Review of influenza impact and low vaccine efficacy in older adults: 2017

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In the week our PM has set out the goal of Aust as longest living nation,

- we find ourselves duelling with Spain inter alia
- We've already achieved the milestone of having a nasty flu named after us - amid suggestions it was like a pandemic

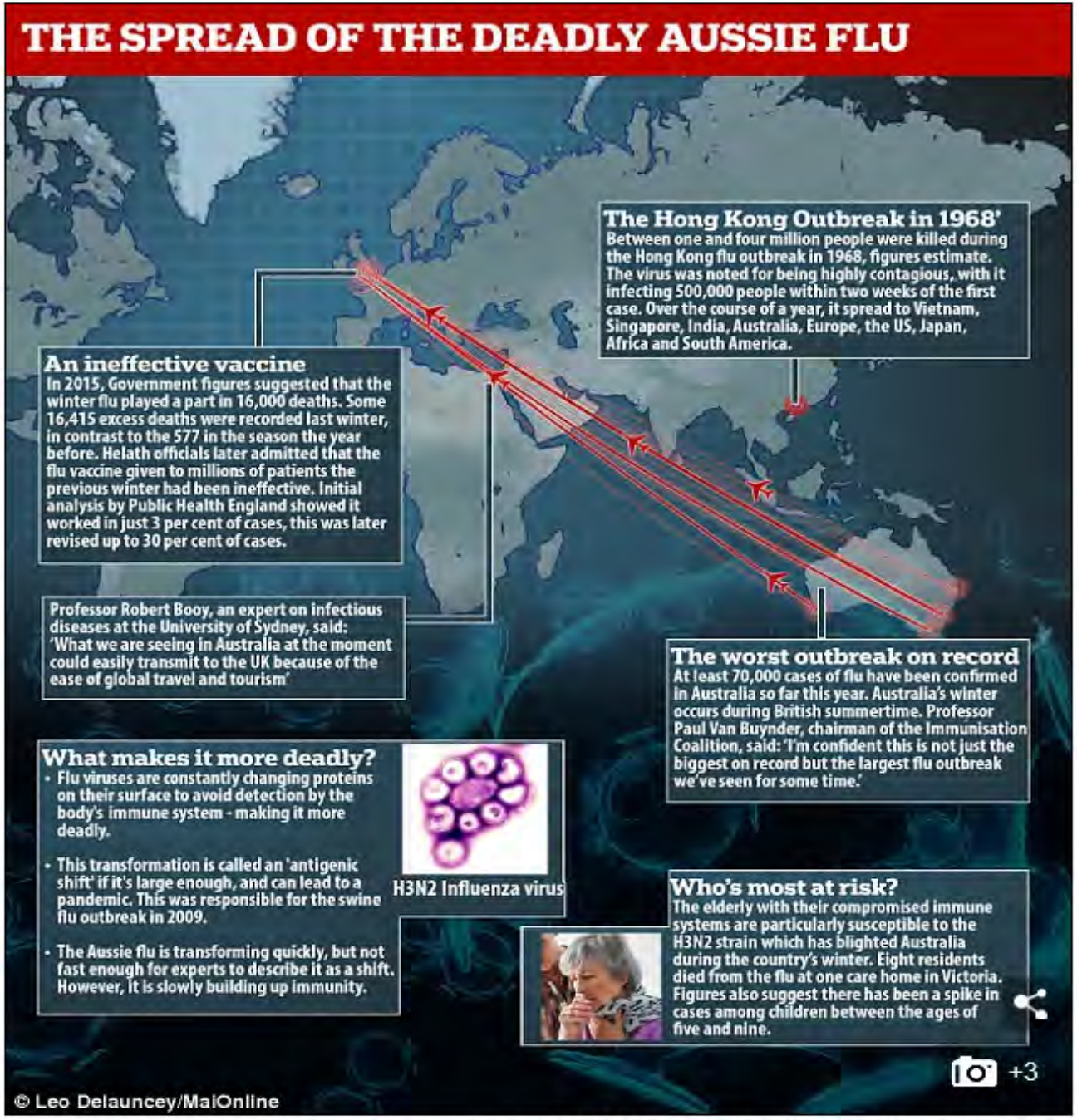
"The DEADLY AUSSIE FLU"

UK news
Nov 2017

Vaccine ineffective

Aussie flu could hit UK

Compared to previous Pandemics



Routine operations could 'cease for several months' if the over-stretched health service falls victim to the bug that is on its way to the UK after blighting Australia, experts warn

"worst outbreak on record"

Who is most at risk?

Older Australians at risk

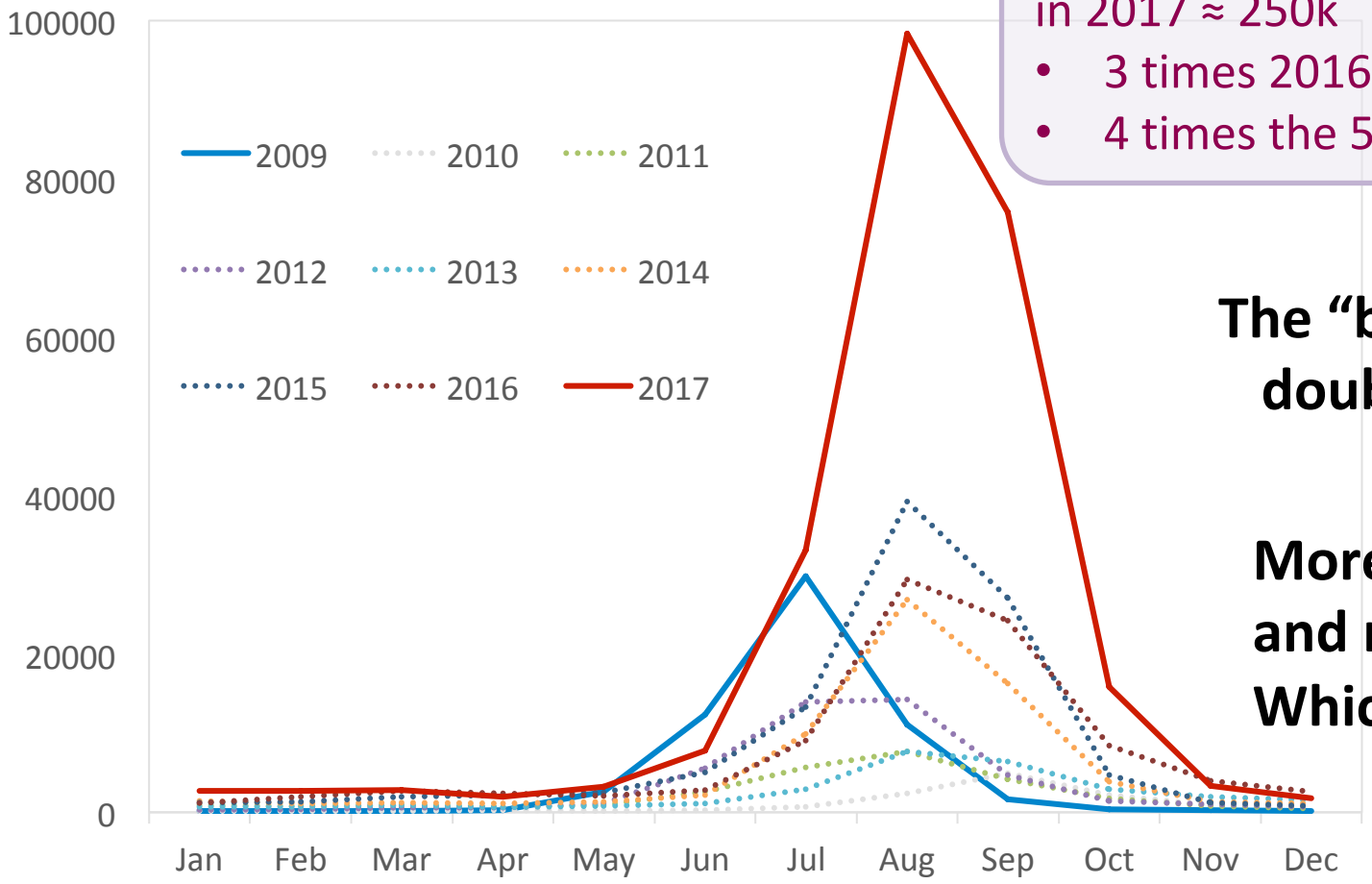
self-interest: male, grey, BMI issues

Beneath a row of trees a group of standing people are “coughing” material onto each other. Below them many people are lying prostrate on the ground

