Seasonal influenza and vaccination strategies—is a paradigm shift needed? A synopsis of the 3rd New Zealand Influenza Symposium, November 2016

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ABSTRACT

Influenza continues to be a global public health problem despite the availability of preventive vaccines and public health vaccination programmes. This paper presents a synopsis of the 3rd New Zealand Influenza Symposium (NZiS) that was hosted by the Immunisation Advisory Centre (IMAC) in November 2016. Experts and service providers convened to discuss current issues in the prevention and management of influenza. One of the key topics discussed was the use of novel vaccines, such as adjuvanted and high-dose vaccines, and antiviral prophylaxis to protect young children and the elderly. Another area of focus was on paradigms of seasonal influenza vaccination strategies that reduce community transmission and provide individual protection to reduce the burden of influenza. The need for better influenza surveillance and country-specific data to guide policy makers and healthcare providers was highlighted in order to improve population health outcomes.

Influenza continues to be a global public health problem despite the wide availability of preventive vaccines and public health vaccination programmes. The 3rd New Zealand Influenza Symposium (NZiS) was held on 2 November 2016 by the Immunisation Advisory Centre (IMAC), an organisation based at the University of Auckland that undertakes research and provides advice about vaccines and vaccine-preventable diseases. The annual event convened international and national influenza experts and service providers to discuss current issues in the prevention and management of influenza. The 3rd NZiS built upon discussions from the two previous symposiums.[1,2] This paper presents a synopsis of the 3rd NZiS, focusing on the key topics discussed, including influenza surveillance, vaccines and antivirals for young children and the elderly, the 2016 seasonal influenza immunisation programme in New Zealand and paradigms of vaccination strategies.

Influenza surveillance mechanisms globally and in New Zealand

Influenza surveillance is vital to facilitate the coordination of prevention and management activities. The World Health Organization's (WHO) Global Influenza Programme (GIP) provides strategic guidance, support and recommendations for preparing and responding to seasonal and pandemic influenza. This global platform relies on the Global Influenza Surveillance and Response System (GISRS) that collects and analyses global surveillance data on influenza virology and epidemiology.[3] The GISRS monitors the evolution of circulating influenza viruses and provides necessary recommendations, particularly regarding seasonal influenza vaccine composition, antiviral susceptibility and diagnostic development.[3] FluNet plays an important role for global influenza virological surveillance by tracking the movement of influenza

virus subtypes based on data reported from national influenza centres and other influenza laboratories around the world.[4] FluID, a web-based tool, complements FluNet by compiling regional influenza epidemiological data into a global dataset.[5] The surveillance information collected at the global level is reported in various formats to help nations strengthen their influenza control programmes.

In New Zealand, influenza surveillance is comprised of sentinel general practice surveillance and non-sentinel laboratory-based surveillance. The Southern Hemisphere Influenza Vaccine Effectiveness Research and Surveillance (SHIVERS) project (2012–2016), which was funded by the Centers for Disease Control and Prevention (CDC) and lead by the Institute of Environmental Science and Research (ESR), has provided a valuable national platform for seasonal influenza control and pandemic preparedness. To date, the study has improved sentinel influenza surveillance capabilities, thereby allowing for a better understanding of influenza disease burden. These findings have had various global and national public health impacts, such as informing vaccination policy and guiding vaccine development for improved health outcomes. For instance, low vaccine coverage and high influenza-associated hospitalisation rates were noted among young children in New Zealand. This finding informed a vaccination policy change so that New Zealand children aged six months to five years old who have been hospitalised or have a history of significant respiratory illness are now eligible for free influenza vaccination.[6,7] Results from SHIVERS have also influenced a revision of the WHO's case definition for severe acute respiratory infection (SARI); the Global Epidemiological Surveillance Standards for Influenza now state that symptom onset is within the past 10 days instead of seven.[7] Moreover, the SHIVERS studies on vaccine effectiveness (VE) have helped inform the WHO's annual vaccine strain selection.[8–11] The SHIVERS study is also contributing to the WHO-led Pandemic Influenza Severity Assessment (PISA), a pilot project aimed at supporting influenza risk assessment to inform better response decisions during a pandemic.[12]

