COVID-19 and influenza

What can we expect this year?

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Last year, influenza vaccination campaigns targeted avoidance of the 'twindemic' of concomitant COVID-19 and influenza. In 2021, a strong vaccination effort will help protect against a major winter outbreak of these diseases.

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Key points

- **In 2020, influenza case numbers between April and September were less than 5% of the previous five-year average.**
- **Although the extent of the upcoming influenza season is unknown, early data suggest a significant outbreak is not likely. However, if there is reduced immunity due to the absent 2020 season and the virus arrives, influenza activity may be high.**
- **With few COVID-19 cases in Australia, there will not be viral competition to stop the spread of influenza here.**
- **For older people, adjuvanted influenza vaccines have been shown to overcome the usual poor immune response due to immunosenescence and chronic, sterile, low-grade inflammation ('inflammaging').**
- **Continuing to improve uptake of influenza vaccine in children will be important in 2021.**
- **Quadrivalent cell-based influenza vaccines are available for the first time this year.**
- **SARS-CoV-2 will continue to be a risk to Australia through overseas arrivals.**
- **A strong vaccination effort by primary care physicians and other healthcare providers will be key this winter.**

Influenza in recent years

In 2019, Australia saw its most intense influenza season since accurate collation of data began, with over 300,000 laboratory confirmed notifications to the National Notifiable Disease Surveillance System.[1] The notifications were mainly for the H3N2 strain of influenza A, which causes disease predominantly in older people. The outbreak occurred despite a record distribution at that time of 14.5 million influenza vaccines in Australia. It was associated with an estimated 3000 deaths.[1]

Amid the high volume of disease in 2019 there were some exciting data about the impact of using an adjuvanted vaccine in the elderly. The aim of influenza vaccination is not preventing influenza disease but maintaining functional capacity, which in elderly people means avoiding the prolonged bed rest of hospitalisation. Queensland surveillance data show that although the amount of illness in people aged over 65 years was comparable in 2017 and 2019 – which were both intense years for influenza – the hospitalisation rate in 2019 was

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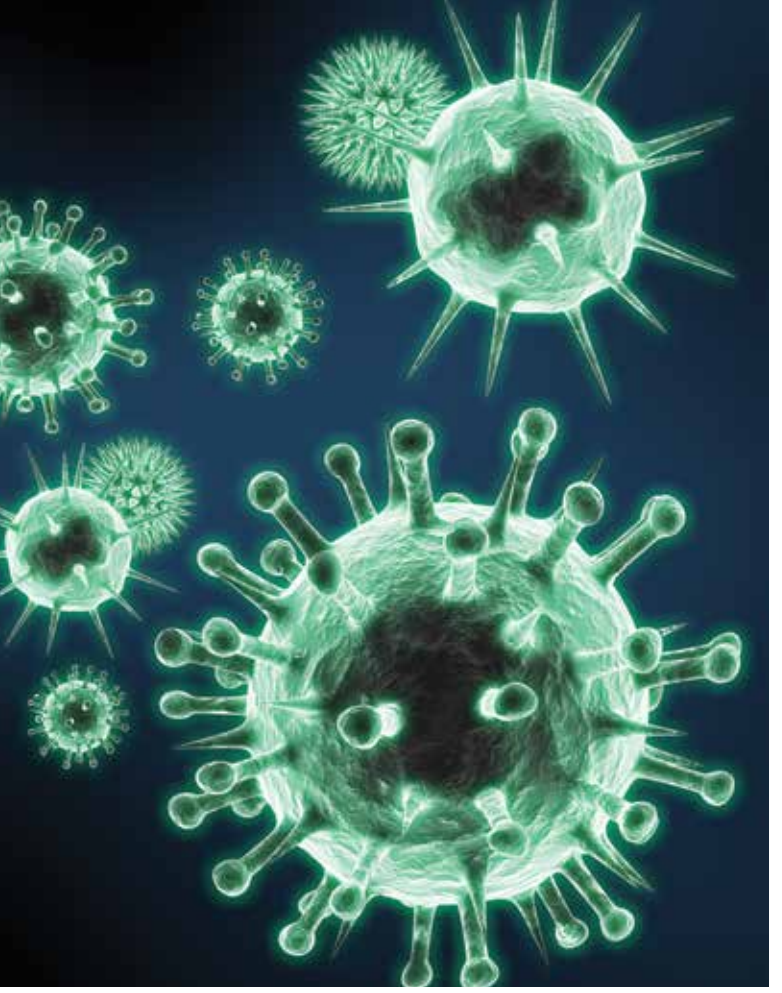

60% lower for this age group.[2,3] This was the first year only adjuvanted vaccine and no other vaccine was used in older people.

Published data from the WHO Collaborating Centre for Reference and Research on Influenza for vaccine effectiveness in the southern winter of 2019 explains this.[4] Vaccine effectiveness against the H3N2 strain was actually highest in the over-65 years age group – a finding never seen previously, when using unadjuvanted vaccines in older people. The adjuvanted vaccine overcame the usual poor immune response that is caused by immunosenescence and the chronic, sterile, low-grade inflammation ('inflammaging') that is present in older people.

