Influenza Related Complications and Deaths in Australian Children: Seasonal Surveillance 2008 -2015

Authors: Yvonne Zurynski, Greta Ridley, Amy Phu, Robert Booy, Elizabeth Elliott *and all clinicians who report to the APSU*

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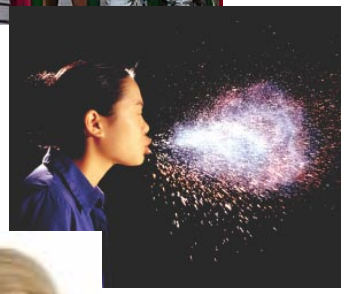
- Influenza is a common *usually mild* disease
- Highest burden:
  - frail elderly
  - very young <2 yrs
  - people with predisposing chronic conditions
- Children are excellent virus reservoirs and efficient virus transmitters
- Severe complications and death occur
- Little data on severe complications and deaths



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National Immunization Program

- **Children considered at risk** (recommended and funded):
  - 6mo to <5yrs ATSI
  - 6mo to < 5yrs Chronic Medical Conditions

- **Other healthy children** (recommended, not funded):

"Annual influenza vaccination is recommended for any person ≥ 6mo of age for whom it is desired to reduce the likelihood of becoming ill with influenza"

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Flu Vaccines for children

- Sanofi's *FluQuadri® Junior* < 3yrs.
- GlaxoSmithKline *Fluarix Tetra®* >3yrs.
- Seqirus (formerly bioCSL) flu vaccine *Fluvax®* is not registered for use in children less than five years of age

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Aim:

To describe:

- Influenza related complications and deaths in Australian children 2008 -2015
- Predisposing conditions
- Vaccination
- Treatment with flu specific antivirals

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Methods

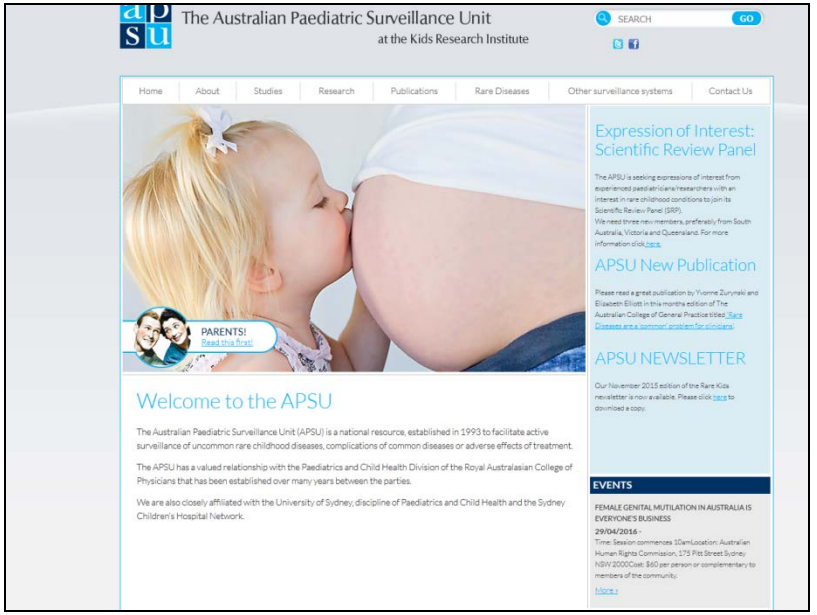
APSU: ~1500 paediatricians

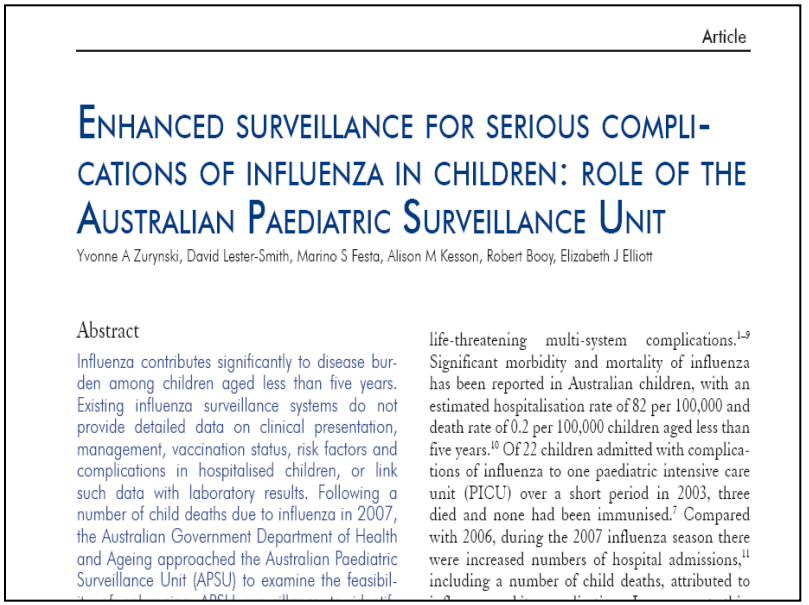
- Monthly reporting
  - 90% report by e-mail
  - Response rates to card >90%

