

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. Vaccine 38 (2020) 7880-7882

Contents lists available at ScienceDirect

# Vaccine

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

# Commentary Expanding global and national influenza vaccine systems to match the COVID-19 pandemic response

# Bruce A. Ruscio<sup>a,\*</sup>, Peter Hotez<sup>b</sup>

<sup>a</sup> Public Health Consultant, United States

<sup>b</sup> National School of Tropical Medicine, Departments of Pediatrics, Molecular Virology & Microbiology, Co-Head, Section of Pediatric Tropical Medicine, Health Policy Scholar, Baylor College of Medicine, United States

# 1. Introduction: Influenza and COVID-19 in the "Global South

Even with the COVID-19 pandemic of 2020, influenza remains a leading global cause of mortality among adults and children. According to the Global Seasonal Influenza-associated Mortality Collaborator Network, approximately 290,000 - 646,000 influenza-associated respiratory deaths occur annually [1]. The Network estimates find that the highest mortality rates now occur in Sub-Saharan Africa and Southeast Asia, with these two regions accounting for more than 40% of the deaths [1]. A related analysis for the year 2019 confirmed that approximately 390,000 respiratory deaths result from influenza, a number corresponding to 2% of all annual respiratory deaths, with two-thirds of the flu deaths among individuals over the age of 65 [2]. Influenza also causes a substantial burden of cardiovascular disease, due to MI, myocarditis, stroke, and other complications [3]. For example, in the 2009 influenza pandemic cardiac complications occurred in approximately 5% of the patients hospitalized with influenza, and almost 50% of the flu patients admitted to intensive care units [3].

## 2. COVID-19 in the global South

COVID-19 is making a significant public health impact on populations living in poverty in the Global South [4]. Currently, Brazil has the second largest number of COVID-19 cases behind the United States, but the numbers of cases and deaths in Brazil are accelerating rapidly such that some projections indicate Brazil may soon become the leading nation in both categories [5]. Outside of Brazil, other Latin American nations have experienced significant increases in COVID-19 cases, including Peru, Chile, Mexico, Ecuador, and Colombia [4]. Globally, the resource-poor nations of India, Pakistan, Bangladesh, Indonesia, South Africa, and Egypt are starting to show evidence of significant COVID-19 epidemics, in addition to a significant epidemic raging in Iran [4]. Overwhelmingly, those living in poverty are at the greatest risk due to crowding in low-income neighborhoods, as well as high rates of co-morbid con-

\* Corresponding author. *E-mail address:* brucearuscio@gmail.com (B.A. Ruscio). ditions such as diabetes, hypertension, and obesity among the poor [6]. Similar to influenza, COVID19 deaths disproportionately occur among older individuals [7–8].

# 3. Influenza and COVID19 syndemics

With the high proportion of influenza deaths in the Global South, and the anticipated march of COVID-19 through these same regions, there emerges the prospect of global syndemics resulting from these two diseases. As influenza co-circulates with COVID-19 there are concerns about the potential co-infections or interactions between these two respiratory viruses. We know that influenza and COVID-19 co-infections can and do occur [9–11], and there will be opportunities to fully explore the clinical impact of these co-infections Fig. 1.

### 4. A vaccine response strategy

In the 2009 H1N1 influenza pandemic, many low- and middleincome countries struggled to use pandemic influenza vaccines effectively because of a constellation of factors. Among these factors were a lack of pandemic planning and limited experience in conducting vaccination campaigns targeting non-pediatric populations, mobilizing financial resources and personnel for vaccine deployment, establishing sufficient cold-chain capacities, implementing regulatory capability, and achieving high rates of vaccine uptake among target groups [12–13]. In contrast, countries with seasonal influenza prevention and control programs were better prepared and achieved more effective pandemic responses [14].

