

RECOMMENDATION FOR SEASONAL INFLUENZA VACCINE COMPOSITION FOR NEW ZEALAND FOR 2022

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1. RECOMMENDATION

The Australian Influenza Vaccine Committee (AIVC) met with a New Zealand representative in Canberra on 6 October 2021 to consult on the influenza vaccine composition for 2022 for New Zealand, Australia and South Africa (Table 1).

Egg-based quadrivalent influenza vaccines:

- an A/Victoria/2570/2019 (H1N1)pdm09-like virus;
- an A/Darwin/9/2021 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage) - like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage) - like virus.

Cell-based or recombinant-based quadrivalent influenza vaccines:

- an A/Wisconsin/588/2019 (H1N1)pdm09-like virus;
- an A/Darwin/6/2021 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

The composition of trivalent influenza vaccines is recommended to include the A(H1N1), A(H3N2) and the B/Victoria lineage virus.

Table 1. Influenza vaccine recommendations for New Zealand, 1991–2022

Decision		Use year	A H3N2	A H1N1	B (Trivalent)	B (Quadrivalent)
NZ & WHO*	2021	2022	A/Darwin/9/2021	A/Victoria/2570/2019	B/Austria/1359417/2021	B/Phuket/3073/2013
NZ & WHO*	2020	2021	A/Hong Kong/2671/2019	A/Victoria/2570/2019	B/Washington/02/2019	B/Phuket/3073/2013
NZ & WHO*	2019	2020	A/South Australia/34/2019	A/Brisbane/02/2018	B/Phuket/3073/2013	B/Washington/02/2019
NZ & WHO*	2018	2019	A/Switzerland/8060/2017	A/Michigan/45/2015	B/Phuket/3073/2013	B/Colorado/06/2017
NZ & WHO*	2017	2018	A/Singapore/INFIMH-16-0019/2016	A/Michigan/45/2015	B/Phuket/3073/2013	B/Brisbane/60/2008
NZ & WHO*	2016	2017	A/Hong Kong/4801/2014	A/Michigan/45/2015	B/Brisbane/60/2008	B/Phuket/3073/2013
NZ & WHO*	2015	2016	A/Hong Kong/4801/2014	A/California/7/2009	B/Brisbane/60/2008	B/Phuket/3073/2013
NZ & WHO*	2014	2015	A/Switzerland/9715293/2013	A/California/7/2009	B/Phuket/3073/2013	B/Brisbane/60/2008
NZ & WHO*	2013	2014	A/Texas/50/2012	A/California/7/2009	B/Massachusetts/2/2012	B/Brisbane/60/2008
NZ & WHO*	2012	2013	A/Victoria/361/2011	A/California/7/2009	B/Wisconsin/1/2010	
NZ & WHO*	2011	2012	A/Perth/16/2009	A/California/7/2009	B/Brisbane/60/2008	
NZ & WHO*	2010	2011	A/Perth/16/2009	A/California/7/2009	B/Brisbane/60/2008	
NZ & WHO*	2009	2010	A/Perth/16/2009	A/California/7/2009	B/Brisbane/60/2008	
NZ & WHO*	2008	2009	A/Brisbane/10/2007	A/Brisbane/59/2007	B/Florida/4/2006	
NZ & WHO*	2007	2008	A/Brisbane/10/2007	A/Solomon Islands/3/2007	B/Florida/4/2006	
NZ & WHO*	2006	2007	A/Wisconsin/67/2005	A/New Caledonia/20/99	B/Malaysia/2506/2004	
NZ & WHO*	2005	2006	A/California/7/2004	A/New Caledonia/20/99	B/Malaysia/2506/2004	
NZ & WHO*	2004	2005	A/Wellington/1/2004	A/New Caledonia/20/99	B/Shanghai/361/2002	
NZ & WHO*	2003	2004	A/Fujian/411/2002	A/New Caledonia/20/99	B/Hong Kong/330/2001	
NZ & WHO*	2002	2003	A/Moscow/10/99	A/New Caledonia/20/99	B/Hong Kong/330/2001	
NZ & WHO*	2001	2002	A/Moscow/10/99	A/New Caledonia/20/99	B/Sichuan/379/99	
NZ	2000	2001	A/Sydney/5/97	A/New Caledonia/20/99	B/Beijing/184/93	
WHO*	2000	2001	A/Moscow/10/99	A/New Caledonia/20/99	B/Beijing/184/93	
NZ & WHO*	1999	2000	A/Sydney/5/97	A/Beijing/262/95	B/Beijing/184/93	
NZ	1998	1999	A/Sydney/5/97	A/Bayern/7/95	B/Beijing/184/93	
WHO**	1997–98		A/Wuhan/359/95	A/Bayern/7/95	B/Beijing/184/93	
NZ	1997	1998	A/Wuhan/359/95	A/Texas/36/91	B/Beijing/184/93	
WHO**	1996–97		A/Wuhan/359/95	A/Singapore/6/86***	B/Beijing/184/93	
NZ	1996	1997	A/Johannesburg/33/94	A/Texas/36/91	B/Beijing/184/93	
WHO**	1995–96		A/Johannesburg/33/94	A/Singapore/6/86	B/Beijing/184/93	
NZ	1995	1996	A/Guangdong/25/93	A/Texas/36/91	B/Panama/45/90	
WHO**	1994–95		A/Shangdong/9/93	A/Singapore/6/86	B/Beijing/184/93	
NZ	1994	1995	A/Beijing/32/92	A/Texas/36/91	B/Panama/45/90	
WHO**	1993–94		A/Beijing/32/92	A/Singapore/6/86	B/Panama/45/90	
NZ	1993	1994	A/Shanghai/24/90	A/Texas/36/91	B/Panama/45/90	
WHO**	1992–93		A/Beijing/353/89	A/Singapore/6/86	B/Yamagata/16/88 or B/Panama/45/90	
NZ	1992	1993	A/Beijing/353/89	A/Victoria/36/88	B/Yamagata/16/88 or B/Panama/45/90	
WHO**	1991–92		A/Beijing/353/89	A/Singapore/6/86	B/Yamagata/16/88 or B/Panama/45/90	

* WHO recommendations are for the Southern Hemisphere winter; ** WHO recommendations are for the Northern Hemisphere winter

2. SUMMARY

New Zealand, a southern hemisphere country with a temperate climate, has a well-established influenza circulation pattern with peak incidences in the winter months. However, the non-pharmaceutical interventions implemented for the control of COVID-19 have had a beneficial impact on reducing transmissions for influenza and other respiratory viral infections in 2020 (Huang *et al.* Impact of the COVID-19 nonpharmaceutical interventions on influenza and other respiratory viral infections in New Zealand. *Nat Commun* **12**, 1001 (2021). <https://doi.org/10.1038/s41467-021-21157-9>). This trend continued in the 2021 winter period that no influenza epidemic or outbreak was reported with almost non-existent of influenza virus circulation in our communities.

No influenza-associated severe acute respiratory illness (SARI) was detected in sentinel hospitals. The narrow and sharp peak of the SARI hospitalization during June-July 2021 was mainly associated with RSV infection.

No influenza-associated acute respiratory illness (ARI) was detected in sentinel general practices (GP). The GP ARI during June-July was mainly associated with RSV infection.

No influenza-associated acute respiratory illness or influenza-like illness (ILI) was detected among community-based longitudinal cohort participants. The ARI or ILI during June-July was mainly associated with RSV infection.

The laboratory-based influenza surveillance tested samples from various surveillance systems as well as samples ordered by clinicians during routine viral diagnosis. A total of 11 influenza viruses were detected and reported through this system. Most of these influenza viruses were detected from returnees while staying at the managed isolation facilities. Of them, influenza A represented 45.5% (5/11) and influenza B 54.5% (6/11) of all influenza viruses. Among A sub-typed, 4 were A(H3N2) viruses. Among B lineage-typed, 3 were influenza B/Victoria lineage viruses.

WHO National Influenza Centre (NIC) at ESR received 4 influenza A(H3N2) and 3 influenza B/Victoria lineage viruses for further characterization. One influenza B virus was isolated in cell culture and antigenic typing was conducted using rabbit antisera raised against B/Washington/02/2019. It was antigenically closely related to B/Washington/02/2019.

3. EPIDEMIOLOGY - NEW ZEALAND INFLUENZA SEASON IN 2021

The national influenza surveillance system in New Zealand is an essential public health tool for assessing and implementing strategies to control influenza. The surveillance system includes hospital-based surveillance (SARI surveillance, Ministry of Health data on publicly funded hospital discharges, laboratory-based surveillance for outpatients and hospital in-patients). The surveillance system also includes community-based surveillance (community-based longitudinal cohort surveillance, sentinel GP based acute respiratory illness surveillance and returnee acute respiratory illness surveillance).

3.1 Hospital-based surveillance

3.1.1 HOSPITAL-BASED SEVERE ACUTE RESPIRATORY ILLNESS (SARI) SURVEILLANCE

Inpatients with suspected respiratory infections admitted overnight to any of the four hospitals (Auckland City Hospital and the associated Starship Children's Hospital, Middlemore Hospital and the associated Kidz First Children's Hospital) in the Auckland District Health Board (ADHB) and Counties Manukau DHB, were screened by research nurses each day. Overnight admission is defined as: "A patient who is admitted under a medical team, and to a hospital ward or assessment unit". Case ascertainment followed a surveillance algorithm. The presence of the components of the case definition was determined through a combination of reviewing the clinician's admission diagnoses and by interviewing patients about their presenting symptoms. Records of all patients admitted overnight to medical wards were reviewed daily to identify anyone with a suspected respiratory infection. These patients were categorised into one of ten admission diagnostic syndrome groups. Research nurses then interviewed the patients and documented the components of the case definition of severe acute respiratory illness (SARI) that were present and ascertain the patients whether meeting the SARI case definition.

The case definition being used is the World Health Organisation (WHO) SARI case definition: "an acute respiratory illness with a history of fever or measured fever of $\geq 38^{\circ}\text{C}$, and cough, and onset within the past 10 days, and requiring inpatient hospitalisation". If a patient with suspected respiratory infection met the SARI case definition, a respiratory sample was collected to test for influenza and other respiratory pathogens. In addition, patient information was captured via a case report form which included patient demographics, presenting symptoms and illness, pre-hospital healthcare, medication usage, influenza vaccination history, co-morbidities, disease course and outcome, including major treatments, ICU admission and mortality, epidemiologic risk factors and laboratory results.

