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# Vaccine

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## Letter to the Editor

### COVID-19 and seasonal influenza: The potential 2021–22 “Twindemic”



Respiratory viruses tend to surge during cold weather. Influenza viruses circulate between birds, humans and other mammals, and cause seasonal flu. Cases usually begin to rise in the northern hemisphere around October each year and peaks the following January or February. In the United States (US) during the last 38-year period, flu activity peaked for 17 seasons in February, seven seasons in December, six seasons in January and six in March (only once in October and once in November) [1]. On the other hand, the season in the southern hemisphere starts around May and peaks between June and August.

The COVID-19 pandemic has heavily impacted influenza activity. Most countries in the northern hemisphere have witnessed elevated influenza activity during February and March 2020; however, the same activity sharply declined since mid-March 2020, concomitant with the spread of SARS-CoV-2. To note how influenza activity has remained low in many countries and regions ever since.

Such an important reduction pattern was due most likely to the implementation of public health and social measures. Although it's impossible to tease out which measure had the biggest impact, mask wearing, social distancing, and handwashing have played a critical role. Additionally, the interruption of most international travel and especially the closure of schools in several countries may have been a key factor in the reduction of influenza virus distribution [2].

Since 1952, the Global Influenza Surveillance and Response System (GIRS) routinely compile and share data from laboratories and public-health institutions in 123 countries that conduct viral genome-sequencing and protein characterization [3]. This enables a detailed picture of the annually most prevalent circulating viruses. Based on the annual findings, the World Health Organization (WHO) convenes a meeting every February and September with experts to recommend which strains of flu should be targeted by the forthcoming vaccines for the northern and southern hemispheres respectively (last ones were from 13 to 23 September on seasonal influenza and from 28 to 30 September on influenza of pandemic potential) [4]. Experts met in February 2021 and formulated recommendations on the selection of four viruses for 2021 vaccine in the northern hemisphere [5].

While the choice of the right viruses is always an issue (flu viruses are constantly changing, thus the vaccine composition is updated each year based on which influenza viruses are making people sick), this year might be even more problematic. Only 1,675 (0.2% of the 818,939 respiratory specimens) flu laboratory confirmed infections were reported in the US during the period between September 2020 and May 2021, which contributed to dramatically fewer flu illnesses, and deaths compared with previ-

ous flu seasons [6]. This is far lower than the 250,396 confirmed infections (16.8% of 1,491,430) reported during 2019–2020 [7]. Similarly, the overall cumulative hospitalization rate for the 2020–21 flu season was 0.8 per 100,000 while it accounted to 66.2 per 100,000 by the end of the 2019–20 flu season [7].

Considering the dearth of information available around which strains of flu are circulating, the Academy of Medical Sciences in Britain claimed that there is an increased likelihood that there will be influenza vaccine mismatch this winter, which could result in more infections and disease [8]. On the other hand, many fewer people have been exposed to the circulating flu viruses in the past year with possibly lower levels of natural immunity in populations. However, acquired immunity to influenza wanes over the course of years [9], with antibodies slowly diminishing and T cell memory responses able to provide a degree of protection (and cross protection) for many years [10].

Attempts to foresee what might happen in 2021 can be drawn from scientific literature. A report from US indicated that the 2012–13 influenza season was unusually early and severe, succeeding the record mild 2011–12 influenza season: authors found that when a winter was mild, on average 72% of the time the next epidemic was more severe than average, with a peak timing occurring 11 days earlier than average, and an epidemic growth rate 40% higher than average [11]. On the other hand, a modeling exercise carried out by the AMS showed that the National Health Service (NHS) could be under pressure with a winter influenza epidemic two times more deadly than normal.

The emerging evidence on the association between reduction of nonpharmacological interventions and the unprecedented surge of respiratory syncytial virus (RSV) might provide helpful insights. The normal RSV seasonal pattern seen in many countries was lost, and the peak of transmission (when it reappeared) was displaced to a non-typical season. While childcares remained opened through most of the lock-down in several setting, the resurgence of RSV occurred after lockdowns, which support the hypothesis of the role of lifting public health and social measures [12]. To note how the evidence is also pointing to the potential important role of adults in RSV transmission [12].

Despite the COVID-19 vaccination pace in several countries in northern hemisphere, the so-called “twindemic”, simultaneous outbreaks of covid-19 and flu, might indeed overwhelm health systems. On the other hand, employee absences due to mild sickness can cause significant disruption to the functioning of society, for example the recent cancellation of flights over Christmas.

Therefore, access to vaccines, both COVID-19 and influenza, becomes even more important together with active and prompt testing as well as public health and social measures. Vaccination in particular remains the best protective measure for prevention of influenza and vaccinating young children could be useful to decrease overall flu transmissibility.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Saverio Bellizzi\*

*Independent Consultant, Medical Epidemiologist, Geneva, Switzerland*

\* Corresponding author.

Catello M. Panu Napodano

*University of Sassari, Sassari, Italy*

Sergio Pinto

*University of Cagliari, Italy*

Giuseppe Pichierri

*Kingston Hospital NHS Foundation Trust, Microbiology Unit, Kingston*

*Upon Thames, United Kingdom*

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