

The impact of the COVID-19 pandemic on the global burden of influenza

Annually, the World Health Organization (WHO) estimates that there are approximately 1 billion human influenza cases of which 3–5 million are considered severe (particularly in children, the elderly, and in the immunocompromised) resulting in between 290 000 and 650 000 deaths.¹ The devastating coronavirus disease 2019 (COVID-19) pandemic, for which there have been over 300 million confirmed cases and over 5 million deaths² has had dramatic effects on the lives of individuals in every region of the world. The public health measures implemented (including social distancing, wearing of face masks, working from home, closure of schools, and travel restrictions) aiming to limit ongoing transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the associated behavioral changes resulting from the pandemic are likely to have had a significant impact on the influenza transmission. Sharp declines in influenza virus circulation were observed in the United States within just 2 weeks of the COVID-19 emergency declaration on March 11, 2020 and the introduction of public health measures.³ Other countries including Taiwan, Korea, Hong Kong, and Singapore all reported similar observations.^{4–7}

In the Southern Hemisphere amongst children in Western Australia, rates of influenza detection in the first 13 weeks of 2020 (before implementation of COVID-19 restrictions) were comparable to those seen in previous seasons.⁸ Following the introduction of local restrictions in Week 14, influenza activity fell and remained at low levels throughout the winter period (Weeks 23–35) relative to previous seasons, even after the subsequent relaxation of COVID-19 restrictions. Influenza detections were 99.4% lower from Weeks 14 to 35 of 2020 when compared to the same period in pre-COVID-19 years (0.03% in 2020 vs. 3.6%–16.4% between 2012 and 2019). The fact that testing rates for influenza in the study region were higher in 2020 compared to previous years suggests that the lower influenza detection rates were not simply attributable to reduced health-seeking behavior and/or reduced testing (hypotheses for which the declines in influenza circulation were initially suggested by some^{3,9,10}). This study, however, did not include hospital admission data. It is important to note that unlike with COVID-19 where the disease burden in children appears to be relatively low compared to in adults,¹¹ influenza is responsible for significant morbidity in children (at times resulting in hospital admission rates on a par with the excess admission rates observed in at-risk adults¹²).

Influenza data reported to the WHO's FluNet platform from three Southern Hemisphere regions (Australia, Chile, and South Africa) demonstrated extremely low influenza activity during

June–August 2020, a period of the year that corresponds to the Southern Hemisphere winter influenza season. In the Northern Hemisphere, the 2019–2020 influenza season was cut short by approximately 6 weeks compared to previous years (2016–2019) despite exhibiting relatively high influenza activity in January 2020 (before the COVID-19 pandemic declaration) suggesting that it could be a particularly severe influenza season.¹³ The sudden fall in influenza activity in the Northern Hemisphere in the 2019–2020 influenza season occurred in early April 2020 just weeks after the declaration of the COVID-19 pandemic.¹³ In Hong Kong, the 2019–2020 winter influenza season was 63.2% shorter compared to 2015–2019 and the number of deaths from laboratory-confirmed influenza in adults was 62.3% lower.¹⁴ A study investigating the effect of enhanced public health intervention in China during the COVID-19 epidemic reported a 6.25% decrease in the positive influenza rate in 2020 compared to the previous 5 years.¹⁵ In view of the ongoing COVID-19 pandemic, these observations continued in 2021 as demonstrated by a population-based Canadian study which found that during 2020–2021 influenza A and B rates decreased to 0.0015 and 0.0028 times that of prepandemic levels, respectively.¹⁶ A finding which has been echoed in several other parts of the world.^{17–19}

The degree to which influenza vaccination rates played a role in the highly attenuated winter influenza seasons across several regions of the world is not entirely clear. Increased influenza vaccination uptake and reduced global travel may have been contributory factors. In Australia, between the beginning of March and mid-April 2020, over 2.1 million influenza vaccines had been administered compared to 235 000 and 624 000 at the same times of year in 2018 and 2019, respectively.²⁰ Interestingly, a cross-sectional self-administered anonymous questionnaire survey conducted amongst nurses in Hong Kong (806 responses) between February and March 2020 showed a similar influenza vaccine acceptance rate in 2019 (47.5%) when compared to their intention to accept the influenza vaccine in 2020 (44.7%).²¹ This is similar to the findings from a study of healthcare workers in Hong Kong during the 2009 H1N1 pandemic that found no difference in H5N1 vaccination acceptance at the different WHO alert levels.²² However, these observations amongst the studied healthcare workers in Hong Kong are not necessarily echoed amongst nonhealthcare workers in Hong Kong or amongst people in other parts of the world. Findings from a United Kingdom observational study by Bachtiger and colleagues of 6641 respondents certainly differed in that the COVID-19 pandemic has