Influenza vaccines and antivirals for vulnerable groups

More effective influenza vaccines for young children and the elderly

Influenza disproportionately affects young children (aged between six months and five years) and the elderly (aged more than 65 years); these vulnerable groups typically experience more severe complications.[13] Vaccination prevents influenza-related illness and complications and is routinely recommended for everyone aged six months and older who do not have a contraindication, particularly those who are at high risk.[13] The live attenuated influenza vaccine (LAIV) and the inactivated influenza vaccine (IIV) are the two currently internationally licensed and most commonly used seasonal influenza vaccines. Although young children and the elderly experience the greatest influenza disease burden, research shows that the seasonal influenza vaccines can be less effective among these populations.[14] Given the findings from recent VE studies and the development of novel vaccines, there is ongoing debate concerning which type of vaccine should be recommended for these vulnerable groups to confer optimal protection.

Among young children, there has been a long-standing recommendation for the use of LAIV due to its similar or superior vaccine efficacy and effectiveness compared to that of IIV.[15–17] However, recent evidence from the US revealed that the quadrivalent LAIV had low effectiveness, particularly against the influenza A(H1N1) virus (A[H1N1] pdm09).[18,19] Accordingly, the CDC's Advisory Committee on Immunisation Practices (ACIP) made an interim recommendation that LAIV should not be used during the 2016–17 influenza season.[20,21] Conversely, data from Europe reported reasonable VE of the quadrivalent LAIV that conferred moderate to good levels of protection among young children.[22–23] These data support the continued use of LAIV for young children as part of routine paediatric vaccination programmes in Finland and the UK.[24] Given the sub-optimal efficacy of IIV and LAIV reported by some studies, adjuvanted trivalent IIV (ATIV) is increasingly being considered for use among young children as

adjuvants enhance one's immune response to vaccines. Studies have revealed that ATIV is more efficacious compared to trivalent IIV and elicits a stronger, more persistent immune response thus supporting the use of ATIV for influenza vaccination in young children despite concerns of increased reactogenicity.[25,26]

The conventional trivalent IIV is less immunogenic and efficacious among the elderly compared to young adults, owing to the effects of immunosenescence; thereby, only a modest level of protection is conferred in the elderly population.[27–28] Supporting this, pooled SHIVERS data from 2013–2015 suggests that effectiveness for the elderly may be lower with a point estimate for VE of 40% (95% confidence interval [CI] 14–58%) compared to 55% (95% CI 38–68%) for those under 17 years old.[8–11] The development of novel vaccines is one of the various strategies used to improve vaccine-induced protection and improve clinical outcomes against influenza among the elderly.[28] A recent review and meta-analysis showed that ATIV had superior efficacy compared to non-adjuvanted vaccines in reducing influenza-related illness and complications among the elderly.[29] Moreover, data suggest that ATIV results in higher antibody titres for A(H3N2), the subtype of most concern for the elderly, and confers increased serological protection against drifted strains compared to non-adjuvanted vaccines.[30] High-dose (HD) vaccines containing four times the amount of hemagglutinin (HA) versus the standard dose (SD) vaccine have also been designed to elicit a greater antibody response among the elderly.[28] Data from large multicentre, randomised control trials suggest that the HD trivalent IIV is safe, well tolerated and elicits a superior immune response compared to the SD vaccine among the elderly for all included vaccine strains.[31–33]

