Influenza Updates

The newsletter of the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne

@WHOCCFluMelb

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Reflection on 2021: Thank you, and Happy Holidays

As the year draws to a close, we would like to thank all of the laboratories that sent us influenza samples in 2021.

It has been an exceptionally quiet year for influenza around the world, due in part to restrictions on travel and social distancing measures that have been in place for the COVID-19 pandemic.

The Centre continued to receive far fewer influenza samples than usual and the other CCs had a similar experience. The Centre staff adjusted their work schedules and routines in accordance with public health guidance and kept the Centre open through another challenging period in Victoria. They have once again earned a big thank you- what a wonderful team effort!

It is difficult to predict when, where and how much influenza activity will return and which virus(es) will circulate. However, we met virtually and made recommendations for the composition of the 2022 southern hemisphere vaccine based on the available data. We are now turning our attention to the northern hemisphere winter and, with your help, will continue to monitor influenza activity. The February vaccine composition meeting will be in Geneva, Switzerland.

We wish you all the very best for the holiday season and look forward to working with you again in 2022.

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WHO Collaborating Centre for Reference and Research on Influenza
VIDRL

Doherty Institute
THE UNIVERSITY OF MELBOURNE
The Royal Melbourne Hospital

A joint venture between The University of Melbourne and The Royal Melbourne Hospital

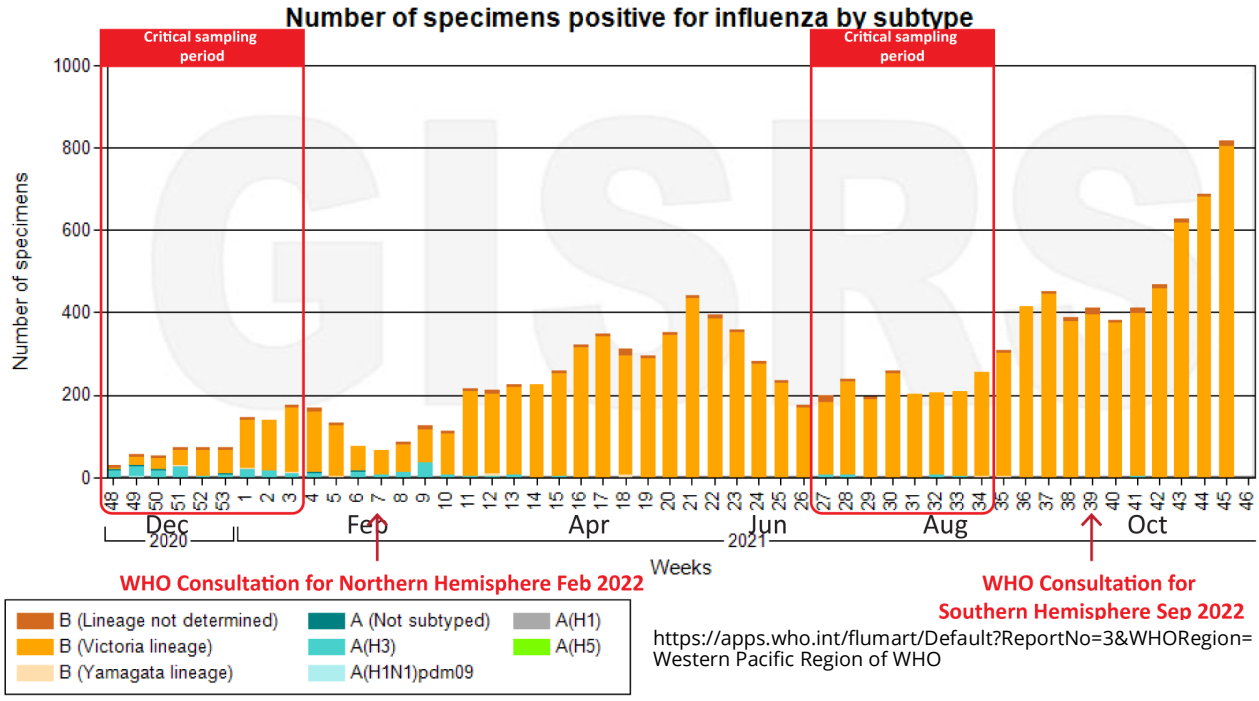
WHO Shipping Fund Project reminder

In anticipation of the WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2022-2023, which will be held in February 2022, this is a reminder that the WHO Shipping Fund Project (SFP) is available to assist National Influenza Centres in shipping samples to WHO Collaborating Centres up to four times per year.

