

INFLUENZA EPIDEMIOLOGY IN PATIENTS ADMITTED TO SENTINEL AUSTRALIAN HOSPITALS IN 2015: THE INFLUENZA COMPLICATIONS ALERT NETWORK

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Abstract

The Influenza Complications Alert Network (FluCAN) is a sentinel hospital-based surveillance program that operates at sites in all states and territories in Australia. This report summarises the epidemiology of hospitalisations with laboratory-confirmed influenza during the 2015 influenza season. In this observational study, cases were defined as patients admitted to one of the sentinel hospitals with an acute respiratory illness with influenza confirmed by nucleic acid detection. During the period 1 April to 30 October 2015 (the 2015 influenza season), 2,070 patients were admitted with confirmed influenza to one of 17 FluCAN sentinel hospitals. Of these, 46% were elderly (≥ 65 years), 15% were children (< 16 years), 5% were Indigenous Australians, 2.1% were pregnant and 75% had chronic co-morbidities. A high proportion were due to influenza B (51%). There were a large number of hospital admissions detected with confirmed influenza in this national observational surveillance system in 2015 with case numbers similar to that reported in 2014. The national immunisation program is estimated to avert 46% of admissions from confirmed influenza across all at-risk groups, but more complete vaccination coverage in target groups could further reduce influenza admissions by as much as 14%. *Commun Dis Intell* 2016;40(4):E521–E526.

Keywords: influenza; hospitalisation; morbidity; FluCAN

Introduction

Influenza is a common respiratory viral infection that affects up to 5% to 10% of the population each year.¹ Although the proportion of cases requiring hospitalisation is low, because infection with influenza virus is relatively widespread, the incidence of hospitalisation from influenza is of public health significance.² In this report we describe the epidemiology of hospitalisation with laboratory-confirmed influenza in the 2015 season in Australia.

Methods

The Influenza Complications Alert Network (FluCAN) is a national hospital-based sentinel

surveillance system in Australia.³ Since 2011, the participating sites have been Canberra Hospital (ACT), Calvary Hospital (ACT), Westmead Hospital (NSW), John Hunter Hospital (NSW), Children's Hospital at Westmead (NSW), Alice Springs Hospital (NT), Royal Adelaide Hospital (SA), Mater Hospital (Qld), Princess Alexandra Hospital (Qld), Cairns Base Hospital (Qld), Royal Hobart Hospital (Tas.), The Alfred Hospital (Vic.), Royal Melbourne Hospital (Vic.), Monash Medical Centre (Vic.), University Hospital Geelong (Vic.), Royal Perth Hospital (WA), and Princess Margaret Hospital (WA).

Ethical approval has been obtained at all participating sites and at Monash University. Hospital bed capacity statistics were obtained from each participating hospital, and national bed capacity was obtained from the last published Australian Institute for Health and Welfare report.⁴

A case was defined as a patient admitted to hospital with influenza confirmed by nucleic acid testing (NAT). For each case, a control was the next tested patient admitted to hospital for an acute respiratory illness where the influenza NAT was negative. Surveillance is conducted from early April to end October (with follow up continuing to the end of November) each year. Admission or transfer to an intensive care unit (ICU) included patients managed in a high dependency unit. The onset date was defined as the date of admission except for patients where the date of the test was more than 7 days after admission, where the onset date was the date of the test. The presence of risk factors and comorbidities was ascertained from the patient's medical record. Restricted functional capacity was defined as those who were not fully active and not able to carry out all activities without restriction prior to the acute illness.⁵

We examined factors associated with ICU admission using multivariable regression. Factors associated with ICU admission were determined using a logistic regression model, with factors retained in the multivariable model if $P < 0.2$.