In 2020, after significant interseasonal circulation of influenza between January and March, Australia saw the 'arrival' of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The associated control mechanisms (mask wearing, travel restrictions, physical distancing, workplace and school closures) led to influenza numbers from April to September being less than 5% of the previous five-year average, and less than 0.5% of the number for the previous year's number of almost 280,000.[1] This disappearance of influenza cases was aided by a high influenza vaccination coverage – the distribution of 18 million vaccine doses in 2020 was a new record. Surveillance data (albeit inaccurate because many doses are not added to the Australian Immunisation Register) showed a 6% increase in vaccination coverage in older people and a record 44% coverage of children between 6 months and 5 years of age.[5]

Vaccination campaigns targeting avoidance of the 'twindemic' of concomitant coronavirus disease 2019 (COVID-19) and influenza infection were important in increasing vaccine uptake and decreasing influenza numbers. More important – almost certainly – were the public health measures used to address COVID-19, including a six-month lockdown of the city of Melbourne.

It was not just influenza numbers that declined during the winter of 2019 as a result of public health messaging. Many other respiratory infections did not circulate at their usual intensity. In Western Australia, notifications of respiratory syncytial virus (RSV) in children dropped by 98% during winter, despite schools being open.[6]

In much of the northern hemisphere in the winter just gone, SARS-CoV-2 was rampaging, aided by a very poor uptake of many public health measures. Helpful measures such as mask wearing became political issues and there was a widespread lack of compliance. Despite this, influenza did not arrive in either Europe or North America. The US Centres for Disease Control and Prevention described the northern winter influenza season case numbers as unusually low, including in children, with one recorded death last winter.[7]

Researchers from Public Health England looking at data for coinfection suggest a possible pathogenic competition between SARS-CoV-2 and influenza viruses may have contributed to low influenza numbers.[8] Influenza is not a colonising virus, so competition is plausible.

Additionally, the marked reduction in international travel almost certainly played a part in the demise of a virus that travels the world from winter to winter.

What can we expect for COVID-19 in the upcoming winter?

SARS-CoV-2 will continue to be a risk to Australia through overseas arrivals. This RNA virus will continue to make mistakes copying itself, leading to variants that will outcompete older strains based on better infectivity. As with recent 'variants of concern', some of these new strains will produce more severe disease and some will have spike proteins that are sufficiently distinct to no longer be neutralised by antibodies that are produced by receipt of our vaccines.

The present Australian Government advice is that Australia's external borders will officially stay closed until the end of June 2021. Whether a high vaccination coverage will lead to an opening of our borders then is unclear. If it does, SARS-CoV-2 will return to the country. This coronavirus is not amenable to eradication in the long term after borders re-open. Eventually we will need to learn to live with it, as we do with influenza each winter.

This winter, although the number of COVID-19 cases will continue to be high in many parts of the world, they will be minimal in a closed-border Australia.

What can we expect for influenza in the upcoming winter?

With few COVID-19 cases in Australia, there will not be viral competition to stop influenza spreading here. There is evidence of public fatigue with masking and public health restrictions elsewhere – the increased time needed to control the fourth wave of

COVID-19 in Hong Kong, for example, was attributed to fatigue and decreased public compliance with recommended infection control measures.[9] Australia cannot continue to rely on strong adoption of public health messages by the populace to keep case numbers of influenza suppressed.

So, will we get an influenza outbreak of significance this winter? Would perhaps the arrival of influenza B or the H1N1 strain of influenza A infecting children who are back at school and in childcare centres lead to high community activity?

Some early data suggests that this will not happen. Overseas arrivals spend 14 days in isolation and would not be infectious with influenza or other respiratory viruses when released. Nor are we seeing influenza cases in the north of Australia, which is often an early clue to what will happen across the rest of the country.

Against this was the unusual resurgence of RSV cases in many states during the summer months. In Western Australia, the speed and magnitude of this increase was greater than the usual winter surge.[10] One contributing factor may have been reduced immunity to RSV through an increase in the number of RSV-naïve children and possibly a waning RSV immunity in older children related to the delayed season. If there is reduced immunity to influenza due to the absent 2020 season and the virus arrives, influenza activity this winter may be high.

The three-month interval in the two-dose regimen of the AstraZeneca COVID-19 vaccine leaves a lot of time for influenza immunisation. We must ensure that older people receive the adjuvanted vaccine and that we continue to improve vaccine uptake in children.

Although the extent of the upcoming influenza season is unknown, we face the risk that community apathy about influenza will reduce the benefit we had last year of very high coverage with influenza vaccines. We cannot allow 'likely low case numbers' to cause the loss of recent gains. The three-month interval in the two-dose regimen of the AstraZeneca COVID-19 vaccine leaves a lot of time for influenza immunisation. We must ensure that older people receive the adjuvanted vaccine and that we continue to improve vaccine uptake in children.

Final comments

Each year our influenza vaccine armamentarium improves. This year we will again have adjuvanted vaccines for the elderly population. In addition, quadrivalent cell-based vaccines are available for the first time this year on the private market for people over 9 years of age. During the production of cell-based vaccines, the virus is grown in cultured cells of mammalian origin (instead of hens' eggs). These vaccines will have improved effectiveness compared with egg-based vaccines in a year when there is 'egg adaptation' during production (i.e. when a strain that is growing poorly adapts to grow more efficiently in the egg environment but thereby changes from the original viral strain that is probably circulating).[11]

A strong influenza vaccination effort by primary care physicians and other healthcare providers – coupled with closed external borders – should ensure that neither COVID-19 nor influenza case numbers are a cause for concern this winter. **RMT**

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