The total numbers of all new hospital inpatient acute admissions and newly assessed and tested patients, including ICU admissions and deaths were collected. This allowed calculation of population-based incidence for SARI and associated influenza cases overall and stratified by age, sex, ethnicity and socio-economic status among the ADHB and CMDHB resident population (from 2013 census data). Incidence rates were calculated along with 95% confidence intervals (95%CI). In addition, this allowed the calculation of the proportion of SARI and associated influenza cases, including ICU admissions and deaths, by overall and stratified patients, among all acute admissions regardless of residence status. An acute admission is defined as an unplanned admission on the day of presentation at the admitting health care facility. Admission may have been from the emergency or outpatient departments of the health care facility, a transfer from another facility or a referral from primary care.

Overall impact on healthcare use in hospitalizations and ICU admissions was low from week 18 (commencing 3 May 2021) through week 34 (ending 29 August 2021). Severe acute respiratory illness (SARI) hospitalization rates were below baseline during weeks 18-23, then had a sharp increase and peaked at weeks 26-27 and then declined (Figure 1). SARI hospitalization rates in 2021 was higher than 2020. No SARI-associated influenza hospitalizations were reported in 2021 (Figure 2).

Figure 1. Weekly hospitalisation rates for SARI in 2021 compared to 2015-2019 and 2020

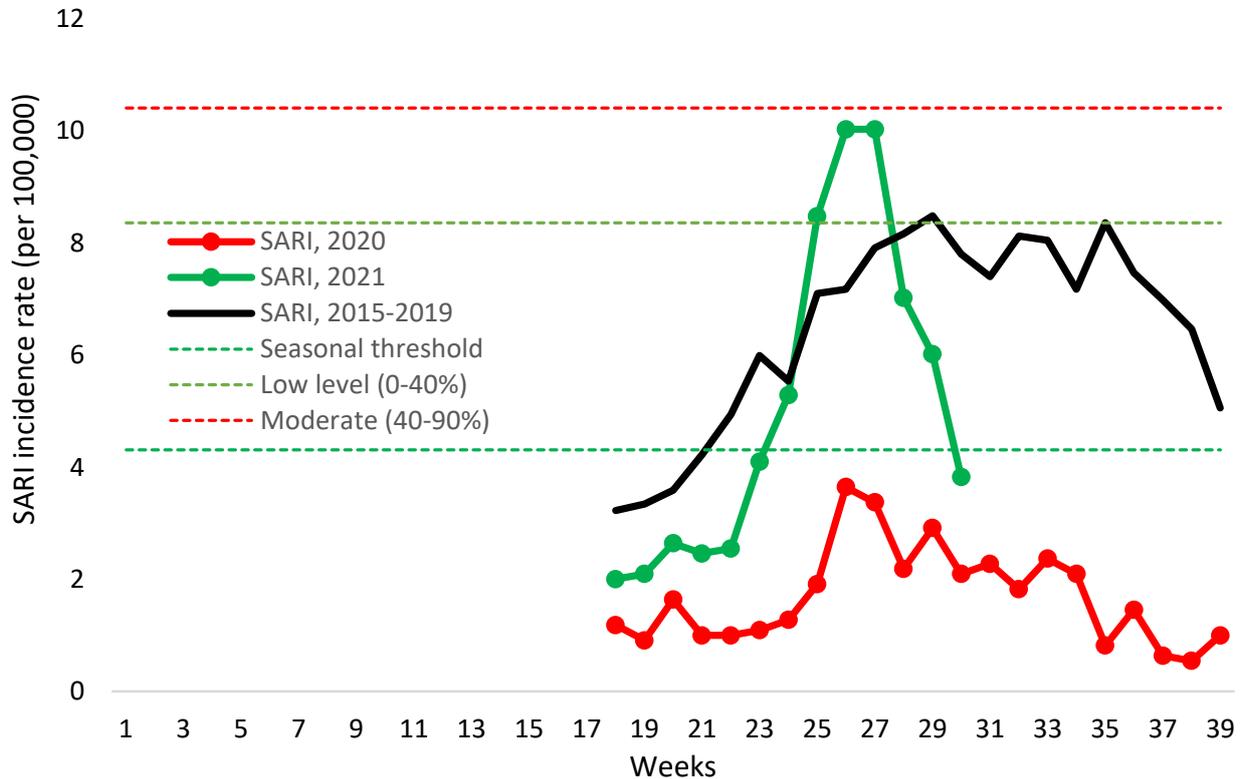
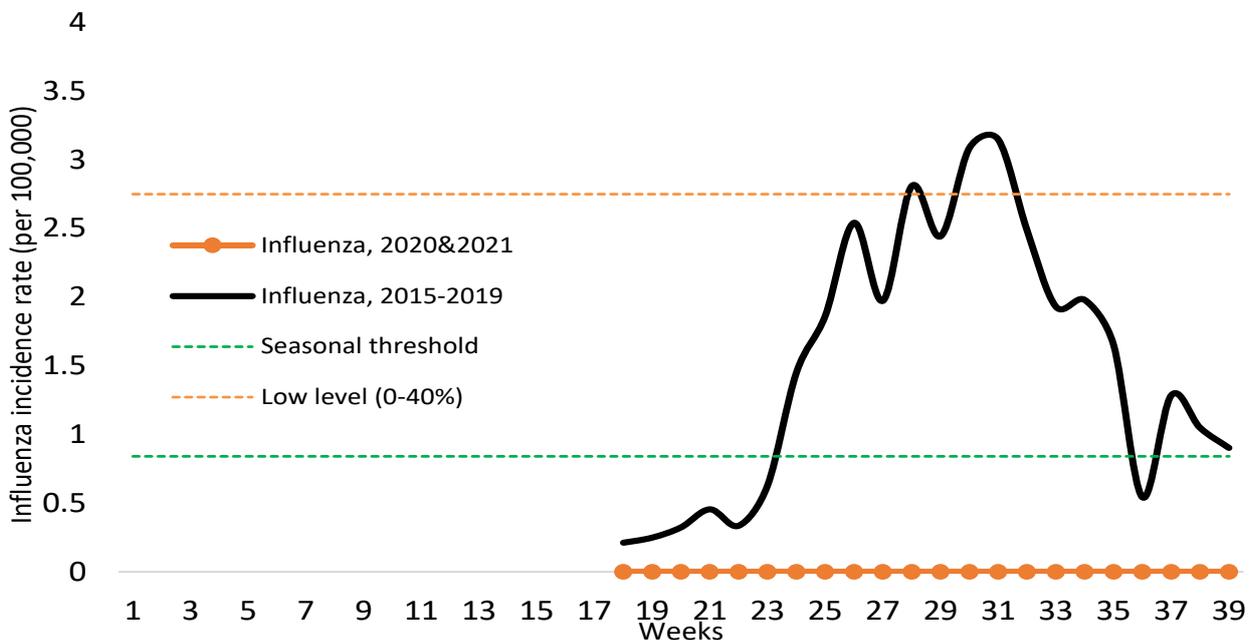


Figure 2. SARI-associated influenza hospitalizations in 2021 compared to 2015-2019 and 2020



From 3 May to 29 August 2021, a total of 2447 patients with suspected respiratory infections were assessed in these hospitals. Of these, 952 (38.9%) patients met the SARI case definition. Among these, 862 were residents of ADHB and CMDHB, giving the SARI incidence rate of 78.6 per 100 000 population (116.6 per 100,000 in 2019) (Table 1). Among the SARI cases who were ADHB and CMDHB residents, none (0.0%) had positive influenza virus results. This gives a SARI related influenza incidence (adjusted for non-testing) of 0.0 per 100 000 population (Note: it was 37.4 per 100,000 in 2019).

Between 3 May and 29 August 2021, of the 952 SARI cases, 54.6% were children aged less than 5 years and 19.3% were adults 65 years and older.

Table 1. Demographic characteristics of SARI cases and related influenza cases, since 3 May 2021

Characteristics	SARI & influenza cases among all hospital patients		SARI & influenza cases among ADHB & CMDHB residents			
	SARI Cases (%)	Influenza positive ¹ (%)	SARI cases	SARI incidence (per 100 000)	Influenza Cases	Influenza incidence (per 100 000)
Overall	952 (38.9)	0 (0.0)	862	78.6	0	0.0
Age group (years)						
<1	253 (44.5)	0 (0.0)	226	1554.3	0	0.0
1–4	267 (63.0)	0 (0.0)	234	435.1	0	0.0
5–19	46 (43.8)	0 (0.0)	40	19.0	0	0.0
20–34	53 (50.5)	0 (0.0)	50	16.3	0	0.0
35–49	48 (38.1)	0 (0.0)	45	21.5	0	0.0
50–64	90 (30.4)	0 (0.0)	86	48.3	0	0.0
65–79	115 (27.2)	0 (0.0)	113	116.6	0	0.0
>80	69 (23.2)	0 (0.0)	68	248.4	0	0.0
Unknown	11 (10.8)	0 ()	0	0.0	0	
Ethnicity						
Māori	219 (44.3)	0 (0.0)	188	143.8	0	0.0
Pacific peoples	314 (47.7)	0 (0.0)	303	174.6	0	0.0
Asian	103 (44.8)	0 (0.0)	99	30.7	0	0.0
European and Other	305 (31.7)	0 (0.0)	272	57.9	0	0.0
Unknown	11 (10.8)	0 ()	0		0	
Hospitals						
ADHB	448 (33.9)	0 (0.0)	377	70.0	0	0.0
CMDHB	504 (44.8)	0 (0.0)	485	87.0	0	0.0
Sex						
Female	462 (39.8)	0 (0.0)	427	76.9	0	0.0
Male	479 (40.5)	0 (0.0)	435	80.3	0	0.0
Unknown	11 (10.7)	0 ()	0	0.0	0	0.0

¹Proportion of cases tested which were positive for influenza viruses

From 3 May to 29 August 2021, 967 SARI specimens have been tested and none (0.0%) were positive for influenza viruses (Table 2). Of the 113 specimens collected from ICU admitted patients with acute respiratory illness, none were positive for influenza viruses. Of the 22 specimens collected from fatal cases with acute respiratory illness, none were positive for influenza viruses.

Additionally, 925 SARI specimens were tested for non-influenza respiratory viruses and RSV is the predominant virus (Table 2).

