Influenza epidemiology, vaccine coverage and vaccine effectiveness in children admitted to sentinel Australian hospitals in 2014: the Influenza Complications Alert Network (FluCAN)

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The Influenza Complications Alert Network (FluCAN) is a sentinel hospital-based surveillance programme operating in all states and territories in Australia. We summarise the epidemiology of children hospitalised with laboratory-confirmed influenza in 2014 and reports on the effectiveness of inactivated trivalent inactivated vaccine (TIV) in children. In this observational study, cases were defined as children admitted with acute respiratory illness (ARI) with influenza confirmed by PCR. Controls were hospitalised children with ARI testing negative for influenza. Vaccine effectiveness (VE) was estimated as 1 minus the odds ratio of vaccination in influenza positive cases compared with test-negative controls using conditional logistic regression models. From April until October 2014, 402 children were admitted with PCR-confirmed influenza. Of these, 28% were aged < 1 year, 16% were Indigenous, and 39% had underlying conditions predisposing to severe influenza. Influenza A was detected in 90% of cases of influenza; influenza A(H1N1)pdm09 was the most frequent subtype (109/141 of subtyped cases) followed by A(H3N2) (32/141). Only 15% of children with influenza received antiviral therapy. The adjusted VE of one or more doses of TIV for preventing hospitalised influenza was estimated at 55.5% (95% confidence intervals (CI): 11.6–77.6%). Effectiveness against influenza A(H1N1)pdm09 was high (91.6% , 95% CI: 36.0–98.9%) yet appeared poor against H3N2. In summary, the 2014 southern hemisphere TIV was moderately effective against severe influenza in children. Significant VE was observed against influenza A(H1N1)pdm09.

Introduction

Influenza is a common respiratory viral infection that affects up to 5–10% of the population each year [1]. Previous studies demonstrate that young children have the highest rate of hospitalisation [2]. A national sentinel surveillance programme for severe influenza was established in Australia in 2009, primarily to monitor hospitalisations in adults with confirmed influenza: the Influenza Complications Alert Network (FluCAN). Given the significant burden of disease in young children and the important role that children play in introducing and spreading influenza virus in the household and the community [3], paediatric influenza surveillance provides public health authorities with important and timely information on disease severity in the early phase of the winter respiratory virus season. Hospital-based sentinel surveillance enables

