Age is not just a number—synopsis of the 5th New Zealand Influenza Symposium 2019

Mary Nowlan, Diana Murfitt, Nikki Turner

ABSTRACT

Presented is a synopsis of the 5th New Zealand Influenza Symposium, which focused on both uptake of the influenza vaccine and the long-term consequences of influenza. Particularly highlighted were the advantages of influenza vaccination for older adults in reducing declines in cognitive and physical health. Research findings from influenza surveillance, future of influenza vaccines and the influenza promotional campaign presented at the symposium are summarised.

The 5th New Zealand Influenza Symposium took a focus on both the uptake of the influenza vaccine and long-term consequences of influenza. The advantages of influenza vaccination for those at increased risk, particularly with ageing, were highlighted. Presented here is a synopsis of the symposium's presentations.

Research helps to inform influenza immunisation programmes

As part of an international collaboration, the Southern Hemisphere Influenza Vaccine Effectiveness Research and Surveillance (SHIVERS) study has monitored influenza in New Zealand since 2012. Sentinel and hospital surveillance are conducted to assess circulating influenza strains for:[1]

- *Transmissibility* as determined by sentinel general practice surveillance for influenza-like illness (ILI) and influenza-associated ILI.
- *Overall impact* as assessed by severe acute respiratory infection (SARI) hospitalisations, SARI-intensive care unit (ICU) admissions and SARI-associated influenza.
- And *seriousness* as reported from the ratio of SARI-ICU admission to influenza-associated hospitalisations—ie, how many cases of influenza-associated SARI are admitted to ICU.

During the 2018 season, the level of influenza illness was low (generally below seasonal threshold), but the seriousness of the circulating influenza was high. The influenza A/H1N1pdm09 strain was predominant. This more recently evolved former pandemic strain appears to be associated with more serious outcomes because it is less attenuated than the older H3N2 strain that was also co-circulating.

Although the circulating influenza serotypes in New Zealand and Australia were similar in 2018, the disease activity was less well aligned. The activity characteristics of the annual influenza season in Australia aligns better with that seen in the Northern Hemisphere.

A pilot serosurvey study was conducted as an extension study of SHIVERS (designated SHIVERS-II). Although the viral surface consists of 70% haemagglutinin (HA)—the target antigen in inactivated influenza vaccines—and 30% neuraminidase (NA), the study identified that the antibody response to influenza infection in unvaccinated individuals was predominantly anti-NA rather than anti-HA. One-third of participants seroconverted to NA inhibition alone, which was

observed more frequently in children less than five years of age and participants who were infected with influenza B.[2] This finding raises the consideration of using NA as a less variable vaccine target than HA.

SHIVERS-II found that around 70–76% of individuals who seroconverted for influenza antibodies were asymptomatic or had a mild febrile illness. Young children had high attack rates, but only a quarter had laboratory-confirmed influenza illness. From this study, it was estimated that the overall infection attack rate of influenza was 32% across all ages within the Auckland population during 2015.[2] The study is being repeated for the 2018 and 2019 seasons in the Wellington region.

