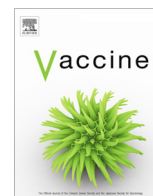




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## Commentary

## Influenza immunization and COVID-19

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## ARTICLE INFO

## Article history:

Received 1 July 2020

Received in revised form 24 July 2020

Accepted 27 July 2020

Available online 29 July 2020

## Keywords:

SARS-CoV-2

COVID-19

Influenza

Vaccination

Immunization

Healthcare personnel

High-risk patients

Pandemic RNA viruses unpredictably evolve, are genetically distinct from circulating strains, and cause sustainable human-to-human transmission and clinical illness. Starting in late 2019, the world was faced with a new coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of coronavirus disease 2019 (COVID-19) [1]. A pandemic was declared on March 11, 2020 and as of July 23 fifteen million cases and 619,150 deaths have been notified globally [1]. In this pandemic several countries experienced an unprecedented surge demand on their healthcare systems, which greatly exceeded their capacity to respond [2–4]. Shortages of healthcare workforce were also noted, with healthcare personnel (HCP), especially those in the frontline, disproportionately affected [5], and high rates of absenteeism were recorded [6].

As the potential of SARS-CoV-2 unfolds [7,8], it is highly likely that a second pandemic wave will occur starting this fall/winter. Although by the time COVID-19 hit the United States and Europe the majority of our influenza season was over, it is likely that we will not be that lucky this fall/winter. The demand that could be imposed on healthcare systems is expected to far exceed that of medical care demands during the influenza seasons alone. This is

attributed to three factors: first, human-to-human transmission of SARS-CoV-2 is much easier compared to influenza [a basic reproduction number ( $R_0$ ) of 3.6 was estimated for SARS-CoV-2 in Northern Italy] [8]; second, a very large proportion of the population remains susceptible; and third, the case fatality rate of COVID-19 is much higher than the case fatality rate for seasonal influenza [3]. Recently Faust and del Rio estimated that COVID-19 deaths are 9.5–44.1-times greater than those recorded during the peak week of influenza deaths during the past seven influenza seasons in the United States, with a 20.5-fold increased mean [3]. The demand that could be placed on healthcare systems could be even worse in countries like Greece, with very limited circulation of SARS-CoV-2 during the first wave.

Seasonal influenza is a major cause of morbidity, mortality, and use of healthcare services globally [9]. In accordance with the World Health Organization (WHO), up to 650,000 deaths are associated with seasonal influenza respiratory infections annually [9]. HCP are at increased risk for influenza infection, and have been often traced as sources of infection for vulnerable patients [10]. The rationale for immunizing HCP against influenza relies on the need to protect them, especially those with co-morbidities, their patients, and to provide healthcare services particularly at a time of high demand [10]. Beyond absenteeism, influenza immunization is expected to reduce presenteeism, which is frequent even among HCP who provide healthcare to high-risk patients.

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Influenza and COVID-19 can present with similar symptoms, and co-infections with a more severe course, complications or a fatal outcome have been recorded [11,12]. Beyond that, COVID-19 and seasonal influenza share the same high-risk groups and both can prove detrimental for older persons and persons with chronic co-morbidities, including obese persons and residents of long-term care facilities [13,14]. For example, in several European countries COVID-19-related deaths in residents of long-term care facilities accounted for 30–60% of all COVID-19 deaths [14]. Therefore, influenza immunization is of critical importance for high-risk groups to reduce the possibility of influenza infection and co-infection with SARS-CoV-2, diagnostic dilemmas, and inappropriate management in terms of antiviral therapy and infection control. A mathematical model developed to assess the effect of mass influenza immunization on the spread of COVID-19 and other respiratory pathogens in the case of an overlapping epidemic with the influenza season, found that increasing vaccine uptake could facilitate the management of respiratory outbreaks coinciding with the peak influenza season, and especially, compensate for the shortage of the detection resources [15]. Furthermore, in the case of co-circulation of influenza virus and SARS-CoV-2, high influenza vaccine uptake rates in a well-matched season between the circulating influenza strains and the vaccine influenza strains, could reduce the epidemiological noise of influenza during the COVID-19 epidemic. Beyond strong immunization recommendations against influenza, of equal critical importance is to ensure routine immunizations, e.g. pneumococcal immunization for the elderly and patients with chronic diseases and pertussis immunization for pregnant women.

Lastly, organizational or accessibility barriers in immunizations that emerged during the COVID-19 pandemic should be addressed. For example access to immunization services was highly jeopardized the past months in several countries, either because vaccinations were averted by the healthcare systems or because of the elimination of healthcare seeking for reasons other than COVID-19 [16].

Given the uncertainties of a second COVID-19 epidemic wave, and when a COVID-19 vaccine might be available, influenza immunization should be regarded as integral component of preparedness and response plans for the COVID-19 pandemic. Prioritizing influenza immunization of pregnant women, persons with co-morbidities, the elderly, and residents of long-term care facilities is absolutely justified. Increasing influenza vaccine uptake by HCP is also imperative in order to protect the essential healthcare services from influenza-associated absenteeism and the vulnerable patients they care for.