Each year July-September

Clinicians are asked to reports cases as they see them

Weekly reporting to the Department of Health and Ageing Surveillance Section





Article

ENHANCED SURVEILLANCE FOR SERIOUS COMPLICATIONS OF INFLUENZA IN CHILDREN: ROLE OF THE AUSTRALIAN PAEDIATRIC SURVEILLANCE UNIT

Yvonne A Zurynski, David Lester-Smith, Marino S Festa, Alison M Kesson, Robert Booy, Elizabeth J Elliott

Abstract

Influenza contributes significantly to disease burden among children aged less than five years. Existing influenza surveillance systems do not provide detailed data on clinical presentation, management, vaccination status, risk factors and complications in hospitalised children, or link such data with laboratory results. Following a number of child deaths due to influenza in 2007, the Australian Government Department of Health and Ageing approached the Australian Paediatric Surveillance Unit (APSU) to examine the feasibil-

life-threatening multi-system complications.[1-9] Significant morbidity and mortality of influenza has been reported in Australian children, with an estimated hospitalisation rate of 82 per 100,000 and death rate of 0.2 per 100,000 children aged less than five years.[10] Of 22 children admitted with complications of influenza to one paediatric intensive care unit (PICU) over a short period in 2003, three died and none had been immunised.[7] Compared with 2006, during the 2007 influenza season there were increased numbers of hospital admissions,[11] including a number of child deaths, attributed to

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Case definition

Any child aged < 15 years with laboratory confirmed influenza AND admitted to hospital AND who have at least one of the following complications:

- Pneumonia (Confirmed on X-ray or microbiology) and Oxygen requirement
- Mechanical ventilation
- Laboratory proven secondary bacterial co-infection; Bacteraemia; Septicaemia
- Encephalitis / encephalopathy
- Seizures (including simple febrile seizure, prolonged or focal seizure or status epilepticus)
- Transverse myelitis
- Polyneuritis/mononeuritis
- Guillain-Barré syndrome
- Reye Syndrome
- Myocarditis; Pericarditis; Cardiomyopathy
- Rhabdomyolysis
- Purpura fulminans
- Disseminated coagulopathy
- Shock (requiring >40 ml/kg fluid resuscitation)
- Acute renal failure
- Death, including death at presentation to hospital

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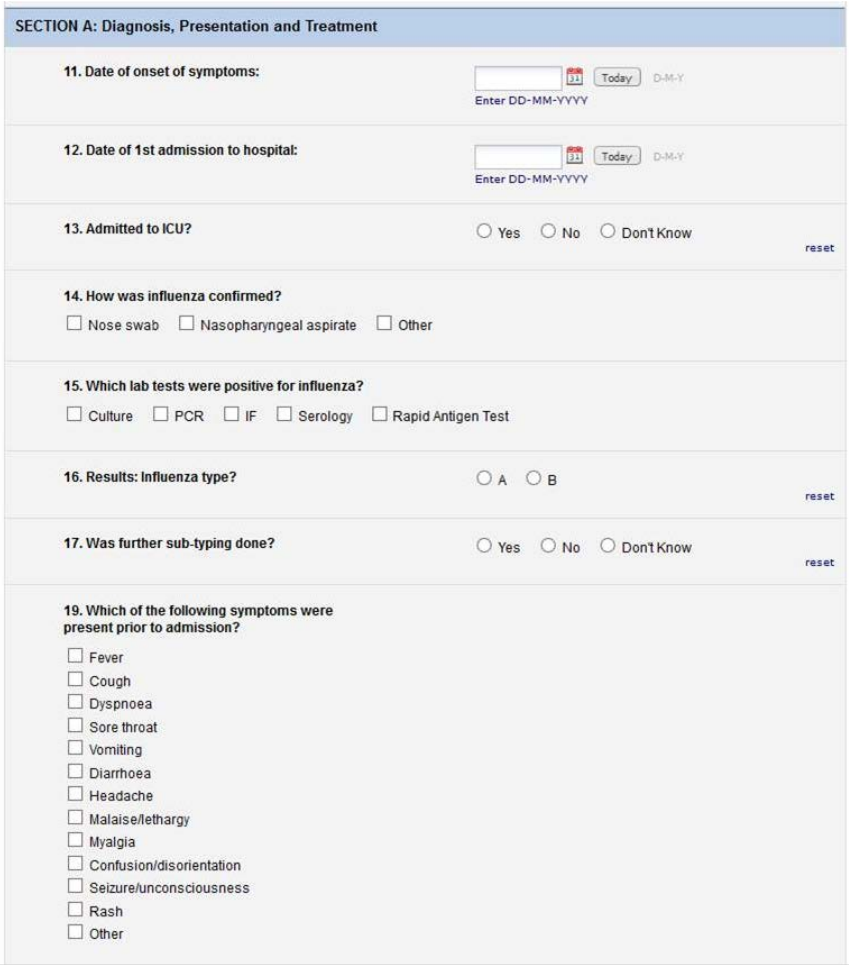
Data collection: paper/fax 2008-13; on-line via REDCap from 2014



