Influenza in 2025:
a program at the crossroads

Chris Blyth

Professor, School of Medicine, UWA

Head, Wesfarmers Centre of Vaccines and Infectious Diseases, TKI

ID physician, Department of Infectious Diseases, PCH

Clinical Microbiologist, PathWest Laboratory Medicine WA

christopher.blyth@uwa.edu.au

“Each year enormous effort goes into producing influenza vaccines for that specific year and delivering them to appropriate sections of the population. Is this effort justified?”

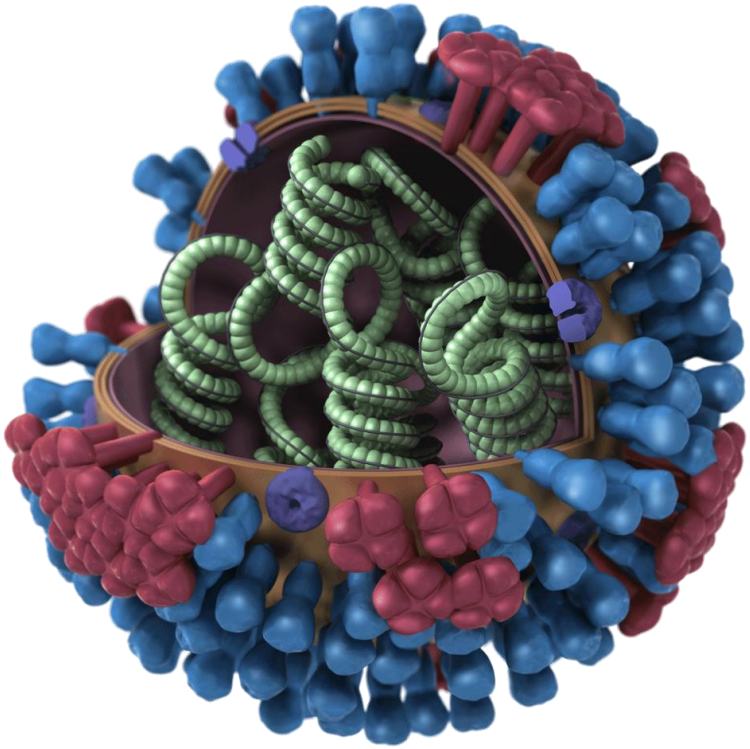
Influenza vaccination: policy versus evidence

Tom Jefferson, 2006

Summary

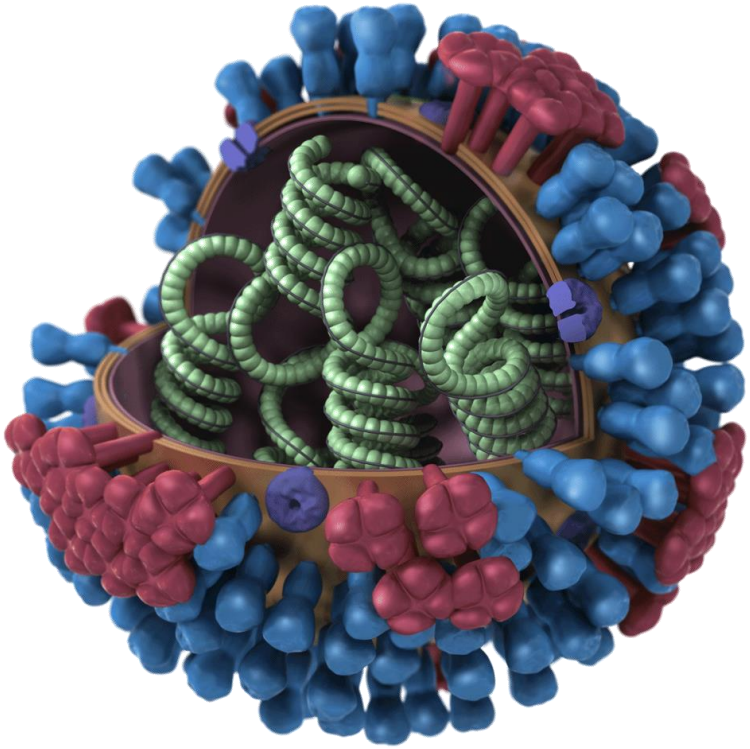
- The virus
- Seasonal influenza and who is at risk?
- Influenza vaccines and do they work?
- Emerging influenza viruses / HPAI
- Next steps

The virus



- Family of enveloped RNA viruses with a segmented genome
  - Influenza A – strain shift and drift
  - Influenza B – strain drift
  - Influenza C – rarely causes disease
- Unique features
  - Haemogglutinin
  - Neuraminidase
  - Segmented genome

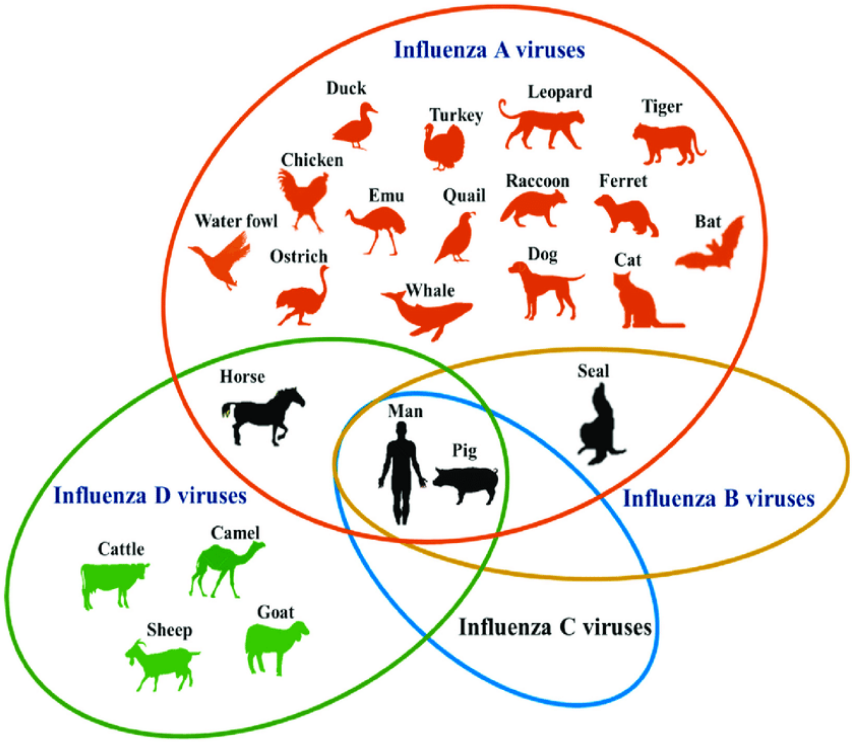
The virus



- RNA polymerases lack the ability to proof-read
  - Mutations occur more frequently with RNA viruses
- Mutations result in periodic changes in haemogglutinin: **Strain drift**
- Strain drift makes immunity short lived: **annual epidemics**

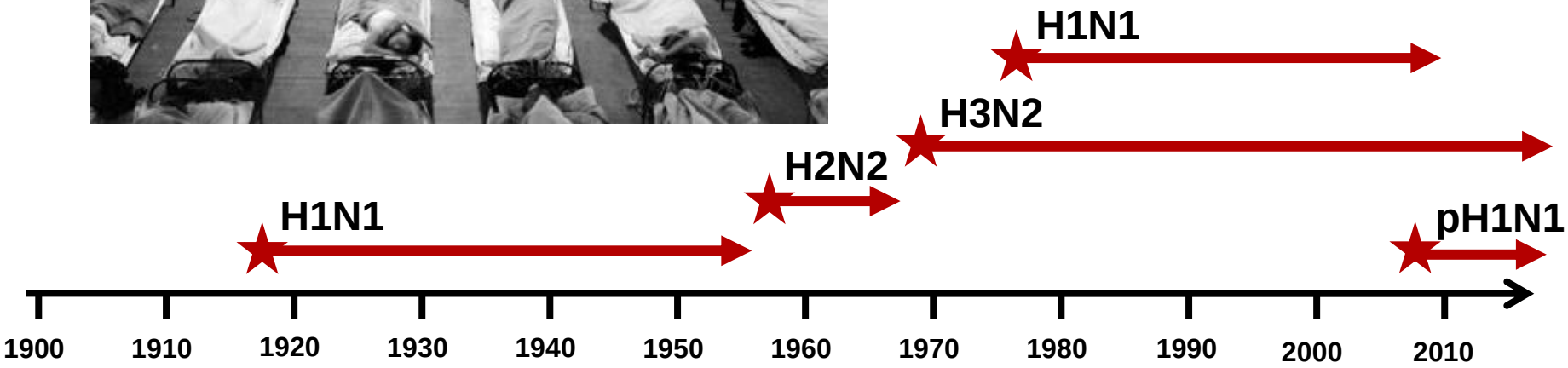
The virus

- A segmented genome allows the genetic reassortment of the influenza genome: **Strain shift**



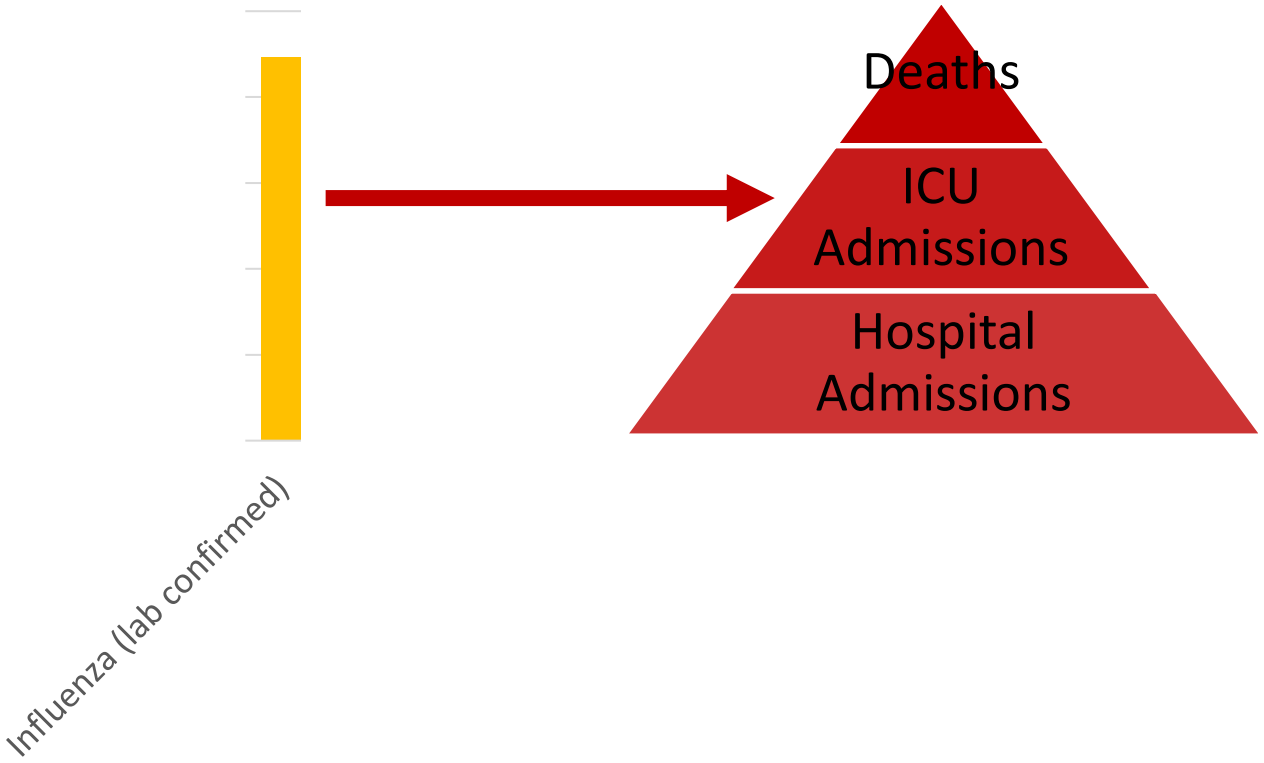
The virus

- No (little) protective immunity exists against new reassorted viruses: **episodic pandemics**

