Influenza Updates

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

@WHOCCFluMelb

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WHO Recommendations for the Southern Hemisphere 2021 Influenza Vaccines

The WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2021 was held as an online event, due to the COVID-19 pandemic. This occurred between 16 September - 02 October 2020, with discussions covering seasonal influenza occurring between 16-24 September, and zoonotic influenza viruses with pandemic potential between 29 September - 02 October.

Following the Consultation, the WHO made the following recommendations:

It is recommended that ***quadrivalent*** vaccines for use in the 2021 southern hemisphere influenza season contain the following:

Egg-based Vaccines

- an A/Victoria/2570/2019 (H1N1)pdm09-like virus;
- an A/Hong Kong/2671/2019 (H3N2)-like virus;
- a B/Washington/02/2019 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

Cell- or recombinant-based Vaccines

- an A/Wisconsin/588/2019 (H1N1)pdm09-like virus;
- an A/Hong Kong/45/2019 (H3N2)-like virus;
- a B/Washington/02/2019 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

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This year there has been reduced influenza surveillance and/or reporting across many countries due to the COVID-19 pandemic. In addition, travel restrictions and other strategies to counteract the spread of the SARS-CoV-2 virus have resulted in an overall decrease in influenza activity. This has meant that there were fewer viruses available for characterisation during the April to August time period compared to recent years.

More details about the recommendations can be found here.

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

Zoonotic influenza viruses with pandemic potential

Influenza A(H5) viruses in poultry and wild birds have diversified over the years into several genetically and antigenically distinguishable clades. Clades 2.3.4.4 (H5N2, H5N5, H5N6 and H5N8) and 2.3.2.1 (H5N1) viruses were reported from several countries. Recent A(H5N6) clade 2.3.4.4g viruses were detected in poultry in Vietnam that reacted poorly with antisera raised against previous CVVs. Low pathogenicity and highly pathogenic A(H7) viruses belonging to different HA lineages were detected in birds in Australia and the USA but they were successfully eradicated through control measures.

Between February and September 2020, no human cases of influenza A(H5) or A(H7) infection were reported. During this period, five cases of avian influenza A(H9N2) G9 clade infection were reported in children in China and one case each of variant (v) swine influenza A(H1N1)v, (H1N2)v and (H3N2)v infection were reported in Brazil, Germany and USA, respectively. All of these infections were mild.

Two new candidate vaccine viruses were recommended:

1. A/chicken/Vietnam/RAHO4-CD-20-421/2020-like (H5N6) clade 2.3.4.4g
2. A/Hessen/47/2020-like A(H1N1)v

For more information, please click here.

AIVC recommendation for the composition of influenza vaccine for Australia in 2021

The Australian Influenza Vaccine Committee (AIVC) met on 7 October to recommend the composition of the influenza virus vaccines for 2021.

The full statement can be accessed here.

Contribution of National Influenza Centres to the vaccine recommendations

We thank everyone who has sent us influenza samples during the COVID-19 pandemic, when influenza activity was very low. Viruses you sent us in the first few months of the year provided essential data on recently circulating strains and helped to inform the choice of recommended vaccine strains. We are especially pleased that the most recently added A(H1N1)pdm09 virus in the vaccine recommendation, A/Victoria/2570/2019, was originally submitted to our Centre by **The Alfred Hospital** in Melbourne.

In this context, we would like to acknowledge the contribution and critical role played by WHO National Influenza Centres and other submitting laboratories in providing influenza samples to WHO Collaborating Centres, not only for the purposes of analysis and surveillance, but also for the provision of potential vaccine candidates. Please continue to send us your samples. The need for constant surveillance remains as the influenza virus continues to circulate and evolve.

A WHO Virtual— E-consultation on 'Adapting influenza sentinel surveillance systems for including COVID-19'

12:00-15:30 (CET) 6-8 October 2020

The overall aim of this e-consultation was to review evidence and develop interim recommendations for adapting and sustaining the WHO GISRS influenza sentinel surveillance to ensure continued influenza surveillance, and wherever possible, monitor COVID-19 virus transmission in the community.