The burden of influenza

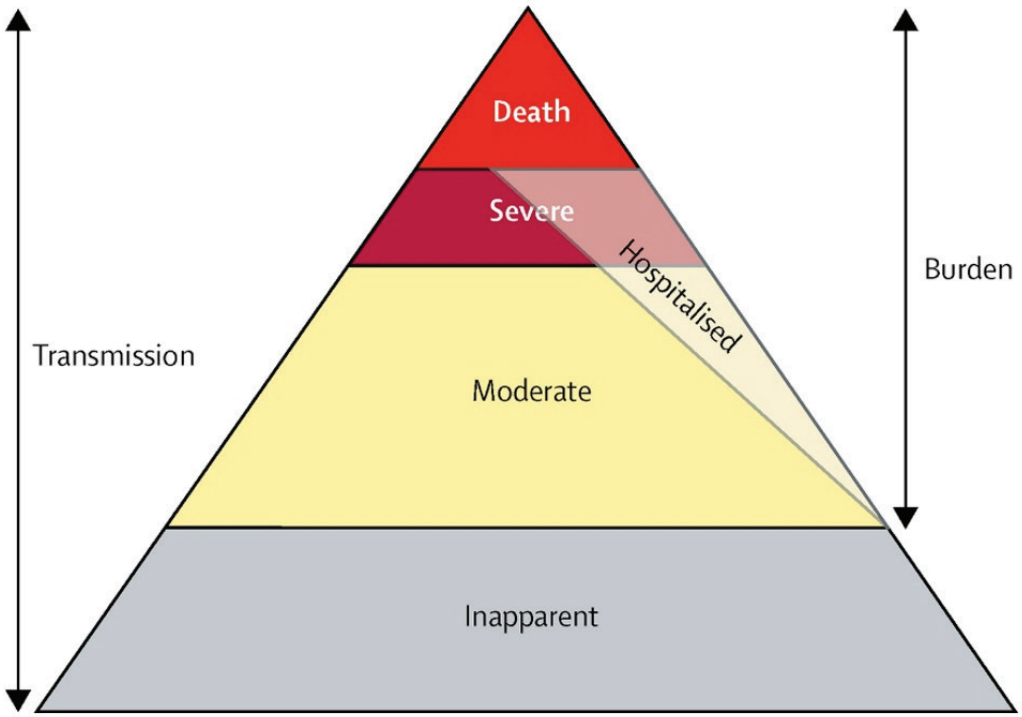
Globally, seasonal influenza has a high burden (Figure 1). An estimated mean of 145,000 deaths were attributed to influenza in 2017 (0.26% of all deaths and 5.6% of all lower respiratory tract infection [LRTI] deaths).

The highest LRTI mortality rates are among adults aged over 70 years and children less than four years.[5] The global mortality rate due to influenza-associated respiratory deaths in those aged over 75 years was more than 10 times the overall rate (estimated 51–99 per 100,000 individuals versus 4.0–8.8 per 100,000 overall). An estimated 42% of the global influenza-associated respiratory deaths were younger than 65 years and 41% were aged over 75 years.[6] These data do not include non-respiratory influenza-associated deaths that are also a contributing factor to mortality.

Influenza vaccines and improving effectiveness for the elderly

Influenza A/H3N2 strains are particularly associated with influenza-related deaths in older people and seasonal influenza vaccines are less effective when these strains predominate. A severe influenza season experienced in Australia during 2017 was partially associated with low vaccine effectiveness (23%) in the elderly. This lower effectiveness is in part due to antigen mutations occurring during vaccine manufacture and H3N2 strains being more difficult to culture than H1N1 or B strains.

Figure 1: Conceptual diagram of the estimated influenza lower respiratory tract infection (LRTI) burden pyramid (from GBD Influenza Collaborators, 2017, open access CC BY4.0 licence) [Inapparent infection not estimated].



The current seasonal influenza vaccines have limitations in older adults, primarily because they are designed to induce anti-HA antibody production. Antibodies alone are insufficient to prevent the virus from entering the lower respiratory tract epithelium once the airway has been infected. Healthy younger people have effective barriers, mucociliary clearance and cough mechanisms to prevent LRTI, but these mechanisms become less effective with age and various comorbidities.

For influenza vaccines to be more effective in older people, greater activation of cell-mediated immunity, in particular cytotoxic T cells, is also required to kill the virus effectively—this is the rationale behind using adjuvants in influenza vaccines (eg, MF59-adjuvanted vaccine, Fluad®). However, data around the effectiveness of such vaccines in older adults remains limited. In Australia, both the high dose (Fluzone®) and the adjuvanted (Fluad®) influenza vaccines were used during 2018 and both appeared to be more effective in the elderly than standard influenza vaccines, based on small numbers. For 2019, only the trivalent adjuvanted vaccine is available so a comparison is not possible in that setting. Neither of these vaccines are yet available in New Zealand.

However, even with vaccine effectiveness of around 25% against H3N2 in older adults, it was argued that positive cost-benefit gains are made by standard influenza vaccinations in terms of reducing hospitalisations and outcomes.

The gold-standard influenza vaccine would be a universal vaccine that targets conserved regions of the virus to protect against multiple strains over several years. Such a vaccine would ideally aim to prevent more than 75% of symptomatic disease across all age groups and have a long-lasting protection to abolish annual reformulation. Various target antigens are under investigation: including neuraminidase, nucleoprotein Matrix P, an external iron channel (M2e), conserved regions of haemagglutinin or chimeric HA technologies (cH6/1).[7] However, each of these targets have limitations in terms of the immune responses and a licensed universal influenza vaccine is at least a decade away.