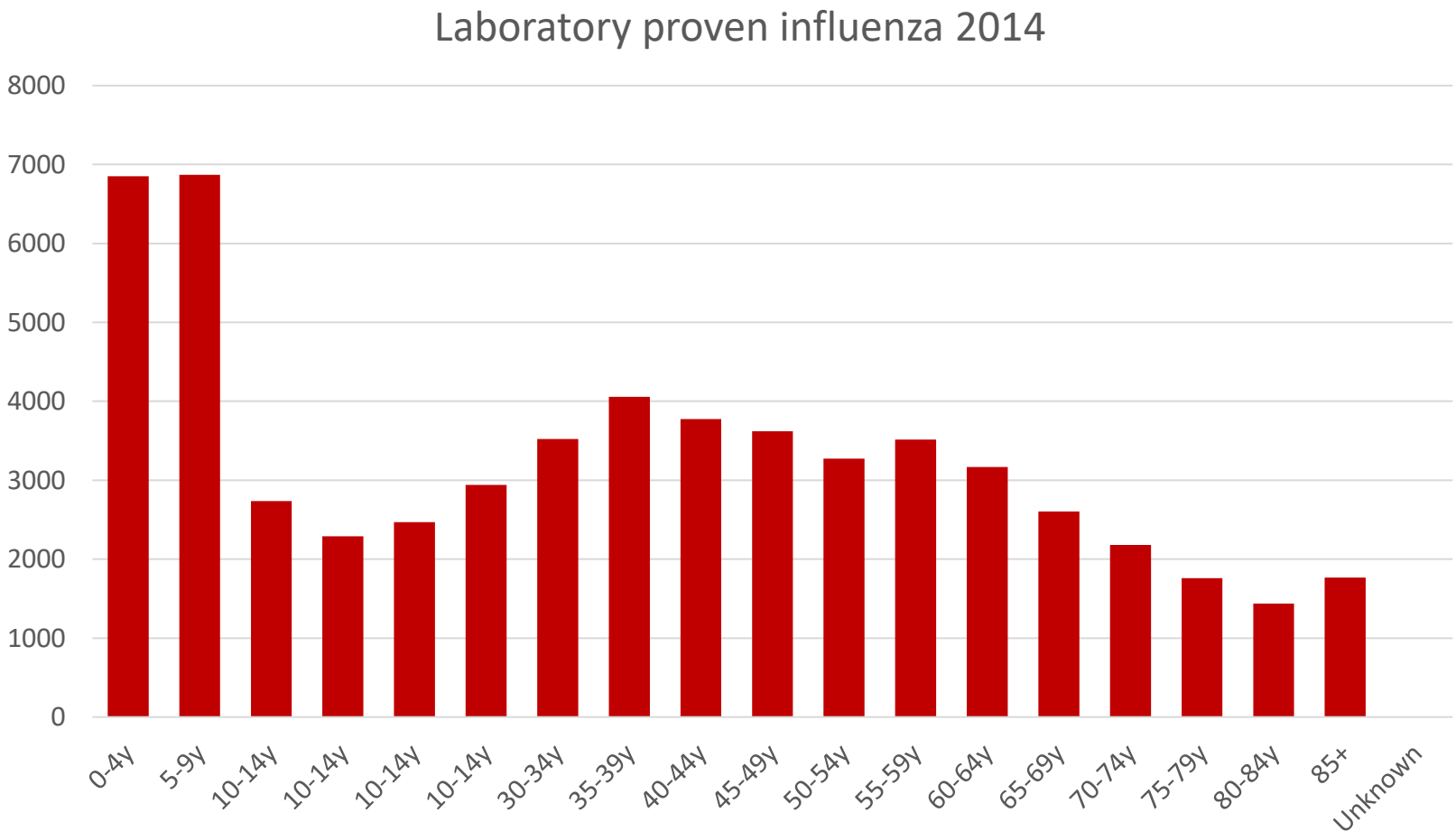


Each year, approximately 10% of the worlds population catch influenza.

How many people get the flu?

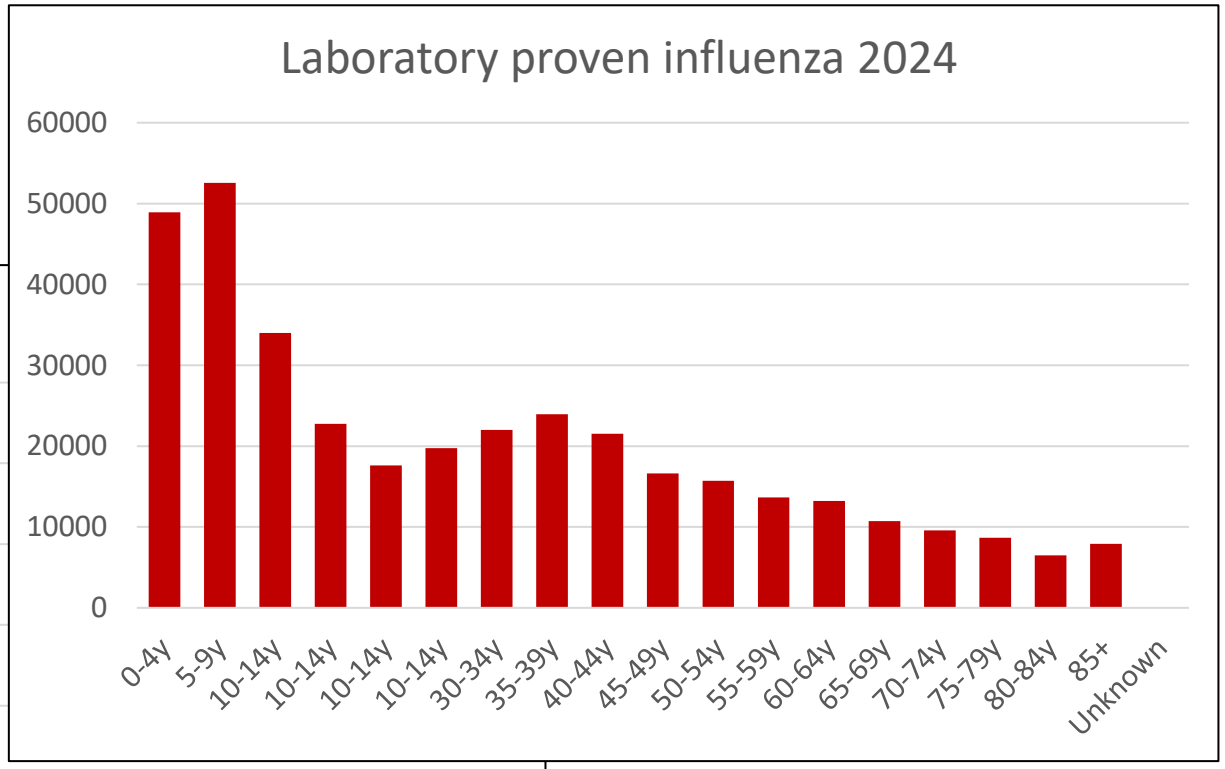


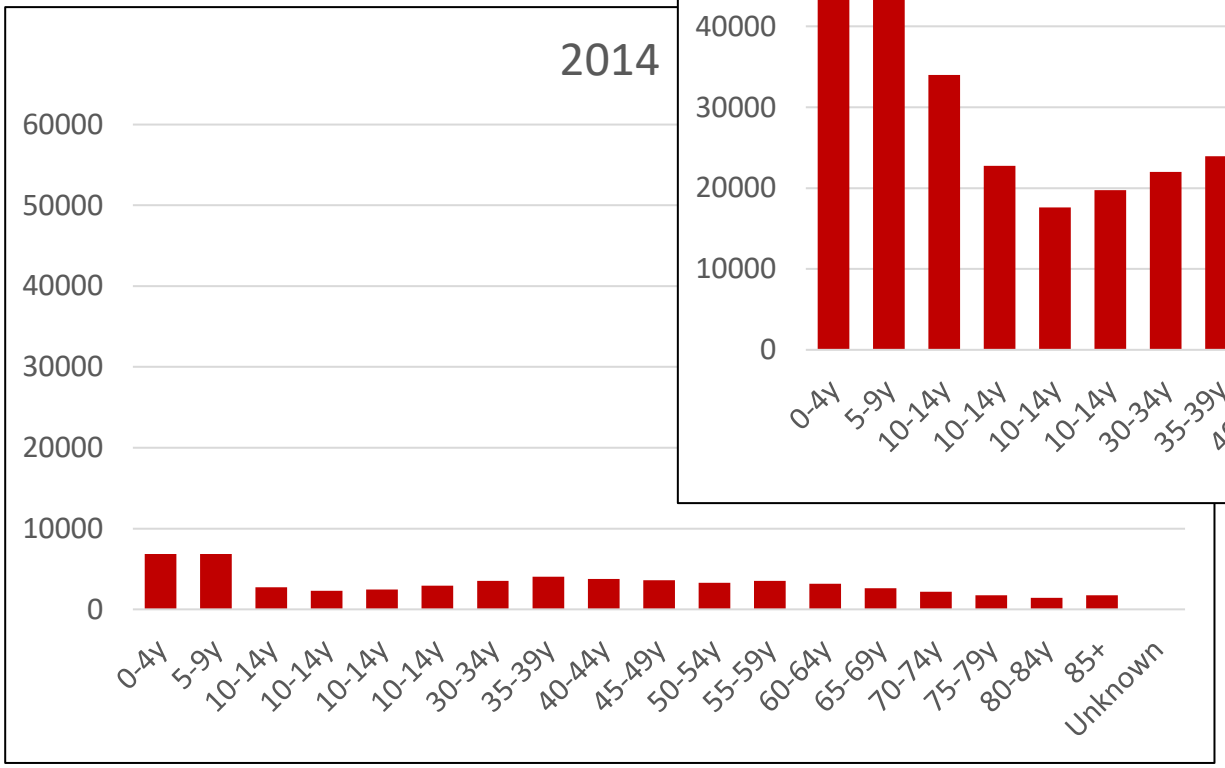
How many people get the flu?



