Influenza Updates

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

@WHOCCFluMelb

Volume 9, Issue 3, December 2020

Reflection on 2020: 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 2020.

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 received far fewer influenza samples than usual and the other CCs had a similar experience. However, we did not know how the influenza season would play out. The Centre staff adjusted their work schedules and routines in accordance with public health guidance and kept the Centre open through a very challenging period in Victoria. They have 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 2021 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 also be a virtual meeting.

We wish you all the very best for the holiday season and look forward to working with you again in 2021.

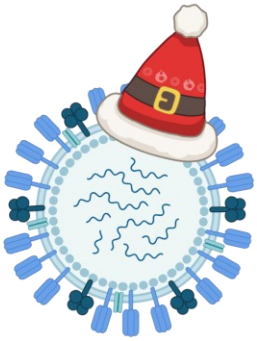


Image made with Biorender.com

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

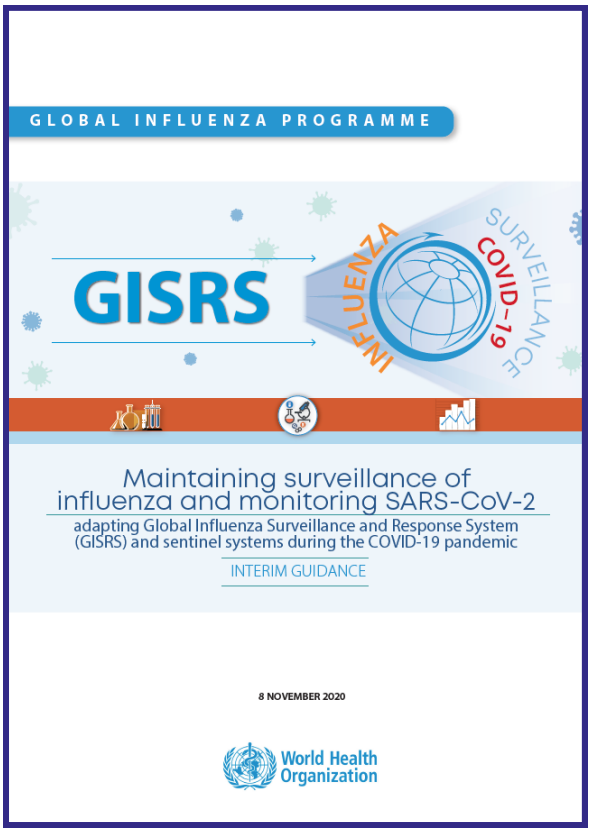
WHO Shipping Fund Project reminder

In anticipation of the WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2021-2022, which will be held in February 2021, 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.

In light of the COVID-19 pandemic, the WHO has released a new Interim Guide titled, '*Maintaining surveillance of influenza and monitoring SARS-CoV-2—adapting Global Influenza surveillance and Response System (GISRS) and sentinel systems during the COVID-19 pandemic*'.

In the lab guidance section (page 17), the report mentions an important point that laboratories shipping clinical samples or isolates to WHO CCs should note:

'With the continued circulation of SARS-CoV-2, the WHO CCs of GISRS would highly prefer to receive influenza-positive clinical specimens that are negative by RT-PCR for SARS-CoV-2 from NICs and other laboratories, and influenza virus isolates derived from clinical specimens that are negative by real-time reverse transcription PCR (RT-PCR) for SARS-CoV-2. It is suggested that influenza isolates be grown only from influenza virus-positive samples that are negative for SARS-CoV-2.'



Therefore, to ensure that the Centre knows whether samples have been tested for SARS-CoV-2, we have modified our sample submission form. This modified form is attached at the end of this Newsletter, and is also available from our website to download.

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 Friday the 25th of December to Monday the 4th of January. Please ensure that all samples are received by us no later than Tuesday the 22nd of December.

WHO Shipping Fund Project reminder continued

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.

