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Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand

The ANZIC Influenza Investigators*

ABSTRACT

BACKGROUND

Planning for the treatment of infection with the 2009 pandemic influenza A (H1N1) virus through health care systems in developed countries during winter in the Northern Hemisphere is hampered by a lack of information from similar health care systems.

METHODS

We conducted an inception-cohort study in all Australian and New Zealand intensive care units (ICUs) during the winter of 2009 in the Southern Hemisphere. We calculated, per million inhabitants, the numbers of ICU admissions, bed-days, and days of mechanical ventilation due to infection with the 2009 H1N1 virus. We collected data on demographic and clinical characteristics of the patients and on treatments and outcomes.

RESULTS

From June 1 through August 31, 2009, a total of 722 patients with confirmed infection with the 2009 H1N1 virus (28.7 cases per million inhabitants; 95% confidence interval [CI], 26.5 to 30.8) were admitted to an ICU in Australia or New Zealand. Of the 722 patients, 669 (92.7%) were under 65 years of age and 66 (9.1%) were pregnant women; of the 601 adults for whom data were available, 172 (28.6%) had a body-mass index (the weight in kilograms divided by the square of the height in meters) greater than 35. Patients infected with the 2009 H1N1 virus were in the ICU for a total of 8815 bed-days (350 per million inhabitants). The median duration of treatment in the ICU was 7.0 days (interquartile range, 2.7 to 13.4); 456 of 706 patients (64.6%) with available data underwent mechanical ventilation for a median of 8 days (interquartile range, 4 to 16). The maximum daily occupancy of the ICU was 7.4 beds (95% CI, 6.3 to 8.5) per million inhabitants. As of September 7, 2009, a total of 103 of the 722 patients (14.3%; 95% CI, 11.7 to 16.9) had died, and 114 (15.8%) remained in the hospital.

CONCLUSIONS

The 2009 H1N1 virus had a substantial effect on ICUs during the winter in Australia and New Zealand. Our data can assist planning for the treatment of patients during the winter in the Northern Hemisphere.

The Australian and New Zealand Intensive Care (ANZIC) study is a collaboration of the ANZIC Society Clinical Trials Group (CTG), the ANZIC Research Centre, the Australasian Society of Infectious Diseases CTG, the Paediatric Study Group of the ANZIC Society, and the ANZIC Society Centre for Outcome and Resource Evaluation. The writing committee (Steven A.R. Webb [chair], M.P.H., Ph.D., F.R.A.C.P., F.J.F.I.C.M., Ville Pettilä, M.D., Ph.D., Ian Seppelt, F.A.N.Z.C.A., F.J.F.I.C.M., Rinaldo Bellomo, M.D., F.R.A.C.P., F.J.F.I.C.M., Michael Bailey, Ph.D., David J. Cooper, M.D., F.R.A.C.P., F.J.F.I.C.M., Michelle Cretikos, M.P.H., Ph.D., Andrew R. Davies, F.R.A.C.P., F.J.F.I.C.M., Simon Finfer, F.R.C.P., F.J.F.I.C.M., Peter W.J. Harrigan, F.J.F.I.C.M., Graeme K. Hart, F.A.N.Z.C.A., F.J.F.I.C.M., Belinda Howe, R.N., Jonathan R. Iredell, Ph.D., F.R.A.C.P., F.R.C.P.A., Colin McArthur, F.J.F.I.C.M., Imogen Mitchell, F.R.A.C.P., F.J.F.I.C.M., Siouxzy Morrison, R.N., M.P.H., Alistair D. Nichol, Ph.D., F.C.A.R.C.S.I., David L. Paterson, Ph.D., F.R.A.C.P., F.R.C.P.A., Sandra Peake, F.J.F.I.C.M., Ph.D., Brent Richards, F.R.A.C.P., F.J.F.I.C.M., Dianne Stephens, F.A.N.Z.C.A., F.J.F.I.C.M., Andrew Turner, F.R.A.C.P., F.J.I.C.M., and Michael Yung, M.D.) takes responsibility for the content and integrity of this article. Address reprint requests to Dr. Webb at the Intensive Care Unit, Royal Perth Hospital, Wellington St., Perth, WA 6000, Australia, or at sarwebb@cyllene.uwa.edu.au.