NNDSS December 2014

How many people get the flu?





NNDSS March 2025

Summary

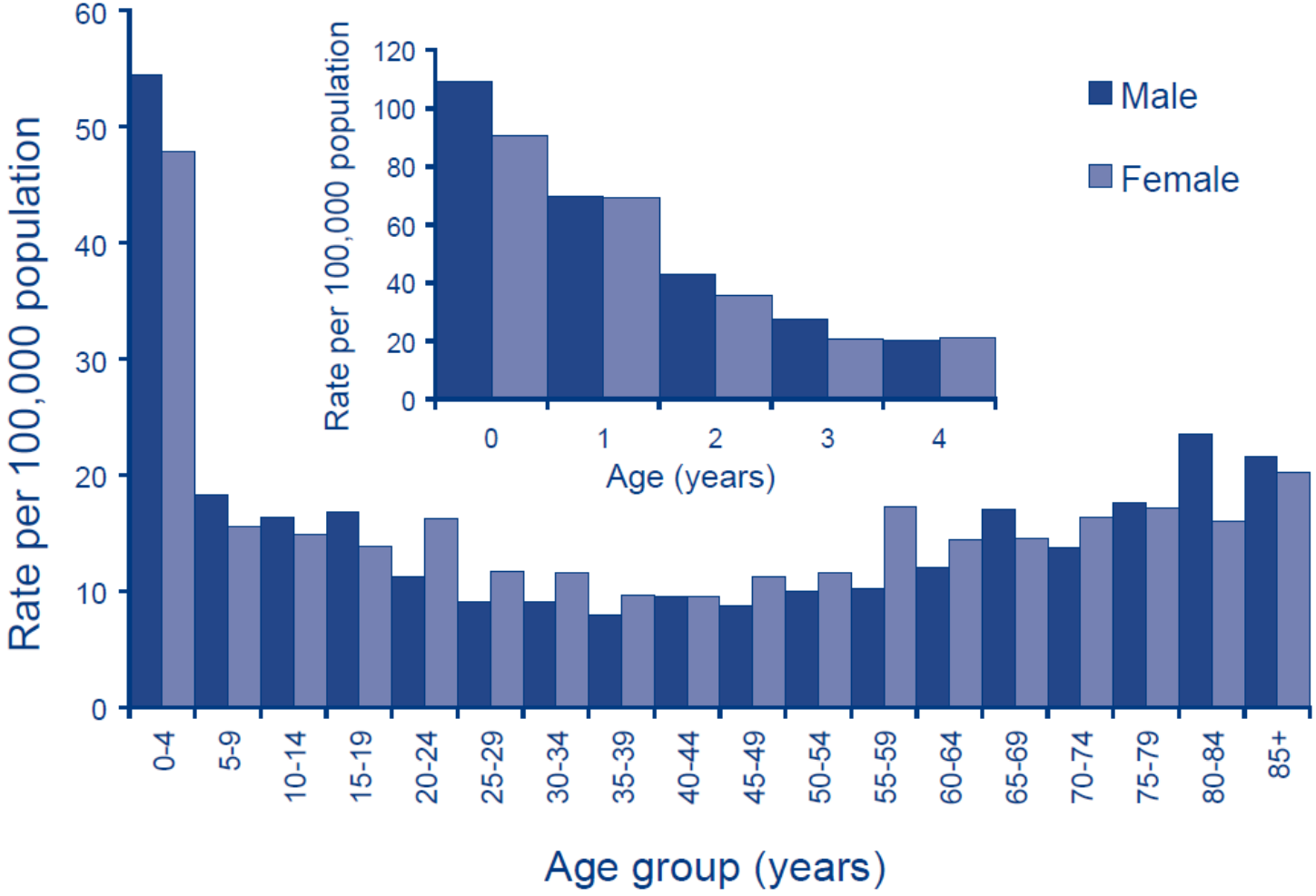
- The virus
- Seasonal influenza and who is at risk?
- Influenza vaccines and do they work?
- Emerging influenza viruses / HPAI
- Next steps

Who is at risk?

- We are all susceptible to influenza infection

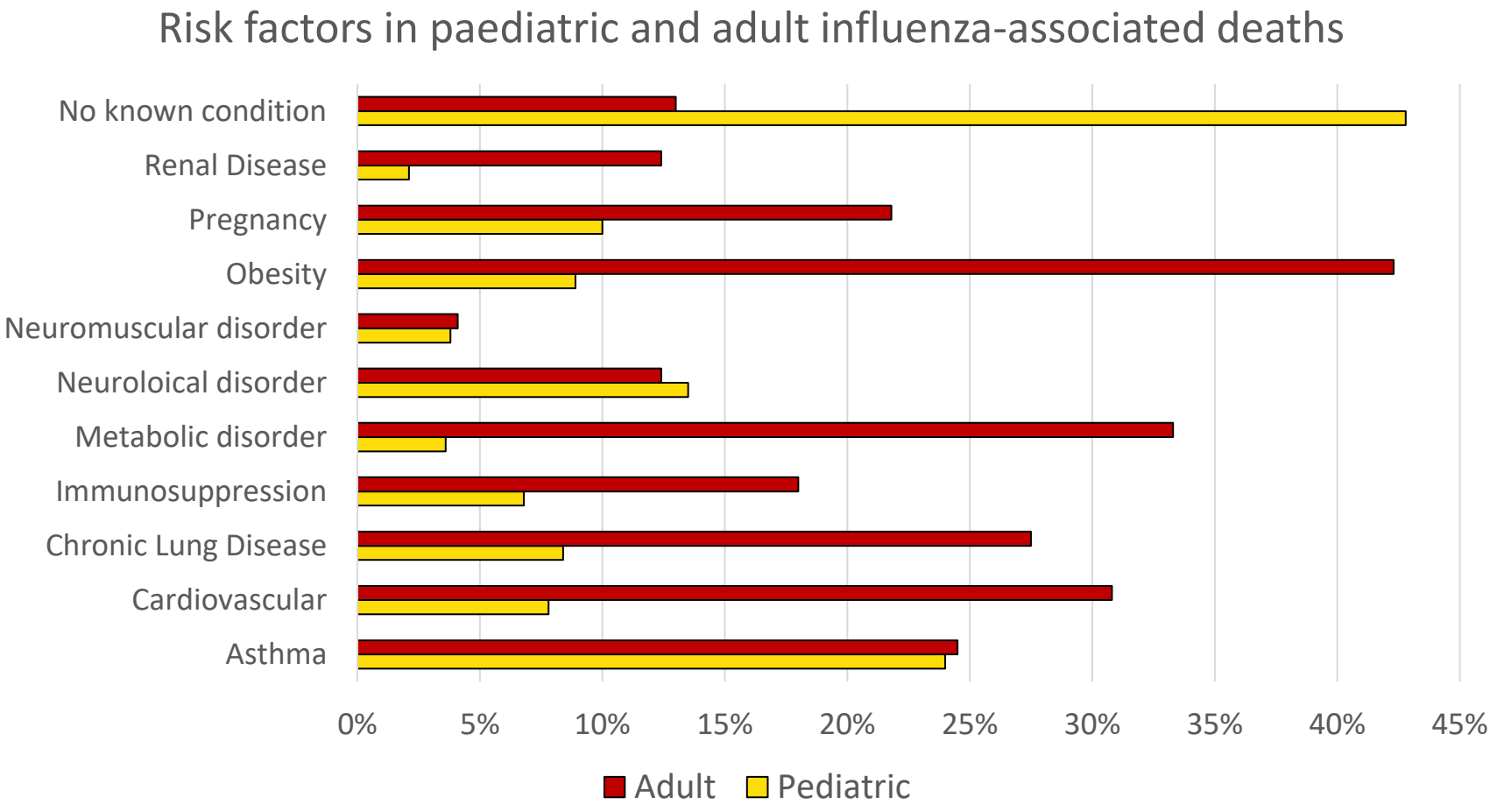
- Specific populations are at greatest risk of morbidity and mortality
  - The young
  - The elderly
  - Those with underlying comorbid conditions
  - Pregnant people
  - Aboriginal people

Influenza in children



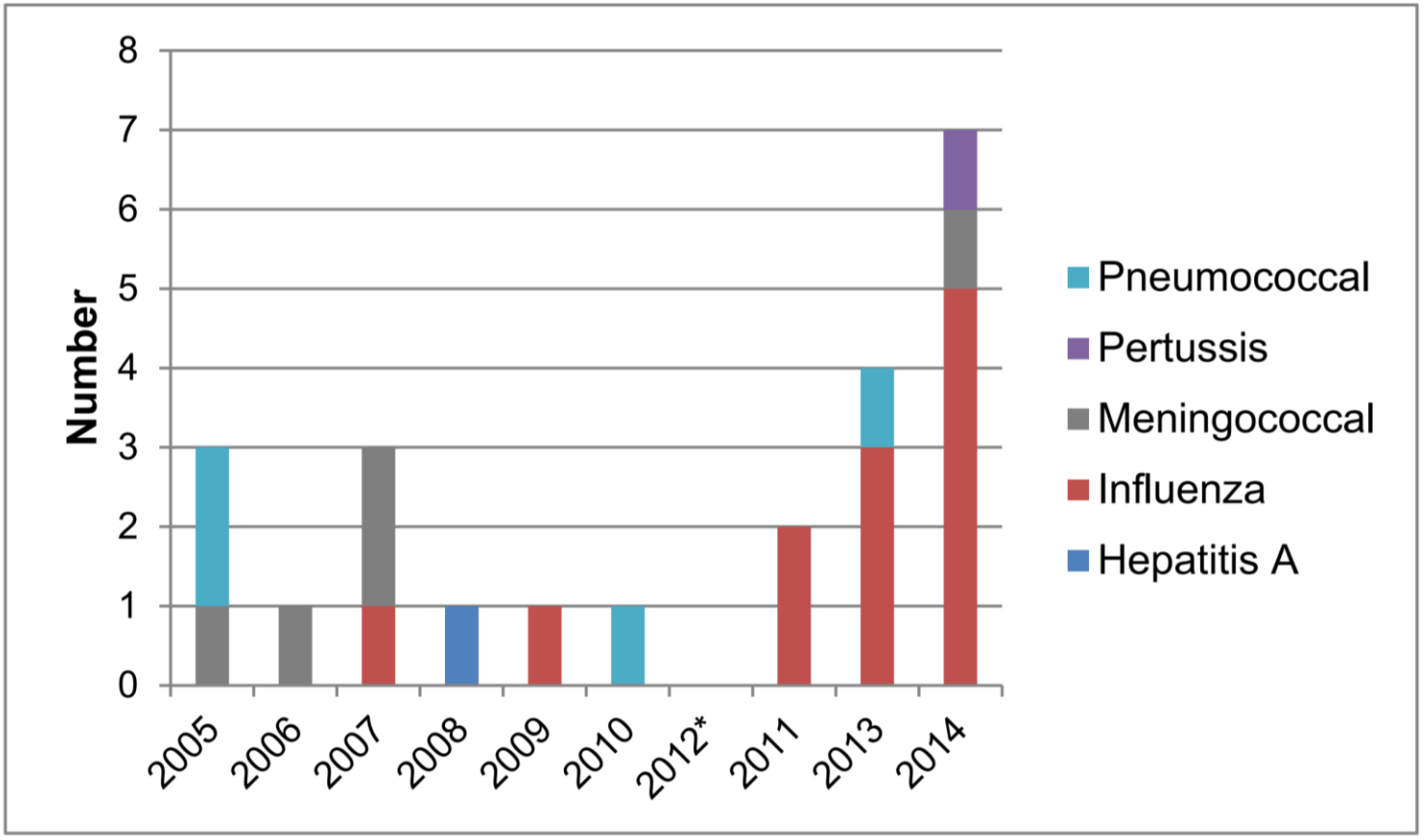
Owen R et al. CDI 2008

Influenza in children



http://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html

Influenza in children



NCIRS NSW report, 2016

Influenza in children

Flu kills three young children

PETA RULE and DEBBIE GUEST

Three children have been killed by the flu in Perth in the past few days, prompting experts to issue an urgent warning that parents should take their children to the doctor as soon as they show signs of the illness.

