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Charamia, N. A., Mansoor, O. D., Murfitt, D., & Turner, N. M. (2016). What's new with the flu? Reflections regarding the management and prevention of influenza from the 2nd New Zealand Influenza Symposium, November 2015. *New Zealand Medical Journal*, 129(1441), 54-62.

<https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2016/vol-129-no-1441-9-september-2016/6999>

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What's new with the flu? Reflections regarding the management and prevention of influenza from the 2nd New Zealand Influenza Symposium, November 2015

Nadia A Charania, Osman D Mansoor, Diana Murfitt, Nikki M Turner

ABSTRACT

Influenza is a common respiratory viral infection. Seasonal outbreaks of influenza cause substantial morbidity and mortality that burdens healthcare services every year. The influenza virus constantly evolves by antigenic drift and occasionally by antigenic shift, making this disease particularly challenging to manage and prevent. As influenza viruses cause seasonal outbreaks and also have the ability to cause pandemics leading to widespread social and economic losses, focused discussions on improving management and prevention efforts is warranted.

The Immunisation Advisory Centre (IMAC) hosted the 2nd New Zealand Influenza Symposium (NZIS) in November 2015. International and national participants discussed current issues in influenza management and prevention. Experts in the field presented data from recent studies and discussed the ecology of influenza viruses, epidemiology of influenza, methods of prevention and minimisation, and experiences from the 2015 seasonal influenza immunisation campaign. The symposium concluded that although much progress in this field has been made, many areas for future research remain.

Background

This paper presents a synopsis of the 2nd New Zealand Influenza Symposium (NZIS) that was hosted by the Immunisation Advisory Centre (IMAC) in November 2015. IMAC is a national organisation based at the School of Population Health at The University of Auckland. IMAC researches aspects of vaccines and vaccine-preventable diseases and is contracted by the Ministry of Health to provide immunisation technical advice and support, health professional training and input into policy development. The 2nd NZIS brought together national and international experts and service providers with the aim of improving the management and prevention of influenza. Building upon the inaugural symposium in 2014,¹ the topics discussed included: the ecology of influenza viruses, disease burden of

influenza, methods to minimise influenza transmission, effectiveness of influenza vaccines and experiences from the 2015 seasonal influenza immunisation campaign and local healthcare service providers.

Ecology of influenza viruses and the impact on humans

Influenza is a contagious respiratory illness caused by influenza viruses, of which there are three types (ie influenza A, B and C) that all belong to the *Orthomyxoviridae* family.² Influenza A viruses are comprised of eight separate strands of ribonucleic acid (RNA) that contain their genetic information and high mutation rates while replicating can lead to the creation of novel viruses.^{3,4} Influenza viruses constantly evolve via antigenic drift and occasionally via antigenic shift enabling these viruses to evade host immune memory from the

last influenza infection by creating variants with different antigenic composition.⁵ These constantly changing viruses require surveillance to identify predominant circulating strains and make recommendations for annual vaccine formulation and pandemic preparation. Many novel type A viruses are currently circulating with pandemic potential, including highly pathogenic avian influenza (HPAI) H5N1 and H7N9 subtypes.⁶

Wild aquatic birds are the natural hosts of all known influenza A virus subtypes although influenza viruses have adapted to infect many species including humans, pigs and other animals.⁷ Most avian influenza viruses (AIVs) have generally remained stable and are usually non-pathogenic to birds.^{8,9} Varying prevalence rates and wide genetic diversity of influenza virus subtypes have been found among animal and environmental reservoirs worldwide.^{10,11} Despite the abundance and diversity of AIVs, these viruses are generally inefficient in infecting humans.⁸ Moreover, many different management interventions appear to aid in reducing the risk of zoonotic infections in identified hot spots; for instance, implementing market rest days, banning overnight markets and separating species in live poultry markets in Asia.^{12,13}

However, it is important to note that AIVs have successfully crossed the species barrier to infect humans and cause disease outbreaks.^{14,15} Most notably, hybrid viruses containing portions of animal viruses have caused the past four influenza pandemics.^{16,17} Thus, continual and coordinated surveillance and management efforts are required to detect and prepare for potential pandemic threats. Evaluative tools, like the influenza risk assessment tool (IRAT) and efforts of the FLURISK Consortium play important roles in helping prioritise efforts towards those influenza viruses currently circulating in animals with the greatest potential pandemic risk.^{18,19}

