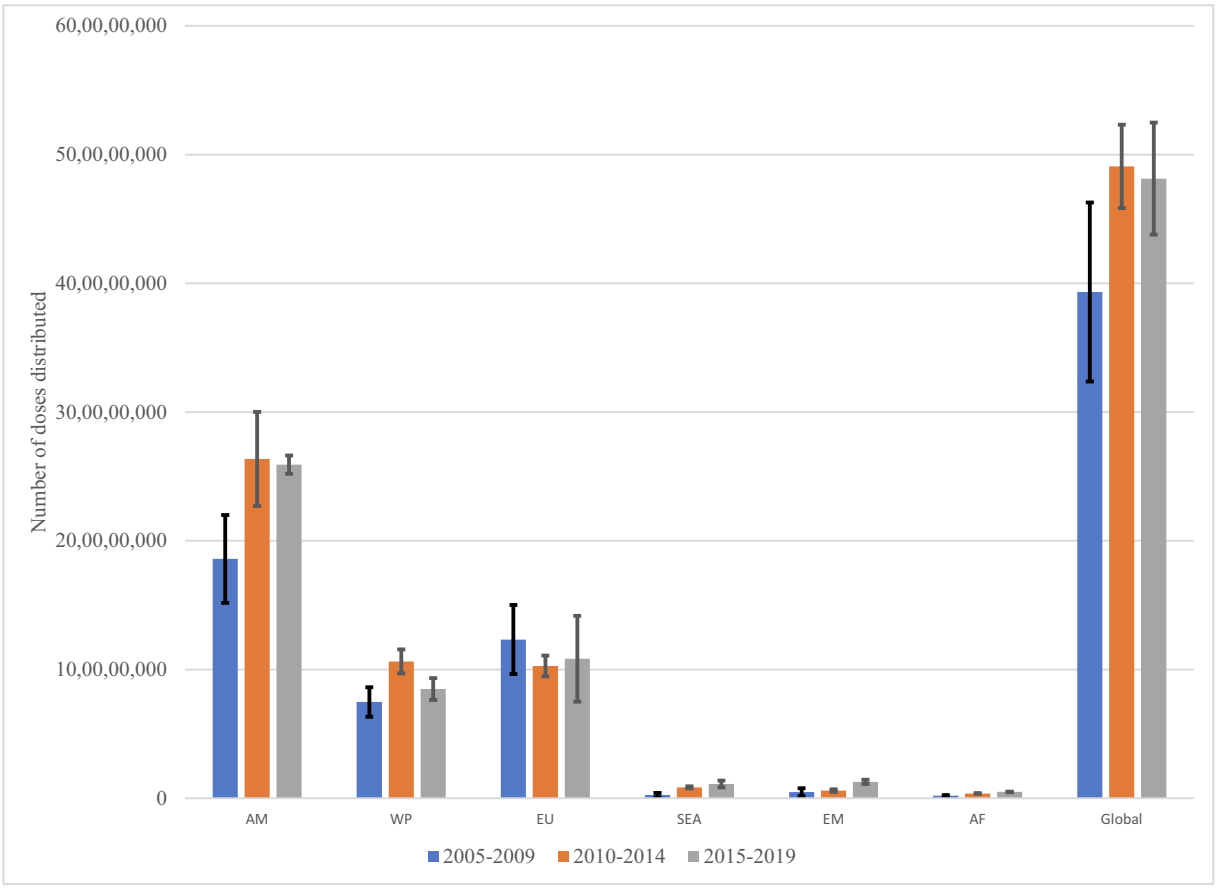

Fig. 2. Five-year average number of doses of seasonal influenza vaccine distributed by WHO region.

the latest year for which there is data (2019). As noted above, the AM region is the only region that exceeds the "hurdle rate" of 15.9%.

Correlation between doses distributed per 1,000 persons and Gross National Income (GNI) – As in the previous IFPMA IVS surveys, we assessed the correlation between doses per 1,000 population and country GNI for 2018 and 2019 (Table 1). Globally the correlation in 2018 and 2019 was weak (r^2 = 0.46, r^2 = 0.52 respectively), but in some regions, like WP, the correlation was moderate (r^2 = 0.64, r^2 = 0.69) and achieved significance. The correlation was not significant in AM and SEA and very weak in AM at r^2 = 0.01, and r^2 = 0.16 in 2018 and 2019 respectively. Just as for the number of doses distributed in each region, gross variations in GNI exist within a region. The intra-regional ranges are shown in Supplemental Fig. 3. The smallest range can be observed in AF and SAE where the highest GNI is considerably lower than in other regions. Nevertheless, even in regions with the greatest variation in GNI, there was little or no association between GNI and dose distribution levels, suggesting that there are other factors that are more critical to vaccine uptake in all regions.

