

Responding to the threat of influenza – what did we learn in 2017?

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Declarations

- No payments received from pharma
- Chair, Advisory Committee for Vaccines (advising TGA/OHP)
- Chair, Influenza Working Group of ATAGI (advising NIP/OHP)

- My views do not represent official policy or the views of advisory committees

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Influenza

- The 2017 season – transmission, severity, impact
- Vaccine coverage and effectiveness
- Maximising direct protection – enhanced formulations, pre-school programs, improving vaccine coverage in high risk groups
- Maximising indirect protection – paediatric programs, HCW programs
- Areas of uncertainty – repeated vaccination, waning immunity
- Public health messaging – balancing advocacy with reality

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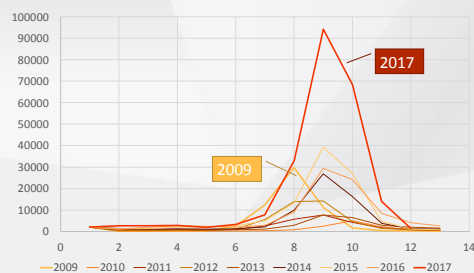
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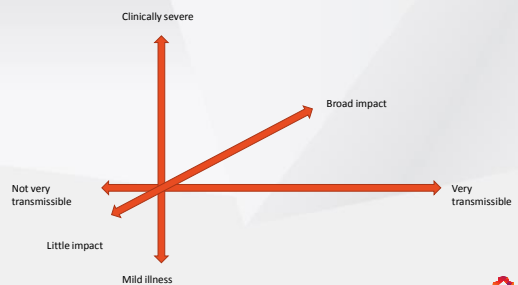
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Monthly notifications (NNDSS)



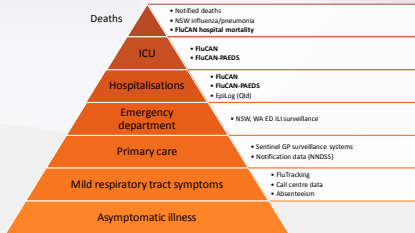
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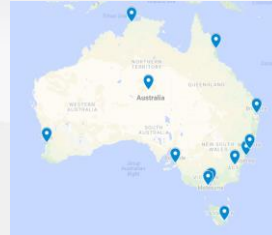
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Surveillance pyramid

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FluCAN 2012-18



- 21 hospitals (incl 6 paediatric hospitals)
- 17 hospitals used for surveillance
- All states/territories
- Metropolitan/regional
- Temperate/tropical
- >14% of national bed capacity
- (TSANZ/ASID collaboration 2009)

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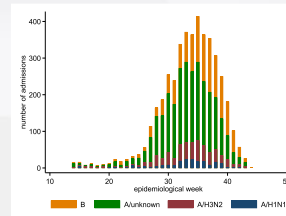
Incidence density test-negative



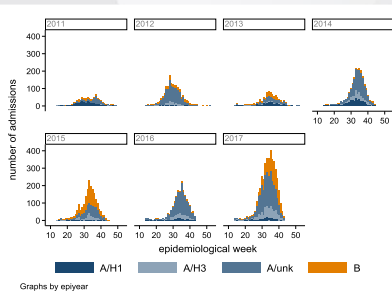
Case = influenza
Control = non influenza ILI matched for date of presentation
Case/control status assigned when test result known
Adjust for confounders

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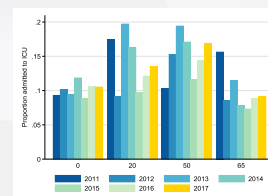
2017 season



- 4259 cases at surveillance hospitals
- (excluding 4 PAEDS sites - >2x 2016)
- 78% chronic comorbidities
- 31% influenza B
- (~31 000 admissions nationally)
- Mortality 155/4236 (3.7%)

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Severity – proportion admitted to ICU



- Overall 8.7%
- Paediatric 10.1%
- Non-elderly adults 11.1%
- Elderly 6.3%
- Indigenous Australians (10.0%)
- Pregnant women (8.7%)

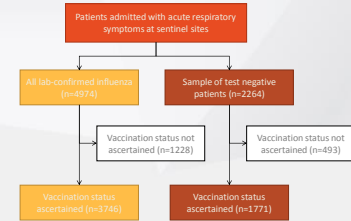
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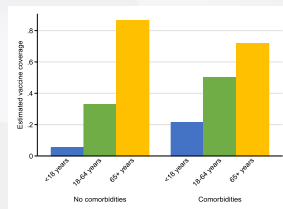
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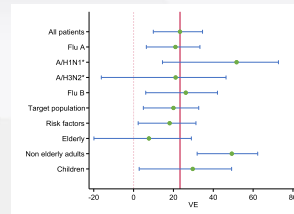
VE analysis

