

An Update on Influenza and Influenza Vaccines 2019

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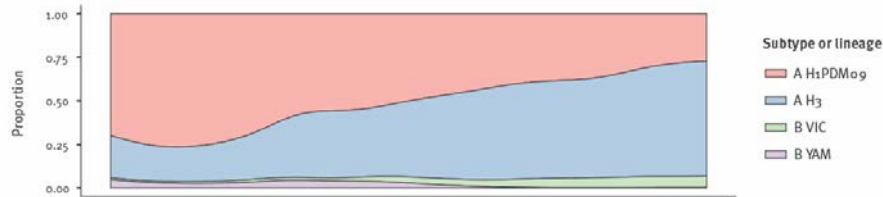
Intense interseasonal influenza outbreaks, Australia, 2018/19

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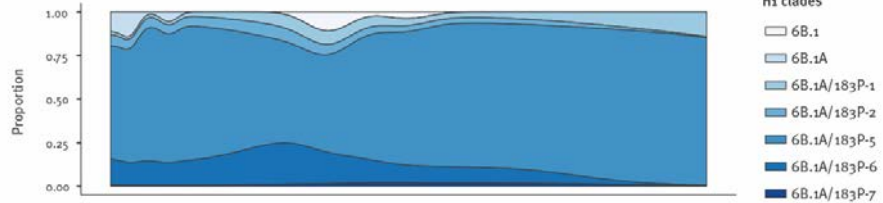
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Ian G Barr^{1,2}, Yi Mo Deng¹, Miguel L Grau³, Alvin X Han^{4,5}, Robin Gilmour⁶, Melissa Irwin⁷, Peter Markey⁸, Kevin Freeman⁹, Geoff Higgins¹⁰, Mark Turra¹⁰, Naomi Komadina¹, Heidi Peck¹, Robert Booy^{11,12}, Sebastian Maurer-Stroh^{4,5,13}, Vijaykrishna Dhanasekaran^{1,3}, Sheena Sullivan^{1,2}

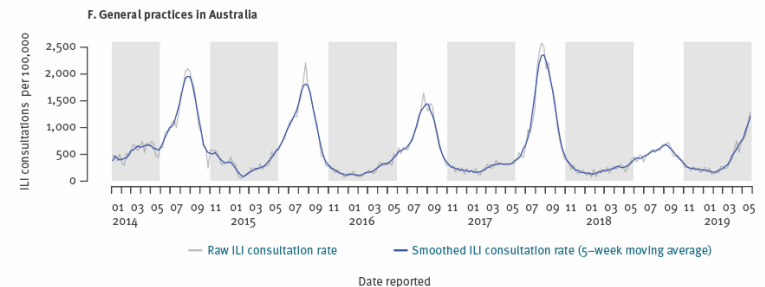
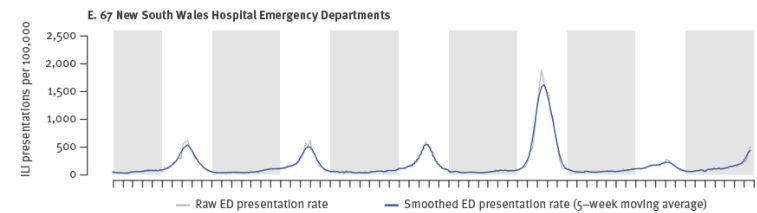
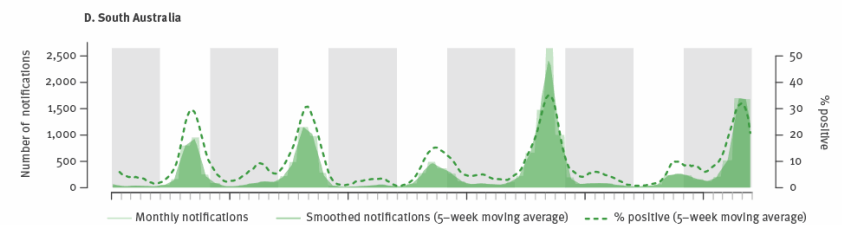
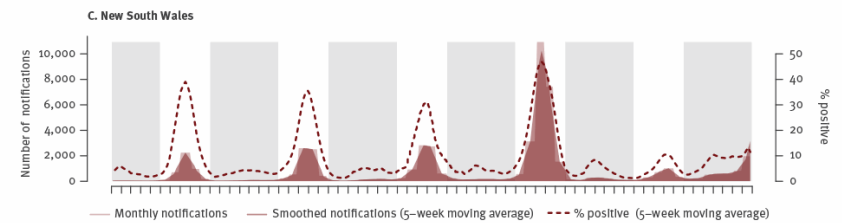
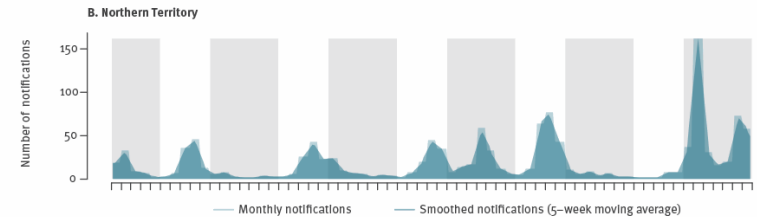
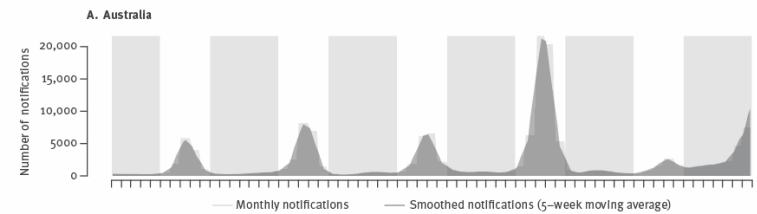
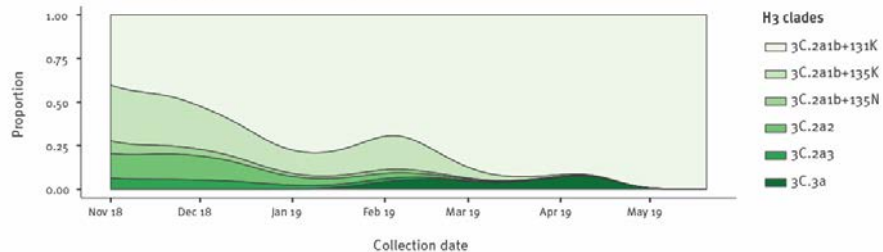
A. All influenza samples (n = 2,965)