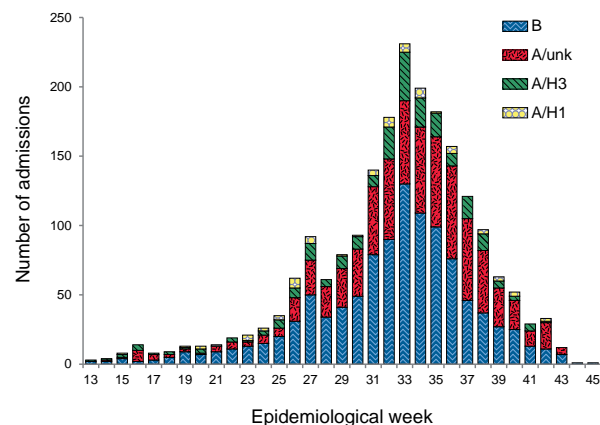
Vaccine coverage was estimated from the proportion of vaccinated test negative control patients in each age group, stratified by the presence of chronic comorbidities. Vaccine effectiveness was estimated from the odds ratio of vaccination in cases vs controls using the formula $VE = 1 - OR$, with the odds ratio calculated from a conditional logistic regression, stratified by site and adjusted for age group, the presence of chronic comorbidities, pregnancy and Indigenous ethnicity. The proportion of avoidable admissions was calculated using the formula $PA = \frac{U - V}{U}$ where U is the number of unvaccinated individuals and V is the number of vaccinated individuals. The proportion of averted admission was calculated using the formula $AA = 1 - PA$.

Results

During the period 1 April to 30 October 2015 (the 2015 influenza season), 2,070 patients were admitted with laboratory-confirmed influenza to one of 17 FluCAN sentinel hospitals. The peak weekly number of admission was in mid-August (week 33) (Figure). The majority of cases were due to influenza B (51%). The proportion due to influenza B varied by site from 49 of 136 cases (36%) at the Royal Hobart Hospital to 60 of 88 cases (68%) at the Princess Alexandra Hospital, Brisbane.

Of these 2,070 patients, 954 (46%) were more than 65 years of age, 320 (15%) were children (<16 years), 93 (4.5%) were Indigenous Australians, and 1,543 (75%) had chronic co-morbidities (Table 1; Table 2). There were 43 pregnant women, which represented 15% of the 277 female patients aged 16–49 years, or 2.1% of the total. Of the 1,686 patients (81%) where influenza vaccination status was ascertained, 805 (48%) had been vaccinated.

Figure: Date of admission in patients hospitalised with confirmed influenza



By week beginning on listed date; representing date of admission (or date of influenza diagnosis if acquired after more than 7 days in hospital).

Table 1: Demographic characteristics of hospitalised adult patients with confirmed influenza

	Influenza type/subtype									
	A/H1		A/H3		A/unknown		B		Total	
Number of cases	69		225		718		1,058		2,070	
	n	%	n	%	n	%	n	%	n	%
Age group										
<16 years	17	24.6	0	0.0	122	17.0	181	17.1	320	15.5
16-49 years	24	34.8	47	20.9	117	16.3	287	27.1	475	22.9
50-64 years	14	20.3	24	10.7	100	13.9	181	17.1	319	15.4
65-79 years	11	15.9	71	31.6	169	23.5	238	22.5	489	23.6
80+ years	3	4.3	83	36.9	210	29.2	171	16.2	467	22.6
Female*	32	46.4	129	57.3	364	50.8	520	49.1	1,045	50.5
Pregnant	3	4.3	8	3.6	8	1.1	24	2.3	43	2.1
Indigenous	1	1.4	5	2.2	34	4.7	53	5.0	93	4.5
State										
ACT	16	23.2	10	4.4	44	6.1	91	8.6	161	7.8
NSW	25	36.2	80	35.6	65	9.1	198	18.7	368	17.8
NT	0	0.0	0	0.0	21	2.9	22	2.1	43	2.1
Qld	5	7.2	20	8.9	74	10.3	153	14.5	252	12.2
SA	0	0.0	6	2.7	182	25.3	117	11.1	305	14.7
Tas.	5	7.2	67	29.8	15	2.1	49	4.6	136	6.6
Vic.	5	7.2	9	4.0	262	36.5	329	31.1	605	29.2
WA	13	18.8	33	14.7	55	7.7	99	9.4	200	9.7

* Sex missing for 1 patient.

Table 2: Risk factors, severity and outcomes in hospitalised adult patients with confirmed influenza