4. Discussion

The IFPMA IVS dose distribution survey is a valuable tool for monitoring year-to-year progress in the utilisation of seasonal influenza vaccine doses and may be a useful proxy for assessing pandemic preparedness. Globally, over the last 16 years, there has been steady but modest progress in global distribution of influenza vaccine doses, rising from 41 per 1,000 population in 2004 to 70 per 1,000 population in 2019. Most of the growth has been driven by AM region and to a lesser extent EU region. In both regions, distribution peaked several years ago (in 2014 in AM and in 2009 in EU), although dose distribution in EU has been trending upwards since 2016. Furthermore, only AM has consistently surpassed the hurdle rate of 15.9% of the population. All WHO regions except AF saw positive trends in vaccine distribution for the 2018–2019 period.

The most notable increase in vaccine dose distribution occurred in the EU region, where distributed doses rose by a remarkable 49% between 2017 and 2018 and then again by another 11% between 2018 and 2019. A positive trend in the 5-year averages is also noted for the EU region, where there was a 5% increase in the 5-year average for the latest period (2014–2019) over the previous period (2010–2014). We also note substantive increases in the 5-year averages over the previous period for SEA, EM and AF: 31%, 113%, and 34% respectively. The 5-year average remained virtually constant for AM (just a 2% decline from 2010 to 2014 to 2015–2019) but dropped by 20% for the WP region where year-to-year distribution has been more variable. However, WP did see a 17% increase in doses distributed per 1,000 population between 2018 and 2019. These findings suggest that for the most recent years there is an upward or stable trend in vaccine dose distribution with a 7% increase between 2017 and 2018 and 6% increase in doses distributer per 1,000 population between 2018 and 2019 globally.

As noted in Fig. 3, there continue to be considerable inequities in the percentage of population that has access to a dose of vaccine across WHO regions. The highest percentage of doses per population are available in AM (26%) and EU (15%) whereas regions like SEA and AF have less than 1%, and WP is in between with 5%. This is an important finding in the context of the ongoing COVID-19