ulidjirri, Gunbalanya (Oenpelli), Northern . Below them many people are lying ne mouth of the King River near Oenpelli. a sacred place, cut down a tree and ate bush Bidjirl, the saltwater bream and Dadbe, the ki and everybody died.

Notifications of lab-confirmed influenza since 2009 pandemic

Number of lab-confirmed cases in 2017 ≈ 250k
- 3 times 2016
- 4 times the 5-yr average



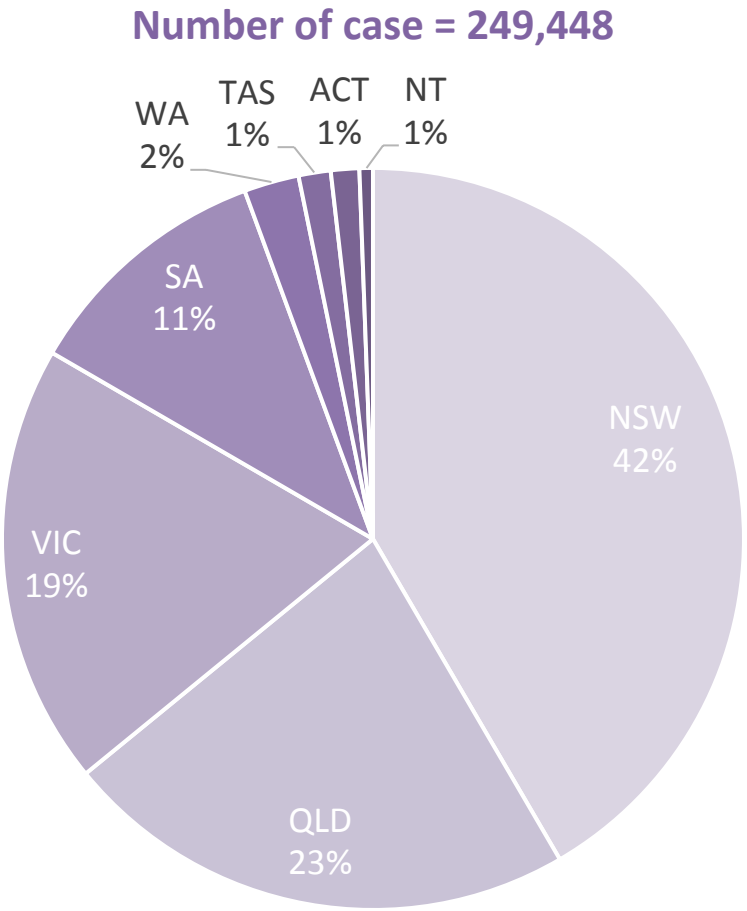
The "both, and" double truth

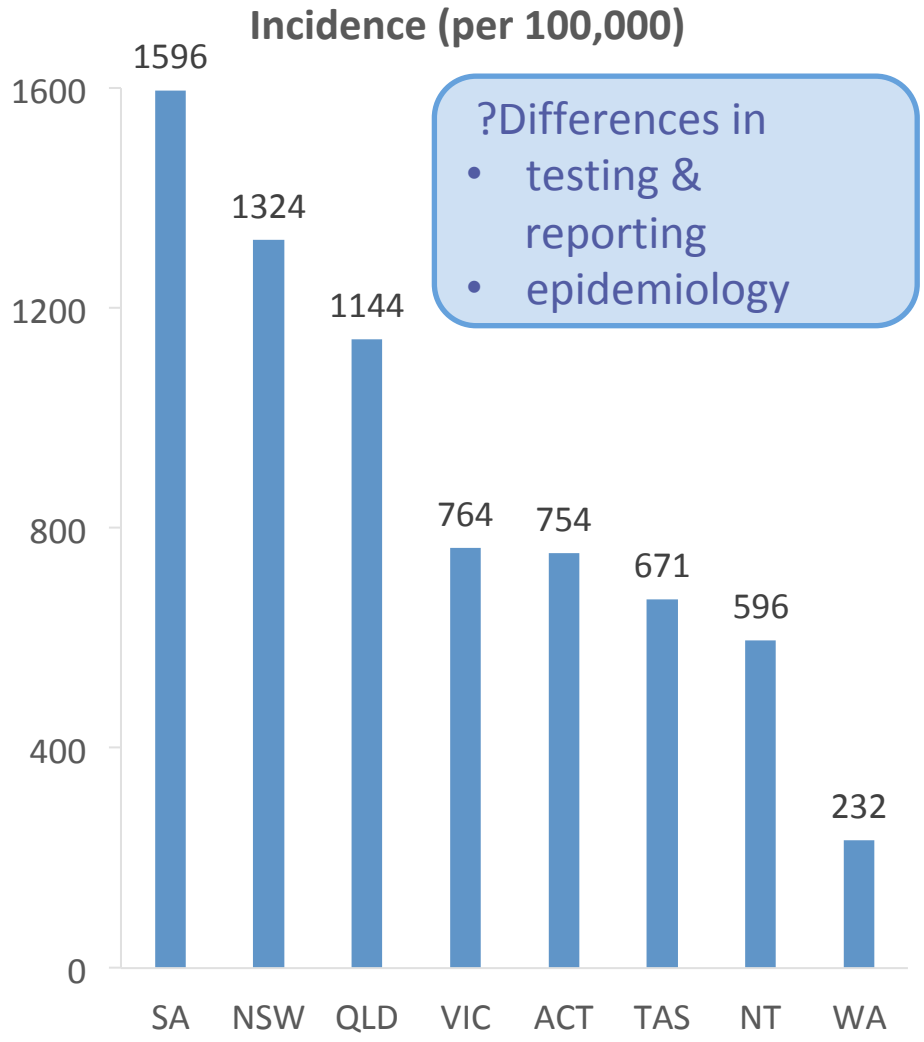
More detection and more cases, Which is more?