SECTION A: Diagnosis, Presentation and Treatment

11. Date of onset of symptoms: Today D-M-Y
Enter DD-MM-YYYY

12. Date of 1st admission to hospital: Today D-M-Y
Enter DD-MM-YYYY

13. Admitted to ICU? ○ Yes ○ No ○ Don't Know reset

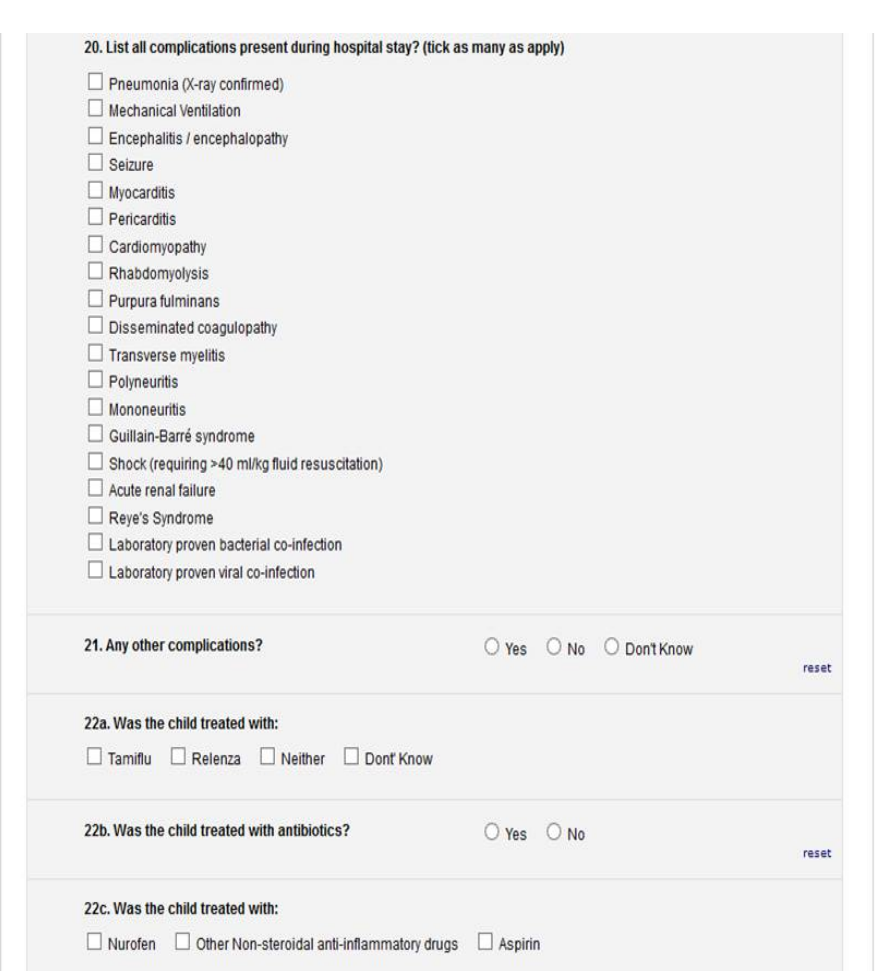
14. How was influenza confirmed?
☐ Nose swab ☐ Nasopharyngeal aspirate ☐ Other

15. Which lab tests were positive for influenza?
☐ Culture ☐ PCR ☐ IF ☐ Serology ☐ Rapid Antigen Test

16. Results: Influenza type? ○ A ○ B reset

17. Was further sub-typing done? ○ Yes ○ No ○ Don't Know reset

19. Which of the following symptoms were present prior to admission?
☐ Fever
☐ Cough
☐ Dyspnoea
☐ Sore throat
☐ Vomiting
☐ Diarrhoea
☐ Headache
☐ Malaise/lethargy
☐ Myalgia
☐ Confusion/disorientation
☐ Seizure/unconsciousness
☐ Rash
☐ Other



20. List all complications present during hospital stay? (tick as many as apply)
☐ Pneumonia (X-ray confirmed)
☐ Mechanical Ventilation
☐ Encephalitis / encephalopathy
☐ Seizure
☐ Myocarditis
☐ Pericarditis
☐ Cardiomyopathy
☐ Rhabdomyolysis
☐ Purpura fulminans
☐ Disseminated coagulopathy
☐ Transverse myelitis
☐ Polyneuritis
☐ Mononeuritis
☐ Guillain-Barré syndrome
☐ Shock (requiring >40 ml/kg fluid resuscitation)
☐ Acute renal failure
☐ Reye's Syndrome
☐ Laboratory proven bacterial co-infection
☐ Laboratory proven viral co-infection

21. Any other complications? ○ Yes ○ No ○ Don't Know reset

22a. Was the child treated with:
☐ Tamiflu ☐ Relenza ☐ Neither ☐ Dont' Know

22b. Was the child treated with antibiotics? ○ Yes ○ No reset

22c. Was the child treated with:
☐ Nurofen ☐ Other Non-steroidal anti-inflammatory drugs ☐ Aspirin