The recommended timing of these shipments is:

- One between the end of December to mid-January and one between the end of June and mid-August, to support the WHO vaccine composition recommendation-making for each hemisphere;
- The third and fourth shipments can be used at your own judgement, which may depend on the seasonality, intensity of the season, the finding of unusual or untypable viruses, or notable outbreaks.

If you have any questions about shipping samples or would like information about accessing the WHO Shipping Fund, please contact us at whoflu@influenzacentre.org.

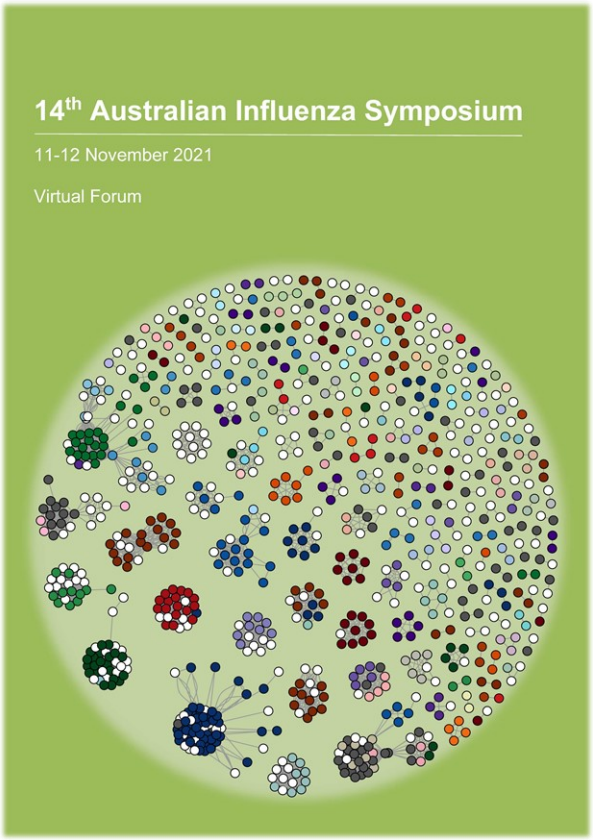


We encourage you to send samples in a timely manner, as soon as possible after collection. Please avoid sending your samples in large batches collected over long periods, as up-to-date data for the current season are the most useful for WHO GISRS surveillance and vaccine formulation.

Please note that the Centre will be closed between Saturday the 25th of December to Monday the 3rd of January. Please ensure that all samples are received by us no later than Tuesday the 21st of December.

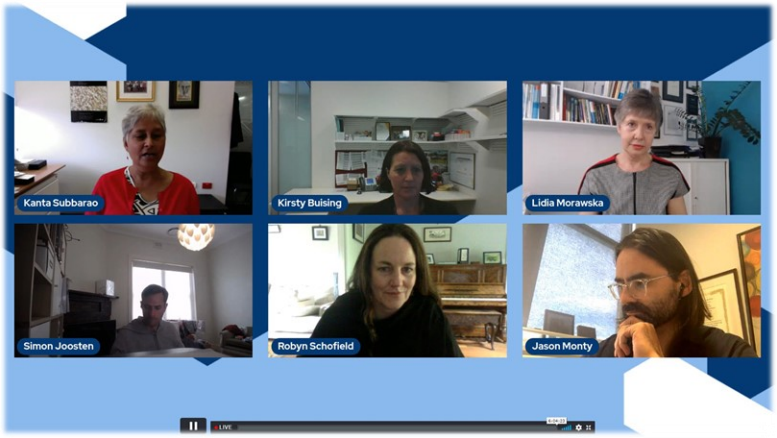
14th Australian Influenza Symposium

We were pleased to hold the 14th Australian Influenza Symposium (AIS) on 11-12 November 2021 as a virtual event hosted by ASN Events. This year we included multiple sessions on COVID -19, as well as influenza and RSV.



