Annual report

Influenza epidemiology in patients admitted to sentinel Australian hospitals in 2016: the Influenza Complications Alert Network (FluCAN)

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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 2016 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. Data are also collected on a frequency matched sample of influenza negative patients admitted with acute respiratory infection as a control group.

During the period 1 April to 30 October 2016 (the 2016 influenza season), there were 1,952 patients admitted with confirmed influenza to one of 17 FluCAN sentinel hospitals. Of these, 46% were elderly (≥65 years), 18% were children (<16 years), 5% were Aboriginal and Torres Strait Islander Peoples, 3% were pregnant and 76% had chronic co-morbidities. A small proportion were due to influenza B (7%). Estimated vaccine coverage was 73% in the elderly (≥65 years), 51% in non-elderly adults with medical comorbidities and 15% in children (<16 years) with medical comorbidities. The estimated vaccine effectiveness in the target population was 13% (95% confidence interval (CI): -5% to 27%).

There were a large number of hospital admissions detected with confirmed influenza in this national observational surveillance system in 2016 with case numbers similar to that reported in 2014 and 2015.

Introduction

Influenza affects up to 5-10% of the population each year[1]. Because infection with influenza virus is relatively widespread, the incidence of hospitalisation from influenza is of public health significance, although the risk of hospitalisation is low[2]. In this report, we describe the epidemiology of hospitalisation with laboratory-confirmed influenza in the 2016 season in Australia.

Methods

The Influenza Complications Alert Network (FluCAN) is a national hospital-based sentinel surveillance system[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 of Health and Welfare report.[4]

An influenza case was defined as a patient admitted to hospital with influenza confirmed by nucleic acid testing (NAT). 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 (HDU). 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 independently associated with ICU admission were determined using a logistic regression model with no variable selection process, as all factors were plausibly related to ICU admission.

Vaccine coverage was estimated from the proportion of vaccinated individuals in each age group, stratified by the presence of chronic comorbidities. Vaccine effectiveness was estimated from the odds ratio of vaccination in cases versus controls using the formula, 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 Aboriginal or Torres Strait Islander ethnicity.

Results

During the period 1 April to 30 October 2016 (the 2016 influenza season), there were 1,952 patients admitted with laboratory-confirmed influenza to one of 17 FluCAN sentinel hospitals. The peak weekly number of admission was in mid-August (week 35) (Figure 1). The majority of cases were due to influenza A (93%). The proportion due to influenza B was higher in the West Australian hospitals (46/180, 26%; Princess Margaret Hospital 34/105, 32%; Royal Perth Hospital 12/75 16%) compared to all other jurisdictions (5.0%).

Of these 1,952 patients, 904 (46%) were >65 years of age, 359 (18%) were children (<16 years), 101 (5%) were Aboriginal and Torres Strait Islander peoples, and 1492 (76%) had chronic co-morbidities (table 1; table 2). There were 50 pregnant women which represented 21% of the 243 female patients aged 16-49, or 3% of the total. Of the 1,599 patients (82%) where influenza vaccination status was ascertained, 752 (47%) had been vaccinated.