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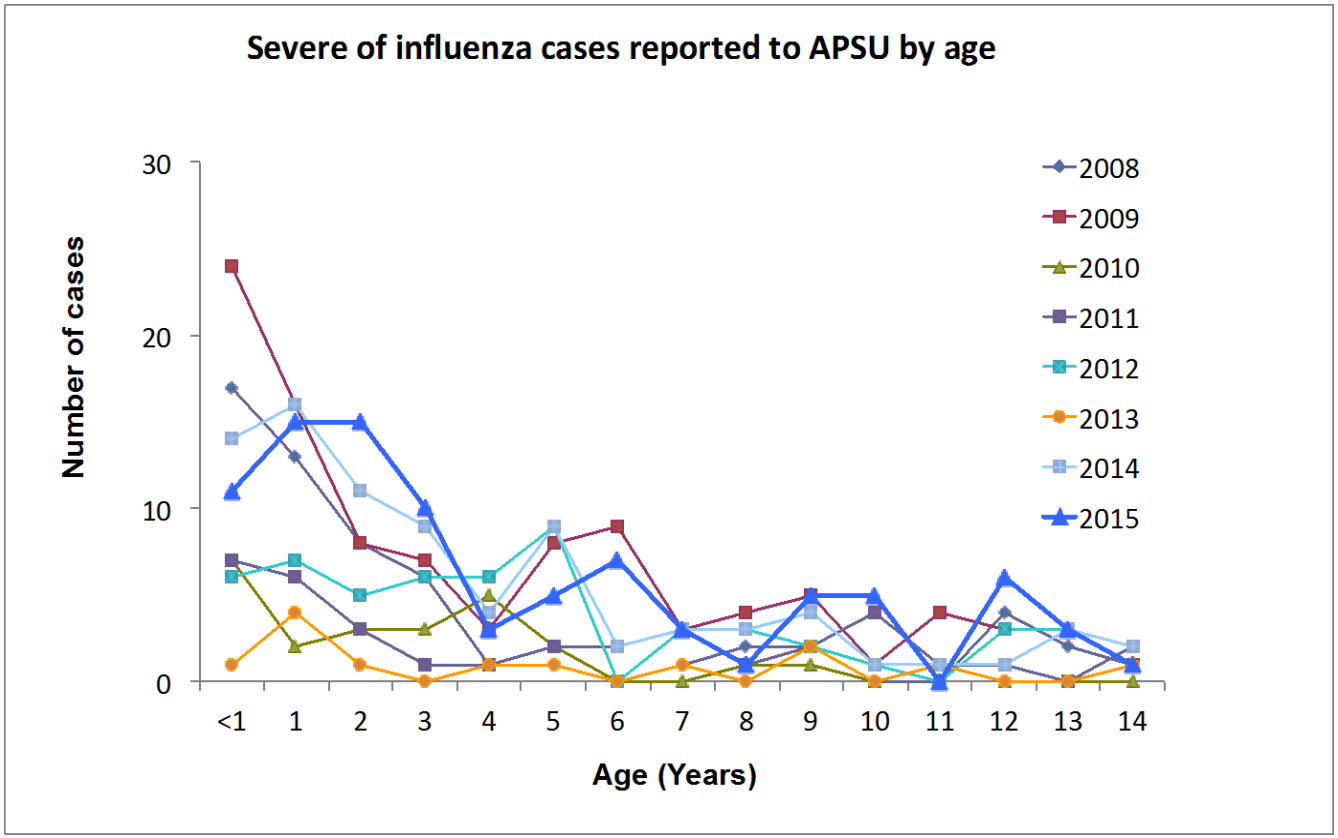
Results:

N = 474 Male: 252 (54%) Female: 210 (46%)

Median Age: 3.5 (0.12 - 14.4) years

Flu A – 329; Flu B – 154



2008: N= 58 2009: N= 99 2010: N= 25 2011: N = 36
2012: N= 56 2013: N=13 2014: N= 83 2015: N= 90

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Results:

- Pre-existing chronic conditions – 174 (36.7%)
  Vaccinated: 18 (10%)

- Previously healthy – 300 (63.3%)
  Vaccinated: 3 (1%)

Vaccination status unknown in ~ 75%

Suggests that clinicians don't ask

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Complications:

283 (59.7%)	Pneumonia
86 (18.0%)	Co-infection (laboratory proven)
71 (15.0%)	Encephalitis/encephalopathy
19 (4.0%)	Rhabdomyolysis
19 (4.0%)	Myocarditis/ cardiomyopathy