The Symposium was attended by over 350 people, including representatives from the biomedical, clinical, research, public health, government, and industry sectors. The Symposium also welcomed a range of national and international speakers, including:

- **Eddie Holmes**, Marie Bashir Institute for Infectious Diseases & Biosecurity, University of Sydney
- **Stanley Perlman**, Department of Microbiology and Immunology, University of Iowa, USA
- **Jenifer Juno**, Department of Microbiology and Immunology, University of Melbourne, Doherty Institute



- **Peter McIntyre**, Department of Women's and Children's Health, University of Otago, Dunedin, NZ
- **Bev Menner**, COVID Vaccine Lead, CSL Limited
- **Keith Chappell**, School of Chemistry and Molecular Biosciences, University of Queensland

Delegates were able to enjoy talks from a diverse range of perspectives during the live sessions, with additional proffered talks provided as pre-recorded videos on the online platform. These videos are still available to delegates for viewing.

The Symposium was also reported on Twitter using the tag #AIS2021Virtual

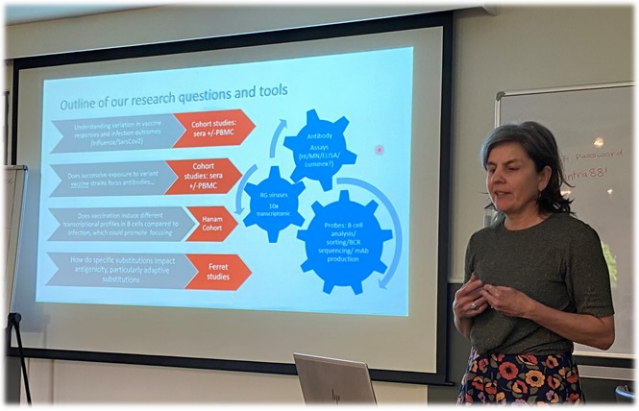
We thank all speakers, session chairs, and delegates. We also thank the team at ASN Events for hosting this virtual event. The next AIS will be held in November 2023.

Centre retreat 2021

The Centre retreat was held 30 November - 1 December 2021 at Peppers Mineral Springs in Hepburn Springs.

Staff from each section were able to reflect and discuss the impact of the COVID-19 pandemic on their work load and strategise for the upcoming year ahead. These discussions also included planning for the next influenza pandemic and how the Centre may approach this, given what we have learnt from the current pandemic.

The research groups also presented data from their various, ongoing research projects, which covered a range of topics including COVID-19 and RSV, in addition to influenza. These presentations highlighted the diversity in expertise and techniques available at the Centre, and allowed us to evaluate what we can offer and collaborate on, both internally and externally, in the future.



Numerous team building activities from the retreat, in conjunction with the above presentations, also brought a more light-hearted side to the two day event, bringing a much needed social aspect after the year we have all experienced.

Featured Article

Head Epidemiologist A/Prof Sheena Sullivan's recent editorial article titled, 'Preparing for out-of-season influenza epidemics when international travel resumes' in the *Medical Journal of Australia* was heavily featured across multiple media outlets.

Editorial

Preparing for out-of-season influenza epidemics when international travel resumes

Sheena G Sullivan

Influenza vaccination for travellers and the resources mobilised during the COVID-19 pandemic could mitigate the effects of an influenza resurgence

In this issue of the *MJA*, Marsh and colleagues[1] report that inter-seasonal influenza activity in New South Wales was unusually high during the 2018–19 summer, and provide compelling evidence for the role of international travel in seeding local influenza epidemics. During December 2018 – March 2019, people with notified influenza infections were 3.7 times as likely to report recent overseas travel as other people; however, the odds were almost seven times as high for people with infections identified during the first two months of summer, suggesting that some of these cases initiated local outbreaks, with subsequent community transmission.[1]

This interpretation is consistent with previous findings that influenza circulation in Australia undergoes serial, local eliminations at the end of winter, with epidemics re-ignited by new viruses imported from overseas via international travel.[2] This phenomenon has never been better exemplified than during the coronavirus disease 2019 (COVID-19) pandemic. In early 2020, influenza activity was higher than normal for the inter-seasonal period, but plummeted with the introduction of COVID-19 restrictions in March 2020.[3] Introduction of new viruses was prevented by the closure of the Australian international border and the requirement that all returning travellers undergo 14 days of hotel quarantine. As a result, we have not confirmed the presence of influenza virus in any community samples sent to our reference laboratory since April 2020. It would seem that the virus has been locally eliminated, but the threat of its re-introduction looms with the imminent re-opening of our border.[4]