Incidence of hospital admissions with influenza

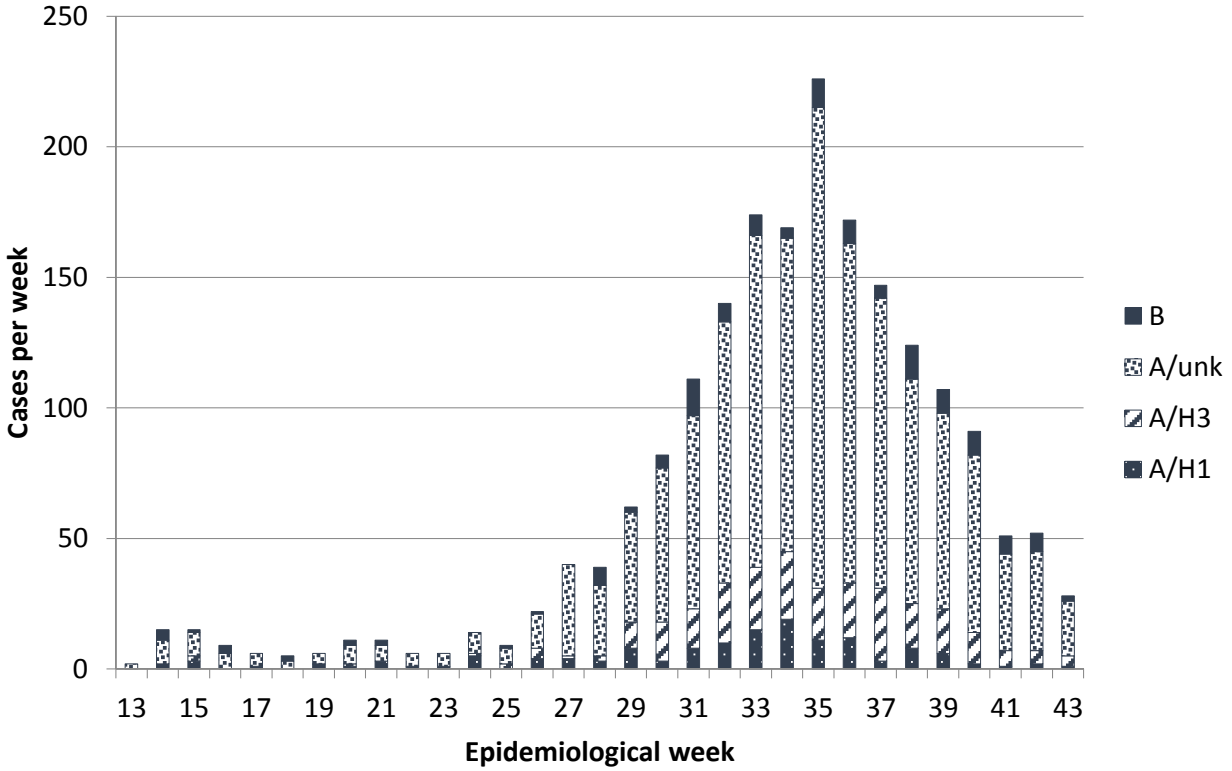
Overall, the peak incidence of admissions with confirmed influenza was 3.2 per 100 hospital beds (in epidemiological week 35), but varied from 0.54 per 100 hospital beds at Princess Alexandra Hospital (QLD) to a 9.7 per 100 hospital beds at Westmead Hospital (NSW).

Presentation and management

For 1,759 patients with laboratory-confirmed influenza where the duration of symptoms was known, the median duration of symptoms prior to admission was 2 days (interquartile range (IQR): 1, 4 days). Of all cases, 65 cases (3%) were diagnosed more than 7 days after admission and therefore were likely to be hospital-acquired. Radiological evidence of pneumonia was present in 363 patients (19%).

Of all cases, 214 patients were admitted to ICU, including 180 patients (9%) were initially admit-

Figure 1: Date of admission in patients hospitalized with confirmed influenza



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

ted to ICU and a further 34 (2%) subsequently transferred to ICU after initial admission to a general ward. The elderly (>65 years) and residents of nursing homes were less likely to be admitted to intensive care. There were no statistically significant differences in the risk of admission to ICU by influenza type in patients admitted to hospital with influenza.

Outcome

The mean length of hospital stay for all patients was 5.6 days. Admission to ICU was associated with a mean hospital length of stay of 11.1 days compared to those not admitted to ICU (4.9 days). Of the 1899 patients where hospital mortality status was documented, 65 patients died (3%), which included 25 patients in ICU. Case fatality was higher in the elderly (51/864; 6%) than in non-elderly adults and children (14/1,035; 1%). Of the 65 deaths, 62 (95%) occurred in patients with comorbidities. The case fatality of influenza-associated pneumonia was 8% (29/359).