Source: National Notifiable Diseases Surveillance System (as of 7th Jan 2018)

Number & incidence of influenza notification in 2017*

by jurisdiction



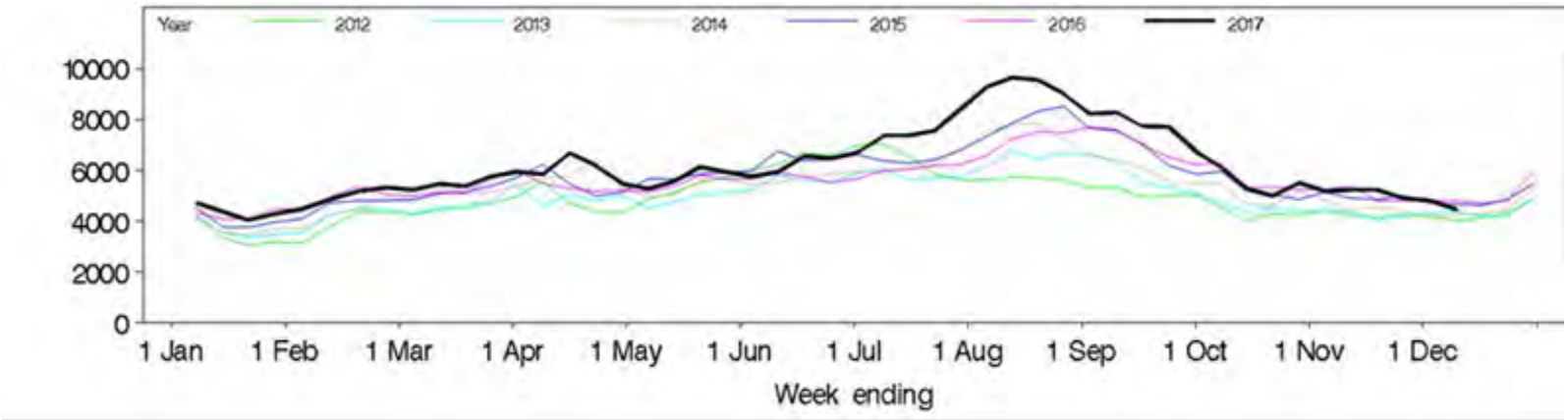


* *Calculated using data from National Notifiable Diseases Surveillance System* (as of 7th Dec) and Australian Bureau of Statistics, 3101.0-Australian Demographic Statistics, Mar 2017

NSW Monthly Influenza Surveillance

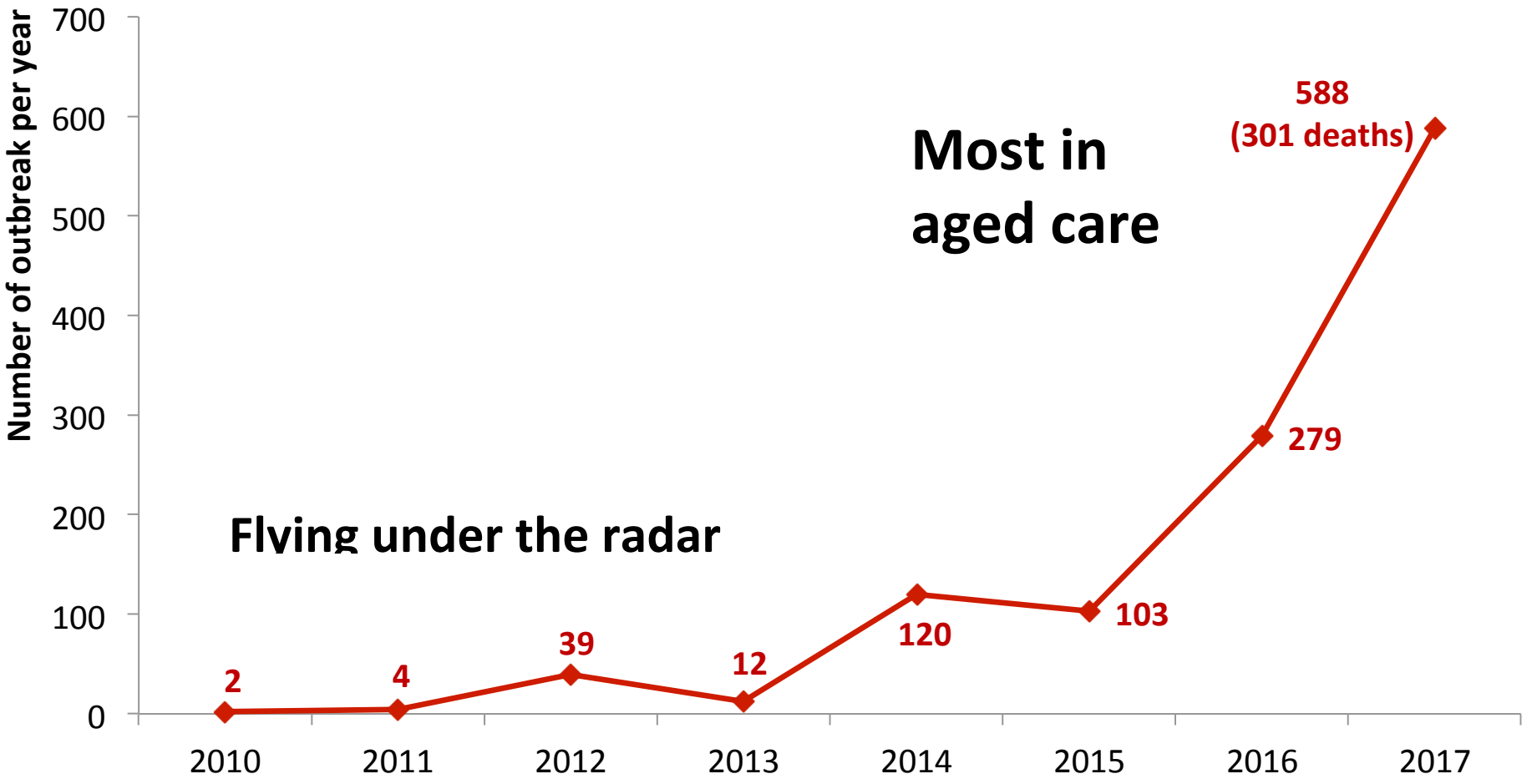
not lab-confirmed: *resp illness, fever & unspecified inf'n*

Emergency Department presentations for any respiratory illness, fever and unspecified infections, for 2017 (black line) compared with 5 previous years (coloured lines), persons of all ages, for 60 NSW hospitals over 6 years