The three children were all under five and lived in the metropolitan area. It is understood each of them died within 24 hours of showing the first signs of the flu, which doctors say was a form of the common influenza A strain. They warned that listlessness, cough and fever were the key symptoms parents should look for and urged them to seek medical advice immediately.

"While we do not want to create unnecessary panic, it is important for parents to be aware that the disease can cause serious illness within 24 hours," Health Department director of communicable disease control Paul Van Buynder said last night.

Two of the deaths were at Princess Margaret Hospital and at least two of the children had also contracted pneumonia as a result of the virus, which could have contributed to their deaths.

Doctors across the State have been warned that they may be inundated by worried parents, prompting the Health Department to advise them of the details of the deaths.

Australian Medical Association president Geoff Dobb said influenza A strain was one of the most common during winter and that West Australians were particularly vulnerable because it had been several years since the last flu epidemic.

He said parents should not be worried if their children simply had a runny nose and headache, though they should look out for a fever above 38C.

"The critical thing is the combination of a fever and a cough," he said. "What we're talking about here is not just having a runny nose and feeling unwell, often people refer to that loosely as having the flu. A true influenza will make you feel really unwell, more severe with cough fever and muscular aches and pain."

He said that unlike the flu, people with a cold may have a sore throat and runny nose, followed by a cough, but without a significant fever.

Parents can call Health Direct on 1800 020 080 for advice and locations of their nearest after-hours clinic.

West Australian Newspaper: 7th July 2007

Influenza in children

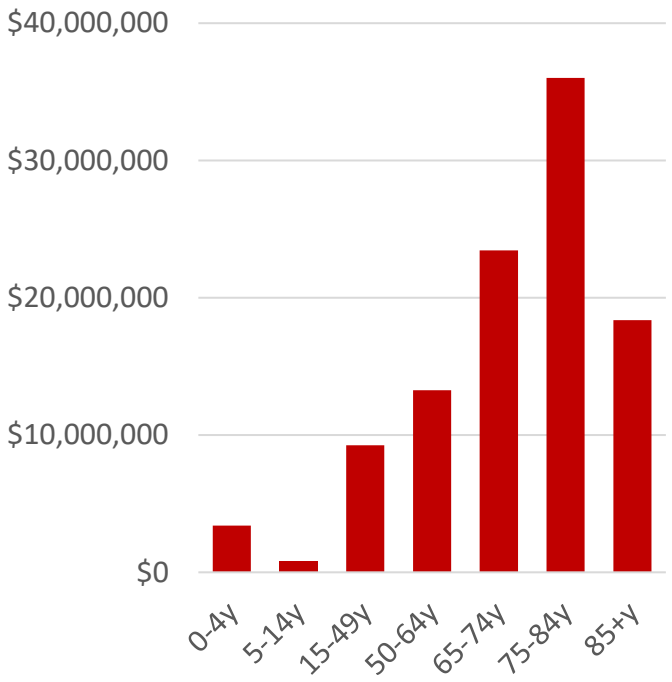
Hospitalised paediatric flu in Australia

- 30-35% are < 2 years; 60-70% are < 5 years
- 5-8% Indigenous
- 35-45% have comorbidities
- 8-14% admitted to intensive care
- Median length of stay 3 days (IQR 1-5d)
- Death is uncommon (but occurs, every year)

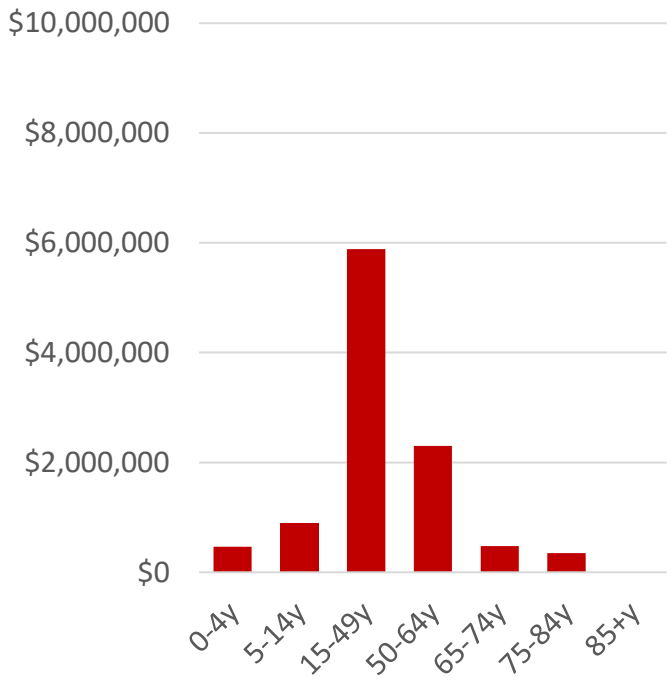
PAEDS-FluCAN data: ongoing

Influenza in the elderly

Estimated costs of influenza: hospitalisation



Estimated costs of influenza: GP visits



$115 million ($72.3–$170.1M) dollars per annum

Newall AT et al, Vaccine 2008

Influenza in the elderly

Hospitalised flu in older Australians

- 30% are 65-79 years; 30% are 80 years+
- 4-6% are Indigenous
- 80% have comorbidities; 5-7% are NH residents
- 1-2% are pregnant
- 8-14% admitted to intensive care
- Median length of stay 6 days (IQR 4-10d)
- In hospital mortality: 3-6% in elderly adults

PAEDS-FluCAN data: ongoing

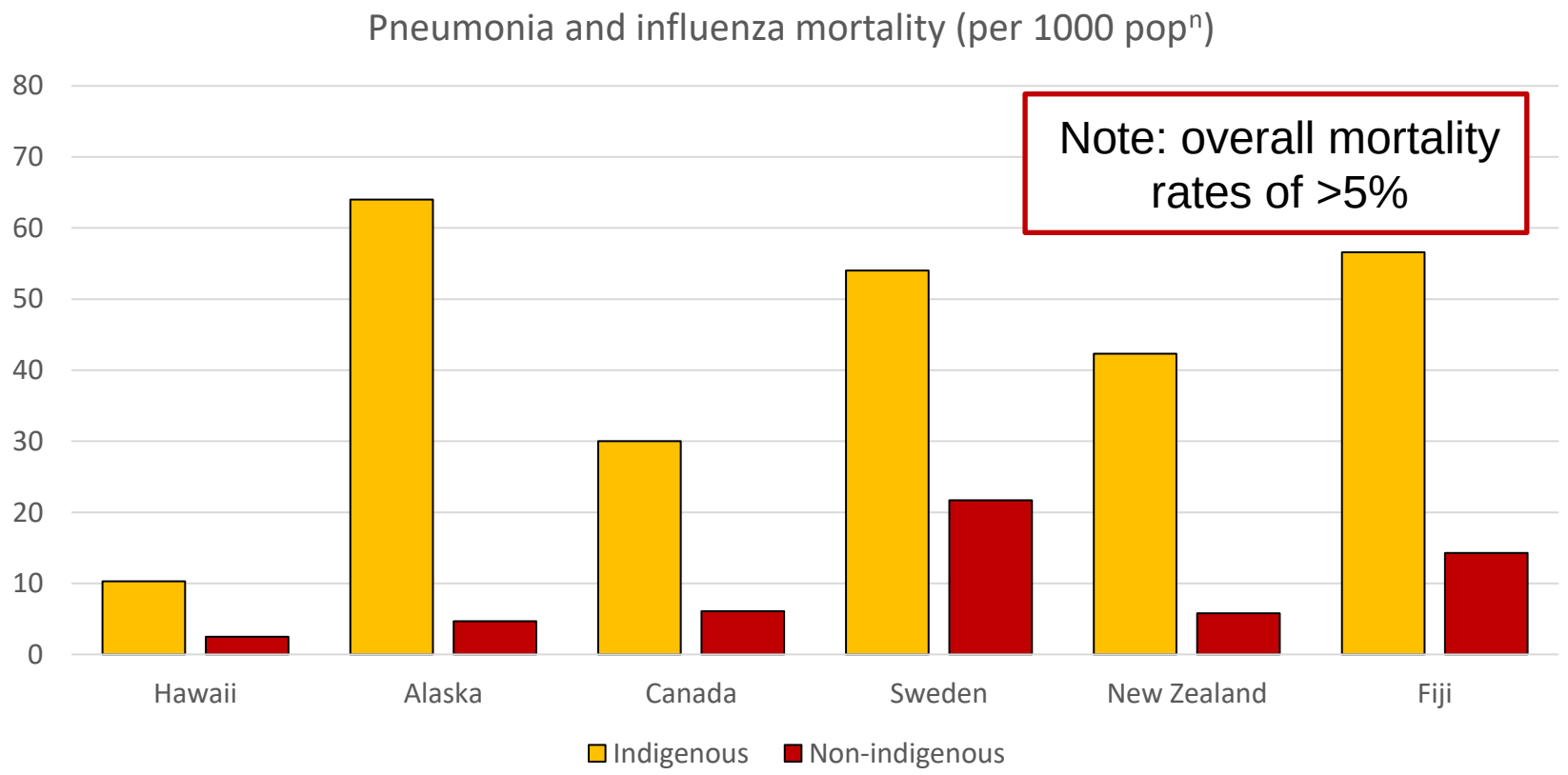
High risk of complications

- Heart disease (Cyanotic CHD, CAD, CHF)
- Chronic lung disease (Bronchiectasis, COPD, sev. asthma)
- Chronic neurological condition
- Immunosuppressive conditions
- Chronic renal failure
- Chronic liver disease
- Obesity
- Diabetes and specific metabolic disorders
- Trisomy 21, Chronic aspirin use (children)