Antiviral prophylaxis among the elderly

Elderly who reside in long-term care facilities (LTCFs) are particularly vulnerable to influenza outbreaks due to their advanced age, underlying heath conditions, congregated living situations and contact with multiple caregivers.[34,35] Various non-pharmaceutical (eg, social distancing, hand hygiene) and pharmaceutical (eg, vaccines, antivirals) measures are used to mitigate influenza outbreaks in LTCFs.[36] Annual seasonal influenza vaccination of residents and staff remains a key strategy to prevent influenza illness; however, the effectiveness of this strategy in these settings can be negatively impacted by suboptimal uptake rates and low vaccine efficacy in the elderly.[36–37] Antivirals reduce viral shedding when administered within 48 hours of symptom onset. Antivirals may also be prescribed for prophylactic purposes and antiviral prophylaxis may be one of the most effective influenza control strategies for the elderly residing in LTCFs where vaccine efficacy is reduced.[36] Research has indicated that offering antivirals prophylactically to all asymptomatic residents during an influenza outbreak can shorten the duration of an outbreak.[38–39] These findings support the prompt detection of an influenza outbreak and administration of antiviral prophylaxis among residents and staff in LTCFs, despite prior vaccination, to control an outbreak.

Seasonal influenza immunisation programme in New Zealand

National strategy and communications

The national strategy is focused on improving influenza immunisation coverage for high-risk groups, including pregnant women, the elderly and those with certain medical conditions. The Ministry of Health (MOH) is working on its infrastructure to support broadening access. These efforts align with recent data collected from the National Immunisation Register (NIR) suggesting that certain ethnic minority groups and pregnant women have particularly low rates of influenza vaccination. Recent research commissioned by the MOH to understand the knowledge and attitudes about influenza vaccination among pregnant women revealed that the most significant barriers were lack of accessible information and experiencing structural barriers for accessing immunisation services.[40]

The MOH recommends that all influenza vaccinations administered are appropriately recorded on the NIR to enable the collection of accurate data. Previous issues affecting coverage data included the inability of vaccinating pharmacists to enter data on the NIR. To improve data accuracy, the MOH has developed a web-based application called "ImmuniseNow" to be implemented in 2017 that will enable pharmacist vaccinators to

record immunisations on the NIR. Another step to supporting priority health professional groups was the addition of two new members to the National Influenza Strategy Group (NISG) to represent the views of pharmacists and midwives.

The 'blue dust' branding was used again for the 2016 seasonal influenza immunisation campaign that uses blue powder imagery to visually symbolise the spread of influenza. There was an increased focus on improving access to online resources for primary care and district health boards (DHBs), along with using various media outlets (eg, radio and television advertisements) to raise public awareness about the campaign. DHB-specific resources were created to increase the effectiveness of the messaging and cater to the local population. These efforts resulted in a successful campaign that achieved the MOH's target of distributing 1.2 million doses. In 2016, according to the NIR, about 50% of influenza vaccinations were recorded. For the eldery population during the 2016 influenza season, a total of 705,655 doses were administered and 56% were recorded on the NIR as having received an influenza vaccination.

Moving forward, the focus of the 2017 campaign will be on raising public awareness about the burden of asymptomatic influenza, using animated infographics as a communication strategy, translating campaign resources into multiple languages to improve accessibility, increasing interaction with primary care and supporting DHBs to share innovative ideas.[41] Some challenges that the campaign will continue to address include how to make system improvements to enable data entry on the NIR, improve immunisation coverage for health care workers and how to deal with the changing media landscape.

District health board strategy

At the DHB level, challenges identified during the immunisation campaign included not having adequate vaccinators, lack of vaccination champions and the need to overcome anti-vaccination sentiments and misconceptions about the influenza vaccine. Low influenza immunisation coverage rates among some DHB staff members was identified as a high priority. Tairawhiti DHB reported the highest workplace influenza immunisation coverage rate and primarily attributed this to hosting a designated 'flu week' for staff vaccinations.[42] Waikato DHB successfully continued the implementation of its mandatory influenza vaccination policy for staff and noted that employee contracts for new hires now state this requirement. Other DHBs shared helpful strategies to improve staff immunisation rates, including promotion by senior leaders in charge, clear communication to staff from senior management and using an influenza-specific trolley containing the equipment required to deliver vaccinations.