More non-specific cases but not that many more…

Institutional influenza outbreaks in NSW, despite ~82% vaccine uptake*



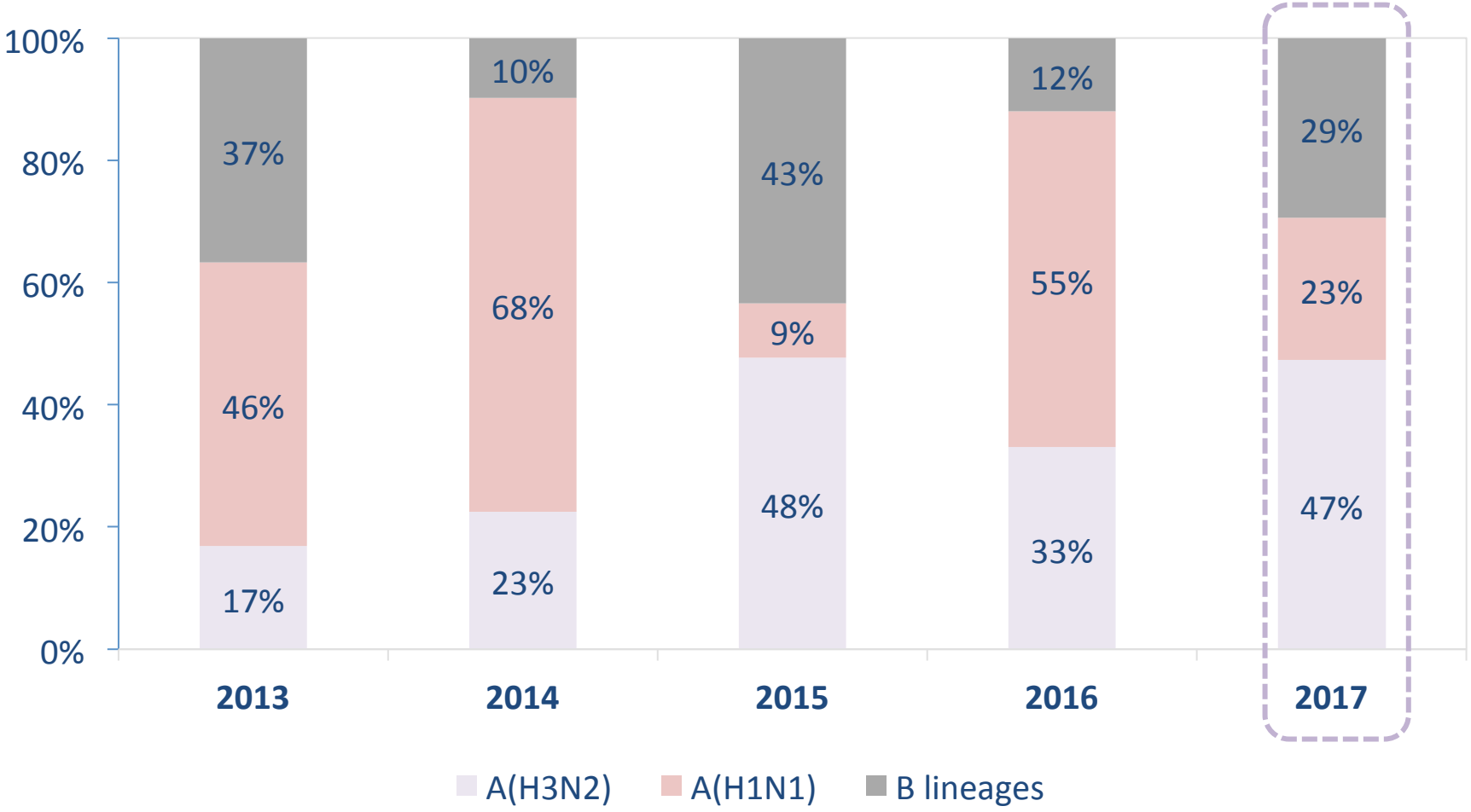
** Booy et al. PLoS One 2012*

† Calculated using the population ratio of NSW vs SA (source of data: Australian Bureau of Statistics, 3101.0-Australian Demographic Statistics)

Multiple strains co-circulating, H3N2 tops - elderly!

Proportional distribution of influenza cases of last 5 years, by strain*

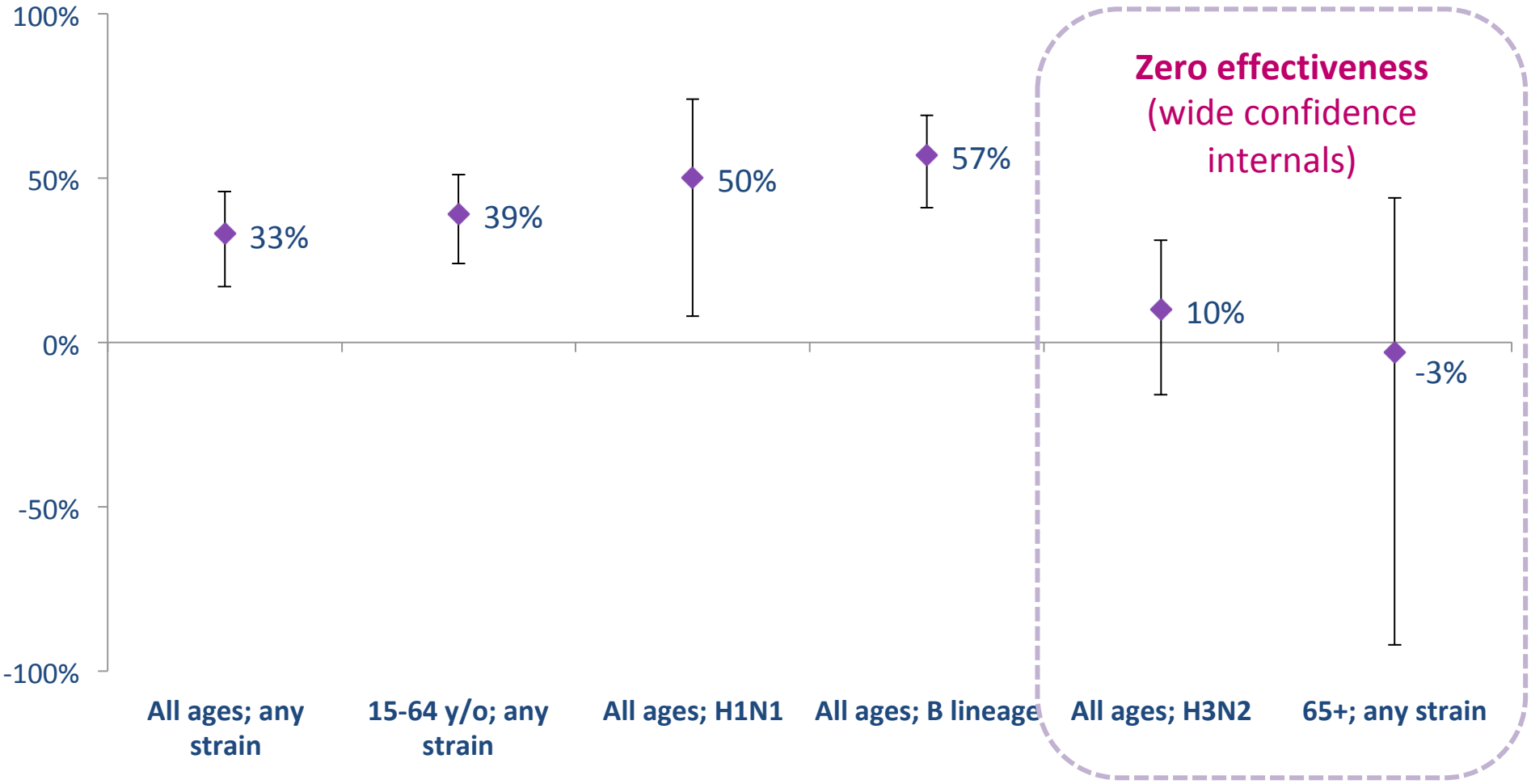
Danger of chasing one's tail.. H3 dominant in elderly



* Based on data from specimens typed by WHO Collaborating Centre in Australia Influenza Surveillance Reports 2013-2017

Flu vaccine effectiveness reduced

QIV effectiveness in GP settings, Australia, May to September 2017*



* **Sullivan et al. Euro Surveill. 2017;22(43):pii=17-00707**

Abbreviation: GP=general practitioner; QIV=quadrivalent influenza vaccine

"The minister has asked the Chief Medical Officer to examine whether there are ways to strengthen the National Immunisation Program, including holding talks with manufacturers on new and strengthened vaccines,"

a spokesman told The Australian (Nov 2017)

CMO: *"This particular strain has undergone some changes during the season and this may also have contributed to occurrence of a larger than usual number of cases in the vaccinated elderly. The DoH is, however, examining what strategies could be implemented to improve vaccine effectiveness in future years."*