~35% had more than one complication

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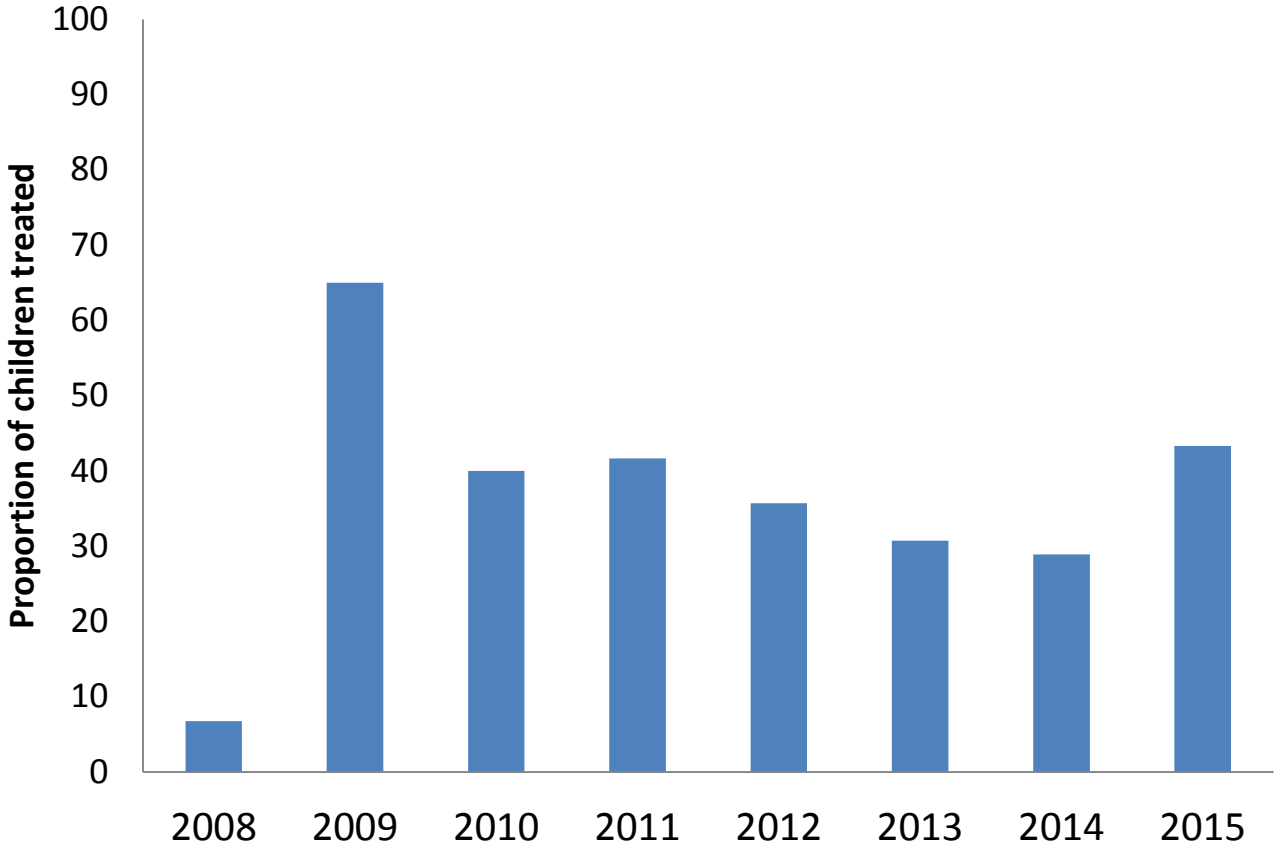
Treatment with Oseltamivir



Total treated 2008-2015:(185)39%

Given after 48 hours in 90%

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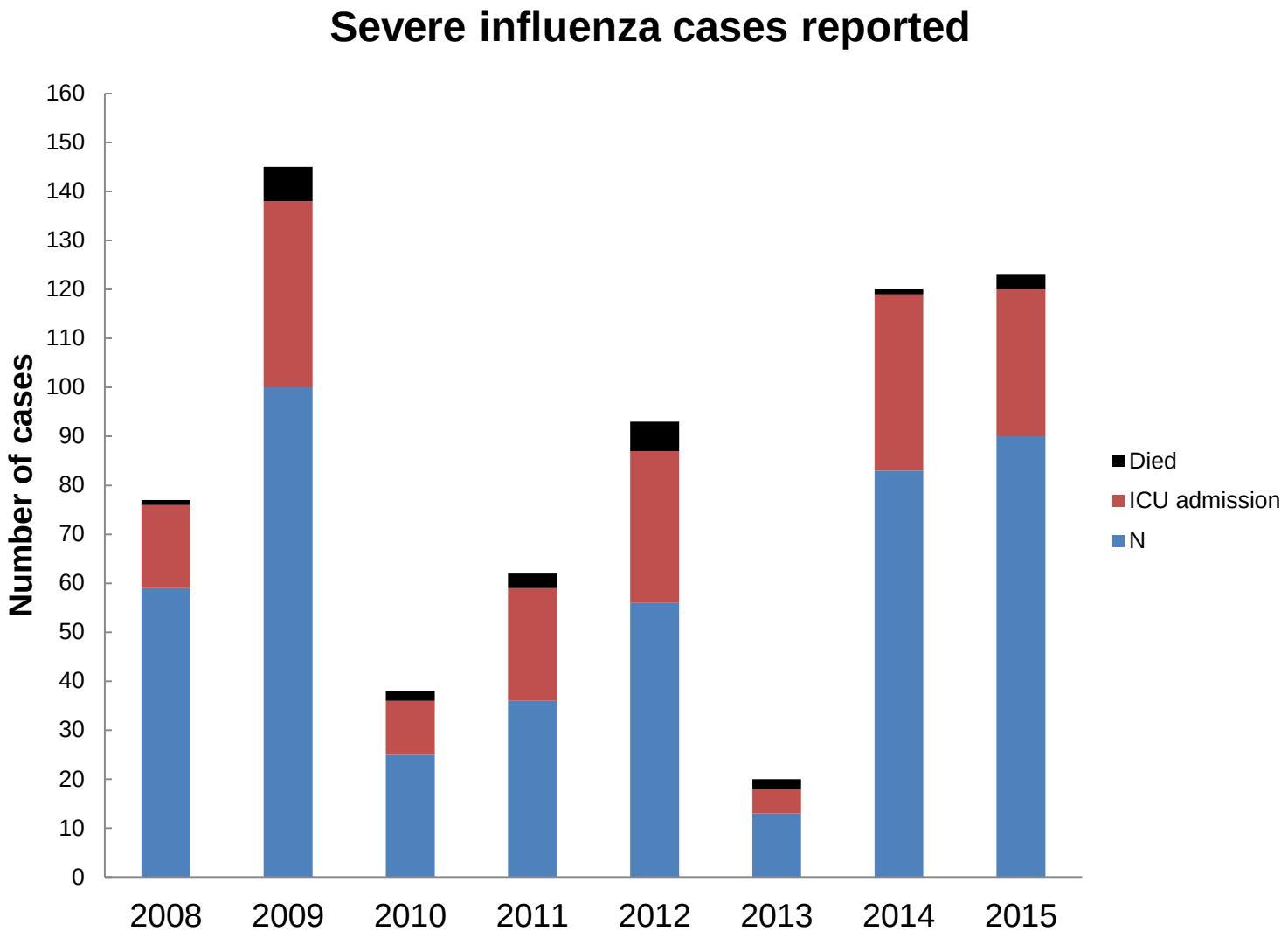
2008-2015
474 cases; 191 ICU admissions; 25 deaths