Date of admission in children hospitalised with confirmed influenza, epidemiological cohort, Influenza Complications Alert Network, Australia, April to October 2014 (n=402)
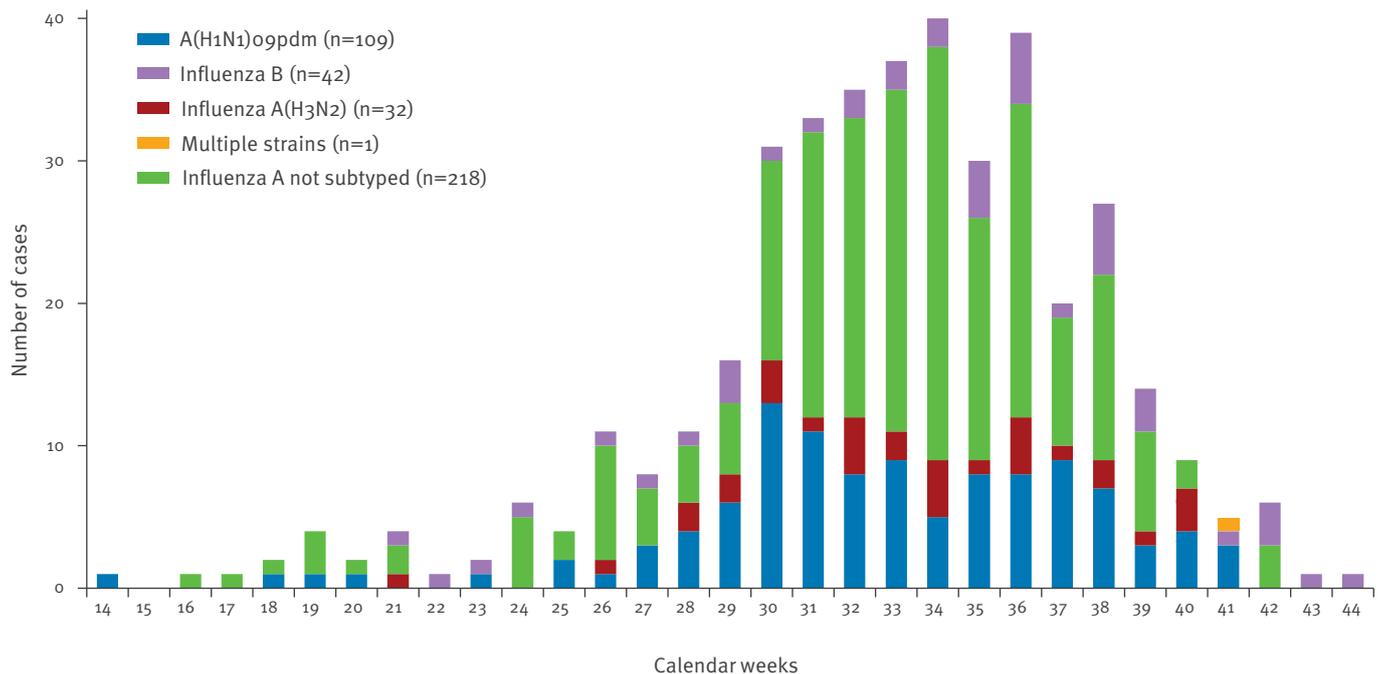
detailed information on the severity of illness to be collected, and complements community- and primary care-based surveillance systems. Comprehensive nationwide clinical data were collected from Australian children admitted to six tertiary paediatric hospitals during the pandemic in 2009 [4]. However, from 2010 to 2013, insufficient numbers of children were prospectively enrolled in existing surveillance programs to ascertain paediatric seasonal influenza activity and severity in Australia. Two tertiary paediatric hospitals (from the separate Paediatric Active Enhanced Disease Surveillance network (PAEDS) [5]) were included in the existing FluCAN sentinel system in 2014.

The Australian Technical Advisory Group on Immunisation (ATAGI) recommends influenza vaccination in all children 6 months and older, yet in 2014, influenza vaccine was only provided free of charge under the National Immunisation Programme (NIP) for children with comorbidities that predispose them to severe outcomes following influenza infection [6]. In Western Australia, a state funded programme has provided free influenza vaccine to all children between 6 months and 5 years of age from 2008 [7-9]. Four brands of inactivated unadjuvanted trivalent influenza vaccine (TIV) were available for use in Australian children: more than 80% of vaccine administered to children in Australia was Vaxigrip or Vaxigrip junior (Sanofi-Pasteur Pty Ltd; personal communication, Brynley Hull, October 2015). Live attenuated and quadrivalent influenza vaccines were not available in Australia in 2014.

Previous studies have demonstrated that inactivated influenza vaccine is protective against influenza [10, 11], yet have concluded that insufficient evidence exists to confirm the effectiveness in the very young. The Western Australian Influenza Vaccine Effectiveness (WAIVE) study has previously estimated vaccine effectiveness (VE) of TIV in children aged 6 to 59 months attending a paediatric emergency department against any laboratory-confirmed influenza at 64.7% (95% confidence interval (CI): 33.7–81.2%) [7]. Insufficient numbers of hospitalised children have been enrolled in this and similar paediatric VE studies to generate robust estimates against hospitalisation. Cowling et al. estimated VE against hospitalisation with laboratory-confirmed influenza to be 61.7% (95% CI: 43.0–74.2%) in Hong Kong (2009–2013) [12].

With nearly 70,000 notifications of laboratory-confirmed influenza, the incidence of disease in 2014 was high compared with previous seasons [13]. Virological surveillance of circulating strains suggested influenza A(H1N1)pdm09 predominated across most jurisdictions throughout the season, but influenza A(H3N2) was predominant in New South Wales and the Australian Capital Territory [14]. In this report, we describe the epidemiology of hospitalisation in children with confirmed influenza and report on VE estimates for the 2014 southern hemisphere inactivated TIV.

