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THE SHIVERS PROJECT

SOUTHERN HEMISPHERE INFLUENZA AND VACCINE EFFECTIVENESS RESEARCH & SURVEILLANCE

SHIVERS-II study update – October 2019

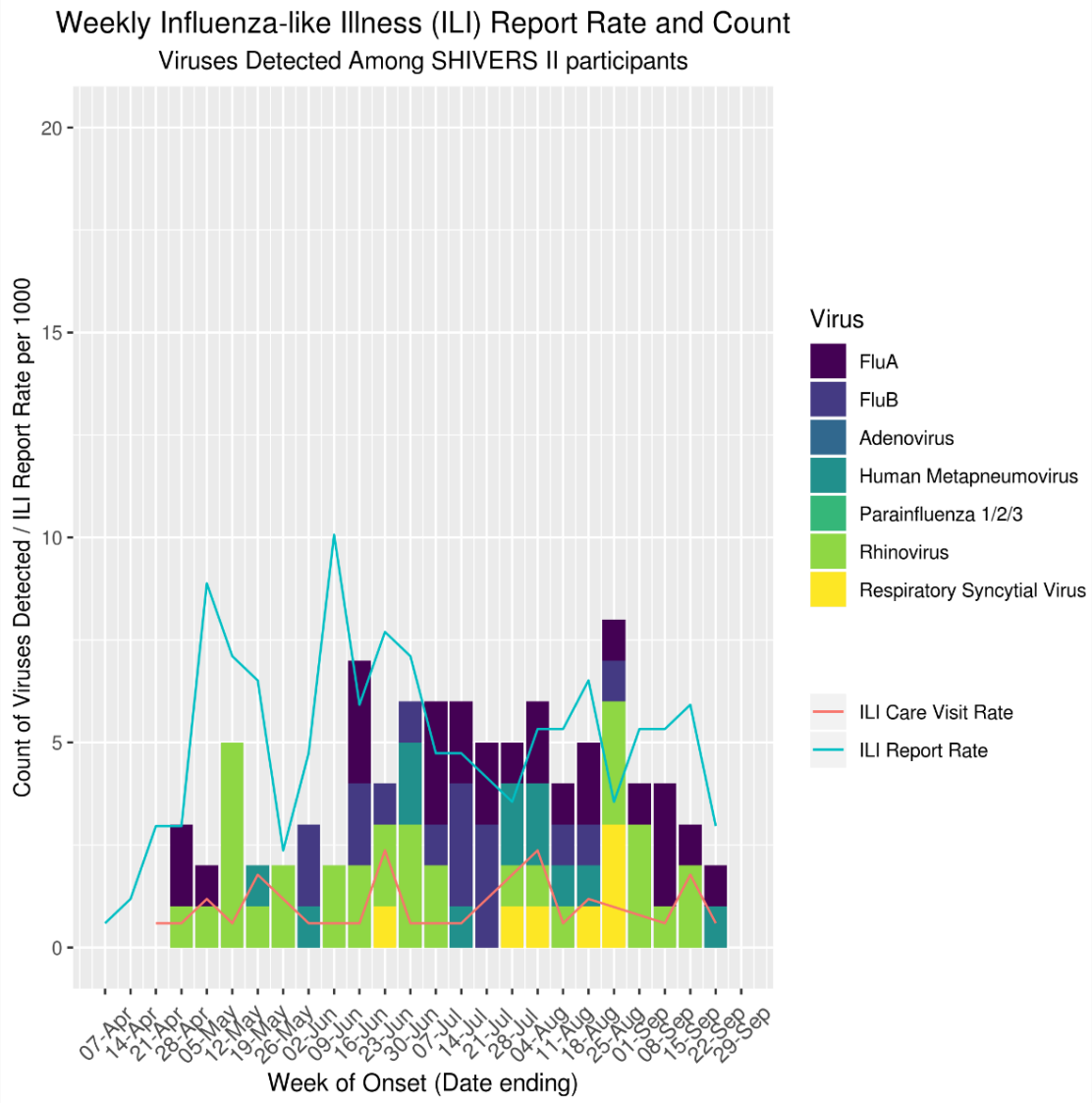
The winter surveillance of the SHIVERS-II 2019 study has finished with weekly surveys on influenza-like illness (ILI) ending on 29 September 2019. A BIG thank you to all our participants for providing your samples and survey information.