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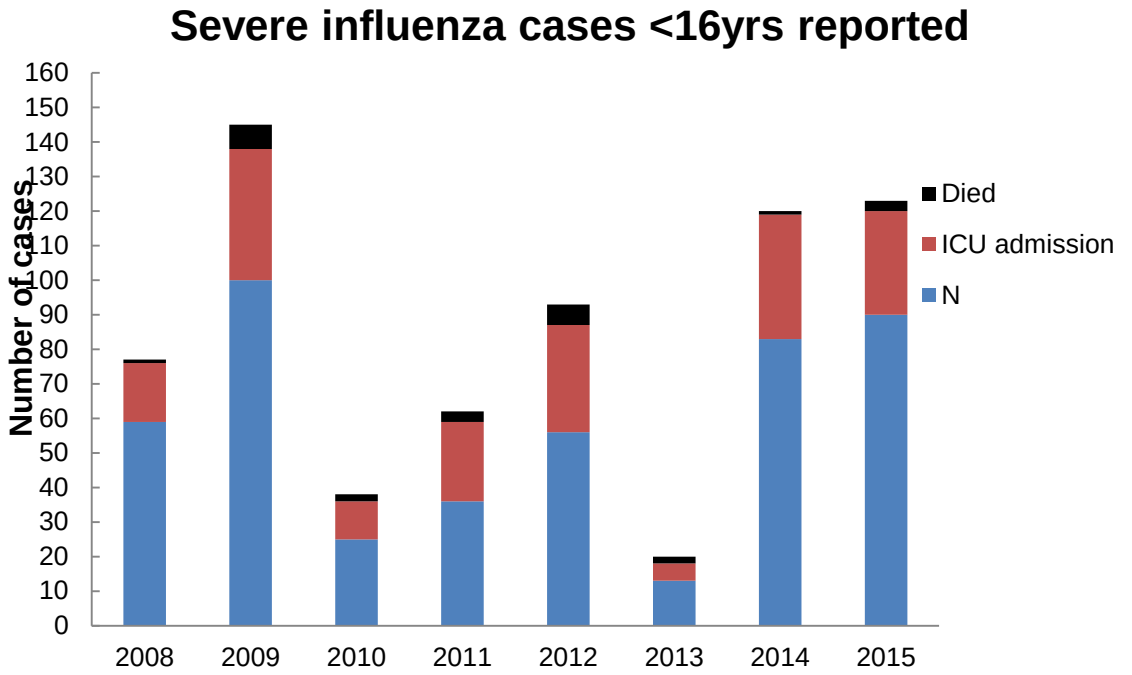
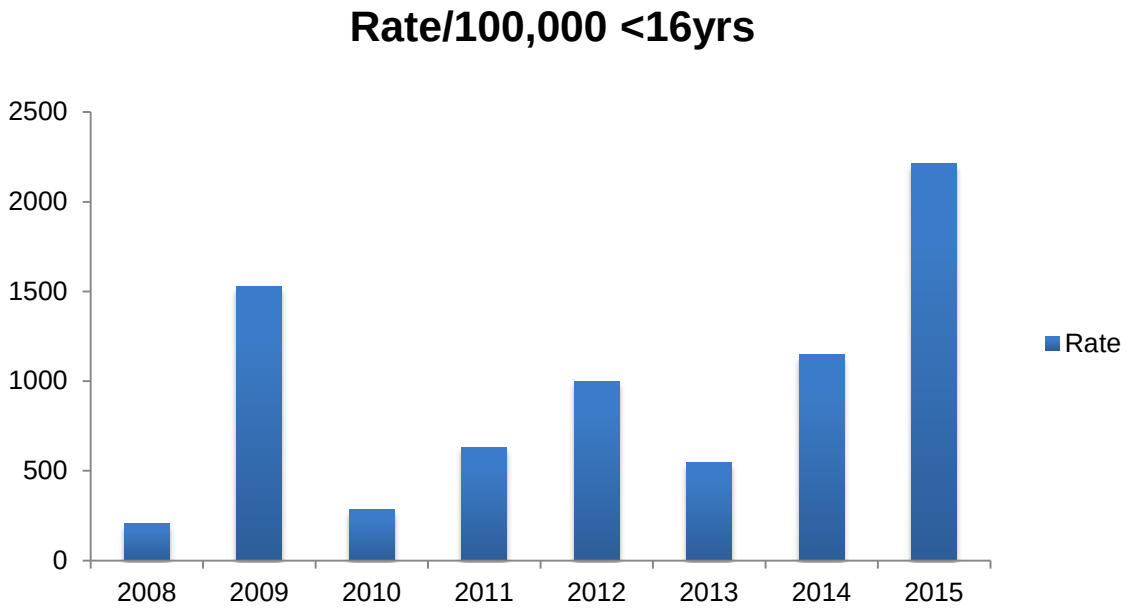
APSU cases