Methods

FluCAN is a national hospital-based sentinel surveillance system [15]. In 2014, surveillance was expanded to include two large specialty paediatric hospitals:

Flowchart of children included in epidemiological and vaccine effectiveness cohorts, Influenza Complications Alert Network, Australia, April to October 2014 (n=747)
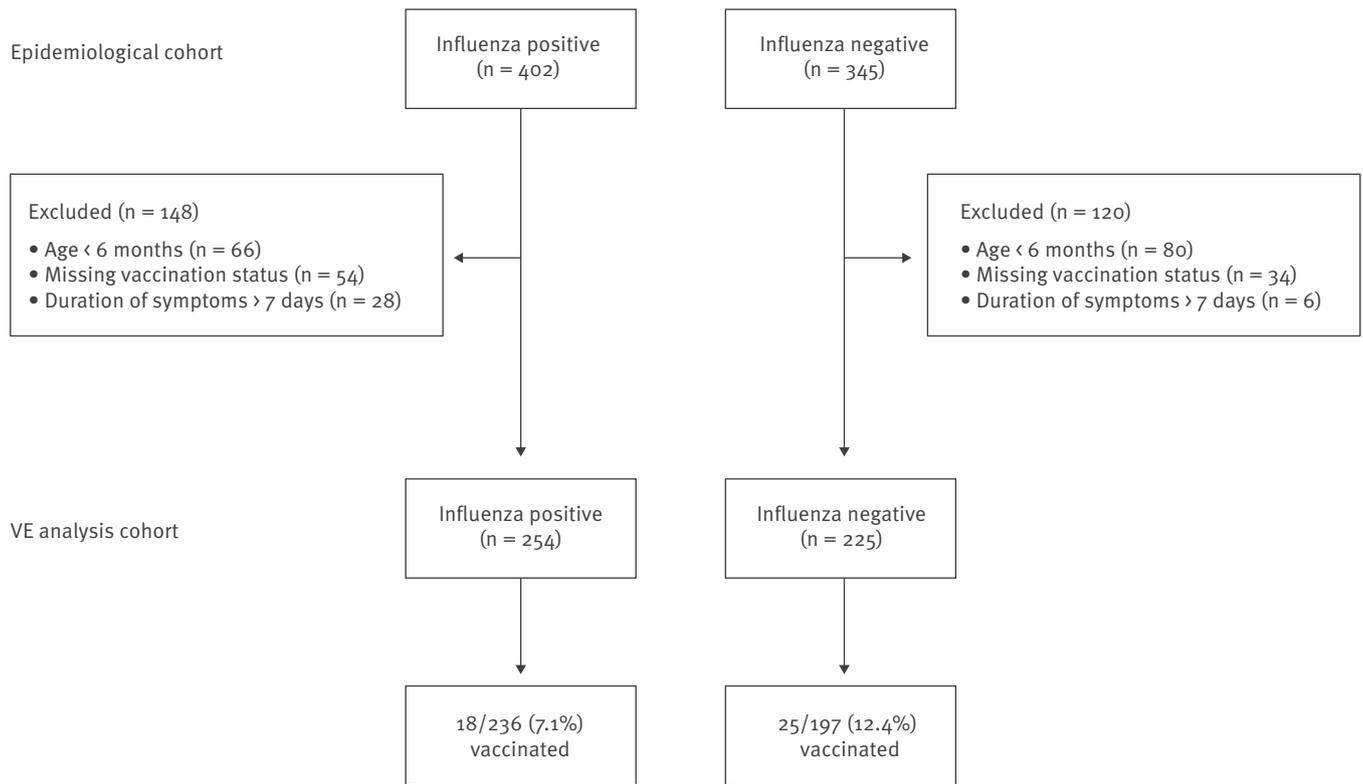
VE: vaccine effectiveness.

Children's Hospital at Westmead (New South Wales) and the Princess Margaret Hospital for Children (Western Australia). In addition, paediatric cases from the other 15 participating sites were also included: Canberra Hospital (ACT), University Hospital Geelong (VIC), Princess Alexandra Hospital (QLD), Cairns Base Hospital (QLD), and Alice Springs Hospital (NT) contributed cases. Ethics approval has been obtained at all participating sites, at Monash University and the Australian National University.