In 2019, we have 1670 participants in the study. Of 1165 who had the flu vaccination this year, 1133 (97%) provided the post-vaccine blood. During the flu season (May to September), we had 42 positive flu cases from the SHIVERS-II participants, nine from the household members. The two flu strains, influenza A (H3N2) and influenza B/Victoria, were the most common viruses detected throughout the flu season.

The 2019 influenza season

The graph below shows the weekly rate of ILI reported by participants on the weekly e-surveys (blue line) during the study period. A rate of around 10 ILI reports per 1000 participants means that about 17 participants reported ILI in that week. The orange line shows the weekly rate of nurse visits to those participants with ILI. The different coloured bars on the graph represent the count of the different respiratory viruses detected among SHIVERS-II participants each week.

This circulation pattern is similar to the national flu surveillance picture https://www.esr.cri.nz/our-services/consultancy/flu-surveillance-and-research/



Weekly Influenza-Like Illness (ILI) Report Rate and Count - SHIVERS-II 2019

Influenza vaccine strain selection

Influenza virus is an enveloped RNA virus with two spike proteins sticking out of the envelop (Figure below). The purple one is called hemagglutinin (HA) – the most abundant surface protein (70% of all surface proteins). The yellow one is called neuraminidase (NA) – the second most abundant surface protein (30%). When the virus enters the human body, the human immune system sees these two spike proteins and generates antibodies to block the virus infection. To avoid human immune responses, the virus is changing constantly - especially around the globular head region of the

hemagglutinin protein. This is how the flu virus outsmarts the human body - antibodies generated against the previous virus are not effective against the newly changed virus.