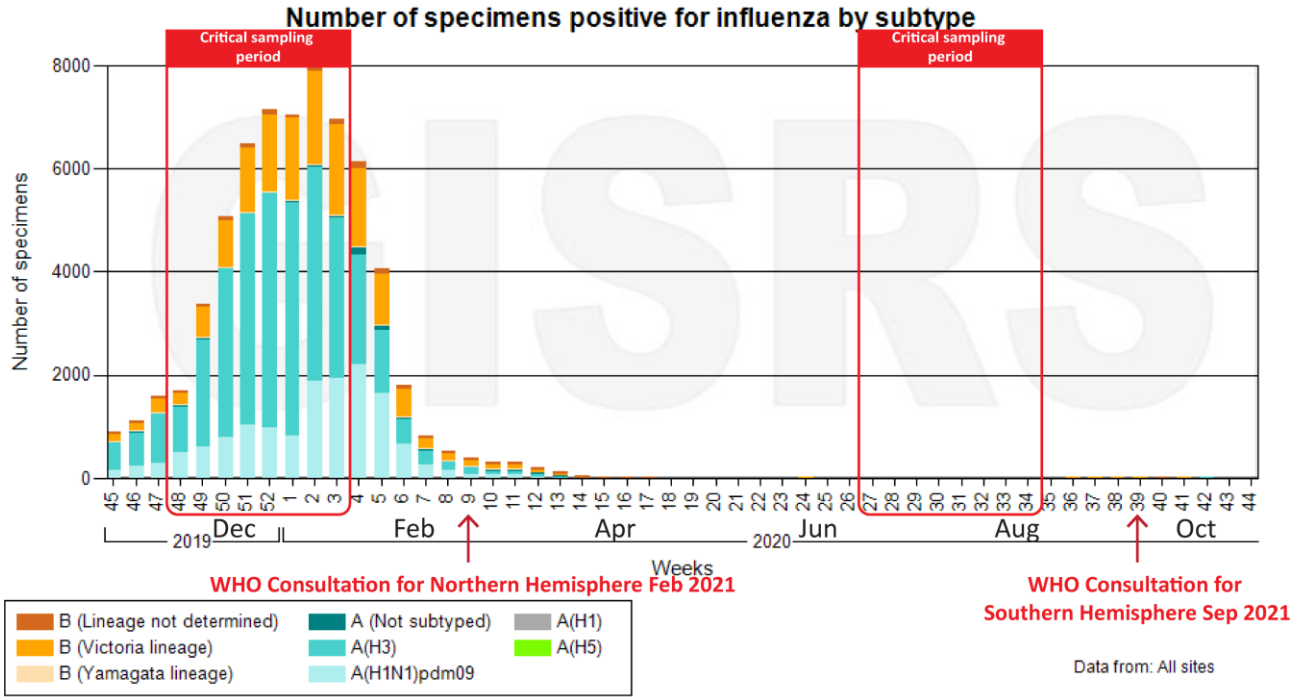
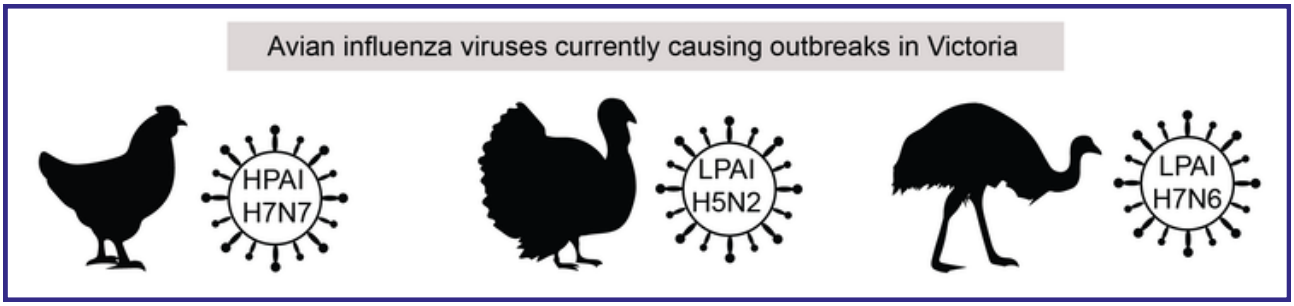


Figure adapted from FluNet: https://www.who.int/influenza/gisrs_laboratory/flunet/charts/en/Influenza viruses detections Western Pacific Region of WHO

Nearly half a million poultry deaths: there are 3 avian influenza outbreaks in Victoria. Should we be worried?