Vaccine coverage and effectiveness

Vaccination status was ascertained in 1,599 of 1,952 cases (82%) and 1,386 of 1,715 test negative control patients (81%). Estimated vaccine coverage was 73% (467/636) in the elderly (≥65 years), 51% (212/414) in non-elderly adults with medical comorbidities and 15% (18/116) in children (<16 years) with medical comorbidities. In the target population, the crude odds ratio of vaccination in cases versus controls was 0.87 (95% confidence interval (CI): 0.73 to 1.02) and the adjusted odds ratio of vaccination was 0.87 (95% CI: 0.73 to 1.05). The estimated vaccine effectiveness in the target population was therefore 13% (95% CI: -5%to 27%). In the elderly (>65 years), there was no evidence of vaccine effectiveness (estimated VE -19%, 95% CI: -52% to 8.0%)

Discussion

In the 2016 season, we have documented more than 1,900 cases of influenza, which represents a similar number of admissions as 2014 (n=2,097)

Table 1: Demographic characteristics of hospitalized patients with confirmed influenza

	Influenza type/subtype				Total
	A/H1	A/H3	A/unknown	B	
Number of cases	139	256	1422	135	**1952**
Age group					
<16 years	32 (23%)	1 (0%)	258 (18%)	60 (44%)	**351 (18%)**
16-49 years	44 (32%)	47 (18%)	279 (20%)	27 (20%)	**397 (20%)**
50-64 years	32 (23%)	40 (16%)	211 (15%)	17 (13%)	**300 (15%)**
65-79 years	25 (18%)	78 (31%)	337 (24%)	18 (13%)	**458 (24%)**
80+ years	6 (4%)	90 (35%)	337 (24%)	13 (7%)	**446 (23%)**
Female*	67 (48%)	144 (56%)	726 (51%)	54 (40%)	**991 (51%)**
Pregnant	5 (4%)	3 (1%)	42 (3.0%)	0 (0.0%)	**50 (3%)**
Aboriginal or Torres Strait Islander peoples	6 (4%)	9 (4%)	76 (5%)	10 (7%)	**101 (5%)**
State					
ACT	22 (16%)	78 (31%)	152 (11%)	16 (12%)	**268 (14%)**
NSW	14 (10%)	14 (6%)	450 (32%)	24 (18%)	**502 (26%)**
NT	0 (0.0%)	0 (0.0%)	43 (3%)	3 (2%)	**46 (2%)**
QLD	7 (5.0%)	21 (8%)	125 (9%)	12 (9%)	**165 (9%)**
SA	0 (0.0%)	6 (2%)	165 (12%)	7 (5%)	**178 (9%)**
TAS	65 (47%)	31 (12%)	29 (2%)	4 (3%)	**129 (7%)**
VIC	14 (10%)	50 (20%)	397 (28%)	23 (17%)	**484 (25%)**
WA	17 (12%)	56 (22%)	61 (4%)	46 (34%)	**180 (10%)**

*Sex missing for 2 patients; reported as number and percentage of patients with type/subtype

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

	Not admitted to ICU	Admitted to ICU	Total
Number of cases	1738	214	**1952**
Pregnancy	43 (3%)	7 (3%)	**50 (3%)**
Medical comorbidities	1316 (76%)	176 (82%)	**1492 (76%)**
Chronic respiratory illness	515 (30%)	71 (33%)	**586 (30%)**
Chronic cardiac disease	567 (33%)	70 (33%)	**637 (32%)**
Diabetes	383 (22%)	46 (22%)	**429 (22%)**
Chronic liver disease	74 (4%)	15 (7.0%)	**89 (5%)**
Chronic neurological illness	280 (16%)	31 (15%)	**311 (16%)**
Chronic renal disease	219 (13%)	28 (13%)	**247 (13%)**
Immunocompromised	260 (15%)	33 (15%)	**293 (15%)**
Malignancy	187 (11%)	25 (12%)	**212 (11%)**
Obesity	198 (11%)	33 (15%)	**231 (12%)**
Nursing home resident	152 (9%)	4 (2%)	**156 (8%)**
Received influenza vaccine	693/1431 (48%)	59/168 (35%)	**752/1599 (47%)**
Influenza type/subtype			
A/H1	126 (7%)	13 (6%)	**139 (7%)**
A/H3	231 (13%)	25 (12%)	**256 (13%)**
A/unknown	1260 (73%)	162 (76%)	**1422 (73%)**
B	121 (7.0%)	14 (7%)	**135 (7%)**
In hospital mortality	40/1692 (2%)	25/207 (12%)	**65/1899 (3%)**