Throughout the pandemic, influenza A(H1N1)pdm09, A(H3N2), and B/Victoria have continued to circulate globally, with evidence of small, sporadic outbreaks, chiefly in tropical and subtropical regions of Asia and Africa (Box), where influenza seasonality is less marked than in temperate regions and year-round, low level activity is typical.[5] Marsh and colleagues[1] found that returned travellers with notified influenza had most frequently arrived from South-East Asia (42 of 168, 25%). However, current circulation patterns suggest that this region is not the most likely source of influenza importation into Australia. Our laboratory has confirmed the presence of influenza viruses in samples collected from travellers in hotel quarantine who have returned from South Asia, particularly those in the Howard Springs facility in the Northern Territory. As the influenza incubation period, infectious period, and serial interval are short,[6] the current duration of hotel quarantine (14 days) has prevented people leaving quarantine while still infectious, even in the context of chains of transmission within travelling groups. However, if quarantine periods are reduced or eliminated, infected travellers may enter the community and instigate local outbreaks.

The report by Marsh and colleagues[1] indicates that, as borders open in late 2021, we should expect the introduction of influenza viruses into Australia and possibly intense out-of-season activity. Re-opening will precede our seasonal influenza vaccination campaign, which usually begins in April. To restrict the entry of influenza viruses, all returning travellers should be required to be vaccinated against influenza prior to travel, as recommended by the New South Wales Ministry of Health in response to the study by Marsh and colleagues.[1] Given the similarities in disease presentation, diagnosis, and management, the wealth of resources made available during the COVID-19 pandemic should also be leveraged to mitigate the consequences of influenza outbreaks. To avoid unclear messaging and to harmonise the response to all respiratory virus outbreaks, this would include testing for influenza as well as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), especially in people in hotel quarantine, and sharing the resources of the special COVID-19 public health divisions that have been established in many jurisdictions.

Any resurgence of influenza will be most harshly felt by older people,[7] particularly those in aged care facilities, among whom influenza mortality is high[8] and the COVID-19 pandemic has already exerted a heavy toll.[9] It behoves us as a nation to protect our older citizens, and it reflects on us poorly when we fail to do so. In addition, influenza is likely to infect a considerable proportion of young children. In contrast to those infected with SARS-CoV-2, many children infected with influenza, especially those less than six months old, may need hospital care.[7] A resurgence of respiratory syncytial virus outbreaks in late 2020/early 2021 has already challenged some paediatric hospitals in Australia.[10] Increased severity of disease among patients co-infected with SARS-CoV-2 and influenza was reported in China in 2020,[11] and this could also have consequences for our healthcare system.

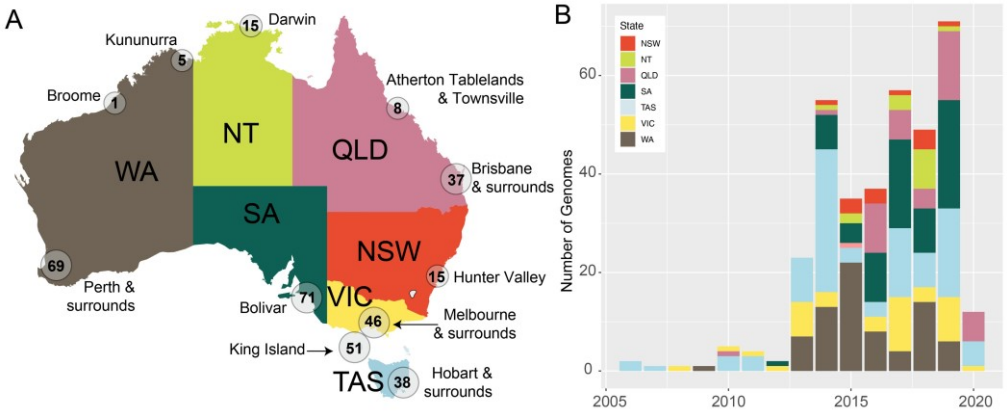
In it, she highlights the likely out-of-season resurgence of influenza once international travel restrictions are lifted in Australia. However, with the use of influenza vaccinations and other resources that were utilised against the COVID-19 pandemic, the effects of this influenza resurgence may be mitigated. To listen to the accompanying podcast interview, click here.

Sullivan SG. Preparing for out-of-season influenza epidemics when international travel resumes. Med J Aust. 2021 Nov 13. doi: 10.5694/mja2.51340. PubMed

Most comprehensive analysis of avian influenza A virus sequences in Australia

A new preprint on bioRxiv, led by Dr. Michelle Wille in collaboration with state laboratories, university groups, and the Australian Centre of Disease Preparedness, comprises the most comprehensive analysis of avian influenza A viruses (AIV) in Australia.

