



IMMUNISATION
COALITION

MASTERCLASS: IMMUNISATION OF OLDER ADULTS

Influenza

Professor Paul Van Buynder



We were young and beautiful

Now we are just beautiful

Demotivation.us



The global burden of seasonal influenza

Each year, influenza related illness:

- Causes **3 million – 5 million** cases of severe illness¹
- Causes up to **650,000** influenza-related respiratory deaths annually¹
- **All** countries are affected
- Significant economic cost. Estimated average **annual total economic burden is USD \$11.2 billion**²



Northern hemisphere
Influenza peak:
November–March

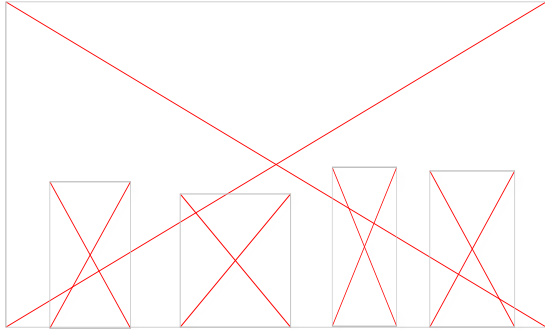
Tropics
Year-round
activity

Southern hemisphere
Influenza peak:
April–September

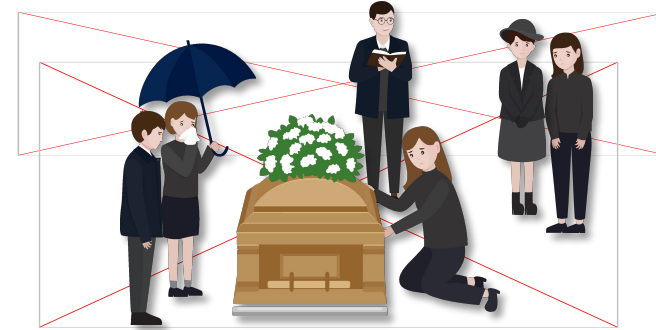
1. Influenza. World Health Organization Web site Jan 2018. <http://www.who.int/mediacentre/factsheets/fs211/en/> Accessed August 2020

2. Putri, Wayan C.W.S. et al , Economic burden of seasonal influenza in the United States , Vaccine. 2018 Jun 22;36(27):3960-3966. Found at: <https://pubmed.ncbi.nlm.nih.gov/29801998/> (Accessed September 2020)

Impact of Influenza in Australia

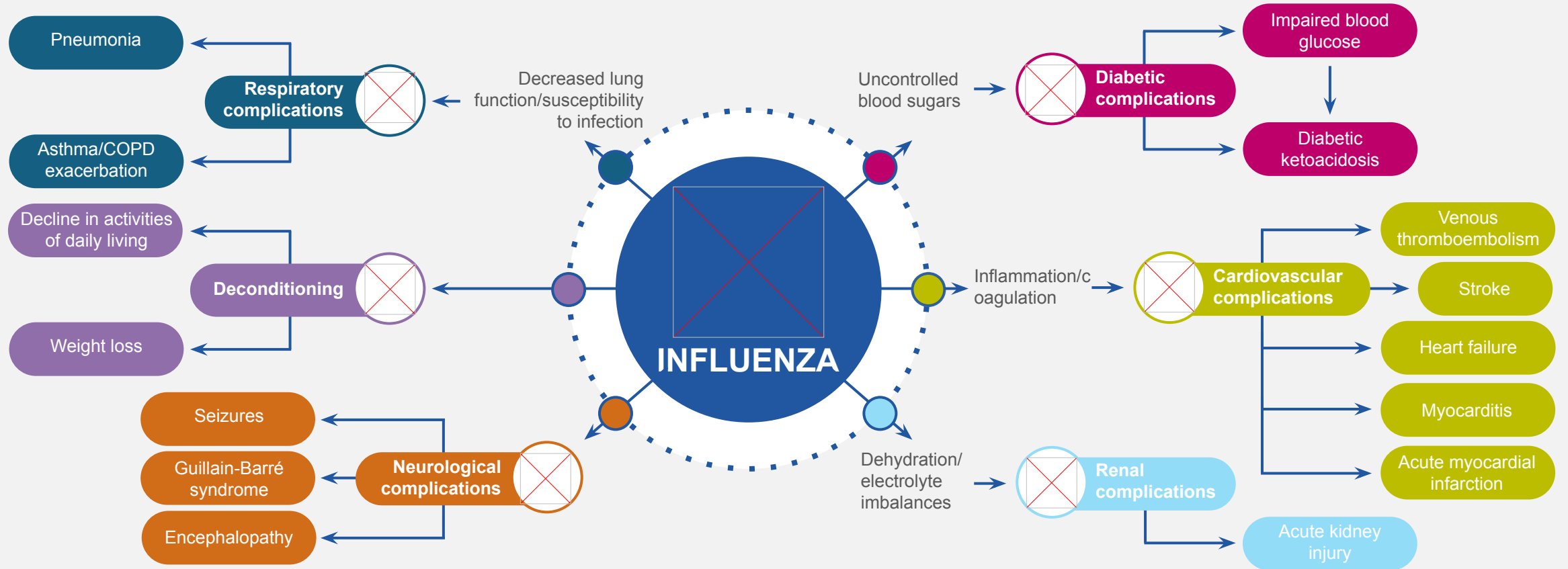


- Annual influenza attack rates in the community are typically **5–10%** but can be as high as **20%** in some years¹
- Influenza contributes to more than 1/3 of the total burden due to all Vaccine Preventable Diseases in Australia.⁴