CDNA – Lab confirmed cases



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Deaths: N=25

State	N (%)	Hospitals
NSW	9 (40)	Westmead -3; Randwick - 1; Bankstown - 3; Lismore Base – 1; Albury Base – 1
Vic	4 (16)	RCH – 2; Gippsland -1; Ballarat Base-1;
Qld	4 (16)	Mater-1; RCH-1; Gold Coast – 1; Nambour- 1; Rockhampton - 1
SA	2 (8)	Women's and Children's -1; Flinders Medical Centre -1
WA	2 (8)	Princess Margaret - 2
Tas	2 (8)	Launceston General - 1; Mersey Community Hospital -1
NT	1 (4)	Royal Darwin - 1

- Tertiary paediatric referral centres: 11 (44%)
- Other Hospitals: 14 (56%)

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Complications Before Death

7 pneumonia
7 mechanical ventilation
    1 ECMO

5 Encephalitis/encephalopathy
1 acute necrotising encephalopathy
4 Seizures
1 intracranial haemorrhage

5 Shock requiring fluid resuscitation

4 Proven Co-infection
1 Disseminated Intravascular Coagulation
1 Rhabdomyolysis
1 metabolic acidosis
1 myositis
4 cardiomyopathy/myocarditis

Most had multiple complications

ICU: 15 (60%)

3 dead on arrival in ED

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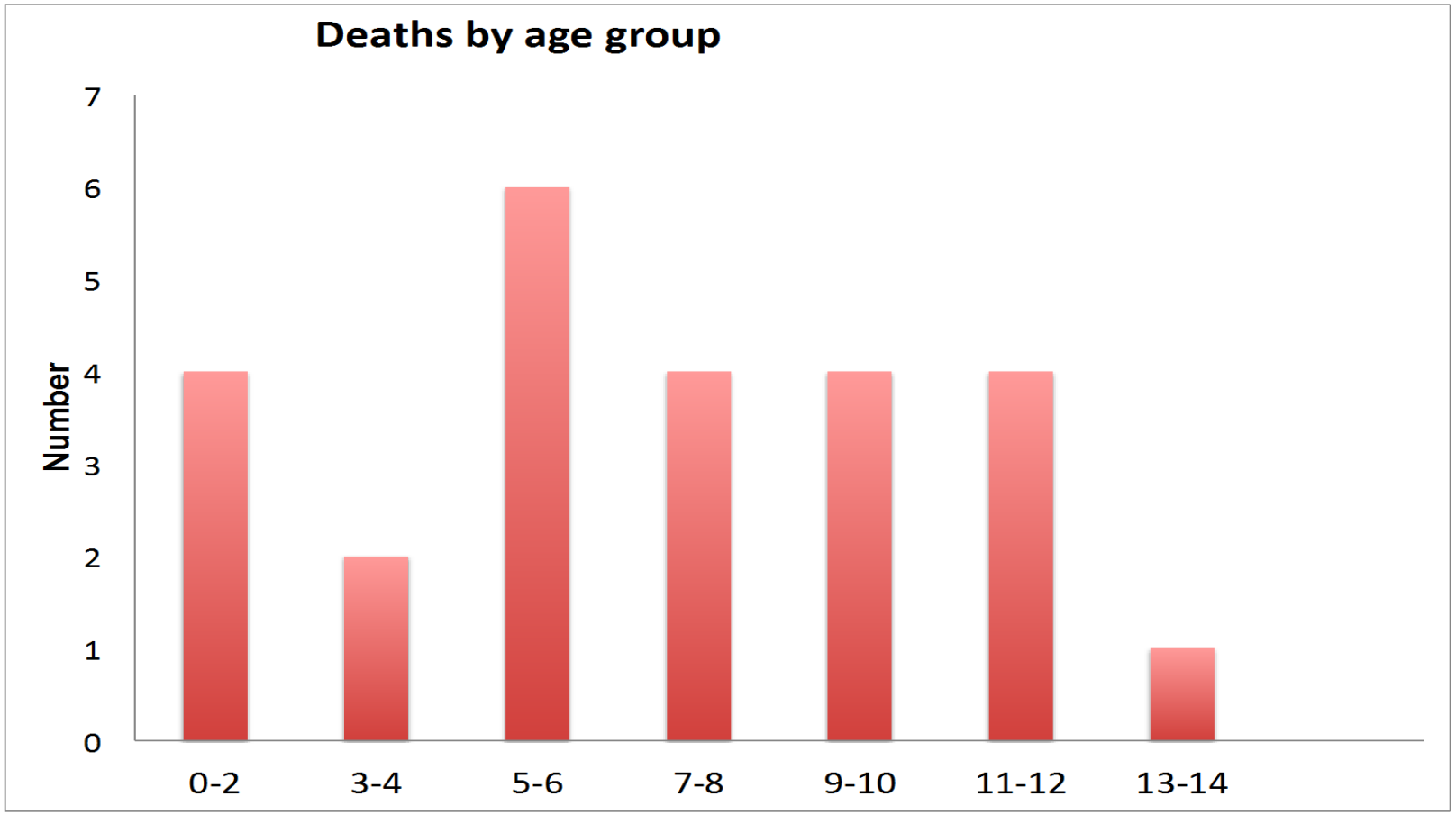