The article reports the generation and analysis of >300 low pathogenic avian influenza genomes. These sequences comprise genomes sequenced over the last 15 years, and from all states and territories. The authors find that Australia is a sink for global AIV diversity; AIV are infrequently introduced to Australia, followed by decades of isolated circulation and eventual extinction. Within Australia, there was no evidence of directional or consistent patterns in virus movement, which is highly reflective of the nomadic nature of ducks. Overall, the results demonstrate that patterns of AIV dynamics in Australia (and the southern hemisphere) are distinct from those in the temperate north.



Wille M. et. al. Australia as a global sink for the genetic diversity of avian influenza A virus. bioRxiv 2021.11.30.470533; doi: 10.1101/2021.11.30.470533

Other Centre news

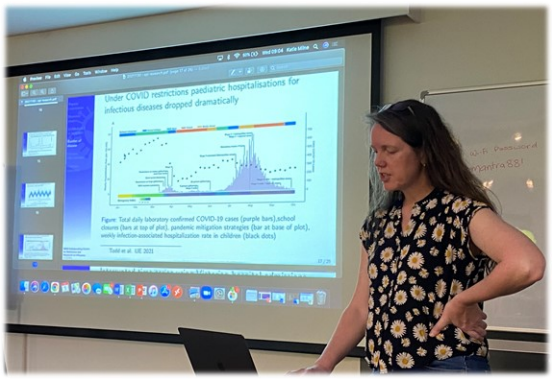
Congratulations once again to Ph. D student Paulina Koszalka for completing her Ph. D Oration titled, 'Assessing antiviral resistance to baloxavir marboxil, an influenza polymerase inhibitor' on 23 November 2021. Paulina is supervised by Centre Director Kanta Subbarao, Prof Stephen Turner from Monash University, A/Prof Vijay Dhanasekaran (now at The University of Hong Kong), and A/Prof Aeron Hurt (now at Roche, Switzerland).

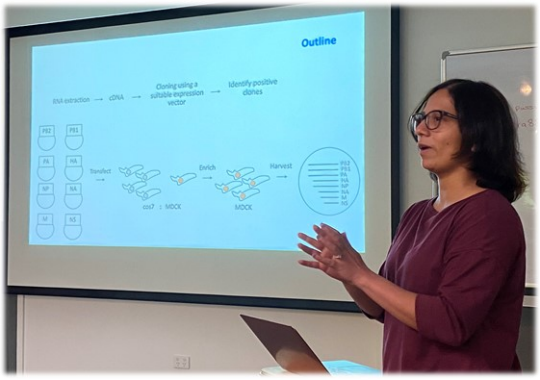
Farewell and good luck

It is with sadness but good wishes that we announce the departure of Vivian Leung and Chris Bailie. We thank Vivian and Chris for their significant contributions to the Centre, and wish them all the very best their futures.

Ms Vivian Leung had been an epidemiologist at the Centre for the past seven years. She has now taken on a permanent position with the Royal Melbourne Hospital.

Dr Chris Bailie had been a MAE student under the supervision of A/Prof Sheena Sullivan at the Centre for the past year and a half. Congratulations on finishing your degree, Chris.





Recent activities at the Centre (1 January— 30 November 2021)

Below is a summary of surveillance activities at the Centre during this current reporting period. Centre activities have remained relatively quiet in 2021 due to decreased influenza cases resulting from social distancing and travel restriction measures implemented in response to COVID-19 across many countries. We anticipate that this decrease in the number of samples will continue while these measures are in place.

Samples received:

The Centre received 287 influenza samples from the laboratories and institutions listed below during the period 1 January — 30 November 2021.

AUSTRALIA: Westmead Hospital, John Hunter Hospital, Northern Hospital, The Children's Hospital at Westmead, Royal Darwin Hospital, Queensland Health Forensic and Scientific Services (QHFSS), SA Pathology, Alfred Hospital, Australian Clinical Labs, Monash Medical Centre, Steritech Ltd., The Department of Health and Human Services, VIDRL

INDIA: National Institute of Virology

NEPAL: National Public Health Laboratory

NEW ZEALAND: Institute of Environmental Science and Research

PAKISTAN: National Institute of Health

PHILIPPINES: Research Institute for Tropical Medicine

SINGAPORE: National Public Health Laboratory

SOUTH AFRICA: National Institute for Communicable Diseases

THAILAND: Thai National Influenza Center

TIMOR-LESTE: Laboratório Nacional de Saúde

Isolation of viruses in eggs:

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 January — 30 November 2021, 14 A (H3N2) and 8 B/Victoria viruses were successfully isolated in eggs at the Centre.