During the 2016/17 UK influenza season, the effectiveness of vaccine against medically attended, laboratory -confirmed influenza in primary care in the elderly could not be demonstrated
(Pebody et al.,2017)

A meta-analysis of data between 2004 and 2015 was also unable to show significant efficacy for the inactivated influenza vaccine in the elderly against the A(H3N2) virus
(Bellongia et al., 2016)

Public Health England did an age-stratified analysis of pooled primary care data since 2010/11 (in press) which showed ***significant effectiveness in the 65-74 age group for all influenza, A(H1N1)pdm09, influenza B and A(H3N2)***

Above the age of 75 years, however, pooled estimates were unable to demonstrate any significant effectiveness across all seasons and all the influenza virus types

UK January 2018

Health officials calling for a “serious debate” about introducing mandatory flu jabs for NHS staff, amidst a deepening winter crisis

Sir Bruce Keogh, NHS medical director, said action was needed to tackle “massive variation” between hospitals, with as few as one third of medical workers vaccinated at some hospital trusts

About one quarter of NHS staff will contract flu during a typical season - of those, more than one third will avoid major symptoms, meaning they are likely to remain in work, spreading infections

Australia Nov 2017

The DoH is, however, examining what strategies could be implemented to improve vaccine effectiveness in future years

Australia's Chief Medical Officer, Brendan Murphy

"This particular strain has undergone some changes during the season and this may also have contributed to occurrence of a larger than usual number of cases in the vaccinated elderly,"

Egg Based Vaccines

NEJM commentary (inclu Sullivan, Fauci, late 2017)

Based on data from Australia, scientists warn that this season's flu shot might be **only 10% effective**

And the reason.. might lie in the method by which the majority of flu vaccines are made: in eggs.

We have the same viral composition this year for flu vaccines in both the Northern & Southern Hemispheres

Australia had already reported
215,280 influenza cases by mid-Oct 2017,
far more than the 59,022 recorded during its 2009 pandemic

CDC Morbidity and Mortality Weekly Report

the low effectiveness was not primarily due to any difference between the vaccine strain and circulating viruses… it seems to be the egg-based vaccine production technology that caused the mismatch

Circulating A(H3N2) viruses are antigenically less similar to egg-grown A(H3N2) viruses used for producing the majority of influenza vaccines in US

Flu viruses propagated in eggs undergo mutational change in the hemagglutinin protein, the primary target of neutralizing antibodies: negatively impacts viral-killing

Hence the importance of new approaches apart from the egg-based manufacturing process:

Recombinant and cell-based platforms

Clinical studies have not yet conclusively proved that cell-culture vaccines are more effective

Mathematical modelling by PHE, for JCVI UK

Even under conservative estimates of effectiveness, enhanced vaccine (eg adjuvanted)

would be highly cost-effective in both the 65-74 and 75 year and over age groups

Given the low influenza vaccine effectiveness seen in the over 65 year olds in seasons dominated by A(H3N2), the Committee (JCVI) said that use of aTIV in those aged over 64 years would be both more effective and cost-effective than the un-adjuvanted vaccines

JCVI: priority for adjuvanted vaccine should be for those aged 75 years and above as this age group appear to derive little benefit from un-adjuvanted vaccine
(JCVI, Oct 2017)

NEJM commentary 2017

encourages people to get vaccinated, even if it only offers 10% protection (Sullivan, Fauci et al)

"However imperfect, current influenza vaccines remain a valuable public health tool, and it is always better to get vaccinated than not to get vaccinated,"

With 150 million doses of flu shots needed yearly in US alone, egg-based vaccine production remains the most reliable, time-proven method and represents the vast majority of vaccines used globally to help prevent influenza

International Perspective (US CDC)

Most deaths occur among people aged over 75 years, and in the world's **poorest regions**

Sub-Saharan Africa accounts for the world's greatest flu mortality risk, followed by the East Med & SE Asia

"**All countries**, rich and poor, large and small, **must work together** to control influenza outbreaks before the arrival of the next pandemic - **building capacity to detect and respond to outbreaks**, and strengthening health systems to improve the health of the most vulnerable" US-CDC

Summary

- Australia has just had the busiest flu season on record – more detection & more disease
- Current vaccines have reduced effectiveness in the elderly, possibly due to mutations while grown in eggs
- Australia is seriously exploring enhanced vaccines for the better protection of the elderly to be protected in the upcoming 2018 season

Flu vaccination in the elderly

There is considerable evidence that immune responses to vaccination decline substantially with age (Haralambieva et al., 2015). Antibody responses in the elderly are lower than in younger adults and this is likely to translate into a lower effectiveness in the elderly for influenza vaccine compared with younger adults (Goodwin et al., 2006; Lang et al., 2012).

During the 2016/17 UK influenza season, the effectiveness of vaccine against medically attended, laboratory -confirmed influenza in primary care in the elderly could not be demonstrated (Pebody et al.,2017).

A meta-analysis of data between 2004 and 2015 was also unable to show significant efficacy for the inactivated influenza vaccine in the elderly against the A(H3N2) influenza virus, which mainly impacts the elderly (Bellongia et al., 2016)

PHE conducted an age stratified analysis of pooled primary care data since 2010/11 (in press) which showed significant effectiveness in the 65-74 age group for all influenza, A(H1N1)pdm09, influenza B and evidence of protection against A(H3N2)

Above the age of 75 years old, however, pooled estimates were unable to demonstrate any significant effectiveness across all seasons and all the influenza virus types

In August 2017, an adjuvanted trivalent inactivated vaccine (aTIV) Fluad®, licensed for use in those aged 65 years and older, gained marketing authorisation in the UK.

The aTIV has been licensed in some countries in Europe since 1997 and in the USA since 2015.

In June 2017, JCVI (JCVI., June 2017) reviewed the published data that the adjuvanted vaccine has higher vaccine immunogenicity and higher effectiveness than non-adjuvanted vaccines in the elderly (Van Buynder et al, Vaccine 2013, Dominich et al., 2017).

Mathematical modelling by PHE indicates that, even under quite conservative estimates of effectiveness, the adjuvanted vaccine would be highly cost-effective in both the 65-74 and 75 year and over age groups (in press).

Given the low influenza vaccine effectiveness seen in the over 65 year olds in seasons dominated by A(H3N2), the Committee agreed that use of aTIV in those aged 65 years and over would be both more effective and cost-effective than the non adjuvanted vaccines currently in use.

JCVI also agreed that the priority for adjuvanted vaccine should be for those aged 75 years and above as this age group appear to derive little benefit from the un-adjuvanted vaccine (JCVI.,October 2017)

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

WHO Report

Announcing the publication of the WHO immunological basis for immunization series module on influenza vaccines

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ABSTRACT

In 2017, the World Health Organization (WHO) published a document aimed at facilitating influenza vaccine introduction and use in low- and middle-income countries. The document "The Immunological Basis for Immunization Series: Influenza Vaccines" is freely available on the WHO website. The main purpose of this document is to give immunization managers and vaccination professionals an authoritative but easily-understood overview of the scientific basis of influenza vaccination and the immunological basis for the WHO position on influenza vaccines. The influenza vaccine document comprises one module of the WHO Immunological Basis for Immunization series. We invite the immunization community to use these references, and we hope the influenza vaccine module will be a valuable resource for persons who manage and monitor influenza vaccine programs, particularly in low- and middle-income countries.