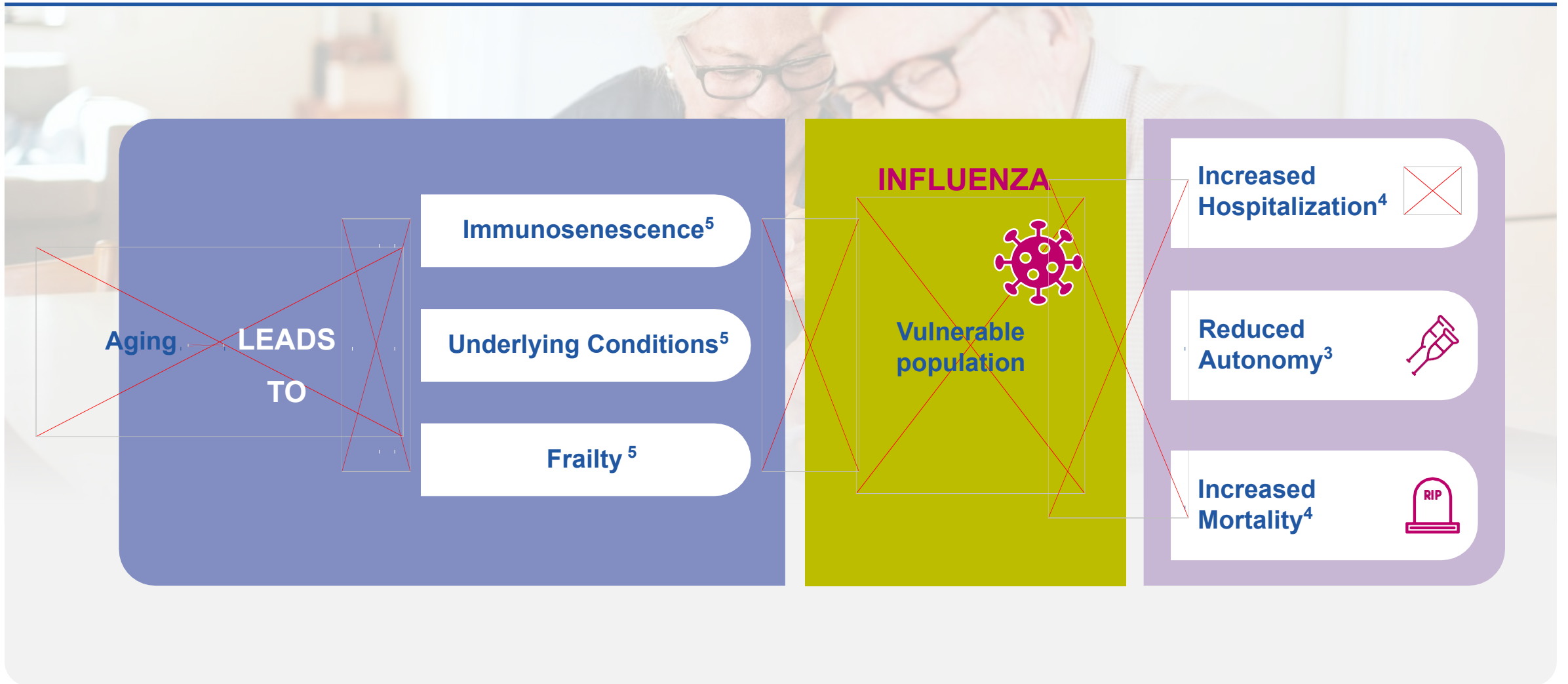
- Each year, influenza & associated complications are estimated to be responsible for approximately:
 - 3,000 deaths in older Australians¹
 - 18,000 hospitalisations²
 - 300,000 doctor visits²
 - 1,500,000 lost work days³

The Broader Impact of Influenza



References: 1-[Macias et al. Vaccine. 2020 Oct 9;S0264-410X\(20\)31209-3.](#)