Participants for the WHO e-consultation included experts invited from:

1. GISRS including NICs, WHO CCs, WHO H5 Reference Laboratories and others
2. National influenza surveillance focal points
3. Partner agencies and research academia
4. WHO regional offices influenza focal points
5. WHO COVID-19 incident management support team in HQ and Regional Offices
6. National COVID-19 task force or equivalent
7. Other relevant expert groups/areas

The expected outcomes from this WHO E-consultation included:

1. Interim epidemiological and laboratory recommendations that will be piloted in the coming Northern Hemisphere Influenza Season
2. Updated understanding of scientific base for sentinel surveillance of influenza and COVID-19 virus

For more information, please follow the link here.

A draft document has been prepared and will be circulated, before a final set of recommendations from the e-consultation is published by the WHO later in the year.

COVID-19 work with the Royal Melbourne Hospital

Vivian Leung (Epidemiologist) and Chris Bailie (Master of Applied Epidemiology scholar) from the Epidemiology group have been working with Infection Prevention and Surveillance Service at the Royal Melbourne Hospital (RMH) to assist with their COVID-19 response. Vivian and Chris were involved in the management of healthcare worker (HCW) contact tracing data, including the development of a contact tracing database. They both currently sit on the COVID-19 HCW infection project group at RMH, which aims to understand SARS-CoV-2 infection among HCWs and provide recommendations for interventions to reduce the risk of COVID-19 transmission.

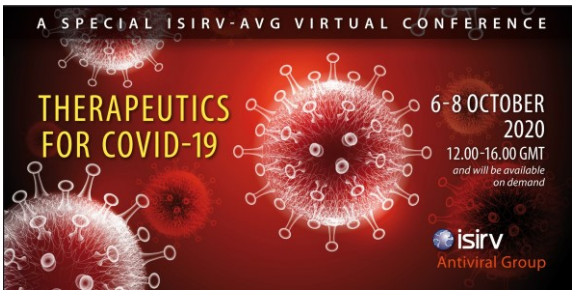
Notable conferences

Special isirv-AVG Virtual Conference on 'Therapeutics for COVID-19'

6-8 October 2020

This special online conference hosted by isirv Antiviral Group addressed the latest advances in the development of therapeutics against COVID-19.

Please use this link to view the final program.



Upcoming meetings and conferences

Many upcoming meetings and conferences have been converted to an online format due to COVID-19.

Australasian Vaccines & Immunotherapeutics Development Meeting (AVID)

9-10 November 2020

This year the 8th AVID meeting will be held as an online forum.

Abstract submission and early bird registration closes on 18 October, while poster submission closes 1 November.

Please use this link for more information on registration details, program, and invited speakers.

Cold Spring Harbor Asia COVID-19/SARS-CoV-2 Rapid Research Reports (virtual)

2-4 November 2020

Hosted by Cold Spring Harbor Asia, this event will cover the latest findings within Coronavirus Biology.

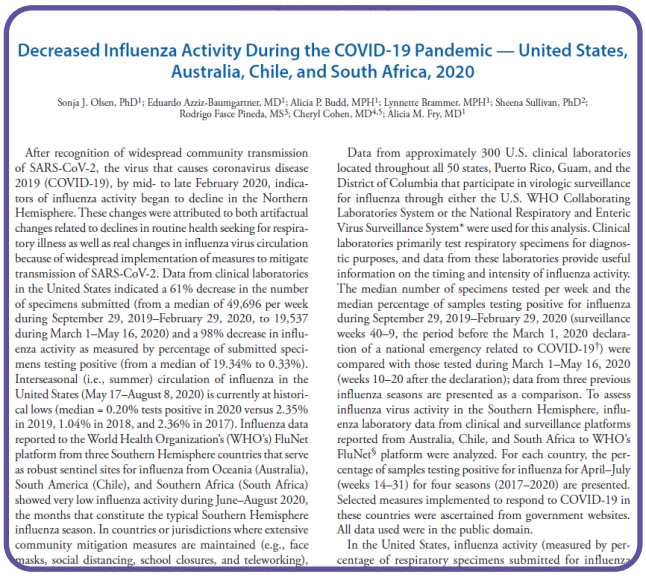
Abstract submission closed 9 October.

Please use this link for more information on registration details, program, and invited speakers.