Influenza epidemiology globally and in New Zealand

Influenza spreads from close personal contact between humans via infectious respiratory droplets and by touching infected surfaces.²⁰ Infection with influenza viruses can cause asymptomatic, mild or severe illness in humans and the main

burden arises from the secondary complications of infection. Influenza type A and B viruses cause seasonal epidemics estimated to cause 250,000 to 500,000 deaths per year worldwide.²⁰ While most of those infected will experience common signs and symptoms (eg high fever, cough, myalgia and sore throat), some may experience more severe complications particularly young children, the elderly and those with chronic medical conditions.²⁰ Recent literature has noted an increased risk of influenza-associated deaths among adults with certain medical conditions, such as acquired immunodeficiency syndrome (AIDS) and pulmonary tuberculosis (PTB), highlighting the importance of prioritizing at-risk groups for influenza vaccination.^{21,22}

In New Zealand, seasonal influenza is not a notifiable condition and influenza surveillance comprises of sentinel general practice surveillance and non-sentinel laboratory-based surveillance. Since 2012, the sentinel influenza surveillance network has been enhanced by the additional surveillance capabilities of the Southern Hemisphere Influenza Vaccine Effectiveness Research and Surveillance (SHIVERS) project (2012–2016), enabling the collection of robust data to better understand the national disease burden of influenza. Data collected from the 2015 winter season showed that influenza-like illness (ILI) consultation rates were within the normal activity range with most infections due to A(H3N2) viruses for the majority of the season until type B strains (B/Victoria and B/Yamagata) predominated in the later portion.²³ Identified risk factors for severe influenza included a range of host, socio-economic, healthcare, environmental and behavioural factors.²⁴ The importance of demographic and socio-economic risk factors were highlighted as the disease burden is consistently highest among young children, the elderly, those of Māori and Pacific peoples ethnicity and those living in socio-economically deprived areas.^{23,25} In addition, the higher risk of getting influenza among pregnant women was noted; between 2012 and 2014, cumulative incidence data reveals that pregnant women were 4.88 times (95% confidence interval [CI] 3.14–7.36) more likely to get influenza compared to non-pregnant women.²³

Prevention and minimisation of influenza

Non-pharmaceutical (eg isolation, quarantine) and pharmaceutical (eg vaccine, antiviral drugs) interventions can mitigate the effects of influenza outbreaks.²⁶ Several non-pharmaceutical interventions limit the spread of influenza and are commonly recommended. Some measures, such as respiratory and hand hygiene, are effective in reducing influenza transmission^{27,28} and are viewed as acceptable, familiar and socially responsible methods.²⁹ The effectiveness of mask wearing has been highlighted, as a recent study reported that surgical face-masks worn by influenza-infected patients resulted in an overall 3.4 fold (95% CI 1.8–6.3) decrease in viral aerosol shedding.³⁰

The best way to prevent seasonal influenza is annual influenza vaccination with an inactivated influenza vaccine (IIV) or a live attenuated influenza vaccine (LAIV), although it is noted that LAIVs are not yet licensed or available in New Zealand. Much research is being dedicated towards estimating vaccine effectiveness (VE) to evaluate the public health benefit of immunisation campaigns and accuracy of vaccine strain selection. Recent research has indicated that the level of protection offered by IIVs used in seasonal influenza vaccination campaigns varies each year and by age group, but generally offers a moderate level of protection for most people.^{31,32}

Starting in 2012 in New Zealand, the SHIVERS project has provided robust and timely estimations of VE of the trivalent IIV and the protection offered in community and hospital settings using a test negative study design.^{33–35} Most recently, during the 2014 influenza season, VE was 42% (95% CI 16%–60%) for preventing laboratory-confirmed influenza hospitalisations and 56% (95% CI 35%–70%) against influenza cases among general practice patients in the community.³⁵ In contrast to New Zealand data, studies from the northern hemisphere reported suboptimal overall VE of the 2014/2015 seasonal influenza vaccine due to a poorly matched A(H3N2) component of the vaccine.^{36,37} One study reported that low VE levels were linked to mutations in the egg-adapted A(H3N2) vaccine strain introduced during the manufacturing process instead of due to antigenic drift of