Table 2. Non-influenza respiratory viruses among SARI cases, 3 May to 29 August 2021

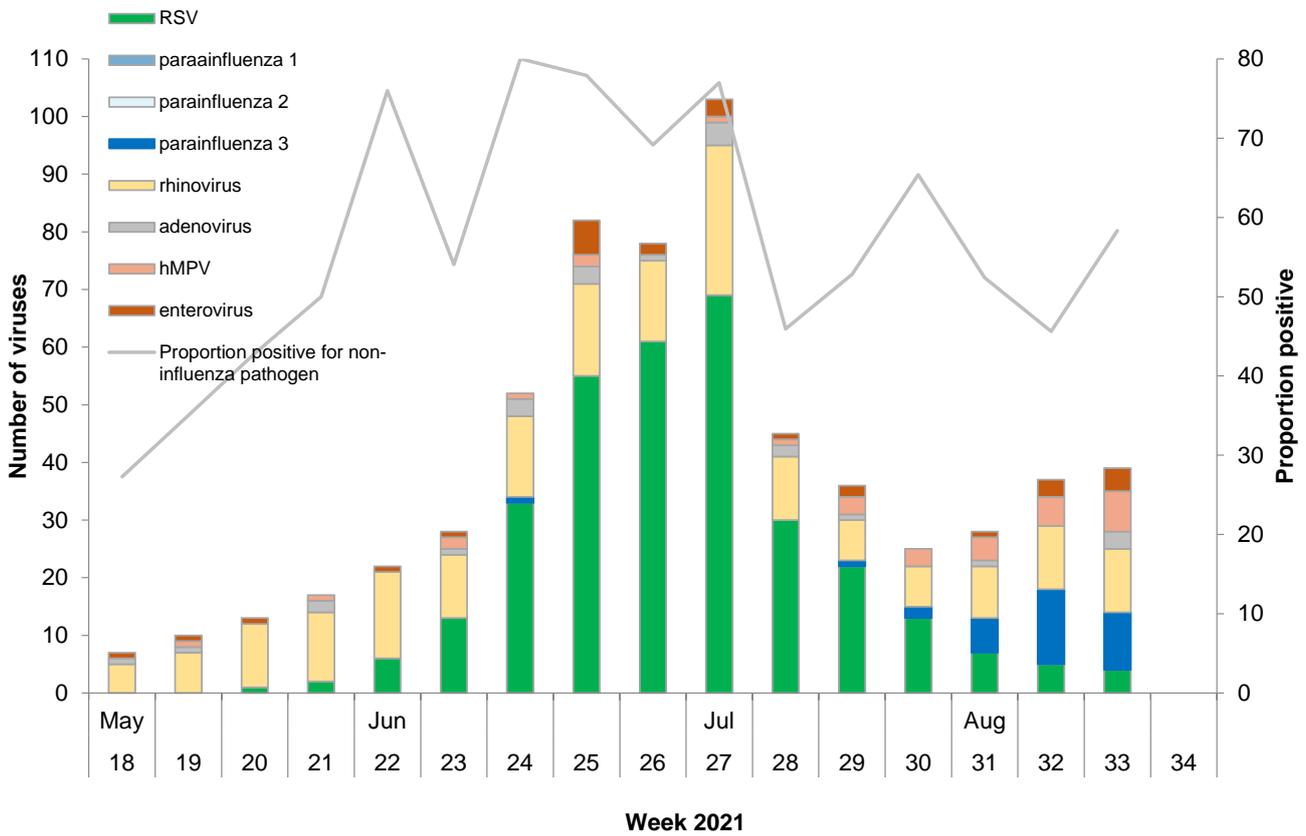
<i>Influenza viruses</i>	SARI	SARI and non-SARI	
	Cases (%)	ICU (%)	Deaths (%)
No. of specimens tested	832	113	22
No. of positive specimens (%) ¹	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A	0	0	0
A (not subtyped)	0	0	0
A(H1N1)pdm09	0	0	0
A(H1N1)pdm09 by PCR	0	0	0
A/Victoria/2570/2019 (H1N1)pdm09 - like	0	0	0
A(H3N2)	0	0	0
A(H3N2) by PCR	0	0	0
A/Hong Kong/2671/2019 (H3N2)-like	0	0	0
Influenza B	0	0	0
B (lineage not determined)	0	0	0
B/Yamagata lineage	0	0	0
B/Yamagata lineage by PCR	0	0	0
B/Phuket/3073/2013 - like	0	0	0
B/Victoria lineage	0	0	0
B/Victoria lineage by PCR	0	0	0
B/Washington/02/2019-like	0	0	0
Influenza and non-influenza co-detection (% +ve)	0 (-)	0 (-)	0 (-)

<i>Non-influenza respiratory viruses</i>	SARI	SARI and non-SARI	
	Cases (%)	ICU (%)	Deaths (%)
No. of specimens tested	790	113	22
No. of positive specimens (%) ¹	482 (61.0)	81 (71.7)	6 (27.3)
Respiratory syncytial virus (RSV)	321	46	2
Parainfluenza 1 (PIV1)	0	0	0
Parainfluenza 2 (PIV2)	0	0	0
Parainfluenza 3 (PIV3)	33	6	0
Rhinovirus (RV)	187	47	3
Adenovirus (AdV)	23	10	1
Human metapneumovirus (hMPV)	31	4	1
Enterovirus	27	8	2
SARS-Cov-2	0	0	0
Single virus detection (% of positives)	355 (73.7)	46 (56.8)	0 (-)
Multiple virus detection (% of positives)	127 (26.3)	35 (43.2)	0 (-)

¹Number of specimens positive for at least one of the listed viruses; note a specimen may be positive for more than one virus

The temporal distribution of the number and proportion of the non-influenza respiratory viruses is shown in Figure 3. RSV was the dominant virus during June-July 2021. Around the end of April 2021, NZ started free quarantine travel between Australia and New Zealand. This may have contributed to community-wide RSV outbreak in NZ in 2021.

Figure 3. Temporal distribution of the number and proportion of non-influenza viruses from SARI specimens, by type and week¹



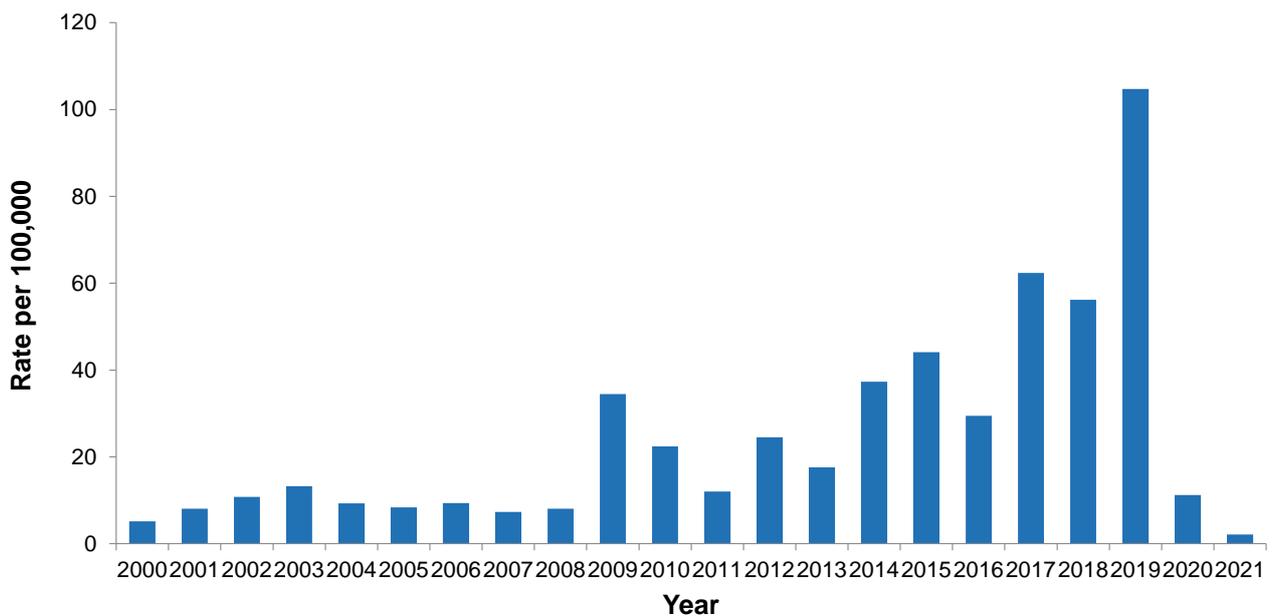
¹Figures for recent weeks will be underestimates due to time lag in receiving laboratory test results

3.1.2 MINISTRY OF HEALTH DATA ON PUBLICLY FUNDED HOSPITAL DISCHARGES

Hospitalisation data for influenza (ICD-10AM-VI code I (J09-J11) for 2021 which correlate with previous versions of ICD-10AM codes J10-J11, were extracted from the New Zealand Ministry of Health's NMDS (by discharge date). In this dataset, people who received less than 1 day of hospital treatment in hospital emergency departments were excluded from any time series analysis of influenza hospitalisations during 2000–2021. Influenza-related hospitalisations were conservatively taken to include only those cases where influenza was the principal diagnosis. Repeat admissions were included, as infections with another influenza A subtype or B virus are possible.

From 1 January to 1 Aug 2021, there were a total of 104 hospitalisations (2.0 per 100,000) for influenza (Figure 4). Influenza hospitalisation coding has not been completed for the year. This data only captured a proportion of influenza-coded cases for the winter season of 2021.

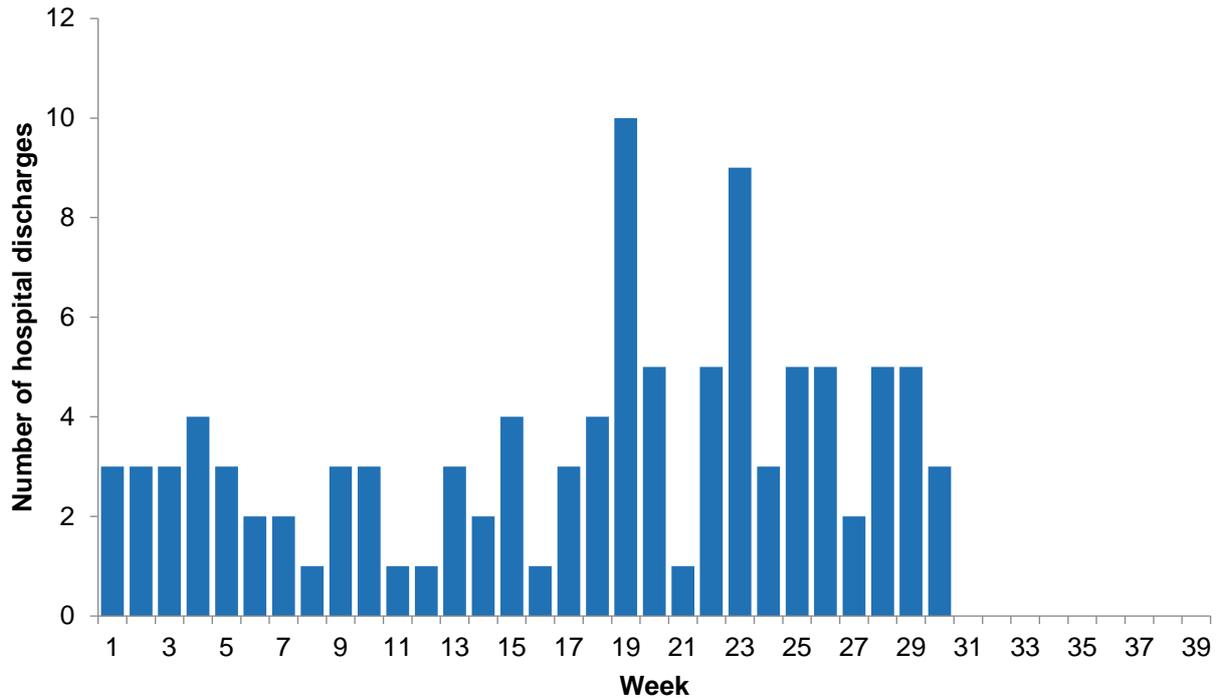
Figure 4. Influenza hospital discharge rates, 2000–2021*



*2021 data from 1 Jan to 1 Aug only; Source: Ministry of Health, NMDS (Hospital Events)

Figure 5 shows influenza hospitalisations by week discharged. The highest number of hospitalisations (10) occurred in week 19 (week ending 16 May 2021).