Michelle Wille, from the Centre, and Stacey Lynch (Agriculture Victoria) wrote an explainer for The Conversation about the highly pathogenic avian influenza outbreaks in Australia. Unlike other parts of the world, there has not been an outbreak of avian influenza in poultry in the Australian state of Victoria since 1992. These outbreaks are more complex than other outbreaks experienced by Australia in the past, as 3 outbreaks were the result of 3 different strains: HPAI H7N7, LPAI H5N2 and LPAI H5N6. For more, check out the full story here.

Featured Research Article

'Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020'

Featuring Associate Professor Sheena Sullivan from the Centre

RAPID COMMUNICATION

Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020

Sheena G Sullivan[1], Sandra Carlson[2], Allen C Cheng[3,4], Monique BN Chilver[4], Dominic E Dwyer[4], Melissa Irwin[5], Jen Kok[4], Kristine Macartney[6,7], Jennifer MacLachlan[8,9], Cara Minney-Smith[10], David Smith[11,12], Nigel Stocks[13], Janette Taylor[4], Ian G Barr[11]

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6. Centre for Infectious Diseases and Microbiology Laboratory Services, New South Wales Health Pathology - Institute of Clinical Pathology and Medical Research, Westmead Hospital, Westmead, Australia
7. Rapid Surveillance, Centre for Epidemiology and Evidence, NSW Ministry of Health, Sydney, Australia
8. National Centre for Immunisation Research and Surveillance and The Children's Hospital Westmead, Sydney, Australia
9. Faculty of Medicine and Health, The University of Sydney, Sydney, Australia
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Citation style for this article: Sullivan Sheena G, Carlson Sandra, Cheng Allen C, Chilver Monique BN, Dwyer Dominic E, Irwin Melissa, Kok Jen, Macartney Kristine, MacLachlan Jennifer, Minney-Smith Cara, Smith David, Stocks Nigel, Taylor Janette, Barr Ian G. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. Euro Surveill. 2020;25(47):pii=2001847.

Article submitted on 23 Oct 2020 / accepted on 26 Nov 2020 / published on 26 Nov 2020

The coronavirus disease pandemic was declared in March 2020, as the southern hemisphere's winter approached. Australia expected co-circulation of severe acute respiratory syndrome coronavirus 2, influenza and other seasonal respiratory viruses. However, influenza notifications were 7,029 (March–September) compared with an average 149,832 for the same period in 2015–2109, despite substantial testing. Restrictions on movement within and into Australia may have temporarily eliminated influenza. Other respiratory pathogens also showed remarkably changed activity in 2020.

The World Health Organization (WHO) declared a coronavirus disease (COVID-19) pandemic on 11 March 2020, as southern hemisphere countries prepared for their usual winter respiratory pathogen epidemics. The announcement prompted concern that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza and other respiratory viruses might co-circulate, straining and possibly overwhelming healthcare systems. In Australia, these fears were not realised and—in contrast to expectations—influenza activity was at an all-time low during the southern hemisphere's 2020 winter. Here, we describe the decreased activity of influenza and other respiratory pathogens in Australia and the measures that have likely contributed to their decline.

Pandemic mitigation measures and influenza and COVID-19 notifications

Key government measures to restrict movement and mixing are displayed in Figure 1A, with severity indicated using the Oxford Stringency Index [1]. Like many other countries, COVID-19 mitigation measures implemented in Australia included working from home, limits on types of indoor and outdoor social gatherings (such as meals, organised sport and religious services) and numbers of attendees, visitor restrictions in hospitals and residential long-term care facilities, increased use of hand sanitisers and other hygiene measures, and physical distancing [2]. The duration and intensity of these measures varied nationwide, with Victoria the only jurisdiction to require persons (aged >12 years) to wear face masks in public and to carry out extended school closures. Domestic inter-jurisdictional borders were closed by five of eight states and territories in late March. National borders were incrementally closed to foreign nationals with all returned travellers required to self-isolate for 14 days in hotel quarantine from 28 March [2].