Older adults are more vulnerable to influenza infection^{1,2}

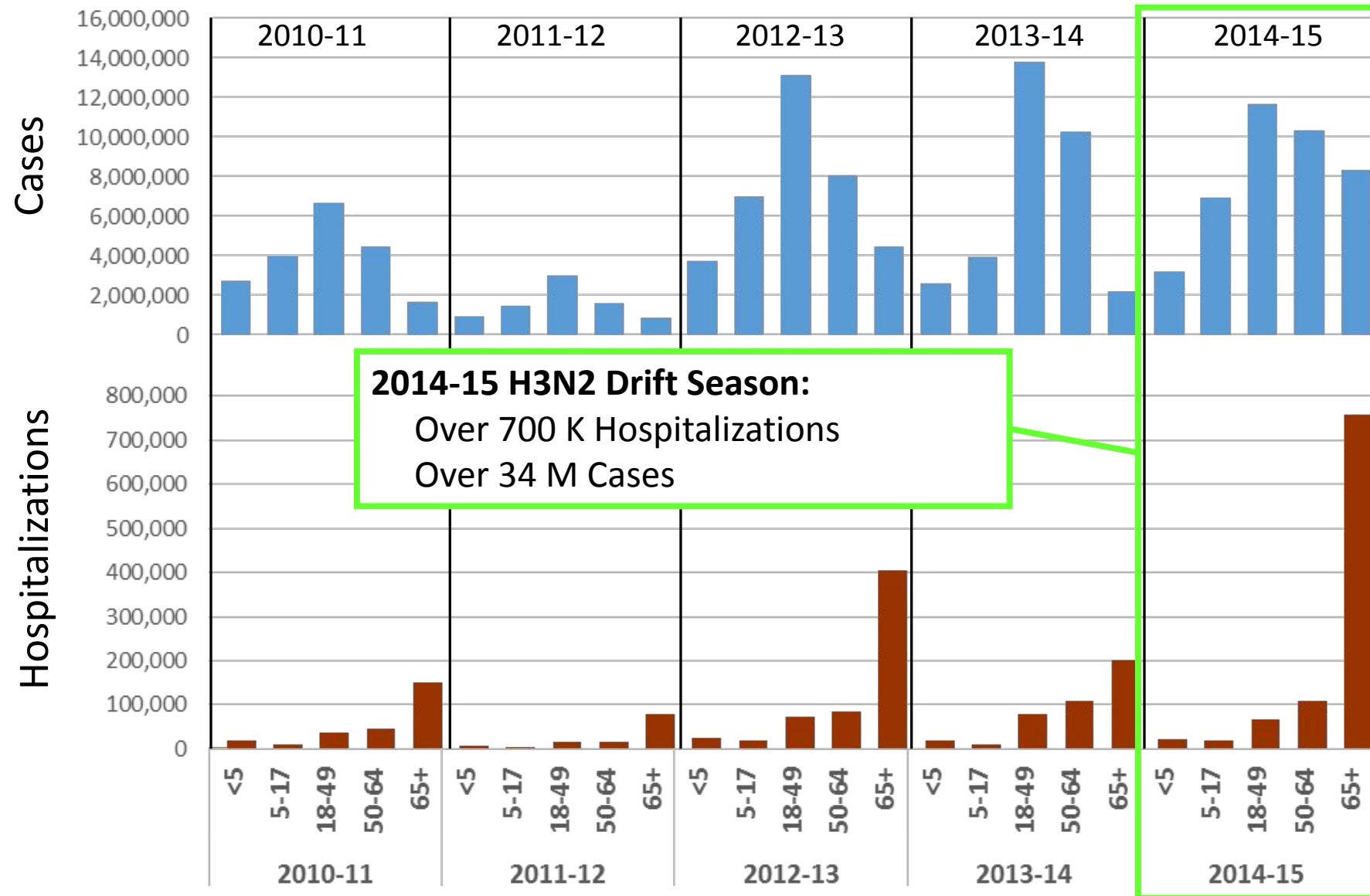


References: 1-<https://www.ecdc.europa.eu/en/seasonal-influenza/facts/factsheet>, 2-CDC. <https://www.cdc.gov/flu/about/disease/65over.htm> Accessed May 31, 2018, 3-Gozalo P et al. J Amer Geriatr Soc. 2012 Jul;60(7):1260-7. 4-<https://www.nfid.org/wp-content/uploads/2019/08/65-flu-fact-sheet.pdf>, 5-Gavazzi G. et al. The Lancet Infectious Diseases; 2002: 2(11), 659-666



“Which kind of Flu?”

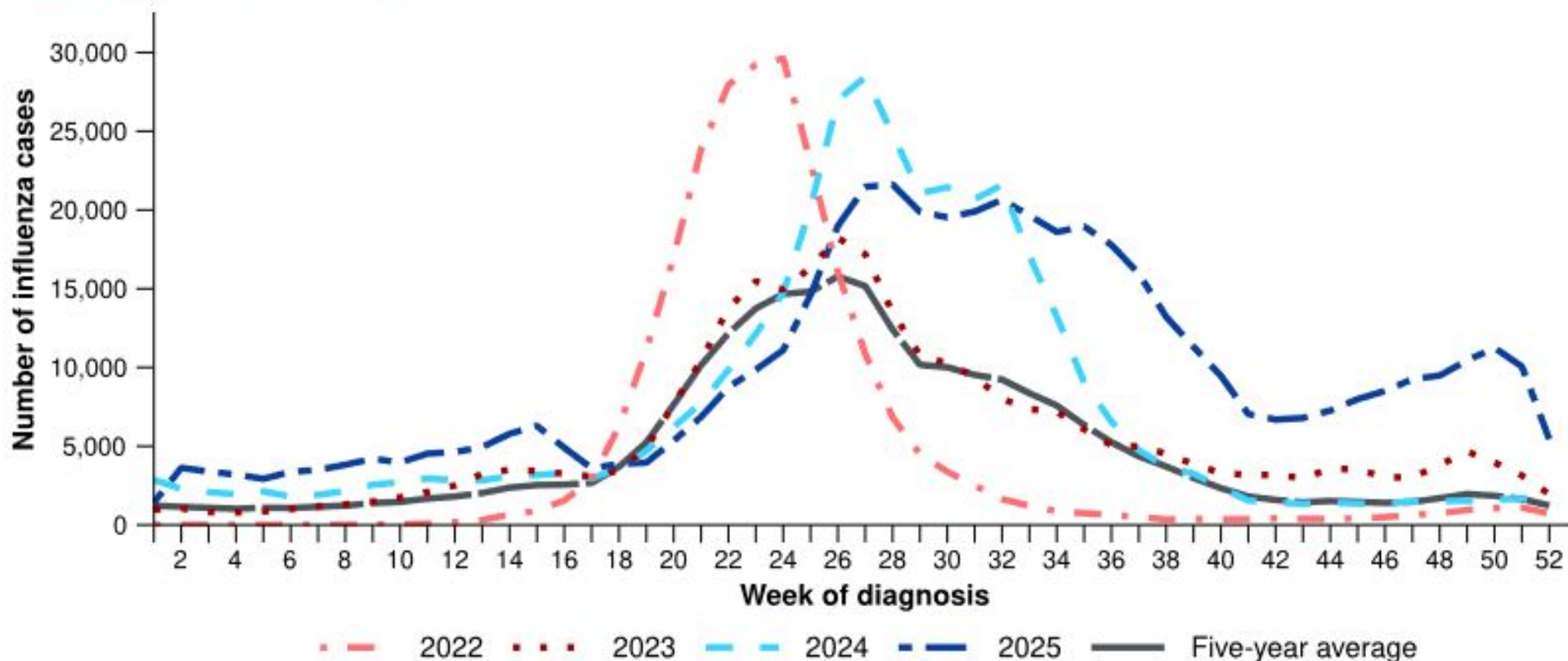
Annual Influenza Impact Varies by Age Group





Australian Respiratory Surveillance Report

Figure 6: Notified influenza cases and five-year average* by year and week of diagnosis, Australia, 2022 to 28 December 2025