B. Influenza A(H1N1)pdm09 clades (n = 278 HA sequences)



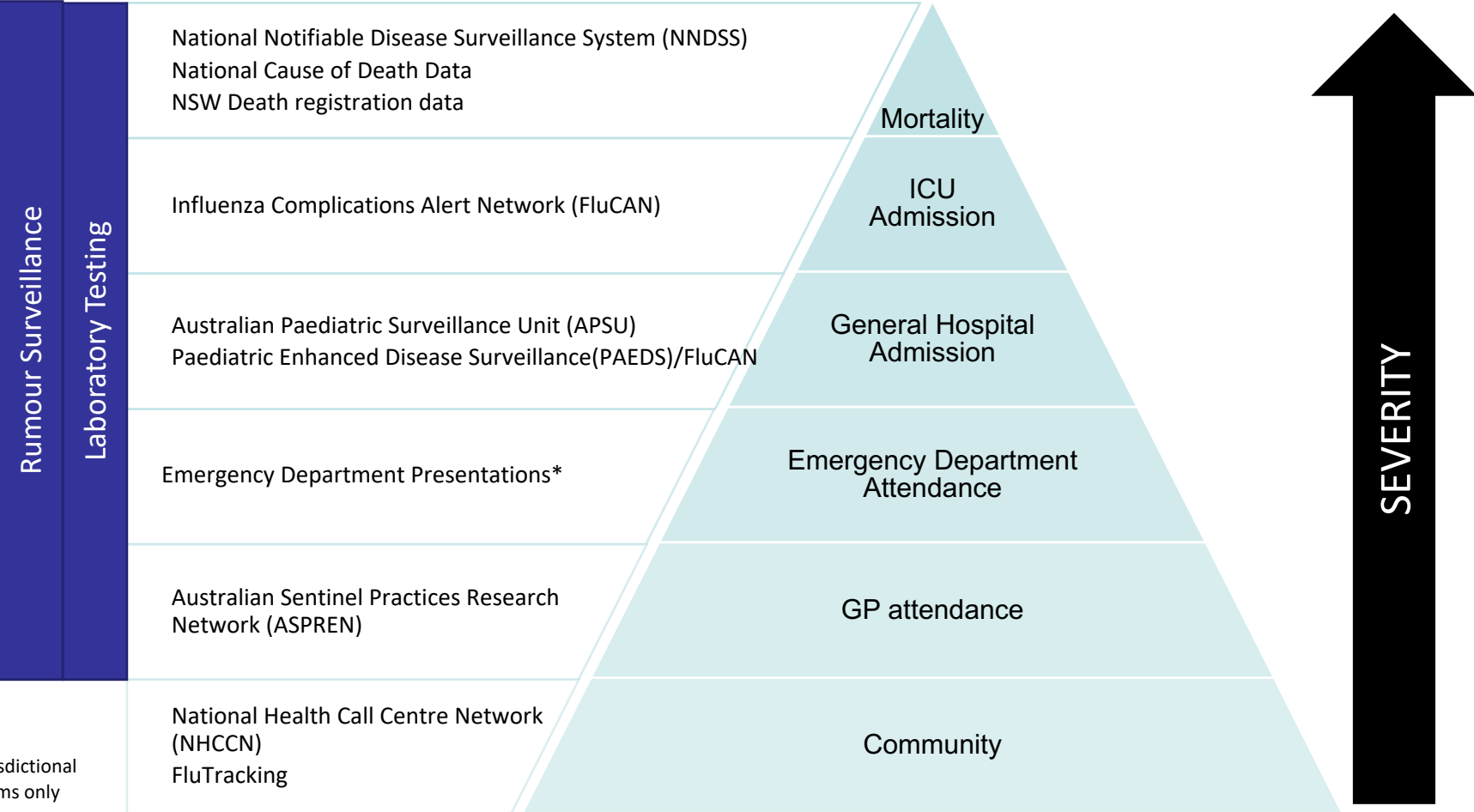
C. Influenza A(H3N2) clades (n = 453 HA sequences)



Interseasonal influenza activity 2019

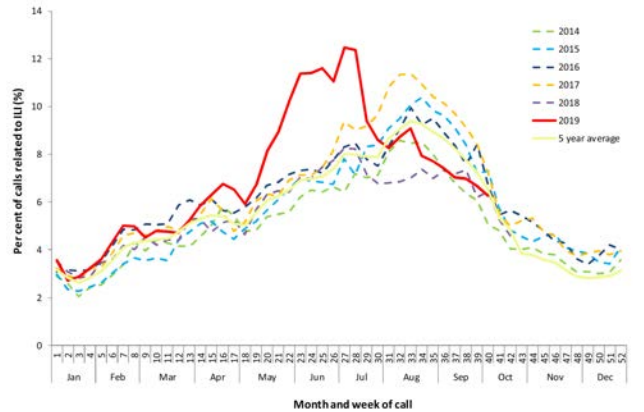
- The 2018-2019 interseasonal period in Australia was exceptional.
- By May, notifications were ~12-fold higher than the average of the last 3 years.
- Institutional outbreaks, deaths, emergency department visits and GP consultations were all high.
- Interseasonal activity disproportionately affected children.
- Weekly rates of positive tests from Jan-May were 8.6-12.2% and 4.8-35.3% in NSW and SA, respectively.

National Influenza Surveillance Scheme

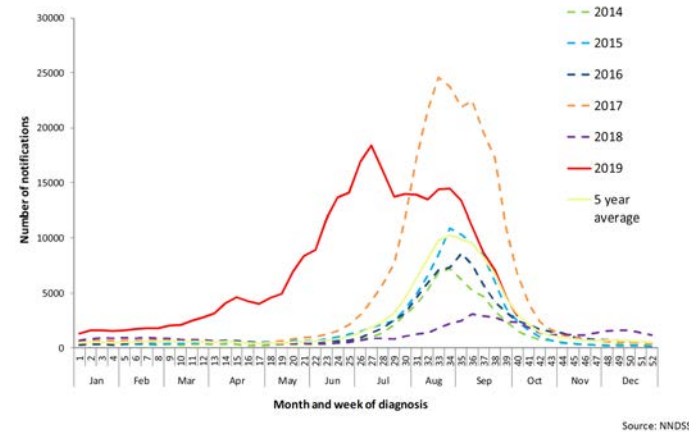


2019 in Australia

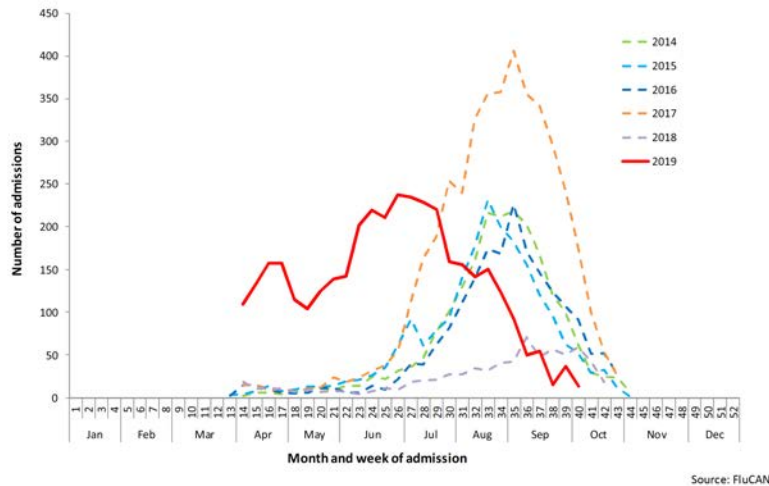
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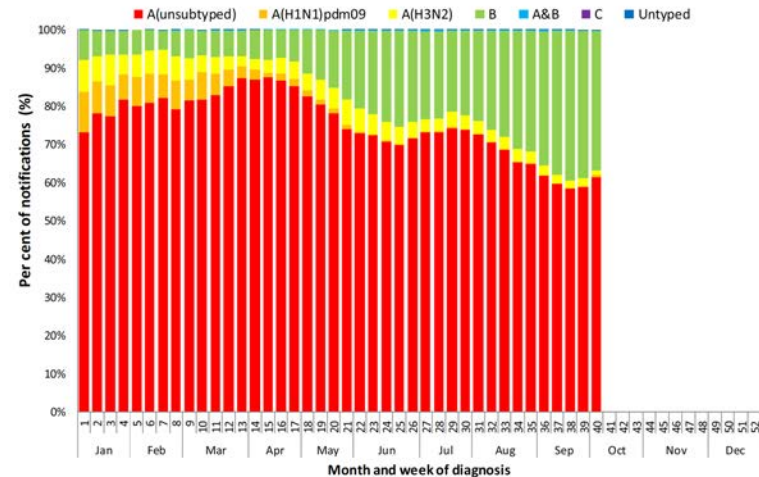
Lab confirmed influenza