Up to 650 000 people die of respiratory diseases linked to seasonal flu each year

News release

14 DECEMBER 2017 | GENEVA - Up to 650 000 deaths annually are associated with respiratory diseases from seasonal influenza, according to new estimates by the United States Centers for Disease Control and Prevention (US-CDC), the World Health Organization and global health partners.

This marks an increase on the previous global estimate of 250,000-500,000 , which dates from over ten years ago and covered all influenza-related deaths, including cardiovascular disease or diabetes. The new figures of 290,000-650,000 deaths are based on more recent data from a larger, more diverse group of countries, including lower middle income countries, and exclude deaths from non-respiratory diseases.

“These figures indicate the high burden of influenza and its substantial social and economic cost to the world,” said Dr Peter Salama, Executive Director of WHO’s Health Emergencies Programme. “They highlight the importance of influenza prevention for seasonal epidemics, as well as preparedness for pandemics.”

The estimates take into account findings from recent influenza respiratory mortality studies, including a study conducted by the United States Centers for Disease Control and Prevention (US-CDC), published in The Lancet on Thursday (14 December).

Australia's Chief Medical Officer has stridently rejected claims a "budget" flu vaccine was partly responsible for this year's horror flu season, as the academic quoted called the reports "inaccurate".

Professor Brendan Murphy called "utterly false" accusations that a cheaper flu vaccine was to blame for hundreds flu-related deaths among the elderly this year.

"No one is trying to save money here ... we are using the best available vaccines in Australia," he said.

"The vaccine purchased by the Australian government and used this year was the best available in Australia at the time, and remains so today," Professor van Buynder said in a statement

IMMUNISATION COALITION

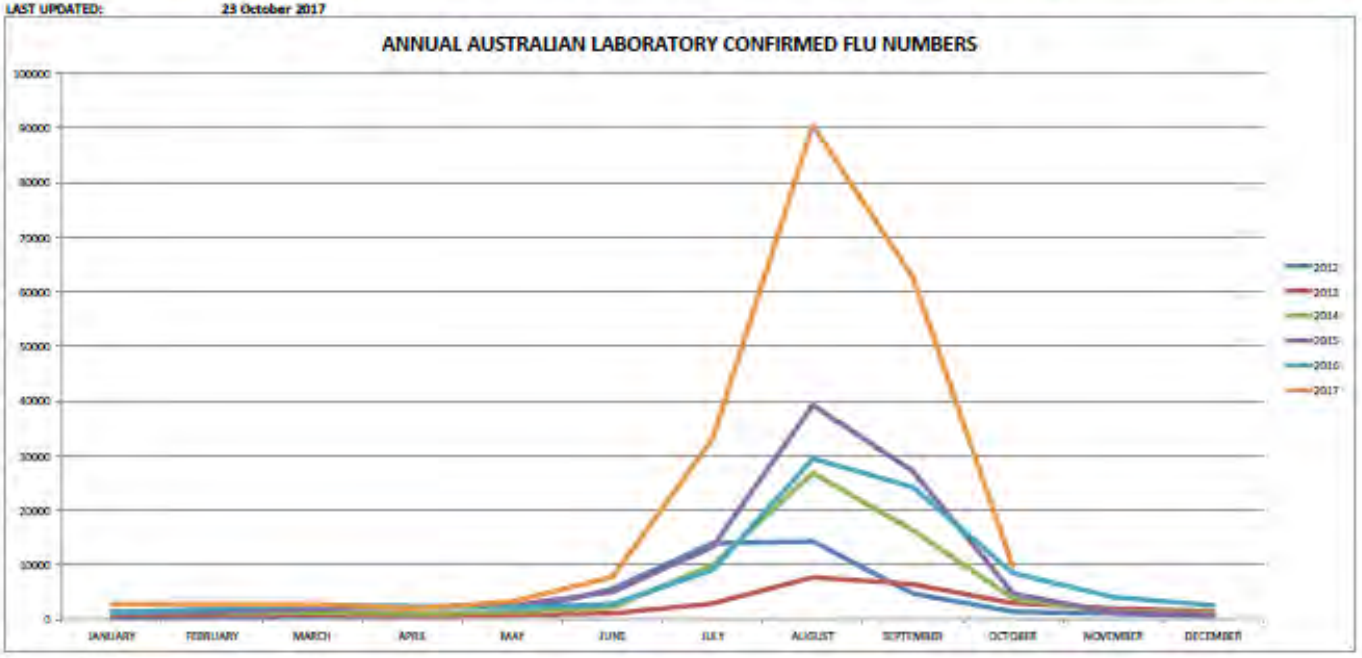
The Immunisation Coalition is the leading voice in whole-of-life immunisation in Australia, protecting all Australians against communicable diseases.

For more information, please visit our website: **www.immunisationcoalition.org.au/news-media/2017-statistics/**

ANNUAL AUSTRALIAN INFLUENZA STATISTICS

YEAR	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER	TOTALS
2012	306	356	610	575	1164	5591	13927	14270	4696	1402	1020	647	44564
2013	717	740	862	635	776	1088	2909	7702	6428	2961	1993	1503	28314
2014	1425	1146	1260	1067	1332	2198	9919	26810	16290	3819	1305	1136	67697
2015	1249	1342	1966	2218	2527	5013	13279	39222	27083	4725	1178	788	100590
2016	1175	1969	2666	2434	2058	2830	9037	29421	24216	8448	4044	2539	90837
2017	2735	2734	2812	1978	3289	7756	33050	90465	62577	9611			217007

LAST UPDATED: **23 October 2017**



Reference: These statistics are taken from the Aust Government Department of Health, National Notifiable Diseases Surveillance System.

Australian Government

Department of Health

CHIEF MEDICAL OFFICER

Early advice on the 2017 Seasonal Influenza Vaccine

Dear Colleague

Vaccination remains the best protection we have against influenza. You, as a vaccination provider, play a key role in informing the community about risks from influenza and of the importance of influenza vaccination.

This year I am particularly concerned about low vaccination rates in Aboriginal and Torres Strait Islander children under five, pregnant women and people who suffer from chronic illness. I ask that you take the necessary steps to recall your patients in these at-risk groups and ensure they are aware of the importance of influenza vaccination.

Key features of the 2017 National Immunisation Program (NIP) influenza vaccines include that:

- Influenza vaccines will be available from mid April 2017, subject to vaccine supply.
- Four age-specific quadrivalent influenza vaccines (QIVs) will be available free to eligible people under the NIP. The four vaccines are:
- FluQuadri Junior® (Sanofi Pasteur) for children from 6 months to under 3 years of age;
- FluQuadri® (Sanofi Pasteur) for people aged 3 years and over;
- Fluarix® Tetra (GSK) for people aged 3 years and older; and
- Afluria Quad® (Seqirus) for people aged 18 years and older.
- The QIVs will cover two A strains of influenza (Michigan and Hong Kong) and two B strains of influenza (Brisbane and Phuket).
  Note: The Michigan strain of influenza is new in 2017.
- The QIVs are also available for purchase on the private market.

Recent evidence suggests that protection following influenza vaccination may begin to wane after three to four months and timing of vaccination should aim at achieving the highest level of protection during the period of influenza virus circulation, usually around August.

Providers should continue to offer vaccination throughout the influenza season. When considering when to vaccinate patients please take note of the special needs of pregnant women (who should receive the vaccine at any stage during pregnancy) and young children 6 months to 9 years of age (who require two doses in the first year they receive the vaccine).