Ahmed R. Nature Immunology 2007

Indigenous populations

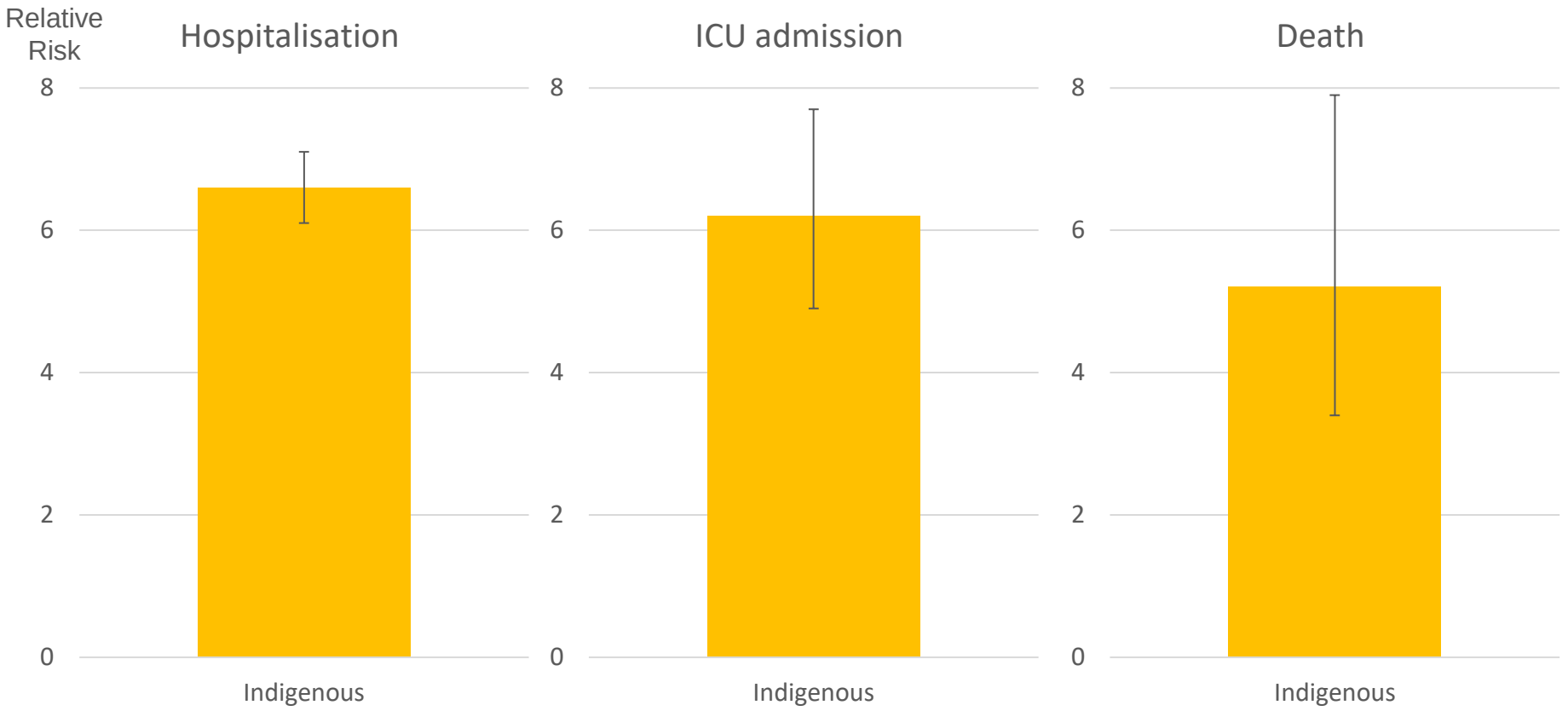
- 1918: Pneumonia and influenza



Mamelund SE. Epidemics 2011

Australian indigenous populations

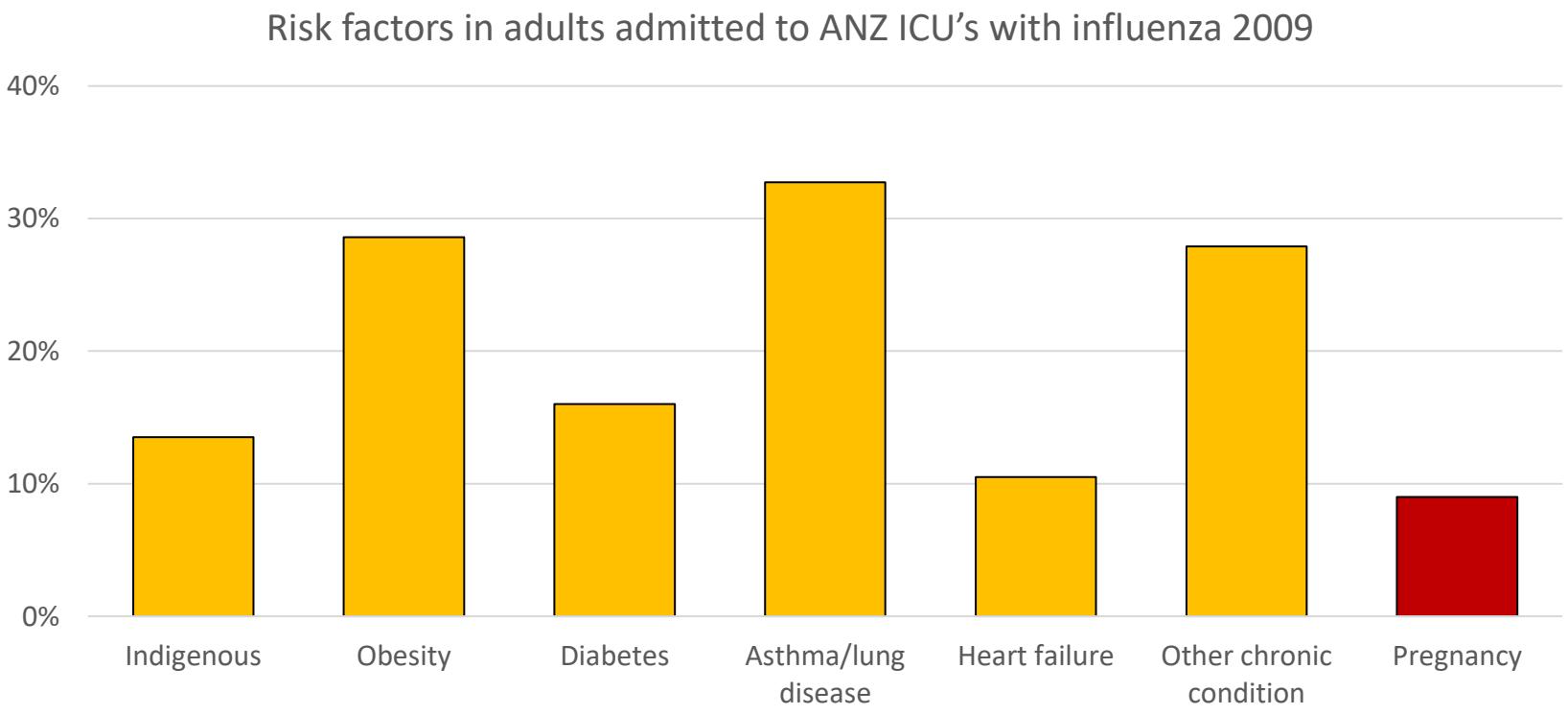
- Pandemic influenza



Kelly H et al Eurosurveillance 2009

Pregnant women

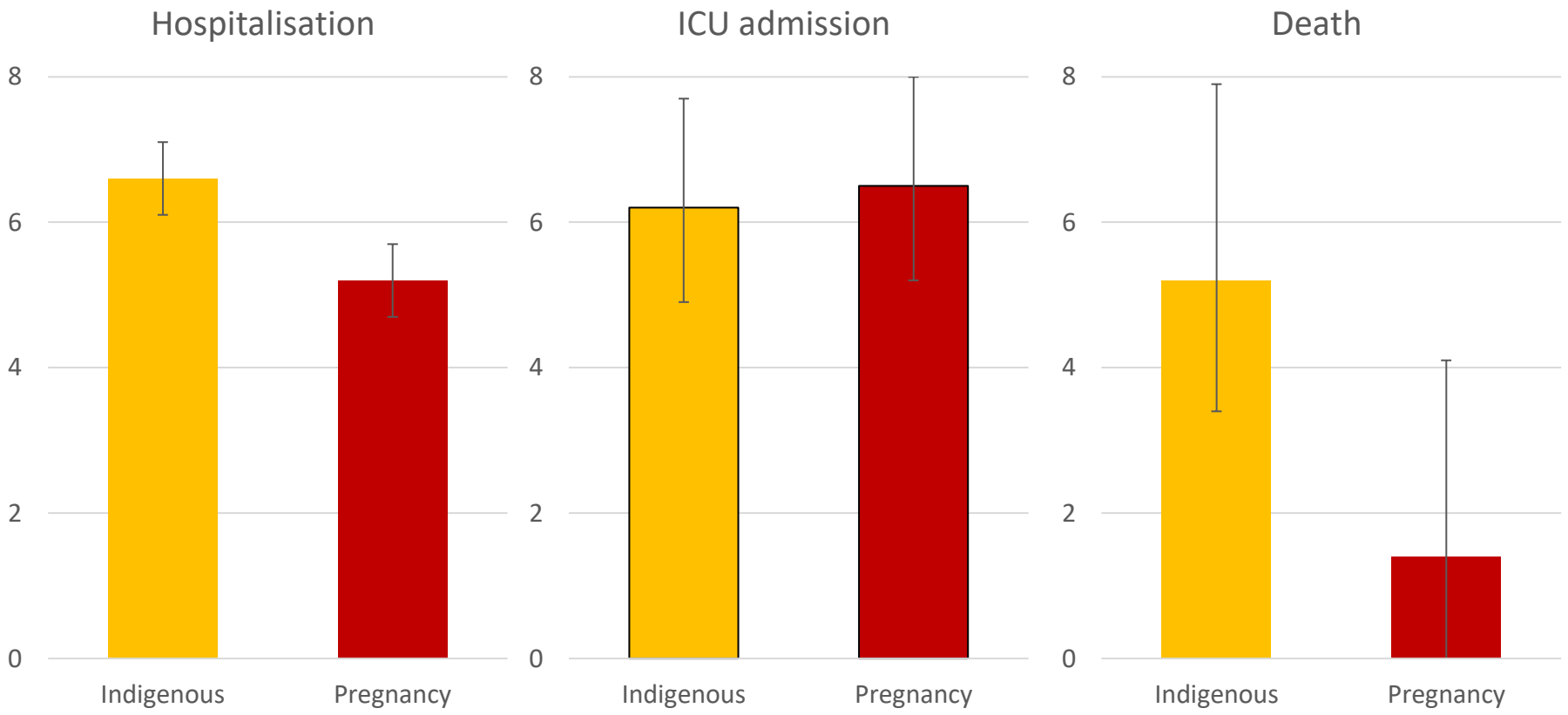
- Pregnancy is an independent risk factor for severe influenza



ANZIC Investigators, NEJM 2009

Pregnant women

- Pregnancy is an independent risk factor



Kelly H et al Eurosurveillance 2009

Who is at risk?