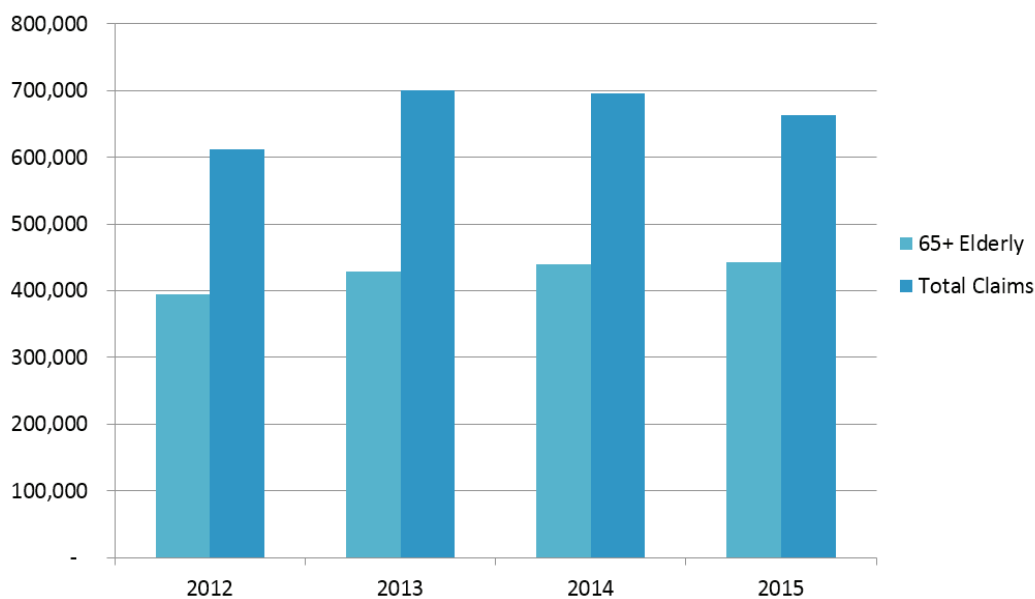
the circulating virus.³⁸ Despite offering only moderate levels of protection, vaccination still prevents influenza-related illness and complications (eg hospitalisation, death) and is recommended for all of those who do not have a contraindication.³⁹

Literature has generally reported LAIVs to have similar or superior vaccine efficacy and effectiveness in children compared to that of IIVs, which supports the long-standing recommendation of LAIVs for this age group.^{31,32,40} However, two recent studies revealed that the quadrivalent LAIV was not effective against the 2009 pandemic influenza A(H1N1) virus (A[H1N1]pdm09) while the trivalent/quadrivalent IIV was effective among children aged 2–17 years old during the 2013/2014 season in the US.^{41,42} The ineffectiveness of the LAIV against the A(H1N1)pdm09 strain in children underscores the need for constant monitoring to ensure the most appropriate type of vaccine is recommended to provide optimal protection.⁴¹

Influenza immunisation programme and service delivery in New Zealand

In 2015, the Ministry of Health's (MOH) seasonal influenza immunisation campaign achieved its target of distributing 1.2 million doses, despite experiencing a late start to the programme. Delays in vaccine availability occurred as a result of adding two new strains to the vaccine.⁴³ Particularly important was the addition of a new A(H3N2) strain as it was noted that A(H3N2) had been responsible for significant disease burden in the older age groups.²³ Pertaining to specific programme goals, provisional data on the funded influenza vaccines given to those aged 65 years and older indicates a steady increase in coverage since 2012, although room for improvement remains (Figure 1).⁴³ Furthermore, progress was made in terms of improving immunisation coverage for healthcare workers (HCWs) (Figure 2).⁴³ The role of pharmacists in the seasonal influenza immunisation campaign was also highlighted as a recent reclassification now allows pharmacists to administer the non-funded influenza vaccine.⁴⁴ The MOH continues to work on enabling pharmacist vaccinators to record immunisations on the National Immunisation Register (NIR).