Benefits of vaccination in older adults

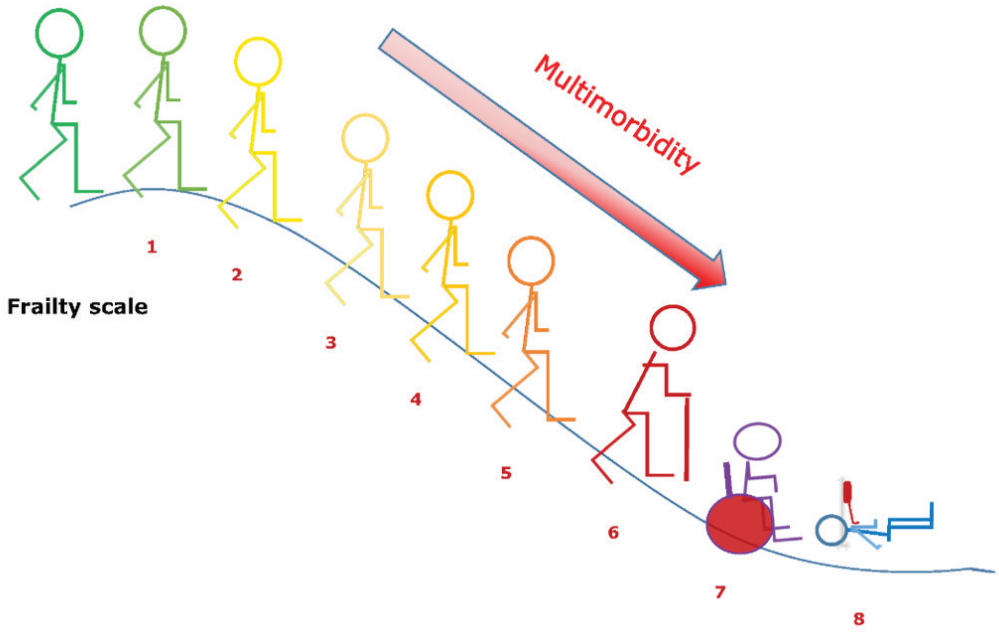
The long-term effects influenza has on older adults in terms of loss of independence and physical and cognitive function was highlighted. Influenza is described as 'barometer of health in older people'; 90% of deaths and 70% of those hospitalised with influenza are older than 65 years. Independent of age, adults aged 50–64 years with comorbidities are also at increased risk from influenza.

Influenza induces a systemic inflammatory response. Although it is often directly associated with respiratory tract illness, systemic symptoms like fever and myalgia indicate a widespread multi-organ effect. Influenza infection is linked with the exacerbation of pre-existing disease, such as renal failure, respiratory disease and diabetes. It has also been shown to trigger cardiovascular events, such as myocardial infarction and ischaemic strokes due to acceleration of atherosclerosis process, to the extent that influenza vaccination is as protective as other routinely used preventatives for coronary disease, such as smoking cessation, anti-hypertensives and statins.[8]

Many older people are more fearful of a loss of independence than of death. Influenza and other infections can lead to 'catastrophic disability' in an older adult, who is seemingly well prior to the infection but showing initial signs of frailty.[9] Hospitalisation and ICU admission can increase frailty resulting from a permanent loss of physical and cognitive function and an inability to perform daily activities.[10] Around 5% of muscle strength is lost for each overnight spent in hospital. However, it takes much more severe disease to reach the same levels of frailty for those who have been vaccinated than for an unvaccinated adult.

A combination of exercise, good nutrition, smoking cessation, medications to treat comorbidity and vaccination are all important components of reducing the risk of increasing frailty in older people. When discussing vaccination needs with patients, it was recommended to assess where the individual sits on the frailty scale to emphasise the risk to their independence if not vaccinated (illustrated in Figure 2).[9]

Figure 2: Influenza infection can lead to a rapid increase in frailty in unvaccinated older adults (reproduced with permission from J McElhaney).



The ethics of vaccination

It was argued ethically that promotion of vaccinations for older people is a fair use of resources. The harms resulting from not vaccinating outweigh the harms due to vaccine ineffectiveness—therefore, vaccinating older people can be deemed effective and justified. Across the whole population, vaccination needs to be considered for the community, not just for individuals, and health professionals have an obligation to offer and accept vaccinations to prevent disease transmission within the community and aged-care facilities.