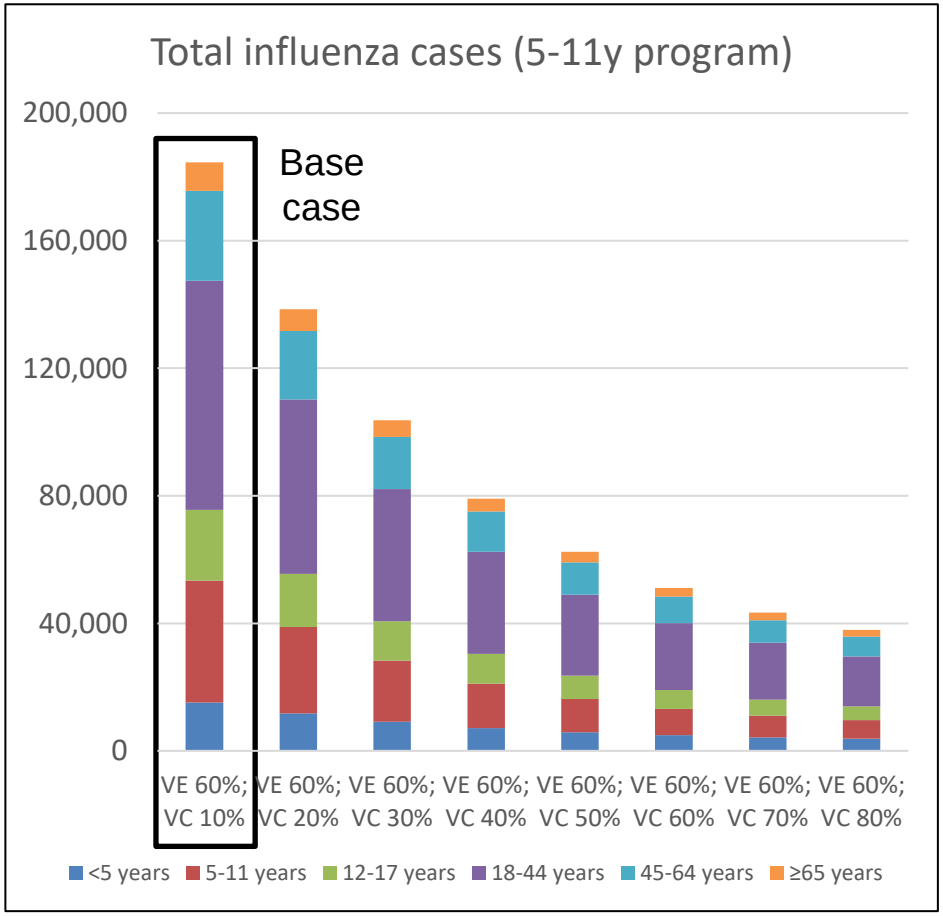
- We are all susceptible to influenza infection
- Specific populations are at greatest risk of morbidity and mortality
- School age children are at greatest risk of transmission

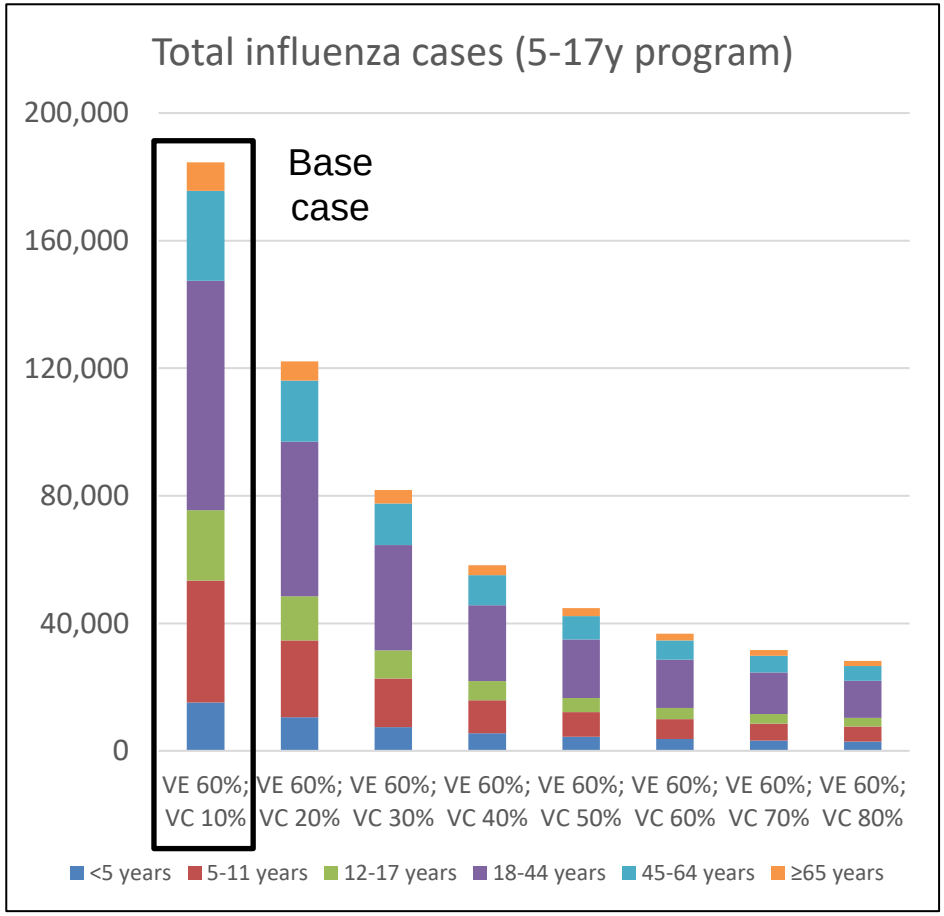
School children

Vaccinate the Vectors

Protect the grandparents

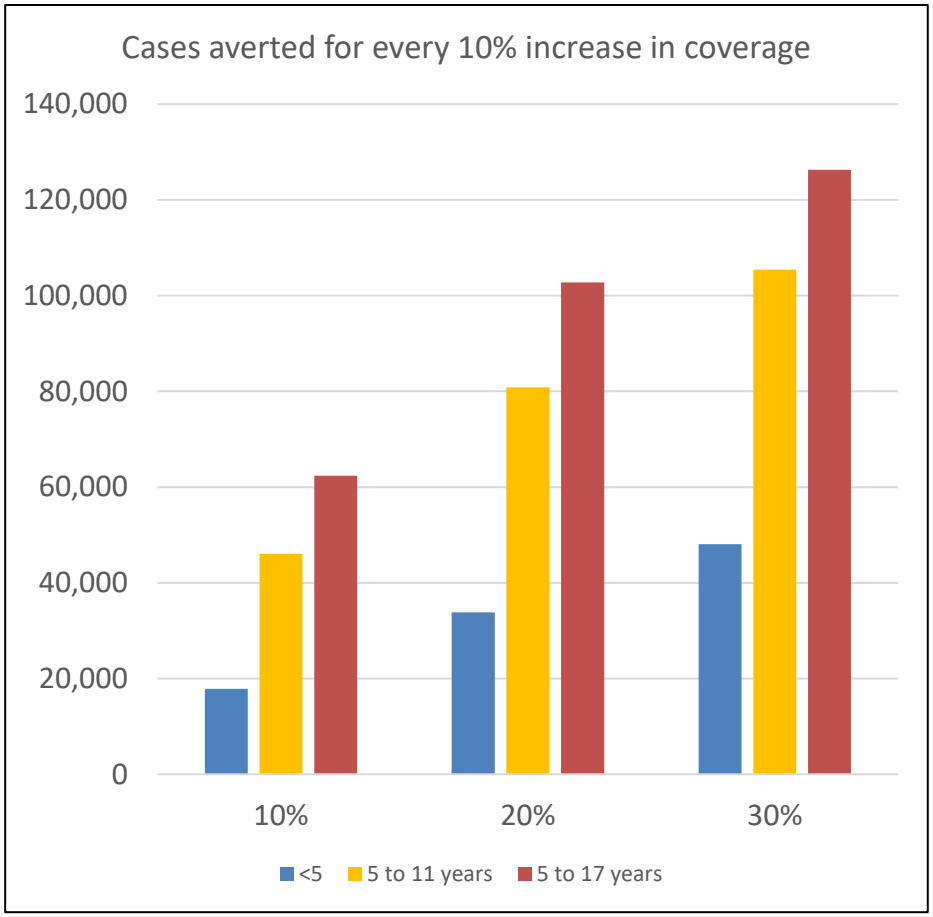
School children

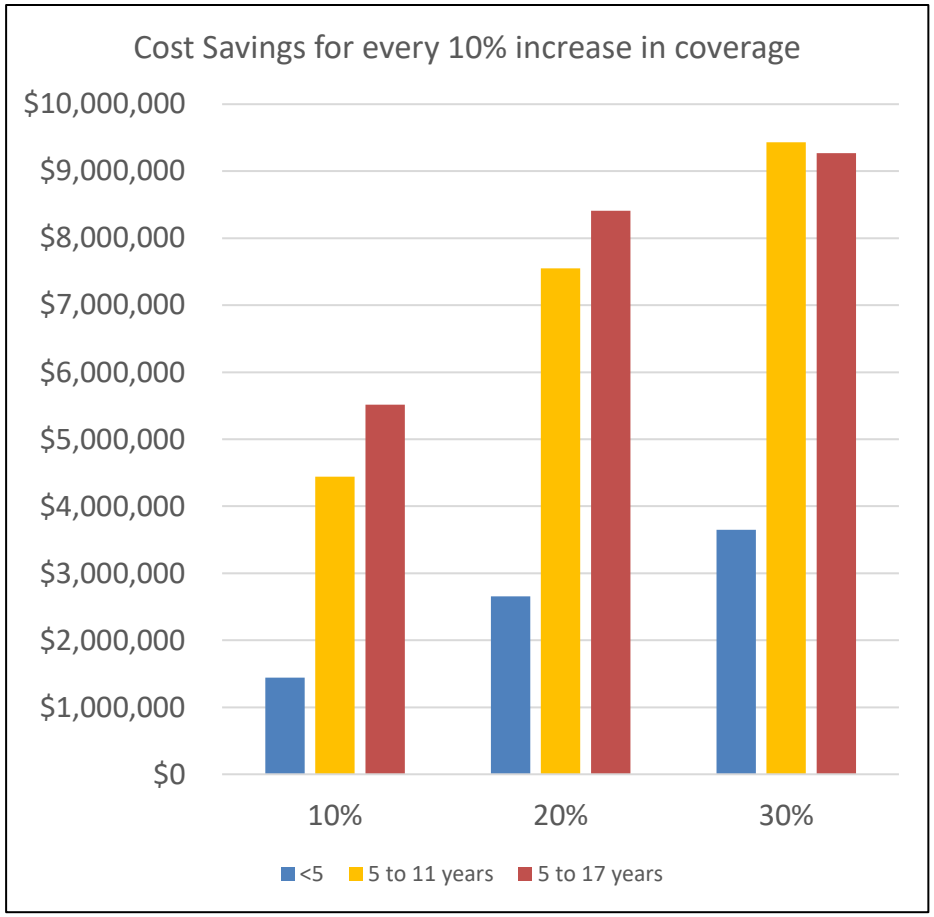




Blyth CC et al, Vaccine X, 2023

School children





Blyth CC et al, Vaccine X, 2023

Who is at risk?