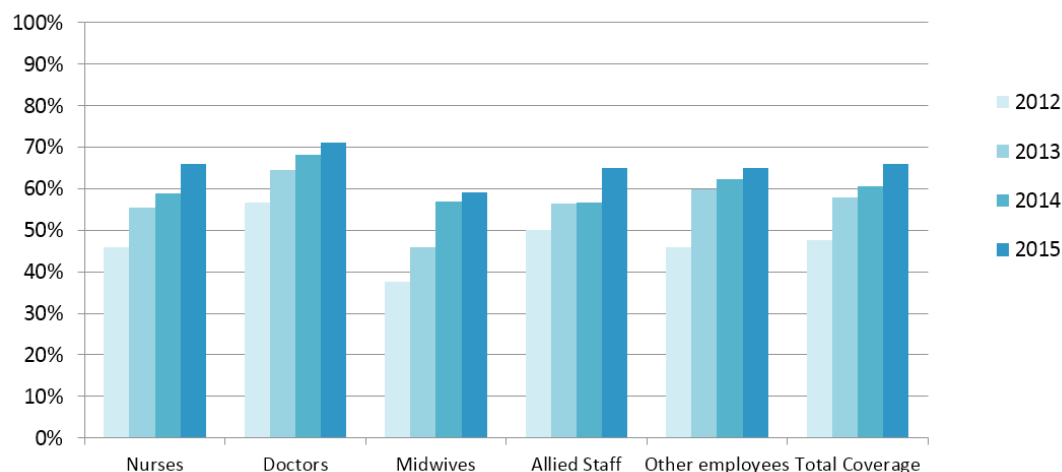
Figure 1: Immunisation benefit claims for funded influenza vaccines among the elderly (65 years and older) in New Zealand, 2012–2015 (provisional data, 11 November 2015).



In 2015, a new multifaceted ‘blue dust’ promotional campaign was introduced to raise public awareness about influenza and the influenza vaccine.⁴⁵ Evaluation of the promotional campaign revealed that the campaign reached 50% of people eligible for the funded vaccination, 41% of the elderly and 80% of pregnant women.⁴⁵ The most commonly reported motivators to immunise were the perceived severity and susceptibility of influenza, social concern of preventing influenza transmission and being offered the funded vaccine.⁴⁵ On the other hand, commonly reported barriers included needle phobia, concern of side effects and preference of building natural immunity.⁴⁵ Results highlighted the critical role HCWs play in recommending influenza vaccinations and the need for high-risk groups in particular (eg the elderly and pregnant women) to understand the associated benefits and risks of vaccination.

During the influenza season, a range of strategies were used to control and manage the spread of influenza at the local level. To provide a service delivery perspective on the influenza programme in 2015, healthcare planners and providers shared their experiences and lessons learnt. In addition to experiencing challenges due to delays in vaccine availability and extending the immunisation programme dates, issues related to the different types of vaccine offered in the funded programme compared with those available for private purchase were reported; in particular some people were requesting the quadrivalent IIV when only the trivalent one was available as part of the funded programme.⁴⁶ Methods used to improve immunisation coverage rates included offering specific immunisation clinics, extended hours, opportunistic vaccinations, and off-site vaccinations (eg residential, home and workplace visits).^{46,47}

Figure 2: Influenza immunisation coverage for District Health Board healthcare workers in New Zealand, 2012–2015.



In preparation for the 2016 influenza season, the need for a team-based approach in planning, improved immunisation education, better reporting and rapid point-of-care testing were noted.^{46,48}

The international debate about whether seasonal influenza vaccination should be mandatory for HCWs was raised. Outbreaks of nosocomial (hospital-acquired) influenza can lead to severe morbidity and mortality and HCWs are at an increased risk of acquiring influenza and subsequently transmitting the disease to vulnerable patients.^{49,50} Increased vaccination of HCWs has been shown to reduce patient mortality rates.⁵¹⁻⁵³ All District Health Boards (DHB) in New Zealand offer funded voluntary influenza vaccination to their staff. In 2015, Waikato District Health Board (WDHB) became the first DHB in New Zealand to implement a 'Vaccinations for Health Care Workers' policy. The policy aimed to increase seasonal immunisation coverage rates among HCWs and reduce influenza transmission in healthcare settings. Similar to a policy introduced in British Columbia, Canada,⁵⁴ it required that employed HCWs receive the season influenza vaccination or don a mask while at work until the end of the season. The CEO of the WDHB reported that the programme was generally successful with 81% of HCWs receiving the vaccination and only 3% claiming medical or religious exemptions, despite some resistance from unions and a few staff members.

Conclusion and recommendations for future work

Overall, the NZiS 2015 concluded that much progress has been made regarding the management and prevention of influenza although many unanswered questions remain. The key areas discussed and recommendations for future work related to research, strategic planning and service delivery are summarised in Table 1.