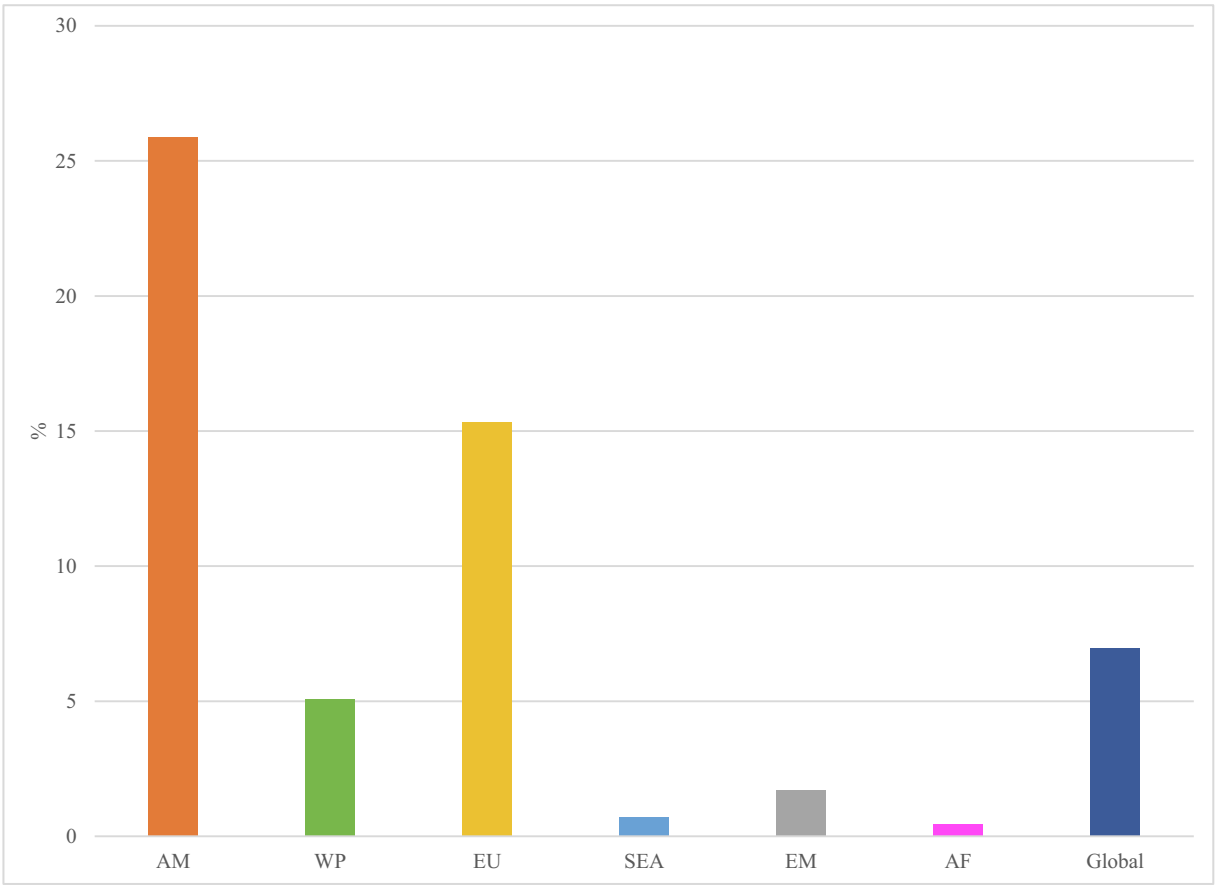

Fig. 3. Percentage vaccine distribution per population in WHO regions in 2019.

Table 1
Correlation between numbers of doses distributed per 1,000 population and GNI for 2018 and 2019, using regression in Microsoft Excel 365.

	2018			2019		
	n	r^2	significance	n	r^2	significance
Global	114	0.46	p = 0.000	133	0.52	p = 0.000
AM	28	0.01	p = 0.550	33	0.16	p = 0.023
WP	11	0.64	p = 0.003	13	0.69	p = 0.000
EU	46	0.65	p = 0.000	48	0.57	p = 0.000
SEA	7	0.55	p = 0.064	8	0.27	p = 0.184
EM	14	0.64	p = 0.000	17	0.65	p = 0.000
AF	8	0.63	p = 0.018	14	0.70	p = 0.000

pandemic and concerns surrounding equitable access to vaccination, as distribution of influenza vaccine doses in many ways reflects access to COVID-19 vaccines and suggests that regions with better access to influenza vaccines also have better access to pandemic vaccines. As of March 2021, 380 million doses of COVID-19 vaccine have been administered with 29% in the US, 13% European Union, 7% United Kingdom and <6% South America [14].

The COVID-19 pandemic may also pose an additional concern regarding uptake of influenza vaccination. While vaccination coverage for the 2020–2021 influenza season has increased in many countries [15,16], the record low number of influenza cases reported in many regions [17,18,19] may lead to complacency in the coming season (2021 southern hemisphere seasons and 2021–2022 northern hemisphere season). Vaccine complacency is a recurring impediment to seasonal vaccination coverage [20,21]. Of particular concern is that the low rate of transmission over the last season may leave the public particularly vulnerable to influenza in the coming season due to waning immunity from lack of exposure and the potential for new strains to arise [22]. One strain change (H1N1 for the 2021 – 2022 northern hemisphere campaign) has already occurred during the COVID-19 pandemic [23]. Thus, influenza viruses still evolve effectively and new emerging strains will likely cause severe seasons, possibly coinciding with the end of the COVID-19 pandemic. An influenza – SARS-CoV-2 syndemic would have devastating public health consequences, hence the importance of optimizing pandemic response capabilities with seasonal influenza vaccination.. Influenza vaccination has a important role to play in mitigating the impacts of COVID-19 by facilitating the management of respiratory outbreaks

by reducing the epidemiological noise of influenza and by securing the infrastructure to deliver other routine immunizations during the pandemic [24].