An influenza case was defined as a paediatric patient (<16 years) admitted to hospital with an acute respiratory illness (ARI) and with influenza confirmed by PCR. Influenza testing was initiated by clinicians based on clinical indications and local guidelines. All influenza cases were confirmed using real-time reverse transcriptase PCR assays using standard primers. All tests were performed in local or referral laboratories accredited by the National Association of Testing Authorities. An ARI was defined by the presence of new respiratory symptoms including cough and rhinorrhoea. A hospital admission was defined as requiring inpatient care outside of the emergency department.

Under FluCAN, surveillance is conducted during the southern hemisphere influenza season (i.e. April to October with follow up continuing to the end of November each year). Admission to an intensive care unit (ICU), including high dependency unit (HDU), was also recorded. The presence of risk factors predisposing to severe outcomes following influenza infection including ethnicity (Indigenous or non-Indigenous Australian) and the presence of underlying conditions (hereafter referred to as comorbidities) was ascertained from the patient's medical record [6]. Comorbidities assessed included congenital heart disease, chronic respiratory and neurological disorders, immunocompromising conditions or immunosuppression, Down syndrome and chronic illnesses such as diabetes mellitus and renal failure [6].

We examined factors associated with ICU admission and the length of hospital stay (LOS) using multivariable regression. Factors associated with ICU admission were determined using a logistic regression model, with factors retained in the multivariable model if $p < 0.20$. Factors associated with LOS were modelled using a linear regression, as the mean duration of stay was the parameter of interest. Standard errors were estimated using bootstrapping (1,000 replicates) to correct for heteroskedasticity.

Demographic characteristics of children hospitalised with confirmed influenza, epidemiological cohort, Influenza Complications Alert Network, Australia, April to October 2014 (n=402)

	Influenza type				Total influenza positive cases
	A(H1N1A(H1N1)09pdm	A(H3N2)	A not subtyped	B	
Number of children	109	32	218	42	402[a]
Age group					
Neonate‹28 days	2 (1.8%)	0 (0.0%)	5 (2.3%)	0 (0.0%)	7 (1.7%)
Infant 28 days to 1 year	29 (26.6%)	9 (28.1%)	60 (27.5%)	8 (19.0%)	107 (26.6%)
1–5 years	40 (36.7%)	16 (50.0%)	94 (43.1%)	15 (35.7%)	165 (41.0%)
5–9 years	23 (21.1%)	5 (15.6%)	34 (15.6%)	12 (28.6%)	74 (18.4%)
10–16 years	15 (13.8%)	2 (6.3%)	25 (11.5%)	7 (16.7%)	49 (12.2%)
Male	62 (56.9%)	16 (50.0%)	107 (49.1%)	24 (57.1%)	209 (52.0%)
Indigenous	9 (8.3%)	3 (9.4%)	48 (22.0%)	3 (7.1%)	63 (15.7%)
Hospital					
Alice Springs	0 (0.0%)	0 (0.0%)	43 (19.7%)	5 (11.9%)	48 (11.9%)
Canberra	15 (13.8%)	14 (43.8%)	0 (0.0%)	2 (4.8%)	31 (7.7%)
Cairns Base	4 (3.7%)	0 (0.0%)	10 (4.6%)	3 (7.1%)	17 (4.2%)
Children›s Hospital, Westmead	0 (0.0%)	0 (0.0%)	135 (61.9%)	16 (38.1%)	151 (37.6%)
Geelong Hospital	0 (0.0%)	0 (0.0%)	21 (9.6%)	0 (0.0%)	22 (5.5%)
Princess Alexandra	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (0.2%)
Princess Margaret	90 (82.6%)	18 (56.3%)	9 (4.1%)	15 (35.7%)	132 (32.8%)

[a] One child with disease due to multiple subtypes included in total

Estimation of vaccination coverage and effectiveness

Vaccination status was obtained from the medical record, by parental report and confirmed, in children‹7 years of age, on the Australian Childhood Immunisation Register (ACIR). In those 10 years and older, 'fully immunised' was defined by receipt of one dose of 2014 TIV more than 2 weeks before presentation. In children age‹10 years, 'fully immunised' was defined as either (i) two doses of TIV at least 21 days apart and at least 2 weeks before presentation or (ii) one dose of TIV at least 2 weeks before presentation and receipt of at least one TIV dose in a previous year [6]. 'Partially vaccinated' children were those aged‹10 years receiving only one dose of vaccination in 2014 without receipt of TIV in previous years. 'Unvaccinated' children where those not receiving TIV in 2014 or receiving the vaccine less than 2 weeks before presentation.