- We are all susceptible to influenza infection
- Specific populations are at greatest risk of morbidity and mortality
- School age children are at greatest risk of transmission

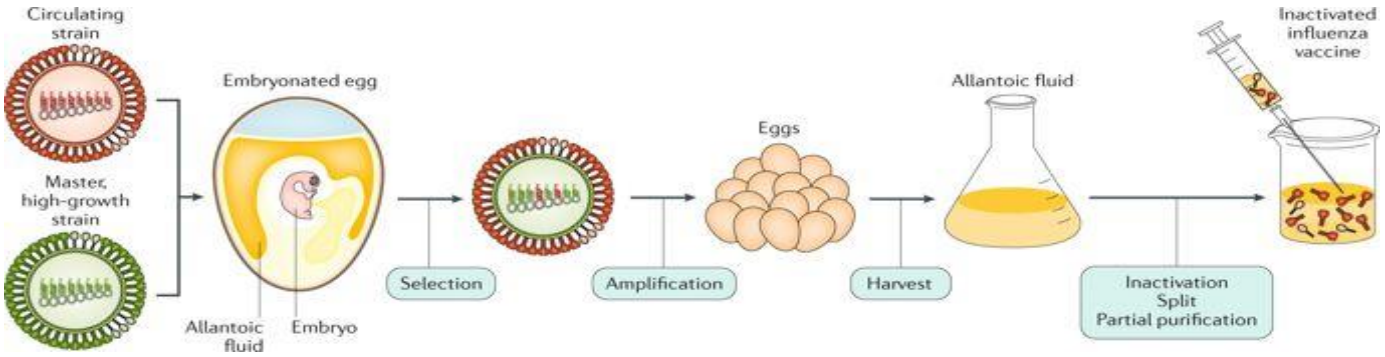
So, although we are all at risk, some are at higher risk
Strategies must be targeted, ensuring we reach those at greatest risk of influenza-associated harm

It will take more than "free-flu vaccine"

Summary

- The virus
- Seasonal influenza and who is at risk?
- Influenza vaccines and do they work?
- Emerging influenza viruses / HPAI
- Next steps

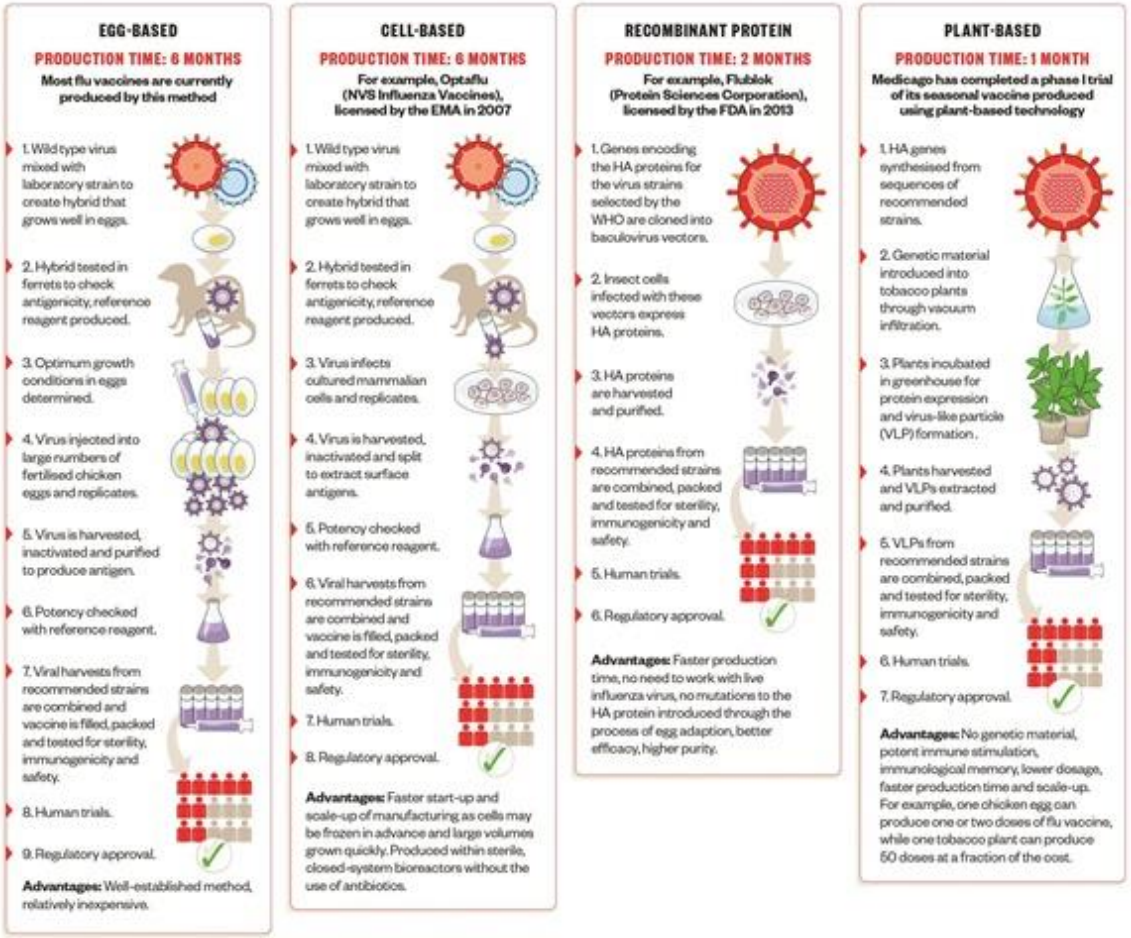
How to make an influenza vaccine?



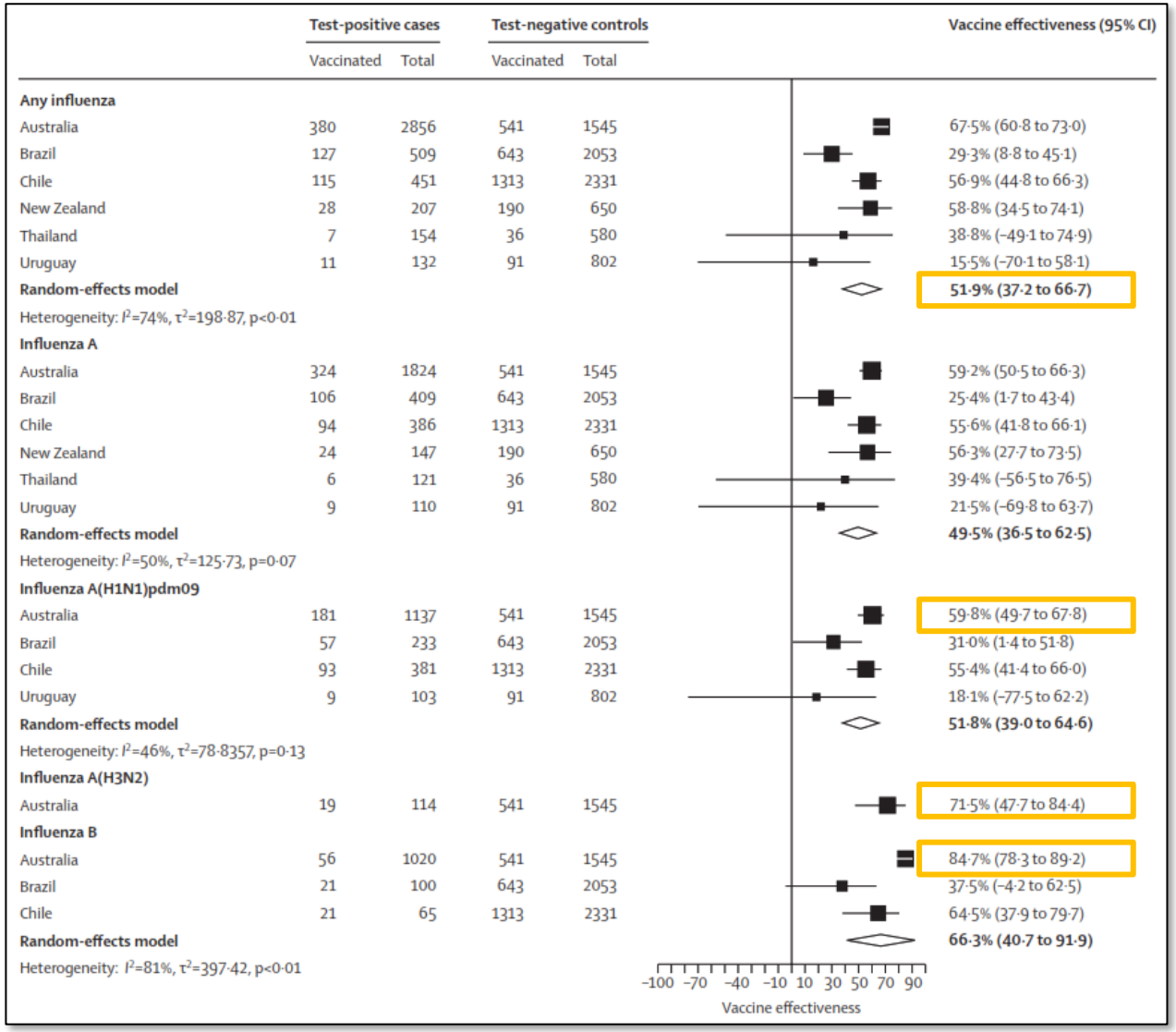
- Chose virus and inject into fertilized egg
- Incubate egg and allow for viral replication
- Collection virus-laden allantoic fluid from egg
- Deactivate and split virus
- Purify hemagglutinin
- Mix with other strains

How to make an influenza vaccine?