and 2015 (n=2,070). Based on the bed capacity of sentinel hospitals, this is likely to represent around 14,000 admissions with confirmed influenza nationally. However, as influenza testing is not performed on all patients with acute respiratory presentations, and influenza may also trigger delayed respiratory presentations (e.g. secondary bacterial pneumonia) and non-respiratory complications (e.g. acute myocardial infarction), this should be regarded as a minimum estimate.

The 2016 year was the first season in which the use of quadrivalent vaccine (containing two influenza A and two influenza B strains) was funded under the National Immunisation Program. However, in comparison with the 2015 season, where more than half of admissions were due to influenza B and both Victorian and Yamagata lineages circulated, the incremental benefit of the quadrivalent vaccine would be expected to be minimal in 2016 as influenza B activity was low. Influenza vaccine effectiveness was noted to be low in the target population in this season in comparison to previous years (and absent in the elderly). Further work is being performed to explore this issue further. Vaccine effectiveness in the elderly has generally been found to be lower than in younger age groups, but a study from the United States found influenza vaccine to be cost-effective in the elderly over four seasons[6].

In recent seasons, there has been ongoing concern about mismatches between the A/H3N2 vaccine and circulating strains, due in part to antigenic change associated with egg adaptation as well as growing genetic diversity within circulating A/H3N2 strains, with North American data suggesting a higher vaccine effectiveness against 3C.3b than 3C.3a and 3C.2a clades [7, 8]. Additionally, work has suggested that the effectiveness of influenza vaccines against A/H1N1pdm may be poorer in a middle aged cohort born before 1980, who were exposed to 163Q A/H1N1/USSR types[9].

The peak incidence of confirmed influenza provides a measure of the impact of influenza. We chose to use acute hospital beds as a denominator because the number of admissions are not readily available in a timely manner, and bed numbers provide a "hard limit" of hospital capacity. The proportion of hospital beds occupied by patients with confirmed influenza can be estimated from the incidence and mean duration of stay – at Westmead Hospital in 2016, a peak weekly incidence of 9.7 per 100 beds roughly equates to 9% of the hospital bed capacity (9.7 admissions per 700 bed days x 5.6 days).

We found that around half of the influenza cases were unvaccinated. Our estimates of vaccine coverage are similar to that of previous years, where around 70-80% of the elderly, around 60% of non-elderly adults with comorbidities and around 20% in children with comorbidities[10-13]. Our estimates of influenza vaccine coverage in the elderly are consistent with recent estimates from a meta-analysis of vaccine coverage in the Australian elderly population collected by a variety of methods, providing reassurance about the validity of hospital controls for this purpose[14]. Additionally, we have recently compared vaccine coverage estimates from hospital, primary care and community-based systems and found them to be broadly consistent.[15]

The systematic review also found an increase in coverage associated with public funding of influenza vaccine since 1999; however, our findings reinforce the need to improve coverage particularly in younger populations with medical comorbidities where publicly funded vaccine has been available since 2010. We found that 93% of admissions with influenza in the elderly occurred in patients with medical comorbidities; this proportion was 71% in non-elderly adults and 44% in children. This suggests that even with an effective influenza vaccine, the current policy of vaccinating only younger individuals with comorbidities would not be expected to provide protection to more than half of children admitted to hospital.

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.

In summary, we detected a large number of hospital admissions with laboratory-confirmed influenza in a national observational study in 2016 comparable to 2014 and 2015 but much higher than in prior years. A consistent finding over several years is that a high proportion of patients with severe influenza, and almost all deaths, occurred in patients with chronic comorbidities.