Vaccination coverage was estimated in patients›6 months of age admitted with ARI who tested negative to influenza by PCR. We used an incidence density test negative design to estimate VE, where controls were selected from influenza-test negative subjects with ARI tested contemporaneously with a case: controls could be test-negative for all pathogens or have an alternative pathogen detected [16-18]. VE was estimated as 1 minus the odds ratio (OR) of vaccination in influenza-positive cases compared with test-negative control patients using methods previously described

[15,19]. Only children›6 months of age and tested within 7 days of admission were included in VE estimates. A conditional logistic regression model using influenza case status as the dependent outcome was constructed from influenza vaccination and adjusted for potential confounders (age group‹2 years and comorbidities). The regression was stratified on site, except for the models that considered VE against H1N1 due to small numbers. Models that included more age groups (‹1 year, 1–4 years, 5–9 years and≥10 years,) and Indigenous status as adjusting variables were considered in sensitivity analyses. In addition, VE estimates excluding children with duration of symptoms of›7 days (as opposed to restriction the analysis to who underwent testing within 7 days) were performed. These adjustments had minimal effect (‹3%) on VE estimates and thus were dropped from the final model. Analyses were performed using Stata 13 for Windows (College Station, Texas, US).

Results

During the period 3 April to 31 October 2014, 402 children were admitted with PCR-confirmed influenza to seven of 17 sentinel hospitals, including 283 admissions to the two specialist paediatric hospitals, and 119 admissions to five non-specialist hospitals (Table 1). The peak rate of admission was in late August (Figure 1). Of these 402 children, 114 (28%) were‹1 year of age, 63 (16%) were Indigenous Australians, and 155 (39%) had underlying comorbidities (Table 1; Table 2).

Risk factors, severity and outcomes in children hospitalised with confirmed influenza, epidemiological cohort, Influenza Complications Alert Network, Australia, April to October 2014 (n=402)

	Not admitted to ICU	Admitted to ICU	Total
Total	**356**	**46**	**402**
Age group			
Neonate < 28 days	5 (1.4%)	2 (4.3%)	7 (1.7%)
Infant 28d - 1 year	93 (26.1%)	14 (30.4%)	107 (26.6%)
1–4 years	147 (41.3%)	18 (39.1%)	165 (41.0%)
5–9 years	68 (19.1%)	6 (13.0%)	74 (18.4%)
10–15 years	43 (12.1%)	6 (13.0%)	49 (12.2%)
Smoking	4 (1.1%)	2 (4.3%)	6 (1.5%)
Others smoking in the household	21 (5.9%)	5 (10.9%)	26 (6.5%)
Chronic medical comorbidities	127 (35.7%)	28 (60.9%)	155 (38.6%)
Chronic respiratory disease	38 (10.7%)	12 (26.1%)	50 (12.4%)
Prematurity	33 (9.3%)	12 (26.1%)	45 (11.2%)
Chronic cardiac disease	21 (5.9%)	3 (6.5%)	24 (6.0%)
Diabetes	4 (1.1%)	1 (2.2%)	5 (1.2%)
Chronic neurological disease	26 (7.3%)	7 (15.2%)	33 (8.2%)
Chronic renal disease	10 (2.8%)	4 (8.7%)	14 (3.5%)
Immunosuppressed	35 (9.8%)	4 (8.7%)	39 (9.7%)
Chronic liver disease	7 (2.0%)	3 (6.5%)	10 (2.5%)
Genetic abnormality	28 (7.9%)	10 (21.7%)	38 (9.5%)
Inborn error of metabolism	4 (1.1%)	3 (6.5%)	7 (1.7%)
Chronic aspirin use	4 (1.1%)	0 (0.0%)	4 (1.0%)
Residential care	1 (0.3%)	1 (2.2%)	2 (0.5%)
Influenza vaccination	11/242 (4.5%)	4/35 (11.4%)	15/277 (5.4%)
Influenza subtype			
A(H1N1)09pdm	92 (25.8%)	17 (37.0%)	109 (27.1%)
A(H3N2)	24 (6.7%)	8 (17.4%)	32 (8.0%)
A not subtyped	199 (55.9%)	19 (41.3%)	218 (54.2%)
B	40 (11.2%)	2 (4.3%)	42 (10.4%)
multiple strains	1 (0.3%)	0 (0.0%)	1 (0.2%)
Mortality	0/317 (0.0%)	1/41 (2.4%)	1/358 (0.3%)