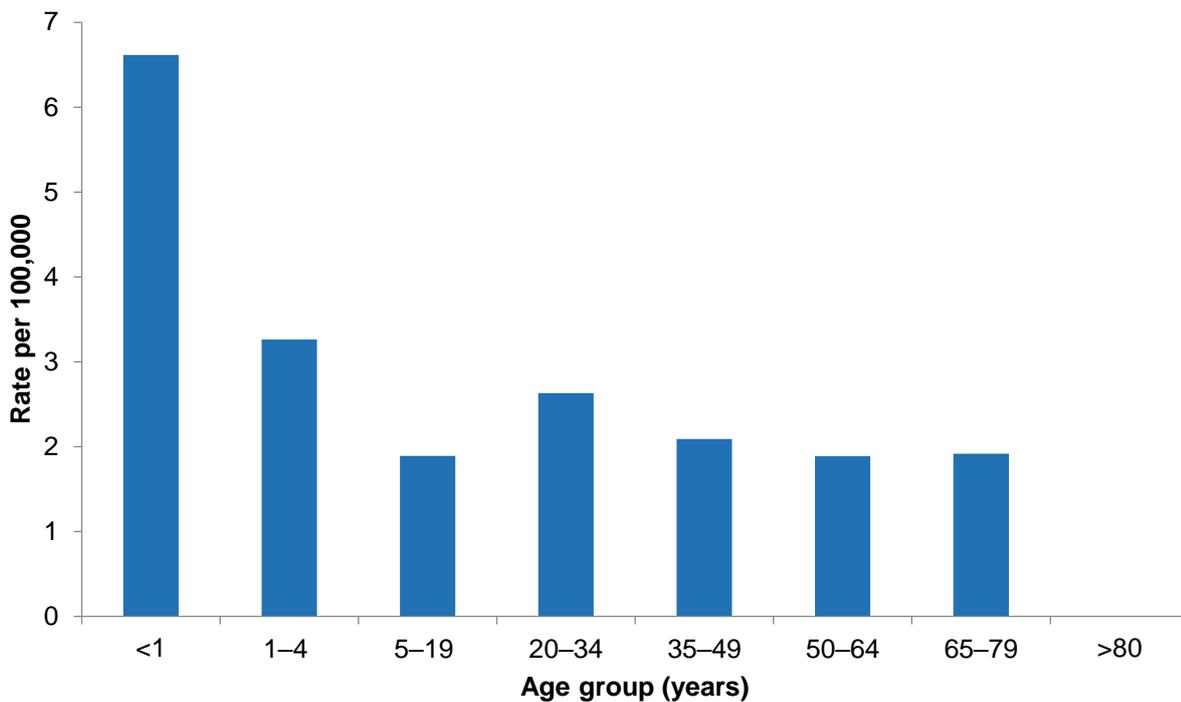
Figure 5. Influenza hospital discharges by week, 2021*



*Data from 1 Jan to 1 Aug only; Source: Ministry of Health, NMDS (Hospital Events)

From 1 January to 1 Aug, the highest influenza hospitalisation rates were recorded among infants < 1 year (6.6 per 100,000) followed by young children aged 1-4 years (3.3 per 100,000) (Figure 6).

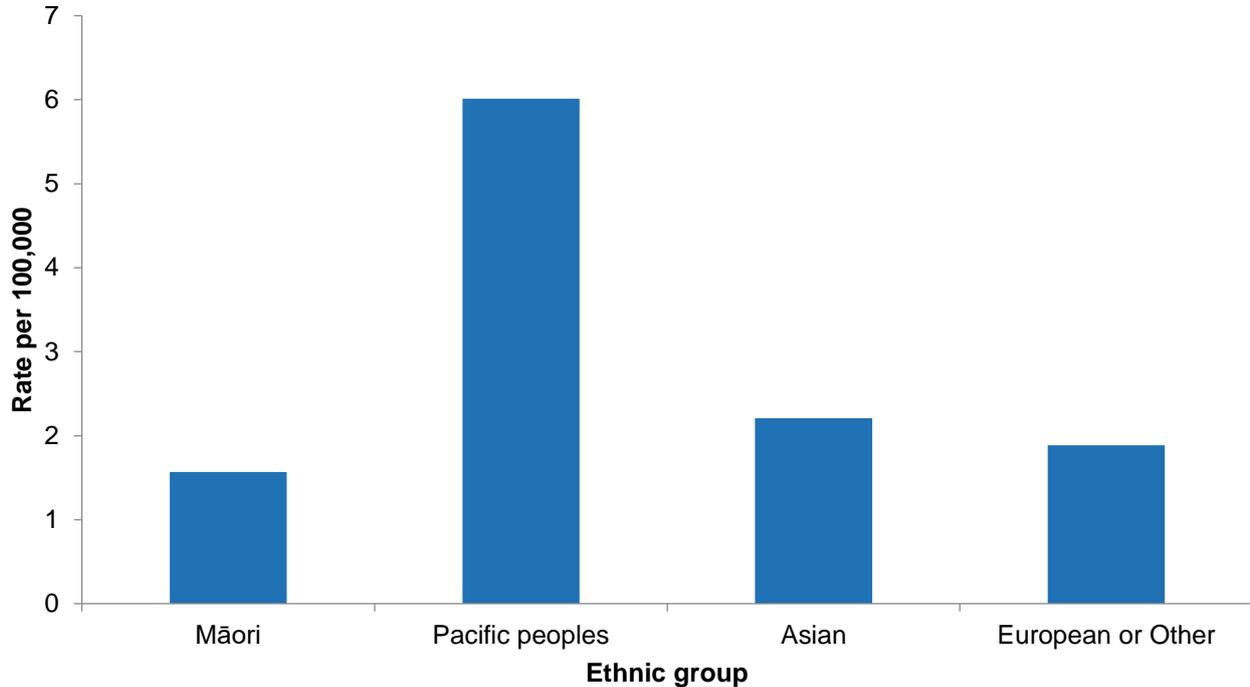
Figure 6. Influenza hospital discharge rates by age group, 2021*



*Data from 1 Jan to 1 Aug only; Source: Ministry of Health, NMDS (Hospital Events)

The ethnic distribution of influenza hospitalisations in 2021 is shown in Figure 7. Pacific peoples had the highest hospitalisation rate (6.0 per 100,000) followed by Asian (2.2 per 100,000 populations). European or Other (1.9 per 100,000) and Maori (1.6 per 100,000 populations) ethnic groups+ had the lowest rates of hospitalisations.

Figure 7. Hospital discharge rates by prioritised ethnic group, 2021*



*Data from 1 Jan to 1 Aug only; Source: Ministry of Health, NMDS (Hospital Events)

3.2 COMMUNITY-BASED SURVEILLANCE

3.2.1 COMMUNITY-BASED LONGITUDINAL COHORT STUDY

SHIVERS-II (the second iteration of the Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance programme) is a prospective adult cohort study in Wellington, NZ. The cohort study is also called WellKiwis Adult study and has been in operation since 2018 enrolling individuals aged 20-69 years, randomly selected from those healthy individuals listed in the general practice's primary care management system. In 2021, SHIVERS-II study staff followed these participants (~1400) and monitored their ILIs and acute respiratory illness (ARI)s.

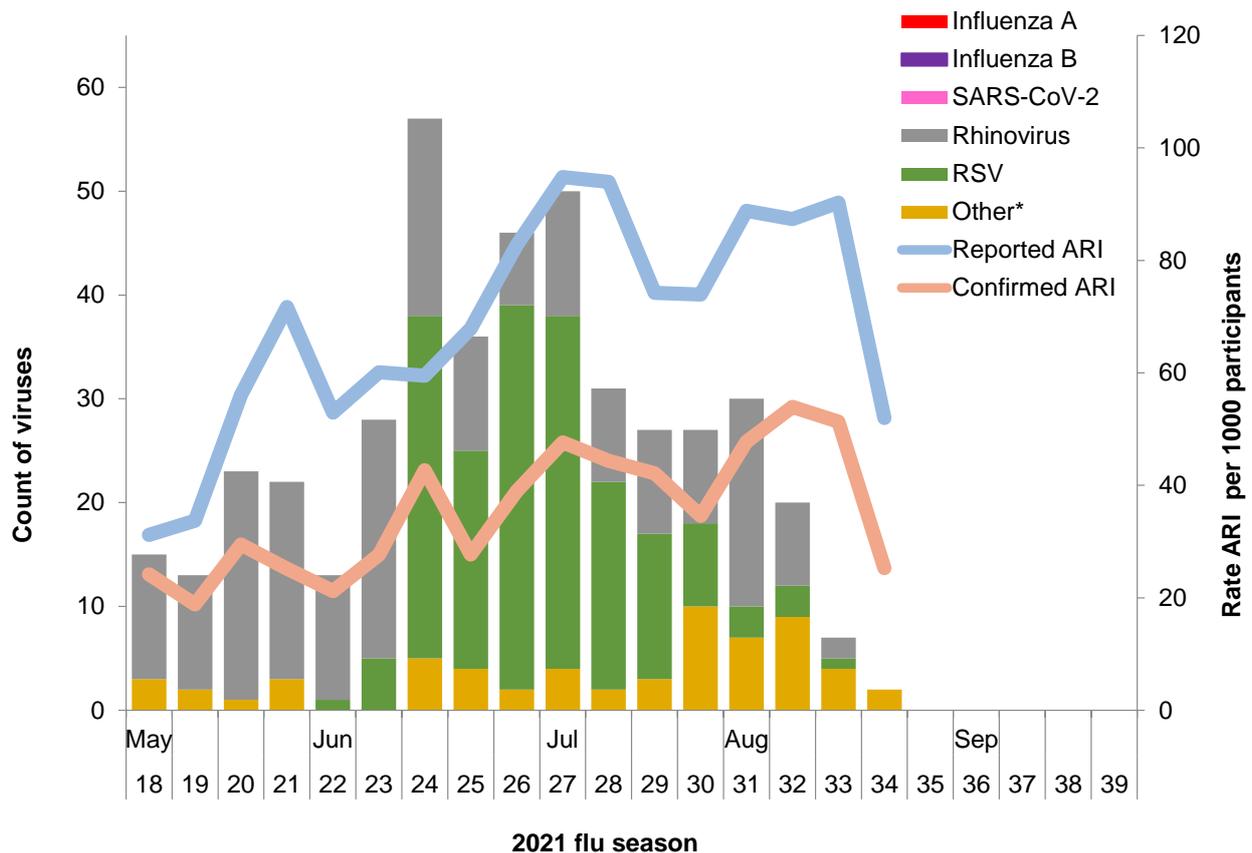
SHIVERS-III (i.e. WellKiwis Infant) is a prospective Wellington infant cohort aiming to recruit 600 infant-mother pairs from Oct 2019-Sept 2022 (200 pairs a year) and follow them until 2026. In 2021, the study staff followed up ~300 infants and monitored their ILIs and ARIs.