Featured Research Article

'Decreased influenza activity during the COVID-19 pandemic - United States, Australia, Chile, and South Africa, 2020 '

Featuring Associate Professor Sheena Sullivan from the Centre



Decreased Influenza Activity During the COVID-19 Pandemic — United States, Australia, Chile, and South Africa, 2020

Sonja J. Olsen, PhD[1]; Eduardo Azziz-Baumgartner, MD[1]; Alicia P. Budd, MPH[1]; Lynnette Brammer, MPH[1]; Sheena Sullivan, PhD[2]; Rodrigo Fasce Pineda, MS[3]; Cheryl Cohen, MD[4,5]; Alicia M. Fry, MD[1]

After recognition of widespread community transmission of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), by mid- to late February 2020, indicators of influenza activity began to decline in the Northern Hemisphere. These changes were attributed to both artifactual changes related to declines in routine health seeking for respiratory illness as well as real changes in influenza virus circulation because of widespread implementation of measures to mitigate transmission of SARS-CoV-2. Data from clinical laboratories in the United States indicated a 61% decrease in the number of specimens submitted (from a median of 49,696 per week during September 29, 2019–February 29, 2020, to 19,537 during March 1–May 16, 2020) and a 98% decrease in influenza activity as measured by percentage of submitted specimens testing positive (from a median of 19.34% to 0.33%). Interseasonal (i.e., summer) circulation of influenza in the United States (May 17–August 8, 2020) is currently at historical lows (median = 0.20% tests positive in 2020 versus 2.35% in 2019, 1.04% in 2018, and 2.36% in 2017). Influenza data reported to the World Health Organization's (WHO's) FluNet platform from three Southern Hemisphere countries that serve as robust sentinel sites for influenza from Oceania (Australia), South America (Chile), and Southern Africa (South Africa) showed very low influenza activity during June–August 2020, the months that constitute the typical Southern Hemisphere influenza season. In countries or jurisdictions where extensive community mitigation measures are maintained (e.g., face masks, social distancing, school closures, and teleworking),

Data from approximately 300 U.S. clinical laboratories located throughout all 50 states, Puerto Rico, Guam, and the District of Columbia that participate in virologic surveillance for influenza through either the U.S. WHO Collaborating Laboratories System or the National Respiratory and Enteric Virus Surveillance System* were used for this analysis. Clinical laboratories primarily test respiratory specimens for diagnostic purposes, and data from these laboratories provide useful information on the timing and intensity of influenza activity. The median number of specimens tested per week and the median percentage of samples testing positive for influenza during September 29, 2019–February 29, 2020 (surveillance weeks 40–9, the period before the March 1, 2020 declaration of a national emergency related to COVID-19†) were compared with those tested during March 1–May 16, 2020 (weeks 10–20 after the declaration); data from three previous influenza seasons are presented as a comparison. To assess influenza virus activity in the Southern Hemisphere, influenza laboratory data from clinical and surveillance platforms reported from Australia, Chile, and South Africa to WHO's FluNet§ platform were analyzed. For each country, the percentage of samples testing positive for influenza for April–July (weeks 14–31) for four seasons (2017–2020) are presented. Selected measures implemented to respond to COVID-19 in these countries were ascertained from government websites. All data used were in the public domain.

In the United States, influenza activity (measured by percentage of respiratory specimens submitted for influenza

Published online in September, this article describes the significant impact that the COVID -19 pandemic has had on influenza activity, both in the Northern and Southern Hemispheres.

The implementation of measures to reduce the transmission of SARS-CoV-2, the causative agent of COVID-19, have been adopted by many different countries across the globe.

Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. Decreased Influenza Activity During the COVID-19 Pandemic - United States, Australia, Chile, and South Africa, 2020. MMWR *Morb Mortal Wkly Rep*. 2020;69(37):1305-1309. Published 2020 Sep 18. doi:10.15585/mmwr.mm6937a6

PubMed link

In addition to a decrease in COVID-19 activity, these strategies have also resulted in the decreased transmission of other respiratory viruses, such as influenza.

Coupled with the use of seasonal vaccines, it is likely that these ongoing measures will reduce influenza activity during the upcoming 2020-2021 Northern Hemisphere influenza season.

Farewell and good luck

It is with sadness but good wishes that we announce the departure of Manisha Patel. We thank Manisha for her significant contributions to the Centre, and wish her all the very best for her future.