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

Variable	Crude OR	p	Adjusted OR*	p
Age				
<16 years	0.9 (0.6, 1.4)	0.713	1.1 (0.7, 1.8)	0.685
16-64 years	1		1	
65+ years	0.6 (0.5, 0.9)	0.007	0.7 (0.5, 0.9)	0.017
Medical comorbidities	1.5 (1.0, 2.1)	0.035	1.9 (1.3, 2.9)	0.001
Aboriginal or Torres Strait Islander peoples	1.6 (0.9, 2.7)	0.11	1.3 (0.7, 2.3)	0.369
Pregnancy	1.3 (0.6, 3.0)	0.488	1.0 (0.4, 2.4)	0.935
Restricted functional status	1.1 (0.8, 1.5)	0.426	1.0 (0.7, 1.4)	0.912
Nursing home resident	0.2 (0.1, 0.5)	0.002	0.2 (0.1, 0.6)	0.003
Influenza type/subtype				
A/H1	0.9 (0.4, 2.0)	0.778	0.9 (0.4, 1.9)	0.701
A/H3	0.9 (0.5, 1.9)	0.85	1.1 (0.5, 2.3)	0.761
B	1		1	
A/unk	1.1 (0.6, 2.0)	0.72	1.2 (0.7, 2.2)	0.561

* all variables included in multivariate model

Figure 2: Incidence of confirmed influenza (per 100 hospital beds) by week and year