Further confounding the situation are national efforts to rollout COVID-19 vaccines during the influenza season, which may impede influenza vaccination uptake either because of the heightened priority of COVID-19 over influenza vaccination or because the earlier recommended 14 day interval between COVID-19 and influenza vaccinations [25,26,27] may limit influenza vaccine uptake in countries where this interval is maintained. Influenza remains a global healthcare challenge, and a syndemic of COVID-19 and influenza would create significant issues with respect to clinical management, diagnosis, and strain upon global health resources. Stowe et al [28] found that coinfection of influenza and SARS-CoV-2 increased the risk of death 6-fold compared to those without either infection, and doubled the risk of ventilation or admission to ICU, and therefore may have a significant impact on demand for health services.

The annual burden of influenza-associated disease, hospitalizations and deaths is well recognised and documented [29,30,31,32], and influenza is known to contribute to social and healthcare costs from NCDs [33,34,35,36,37]. The WHO position paper on the use of influenza vaccination is clear and soundly supported by evidence [29]. Even when vaccine effectiveness is low, large numbers of cases can be prevented [38]. Low vaccination coverage can result from poor appreciation of disease burden by the public, and lack of prioritization within national budgets [38]. However, estimates of the impact of influenza vaccination on disease reduction and broader societal health systems are very compelling in favour of the value of vaccination [39,40,41]. In the US, Kostova et al [40] estimated that between 1 and 5 million influenza cases were averted each season by vaccination. In Europe, Preaud et al [41] estimated that vaccination prevents between 1.6 million and 2.1 million cases of influenza each year and 45,300 to 65,600 hospitalizations and 25,200 to 37,200 deaths. Furthermore, this report and the previous IFPMA IVS survey reports [9,42,43,44] indicate that GNI is not a strong determinant of dose distribution. Influenza therefore remains "a preventable disease not being prevented" [45] and considerable economic and healthcare burden continues to occur because of seasonal influenza [41].

Globally, COVID-19 vaccination strategies have opened the door to new vaccine technologies with the potential to increase vaccine effectiveness through improved T cell mediated responses and these vaccines will most likely be applied to influenza. Much research and development effort continues to be expended on the development of novel 'universal' influenza vaccines that would impart lasting immunity and not require annual revaccination [46,47]. Ultimately, these efforts may inspire further improvement of future influenza immunization programs. At the same time, current seasonal vaccine production capacity is only at 50% [1], so better use of existing vaccines is possible and required from a public health perspective. Making better use of the existing vaccines is critical so that when the next generation of vaccines arrives, the necessary infrastructure and programs are in place to best ensure uptake and impact on public health.

The primary limitation of this study is the exclusion of data from non-IFPMA manufacturers from the survey, however we note that 90% of all influenza vaccine manufacturers globally are covered [10]. In addition, the survey does not consider the impact of vaccination policies and practices on the uptake of vaccines. Since vaccination policies apply to target groups other than persons over 65 years of age, our method underestimates the true coverage gaps in country programs. Nevertheless, this survey provides some of the most comprehensive data on global influenza prevention and can serve as an important proxy parameter for pandemic preparedness.

5. Conclusion

The current IFPMA IVS survey shows a positive tendency in the uptake of influenza vaccines in the last two years (2018 and 2019). The survey also provides an important proxy for country pandemic readiness as influenza vaccination infrastructure is ideally suited for a viral respiratory disease pandemic response. However, while the benefits of seasonal influenza vaccination are clear and well documented by the WHO, vaccine complacency continues to reduce the potential benefits of influenza vaccination at a population level. Fifty percent of the global population has access to only a 6% share of distributed doses. The COVID-19 pandemic provides an opportunity for countries to build or improve existing immunization systems and at the same time enhance their pandemic readiness. The WHO's 2019–2030 strategy and tactics and the efforts of the Ready2Respond collaboration are available to support countries in optimizing the use of existing influenza vaccines. Improving seasonal vaccine uptake rates is not only an important driver for pandemic preparedness, but also for optimizing the annual benefits in the at-risk individuals for whom vaccination is recommended. Increased vaccine uptake can substantially reduce the huge annual influenza-associated societal burden as well as protect vulnerable persons against serious complications from influenza infections.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Abraham Palache reports a relationship with Abbott that includes: consulting or advisory. Abraham Palache, Steven Rockman, Beverly Taylor, Meral Akcay, John K Billington are full-time or contract employees of member companies of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Influenza Vaccine Supply International Task Force (IVS). The IFPMA IVS member companies develop, manufacture and supply the majority of the world's influenza vaccines. Representatives of IFPMA IVS member companies may have other financial interests in those companies. Paula Barbosa is a full-time employee of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

Acknowledgements

The study was commissioned and funded by the IFPMA IVS. The IFPMA IVS provided input into the study design, data collection, analysis, manuscript writing, and decision to submit the manuscript for publication. Consequently, the resultant manuscript is submitted on behalf of IFPMA IVS. The authors gratefully acknowledge the writing services of Shawn Gilchrist, president of S Gilchrist Consulting Services Inc.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2021.08.097.