Published online in *Eurosurveillance* this November, the article describes the significant impact that the COVID-19 pandemic has had on influenza activity in Australia.

Between March and September, there were only 7,029 notifications of influenza, compared to the average 149,832 (2015-2019). This marked decline was also seen in other respiratory viruses as well.

Sullivan SG, Carlson S, Cheng AC, Chilver MB, Dwyer DE, Irwin M, Kok J, Macartney K, MacLachlan J, Minney-Smith C, Smith D, Stocks N, Taylor J, Barr IG. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. *Euro Surveill.* 2020 Nov;25(47). doi: 10.2807/1560-7917.ES.2020.25.47.2001847. PubMed link

With ongoing restrictions to international travel in and out of Australia, it is likely that this trend will continue into the future.

Young Scientist Award: Maria Auladell—ESWI

Ph. D student Maria Auladell has been awarded a Young Scientist Award to present her work at the 7th European Scientific Working group on Influenza (ESWI) conference. This large international conference focuses on influenza, RSV and SARS-CoV-2 pathology, prevention, control and treatment. Dr Auladell's abstract was selected from a large pool for this prize, which is generously supported by Seqirus.

Dr Auladell is co-supervised by Dr Annette Fox from the Centre, and Professor Katherine Kedzierska and Dr Oanh Nguyen from the Department of Microbiology and Immunology. At the conference, Dr Auladell is presenting her work looking at how prior influenza A infections affect the magnitude and breadth of influenza A/H3N2-specific antibodies and B cells induced by the current influenza vaccination.

Knowledge derived from Dr Auladell's Ph. D research will contribute more generally to understanding how human antibodies and B cells respond to constantly evolving RNA viruses, like influenza, and as a consequence, contribute to the design and/or vaccination policy of seasonal influenza vaccines.

Upcoming meetings and conferences

Australian Virology Society Virtual Symposium

7 December 2020

Join the inaugural AVS symposium on *'COVID-19 and Emerging Viral Pathogens'*, which will showcase the latest research on SARS-CoV-2 and challenges in the development of vaccines and treatments, as well as exploring strategies to protect and detect the next viral pandemic.

For more information on registration, event programs and guest speakers, please click here.

Farewell and good luck

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

Ms Angela Todd has been a medical scientist with the Centre for the last three and a half years. She will be taking on a new position as Senior Scientist, at the Microbiological Diagnostic Unit Public Health Laboratory.

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

Below is a summary of surveillance activities at the Centre during this current reporting period. Centre activities have been relatively quiet all year, due to decreased influenza cases resulting from COVID-19 mitigation strategies implemented 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 1879 influenza samples from the laboratories and institutions listed below during the period 1 January — 30 November 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

INDONESIA: Centre for R&D of Biomedical and Basic Health Technology

MALAYSIA: Institute for Medical Research, University Malaya

NEW CALEDONIA: Centre Hospitalier de Nouvelle Calédonie

NEW ZEALAND: Canterbury Health Laboratories, Institute of Environmental Science and Research Limited

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

TIMOR-LESTE: Laboratório Nacional da 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 2020, 9 A(H1N1)pdm09, 12 A(H3N2) and 5 B/Victoria viruses were successfully isolated in eggs at the Centre.