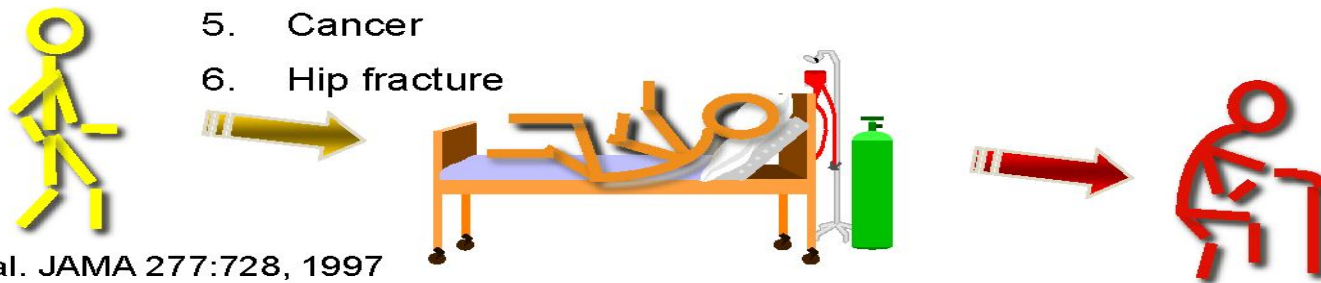
Source: National Notifiable Diseases Surveillance System (NNDSS)

* The years 2020 and 2021 are excluded when comparing the current season to historical periods when influenza virus has circulated without public health restrictions. As such, the five-year average includes the years 2018 to 2019 and 2022 to 2024. Please refer to the [Technical Supplement](#) for interpretation of the five-year average.

Vaccine Preventable Disability

Catastrophic disability

- ❖ Defined as a loss of independence in ≥ 3 ADL
- ❖ 72% who experience catastrophic disability have been hospitalized
- ❖ Leading causes of catastrophic disability
 1. Stroke
 2. CHF
 3. Pneumonia and influenza
 4. Ischemic heart disease
 5. Cancer
 6. Hip fracture



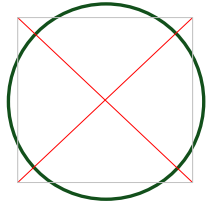
Ferrucci et al. *JAMA* 277:728, 1997

Barker et al. *Arch Int Med* 158:645, 1998

Falsey et al. *N Engl J Med*. 2005;352:1749

Important Considerations for Flu Vaccine Selection

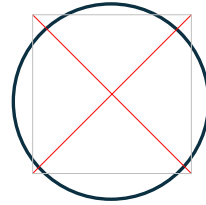
Factors Impacting Vaccine Effectiveness



Viral Factors

e.g. antigenic drift or shift
(natural mutation in circulating
flu strains)

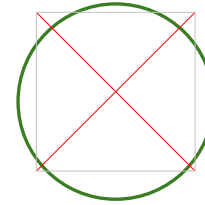
Circulating strains may become
less susceptible to vaccine
induced antibodies¹



Vaccine Factors

e.g. egg-adaptation
(changes introduced during
egg-based manufacturing)

Vaccine-induced antibodies may
be less effective against
circulating strains²



Patient Factors

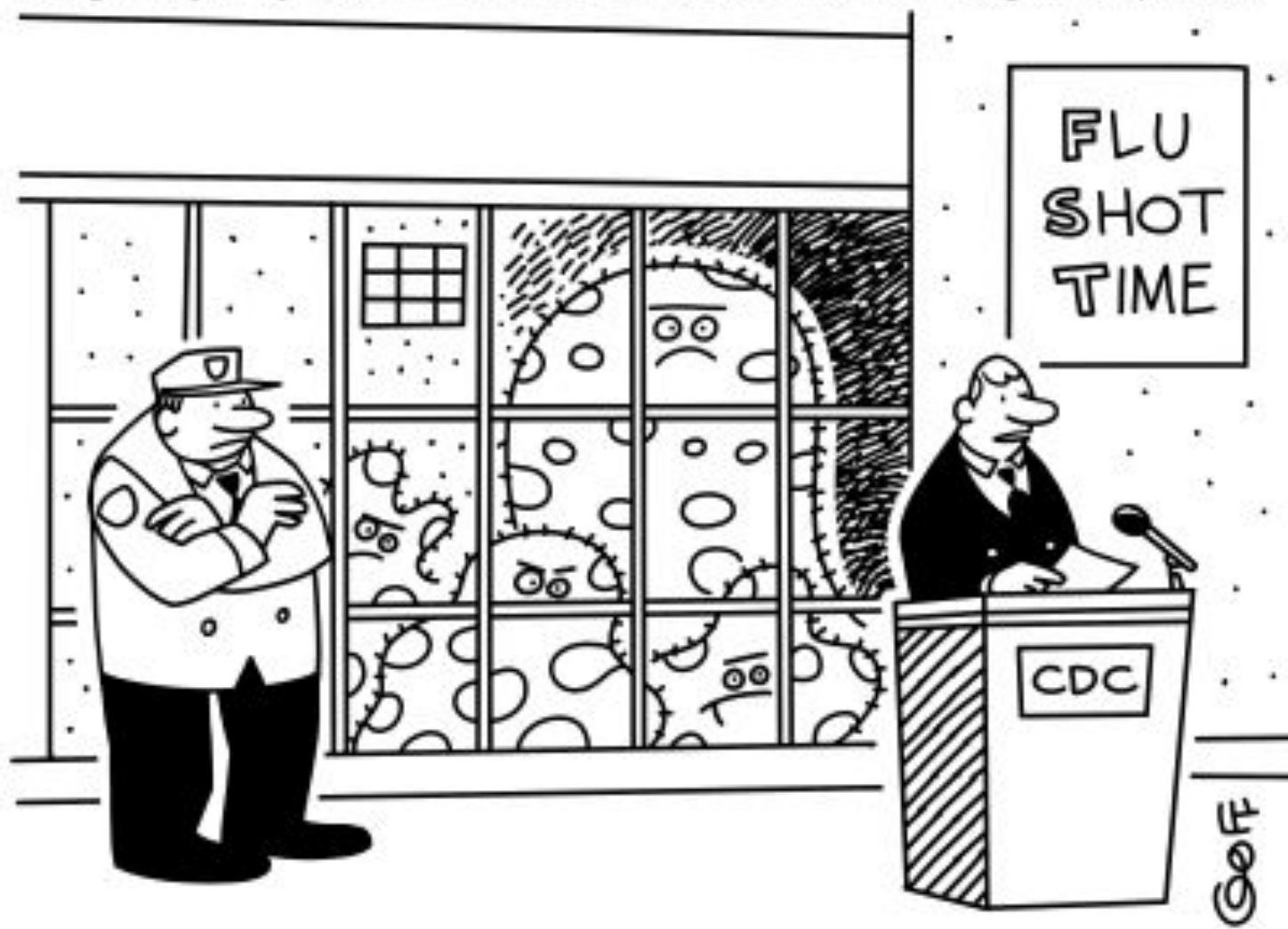
e.g. immunosenescence
(reduced immune
function in older adult patients)