Key issues regarding service delivery

Various healthcare planners and providers shared their perspectives on the delivery of the influenza immunisation campaign. Practice nurses highlighted the importance of opportunistic vaccinations (ie, offering vaccination at every contact point with health services) and offering short appointments specifically for patients to obtain their influenza vaccination.[43] Registered nurses working in occupational health play an important role in administering influenza vaccines to healthy adults at numerous workplaces.[44] While they are not yet able to record the vaccines they administer on the NIR, the potential for occupational health vaccinators to use "ImmuniseNow" was discussed to enable the collection of more accurate data.[44] Midwives promote and deliver the vaccine to pregnant women at ante-natal clinics.[45] Midwives reported providing information sheets specific for pregnant women to raise awareness about the influenza vaccine and used labels in women's files to prompt practitioners to ask about vaccinations.[45]

In 2012, following a national policy change to reclassify the influenza vaccine by the Medicines Classification Committee, pharmacists began to administer the influenza vaccine.[46] This has increased the access and convenience of obtaining an influenza vaccination, along with alleviating some pressure off primary care.[47] Some barriers were noted by pharmacists delivering the influenza vaccine, including the costs associated with training pharmacists to vaccinate, only being approved to deliver the unfunded influenza vaccine, and lack of public awareness that pharmacists can vaccinate.[47]

Alternative paradigms for influenza vaccination strategies

Despite reasonably good influenza vaccine uptake rates and efforts to broaden access and improve infrastructure in New Zealand, room for improvement remains regarding the implementation of vaccine policies that will maximise public health benefits and efficiently use resources. In New Zealand, the main focus of the existing seasonal influenza campaign is on individual protection and specifically targets high-risk groups. An alternative strategy that appears to be effective is to focus on limiting community-level transmission (ie, a herd immunity approach), which would involve universal childhood vaccination. Evidence suggests that children are the main drivers of influenza transmission; thus, vaccinating healthy children can potentially provide direct protection to the child and indirect protection to the rest of the population due to the benefits of herd immunity.[48–51] Modelling and economic evaluation studies suggest that adding children to existing influenza programmes would be cost-effective and reduce transmission and morbidity and mortality rates.[48,51,52]

In the UK, the Joint Committee on Vaccination and Immunisation (JCVI) made a recommendation in 2012 to extend the annual influenza vaccination programme to all healthy children aged 2–16 years old using the LAIV.[53] Since the 2013–2014 season, the UK has been rolling out this childhood programme to complement the existing individual-protection strategy based on age and risk-based policy.[53] Given the considerable operational and resource challenges associated with implementing a general practitioner office and school-based LAIV programme, it was rolled out as a pilot programme in primary schools with phased extensions occurring yearly.[53,54] The programme has been implemented successfully, resulting in an overall coverage rate of 52.5% in the initial pilot areas.[54,55] Research to date indicates that the childhood LAIV programme has resulted in an overall reduction in cumulative influenza-like illness incidence and influenza positivity in pilot areas versus control areas.[22,55,56] Given this success, the JCVI plans to continue the roll-out of this programme and strengthen surveillance to monitor the associated impact. This evidence may prompt other countries to adopt a similar vaccination policy to reduce the burden of paediatric influenza.[54]

Conclusion

The third NZiS brought together various experts and providers in the field of influenza prevention and management. The presentations at the symposium summarised key issues and experiences, along with stimulating interesting discussions about future improvements. Given that young children and the elderly are disproportionately impacted by influenza, continued focus is warranted regarding the optimal use of novel vaccines and antivirals for these vulnerable groups. Moreover, as some countries shift away from traditional influenza vaccination strategies and include extensions for certain sub-groups, much debate remains regarding which strategy is best to provide optimal population protection and not just individual protection. To make informed decisions, policy makers and programme planners will require country-specific data by age group on disease burden, transmission dynamics and cost-effectiveness. These suggested areas of future work are underscored by the need for more timely and accurate influenza surveillance data to better inform response decisions and vaccination programmes for improved population health outcomes.

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