SHIVERS-IV (i.e. WellKiwis Household) is a prospective Wellington household cohort in Wellington, NZ. Households with at least one child aged 19 years or younger are invited to participate from SHIVERS-II and III participants and individuals randomly selected from participating general practice's patient list. Enrolled participants are to be followed for 7 years during 2021-2028. In 2021, the study staff followed up ~950 household members and monitored their ILIs and ARIs.

During May-September 2021, SHIVERS-II, III and IV study staff sent weekly surveys to participants regarding their respiratory illness. Due to COVID-19, the ARI case definition in 2021 has changed to: “acute respiratory illness with fever or feverishness and/or one of following symptoms (cough, running nose, wheezing, sore throat, shortness of breath, loss of sense of smell/taste) with onset in the past 10 days.” The case definition for ILI during was the same: “acute respiratory illness with cough and fever/measured fever of $\geq 38^{\circ}\text{C}$ and onset within the past 10 days”. For those participants who met the case definition for ILI and ARI, research nurses visited the participant and take a nasopharyngeal or nasal or throat swab to test for influenza, RSV and other respiratory viruses and SARS-CoV-2.

Figure 8 shows the weekly rate of influenza like illness (ILI) and associated viruses detected among the SHIVERS-II, III, IV cohort participants during the winter surveillance period in 2021. RSV was the dominant virus during June-July 2021. Around the end of April 2021, NZ started free quarantine travel between Australia and New Zealand. This may have contributed to community-wide RSV outbreak in NZ in 2021.

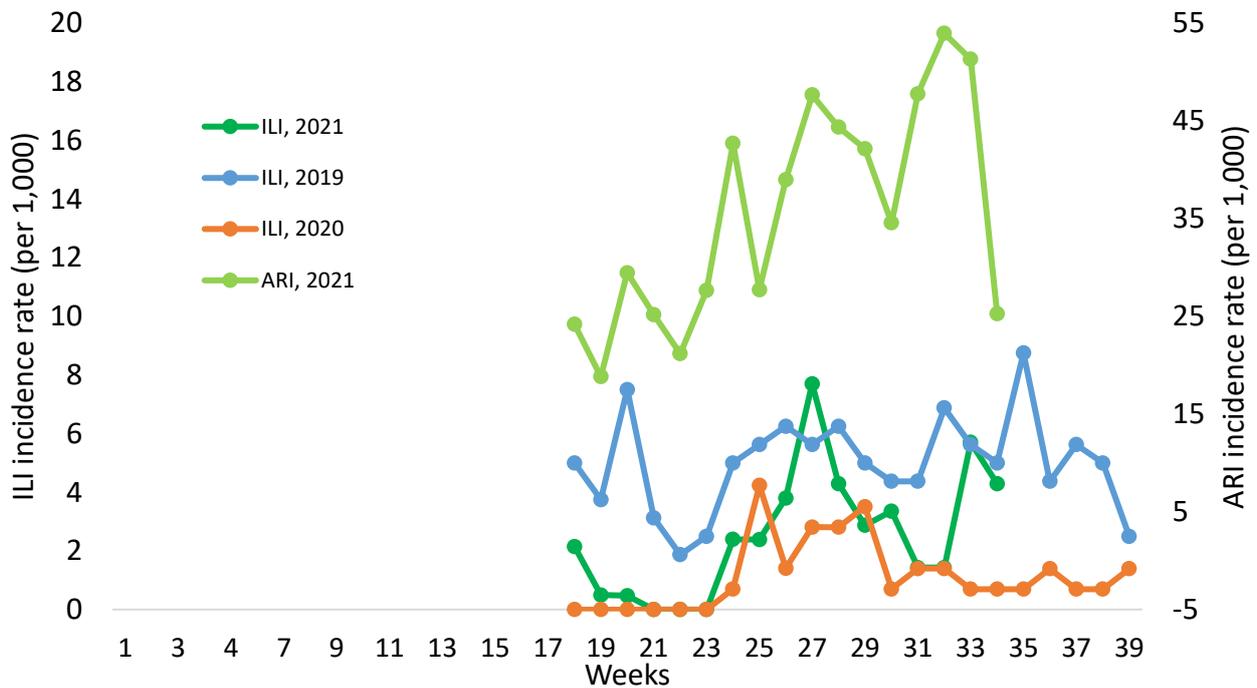
Figure 8. Weekly incidence rate of acute respiratory illness and associated viruses in 2021



*Note: other viruses include enterovirus, adenovirus, parainfluenza virus types 1-3 and human metapneumovirus. The left axis indicates number of respiratory viruses detected among participants each week. The different coloured bars on the graph represent the count of the different respiratory viruses detected. The right axis shows weekly ILI rates - the blue line is the weekly rate of ILI reported by participants (per 1000), and the orange line the rate of nurse-confirmed ILI meeting the case definition. National Level 4 lockdown occurred 17-31 August 2021.

The ILI rates in 2021 was higher than the previous years of 2019 and 2018, however, ARI incidence in 2021 was higher than the ILI rate in 2021 (Figure 9).

Figure 9. Weekly incidence rates in 2021, compared to 2020 and 2019



From 3 May to 29 August 2021, 663 respiratory specimens have been tested and none (0.0%) were positive for influenza viruses.

Additionally, 659 specimens were tested for non-influenza respiratory viruses (Table 3).

Table 3 Non-influenza respiratory viruses among ILI cases, since 3 May 2021

<i>Non-influenza respiratory viruses</i>	WellKiwis Households	Wellkiwis Infants	WellKiwis Adults	Total
No. of specimens tested	274	203	182	659
No. of positive specimens (%) ¹	160 (58.4)	152 (74.9)	98 (53.8)	410
Respiratory syncytial virus (RSV)	77	64	38	179
Parainfluenza 1 (PIV1)	3	0	2	5
Parainfluenza 2 (PIV2)	0	0	0	0
Parainfluenza 3 (PIV3)	3	11	2	16
Rhinovirus (RV)	75	72	58	205
Adenovirus (AdV)	8	12	4	24
Human metapneumovirus (hMPV)	5	2	0	7
Enterovirus	2	9	0	11
SARS-CoV-2	0	0	0	0
Single virus detection (% of positives)	148 (92.5)	135 (88.8)	92 (93.9)	375
Multiple virus detection (% of positives)	12 (7.5)	17 (11.2)	6 (6.1)	35

3.2.2 SENTINEL GENERAL PRACTICE ACUTE RESPIRATORY ILLNESS SURVEILLANCE

Prior to 2020, influenza-like illness (ILI) surveillance through sentinel general practices was the main means of identifying seasonal influenza activity in New Zealand communities. The COVID-19 pandemic has changed the landscape at the primary care level through intensive screening for COVID-19 both at general practices and community-based assessment centres for patients presenting with any acute respiratory illness. However, this situation also creates new opportunity of tracking influenza and other respiratory viruses by testing those samples already collected for COVID-19 with no additional effort from practices.

In 2021, we piloted a sentinel general practice-based Acute Respiratory Illness (ARI) surveillance using routine swabs indicated for COVID-19 testing (i.e. no change in practice) among voluntary sentinel general practices. Our aim is to identify an efficient, fit-for-purpose public health surveillance system which does not impact on clinical workload in a new and rapidly evolving environment where respiratory viral infections may be caused by COVID-19, influenza and non-influenza respiratory viruses. This pilot is called SHIVERS-V, the fifth iteration of SHIVERS (Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance).

Acute respiratory illness is manifested by a range of symptoms such as cough, fever, sore throat, and runny nose. Many respiratory viruses can cause ARI including SARS-CoV-2 (causing COVID-19), influenza and other non-influenza respiratory viruses.

The specific aims of ARI surveillance in primary care are to:

1. Align with the current COVID-19 clinical guidelines in general practices while expanding testing to include influenza and non-influenza respiratory viruses in addition to COVID-19.
2. Utilise the current mechanism for COVID-19 data collection through use of the routine laboratory electronic order/specimen request form:
 - No extra work is required during the standard clinical consultation, beyond ticking the correct box in the existing request form (i.e. testing request for COVID-19/influenza/non-influenza virus).
 - Patient demographic information pre-populated from the Practice Management System as usual.
3. Provide valuable information on influenza disease burden, epidemiology, etiology, risk factors and vaccine effectiveness in the COVID-19 era to guide early detection of influenza epidemics/pandemics, inform vaccination policy, vaccine strain selection and other public health measures.

ARI case definition: it is consistent with the current Ministry of Health definition on COVID-19 when to take swabs in primary care (<https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-information-health-professionals/case-definition-and-clinical-testing-guidelines-covid-19#guidance>) (updated on 7 May 2021)

Any acute respiratory infection with at least one of the following symptoms (with or without fever):

- *new or worsening cough,*
- *fever (at least 38°C),*
- *shortness of breath,*
- *sore throat,*
- *coryza (runny nose),*
- *anosmia (loss of sense of smell),*
- *dysgeusia (altered sense of taste).*

People meeting the above clinical criteria should be tested.