Hospitalizations



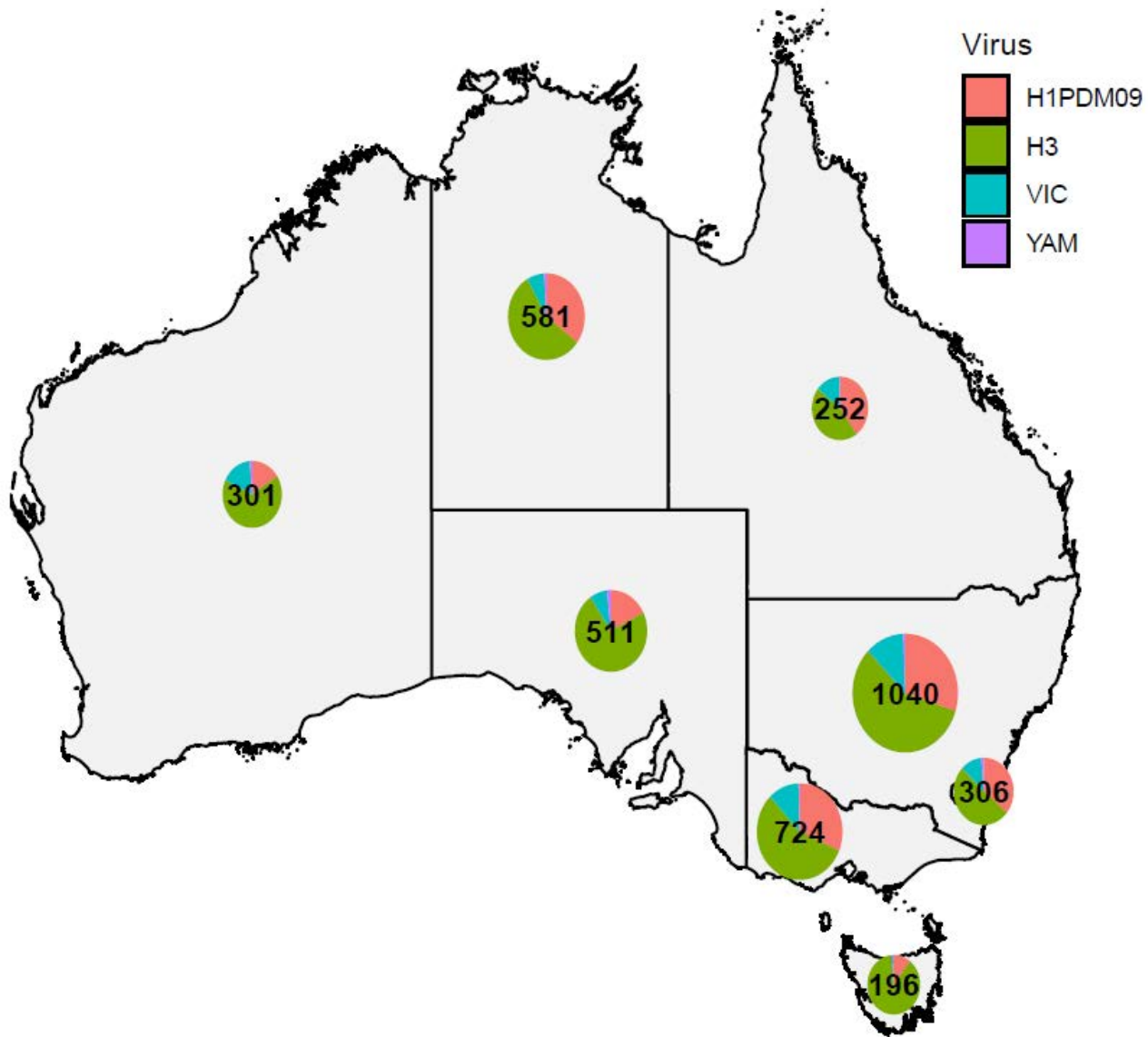
Typing



2019 – season lasted approx 30 weeks

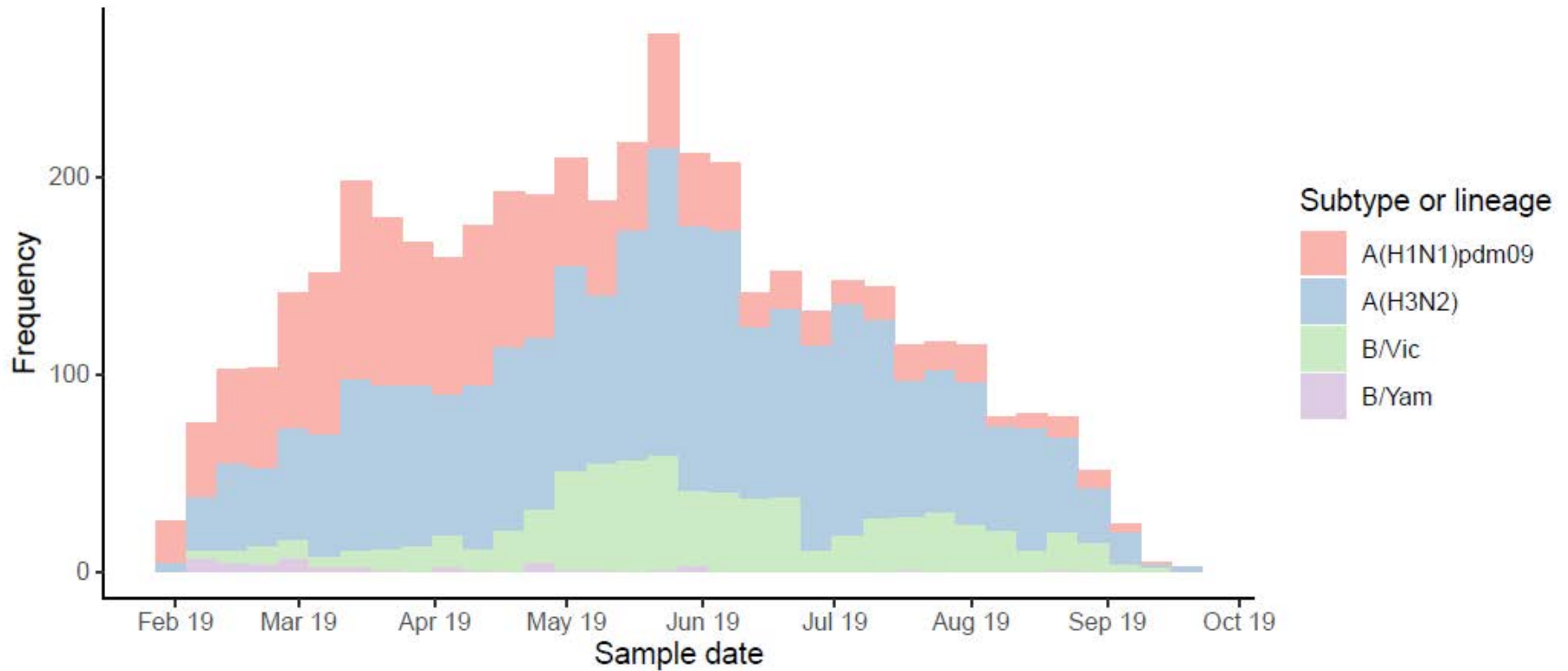
Australian Influenza Surveillance Report 6 Oct 2019