References

[1] World Health Organization. Report of the Third WHO Consultation on the Global Action Plan for Influenza Vaccines. Geneva, Switzerland, 15–16 November 2016. Available at: http://apps.who.int/iris/bitstream/handle/10665/259727/WHO-HIS-TTi-17.6-eng.pdf;jsessionid=8226CB8099F043948B-45AB5E283D95EA?sequence=1. Accessed April 22, 2021.

[2] World Health Organization. Global influenza strategy 2019-2030. World Health Organization; 2019. Available at: http://www.who.int/iris/handle/10665/311184. Accessed Aug 2, 2019.

[3] World Health Organization. Pandemic Influenza Risk Management: A WHO guide to inform and harmonize national and international pandemic preparedness and response. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO. Available at: http://apps.who.int/iris/bitstream/handle/10665/259893/WHO-WHE-IHM-GIP-2017.1-eng.pdf;jsessionid=C57DD85154E5CB99358377BA5219ACE5?sequence=1. Accessed April 28, 2021.

[4] World Health Organization. WHO Pandemic Influenza Vaccine Response Operational Plan Draft Annotated Outline 1 December 2020. Available at : https://extranet.who.int/dataformv3/upload/surveys/776836/files/Draft%20WHO%20Pandemic%20Influenza%20Vaccine%20Response%20Operational%20Plan%20Annotated%20Outline_1%20December%202020.pdf. Accessed April 28, 2021.

[5] World Health Organization. Influenza Vaccine Response during the Start of a Pandemic. Report of a WHO Informal Consultation held in Geneva, Switzerland, 29 June - 1 July 2015. Available at: https://apps.who.int/iris/bitstream/handle/10665/207751/WHO_OHE_PED_GIP_2016.1_eng.pdf;sequence=1. Accessed July 29, 2021.

[6] World Health Organization. Influenza Vaccine Response during the Start of a Pandemic. Report of the Second WHO Informal Consultation held in Geneva, Switzerland 21 -22 July 2016. Available at: https://apps.who.int/iris/handle/10665/254743. Accessed July 29, 2021.

[7] World Health Organization. Influenza Vaccine Response During the Start of a Pandemic. Report of the Third WHO informal consultation, 7-9 June 2017, Geneva, Switzerland. Available at: https://apps.who.int/iris/handle/10665/325973. Accessed July 29, 2021.

[8] Ready2Respond. Available at: https://ready2respond.org/. Accessed April 28, 2021.

[9] Palache A. Seasonal influenza vaccine provision in 157 countries (2004–2009) and the potential influence of national public health policies. Vaccine 2011;29(51):9459–66. https://doi.org/10.1016/j.vaccine.2011.10.030. Epub 2011 Oct 21.

[10] International Federation of Pharmaceutical Manufacturers and Associations. Influenza vaccine supply (IVS) international task force. Available at: https://www.ifpma.org/subtopics/influenza-vaccine/. Accessed April 22, 2021.

[11] International Federation of Pharmaceutical Manufacturers and Associations. Improving pandemic preparedness. Seasonal influenza vaccination series: Paper 5. 2013. Available at: https://www.ifpma.org/wp-content/uploads/2016/01/IFPMA-IVS-Eng-FactSheet5-01.13.pdf

[12] United Nations Department of Economic and Social Affairs / Population Division. World Population Prospects 2019. Available at: https://population.un.org/wpp/Download/Standard/Population/

[13] World Bank. Population, total. Available at: https://data.worldbank.org/indicator/SP.POP.TOTL. Accessed April 28, 2021.

[14] OECD. Access to COVID-19 vaccines: Global approaches in a global crisis. March 18, 2021. Available at: https://www.oecd.org/coronavirus/policy-responses/access-to-COVID-19-vaccines-global-approaches-in-a-global-crisis-c6a18370/. Accessed May 21, 2021.