Reduced immune response to
vaccination³

Utilisation Factors

e.g. lack of patient demand and/or provider recommendation leading to under-vaccination^{4,5}

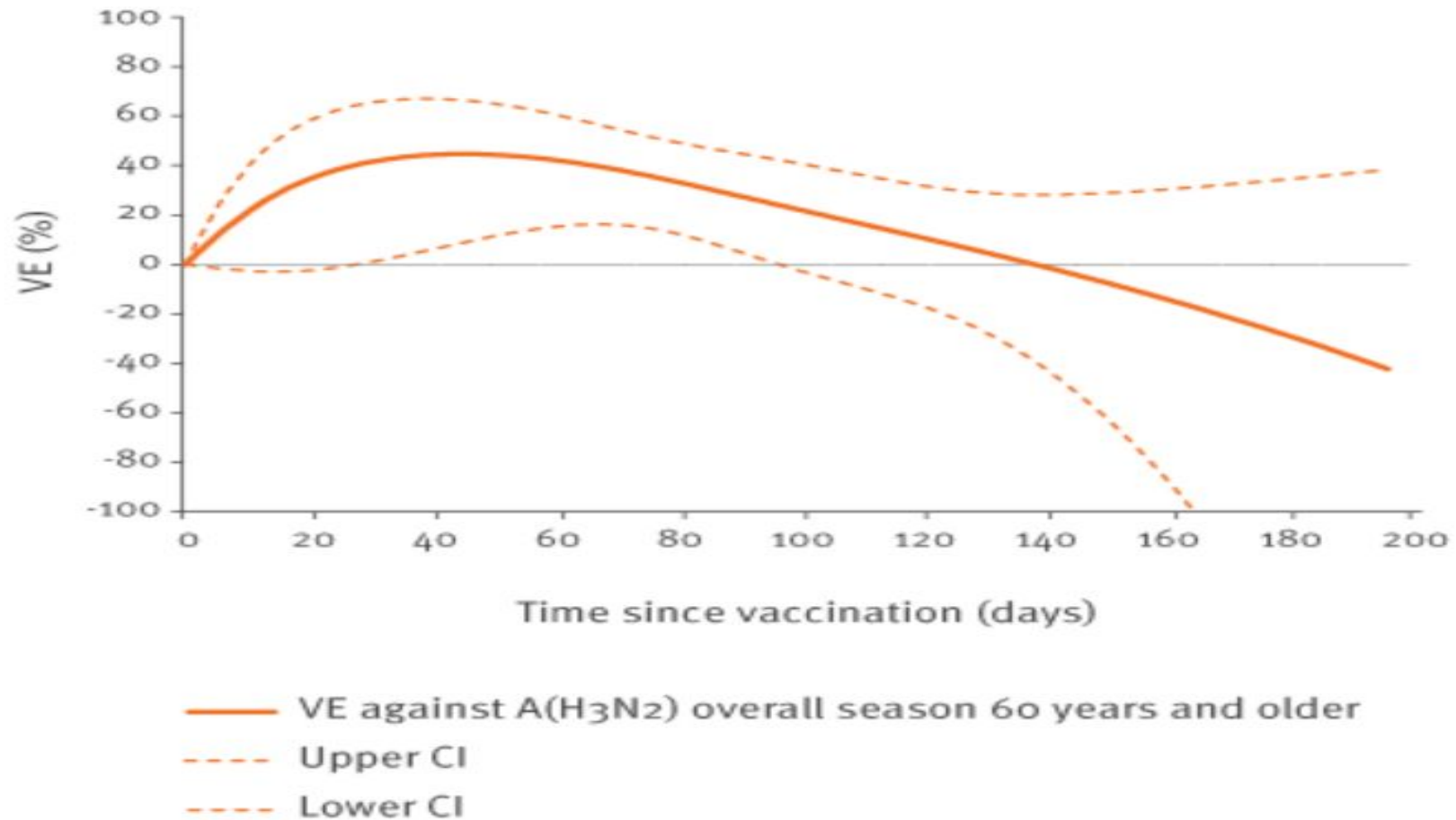
1. van den Brand JMA et al. *J Virol*. 2011;85(6):2851-2858. 2. Skowronski DM et al. *PLoS One*. 2014;9(3):e92153. 3. McElhaney JE. *Aging Health*. 2008;4(6):603-613. 4. Menzies RI et al. *Med J Aust*. 2017;206(6):238-239. 5. Rao S et al. *Hosp Pediatr*. 2016;6(9):513-519.