More than half of all countries still lack access to robust seasonal influenza immunization programs, with most deaths and severe disease from seasonal influenza epidemics occurring in Global South countries [15–19]. In response, the WHO established a comprehensive Global Influenza Strategy for 2019–2030, focused on surveillance and disease prevention, including expanded vaccinations [20]. This strategy and existing global influenza infrastructure may provide a key platform for folding in COVID-19 vaccinations. For example, a modeling exercise has determined that increasing the uptake of influenza vaccines has an overall pos-







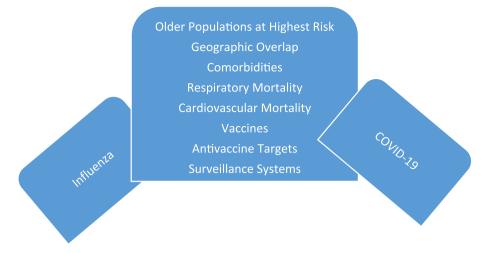


Fig. 1. Overlap and Synergies of Influenza and COVID19 as Global Health Threats.

itive impact in terms of managing outbreaks of COVID-19 or influenza-like respiratory illnesses [21].

Pairing COVID19 and influenza vaccinations may offer a highly cost-effective means to prevent needless deaths from these two leading causes of respiratory and cardiovascular illnesses. We recommend a health economic modeling assessment to confirm these efficiencies and cost-savings, and begin plans to implement pilot programs for administering both vaccines as a component of global introduction schemes.

In parallel there will be increased needs for data sharing with the potential for linking influenza to COVID-19 databases to better understand the epidemiology and the impact of public health interventions on co-circulating influenza and COVID-19, among other needed analyses. For example, preliminary information from the current southern hemisphere influenza season in countries with robust influenza surveillance program, that have implemented COVID public health measures (e.g., face masks, social distancing), are experiencing lower influenza activity [22].

Finally, there must be enhanced global collaborative efforts to develop effective communication strategies specific to vaccine hesitancy [23–24], and influenza and COVID-19 disease risks and the benefits of vaccines for communities and policy makers.

#### 5. Concluding remarks

There are opportunities to link the prevention of these two illnesses through both non-pharmaceutical interventions and vaccination at the individual, community, national, and medical system capacity levels. A global coordinated strategy that builds on influenza vaccine infrastructure and supports development of new robust seasonal influenza systems will help ensure an effective COVID-19 vaccine response, while also driving needed attention to seasonal flu. It could produce a long-term return in terms of reducing the health and economic burden of seasonal influenza, and advance readiness for the next pandemic. With the rise of influenza in the Southern Hemisphere and soon in the Northern Hemisphere, we must act now.

## **Declaration of Competing Interest**

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: PJH has developed subunit vaccines against SARS and

MERS coronavirus infection and is involved in the process of developing a vaccine against SARS-CoV-2.