Presentation and treatment

In 395 patients with influenza where the duration of symptoms was known, the median duration of symptoms before admission was 3 days (interquartile range (IQR): 2, 5 days). Only 64 (15%) of patients with influenza, received oseltamivir; of these, 24 patients were known to have received oseltamivir within 48 hours of symptom onset.

Admission to intensive care

Of all influenza cases, 40 (10%) were initially admitted to intensive care (ICU) and a further six (1%) patients were subsequently transferred to ICU after initial admission to a general ward. The presence of comorbidities was associated with intensive care admission: OR 2.80 (95% CI: 1.49–5.27, p=0.001). Influenza B appeared associated with a lower risk of admission to ICU but this difference was not statistically significant: OR 0.36 (95% CI: 0.08–1.53, p=0.16). In a multivariate model, only the presence of one or more comorbidity was associated with ICU admission (Table 3).

Outcome

The mean LOS of all patients was 3.7 days. The presence of comorbidities was associated with an increase in mean hospital length of stay of 2.6 days. Other factors associated with prolonged length of stay included ICU admission and being Indigenous but these differences were not statistically significant (data not shown). The duration of hospital stay was similar in patients that received antivirals within 48 hours of symptom onset (median: 2.5 days; IQR: 2, 6 days), compared with those who received antivirals more than 48 hours after symptom onset (median: 4 days; IQR: 1, 7 days) and who did not receive antivirals (median: 2 days; IQR: 1, 3 days).

One in-hospital death was reported, in a 13-year-old boy with no known comorbidities.

Factors associated with admission to intensive care in patients hospitalised with confirmed influenza, epidemiological cohort, Influenza Complications Alert Network, Australia, April to October 2014 (n=402)

Variable	Crude OR (95% CI)	p value	AOR (95% CI)	p value
Infant‹12 months	1.40 (0.73, 2.69)	0.306	1.86 (0.94, 3.69)	0.076
Medical comorbidities	2.80 (1.49, 5.27)	0.001	3.20 (1.66, 6.16)	0.001
Indigenous Australian	0.79 (0.32, 1.94)	0.603	NI	NA
Influenza type				
Influenza A	1 (referent)		1 (referent)	
Influenza B	0.36 (0.08, 1.53)	0.166	NI	NA

AOR: adjusted odds ratio; CI: confidence interval; NA: not applicable; NI: not included in final model; OR: odds ratio.

Vaccine coverage

Vaccine coverage for all children ›6 months of age, as shown in Figure 2, was low. Of the 225 children who tested negative for influenza within 7 days of onset of illness, 28 children had received at least one dose of vaccine in 2014 (estimated full or partial vaccine coverage: 12.4%). Eighteen children were regarded as fully vaccinated (estimated full coverage: 8.0%) Of those with comorbidities (eligible to receive influenza vaccine under the NIP), only 16 of 89 children had received at least one dose of vaccine in 2014 (estimated full or partial coverage: 18.0%), of whom only nine children were regarded as fully vaccinated (estimated full coverage: 10.1%).

Vaccine effectiveness

In children aged ›6 months, the crude VE of full or partial vaccination (i.e. children who received at least one dose of vaccine in 2014) was estimated as 48.8% (95% CI: 1.1–73.5%; Table 4). After adjusting for age group and comorbidities, the adjusted full/partial VE was estimated as 55.5% (95% CI: 11.6–77.6%). VE differed by infecting strain (Table 4) with poor VE against circulating influenza A(H3N2) noted. Only one child with A(H1N1) infection was partially vaccinated with no vaccine breakthrough cases in fully vaccinated children identified: adjusted fully/partial VE estimate for A(H1N1) was 91.6% (95% CI: 36.0–98.9%).