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

Antigenic analysis
1223 viruses analysed by haemagglutination inhibition (HI) assay

Antiviral drug susceptibility
1225 viruses analysed by neuraminidase inhibition (NAI) assay

Sequencing
686 viruses analysed
554 HA genes
542 NA genes
467 MP genes
172 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	56		34	1
Brunei	29	4					27	4					15	4			
Cambodia	39	60			33		39	60		33			19	48		11	
Indonesia	14	18			12		14	18		12			8	12		5	
Malaysia	172	24			5		172	24		5			37	10		5	
New Caledonia	11				1		11			1			9			1	
New Zealand	21	3			2		20	3		3			8	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	13		1	16		8	13		16			6	4	2	13	
Thailand	30	20			17		30	21		17			20	19		12	
Timor-Leste														2			
Total	**785**	**267**	**1**	**1**	**165**	**4**	**781**	**272**	**1**	**166**	**4**	**1**	**293**	**166**	**2**	**95**	**1**

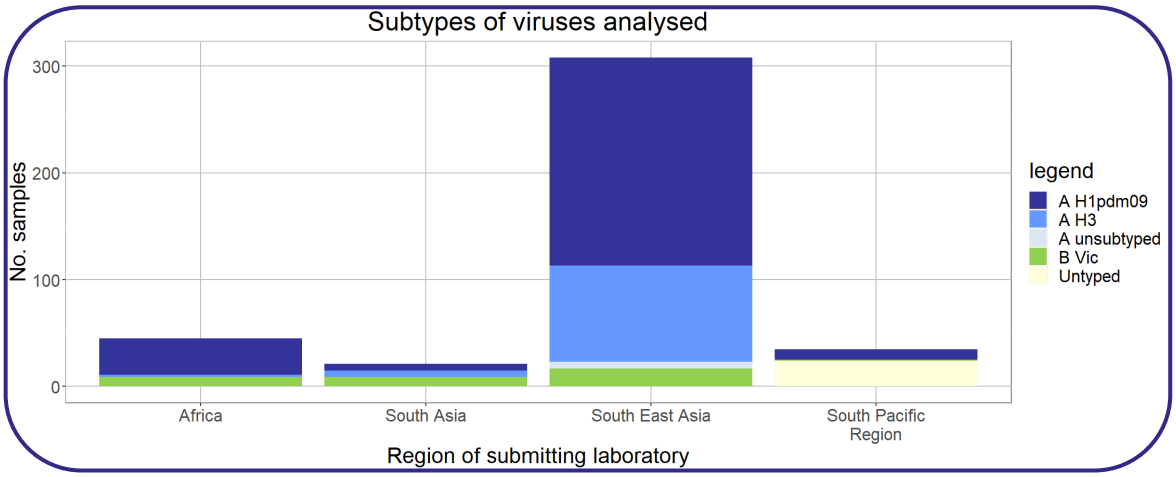
* *Subtypes and lineages are based on analysis of HA and in some cases confirmed by genetic analysis of NA.*

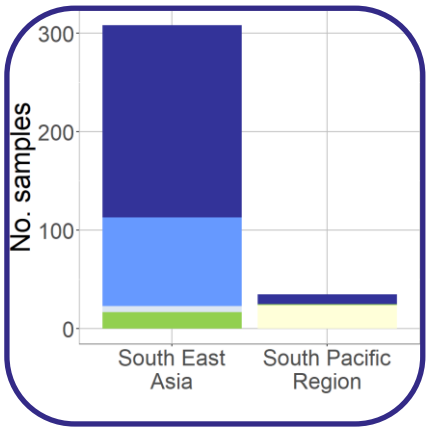
Surveillance update: Virus activity 1 January — 30 November 2020

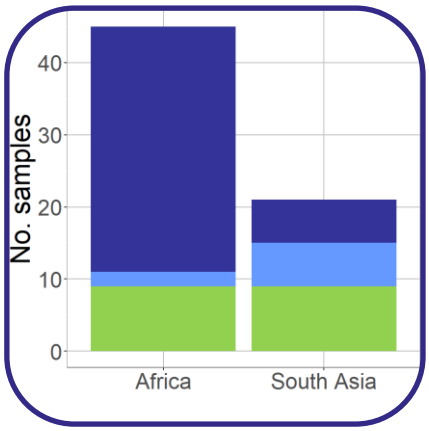
The data below are results for viruses collected between 1 January and 30 November 2020 that have been analysed at the Centre as of 1 December 2020.