Recent activities at the Centre (1 January— 30 November 2021) continued

Antigenic analysis
88 viruses analysed by haemagglutination inhibition (HI) assay

Antiviral drug susceptibility
104 viruses analysed by neuraminidase inhibition (NAI) assay

Sequencing
88 viruses analysed
86 HA genes
86 NA genes
75 MP genes
57 NS genes

Country of submitting laboratory	No. of viruses analysed by HI assay*				No. of viruses tested by NAI assay*				No. of viruses sequenced by NGS or Sanger sequencing			
	A(H1N1)pdm09	A(H3N2)	A (H3N2)v	B/Victoria	A(H1N1)pdm09	A(H3N2)	A (H3N2)v	B/Victoria	A(H1N1)pdm09	A(H3N2)	A(H3N2)v	B/Victoria
Australia	1	29	1	1	1	29	1	3	3	33	2	5
India	6			1	6	8						
Nepal										2		1
New Zealand		2				3		1		3		1
Philippines		4		4		4		4		4		4
Singapore		3		17		3		17				
South Africa				12				12		1		12
Thailand						4				5		
Timor-Leste		8				8				12		
Total	**7**	**46**	**1**	**34**	**7**	**59**	**1**	**37**	**3**	**60**	**2**	**23**

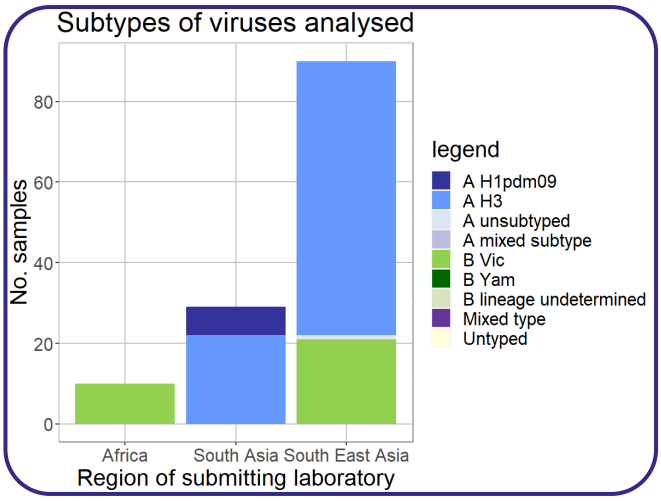
* *Subtypes and lineages are based on analysis of HA and in some cases confirmed by genetic analysis of NA.*

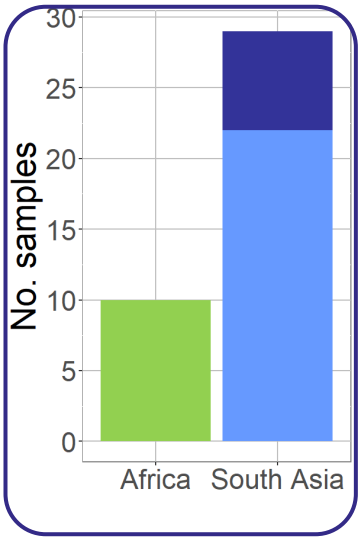
Surveillance update: Virus activity 1 January — 30 November 2021

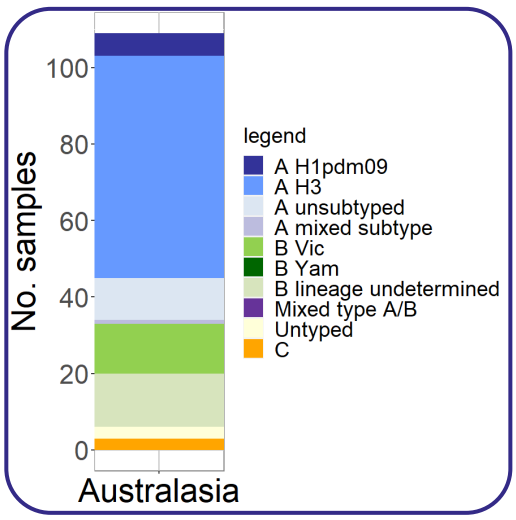
The data below are results for viruses collected or sampled between 1 January and 30 November 2021 that have been analysed at the Centre as of 7 December 2021.