Ms Manisha Patel has been a research assistant with the Centre for the last couple of years. She will be taking on a new position as a Medical Scientist with the Immunology team at the Royal Melbourne Hospital.

Recent activities at the Centre (1 January — 30 September 2020)

Below is a summary of surveillance activities at the Centre during this current reporting period. Centre activities have been relatively quiet in recent months 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 1782 influenza samples from the laboratories and institutions listed below during the period 1 January — 30 September 2020.

AUSTRALIA: Canberra Hospital, Westmead Hospital, The Children's Hospital at Westmead, Royal Darwin Hospital, Queensland Health Forensic and Scientific Services, SA Pathology, Hobart Pathology, North West Pathology, Alfred Hospital, Australian Clinical Labs, Royal Children's Hospital, Royal Melbourne Hospital, VIDRL, Pathwest QEII Medical Centre

BRUNEI: RIPAS Hospital

CAMBODIA: Institut Pasteur du Cambodge

MALAYSIA: Institute for Medical Research, University Malaya

NEW CALEDONIA: Centre Hospitalier de Nouvelle Calédonie

NEW ZEALAND: Canterbury Health Laboratories

PHILIPPINES: Research Institute for Tropical Medicine

SINGAPORE: National Public Health Laboratory

SOLOMON ISLANDS: National Referral Hospital

SOUTH AFRICA: National Institute for Communicable Diseases

SRI LANKA: Medical Research Institute

THAILAND: Thai National Influenza Center

Isolation of viruses in eggs:

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 January — 30 September 2020, 9 A(H1N1)pdm09, 10 A(H3N2) and 5 B/Victoria viruses were successfully isolated in eggs at the Centre.

Antigenic analysis
1166 viruses analysed by haemagglutination inhibition (HI) assay

Antiviral drug susceptibility
1160 viruses analysed by neuraminidase inhibition (NAI) assay

Sequencing
577 viruses analysed
504 HA genes
493 NA genes
419 MP genes
139 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 mixed subtype	A unsubtyped	B/Victoria	B/Yamagata	A(H1N1)pdm09	A(H3N2)	A mixed subtype	B/Victoria	B/Yamagata	Mixed type A/B	A(H1N1)pdm09	A(H3N2)	B lineage	B/Victoria	B/Yamagata
Australia	334	90	1		46	1	333	94	1	46	1	1	138	55		34	1
Brunei	29	4					27	4					12	4			
Cambodia	39	60			33		39	60		33			18	48		11	
Indonesia	7	5			11		5	5		11			3	4		3	
Malaysia	172	24			5		172	24		5			36	10		5	
New Caledonia	11				1		11			1			6			1	
New Zealand	16	3			2		16	3		2			6	3		2	
Philippines	11	3			4		11	3		4			9	3		3	
Singapore	78	25			20	3	78	25		20	3			1			
South Africa	38	7			9		38	7		9			24	4		9	
Sri Lanka	8	8		1	14		2	9		14			5	2	2	10	
Thailand	17	12			14		16	13		14			12	13		10	
Total	**760**	**241**	**1**	**1**	**159**	**4**	**748**	**247**	**1**	**159**	**4**	**1**	**269**	**147**	**2**	**88**	**1**

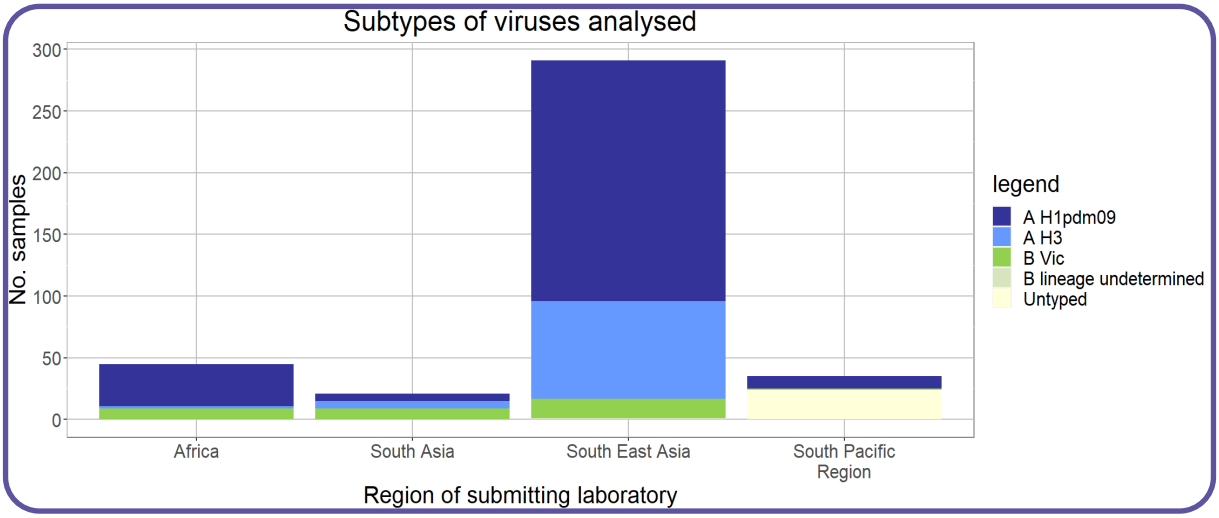
* *Subtypes and lineages are based on analysis of HA and in some cases confirmed by genetic analysis of NA.*