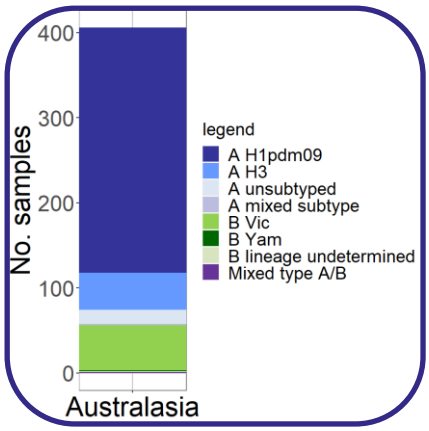
Virus types/subtypes*
The type and subtype/lineage of 815 viruses have been determined.

65.4% A(H1N1)pdm09
17.4% A(H3N2)
10.9% B/Victoria
0.1% B/Yamagata









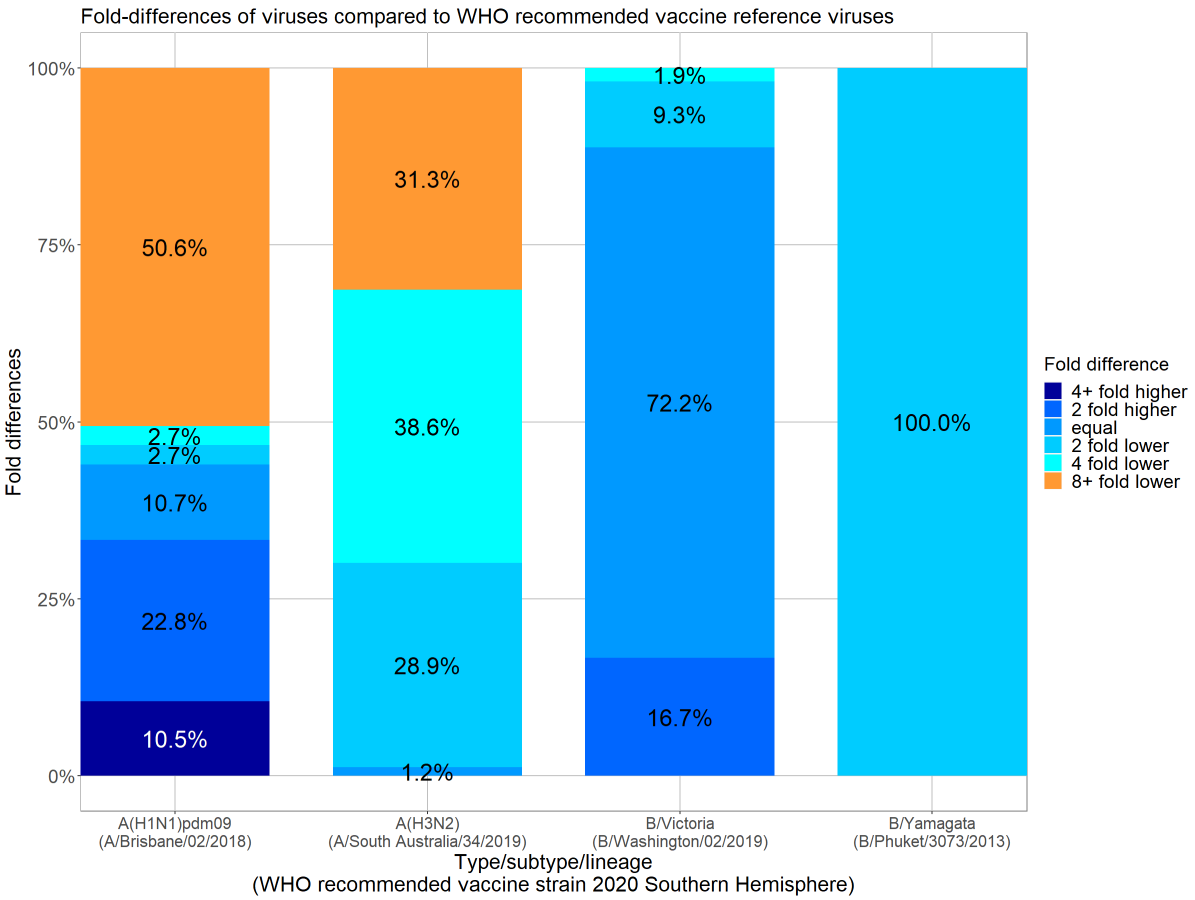
**Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

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

Antigenic analysis*

A total of 1176 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.