increased the acceptance rate of the influenza vaccination (in those previously eligible for the influenza vaccine) from 79.6% up to 91.2% for 2020–2021 influenza season.²³ Of note, amongst previously influenza vaccine eligible respondents in their study with school-age children, 82.5% of those intending to vaccinate themselves also intended to vaccinate their children whereas 25.8% of those unwilling to vaccinate themselves would, however, vaccinate their children. Recent Public Health England (PHE) data supports the findings of Bachtiger et al.²³ in that influenza vaccine uptake for 2020–2021 was the highest it had ever been at the time of the study for those aged over 65 years and in 2–3 year olds.²⁴ US national survey data indicated that 59% planned to be vaccinated against influenza during the 2020–2021 influenza season (compared to 52% who had planned to be vaccinated in 2019); 28% responded that the COVID-19 pandemic made them more likely to receive the influenza vaccination during the 2020–2021 influenza season.²⁵

It is known that infection of a host with a particular virus can reduce the risk of infection with a different virus within the same individual, termed viral interference, which has raised the question by some as to whether this could explain, at least in part, the diminished influenza activity during the COVID-19 pandemic. This question currently remains unanswered, however, there have been numerous reports of cases of SARS-CoV-2 and influenza coinfection, and reported coinfection rates in the literature range from 0.08% up to 90% depending on the region.²⁶ In addition, the human receptor for SARS-CoV-2 is angiotensin-converting enzyme 2²⁷ whereas sialic acid serves as the receptor for the influenza virus therefore the two viruses are not competing for the same cellular receptors for cell entry. It is, however, important to be aware that utilization of the same cellular receptor is not a prerequisite for viral interference as has been demonstrated by rhinovirus-induced inhibition of influenza infection through rhinovirus-induced activation of human antiviral defenses within the human respiratory epithelium.²⁸ The SARS-CoV-2-influenza viral interference hypothesis is, however, unsupported by the observed declines in influenza activity in the US even prior to widespread SARS-CoV-2 transmission across most of the country,³ although lower SARS-CoV-2 testing rates at that early stage and/or a possible natural end to the 2019–2020 influenza season could have influenced these observations. Interestingly, PHE data (looking at 2019, 256 individuals who were tested for both SARS-CoV-2 and influenza between January 20 and April 25, 2020) found that the risk of testing positive for SARS-CoV-2 was 58% lower among influenza-positive cases.^{29,30} Data from New York (of 16 408 patients tested for SARS-CoV-2 between March 16 and April 20, 2020) revealed that the influenza infection rate was 0.08% in individuals in whom SARS-CoV-2 was detected compared to 1.54% (×19-fold greater) in individuals who tested negative for SARS-CoV-2.³¹ Inferences with regard to viral interference between SARS-CoV-2 and influenza cannot be clearly made from these data. PHE data showed that the mortality was high at 43.1% in the 58 people with confirmed SARS-CoV-2-influenza coinfection; a mortality rate 2.72 times higher than in SARS-CoV-2 mono-infection (and 5.92 times higher than in individuals infected with neither virus) and therefore potentially

synergistic effects between the two viruses has been suggested by the investigators³⁰ which is in stark contrast to SARS-CoV-2-influenza viral interference hypothesis. It is unclear whether the particularly high mortality rate in coinfecting individuals could possibly be attributed in part to behavioral changes amongst medical personnel in initiating anti-influenza treatment. In previous influenza seasons, many patients would be empirically prescribed a neuraminidase inhibitor when admitted to a healthcare facility with an influenza-like illness. In light of the COVID-19 pandemic, efforts have been primarily focused on initiating therapies for COVID-19 which could potentially lead to delays in starting anti-influenza treatment. The timing of treatment initiation for influenza is important given that most studies have suggested that oseltamivir is most effective when initiated within 48 h of illness onset.³² However, if influenza activity remains at such low levels then this may be less of an issue than envisaged.

There are valuable lessons and insights gained from the public health strategies (including mass vaccination) implemented during ongoing the COVID-19 pandemic, many of which may be important in reducing influenza-associated morbidity and mortality in the years ahead.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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