Some people may present with less typical symptoms such as only fever, diarrhoea, headache, myalgia (muscle aches), nausea/vomiting, or confusion/irritability. For people with less typical symptoms, if there is not another more likely diagnosis, they should also be tested.

Eligibility criteria for sample collection: All consultation-seeking patients with symptoms consistent with COVID-19 are eligible for ARI swabbing. Patients who do not have symptoms consistent with COVID-19 but are required or are seeking COVID-19 testing for other reasons (eg. travel, routine testing of border workers, or asymptomatic contacts etc.) are not eligible for ARI testing.

Electronic order/Specimen request form: Wellington Southern Community Laboratory (WSCL) and Labtests to provide additional testing option on their electronic order/specimen (e-order) form. GPs or nurses can choose to: either test for COVID-19/influenza/non-influenza for those patients agreeing ARI testing or test for COVID-19 alone for those patients declining ARI testing. Patient demographic information will be pre-populated from PMS to this form.

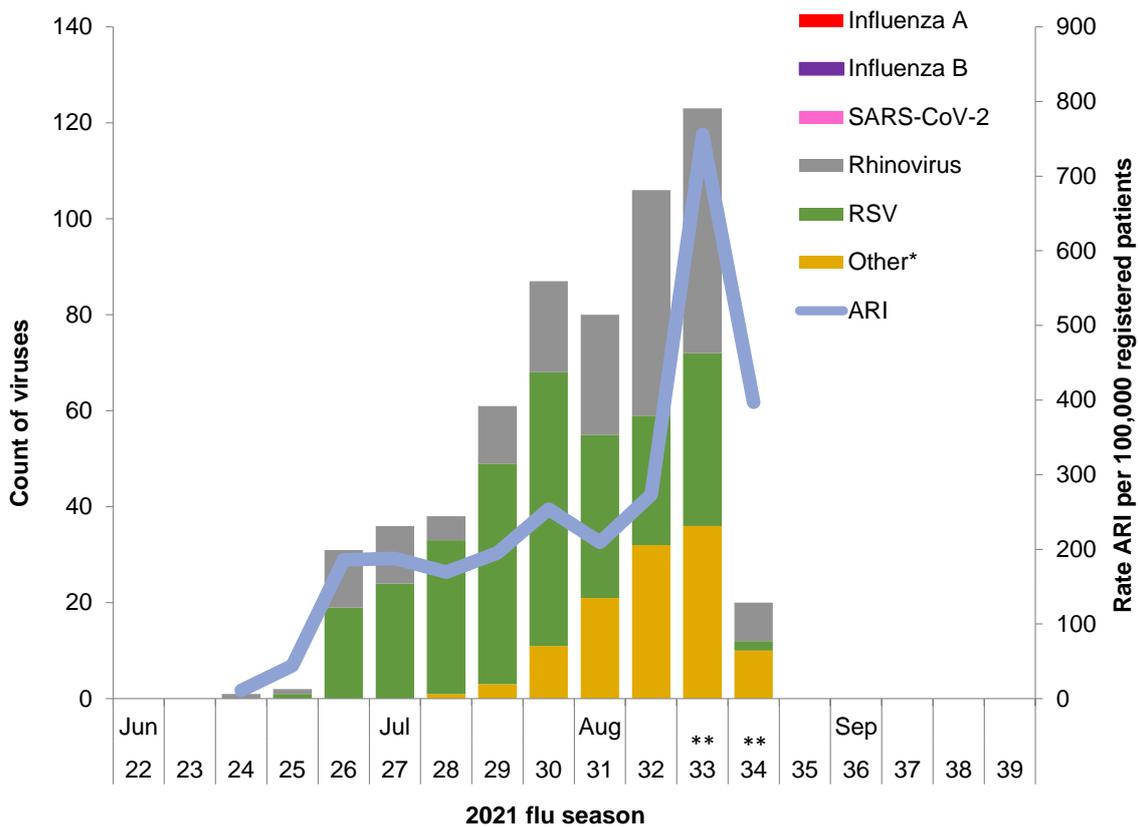
Laboratories: WSCL in Wellington and Labtests in Auckland and ESR's WHO National Influenza Centre are involved in testing. Laboratory identification included molecular detection using the polymerase chain reaction (PCR) for SARS-CoV-2, influenza A&B, and non-influenza respiratory viruses (respiratory syncytial virus, parainfluenza virus types 1, 2, 3 and 4, rhinovirus, adenovirus, human metapneumovirus).

Practice denominator: The number of the enrolled patients, including age, sex, ethnicity (and addresses to allow geocoding for the NZ Deprivation index). This will be collected once the practice agrees to take part in this pilot. Consultation rates were calculated using the registered patient populations of the participating practices as a denominator.

Data from Practice Management system: At the end of the influenza season, additional data will be collected on ARI patients, including respiratory symptoms or illness, underlying conditions, travel history, vaccination status etc

Figure 10 shows the weekly rate of acute respiratory illness and associated viruses detected in this sentinel general practice-based ARI surveillance between Week 24 (starting 14 June) to week 34 (ending 29 August) 2021. RSV was the dominant virus during June-July 2021.

Figure 10. Weekly incidence rate of acute respiratory illness and associated viruses in 2021



*Note: other viruses include enterovirus, adenovirus, parainfluenza virus types 1-3 and human metapneumovirus. The left axis indicates number of respiratory viruses detected among registered patients with acute respiratory illnesses each week. The different coloured bars on the graph represent the count of the different respiratory viruses detected. The right axis shows weekly ARI rates - the purple line is the weekly rate of ARI reported by registered patients (per 100,000), meeting the case definition. **: The 2021 national lockdown at Level 4 may lead to health seeking behaviour changes among consultation seeking patients which may contribute to a higher than usual ARI rate.

From 14 June to 29 August 2021, 1374 respiratory specimens have been tested and none (0.0%) were positive for influenza viruses. Additionally, 1374 specimens were tested for non-influenza respiratory viruses (Table 4).

Table 4 Non-influenza respiratory viruses among GP consultation seeking patients with ARI, since 14 June 2021

Non-influenza respiratory viruses	Total
No. of specimens tested	1374
No. of positive specimens (%)	559 (40.7)
Respiratory syncytial virus (RSV)	278
Parainfluenza 1 (PIV1)	0
Parainfluenza 2 (PIV2)	0
Parainfluenza 3 (PIV3)	83
Rhinovirus (RV)	193
Adenovirus (AdV)	10
Human metapneumovirus (hMPV)	21
Enterovirus	0
SARS-CoV-2	0
Single virus detection (% of positives)	534 (95.5)
Multiple virus detection (% of positives)	25 (4.5)

3.2.3 RETURNEES ACUTE RESPIRATORY ILLNESS SURVEILLANCE

As NZ has not had any laboratory confirmed influenza outbreaks nor epidemics detected in our community since the implementations of border restrictions in 2020, it is likely that overseas returnees will be the source of influenza virus re-introduction and subsequent spread in NZ.

In 2021, we conducted a clinical audit (part of the SHIVERS-V project) of left-over specimens currently being tested for COVID-19 among those overseas returnees with acute respiratory symptoms staying at managed isolation facilities. The specific aim of the clinical audit is to understand and potentially improve the experience, process, safety and efficiency of hospital laboratory testing regimes in a new and uncertain environment of respiratory viral infections that may be caused by COVID-19, influenza and other non-influenza respiratory viruses:

- Evaluate hospital laboratory testing regimes by systematically testing for influenza virus (and some non-influenza respiratory viruses) from the specimens that have already been tested for COVID-19 among those returnees who presented acute respiratory symptoms on arrival or during their stay at the managed isolation facilities while border restrictions are in place.
- Refer any influenza positive specimen (and a sample of non-influenza respiratory virus positive specimens) to ESR's National Influenza Centre in a de-identifiable manner for whole genome sequencing.

ARI case definition: it is consistent with the current Ministry of Health definition on COVID-19 for acute respiratory illness.

Any acute respiratory infection with at least one of the following symptoms (with or without fever):

- *new or worsening cough,*
- *fever (at least 38°C),*
- *shortness of breath,*
- *sore throat,*
- *coryza (runny nose),*
- *anosmia (loss of sense of smell),*
- *dysgeusia (altered sense of taste).*

People meeting the above clinical criteria should be tested.

Some people may present with less typical symptoms such as only fever, diarrhoea, headache, myalgia (muscle aches), nausea/vomiting, or confusion/irritability. For people with less typical symptoms, if there is not another more likely diagnosis, they should also be tested.

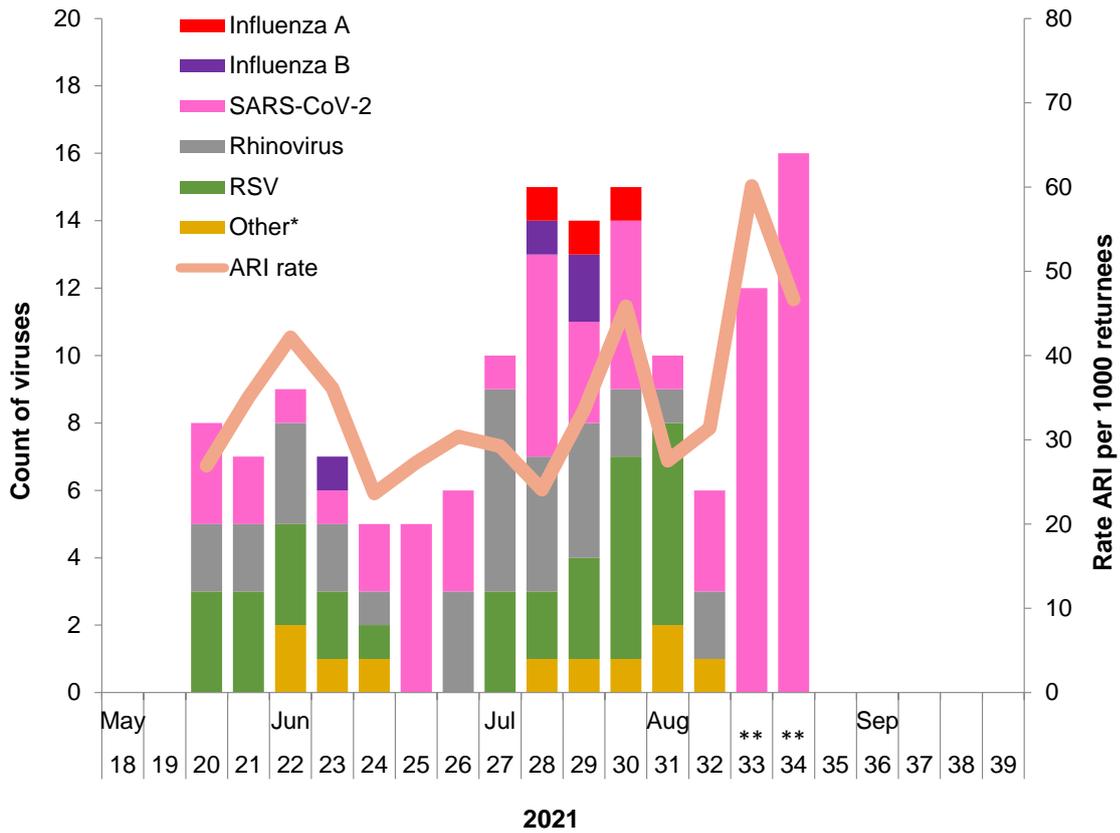
Laboratories: ADHB, CMDHB, CDHB, CCDHB, BOPDHB laboratories and ESR's WHO National Influenza Centre are involved in testing. Laboratory identification included molecular detection using the polymerase chain reaction (PCR) for SARS-CoV-2, influenza A&B, and non-influenza respiratory viruses (respiratory syncytial virus, parainfluenza virus types 1, 2, 3 and 4, rhinovirus, adenovirus, human metapneumovirus).