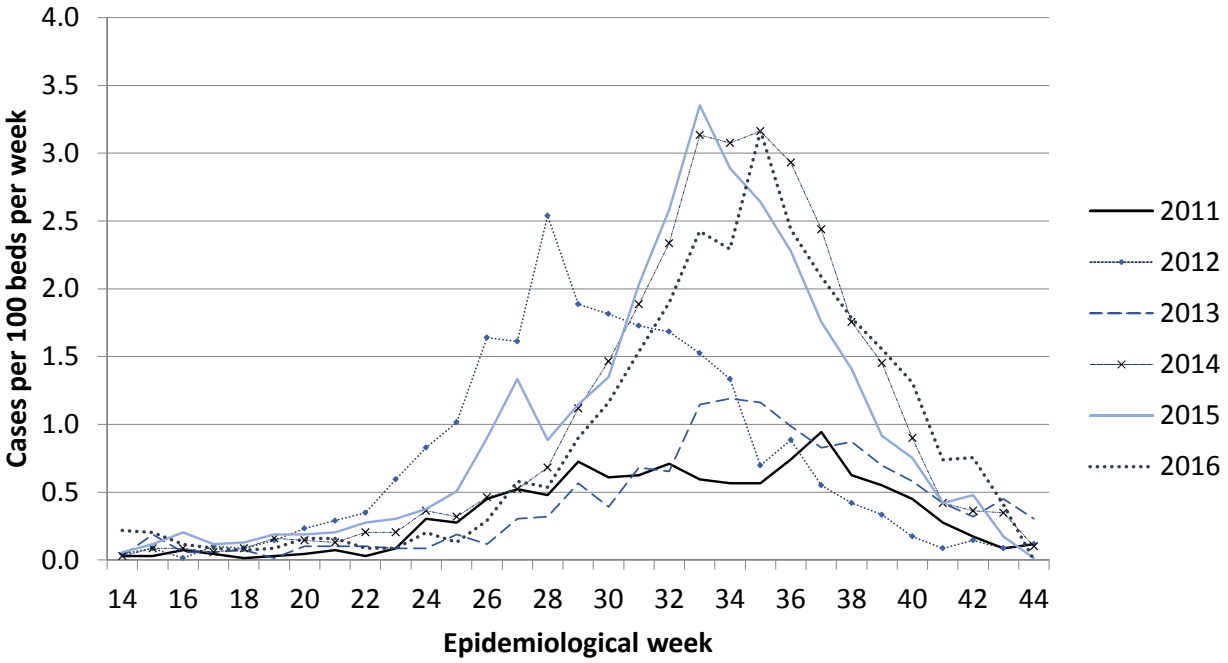
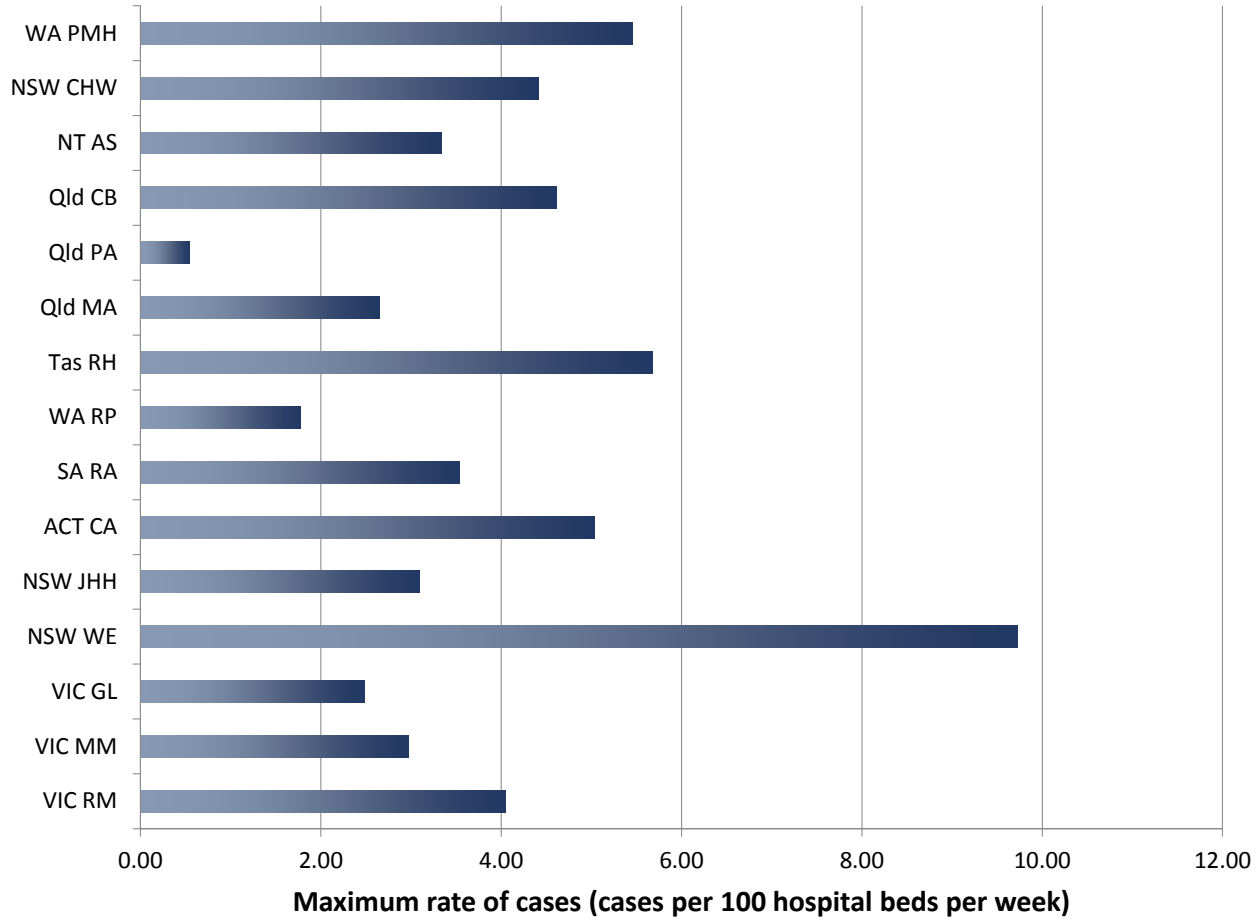


Figure 3: Peak incidence of confirmed influenza (per 100 hospital beds) by hospital



RM: Royal Melbourne; MM: Monash Medical Centre, GL: University Hospital Geelong, WE: Westmead Hospital, JHH: John Hunter Hospital, CA: Canberra and Calvary Hospitals, RA: Royal Adelaide, RP: Royal Perth Hospital, RH: Royal Hobart Hospital, MA: Mater Hospital, PA: Princess Alexandra Hospital, CB: Cairns Base Hospital, AS: Alice Springs Hospital, CHW: Children's Hospital at Westmead, PMH: Princess Margaret Hospital