**“We all have less than a month
before they are let out.”**

Duration of Influenza Vaccine Effectiveness against H3N2 in adults aged ≥ 60 years (2011/2012-2014/2015)

VE declines progressively across the influenza season and this may be as much as 8% per month



The Current Need

- 1. Higher Immune response:** Influenza vaccines are less effective in older adults due to immunosenescence
- 2. Breadth of protection:** Influenza vaccines are even less effective in older adults during seasons when drift and strain mismatch occur
- 3. Persistence:** Influenza vaccine effectiveness wanes significantly during the season

Strategies in Use currently

Adjuvanted Vaccine

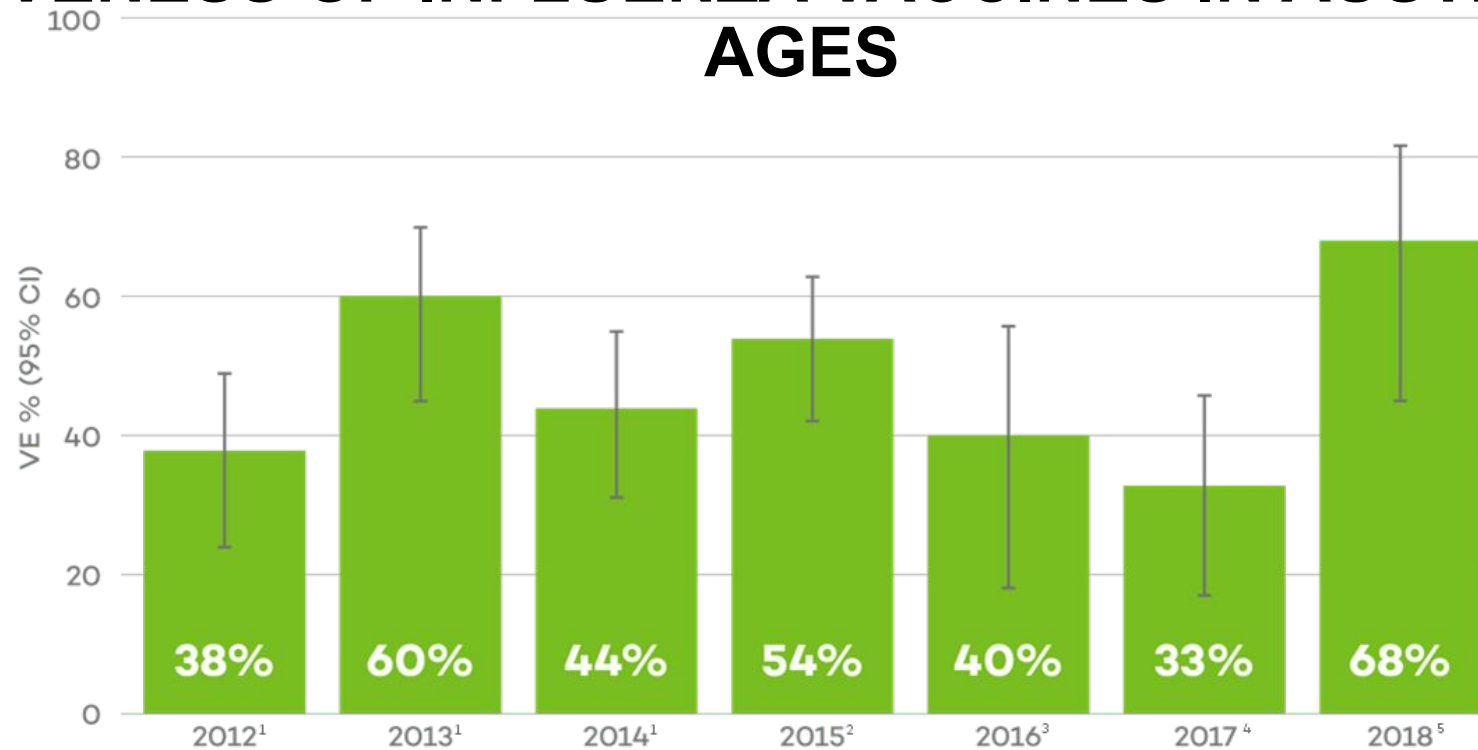
High Dose Vaccine

Cell Derived Vaccine

CURRENT VACCINES HAVE SUBSTANTIAL IMPACT ON DISEASE BURDEN

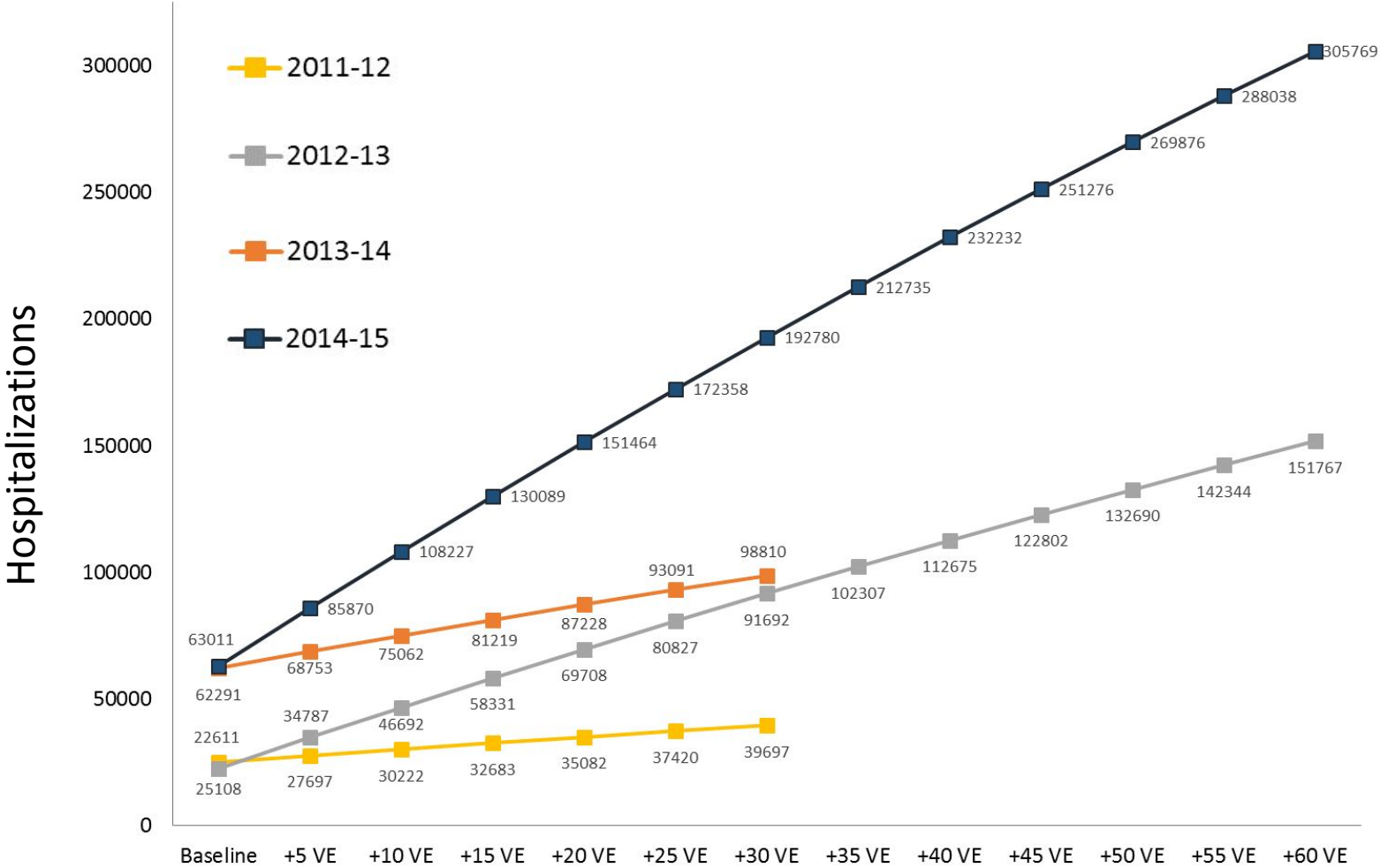
– But there is room for improvement

EFFECTIVENESS OF INFLUENZA VACCINES IN AUSTRALIA – ALL AGES