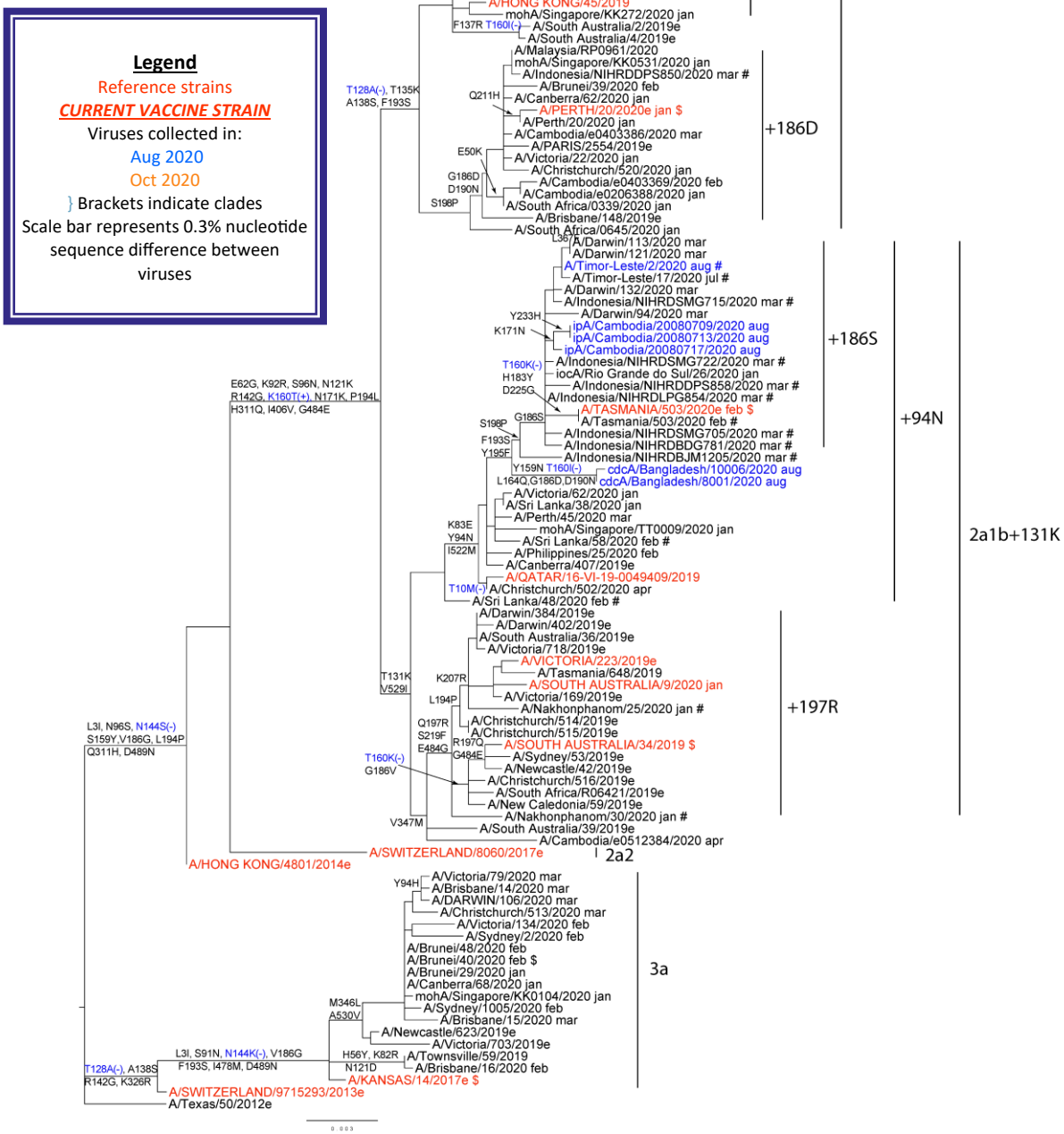
* *Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

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

Genetic analysis: focus on A (H3N2)

Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis shows a small increase in the proportion of viruses in the 2a1b clade.