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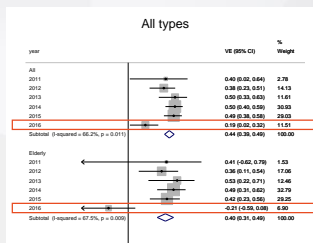
Vaccine coverage

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Vaccine effectiveness against hospitalisation

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Historical context

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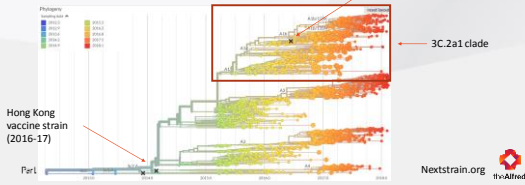
The “perfect storm”

- A/H3 subtype predominating
 - Tends to affect elderly
 - Genetically diverse subtype compared to A/H1 and B
- Egg adaptation of H3 vaccine strain
 - Fewer vaccine candidates
 - Difficult to match against diverse H3 strains
- Poorly protective vaccine-induced antibodies
 - Vaccine poorly immunogenic in high risk groups
 - A/H3 vaccine issues

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H3N2 diversity

- Significant genetic diversity within H3N2 circulating strains
- Various clades – recent strains in 3C.2a1
- Recent diversification in 2a1 clade



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New vaccines for elderly – FluZone HD

- 4x antigen content of standard IIV
- TIV (not QIV)
- Evidence of increased protection in RCT
 - 24% more effective than TIV
 - Two seasons with predominant H3
- Also protection demonstrated against non-specific endpoints eg pneumonia
- 24% represents relative protection
 - If standard vaccine 40% effective, expect 50% effectiveness with new vaccine



DiazGranados NEJM 2014

New vaccines for elderly - Fludax

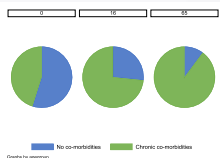
- MF59 adjuvanted vaccine
- Also TIV (not QIV)
- Evidence of increased protection in observational study
 - Hospitalisation with influenza
 - 17% more effective than TIV
 - Multiple seasons



Mennino AJE 2012

Paediatric influenza

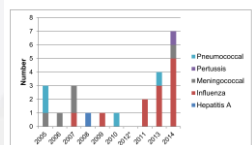
Risk factors by age group



FluCAN hospitalisations

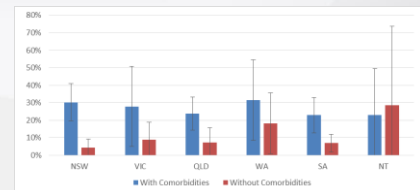
Paediatric deaths from vaccine preventable diseases, NSW

Figure 17 Preventable and potentially preventable deaths, 2005 - 2014

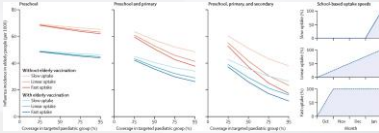


NCIRS NSW report, 2016

Current estimated paediatric coverage



UK paediatric influenza program



- Paediatric program gives both direct and indirect protection
- Greater effect if more children vaccinated (and if uptake rapid)
- May be more cost effective than vaccinating elderly

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Hodgson Lancet Pub Health 2017



Mandatory vaccination of HCW?

For

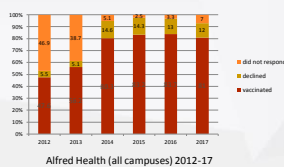
- Very high coverage ensured, precedent established
- Nosocomial influenza can be severe in inpatients
- Influenza vaccine less immunogenic in elderly, immunosuppressed
- Some evidence that vaccinating staff reduces risk in patients (low quality evidence)
- When effective, vaccine is probably cost effective in reducing staff illness

Against

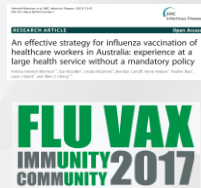
- Reasonable coverage achievable without mandate; if offered, most staff will get vaccinated
- Difficult to justify if vaccine poorly protective
- Continuous masking not supported by evidence
- Better protection from respiratory viruses achieved by addressing "presenteeism"
- Practical issues in re-deploying unvaccinated staff: specialized areas, medical contraindications

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Healthcare workers



Alfred Health (all campuses) 2012-17

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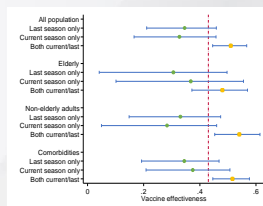
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Repeated vaccination

- Vaccination serially correlated
- No evidence of impaired VE in FluCAN
- Mixed results – some studies demonstrate impaired vaccine protection with repeated doses
- Potential for confounding by natural infection

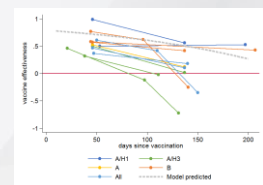


Cheng CID 2017



Waning protection

- Systematic review of all studies comparing early vs late VE
- 7 studies identified
 - Heterogeneity in population, season, country, definitions
 - generally consistent fall in VE with time since vaccination
- Implications for policy?
- Revaccination?