Virus types/subtypes*
The type and subtype/lineage of 239 viruses have been determined.

5.5% A(H1N1)pdm09
61.3% A(H3N2)
18.5% B/Victoria





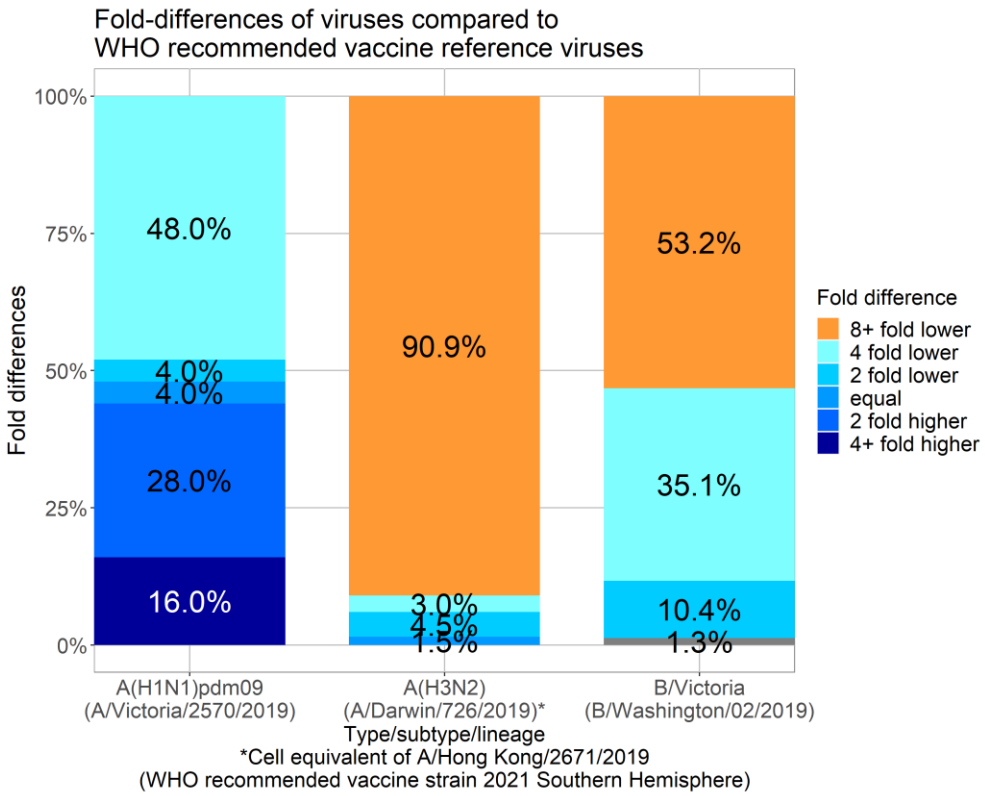


**Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

Antigenic analysis*

A total of 274 viruses were tested using the haemagglutination inhibition (HI) assay.

Viruses were identified as low-reactors if their titre with reference antiserum was at least 8-fold lower than the titre of the reference virus. Almost all A(H3N2) viruses, and half of the B/Victoria viruses were low reactors to their respective reference strains.