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

Antiviral drug susceptibility testing:
1176 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 viruses showed 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	509	1	2	507	2	3	512			509	3	
A(H3N2)	129			129			129			129		
B/Victoria	71			70	1		71			70	1	
B/Yamagata	1			1			1			1		
Mixed type A/B	1			1			1			1		
Total	**711**	**1**	**2**	**708**	**3**	**3**	**714**			**710**	**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		*		

WHO Collaborating Centre for Reference and Research on Influenza

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Email: whoflu@influenzacentre.org http://www.influenzacentre.org

Details of samples sent to WHO Collaborating Centre, Melbourne, Australia

Name and Address of Laboratory:

Name of person completing the form:

Date:

Please complete all columns with a red heading where possible

	Virology										Patient and epidemiological information								
	Sample sent	Clinical Sample						Virus isolate											
	Clinical specimen identifier[1] (Unique identifier)	Sample type[2]	Specimen collection date (dd/mm/yyyy)	Ct value	Influenza Type[3]	Sub-type[4]	Lineage[5]	Virus passage history[6]	Strain designation[7]	SARS-CoV-2 test Result[8]	Date of birth (dd/mm/yyyy)	Sex	City or district of residence	Influenza vaccination[9]	Antiviral treatment[10]	Patient setting[11]	Health status[12]	**Comments[13]**
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Help Notes

1) Column B: The identifier code applied to the clinical specimen by the sending laboratory

2) Column D: Indicate the sample type sent to the CC: Isolate, Specimen, Isolate+Specimen, RNA/DNA, Tissue

3) Column F: Influenza type e.g. A, B

4) Column G: A virus subtype: e.g. H1N1pdm09, H3N2

5) Column H: B virus lineage: Vic = B/Victoria, Yam = B/Yamagata

6) Column I: Number of passages in cells (specify cell-line) and/or eggs (e.g. MDCK1, SIAT2, E1 or MDCK2/E1)

7) Column J: The virus name given by the sending laboratory; Influenza type/animal (if not human) / Location (country or region or state or town) / Unique identifier (often specimen number) / Year (yyyy) of sample collection e.g. A/California/7/2009 or B/Victoria/60/2008

8) Column K: Indicate test result if patient was tested for SARS-CoV-2 (COVID-19)

9) Column O: Indicate if current seasonal influenza vaccine was administered

10) Column P: Indicate if antiviral treatment was administered

11) Column Q: Indicate "patient setting" when specimen was collected e.g.: hospitalised inpatient, hospitalised outpatient, community GP, surveillance GP, emergency, or other (specify in comments)

12) Column R: Indicate "health status" of the patient when the specimen was collected e.g.: immunocompromised, ICU, deceased, pregnant, or other (specify in comments)

13) Column S: Please provide a description for "other" if this option was selected. Any other relevant information can also be included here.

Please write "Unknown" if information is not available

Sample type	Sample Type	Influenza Type	Subtype	Lineage
V	Isolate	A	H1N1pdm09	Vic
cs	Specimen	B	H3N2	Yam
R	Isolate+Specimen	C		
D	RNA/DNA	D		
Other	Tissue	Mixed		

SARS-CoV-2 test result	Sex	Influenza Vaccination	AV treatment
Positive	F	Yes	Oseltamivir (Tamiflu)
Negative	M	No	Zanamivir (Relenza)
Not tested	Unknown	Unknown	None
Unknown			Unknown

Patient Setting	Health Status
Hospitalised Inpatient	Immunocompromised
Hospitalised Outpatient	ICU
Emergency	Deceased
Community GP	Pregnant
Surveillance GP	Unknown
Outbreak	Other
Unknown	
Other	