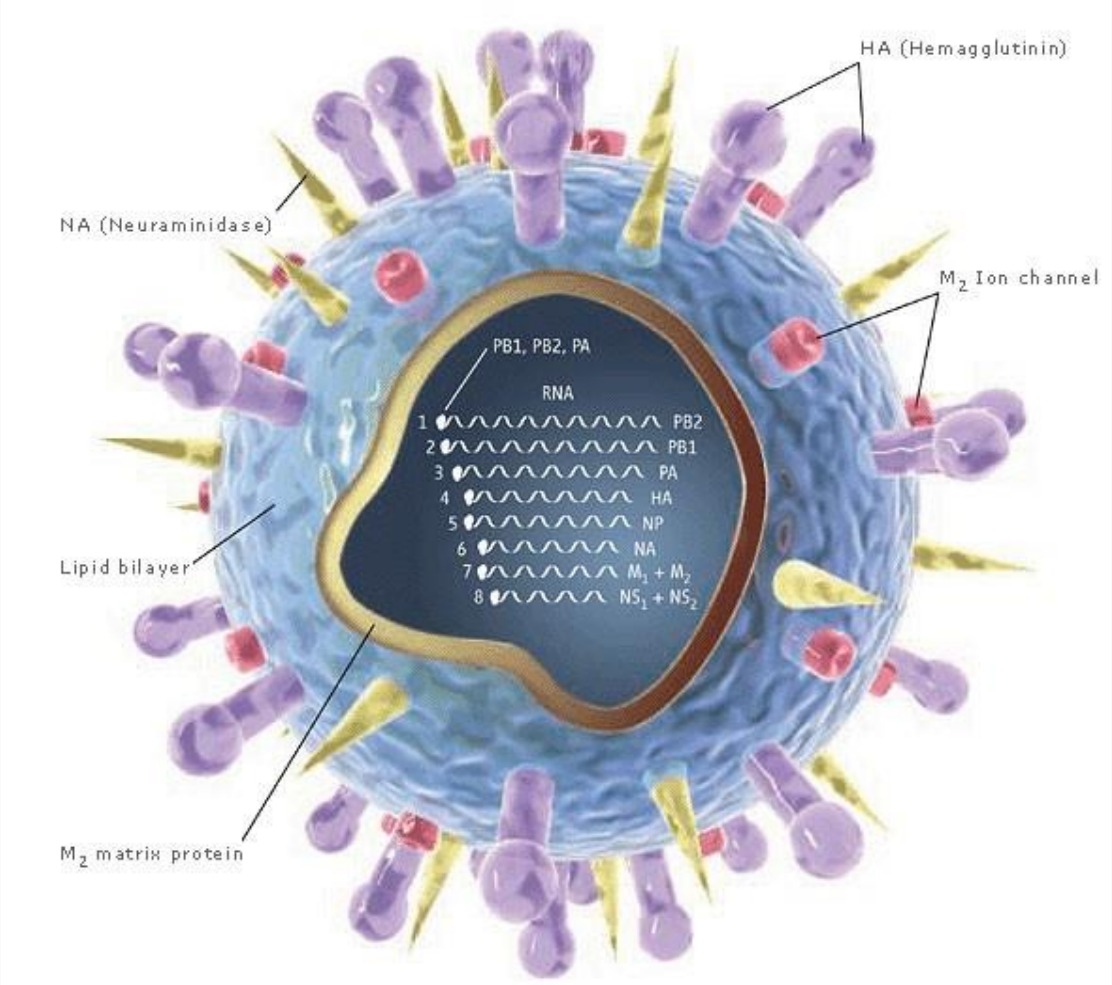


Illustration: Chris Bickel/Science. Reprinted with permission from Science Vol. 312, page 380 (21 April 2006) © 2006 by AAAS

Influenza vaccination remains the cornerstone of global and national public health efforts to reduce the impact of both seasonal and pandemic influenza. The vaccine strains are more effective when they match well with predominant strains in a population (i.e. those circulating most widely and representative viruses among all strains detected). Since the early 1970s, the World Health Organization (WHO) has provided two formal recommendations on influenza vaccine composition based on yearly influenza surveillance data, one in September for Southern Hemisphere and another in February for Northern Hemisphere.

The data generated from SHIVERS-II, combined with New Zealand's sentinel general practice and hospital surveillance data, has been submitted to the WHO and the Australian Influenza Vaccine Committee (AIVC) on recommendations on seasonal influenza vaccines to be used for Southern Hemisphere (including NZ) for the following year (2020):

- an A/Brisbane/02/2018 (H1N1) pdm09-like virus
- an A/South Australia/34/2019 (H3N2)-like virus
- a B/Washington/02/2019-like (B/Victoria lineage) virus; and
- a B/Phuket/3073/2013-like (B/Yamagata lineage) virus

Household transmission

This year we began a new component of the SHIVERS-II study which was to discover more about how the flu virus spreads from person to person in a household. The household provides a very important setting because previous studies found that transmission (i.e. spread) in households tends to be frequent and can count for up to 30% of influenza virus transmission. Another advantage is that we can track flu infections among close contacts of primary flu positive cases, because we can easily count how many household members within a family. Household transmission also helps us determine those people who had flu virus infection but either showed very mild illness or no symptoms at all. All this information is valuable in supporting local, national and international public health authorities to make decisions around managing the spread of flu in the community, and most importantly in the event of a pandemic.

In this pilot year of the Household Transmission arm of the study, once a SHIVERS-II participant confirmed positive for the influenza virus, the household became eligible for this sub-study. Household members (one or more) were asked if they were willing to have swabs and paired blood samples taken, and records of any symptoms. In 2019, 20 households took part, making a total of 57 household members including the SHIVERS-II participants, in this study. There was a total of nine close contacts on top of the SHIVERS-II participants who had laboratory-confirmed influenza virus infection from six households. It meant about a 25% (9/37) chance of flu being transmitted to other household members once someone already had an influenza infection among these households. This is much higher than the overall influenza virus positive rate (2.5%, 42/1670) in the SHIVERS-II cohort. The overall influenza virus positive rate in the SHIVERS-II cohort may reflect the chance of becoming infected with influenza in people aged 20-69 years.