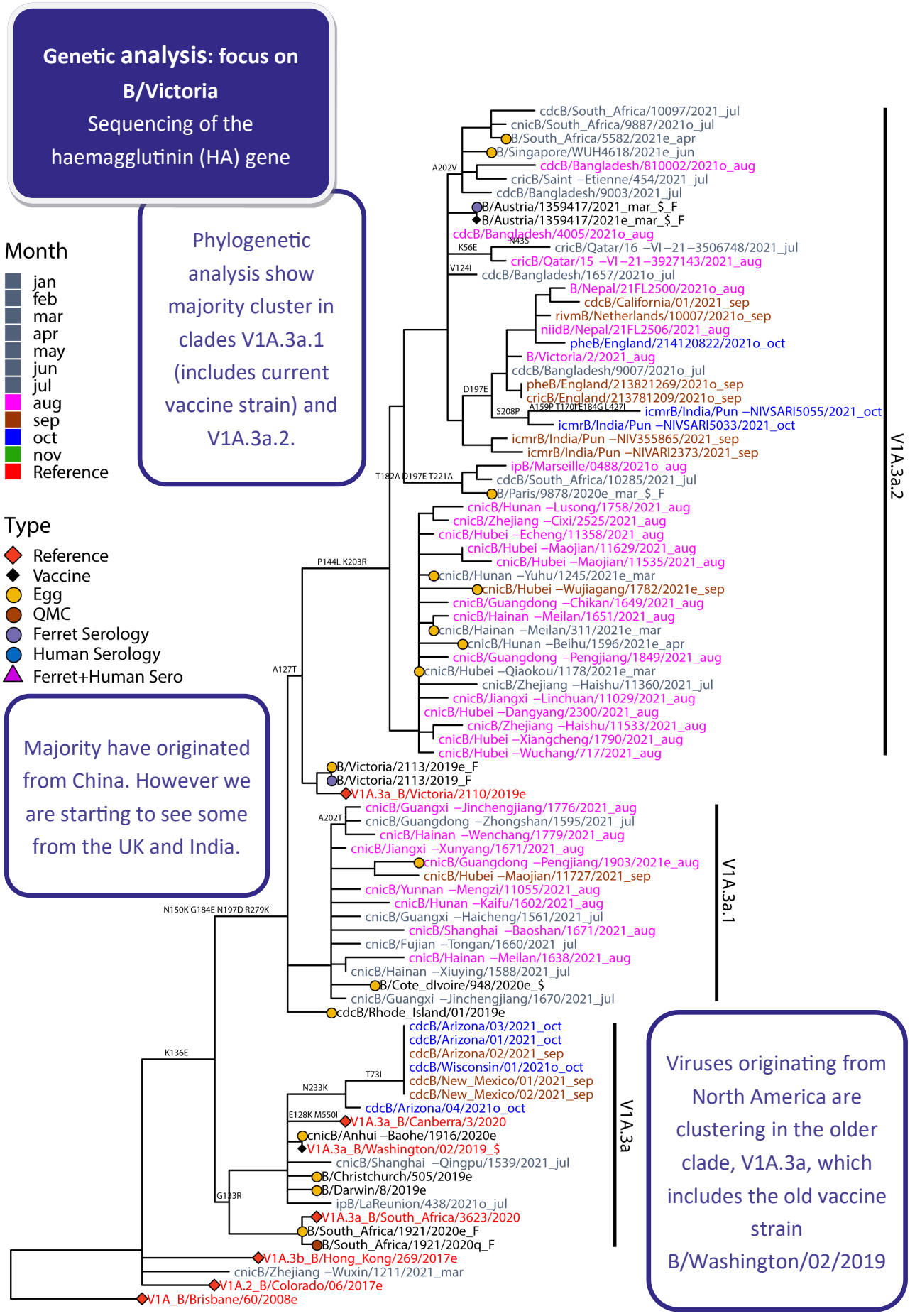


* *Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

Genetic analysis: focus on B/Victoria

Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis show majority cluster in clades V1A.3a.1 (includes current vaccine strain) and V1A.3a.2.



Majority have originated from China. However we are starting to see some from the UK and India.

Viruses originating from North America are clustering in the older clade, V1A.3a, which includes the old vaccine strain B/Washington/02/2019

Surveillance update: Virus activity 1 January — 30 November 2021 continued

Antiviral drug susceptibility testing:
274 viruses tested by neuraminidase inhibition (NAI) assay

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir, and laninamivir showed that no viruses had highly reduced inhibition by one or more neuraminidase inhibitors (NAI).

Type/ subtype/ lineage	Oseltamivir			Peramivir			Laninamivir			Zanamivir		
	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition
A(H1N1) pdm09	7			7			7			7		
A(H3N2)	56			56			56			56		
A(H3N2)v	1			1			1			1		
B/Victoria	35			35			35			35		
Total	**99**			**99**			**99**			**99**		

Normally, viruses with reduced inhibition by antiviral drugs in the NAI assay undergo genetic analysis of the neuraminidase gene to detect mutations associated with the functional change. The relationship between reduced inhibition and the clinical effectiveness of a neuraminidase inhibitor is not well understood. Further studies would be required to determine whether a virus with reduced inhibition in the NAI assay is clinically resistant.

WHO Collaborating Centre for Reference and Research on Influenza

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