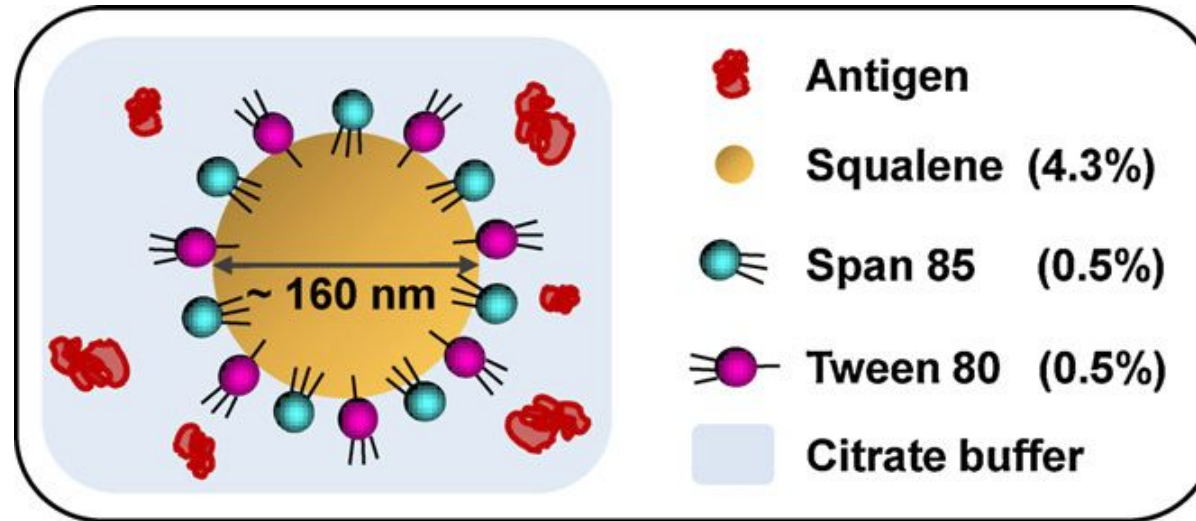
Note: Data pooled from multiple sources. For GP visits, complete case analysis only for 2012-2014, imputed analysis for 2015-2017.

Averted Hospitalizations for Incremental VE Improvements 2011-15 Influenza Seasons, U.S.



- For the 2014-15 drift H3 season, an improvement of +5% averts 86K hospitalizations, +10% averts 108K, and +40% averts 232K
- Even at low VE, influenza morbidity in 65+ may be reduced with incremental VE increases

Adjuvanted Trivalent Influenza Vaccine



The MF59[®] adjuvant contained in aTIV is an oil-in-water emulsion composed of squalene as the oil phase, stabilized with the surfactants polysorbate 80 and sorbitan trioleate, in citrate buffer

Seqirus UK Limited. FLUAD[®] Product Monograph 2017 – 2018;

O'Hagan DT, Ott GS, De Gregorio E, Seubert A. The mechanism of action of MF59 - an innately attractive adjuvant formulation. *Vaccine*. 2012;30(29):4341-4348. doi:10.1016/j.vaccine.2011.09.061.