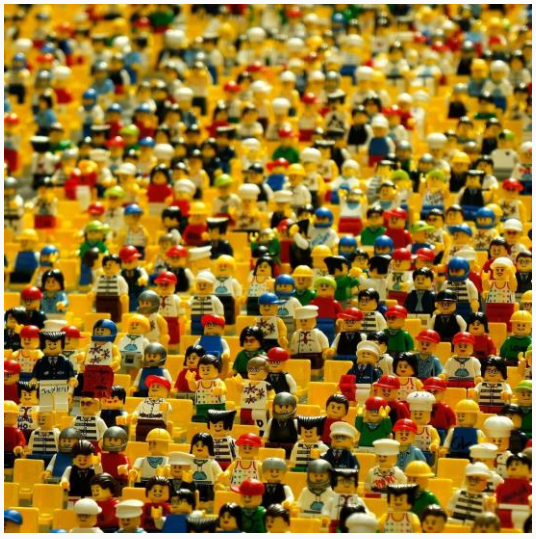
Our story –Children bring Flu B home to parents

Influenza virus has two types (A and B) causing outbreaks in humans. Traditionally, most attention has been directed to influenza A. However, influenza B can also cause

considerable illness in communities, particularly in school aged children (5-19 years). Since the 1970s, influenza B viruses have evolved into two distinct lineages - the B/Victoria and B/Yamagata lineages. For reasons not completely understood, B/Victoria lineage virus remained geographically restricted to Asia until 2001. Then B/Victoria virus spread to Hawaii, reached Australia and New Zealand in 2002 and began its circulation worldwide. Since reaching New Zealand, this B/Victoria lineage has co-circulated with B/Yamagata lineage viruses. B/Victoria lineage viruses predominated over the B/Yamagata lineage viruses every three years during 2002-2011 and now every four years during 2011-2019. It has become the predominant strain in 2019 flu season, identified both in the SHIVERS-II cohort, as well as other GP and hospital surveillance systems.

Among the SHIVERS-II cohort and household transmission studies, we found this year for the most part, influenza B was circulating earlier than influenza A. ILI peaked around mid August for our SHIVERS-II participants, which was a little later than the national average, see the weekly graph above.

Anyone familiar with young children knows, it is the day care and early school years when they bring “anything and everything” home. This is exactly what we found in our households, our participants weren’t usually the first in the chain to become unwell, the children had influenza first.



Japanese story on herd immunity

Influenza can cause serious illness and even death, especially among elderly people. Japan, unlike most developed countries, introduced a mandatory vaccination programme for school aged children during 1962 – 1987. Then the policy was relaxed and repealed in 1994.

A study in 2001 (Reichert et al, 2001) noticed this vaccination programme was associated in reducing deaths amongst the older populations in Japan. It is possible, when most school children were vaccinated, it provided herd immunity and thus protected the elderly, those most vulnerable in our communities. Researchers determined a large proportion of elderly people cohabitated with their adult children and school aged grandchildren in Japan (60-90% lived with

adult children and 60-70% with grandchildren as well). Thus, the high levels of vaccine coverage achieved among schoolchildren is likely to have directly prevented the transmission of influenza virus to their grandparents.

The key to this story is as the vaccination of schoolchildren was discontinued, the proportion of deaths among elderly in Japan increased. However, the authors did agree that when there is comprehensive vaccination in older and chronically ill people, a reduction in mortality (death) at a rate similar to that observed with the vaccination of schoolchildren can also be seen.

Reichart, T. A., Sugaya, N., Fedson, D. S., Glezen, W. P., Simonsen, L. and Tashiro, M. (2001). The Japanese Experience with Vaccinating Schoolchildren Against Influenza. *N Engl J Med*, 344 (12), 889-896. doi:10.1056/nejm200103223441204

Introducing new SHIVERS team members for 2019

Meet Hannah Schrader (seen here with her niece)

Hannah joined our team as our new project coordinator in the middle of the year, jumping right into flu season. Hannah hails from the deep south and has two brothers and one sister. More recently, she was the events coordinator for the New Zealand Veterinary Association. Hannah takes care of the day-to-day finances, administration and scheduling of projects for the SHIVERS project.

2019 Regional Public Health Nurses:

Our RPH nurses for the 2019 flu season L to R: Amanda DeCleene, Cath O'Connor, Ana Enriquez and Fiona Glover, standing in front of one of the labs at ESR in Wallaceville.

Regional Public Health (RPH) are the SHIVERS-II collaborating organisation that provides registered nurses to visit our participants. Our nurses have a wide range of experience and skills – from triage in ED (Emergency Department) to breast screening to MAPU (Medical Assessment and Planning Unit) to outback medicine in Australia.

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