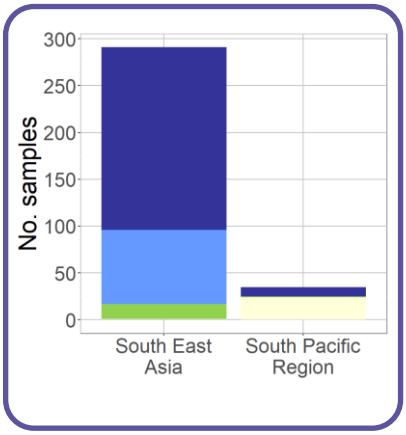
Surveillance update: Virus activity 1 January—30 September 2020

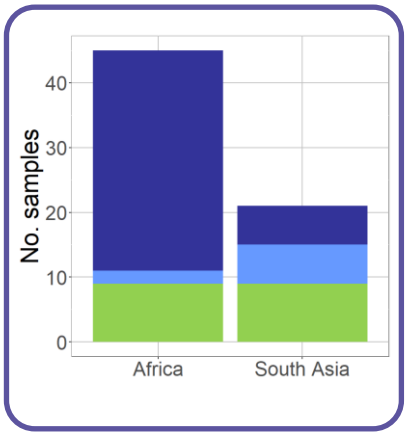
The data below are results for viruses collected between 1 January and 30 September 2020 that have been analysed at the Centre as of 6 October 2020.

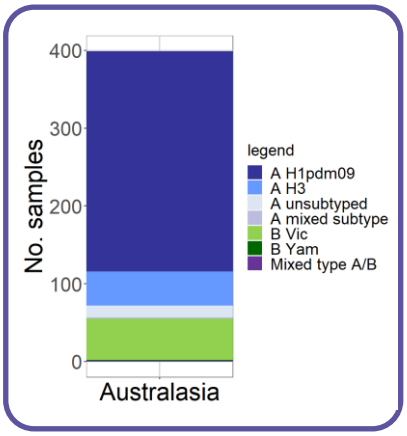
Virus types/subtypes*
The type and subtype/lineage of 791 viruses have been determined.