Viruses tested at WHO CC from Australia

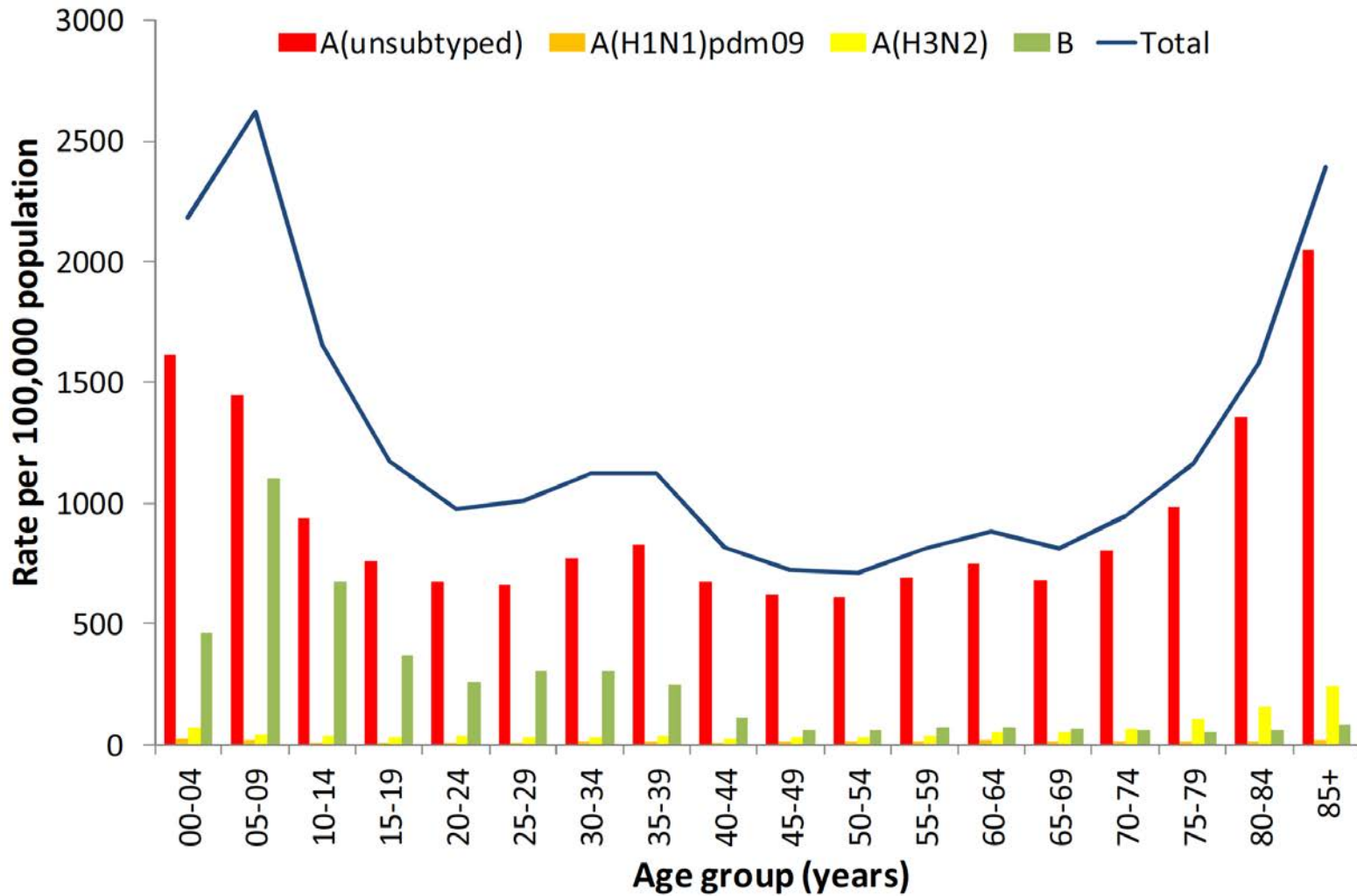


Slide courtesy of Ian Barr

Type and subtype of influenza viruses submitted to WHO CC Feb-Oct 2019

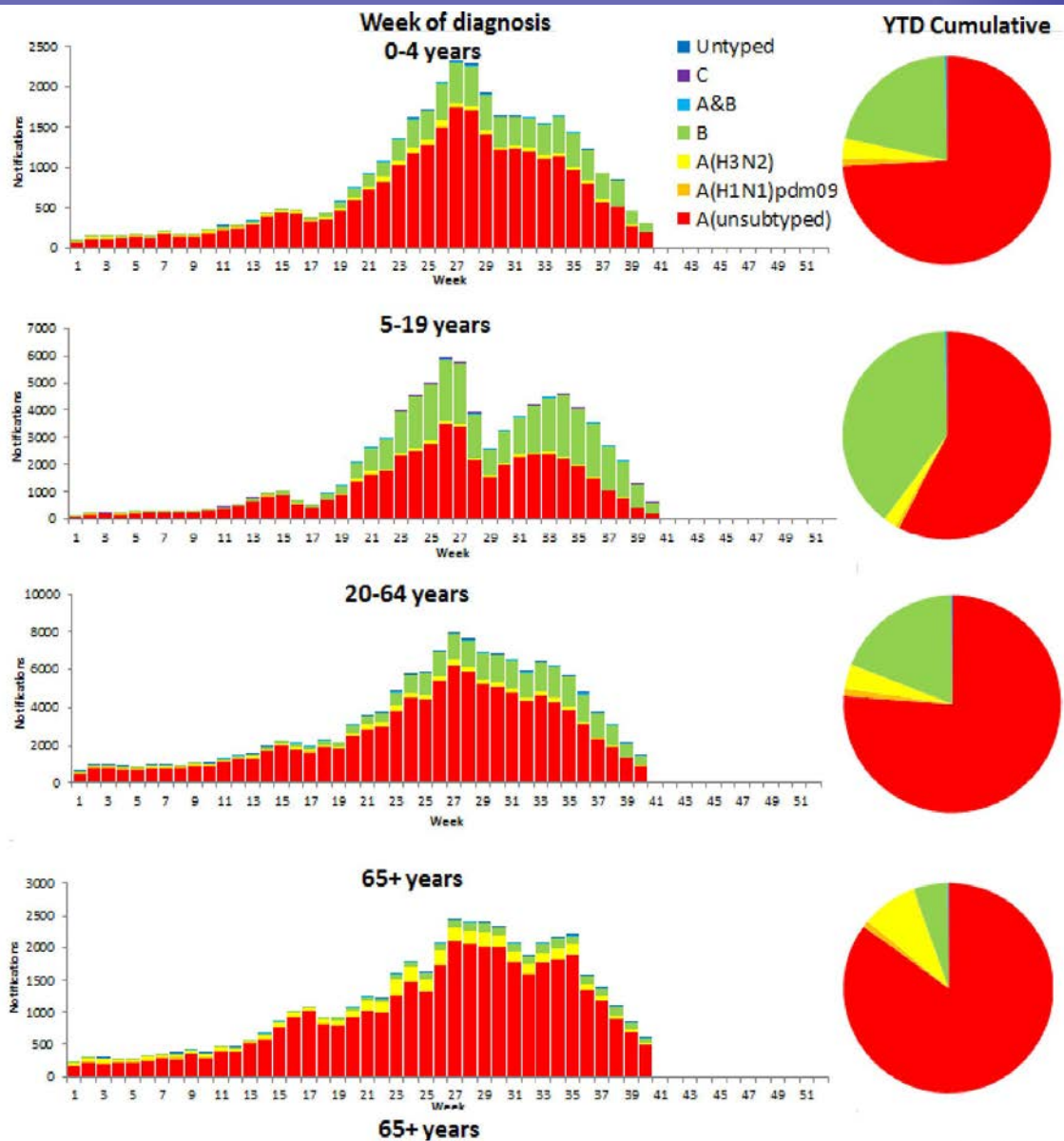


Notifications by age



Source: NNDSS

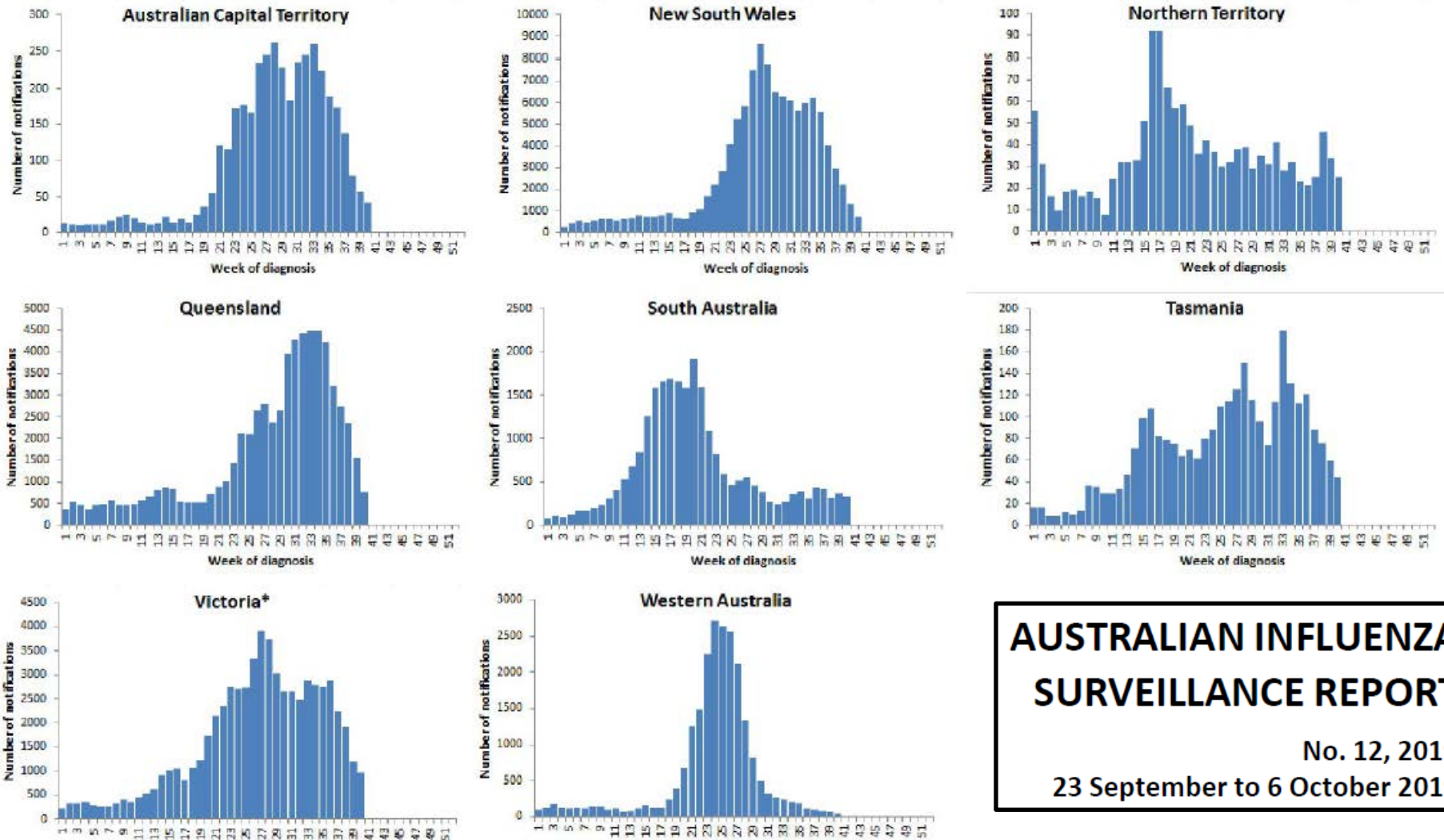
Notifications by week of diagnosis and age



Source: NNDSS

Lab confirmed influenza cases by state by week

Figure 8. Notifications of laboratory confirmed influenza*, 1 January to 6 October 2019, by state or territory and week.



**AUSTRALIAN INFLUENZA
SURVEILLANCE REPORT**
No. 12, 2019
23 September to 6 October 2019

FluCAN influenza hospitalisations in Australia

Year*	Total # hospitalised	% cases admitted to ICU	Other information
2014 (up to 26 Sep)	(1,583)¹	10	94% influenza A
2015 (up to 9 Oct)	1,873	6.9	47% ≥65y (73% had significant risk factors present on admission)
2016 (up to 14 Oct)	1,767	10	18% <15y, 845 (45%) >65y
2017 (up to 27 Oct)	3,969	8.9	2.3 times 5 year average 14% ≤15y; 33% 16-64y; 52% ≥65y
2018 (up to 9 Oct)	725	8.1	One-third the number of hospitalisations than the 5 year average for the same period (n=2,226).
2019 (up to 6 Oct)	3,915	6.3	Bed occupancy highest @ wk 28 (June 24-30) at 6.7%

*FluCAN surveillance runs 1 April – 30 Oct each year

Number reported only from surveillance hospitals;