<5 yrs old: 6 (2.1%) died

5-14 yrs old: 19 (11.3%) died

P < 0.01

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Underlying condition

15 (60%) had a chronic condition

- 3 Neuromuscular disorders
- 2 Cerebral Palsy
- 2 Malignancy or other immunodeficiency
- 1 Gastrointestinal disorders (GORD, fundoplication)
- 2 Congenital heart disease
- 1 CHARGE syndrome
- 1 Panhypopituitarism
- 3 Undiagnosed rare genetic syndrome

2 vaccinated for flu

10 (40%) were healthy

None vaccinated for flu

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Previously Healthy Children – Examples

2009

- 12 yo, fever, cough, headache, malaise, sore throat, myalgia
- Admitted to hospital
- Not tested for influenza
- No Oseltamivir
- Discharged home after 2 days in hospital
- Developed serious pneumonia – dead on arrival at hospital 2 days later
- Flu A H1N1 2009 confirmed on autopsy

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Previously Healthy Children - Examples

2015

- 4.3yo; Flu B
- Usual flu symptoms (fever, malaise, cough etc.)
- Deteriorated quickly in hospital
- Seizure
- Encephalitis / encephalopathy, acute necrotising encephalopathy
- Shock (requiring >40ml/kg fluid resuscitation)
- Persistent metabolic acidosis,
- ? Secondary infection
- Cefotaxime, IV aciclovir, Vancomycin, Gentamicin

- Died 2 days later

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Summary

Severe complications:
•Only 39% were treated with flu specific antivirals
•Of the treated 90% were treated late (>48hrs)

Vaccination:
•10% children with chronic disorders

Deaths:
•every year 2008-2015 (total 25)
•more common among older children ≥ 5 years
•~ 60% chronic conditions and **40% previously healthy**
•general hospitals (66%) rather than paediatric referral centres

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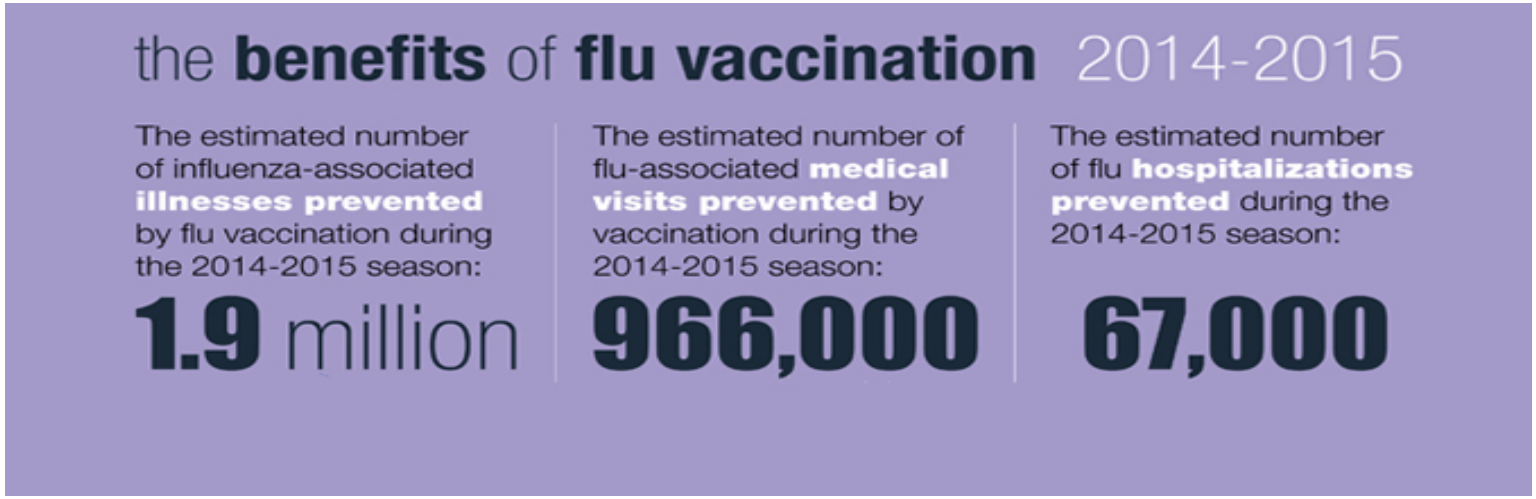
Conclusions

- Better awareness among clinicians
- Earlier detection
- Earlier treatment and referral to paediatric centre
- Vaccination
- Ongoing surveillance to monitor the effectiveness of any prevention and intervention strategies

CDC:



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Thank You

- Co-Authors
- Australian Department of Health and Ageing
- ***all APSU clinicians for reporting cases***

Questions?

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