For elderly adults with multi-comorbidities, the seasonal influenza vaccines are less effective and therefore, the best protection is likely to come through vaccination of those around them (ring protection). Children are especially significant source of infection to adults. Vaccine uptake in children as well as older people, particularly in smaller communities, is likely to improve vaccine effectiveness in their grandparents.[11]

Improving vaccination coverage for older people and reducing inequity

Uptake of influenza vaccine needs to be encouraged at a younger age, rather than waiting until 65 years of age, especially for those with certain medical conditions with increased risk from influenza who are eligible to funded vaccine.

National Immunisation Register (NIR) coverage of influenza vaccination is improving in New Zealand, but adults aged 65 years or older of Māori and Asian ethnicity have the lowest uptake despite being eligible for funded influenza vaccine. For 2018, influenza vaccine uptake for these adults was 45% for Māori and 52% for Asian compared with 56% overall and 63% for Pacific ethnicities.

Increasing acceptance and uptake of the influenza vaccine by older Māori has been achieved successfully in the Whanganui district, with 70% coverage (compared with 45% nationally). Gaps were closed through close liaison with general practices, presenting data on coverage to the practices face-to-face and ensuring staff levels are maintained to cover sick leave. They found that practices with fewer immunised staff were likely to have lower patient immunisation rates.

One challenge around monitoring influenza immunisation coverage is to record all vaccinations given in general practice, pharmacy and in occupational health settings on the NIR. Excellent progress has now been made to enable pharmacies to enter vaccinations on to the NIR. However, other providers such as occupational health are as yet unable to access the NIR directly. Working collaboratively can help to ensure

more people are vaccinated and to provide a more accurate picture of where resources may be required.

Encouraging greater uptake of influenza vaccines through social media

The national Fight Flu public influenza immunisation campaign utilises social media through Facebook, and in 2018, was particularly successful for engagement with pregnant women. However, the role of social media in promoting vaccine uptake is a double-edged sword.

The most predominant sources of news and fake news for those aged 18–49 years are YouTube and Facebook, with younger adults tending to use YouTube, and there are around 3.5 million social media users in New Zealand. Social media and the internet significantly influence immunisation decisions, particularly negative influences which instil doubt through online discussion forums.[3]

Social media for news is changing with WhatsApp—in which, audiences can be targeted without specific advertising. Vaccine debates are being fuelled by targeted forums from anti-vaccination groups, but also driven by automated bots/trolls. Pressure is building to reduce misinformation and anti-vaccination sentiment with reports from UK Royal Society of Public Health declaring that social media 'giants' need to take responsibility for the misinformation that could result in dangerous consequences.[4]

Strategy for New Zealand influenza programme in 2019

In recent years, the peak of the influenza season occurred in August in New Zealand, and due to declining vaccine effectiveness during the season, it is more feasible to start vaccinating later than March, as for previous years. Hence, the decision to commence the funded influenza immunisation programme from 1 April 2019 onwards.

For the 2019 season, more culturally and language appropriate promotional material is being used, particularly to target Māori and Asian ethnicities, to engage with more adults and to encourage all older people to receive influenza vaccine.

An important aim is to educate health professionals about the risks of influenza to independence and the effect of influenza infection on cardiovascular health, so that they can better explain the benefits of being vaccinated to their patients.

The key goals for the 2019 influenza immunisation programme are to achieve more than 25% population-wide coverage and specifically to encourage greater uptake by those at high risk from influenza, including those aged 65 years or older, healthcare workers, pregnant women and all ages with certain medical conditions.

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Author information:
Mary Nowlan, Research Assistant and Medical Writer, Immunisation Advisory Centre, Department of General Practice and Primary Care, University of Auckland, Auckland; Diana Murfitt, Senior Advisor, Emergency Management - Pandemic Readiness, Ministry of Health, Wellington; Nikki Turner, Associate Professor, Director of the Immunisation Advisory Centre, Department of General Practice and Primary Care, University of Auckland, Wellington.

Corresponding author:
Dr Nikki Turner, The Immunisation Advisory Centre, Private Bag 92019, Auckland 1142.
n.turner@auckland.ac.nz

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