66.8% A(H1N1)pdm09
16.6% A(H3N2)
11.1% B/Victoria
0.1% B/Yamagata









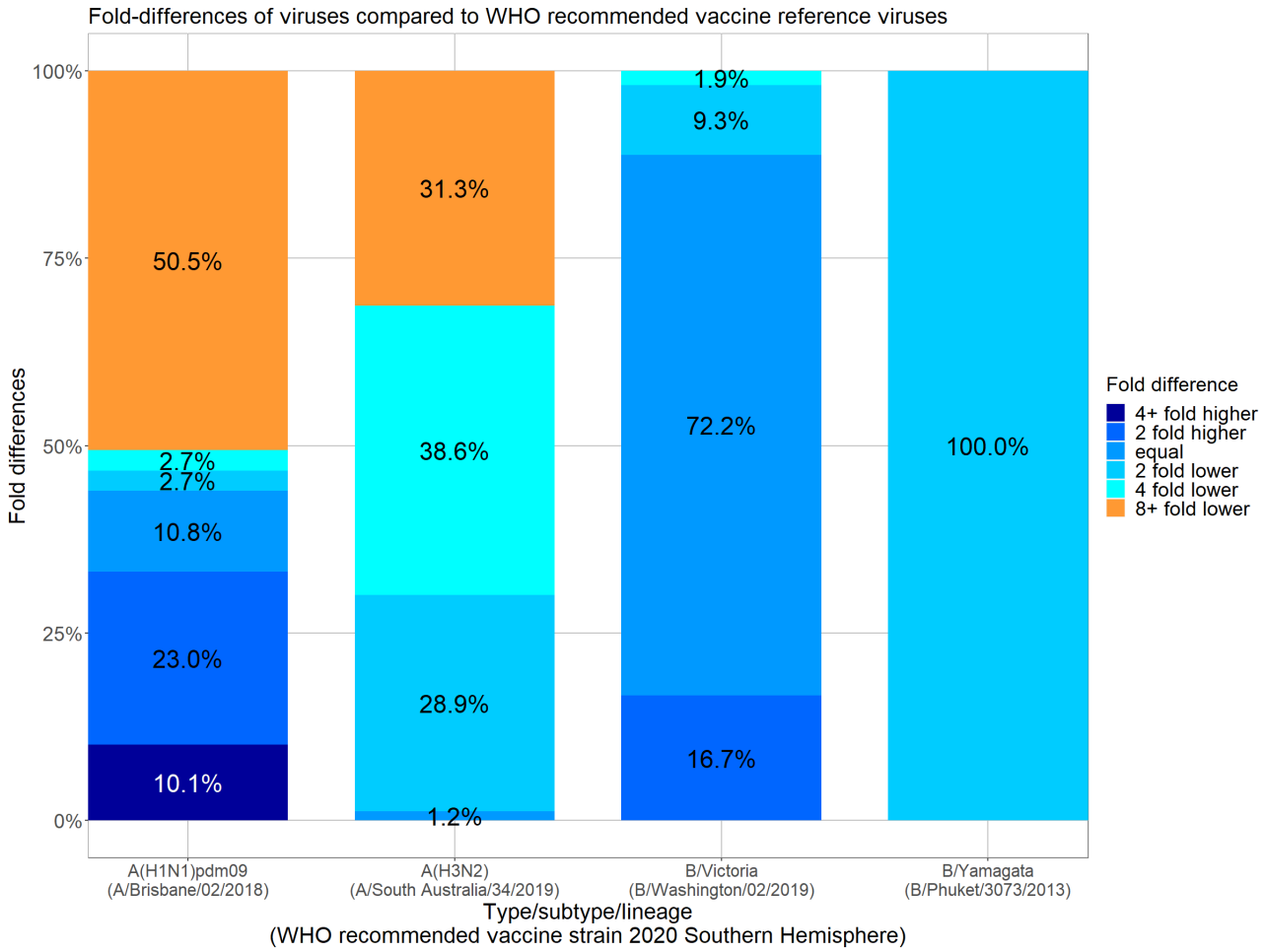
**Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

^ The Pacific region comprises countries in Polynesia, Melanesia and Micronesia.

Antigenic analysis*

A total of 1140 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. Half of A(H1N1) pdm09 viruses, and almost a third of A(H3N2) viruses were low reactors to their respective reference strains.