¹Estimated from graph

NNDSS reported influenza associated deaths

Year	Deaths #	Median age y	Virus type/subtype	NNDSS notifications/death
2014	72	72	100% Influenza A	873
2015	97	85	B and A(H3N2)	923
2016	92	80	87% Influenza A	225
2017	745	86	78% influenza A	318
2018	57	80	75% influenza A	847
2019*	812	86	80% influenza A	367

*Up to 6.10.19

Australian Influenza Surveillance Report

Year	2014	2015	2016	2017	2018	2019*
Number of outbreaks	121	103	252	543	42	379

Summary

- Australia had exceptional inter-seasonal influenza activity (Dec-Feb)
- We then had an early start to our influenza season with large numbers of notifications, hospitalisations and deaths
- Mainly influenza A (H3>H1) & B-Vic
- The early and severe start to the season prompted distribution of a record 12.5 million doses of vaccine.
- Very low numbers of influenza viruses with highly reduced sensitivity to NAI

Currently licensed influenza vaccines



Principle: Induction of a protective immune response against the haemagglutinin protein

- Based on serum antibody response to the hemagglutinin (HA) protein
- Offered as trivalent or quadrivalent formulations to cover epidemic influenza A and B viruses
 - Trivalent vaccines contain A/H1N1, A/H3N2 and one B strain
 - Quadrivalent vaccines contain A/H1N1, A/H3N2, B Yamagata-lineage and B Victoria-lineage viruses.

2019 Influenza vaccines in Australia

- Annual vaccination is recommended for all persons ≥ 6 months of age
- The standard vaccine is quadrivalent influenza vaccine (QIV)
- For **adults ≥ 65 years of age**, two higher immunogenicity trivalent influenza vaccine (TIV) formulations are available and NIP-funded
 - A high-dose vaccine
 - An adjuvanted vaccine
 - These 'enhanced' vaccines are preferentially recommended over QIV for adults ≥ 65 years of age
 - There is no preference for use between the two TIVs

Individuals eligible for free influenza vaccine under the National Immunisation Program

- Aboriginal or Torres Strait Islander children aged ≥ 6 m
- All adults aged ≥ 65 years
- All persons aged >6 mo who have certain medical conditions which increase the risk of influenza disease complications

Cardiac disease, chronic respiratory conditions, chronic neurological conditions, immunocompromising conditions, diabetes or metabolic disorders, renal disease, haematologic disorders, long term aspirin therapy in children aged 6 mo to 10 years

- Pregnant women (during any stage of pregnancy)

Vaccine composition recommended for 2019 southern hemisphere

- H1N1pdm09: A/Michigan/45/2015-like
- H3N2: **A/Switzerland/8060/2017-like***

Quadrivalent vaccine:

B/Yam: B/Phuket/3073/2013-like

B/Vic: **B/Colorado/06/2017-like***

Trivalent vaccine:

B/Vic: **B/Colorado/06/2017-like*#**

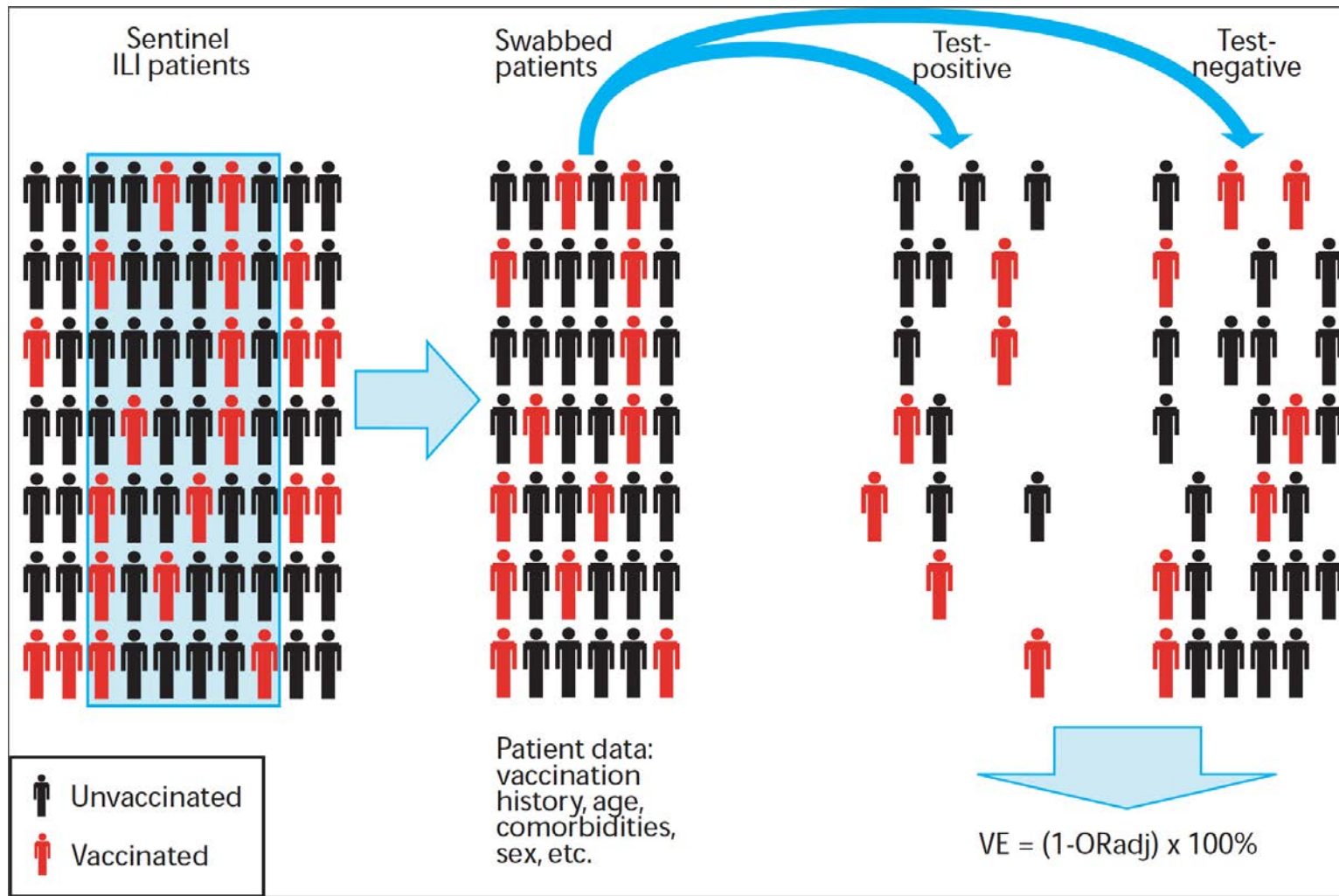
* **Changes to 2018 recommendations**

AIVC recommended B/Yam: B/Phuket/3073/2013-like for Australia and NZ

How did the circulating viruses in 2019 compare with the vaccine viruses?