- Egg-free technologies being utilised



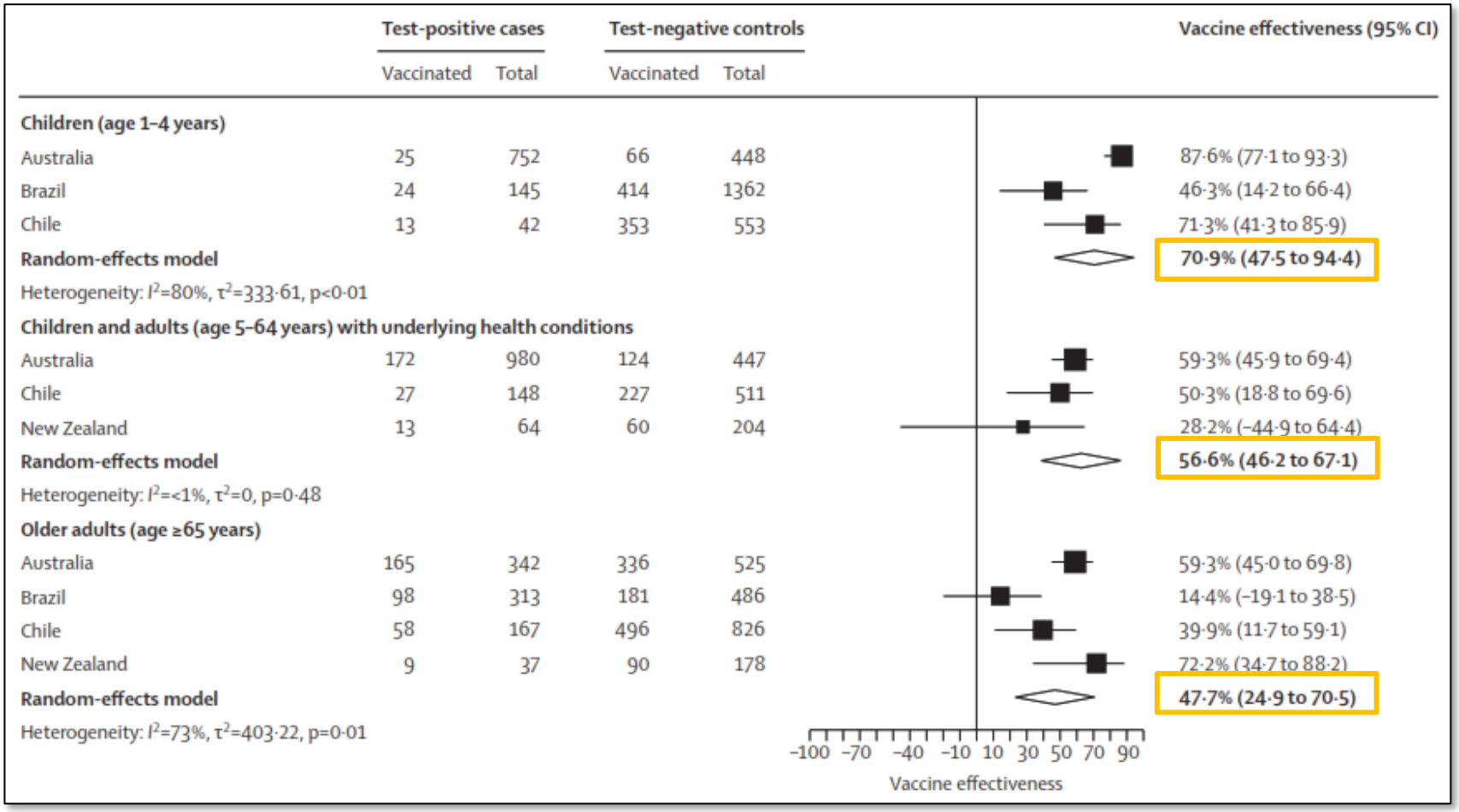
Do they work?



	Test-positive cases		Test-negative controls		Vaccine effectiveness (95% CI)
	Vaccinated	Total	Vaccinated	Total	
Any influenza					
Australia	380	2856	541	1545	67·5% (60·8 to 73·0)
Brazil	127	509	643	2053	29·3% (8·8 to 45·1)
Chile	115	451	1313	2331	56·9% (44·8 to 66·3)
New Zealand	28	207	190	650	58·8% (34·5 to 74·1)
Thailand	7	154	36	580	38·8% (−49·1 to 74·9)
Uruguay	11	132	91	802	15·5% (−70·1 to 58·1)
Random-effects model					**51·9% (37·2 to 66·7)**
Heterogeneity: I^2=74%, τ^2=198·87, p<0·01					
Influenza A					
Australia	324	1824	541	1545	59·2% (50·5 to 66·3)
Brazil	106	409	643	2053	25·4% (1·7 to 43·4)
Chile	94	386	1313	2331	55·6% (41·8 to 66·1)
New Zealand	24	147	190	650	56·3% (27·7 to 73·5)
Thailand	6	121	36	580	39·4% (−56·5 to 76·5)
Uruguay	9	110	91	802	21·5% (−69·8 to 63·7)
Random-effects model					**49·5% (36·5 to 62·5)**
Heterogeneity: I^2=50%, τ^2=125·73, p=0·07					
Influenza A(H1N1)pdm09					
Australia	181	1137	541	1545	59·8% (49·7 to 67·8)
Brazil	57	233	643	2053	31·0% (1·4 to 51·8)
Chile	93	381	1313	2331	55·4% (41·4 to 66·0)
Uruguay	9	103	91	802	18·1% (−77·5 to 62·2)
Random-effects model					**51·8% (39·0 to 64·6)**
Heterogeneity: I^2=46%, τ^2=78·8357, p=0·13					
Influenza A(H3N2)					
Australia	19	114	541	1545	71·5% (47·7 to 84·4)
Influenza B					
Australia	56	1020	541	1545	84·7% (78·3 to 89·2)
Brazil	21	100	643	2053	37·5% (−4·2 to 62·5)
Chile	21	65	1313	2331	64·5% (37·9 to 79·7)
Random-effects model					**66·3% (40·7 to 91·9)**
Heterogeneity: I^2=81%, τ^2=397·42, p<0·01					

Gharpure R et al, Lancet Global Health 2025

Do they work – moderately protective?



Gharpure R et al, Lancet Global Health 2025

Do they work – moderately protective?

Vaccine / Registered age group	**Vaxigrip Tetra** 0.5 mL (Sanofi)	**Flucelvax Quad** 0.5 mL (CSL Seqirus)	**FluQuadri** 0.5 mL (Sanofi)	**Afluria Quad** 0.5mL (CSL Seqirus)	**Influvac Tetra** 0.5 mL (Viatris)	**Fluad Quad** 0.5 mL (CSL Seqirus)	**Fluzone High-Dose** 0.7 mL (Sanofi)
6 months to <5 years	✓	✓	✓	X	✓	X	X
≥5 to <60 years	✓*	✓*	✓	✓	✓	X	X
≥60 to <65 years	✓*	✓*	✓	✓	✓	X	✓
≥65 years	✓	✓	✓	✓	✓	✓	✓

Egg-based influenza vaccines	Cell-based influenza vaccines
A/Victoria/4897/2022 (H1N1)pdm09-like virus	A/Wisconsin/67/2022 (H1N1)pdm09-like virus
A/Croatia/10136RV/2023 (H3N2)-like virus	A/District of Columbia/27/2023 (H3N2)-like virus
B/Austria/1359417/2021 (B/Victoria lineage)-like virus	B/Austria/1359417/2021 (B/Victoria lineage)-like virus
B/Phuket/3073/2013 (B/Yamagata lineage)-like virus	B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

Summary

- The virus
- Seasonal influenza and who is at risk?
- Influenza vaccines and do they work?
- Emerging influenza viruses / HPAI
- Next steps

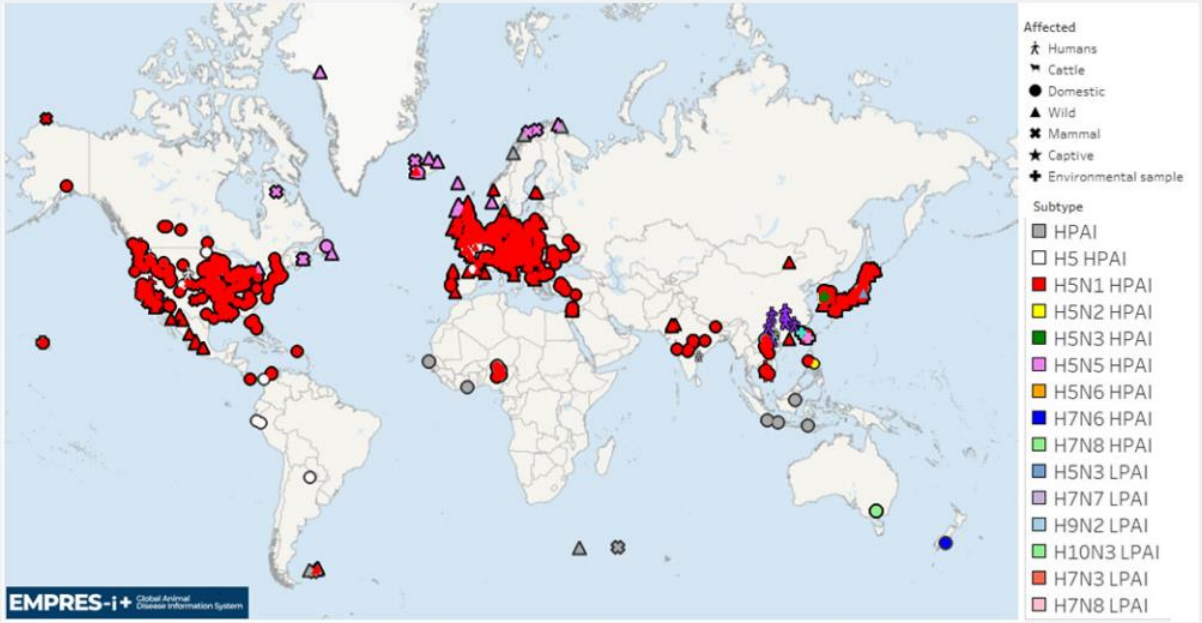
Emerging influenza viruses

Influenza A is known to circulate in many animals

- HPAI: highly pathogenic avian influenza
- LPAI: low pathogenic avian influenza

pathogenicity in birds

Map 1. *Global distribution of AIV with zoonotic potential* observed since 1 October 2024 (i.e. current wave)*



HPAI A/H5N1 2.3.4.4b

- First detected in Europe in 2020





https://www.cdc.gov/bird-flu/spotlights/h5n1-response-03192025.html

HPAI A/H5N1 2.3.4.4b

- Currently limited impact on human health
  - 70 human cases reported in US since April ’24
    - 41 following exposure to cattle
    - 24 following exposure to poultry/birds
  - 64 cases detected through targeted testing
  - 6 cases detected through routine testing
  - 1 death

https://www.cdc.gov/bird-flu/spotlights/h5n1-response-03192025.html

Emerging flu viruses - Australia

The only continent free of A/H5N1 2.3.4.4b

- Federal government funded strategies to strengthen surveillance, preparedness and response capability
- A federal response will be led by Dept of Agriculture, Fisheries and Forestry (DAFF)

Emerging flu viruses - Australia

A number of recent HPAI outbreaks detected in Australia

- HPAI H7N8 – Victoria (2025)
- HPAI H7N3 – Victoria (2024)
- HPAI H7N9 – Victoria (2024)
- HPAI H7N8 - NSW, ACT (2024)

HPAI outbreaks are the result of Australian lineage LPAI strains ‘spilling over’ from wild birds into poultry farms, where the virus mutated to become HPA

A program at the crossroads

- The virus
- Seasonal influenza and who is at risk?
- Influenza vaccines and do they work?
- Emerging influenza viruses / HPAI
- Next steps

A program at the crossroads

Declining use of flu vaccines, particularly in high risk populations, will lead to increased morbidity and mortality

No single intervention will turn around this trend: greater collaborative efforts are required