Sarah Moberley, unpublished data



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Public health messaging

- Hyperbolic predictions and unreasonable claims potentially erode trust

“This will be the worst season ever and the vaccine will protect you”

Vs

“Influenza is common; although usually mild, severe disease can occur even in otherwise healthy adults and children. The vaccine is far from perfect, but is one of the best tools we have to reduce your risk of complications”

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Target audience

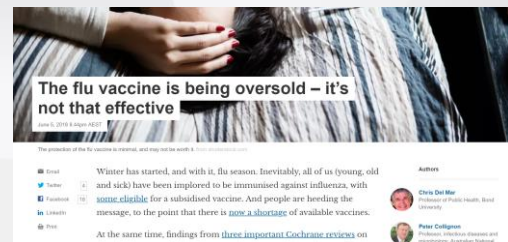
- Importance of recommendation from health professionals
- Target: other healthcare workers

Understanding the barriers to uptake of antenatal vaccination by women from culturally and linguistically diverse backgrounds: A cross-sectional study

Sushena Krishnaswamy, Allen C. Cheng, Euan M. Wallace, Jim Buttery & Michelle L. Giles

	dTPa Crude OR	Adjusted OR	IIV Crude OR	Adjusted OR
Previous dTPa / IIV				
No	Ref	Ref	Ref	Ref
Yes	2.9 (1.9–4.3)	<0.001	0.63	3.9 (2.7–5.7)
HCW recommended				
No	Ref	Ref	Ref	Ref
Yes	24.9 (15.3–40.7)	<0.001	9.9 (4.6–21.3)	<0.001
				16.2 (10.1–25.9)
				<0.001

Krishnaswamy Hum Ther Imm 2018

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Conclusions

- Vaccine effectiveness moderate at best
 - Vaccine match issues persist
- Available tools to reduce impact of influenza
 - Improve vaccine coverage esp in vulnerable groups
 - More immunogenic vaccines. FluZone HD, Fluid in 2018 – marginal benefit over QIV
 - Childhood immunisation
 - Harness indirect protection?
- Research required
 - Evaluate effectiveness of new vaccines
 - Determine whether alternative vaccine platforms may reduce adaptation problems
 - Universal flu vaccine

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Acknowledgements

FuCAN investigators

- Dominic Dwyer
- Mark Holmes
- Louis Irving
- Grant Waterer
- Tony Korman
- Louise Cooley
- Anna Howell
- Deb Friedman
- Peter Wark
- Graham Simpson
- John Ugham
- Simon Bowler
- Saranya Senenayake
- Tom Kotsimbos
- Paul Kelly

PAEDS/AusVaxSafety

Kristine Macartney
Christopher Blyth
Helen Marshall
Julia Clark
Josh Francis
Jim Buttery

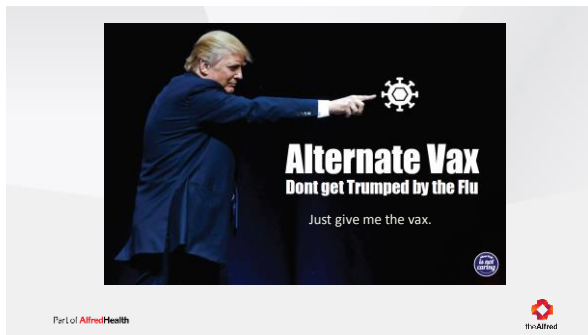
Infection Prevention Unit, Alfred Health

Pauline Bass
Kristine Heinrich-Morrison
Sue McLellan
Jonathan Chirines

Systematic review

TGA, OHP, NCIRS
Michelle Giles, Sush Krishnaswamy

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Vaccine shortages

- Unprecedented demand – more vaccine distributed in by mid May than in all of 2017
- Distribution chain complex: national => state => primary care
 - New childhood programs, aged care worker mandates
 - Mixed stock with healthcare workers
 - Complexity in forecasting demand with different vaccine types/age group limits
 - Off label use – two dose/combination TIV/QIV
- Need for better stock management and distribution data
- Need for prioritisation for future vaccines

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