As many viruses pose a potential pandemic threat, it is important that continued effort is directed towards influenza surveillance and identifying effective management interventions to reduce the incidence of zoonotic infections globally. In New Zealand, the SHIVERS project has established robust surveillance capabilities and identified groups that experience a higher disease burden. Future research should be directed towards reducing these identified inequities based on age, ethnicity and socio-economic deprivation. Moreover, research is needed to improve the vaccine effectiveness of influenza vaccinations and better understand what type of vaccine is best suited for particular age groups. To improve vaccination coverage rates, shared experiences indicated that future campaigns should consider extending the programme dates and improving educational efforts. There also appears to be growing interest for strengthening policies related to influenza vaccination of HCWs.

Table 1: Summary of key issues and suggested areas for future work identified by participants attending the 2nd New Zealand Influenza Symposium, November 2015.

Ecology of influenza viruses	<ul style="list-style-type: none"> • Surveillance of avian influenza viruses with pandemic potential • Identification of effective management interventions to reduce influenza transmission from animal sources to humans
Influenza epidemiology	<ul style="list-style-type: none"> • Surveillance of circulating influenza viruses • Reduce inequities of influenza disease burden • Understand the extent and implications of asymptomatic influenza
Influenza vaccines	<ul style="list-style-type: none"> • Improve vaccine effectiveness and level of protection of influenza vaccine • Improve A(H3N2) vaccine component and manufacturing process • Understand effectiveness of LAIV versus IIV in young children (in particular for protection against A[H1N1]pdm09 strain) • Value of trivalent versus quadrivalent IIV • Public's perception of trivalent versus quadrivalent IIV • Understand intra-seasonal waning immunity • Understand the impact of repeat immunisations (improves overall protection or not)
National influenza immunisation programme	<ul style="list-style-type: none"> • Methods to reach people eligible for funded vaccines to improve vaccination coverage rates (focus on identified motivators and barriers to immunise) • Improve vaccination rates of the elderly population and pregnant women (need to target educational efforts to understand risks and benefits) • Explore ways to better utilise pharmacist vaccinators
Healthcare service delivery	<ul style="list-style-type: none"> • Explore evidence to support the implementation of mandatory seasonal vaccination or mask policy for HCWs • Improve influenza vaccine service delivery by allowing registered nurses to vaccinate without a prescription or a standing order (similar to pharmacist vaccinators)

Competing interests:

The Immunisation Advisory Centre and Regional Public Health are funded by the Ministry of Health to promote the delivery and uptake of influenza immunisation as part of the national immunisation programme. Dr Mansoor reports my current employer, RPH is funded to promote influenza vaccine. I have undertaken work on maternal influenza immunization or WHO. Dr Turner reports other from SHIVERS study: CDC funded, outside the submitted work.

Acknowledgements:

The authors and the Immunisation Advisory Centre would like to thank the presenters and session chairs for their contributions: Bob Buckham (Pharmaceutical Society of New Zealand), Carolyn Clissold (Capital and Coast District Health Board), Shirley Crawshaw (Ministry of Health), Sue Huang (Institute of Environmental Science and Research), Michelle Kapinga (National Influenza Specialist Group), Heath Kelly (Australian National University, Victorian Infectious Diseases Reference Laboratory), Osman Mansoor (Regional Public Health), Margo Martin (Island Bay Medical Centre), Richard Medlicott (Island Bay Medical Centre), Diana Murfitt (Ministry of Health), Nigel Murray (Waikato District Health Board), Annette Nesdale (Regional Public Health), Phil Schroeder (Canterbury Primary Response Group), Nikki Turner (Immunisation Advisory Centre), Richard Webby (St. Jude's Children's Research Hospital), Marc-Alain Widdowson (Centers for Disease Control and Protection). We would also like to thank Barbara McArdle (Immunisation Advisory Centre) for organising and coordinating the symposium.

Author information:

Nadia A Charania, Lecturer, Department of Public Health, Auckland University of Technology, Auckland; Osman D Mansoor, Public Health Physician, Regional Public Health, Lower Hutt; Diana Murfitt, Senior Advisor - Immunisation, Service Commissioning, Ministry of Health, Wellington; Nikki M Turner, Associate Professor, Department of General Practice and Primary Health Care, University of Auckland, Auckland.

Corresponding author:

Dr Nadia A Charania, Department of Public Health, Auckland University of Technology, 90 Akoranga Drive, Northcote, Auckland.
nadia.charania@aut.ac.nz

URL:

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