In children aged ›6 months, the crude VE based on children who were regarded as fully vaccinated in 2014 was estimated as 30.5% (95%CI -45.7 to 66.8%). After adjusting for age group (age‹2 years), and chronic medical comorbidities, the adjusted VE was estimated as 41.1% (95% CI: -26.7 to 72.6%).

Discussion

Inclusion of two tertiary paediatric hospitals (from the separate Paediatric Active Enhanced Disease Surveillance network; PAEDS [5]) into the existing FluCAN sentinel system has allowed us to report on influenza in 3,400 hospitalised children and adults in 2014 (unpublished data), inclusive of metropolitan and regional hospitals, specialist paediatric and adult hospitals and hospitals in tropical and subtropical regions. By collecting data on control patients with ARI who tested negative for influenza, vaccine coverage (particularly in vulnerable patients) and VE against severe influenza can also be accurately estimated [20]. Here we report the first significant VE estimate against hospitalised influenza in Australian children.

In 2014, we recorded over 400 paediatric admissions in the FluCAN system. When compared with children with influenza requiring hospitalisation in 2009 (n=601 across six paediatric hospitals), a number of similarities and differences were identified. In both cohorts, more than 50% of children did not have any underlying comorbidities, highlighting that healthy children form a significant proportion of those requiring hospital admission. Indigenous Australians are at increased risk of hospital admission with influenza; national hospitalisation discharge data indicate that indigenous children aged ‹5 years are hospitalised more than twice as frequently with influenza compared with their non-indigenous peers [21]. This finding has prompted the inclusion of Indigenous children‹5 years of age as eligible for NIP-funded influenza vaccination from 2015 onwards. The higher proportion of indigenous children enrolled in this study in 2014 (16.0% vs 4.5% in 2009) needs to be interpreted with caution as recruitment from sites with sizable indigenous populations (e.g. Alice Springs Hospital) occurred in 2014 and not in 2009. The proportion of Indigenous children with influenza in the study (excluding those admitted to Alice Springs Hospital) was 6.5% (23/354). This is compared with the national average of 4.4% [22].

For all children, similar outcomes were observed in 2014 compared with 2009, respectively: 11.4% and 9.9% of children were admitted to ICU, and mortality was 0.3% and 0.9% respectively. Despite the availability of free vaccine through the NIP for children with comorbidities from 2010, uptake of seasonal TIV in those at greatest risk has not significantly changed since 2009: in 2014 only 21.0% of controls with comorbidities were vaccinated compared with 18.4% in 2009 [4]. Another striking difference is the infrequent use of antiviral medications in 2014 compared with the pandemic year, 2009 (15% vs 47%). The effectiveness of

Strains	Number of cases and controls				Unadjusted VE (95% CI)	Adjusted VE[a] (95% CI)
	Vaccinated cases	Unvaccinated cases	Vaccinated controls	Unvaccinated controls		
Vaccinated cases inclusive of fully and partially vaccinated children						
All strains[b]	18	236	28	197	48.8% (1.1%, 73.5%)	55.5% (11.6%, 77.6%)
H1N1	1	72	28	197	90.2% (26.9%, 98.7%)	91.6%[c] (36.0%, 98.9%)
H3N2	13	90	28	197	6.2% (-110.7%, 58.2%)	-4.0% (-138.9%, 54.7%)
B	2	22	28	197	66.0% (-163.3%, 95.6%)	65.0% (-179.4%, 95.6%)
Vaccinated cases inclusive of fully vaccinated cases only						
All strains[b]	15	236	18	197	30.5% (-45.7%, 66.8%)	41.1% (-26.7%, 72.6%)
H1N1	0	72	18	197	100%	100%[c]
H3N2	11	90	18	197	3.5% (-154.1%, 63.4%)	-13.6% (-204.1%, 57.6%)
B	2	22	18	197	47.3% (-317.0%, 93.3%)	51.5% (-294.4%, 94.0%)

CI: confidence intervals; VE: vaccine effectiveness.