We call for public health authorities globally to work on raising influenza vaccine uptake rates prioritizing high-risk groups and HCP. In countries where HCP are immunized against influenza on a voluntary basis, like in almost all European countries, the implementation of mandatory immunization policies should be highly considered in the context of the ongoing pandemic [17,18]. Because concerns exist that manufacturers may divert manufacturing capacity to COVID-19 and other vaccines, we call upon manufacturers to insure an *increased* supply of influenza vaccines as early in the fall season as possible in order to allow large-scale immunization programs hopefully prior to a second wave of COVID-19.

#### Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing

interests: Dr. Poland is the chair of a Safety Evaluation Committee for novel investigational vaccine trials being conducted by Merck Research Laboratories. Dr. Poland offers consultative advice on vaccine development to Merck & Co. Inc., Avianax, Adjuvance, Valneva, Medicago, Sanofi Pasteur, GlaxoSmithKline, Emergent Biosolutions, and Dynavax. Dr. Poland holds patents related to vaccinia and measles peptide vaccines. These activities have been reviewed by the Mayo Clinic Conflict of Interest Review Board and are conducted in compliance with Mayo Clinic Conflict of Interest policies.

Dr Maltezou: nothing to declare.

Dr. Kalliopi Theodoridou: nothing to declare

#### References

- [1] World Health Organization. Coronavirus disease (COVID-19) pandemic, available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019> (last accessed: July 24, 2020).
- [2] Verelst F, Kuylen E, Beutels P. Indications for healthcare surge capacity in European countries facing an exponential increase in coronavirus disease (COVID-19) cases, March 2020. *Eurosurveill* 2020;25:2000323.
- [3] Faust JS, del Rio C. Assessment of deaths from COVID-19 and from seasonal influenza May 14. *JAMA Intern Med* 2020. <https://doi.org/10.1001/jamainternmed.2020.2306>.
- [4] Flores S, Gavin N, Romney ML, Tedechi C, Olsen E, Heravian A, et al. COVID-19: New York City pandemic notes from the first 30 days. *Am J Emerg Med* 2020; S0735-6757(20):30283-7.
- [5] Heinzerling A, Stuckey MJ, Scheuer T, Xu K, Perkins KM, Resseger H, et al. Transmission of COVID-19 to health care personnel during exposures to a hospitalized patient – Solano County, California, February 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:472-6.
- [6] Maltezou HC, Dedoukou X, Tseroni M, Tsonou P, Raftopoulos V, Papadima K, et al. SARS-CoV-2 infection in healthcare personnel with high-risk occupational exposure: evaluation of a seven-day exclusion from work policy. *Clin Infect Dis* 2020 Jun 29;ciaa888. doi: 10.1093/cid/ciaa888.
- [7] Rocklöv J, Sjödin H, Wilder-Smith A. COVID-19 outbreak on the diamond princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures taaa030. *J Travel Med* 2020;27.
- [8] Distante C, Piscitelli P, Miani A. Covid-19 outbreak progression in Italian regions: approaching the peak by the end of March in Northern Italy and first week of April in Southern Italy. *Int J Environ Res Public Health* 2020;17(9). E3025.
- [9] Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modeling study. *Lancet* 2018;391:1285-300.
- [10] Maltezou HC, Poland GA. Immunization of health-care providers: necessity and public health policies. *Healthcare* 2016;4. pii:E47.
- [11] Hashemi SA, Safamanesh S, Ghafouri M, Taghavi MR, Mohajer Zadeh Heydari MS, Namdar Ahmadabad H, et al. Co-infection with COVID-19 and influenza A virus in two died patients with acute respiratory syndrome, Bojnurd. *Iran. J Med Virol* 2020. <https://doi.org/10.1002/ijmv.26014>.
- [12] Ma S, Lai X, Chen Z, Tu S, Qin K. Clinical characteristics of critically ill patients co-infected with SARS-CoV-2 and the influenza virus in Wuhan. *China. Int J Infect Dis* 2020;96:683-7.
- [13] Petrilli CM, Jones SA, Yang J, Rajagopalan H, O' Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *Br Med J* 2020 May;22(369). m1966.
- [14] Danis Kostas, Fonteneau Laure, Georges Scarlett, Daniau Côme, Bernard-Stoecklin Sibylle, Domegan Lisa, et al. High impact of COVID-19 in long-term care facilities, suggestion for monitoring in the EU/EEA, May 2020. *Euro Surveill* 2020;25(22). <https://doi.org/10.2807/1560-7917.ES.2020.25.22.2000956>.
- [15] 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 capacity. *Math Biosci* 2020;325. 108378.
- [16] Saxena S, Skirrow H, Bedford H. Routine vaccination during covid-19 pandemic response Falls in uptake must be reversed quickly. *Br Med J* 2020;369. m2392.
- [17] Maltezou HC, Theodoridou K, Ledda C, Rapisarda V, Theodoridou M. Vaccination of healthcare workers: is mandatory vaccination needed?. *Expert Rev Vaccines* 2019;18:5-13.
- [18] Maltezou HC, Botelho-Nevers E, Brantsæter AB, Carlsson RM, Heininger U, Hübschen JM, et al. Vaccination policies of healthcare personnel in Europe: update to current policies. *Vaccine* 2019;37:7576-84.