	Not admitted to ICU		Admitted to ICU		Total	
	n	%	n	%	n	%
Number of cases	1,916		154		2,070	
Pregnancy	41	2.1	2	1.3	43	2.1
Medical comorbidities	1,421	74.2	122	79.2	1,543	74.5
Chronic respiratory illness	625	32.6	58	37.7	683	33.0
Chronic cardiac disease	399	20.8	43	27.9	442	21.4
Diabetes	70	3.7	8	5.2	78	3.8
Chronic liver disease	323	16.9	28	18.2	351	17.0
Chronic neurological illness	233	12.2	22	14.3	255	12.3
Chronic renal disease	513	26.8	49	31.8	562	27.1
Immunocompromised	190	9.9	24	15.6	214	10.3
Malignancy	304	15.9	28	18.2	332	16.0
Obesity	255	13.3	22	14.3	277	13.4
Nursing home resident	149	7.8	3	1.9	152	7.3
Received influenza vaccine	760/1,564	48.6	46/123	37.4	806/1,687	47.8
Influenza type/subtype						
A/H1	60	3.1	9	5.8	69	3.3
A/H3	215	11.2	10	6.5	225	10.9
A/unknown	666	34.8	52	33.8	718	34.7
B	975	50.9	83	53.9	1,058	51.1
In hospital mortality	22	1.1	21	13.6	43	2.1

Presentation and management

For 1,546 patients with laboratory-confirmed influenza where the duration of symptoms was known, the median duration of symptoms prior to admission was 3 days (interquartile range (IQR): 2, 5 days). Of all cases, 102 cases (4.9%) were diagnosed more than 7 days after admission and therefore were likely to be hospital-acquired. Radiological evidence of pneumonia was present in 377 patients (18%).

Of all cases, 107 patients (5.2%) were initially admitted to ICU and a further 47 (2.3%) were subsequently transferred to ICU after initial admission to a general ward. There were no statistically significant differences in the risk of admission by influenza type. Factors associated with ICU admission are detailed in Table 3.

Outcome

The mean length of hospital stay for all patients was 5.0 days. Admission to ICU was associated with a mean hospital length of stay of 12.7 days compared with those not admitted to ICU (4.4 days). Of the 2,053 patients where hospital mortality status was documented, 43 patients died (2.1%), which included 21 patients in ICU. Case fatality

was higher in the elderly (31/950; 3.3%) than in non-elderly adults (11/786; 1.4%). Of the 43 deaths, 40 (93%) occurred in patients with comorbidities. The case fatality of influenza-associated pneumonia was 5.9%.

Vaccine coverage and effectiveness

Vaccination status was ascertained in 1,687 of 2,070 cases (81%) and 1,293 of 1,636 test negative control patients (79%). Estimated vaccine coverage was 80.2% (478/596) in the elderly (≥ 65 years), 57.9% (219/378) in non-elderly adults with medical comorbidities and 26.9% (21/78) in children (< 16 years) with medical comorbidities. In the target population, the crude odds ratio of vaccination in cases vs controls was 0.57 (95% CI: 0.48, 0.69) and the adjusted odds ratio of vaccination was 0.54 (95% CI: 0.45, 0.66). The estimated vaccine effectiveness in the target population was therefore 45.3% (95% CI: 34.2%, 54.5%).

Avoidable and averted hospitalisations

Of the 2,070 admissions, 1,645 involved patients at risk of severe influenza. This included 956 elderly patients (of which 19.8% were estimated to be unvaccinated); 551 non-elderly adults with comor-

Table 3: Factors associated with admission to intensive care in patients hospitalised with confirmed influenza

Variable	Crude odds ratio	P	Adjusted odds ratio*	P
Age				
<16 years	0.89 (0.56, 1.42)	0.615	0.75 (0.43, 1.33)	0.326
16–64 years	1 (referent)		1 (referent)	
65+ years	0.62 (0.43, 0.90)	0.011	0.59 (0.40, 0.88)	0.011
Medical comorbidities	1.33 (0.89, 1.99)	0.167	1.61 (1.05, 2.48)	0.03
Indigenous	1.18 (0.56, 2.48)	0.662	0.99 (0.46, 2.10)	0.975
Pregnancy	0.60 (0.14, 2.51)	0.486	0.48 (0.11, 2.05)	0.324
Restricted functional status	0.98 (0.70, 1.36)	0.894	0.76 (0.51, 1.12)	0.168
Nursing home resident	0.24 (0.07, 0.75)	0.014	0.23 (0.07, 0.76)	0.016
Influenza type/subtype				
A/H1	1.76 (0.84, 3.68)	0.131	1.68 (0.80, 3.54)	0.169
A/H3	0.55 (0.28, 1.07)	0.078	0.62 (0.31, 1.23)	0.169
B	1 (referent)		1 (referent)	
A/unknown	0.92 (0.64, 1.32)	0.638	0.95 (0.66, 1.37)	0.794

* All variables included in multivariate model.

bidities (42.1% unvaccinated) and; 138 children with comorbidities (72.1% unvaccinated). Based on the estimated vaccine effectiveness in this study of 45.3%, complete vaccination would result in 85 (8.9%) fewer admissions of elderly patients, 82 (18.9%) fewer admissions of non-elderly patients with comorbidities and 41 (32%) fewer paediatric admissions with confirmed influenza in participating sentinel hospitals. Conversely, the current vaccination program was estimated to have averted 49.5% of admissions in the elderly, 41.4% of admissions in non-elderly adults with comorbidities and 24.7% of admissions in children with comorbidities with confirmed influenza.