[a] adjusted for age > 2 years, and comorbidities

[b] Inclusive of patients with untyped influenza A infection, H1N1, H3N2 and influenza B.

[c] 1 patient with A(H1N1) was partially vaccinated and none fully vaccinated. Non-conditional logistic regression used

oseltamivir in children and adults with influenza has recently been debated following meta-analyses by Jefferson et al. and Dobson et al. with conflicting methods, results and conclusions [23,24]. Data pooled by Jefferson et al. demonstrates that oseltamivir reduces the length of symptoms by 29 hours (95% CI: 12 to 47 hours; p = 0.001) at the expense of increased rates of vomiting in children [23]. Despite no appreciable difference in complications or hospitalisation being noted, the numbers of children in both the intervention and control arms of these analyses are very small. Given the current evidence, oseltamivir is most likely to benefit patients at high risk of hospitalisation and patient with influenza requiring hospitalisation [25]. Future work should focus on ways to improve both vaccine uptake and antiviral use, particularly among children with comorbidities or other risk factors for severe influenza.

VE estimates are now generated using test-negative design in multiple populations to guide vaccine strain choice. Existing southern-hemisphere systems and VE studies have either focused on children (and adults) presenting for outpatient or emergency care [7,26,27] or enrolled insufficient numbers of children to generate robust estimates for hospitalised influenza in children, particularly in any single influenza seasons [9,26,27]. The addition of large paediatric sites to the FluCAN network, has enabled calculation of VE estimates against hospitalised influenza for children aged < 16 years in a single season. Moreover, the VE point estimate (55.5% (95% CI: 11.6–77.6%)) is comparable to that observed in hospitalised adults (51.5% (95% CI: 41.6–59.7%), unpublished data), albeit with less precision. Restricting the estimate to those fully vaccinated resulted in a lower point estimate (41.1% (95% CI: -26.7–72.6%)) but given the small numbers of vaccinated cases and controls and wide confidence intervals, this result needs to be interpreted with caution, Similar differences in VE between different influenza strains were also observed (data not shown). The addition of data from more paediatric hospitals, or over subsequent seasons, would assist in providing VE estimates against specific influenza strains and in subgroups of interest, for example the children aged 6 months to 2 years in whom data on VE is sparse.

There are a number of limitations to this study. The decision to test was left to the treating clinician using local guidelines. The impact of this is expected to be small as influenza tests are routinely recommended for infection control purposes in children requiring hospital admission with acute respiratory symptoms. It remains possible that the decision to test might have been influenced by vaccination status. As in all observational studies, a biased estimate of VE may result from unmeasured confounding or misascertainment of vaccination status or outcome. Case ascertainment was likely incomplete due to the underutilisation of influenza laboratory testing by treating clinicians, despite the diagnosis of influenza having implications for infection control and antiviral use in hospitals.

Delayed presentations or secondary bacterial pneumonia may be associated with false negative influenza tests as the influenza infection may be cleared at the time of presentation. Influenza subtyping was not available for the majority (55%) of patients, thereby limiting our ability to determine the relative burden of influenza A types and calculate accurate VE estimates by strain. Furthermore, the antigenic characteristics of influenza viruses from cases was not performed and as such we are unable to determine the relatedness of circulating strains with influenza strains included in the 2014 seasonal vaccine. The inability to determine vaccination status in all children was a limitation although no significant differences were noted when influenza status and risk factors of those with known vaccination status were compared with children with unknown vaccination status (data not shown). Low vaccine uptake was a major limitation impacting on our ability to more precisely calculate VE.

In summary, we describe more than 400 children hospitalised with seasonal influenza in Australia, of whom 10% required ICU admission. Influenza A was detected in 90% of cases with influenza A(H1N109)pdm the most frequent subtype. Vaccine uptake in those with and without comorbidities remains poor. Use of influenza antivirals in children is infrequent. TIV appeared moderately effective against hospitalisation with any influenza in 2014, but was more effective against the influenza A(H1N109)pdm subtype.

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Conflict of interest

Authors' contributions

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