### References

- Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet 2018;391(10127):1285–300.
- [2] Paget J, Spreeuwenberg P, Charu V, Taylor RJ, Iuliano AD, Bresee J, et al. Global mortality associated with seasonal influenza epidemics: New burden estimates and predictors from the GLaMOR Project. J Glob Health. 2019;9 (2):020421.
- [3] Filgueiras-Rama D, Vasilijevic J, Jalife J, Noujaim SN, Alfonso JM, Nicolas-Avila JA, et al. Human Influenza A virus causes myocardial and cardiac-specific conduction system infection associated with early inflammation and premature death. Cardiovasc Res 2020.
- [4] World Health Organization. COVID-19 situation reports 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/ 20200928-weekly-epi-update.pdf?sfvrsn=9e354665\_6. Accessed Oct 8, 2020.
- [5] Marshall E, Ribeiro G. Brazil breaks into Covid-19 top 3, but could already be number 1: @brazilianreport; 2020 updated 2020-05-19. Available from: https://brazilian.report/society/2020/05/19/brazil-breaks-into-covid-19-top-3-but-could-already-be-number-1/. Accessed May 31, 2020.
- [6] Hotez PJ, Bottazzi ME, Singh SK, Brindley PJ, Kamhawi S. Will COVID-19 become the next neglected tropical disease?. PLoS Negl Trop Dis. 2020;14(4): e0008271.
- [7] Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people?. Aging (Albany NY) 2020;12.
- [8] Zhao HL, Huang YM, Huang Y. Mortality in Older Patients with Covid-19. J Am Geriatr Soc. 2020.
- [9] Wu D, Lu J, Ma X, Liu Q, Wang D, Gu Y, et al. Coinfection of Influenza Virus and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2). Pediatr Infect Dis J. 2020;39(6):e79.
- [10] Wu S. Co-infection with SARS-CoV-2 and Influenza A Virus in Patient with Pneumonia, China - Volume 26, Number 6–June 2020 - Emerging Infectious Diseases journal - CDC. Emerg Infect Dis 2020;26(6).
- [11] Ma S, Lai X, Chen Z, Tu S, Qin K. Clinical Characteristics of Critically III Patients Co-infected with SARS-CoV-2 and the Influenza Virus in Wuhan. Int J Infect Dis: China; 2020.
- [12] Ropero-Alvarez AM et al. Expansion of seasonal influenza vaccination in the Americas. BMC Public Health 2009;9:361.
- [13] Richard Mihigo, Claudia Vivas Torrealba, Kanokporn Coninx, Deo Nshimirimana, Marie Paule Kieny, Peter Carrasco, Lisa Hedman, Marc-Alain Widdowson, 2009 Pandemic Influenza A Virus Subtype H1N1 Vaccination in Africa—Successes and Challenges, The Journal of Infectious Diseases, Volume 206, Issue suppl\_1, 15 December 2012, Pages S22–S28, https://doi.org/ 10.1093/infdis/jis535
- [14] Porter RM et al. Does having a seasonal influenza program facilitate pandemic preparedness? An analysis of vaccine deployment during the 2009 pandemic. *Vaccine*. Elsevier 2020;38(5):1152–9.
- [15] Ortiz JR, Perut M, Dumolard L, Wijesinghe PR, Jorgensen P, Ropero AM, et al. A global review of national influenza immunization policies: Analysis of the 2014 WHO/UNICEF Joint Reporting Form on immunization. Vaccine. 2016;34 (45):5400–5.
- [16] Lafond KE, Nair H, Rasooly MH, Valente F, Booy R, Rahman M, et al. Global Role and Burden of Influenza in Pediatric Respiratory Hospitalizations, 1982–2012: A Systematic Analysis. PLoS Med 2016;13(3):e1001977.

- [17] Iuliano AD, Roguski KM, Chang HH, et al. Estimates of global seasonal influenza-associated respiratory mortality: A modelling study. [Published online ahead of print December 31, 2017 Lancet.doi:10.1016/S0140-6736(17) 33293-2.
- [18] Ortiz JR, Perut M, Dumolard L, et al. A global review of national influenza immunization policies: Analysis of the 2014 WHO/UNICEF Joint Reporting Form on immunization. Vaccine. 2016;34(45):5400–5. <u>https://doi.org/ 10.1016/j.vaccine.2016.07.045</u>.
- [19] World Health Organization [Internet site]. Immunization coverage, WHO/ UNICEF joint reporting process. Geneva: WHO; 2019 Available at: https:// www.who.int/immunization/monitoring\_surveillance/data/en/
- [20] World Health Organization. Global Influenza Strategy. WHO. 2019-2030. Available from: https://apps.who.int/iris/handle/10665/311184, accessed June 14, 2020
- [21] Li Q, Tang B, Bragazzi NL, Xiao Y, Wu J. Modeling the impact of mass influenza vaccination and public health interventions on COVID-19 epidemics with limited detection capability. Math Biosci. 2020;325:108378.
- [22] Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. Decreased Influenza Activity During the COVID-19 Pandemic - United States, Australia, Chile, and South Africa, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(37):1305-1309. Published 2020 Sep 18. doi:10.15585/mmwr.mm6937a6
- [23] Hotez PJ, Nuzhath T, Colwell B. Combating vaccine hesitancy and other 21st century social determinants in the global fight against measles. Curr Opin Virol. 2020;41:1–7.
- [24] Hotez P. COVID19 meets the antivaccine movement. Microbes Infect. 2020; 22 (4): 162-4. doi: 10.1016/j.micinf.2020.05.010. Online ahead of print.