I will write to you again in April with further details about the Program, along with a vaccination provider factsheet, promotional posters and consumer fact sheets for your practice or clinic.

Please share this information with others in your practice, including locums, who administer or prescribe vaccines.

Thank you for your continued support of the NIP seasonal influenza vaccine.

Sanofi Pasteur, the manufacturer of the Fluzone High Dose vaccine — it contains four times the amount of antigen (the part of the vaccine that prompts the body to make antibodies) — has begun the early stages of gaining approval by the Therapeutic Goods Administration to bring the super dose to Australia.

Dr Ian Barr said the prevalent A-strain H3N2 tended to affect the entire population. Picture: Aaron Francis

Sarah Hawthorn, 33, from Cobram, who is fighting for life in hospital after getting the flu

A young mother is fighting for her life in a Melbourne hospital having never held her newborn son after contracting a powerful flu strain.

The mother is the latest victim in a deepening crisis that has prompted Health Minister Greg Hunt and the nation's top doctor to investigate "new and strengthened vaccines" available overseas.

The nation's deadly flu season started early and has already claimed more than 100 lives, including eight-year-old cub scout Rosie Andersen, and has left 33-year-old mother Sarah Hawthorn clinging to life in an induced coma since the end of August, unaware her first child was delivered safely six weeks early.

Immunologists told The Australian a quadruple-strength flu shot available for years in the US would have had a "significant impact" in protecting older Australians and potentially other vulnerable people


FUSH & CHUPS

The painting, in ochre, is in portrait format. Beneath a row of trees a group of standing people are “coughing” material onto each other. Below them many people are lying prostrate on the ground.

The painting represents the events which occurred at a big ceremony at Mangarranki, near the mouth of the King River near Oenpelli. People came from everywhere to attend the ceremony. Two brothers, tired and hungry from travelling, trespassed on a sacred place, cut down a tree and ate bush honey. For this they were infected with Komnud, an influenza that manifests itself as a cough, by two spirit brothers, Bidjirl, the saltwater bream and Dadbe, the brown snake, who were protecting the sacred place. The Komnud passed through the whole gathering at Mangarrangki and everybody died.

(Story taken from authentication document supplied with the painting)

Flu Vaccination Rates Among Healthcare Workers Have Plateaued 2017

Vaccination rates have flattened out over the last few years among healthcare workers, US Centers for Disease Control and Prevention (CDC)

Overall, 78.6% of respondents said they had been vaccinated, according to data published in the September 29 issue of *Morbidity and Mortality Weekly Report,* an increase of 15 percentage points since the 2010-2011 season. But the percentage was similar to those of the 2013-2014 and 2015-2016 seasons.

Vaccination was highest among physicians, at 96%; 92% of nurse practitioners and physician assistants and 93% of nurses and pharmacists had received a shot, compared with 80% of other clinicians, 69% of assistants and aides, and 74% of nonclinical healthcare staff.

Ninety-two percent of those working in a hospital setting had received a flu shot, compared with 76% of those in an ambulatory setting and just 68% of those in a long-term-care setting. When the employer mandated vaccination, rates were higher — 97% compared with 45% in settings where vaccination was not required, promoted, or offered on-site, said the CDC.

March 10, 1999

Effectiveness of Influenza Vaccine in Health Care Professionals

- A Randomized Trial

James A. Wilde, MD; Julia A. McMillan, MD; Janet Serwint, MD; et alJeanne Butta, RN; Mary Ann O'Riordan, MS; Mark C. Steinhoff, MD Author Affiliations

JAMA. 1999;281(10):908-913. doi:10.1001/jama.281.10.908

Abstract

Context Data are limited and conflicting regarding the effectiveness of influenza vaccine in health care professionals.

Objective To determine the effectiveness of trivalent influenza vaccine in reducing infection, illness, and absence from work in young, healthy health care professionals.

Design Randomized, prospective, double-blind, controlled trial over 3 consecutive years, from 1992-1993 to 1994-1995.

Setting Two large teaching hospitals in Baltimore, Md.

Participants Two hundred sixty-four hospital-based health care professionals without chronic medical problems were recruited; 49 participated for 2 seasons; 24 participated for 3 seasons. The mean age was 28.4 years, 75% were resident physicians, and 57% were women.

Intervention Participants were randomly assigned to receive either an influenza vaccine or a control (meningococcal vaccine, pneumococcal vaccine, or placebo). Serum samples for antibody assays were collected at the time of vaccination, 1 month after vaccination, and at the end of the influenza season. Active weekly surveillance for illness was conducted during each influenza epidemic period.

Main Outcome Measures Serologically defined influenza infection (4-fold increase in hemagglutination-inhibiting antibodies), days of febrile respiratory illness, and days absent from work.

Results

We conducted 359 person-winters of serologic surveillance (99.4% follow-up) and 4746 person-weeks of illness surveillance (100% follow-up). Twenty-four (13.4%) of 179 control subjects and 3 (1.7%) of 180 influenza vaccine recipients had serologic evidence of influenza type A or B infection during the study period. Vaccine efficacy against serologically defined infection was 88% for influenza A (95% confidence interval [CI], 47%-97%; *P*=.001) and 89% for influenza B (95% CI, 14%-99%; *P*=.03). Among influenza vaccinees, cumulative days of reported febrile respiratory illness were 28.7 per 100 subjects compared with 40.6 per 100 subjects in controls (*P*=.57) and days of absence were 9.9 per 100 subjects vs 21.1 per 100 subjects in controls (*P*=.41).

Conclusions

Influenza vaccine is effective in preventing infection by influenza A and B in health care professionals and may reduce reported days of work absence and febrile respiratory illness. These data support a policy of annual influenza vaccination of health care professionals

Egg Based Vaccines

Based on data from Australia, which already had its flu season, scientists warn that this season's flu shot might be only 10% effective. And the reason for such a low level of protection might lie in the method by which the majority of flu vaccines are made: in eggs.

But with 150 million doses needed every year in the U.S. alone, egg-based vaccine production remains the best option, according to a Sanofi Pasteur executive.

Health officials picked the same viral composition this year for flu vaccines in both the Northern and Southern Hemispheres, so scientists used Australia's health records to get an idea of what the north might expect heading into its season. As Australia had already reported 215,280 influenza cases by mid-October, far more than the 59,022 recorded during its 2009 pandemic, a team disclosed the 10% estimate in a New England Journal of Medicine commentary. Anthony Fauci, M.D., head of the National Institute of Allergy and Infectious Diseases, co-authored the piece.

The U.S. is currently experiencing worse influenza prevalence than in previous years, with seven states already seeing widespread flu activity as of Dec. 2, according to the CDC's surveillance.

Influenza viruses are notorious for their mutations, a phenomenon known as antigenic drift, and each year experts try to predict the strains that will circulate months ahead of the coming season so vaccines can be manufactured in time. If the virus evolves, creating a mismatch between circulating strains and the vaccine composition, it can lead to lower effectiveness.

But for this season, scientists perceive a different problem. Flu viruses didn't significantly change after the vaccine composition was determined, the CDC's most recent Morbidity and Mortality Weekly Report reported, and a preliminary analysis of the Australian data suggests that the low effectiveness was not primarily due to any difference between the vaccine strain and circulating viruses. Instead, it seems to be the egg-based vaccine production technology that caused the mismatch, according to the team.

"[C]irculating A(H3N2) viruses are antigenically less similar to egg-grown A(H3N2) viruses used for producing the majority of influenza vaccines in the United States," the CDC report said.