Eligibility criteria for testing: A regular review of the electronic daily extract from éclair database for each DHB laboratory will be conducted to identify returnees with suspected respiratory infections who may meet the ARI case symptom definition or conditions. If there is any left-over specimen available after the COVID-19 testing, such specimens will be subjected to test for influenza (and other non-influenza respiratory viruses).

Returnee denominator: The number of the returnees (including age, sex, ethnicity) with or without acute respiratory illness are collected as a denominator.

Figure 11 shows the weekly rate of acute respiratory illness and associated viruses detected among returnees with ARI between week 20 (starting 17 May) to week 34 (ending 29 August) 2021.

Figure 11. Returnees weekly incidence rate of acute respiratory illness and associated viruses in 2021



*Note: other viruses include enterovirus, adenovirus, parainfluenza virus types 1-3 and human metapneumovirus
 The left axis indicates number of respiratory viruses detected among returnees with acute respiratory illnesses each week. The different coloured bars on the graph represent the count of the different respiratory viruses detected.
 The right axis shows weekly ARI rates - the orange line is the weekly rate of ARI reported by overseas travellers (per 1000), meeting the case definition). **: The 2021 national lockdown at Level 4 has led to some laboratories prioritised testing for COVID-19 over influenza and other respiratory viruses.

From 17 May to 29 August 2021, 632 respiratory specimens have been tested and 7 (1.1%) were positive for influenza viruses among overseas returnees. Additionally, 632 specimens were tested for RSV and 272 specimens tested for parainfluenza 1,2,3, rhinovirus, adenovirus and human metapneumovirus (Table 5).

Table 5 Respiratory viruses among overseas travellers with acute respiratory illnesses, since 17 May 2021

<i>Respiratory viruses</i>	<i>Cases tested</i>	<i>Cases positive</i>	<i>Positivity rate (%)</i>
Influenza A	632	3	0.5
Influenza B	632	4	0.6
SARS-CoV-2	1035	66	6.4
Respiratory Syncytial Virus (RSV)	632	22	3.5
Parainfluenza 1 (PIV 1)	272	0	0.0
Parainfluenza 2 (PIV2)	272	0	0.0
Parainfluenza 3 (PIV3)	272	6	2.2
Rhinovirus (RV)	272	34	12.5
Adenovirus (AdV)	227	2	0.9
Human metapneumovirus (hMPV)	272	2	0.7

4. RECENT STRAIN CHARACTERISATIONS

The laboratory-based surveillance for influenza is carried out all-year-around by the New Zealand virus laboratory network consisting of the WHO National Influenza Centre (NIC) at ESR and 6 hospital laboratories at Auckland, Waikato, Wellington, Christchurch and Dunedin, serving nearly 70% of the NZ population. This laboratory network tests specimens ordered by clinicians for hospital in-patient and outpatients during routine viral diagnosis. In addition, this laboratory network conducts testing for public health surveillance including hospital based SARI and sentinel GP-based surveillance and SHIVERS research.

The WHO National Influenza Centre at ESR receives samples from local hospital laboratories for further typing from active surveillance (sentinel general practice based ILI/ARI and hospital-based SARI) as well as passive surveillance (i.e. mainly hospital in-patient and outpatients during routine viral diagnosis).

4.1 CIRCULATING STRAINS IN 2021

A total of 11 influenza viruses were detected and reported through any surveillance system in 2021. Most of these influenza viruses were detected from returnees while staying at the managed isolation facilities. Of them, influenza A represented 45.5% (5/11) and influenza B 54.5% (6/11) of all influenza viruses (Table 6). Among A sub-typed, 4 were A(H3N2) virus. Among B lineage-typed, 3 were influenza B/Victoria lineage viruses.

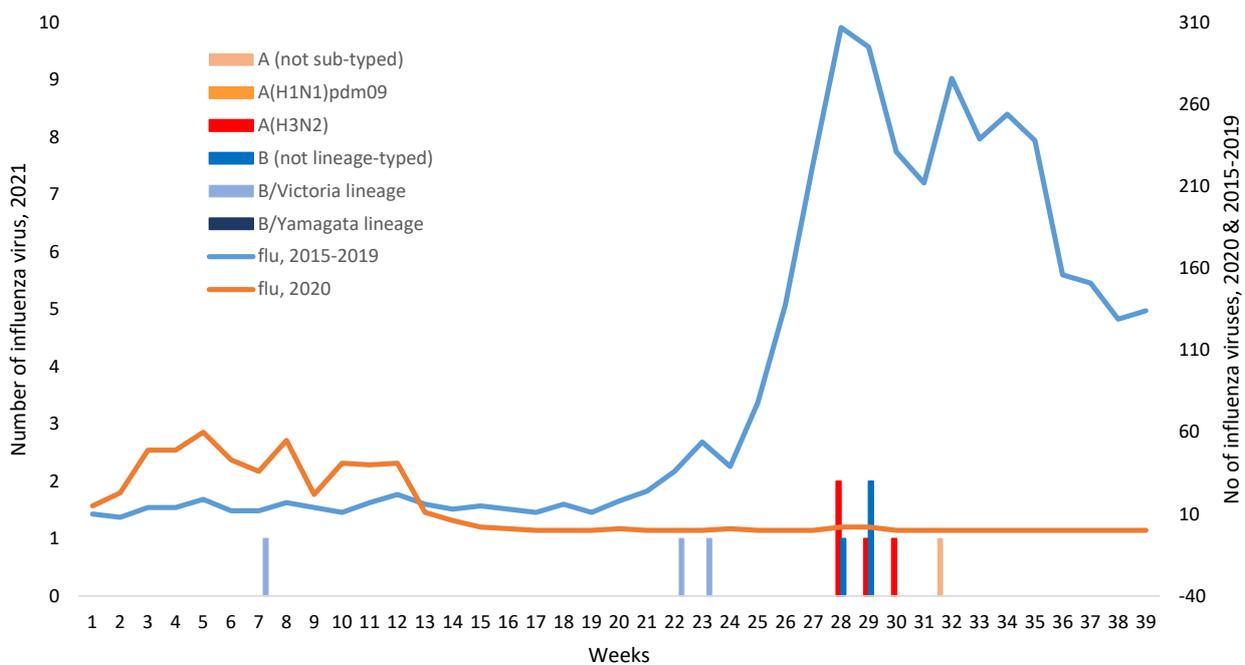
Table 6. Influenza virus identifications by type and sub-type and lineage-typed, 2020

Viruses	All viruses (%)	Sub-typed and lineage-typed (%)
Influenza A	5	4
Influenza A (not sub-typed)	1	
Influenza A(H1N1)pdm09	0	
A(H1N1)pdm09 by PCR		
A/Victoria/2570/2019 (H1N1)pdm09-like		
Influenza A(H3N2)	4	4
A(H3N2) by PCR	4	
A/Hong Kong/2671/2019 (H3N2)- like		
Influenza B	6	3
Influenza B (not lineage-typed)	3	
B/Yamagata lineage		
B/Yamagata lineage by PCR		
B/Phuket/3073/2013-like		
B/Victoria lineage	3	3
B/Washington/02/2019	1	
B/Victoria lineage by PCR	2	
Total	11	7

Figure 12 shows the influenza virus identifications by type and sub-type for each week throughout 2021. NZ is a southern hemisphere country with a temperate climate. NZ has a well-established influenza circulation pattern with peak incidences in the winter months. The 2021 (and 2020) winter is unprecedented that no influenza epidemic or outbreak was reported during the winter influenza surveillance period. This is probably due largely to the COVID-19 related non-pharmaceutical interventions which have been implemented since 25 March 2020 till now.

A total of 11 influenza viruses were detected and reported through laboratory-based surveillance and returnee ARI surveillance. One virus detected in week 7 and the remaining 10 viruses during weeks 18-34.

Figure 12. Total influenza viruses by type and week specimen taken in 2021 compared to 2020 and 2015-2019



4.2 INFLUENZA A(H1N1)PDM09

WHO National Influenza Centre (NIC) at ESR did not receive any influenza A(H1N1)pdm09 clinical samples.

Only 9 A(H1N1)pdm09 viruses with collection dates between February to September 2021 were characterized at the Melbourne WHOCC from 3 countries. All A(H1N1)pdm09 viruses belonged to phylogenetic subclade 6B.1A with subclades 5A2 detected (i.e. 6B.1A5A2). No viruses of 6B.1A5A1 subgroup were detected however this subgroup was widely detected in Western Africa.

The antigenic characteristics of 7 A(H1N1)pdm09 viruses were assessed with post-infection ferret antisera in haemagglutination inhibition (HI) assay. All viruses were well inhibited by ferret antisera raised to cell and egg propagated A/Victoria/2570/2019-like viruses but poorly inhibited by ferret antisera raised against cell or egg propagated A/Brisbane/02/2018-like viruses.