[15] Bachtiger P, Adamson A, Chow JJ, Sisodia R, Quint JK, Peters NS. The impact of the COVID-19 pandemic on the uptake of influenza vaccine: UK-wide observational study. JMIR Public Health Surveill 2021;7(4):. https://doi.org/10.2196/26734e26734.

[16] Centers for Disease Control and Prevention. Influenza (flu). Weekly National Flu Vaccination Dashboard. Available at: https://www.cdc.gov/flu/fluvaxview/dashboard/vaccination-dashboard.html. Accessed April 29, 2021.

[17] Olsen SJ, Azziz-Baumgartner E, Budd AP et al. Decreased influenza activity during the COVID-19 pandemic — United States, Australia, Chile, and South AFica, 2020. MMWR Morb Mortal Wkly Rep 2020; 69:1305–1309. DOI: http://dx.doi.org/10.15585/mmwr.mm6937a6external icon.

[18] Centers for Disease Control and Prevention. Weekly U.S. Influenza Surveillance Report. Available at: https://www.cdc.gov/flu/weekly/index.htm. Accessed April 29, 2021.

[19] World Health Organization. Influenza update – 390. 29 March 2021, based on data up to 14 March 2021. Available at: https://www.who.int/publications/m/item/influenza-update-n-390. Accessed July 29, 2021.

[20] González-Block MA, Gutiérrez-Calderón E, Pelcastre-Villafuerte BE, et al. Influenza vaccination hesitancy in five countries of South America. Confidence, complacency and convenience as determinants of immunization rates. PLoS ONE 2020;15(12):. https://doi.org/10.1371/journal.pone.0243833e0243833.

[21] Schmid P, Rauber D, Betsch C, Lidolt G, Denker ML. Barriers of influenza vaccination intention and behavior – a systematic review of influenza vaccine hesitancy, 2005–2016. PLoS ONE 2017;12(1):e0170550.

[22] Laurie KL, Rockman S. Which influenza viruses will emerge following the SARS-CoV-2 pandemic? Influenza Other Respi Viruses. 2021;00:1–4. https://doi.org/10.1111/irv.12866.

[23] World Health Organization. Recommended composition of influenza virus vaccines for use in the 2021-2022 northern hemisphere influenza season. 26 February, 2021. Available at: https://www.who.int/publications/i/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2021-2022-northern-hemisphere-influenza-season. Accessed July 29, 2021.

[24] Maltezou HC, Theodoridou K, Poland G. Influenza immunization and COVID-19. Vaccine. 2020;38(39):6078–9. https://doi.org/10.1016/j.vaccine.2020.07.058.

[25] Centers for Disease Control and Prevention. Vaccines and immunization. interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States. Available at: https://www.cdc.gov/vaccines/COVID-19/info-by-product/clinical-considerations.html#Administration. Accessed April 29, 2021.

[26] World Health Organization. Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222, SII Covishield, SK Bioscience). Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1

[27] Australian Technical Advisory Group on Immunization (ATAGI). Advice on the relative timing of administering influenza and COVID-19 vaccines in 2021 Version 2.0. Available at: https://www.health.gov.au/sites/default/files/documents/2021/03/COVID-19-vaccination-atagi-advice-on-influenza-and-COVID-19-vaccines.docx. Accessed April 29, 2021.

[28] Stowe J, Tessier E, Zhao H, et al. Interactions between SARS-CoV-2 and influenza, and the impact of coinfection on disease severity: a test-negative design. Int J Epidemiol 2021:dyab081. https://doi.org/10.1093/ije/dyab081.

[29] World Health Organization. Vaccines against influenza - WHO position paper – November 2012. Wkly Epidemiol Rec 2012 Nov 23;87(47):461–76.

[30] Gasparini R, Amicizia D, Lai PL, Panatto D. Clinical and socioeconomic impact of seasonal and pandemic influenza in adults and the elderly. Hum Vaccin Immunother 2012;8(1):21–8. https://doi.org/10.4161/hv.8.1.17622. Epub 2012 Jan 1.

[31] Heikkinen T, Tsolia M, Finn A. Vaccination of healthy children against seasonal influenza: a European perspective. Pediatr Infect Dis J 2013;32(8):881–8. https://doi.org/10.1097/INF.0b013e3182918168.