In fact, a recent study has already attributed last year's low flu shot efficacy to the egg-based production process, a theory that the NEJM study supports. As the earlier group of researchers concluded, flu viruses propagated in eggs undergo certain changes in the hemagglutinin protein—the primary target of neutralizing antibodies—and that could negatively impact our body's virus-killing responses.

With that, scientists now stress the importance of a universal flu vaccine and are championing new paths away from the egg-based manufacturing process.

Recombinant and cell-based platforms are two other vaccine technologies currently available. Sanofi, through its recent acquisition of Protein Sciences, markets the Flublok family, the only recombinant-based flu shots approved in the U.S., and the platform grows vaccine virus in cells. Seqirus' Flucelvax is also the only FDA-approved cell-based flu vaccine. Seqirus just started manufacturing its entirely cell-based flu vaccines on a commercial scale this season.

In a statement sent to FierceVaccines, Sanofi Pasteur's associate VP and North America regional medical head, David Greenberg, M.D., noted that no clinical studies have conclusively proved that cell-culture vaccines are more effective. He also pointed out that, with 150 million doses of flu shots needed each year in the U.S. alone, "egg-based vaccine production remains the most reliable, time-proven method and represents the vast majority of vaccines used globally to help prevent influenza."

But the company also said it “continuously assesses new technologies to improve production capabilities,” including the benefits of Flublok and development of a universal flu vaccine that would be effective despite antigenic drift and mismatch.

Published last month, the University of Pennsylvania study found that most people among the studied group who had strong antibody responses in the 2016-17 season had received the recombinant flu vaccine.

Regardless, before alternative technologies become widely adopted, experts still encourage people to get the flu shots, even if it only offers 10% protection. “However imperfect, though, current influenza vaccines remain a valuable public health tool, and it is always better to get vaccinated than not to get vaccinated,” the NEJM authors wrote.

Editor's Note: *The story has been updated with two statements from Sanofi Pasteur. It also clarifies that recombinant flu vaccines are also grown in cell culture.*

Flu vaccination in the elderly

There is considerable evidence that immune responses to vaccination decline substantially with age (Haralambieva et al., 2015). Antibody responses in the elderly are lower than in younger adults and this is likely to translate into a lower effectiveness in the elderly for influenza vaccine compared with younger adults (Goodwin et al., 2006; Lang et al., 2012).

During the 2016/17 UK influenza season, the effectiveness of vaccine against medically attended, laboratory -confirmed influenza in primary care in the elderly could not be demonstrated (Pebody et al.,2017).

A meta-analysis of data between 2004 and 2015 was also unable to show significant efficacy for the inactivated influenza vaccine in the elderly against the A(H3N2) influenza virus, which mainly impacts the elderly (Bellongia et al., 2016).

PHE have also conducted an age stratified analysis of pooled primary care data since 2010/11 (in press) which showed significant effectiveness in the 65-74 age group for all influenza, A(H1N1)pdm09, influenza B and evidence of protection against A(H3N2).

Above the age of 75 years old, however, pooled estimates were unable to demonstrate any significant effectiveness across all seasons and all the influenza virus types.

In August 2017, an adjuvanted trivalent inactivated vaccine (aTIV) Fluad®, licensed for use in those aged 65 years and older, gained marketing authorisation in the UK.

The aTIV has been licensed in some countries in Europe since 1997 and in the USA since 2015.

In June 2017, JCVI (JCVI., June 2017) reviewed the published data that the adjuvanted vaccine has higher vaccine immunogenicity and higher effectiveness than non-adjuvanted vaccines in the elderly (Van Buynder et al, Vaccine 2013, Dominich et al., 2017).

Nearly all deaths among children under five with influenza-related lower respiratory tract infections occur in developing countries, but the effects of seasonal influenza epidemics on the world's poorest are not fully known.

WHO is working with partners to assess the global influenza burden of disease by providing guidance and expertise to Member States to measure the influenza disease burden and its economic consequences.

Further surveillance and laboratory studies of other diseases such as cardiovascular disease, which can be influenza-related, are expected to yield substantially higher estimates over the next few years.

Australia is not immune to potentially deadly infectious diseases pandemics, the World Health Organisation regional director has warned.

Speaking on Monday October 201 at the WHO regional Committee Meeting for the Western Pacific in Brisbane, Dr Shin Young-soo said it was not a matter of "if" but "when" the next emerging disease tested health security responses in the region.

His warning came as federal Health Minister, Greg Hunt announced Australia would commit $20 million to a regional pandemic preparedness and response plan to protect both Australia and its neighbours from future outbreaks.

Mr Hunt said Australia was well-prepared to respond to pandemics within its borders, with a centralised emergency response centre and national drug inventories.

"[But] the real challenge is within the region if there is an emergence of a new wave of zika [or] you could have the equivalent of the Asian bird flu," he said.

The next threat to the region could be ebola or the rapid spread of tuberculosis, Mr Hunt said.

"Safety at home in this space generally comes from safety in the region," he said.

The funding will be used to beef up emergency response systems within countries, and to mobilise Australian medical and security personnel or enlist private contractors to work on the front lines during outbreaks.

In 2014, Aspen Medical won a $20 million Australian government contract to open a 100 bed ebola clinic in Sierra Leone, but faced opposition from critics who argued Australian Medical Assistance Teams (AUSMATs) should have been deployed.

Regional director Dr Shin said the western Pacific, home to 1.9 billion people, was "the most outbreak- and disaster-prone region in the world".

"Australia is not immune to health challenges ... emerging diseases threaten us all," he said.

Dr Shin said infectious diseases don't respect borders and can spread in a matter of hours. "No country is safe until all are safe," he said.

The funding is part of a $300 million health security initiative announced at the weekend by Foreign Affairs Minister Julie Bishop.

Australia's health security was linked to the health security of countries in the Indo-pacific region. A major disease outbreak could have severe health and economic consequences for all countries, including Australia, potentially disrupting trade, investment and people movement, according to the Department of Foreign Affairs and Trade.

The five-year plan will also support research into improving diagnostics and treatment for multi-drug resistant TB and malaria, fast-tracking new medicine registration, and establishing a health security corps embedded within government, research and health organisations in the region.

Mr Hunt said the initiative was "a sign of international cooperation and it's also in our own national interests".

"It means we have stronger and better health outcomes within our region and it is about ensuring we have better health security for Australia, but above all else it's about doing the right things.“

On Monday Mr Hunt signed Australia’s first regional health security agreement with WHO, becoming the first developed nation in the region to do so. As part of the agreement, Australia will be the subject of an external review of its disaster and epidemic preparedness.

The agreement focuses on health security, universal access to healthcare, medical regulations and health system co-operation to respond to disaster and epidemics.

'The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant. Here is a hypothetical illustration. Mr X has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin the treatment fails. Mrs X dies. Who is primarily responsible for Mrs X's death?'

Sir Alexander Fleming,
Nobel Lecture, 1945

Dr. Santosham has been a pioneer of the Hib scientific field through his instrumental role in a 30-year campaign to understand the global burden and epidemiology of the disease in various populations. Dr. Santosham, citing his early childhood experiences in India as his foundation, was driven to focus on issues of vaccine access and coverage for the world's most vulnerable and underserved populations. Over the past decade, Dr. Santosham has served as a leader in global, regional, and country-focused post-licensure work that moved evidence to policy, and onward to implementation and scale-up, ensuring that children around the world, especially those most in need, had access to these life-saving vaccines.