MF59[®] is a registered trademark of Novartis AG

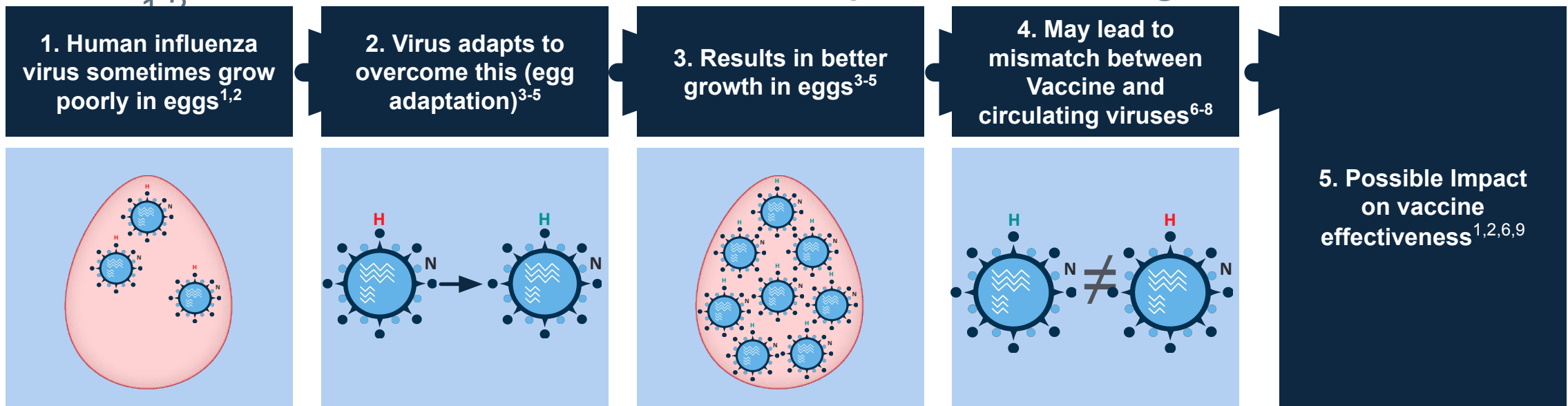
aTIV outcome in Australia in 2019

- 2017 and 2019 were both big years with very high notifications in over 65 year group in a largely H3N2 year
- Qld data showed that in 2019 hospitalisations were down 60% cf 2017
- aTIV in elderly in 2019, non-adjuvanted in 2017

Age	Vaccine	VE (H3N2)	95% CI
All	QIV	37%	(24 - 59)
Under 18	QIV	34%	(-2 - 58)
18-64	QIV	39%	(23 - 53)
65 years +	aTIV	50%	(16 - 70)

Egg adaptations can cause important changes in the viruses used to make vaccines^{1,2}

Some influenza viruses need to adapt in order to grow well in



A key area of influenza vaccine innovation is the use of non-egg based manufacturing technology
□ e.g. growth of virus in Cell Culture and production of recombinant Haemagglutinin (HA)

H=haemagglutinin; N=neuraminidase.

1. Harding AT *et al.* *Vaccines*. 2018;6(2):19. 2. CDC. www.cdc.gov/flu/vaccines-work/vaccineeffect.htm Accessed Sept 2020. 3. Wu NC *et al.* *PLoS Pathog*. 2017;13(10):e1006682. 4. Zost SJ *et al.* *Proc Natl Acad Sci USA*. 2017;114(47):12578-83. 5. Barr I *et al.* *Vaccine*. 2014;32(37):4713-25. 6. Skowronski DM *et al.* *PLoS One*. 2014;9(3):e92153. 7. WHO. www.who.int/influenza/vaccines/virus/candidates_reagents/summary_a_h3n2_cvv-cell_sh20.pdf?ua=1 Accessed Sept 2020. 8. WHO. www.who.int/influenza/vaccines/virus/recommendations/201909_recommendation.pdf?ua=1 Accessed Sept 2020. 9. Rajaram S *et al.* *Ther Adv Vaccines Immunother*. 2020;8:1-10.

High dose (HD) influenza vaccine: presentation

Countries with HD-TIV or HID-QIV licensed

HD vaccine is a split influenza vaccine containing 60 mcg of hemagglutinin (HA) per strain

- Contains 4x the amount of HA compared to standard dose influenza vaccines
- A trivalent formulation Fluzone HD® (0.5mL) is licensed in US, Canada, Australia¹, Brazil, UK and NZ.
- A quadrivalent formulation (0.7mL) was licensed in November 2019 in the US², and then subsequently in 2020 in Canada⁴, EU (Efluelda®)³ & Australia⁵.

HD vaccine is indicated for prevention of influenza in people 60⁷ or 65² years of age and older depending on the countries

166M doses of HD Vaccine have been distributed as of the 2020-21 season⁶

References: 1-Australian product information – Fluzone High Dose. <https://apps.medicines.org.au/files/swpfluhd.pdf>, 2-US FDA Product Insert Fluzone High Dose Quadrivalent <https://www.fda.gov/media/139731/download>, 3-https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2131-015-001_27042020121105.pdf, 4-Health Canada Product Monograph Fluzone High Dose Quadrivalent <https://health-products.canada.ca/dpd-bdpp/info.do?lang=en&code=99020>, 5-Australia Package Insert Fluzone High Dose Quadrivalent <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2020-CMI-02062-1&d=202009301016933>, 6-Diaco M et al. Vaccine: 2021 Jan 20;S0264-410X(20)31147-6, 7-Paul Ehrlich Institut: https://www.pei.de/EN/medicinal-products/vaccines-human/influenza-flu/influenza-flu-node.html;jsessionid=1F785C0B41685CE27618ADFAC91D2947.intranet241?cms_tabcounter=0

Recent Reviews

- **1. Prevention of Disease**

- Cochrane review (Demicelliet al.) Vaccination more than halves the risk of disease in a single season

- **2. Major Health Consequences**

- Influenza vaccine reduces the risk of stroke in older adults by 16% (Tavabe et al 2023)
- Vaccinated cancer patients have longer progression-free survival and longer overall survival (Lopez-Olivo et al 2022)

- **3. Mortality**

- Italian cohort study of older adults in GP groups with a vaccination rate of over 55% revealed a 43% reduction in risk (Lapi et al 2022)

2026 vaccines

Vaccine	Licensed	Funding
aTIV (Fluad)	□ 50 years	□ 65years
High Dose TIV (Fluzone HD)	> 60 Years	Nil
cTIV (Flucelvax)	>6 months	Not >65 years
eTIV (various)	>6 months	Not >65 years

Both aTIV and HD TIV are preferentially recommended for older persons 65 years and older.

Only aTIV is funded for 65 years and older

They are licensed for broader groups