[32] Iuliano AD, Roguski KM, Bresee JS, for the Global Seasonal Influenza-associated Mortality Collaborator Network. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet 2018; 391 (10127): 1285-1300. doi: 10.1016/S0140-6736(17)33293-2. Epub 2017 Dec 14.

[33] Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P. Risk of myocardial infarction and stroke after acute infection or vaccination. New Engl J Med 2004;351:2611–8. https://doi.org/10.1056/NEJMoa041747.

[34] US Centers for Disease Control and Prevention. Flu and people with diabetes. Available at: https://www.cdc.gov/flu/highrisk/diabetes.htm. Accessed Aug 2, 2019.

[35] UK Health Protection Agency. Surveillance of Influenza and other Respiratory Viruses in the UK 2010/2011. London, UK; 2011. Available at: https://webarchive.nationalarchives.gov.uk/20140629102627/http:/hpa.org.uk/webc/HPAwebFile/HPAweb_C/1296687414154. accessed Aug 2, 2019.

[36] Madjid M, Miller CC, Zarubaev VV, Marinich IG, Kiselev OI, Lobzin YV, et al. 3rd influenza epidemics and acute respiratory disease activity are associated with a surge in autopsy-confirmed coronary heart disease death: results from 8 years of autopsies in 34,892 subjects. EU Heart J 2007;28(10):1205–10. https://doi.org/10.1093/EUheartj/ehm035. Epub 2007 Apr 17.

[37] Plans-Rubio P. Prevention and control of Influenza in persons with Chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2007;2(1):41–53.

[38] Palache A. Global seasonal influenza disease and vaccination: a paradox with substantial public health implications. Int Med Rev 2018;4(11):1–22. https://doi.org/10.18103/imr.v4i12.775.

[39] Reed C, Chaves SS, Daily Kirley P, Emerson R, Aragon D, Hancock EB, et al. Estimating influenza disease burden from population-based surveillance data in the United States. PLoS ONE 2015;10(3):. https://doi.org/10.1371/journal.pone.0118369e0118369.

[40] Kostova D, Reed C, Finelli L, Cheng P-Y, Gargiullo PM, Shay DK, et al. Influenza Illness and Hospitalizations Averted by Influenza Vaccination in the United States, 2005–2011. PLoS ONE 2013;8(6):. https://doi.org/10.1371/journal.pone.0066312e66312.

[41] Preaud E, Macabeo B, Markas N, et al. Annual public health and economic benefits of seasonal influenza vaccination: a European estimate. BMC Public Health. 2014 Aug;7(14):813. https://doi.org/10.1186/1471-2458-14-813.

[42] Palache A, Oriol-Mathieu V, Fino M, Xydia-Charmanta M. Seasonal influenza vaccine dose distribution in 195 countries (2004–2013): little progress in estimated global vaccination coverage. Vaccine 2015;33(42):5598–605. https://doi.org/10.1016/j.vaccine.2015.08.082.

[43] Palache A, Oriol-Mathieu V, Abelin A, Music T. Seasonal influenza vaccine dose distribution in 157 countries (2004–2011). Vaccine 2014;32(48):6369–76. https://doi.org/10.1016/j.vaccine.2014.07.012. Epub 2014 Nov 1.

[44] Palache A, Tsai T, Vasiliev Y, et al. Global influenza vaccine distribution survey demonstrates urgency of implementation of objective 3 of WHO influenza strategy 2019-2030. Internal Medicine Review 2020; 6 (2). Available at: https://internalmedicinereview.org/index.php/imr/article/viewFile/850/pdf. Accessed April 29, 2021.

[45] Mostow SR. Influenza–a preventable disease not being prevented. Am Rev Respir Dis 1986;134(1):1. https://doi.org/10.1164/arrd.1986.134.1.1.

[46] Wong T, Ross TM. Steps toward a universal influenza vaccine: research models and comparison of current approaches. In Steps Forwards in Diagnosing and Controlling Influenza. IntechOpen. Ed Manal Mohammad Baddour. 2016. https://doi.org/10.5772/64369.

[47] National Institutes of Allergy and Disease. Universal influenza vaccine research. Available at: https://www.niaid.nih.gov/diseases-conditions/universal-influenza-vaccine-research. Accessed April 29, 2021.