- A(H1N1)pdm 09
 - Large number of viruses analysed; mostly genetically & antigenically similar to the vaccine virus
- A(H3N2)
 - Large number of viruses sequenced; some antigenic differences from the vaccine virus
- B-Victoria lineage (recommended for SH quadrivalent and trivalent vaccines)
 - Dominant B-lineage in circulation
 - Many triple amino acid “deletion variants” (3-Del); antigenically different from double deletion virus in the vaccine
- B-Yamagata lineage (recommended for SH quadrivalent vaccines and in Australia and NZ trivalent vaccines)
 - Very few B/Yam viruses, all similar to the vaccine virus

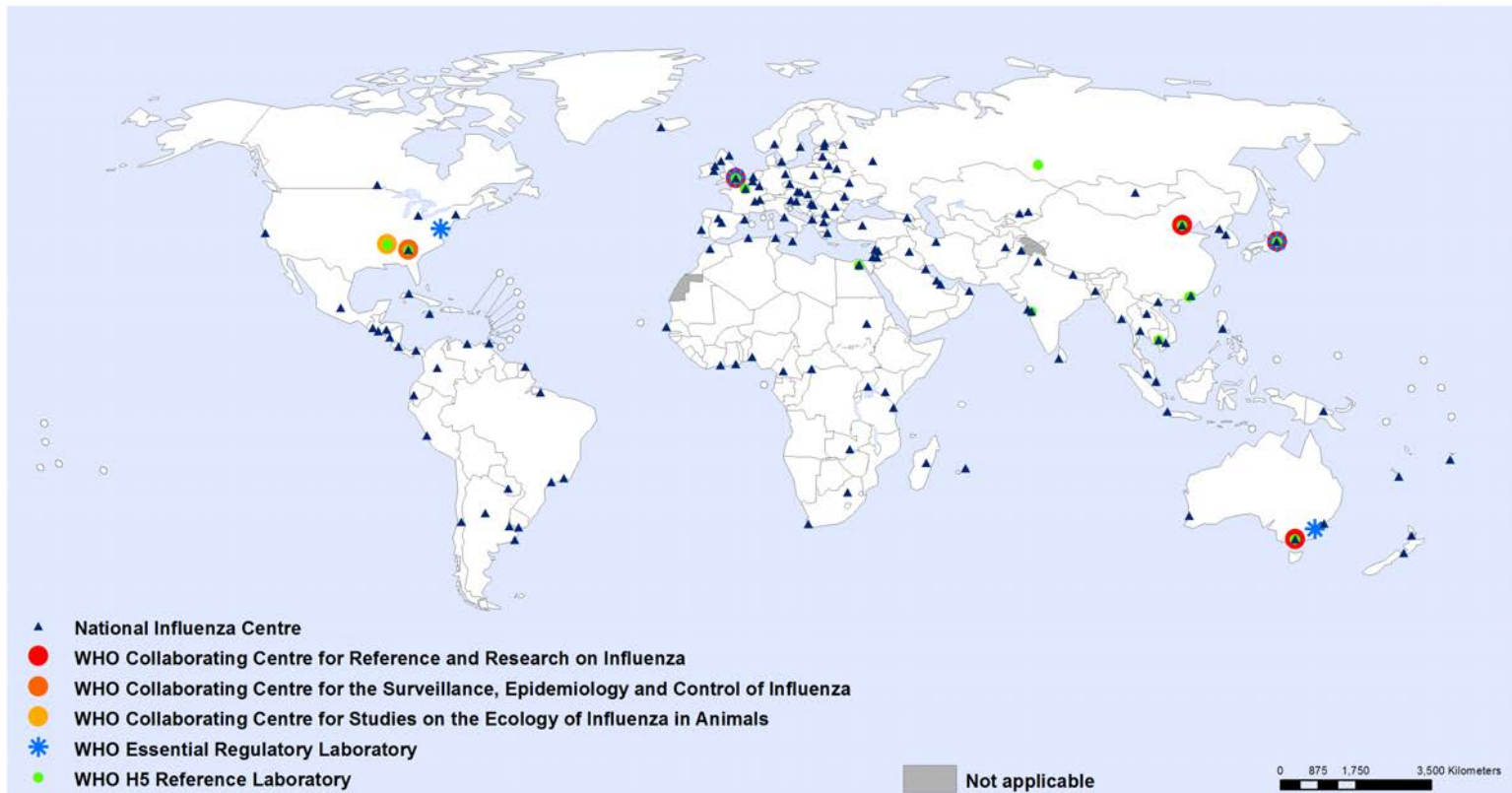
Assessing influenza vaccine effectiveness: test negative design



WHO GISRS network

WHO Global Influenza Surveillance and Response System

28 September 2015



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), WHO
Map Production: Global Influenza Programme
World Health Organization



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Oldest network in WHO: begun in 1952, 144 NIC's in 114 countries, 5 WHO CC's for human influenza + 1 for animal influenza + 4 essential regulatory labs,

WHO vaccine strain recommendation process

A WHO committee meets twice a year to recommend suitable strains to be included in the vaccine for the upcoming influenza season:

- northern hemisphere winter (decided in February)
- southern hemisphere winter (decided in September)

Surveillance and vaccine candidate data are compiled and shared between WHO Collaborating Centres.

A vaccine strain change is recommended only if the following are widely observed amongst circulating viruses:

Antigenic changes

Marked changes in the antigenic profile in 2-way HI assays compared with previous vaccine strains



Sequence changes

Changes in HA gene sequences, especially at known antigenic and receptor-binding sites