Human serology studies used 15 serum panels, from children (6 months to 17 years), adults (18-64 years) and older adults (≥ 65 years) who had received egg-based quadrivalent inactivated vaccines

(standard, high dose or with adjuvant) or cell culture-based quadrivalent inactivated vaccine. Egg-based vaccine formulations for the northern hemisphere in 2020-2021 (NH 2020-21: 13 serum panels) contained antigens from A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like, A/Hong Kong/2671/2019 (H3N2)-like, B/Washington/02/2019-like (B/Victoria lineage) and B/Phuket/3073/2013-like (B/Yamagata lineage) viruses. Cell culture-based NH 2020-21 vaccines contained A/Hawaii/70/2019 (H1N1)pdm09-like and A/Hong Kong/45/2019 (H3N2)-like virus antigens as well as the required influenza B components. The vaccine formulations for the southern hemisphere in 2021 (SH 2021: 2 serum panels) contained a change in the A(H1N1)pdm09 component. The egg- and cell culture-based vaccines contained A/Victoria/2570/2019 (H1N1)pdm09-like and A/Wisconsin/588/2019 (H1N1)pdm09-like viruses, respectively.

In serum panels from recipients of NH 2020-21 vaccines, when compared to titres against cell culture-propagated A/Hawaii/70/2019 (H1N1)pdm09-like **5A1** vaccine viruses, post-vaccination HI geometric mean titres (GMTs) against cell culture-propagated **5A2** viruses were significantly reduced in almost all serum panels. GMTs against most cell culture-propagated **5A1** viruses were not significantly reduced. In serum panels from recipients of SH 2021 vaccines, when compared to titres against cell culture-propagated A/Wisconsin/588/2019 (H1N1)pdm09-like **5A2** vaccine viruses, post-vaccination HI GMTs against the majority of recent **5A1** and **5A2** cell culture-propagated viruses were not significantly reduced.

In summary, very few influenza A(H1N1)pdm09 viruses were circulating in southern hemisphere during the 2021 winter season. The majority of influenza A(H1N1)pdm09 viruses were antigenically and genetically similar to the 2021 vaccine virus A/Victoria/2570/2019 (H1N1)pdm09. Based on all of the available data, the WHO consultation recommended to continue to use the same vaccine strain containing an A/Victoria/2570/2019 (H1N1)pdm09-like strain for 2022. The AIVC accepted this recommendation.

(Abridged from the Weekly Epidemiological Record (WER), 2021 96(42):509-520 and a report to AIVC by Dr Ian Barr, WHO Collaborating Centre for Influenza, Melbourne).

4.3 INFLUENZA A(H3N2)

WHO National Influenza Centre (NIC) at ESR received 4 influenza A(H3N2) clinical samples and none yielded cell culture isolates.

114 A(H3N2) viruses with collection dates between February to September 2021 were characterized at the Melbourne WHOCC from 9 countries with most coming from Australia. It showed an overall reduced heterogeneity in the HA and NA gene compared to previous years. The majority (95%, 37/39) of A(H3N2) viruses belonged to the phylogenetic clade 3C.2a1b with a minority (5%, 2/39) of A(H3N2) 3C3a viruses detected. Within the 3C.2a1b subclade, two further subgroups (3C.2a1b.2a1 and 3C.2a1b.2a2) were identified.

A(H3N2) viruses have become increasingly difficult to test with the haemagglutination inhibition assay (HI). Some viruses have low or no HA titre with guinea pig RBC even though there is ample virus present (as detected by other methods). Particular mutations or polymorphisms in the NA of recent H3N2 viruses (especially the D151G) appear to allow some level of binding to red blood cells (RBC), thus interfering with the inhibition of viruses between HA and RBC using post-infection ferret sera. To overcome this problem a number of WHOCCs have been performing their HI assays in the presence of 20nM oseltamivir carboxylate in order to prevent this NA binding. This appears to improve the discrimination between antigenically drifted vs not-drifted viruses. However, about 35% of these viruses have a drop in HA titre to a point whereby these viruses cannot be assayed by HI anymore. Alternatively, virus neutralization assays such as the microneutralisation or plaque reduction assays or focus reduction assays (FRA) can be used where the NA binding is not relevant.

Antigenic characterisation of A(H3N2) viruses was performed by HI and virus neutralization (VN) assays. Ferret antisera raised against cell culture-propagated A/Hong Kong/45/2019-like viruses (**1b**: e.g. A/Darwin/726/2019), representing the cell/recombinant-based vaccine viruses for the NH 2020-21 and SH 2021 influenza seasons, recognised **1a** viruses well. Of the two new virus groups that have emerged, those in **2a1** were recognised less well and those in **2a2** were recognised poorly. Ferret antisera raised against egg-propagated A/Hong Kong/2671/2019-like viruses (**1b**), representing the egg-based vaccine viruses for the NH 2020-21 and SH 2021 influenza seasons, recognised all test viruses poorly.

In HI assays, viruses with HA genes belonging to 3C.2a1b subclades **1a** and **2a1** were recognised well by ferret antisera raised against cell culture-propagated A/Cambodia/e0826360/2020 (NH 2021-22 **2a1** vaccine virus) while **2a2** viruses were recognised less well. Ferret antisera raised against egg-propagated A/Cambodia/e0826360/2020 showed a similar pattern. In contrast, ferret antisera raised against **2a2** viruses, such as cell culture-propagated A/Darwin/6/2021 or egg-propagated A/Darwin/9/2021, reacted well with **2a2** viruses but reacted poorly with **2a1**, **1a** and clade 3C.3a viruses.

Human serology studies were conducted with serum panels as described above using HI and virus neutralization assays. When compared to titres against cell culture-propagated A/Hong Kong/45/2019-like vaccine viruses, post-vaccination GMTs of most serum panels were significantly reduced against the majority of cell culture-propagated **2a1** and **2a2** viruses. Reductions were less pronounced for **1a** and clade 3C.3a viruses.

In summary, most of influenza A(H3N2) viruses collected in the period February through August 2021 had HA genes that belonged to genetic groups 3C.2a1b.**2a1** and 3C.2a1b.**2a2**. The majority of recently circulating viruses were 3C.2a1b.**2a2** and were poorly recognised by ferret antisera raised against cell- and egg- propagated reference viruses representing the A(H3N2) vaccine components of the SH 2021 influenza season. However, ferret antisera raised against 3C.2a1b.**2a2** viruses, such as cell culture-propagated A/Darwin/6/2021 or egg-propagated A/Darwin/9/2021, inhibited 3C.2a1b.**2a2** test viruses well. Human serology assays showed post-vaccination GMTs were significantly reduced against circulating 3C.2a1b.**2a1** and 3C.2a1b.**2a2** viruses. Based on all available data, the WHO Consultative Group recommended the H3 component of the vaccines containing a cell culture-propagated A/Darwin/6/2021 or egg-propagated A/Darwin/9/2021-like strain. AIVC accepted this recommendation.

(Abridged from the Weekly Epidemiological Record (WER), 2021 96(42):509-520 and a report to AIVC by Dr Ian Barr, WHO Collaborating Centre for Influenza, Melbourne).

4.4 INFLUENZA B

Two distinct lines of influenza B have co-circulated in many countries during recent years. This dates from the late 1980s when the B/Panama/45/90 variant of influenza B was first observed. This strain and its further variants of the Yamagata/16/88 lineage (most recently representative strain-B/Phuket/3073/2013) spread worldwide, whereas strains of the previous B/Victoria/2/87-like viruses continued to circulate in Asia and subsequently underwent independent evolution as an antigenically distinct lineage (most recent representative strain-B/Colorado/6/2017). For reasons not wholly understood, these remained geographically restricted to Asia until 2001. In 2002 the B/Victoria/2/87 lineage viruses were the predominant viruses worldwide.

In 2021, the WHO National Influenza Centre at ESR received 3 influenza B clinical samples and one influenza B virus was isolated by cell culture. Antigenic typing was conducted using rabbit antisera raised against B/Washington/02/2019 supplied by the WHO Collaborating Centre (WHOCC) in Melbourne. It was antigenically closely related to B/Washington/02/2019.

A total of 43 influenza B isolates with collection dates between February to September 2021 were characterized at the Melbourne WHOCC. No B/Yamagata lineage viruses were available for characterization. Sequence analysis of the HA1 gene of the recent B/Victoria lineage viruses showed that they mostly belonged to genetic group V1A. All B/Victoria viruses had a HA triple deletion (162-164). Viruses with HA genes encoding further substitutions of N150K, G184E, N197D and R279K in HA1 have predominated (group 1A.3a), with two main subgroups having emerged. One subgroup had additional HA1 substitutions V220M and P241Q (3a1) which was seen almost exclusively in China, and the other had HA1 substitutions A127T, P144L and K203R (3a2) which was seen in Asia, Africa, Oceania, Europe and North America. While 3a1 viruses predominated in China earlier in 2021, the number and the proportion of 3a2 viruses have increased steadily over recent months to become predominant. 3a2 viruses have shown further genetic divergence with additional HA1 amino acid substitutions identified in viruses from certain geographic locations.

Post-infection ferret antisera raised against both cell culture- and egg-propagated B/Washington/02/2019-like (1A.3) viruses recognised 3a viruses poorly. Antisera raised against B/Sichuan-Jingyang/12048/2019-like viruses (3a1) inhibited viruses in this subgroup well but inhibited 3a2 viruses less well. Antisera raised against B/Austria/1359417/2021-like viruses (3a2) inhibited viruses from this subgroup well but inhibited 3a1 viruses less well and B/Washington/02/2019-like viruses poorly.

Serum panels from recipients of both NH 2020-2021 and SH 2021 vaccines described above, with one additional NH 2020-2021 serum panel from children, were used in human serology studies of B/Victoria lineage viruses. When compared to titres against cell culture-propagated B/Washington/02/2019-like vaccine virus, post-vaccination HI GMTs against some cell culture-propagated 3a1 viruses were significantly reduced. With the exception of sera from older adults, reductions in titres to many 3a2 viruses were observed in most other serum panels.

In summary, all influenza B viruses collected in the period February through August 2021 were of the B/Victoria/2/87 lineage and no B/Yamagata lineage viruses were available for characterisation. Most recent viruses belonged to the antigenically distinct 1A.3a1 (V220M and P241Q) or 1A.3a2 (A127T, P144L and K203R) subgroups, with the latter showing a wider geographic spread. The great majority of these viruses showed reductions in inhibition by post-infection ferret antisera raised against both cell culture- and egg-propagated 1A.3 viruses, such as the current vaccine virus B/Washington/02/2019. Post-infection ferret antisera raised to B/Austria/1359417/2021-like viruses (1A.3a2) inhibited viruses from this group well. Human serology assays showed significant reduction of post-vaccination GMTs against 1A.3a1 and 1A.3a2 viruses. Based on all available data, the WHO Consultative Group recommended the B/Austria/1359417/2021-like virus (B/Victoria/2/87-lineage) and B/Phuket/3073/2013-like virus (B/Yamagata/16/88-lineage) as quadrivalent vaccine strains. AIVC accepted this recommendation.

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