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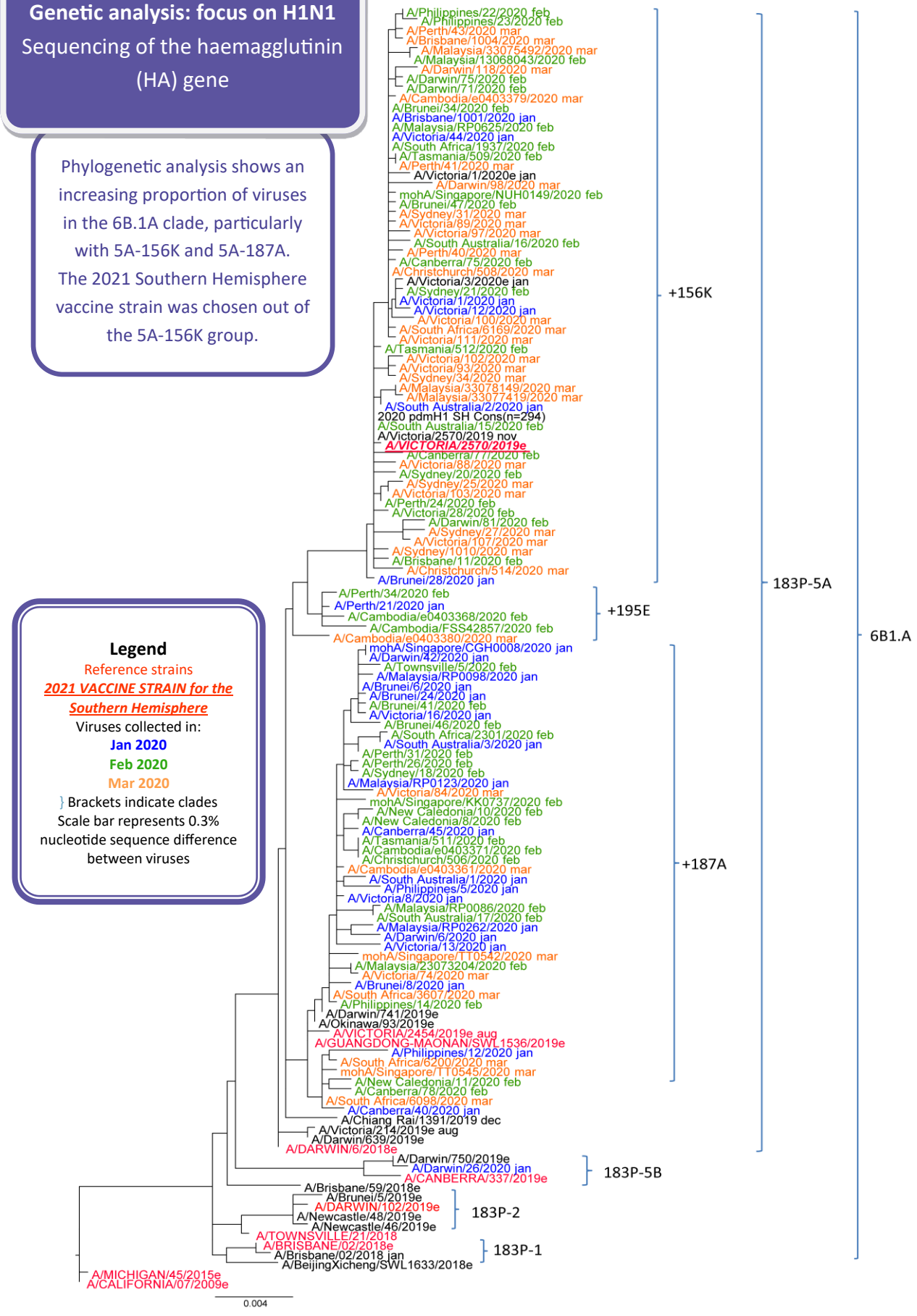
Genetic analysis: focus on H1N1

Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis shows an increasing proportion of viruses in the 6B.1A clade, particularly with 5A-156K and 5A-187A. The 2021 Southern Hemisphere vaccine strain was chosen out of the 5A-156K group.



Legend

Reference strains

2021 VACCINE STRAIN for the Southern Hemisphere

Viruses collected in:

Jan 2020

Feb 2020

Mar 2020

} Brackets indicate clades

Scale bar represents 0.3% nucleotide sequence difference between viruses

Surveillance update: Virus activity 1 January—30 September 2020 continued

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

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir, and laninamivir showed that 3 A(H1N1)pdm09 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	476	1	2	474	2	3	479			476	3	
A(H3N2)	104			104			104			104		
Mixed type A/B	1			1			1			1		
B/Victoria	65			64	1		65			64	1	
B/Yamagata	1			1			1			1		
Total	**647**	**1**	**2**	**644**	**3**	**3**	**650**			**646**	**4**	

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.

Viruses with highly reduced inhibition to one or more NAI

Type/subtype/lineage		Country of submitting laboratory	NAI(s) with highly reduced inhibition (marked with *)			
			Oseltamivir	Peramivir	Laninamivir	Zanamivir
A(H1N1)pdm09	A/Perth/22/2020	Australia	*	*		
	A/Perth/24/2020	Australia	*	*		
	A/Brisbane/13/2020	Australia		*		

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