Discussion

In the 2015 season, we documented more than 2,000 cases of influenza, which represents a similar number of admissions to those in 2014 (n=2,097). This was the largest number of admissions documented since hospital-based surveillance commenced in 2009. Based on the bed capacity of sentinel hospitals, this is likely to represent around 17,000 admissions with confirmed influenza nationally. However, as influenza testing is not performed on all patients with acute respiratory presentations, and influenza may also trigger non-respiratory complications such as acute myocardial infarction, this should be regarded as a probable underestimate.

While the peak and duration of case counts, demographics and medical comorbidities were similar

to cases in 2014, a striking difference in 2015 was the high proportion of admissions associated with influenza B. Influenza B is often thought to be associated with a milder illness than influenza A. Studies examining excess mortality associated with the influenza season suggest that mortality was lower in influenza B seasons compared with seasons where A/H3N2 predominated.^{6–8} We found that the proportion of admissions associated with influenza B was similar to that described in primary care surveillance systems, suggesting that the risk of hospitalisation following infection is similar.

Previous studies have also noted a lower clinical severity of illness associated with influenza B, with pneumonitis or pneumonia being uncommonly reported.^{9,10} In contrast, we found that the proportion of patients requiring intensive care admission was similar for those with influenza B compared with influenza A. A lower proportion of elderly patients were admitted to ICU than non-elderly adults, and this difference was not accounted for by the higher prevalence of medical comorbidities in the elderly. Of all female patients of childbearing age, 16% were pregnant. This was a similar proportion to that observed in previous seasons (20.9% of female patients aged 16–49 years who were pregnant during the 2010–14 seasons), and is likely to reflect the susceptibility of pregnant women to severe influenza.

No data were available on the influenza lineages associated with hospitalisation in this surveillance

system, but other surveillance systems have noted co-circulation of both Victoria and Yamagata lineages of influenza B, in all jurisdictions except the Northern Territory (dominated by B/Victoria lineages) and Western Australia (dominated by B/Yamagata lineages). As the trivalent influenza vaccine only contains one influenza B lineage, this may be associated with an attenuated vaccine effectiveness. The Australian Government has recently announced that influenza vaccines funded under the National Immunisation Program in 2016 will be quadrivalent. It remains to be seen if this change will be associated with a change in the proportion of admissions associated with influenza B infection.

We found that around half of the influenza cases were unvaccinated. Our estimates of vaccine coverage is similar to that of previous years, where around 70% to 80% of the elderly, around 60% of non-elderly adults with comorbidities and 30% of children with comorbidities were vaccinated.^{11,12} We estimated that up to 209 admissions, or 14% of the admissions with confirmed influenza in the at-risk population at these 17 hospitals are potentially avoidable by improving influenza vaccination coverage in the target group. Conversely, this suggests that there would have more than 2,800 admissions involving patients at risk of influenza in the absence of vaccination and the proportion of admissions in the target group averted by vaccination was 46%. These figures are higher than estimated for the United States of America population, where influenza vaccination is actively promoted for the whole population, rather than specific risk groups.¹³

There are several limitations to this surveillance system. There may be under-ascertainment of influenza due to poor quality sample collection or the lack of use of influenza laboratory tests, 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 by the time of presentation. Ascertainment in tropical regions is limited by sampling in the winter/dry season only. We have previously found that around 5% of influenza cases in hospital were acquired after admission,¹⁴ and the incremental benefit of immunising close contacts (healthcare workers and household contacts) has not been considered.

In summary, we detected a large number of hospital admissions with laboratory-confirmed influenza in a national observational study in 2015 comparable with 2014 but much higher than

in prior years. A high proportion of patients with severe influenza, and almost all deaths, occurred in patients with chronic comorbidities.

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