Serology changes

Poor recognition by serum panels from human recipients of the previous vaccine

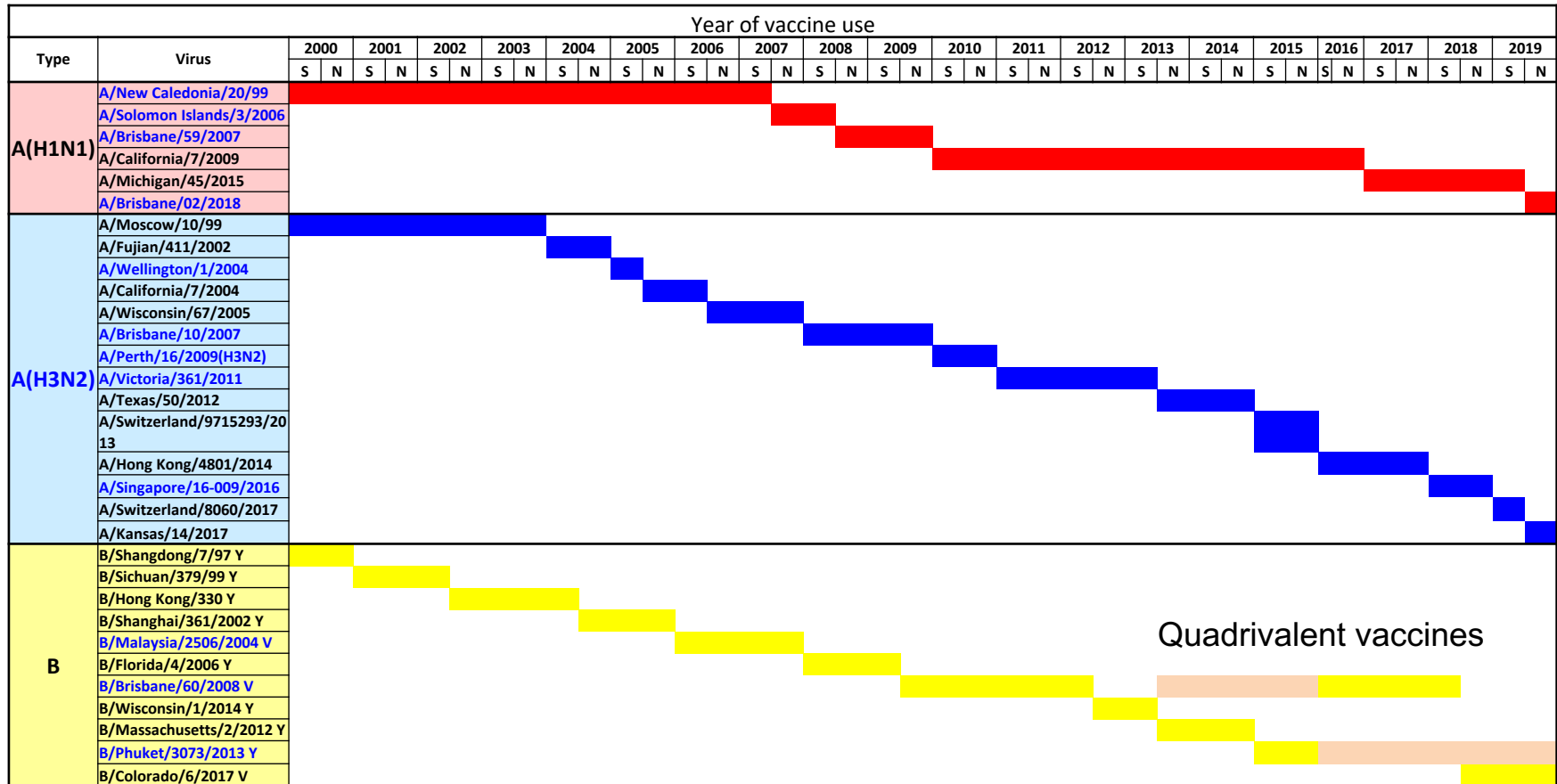


Availability of suitable candidate vaccine strains



National authorities make the final decision for their country.
Vaccine production takes about 6 months

WHO prototype vaccine viruses 2000-2019 (egg isolates)



Viruses in blue=Prototype vaccine viruses isolated at Melbourne CC

- **H1N1pdm – A/Brisbane/02/2018****
- **H3 – A/South Australia/34/2019****

Trivalent vaccine:

- **B/Washington/02/2018-like (B/Vic)**

Quadrivalent vaccine:

- **B/Phuket/3073/2013-like (B/Yam)****
- **B/Washington/02/2018-like (B/Vic)**

***Changes to 2019 SH recommendations**

****Originally isolated at Melb WHO CC**

Antiviral drugs: the NA inhibitors

Oseltamivir

- Oral
- Global
- Market leader



Zanamivir

- Inhaled
- Global



Peramivir

- IV
- Japan, S. Korea, China, US, Australia (pending)



Laninamivir

- Inhaled (single)
- Long acting
- Japan



There are other antivirals on the horizon...some licensed and others in phase III trials

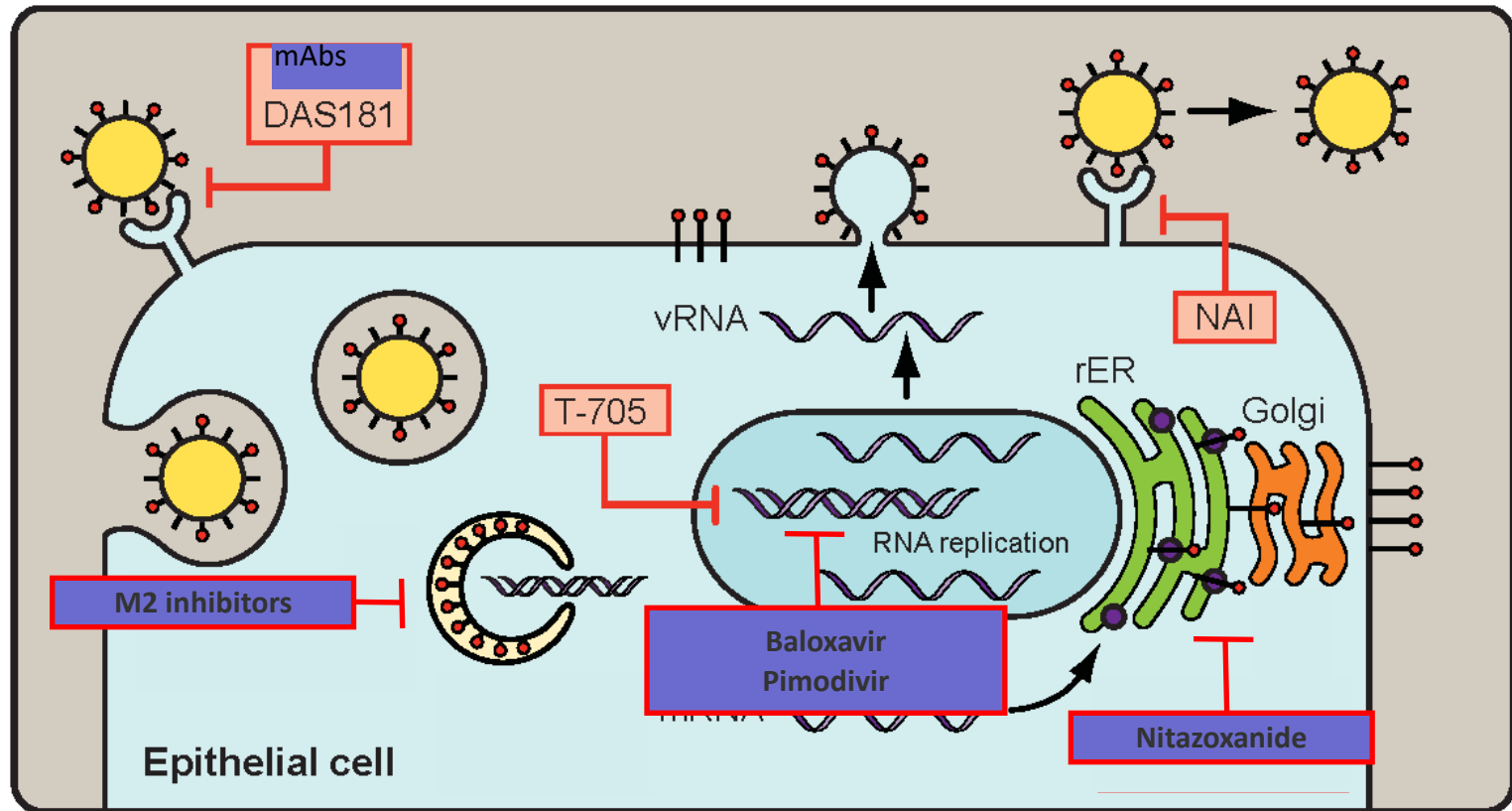


Figure taken modified from: Drugs in development for influenza. Boltz DA, Aldridge JR Jr, Webster RG, Govorkova EA. *Drugs*. 2010 Jul 30;70(11):1349-62.

Acknowledgements



- NICs and labs that have sent us samples
- WHO Influenza website data
- Australian NNDSS database
- Staff at Melbourne WHO CC
- Other WHO CC's

The Melbourne WHO Collaborating Centre for Reference and Research on Influenza is supported by the Australian Government Department of Health