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Infection with the 2009 pandemic influenza A (H1N1) virus emerged in Mexico toward the end of the 2008–2009 influenza season in the Northern Hemisphere. As of September 6, 2009, the World Health Organization had reported over 277,607 laboratory-confirmed cases of 2009 H1N1 influenza, with at least 3205 deaths.[1] From June through August 2009, Australia and New Zealand experienced the combined effect of the pandemic and winter in the Southern Hemisphere. The reported incidence of infection with the 2009 H1N1 virus during winter in Australia and New Zealand was 8 times that reported for the same period in the United States.[1,2] This resulted in a substantial increase in demand for hospital services, particularly critical care services.

Reports of critical illness caused by 2009 H1N1 influenza during summer in the Northern Hemisphere contain insufficient data to provide reliable estimates of the burden of critical illness to be expected during winter in the Northern Hemisphere.[3-9] Although the successful deployment of a safe and effective vaccine may modify the burden of disease,[10,11] population-based data from Australia and New Zealand can currently provide a reasonable estimate of the likely effect of 2009 H1N1 influenza during the Northern Hemisphere winter. In addition, the data can be used to identify persons who are at high risk of developing severe disease.

In this report, we describe the incidence of intensive care unit (ICU) admission, demographic characteristics, treatment, use of critical care resources, and outcome for all patients with laboratory-confirmed infection with the 2009 pandemic influenza A (H1N1) virus admitted to ICUs in Australia and New Zealand during the winter of 2009 in the Southern Hemisphere.

METHODS

We performed a multicenter inception-cohort study involving 187 ICUs in Australia and New Zealand — all the ICUs (adult, pediatric, or adult and pediatric) in the two countries.[12] The ICUs had a total of 1879 beds, of which 1449 were equipped for mechanical ventilation. Each center obtained approval from the institutional ethics committee. The requirement for written informed consent from individual patients was waived at all sites.

From June 1 through August 31, 2009, we identified all patients admitted to the ICU with confirmed infection with the 2009 pandemic influenza A (H1N1) virus. The 2009 H1N1 influenza was confirmed by means of a polymerase-chain-reaction (PCR) assay or serologic analysis. The 2009 pandemic influenza A (H1N1) virus and seasonal subtypes (preexisting H1N1 and H3N2 strains) were confirmed by PCR assay. The PCR assay was conducted initially at reference laboratories in each region and later, as the pandemic evolved, at local laboratories. The performance of these laboratories was accredited by the National Association of Testing Authorities in Australia or by International Accreditation New Zealand. In addition, the 2009 H1N1 virus could be confirmed in a single reference laboratory by means of a hemagglutination-inhibition assay to detect antibodies specific for the 2009 H1N1 virus. Population data for Australia and New Zealand and their constituent regions were obtained from Australian Bureau of Statistics[13] and Statistics New Zealand.[14]

We collected several types of data for the patients: the dates and times of admission to the hospital and the ICU; age; race or ethnic group, including indigenous group (reported by patients or their next of kin or, for patients under 18 years of age, by a parent or guardian); sex; pregnancy or childbirth less than 28 days previously (for women); coexisting conditions, which for patients 16 years of age or older were any condition that is defined within the Chronic Health Evaluation component of the Acute Physiology, Age, and Chronic Health Evaluation (APACHE III, for which scores can range from 0 to 299, with higher scores indicating a greater severity of illness),[15] and for patients under 16 years of age, defined as prematurity, immunodeficiency, cystic fibrosis, congenital heart disease, neuromuscular disorder, or chronic neurological impairment; history of asthma or another chronic pulmonary disease, chronic heart failure, or diabetes; measured or estimated weight and height (for calculation of the body-mass index [BMI]); date and time of first symptoms; presence and type of influenza syndrome, including viral pneumonitis or the acute respiratory distress syndrome, secondary bacterial pneumonia, exacerbation of airflow limitation due to either asthma or chronic obstructive pulmonary disease, or intercurrent illness; and airway status at the time of ICU admission (presence or absence of endotracheal intubation, tracheotomy, sealed face mask, and any artificial airway).

We categorized patients according to the age

groups used in a previous report: 0 to 1 year of age, 1 to 4 years, 5 to 24 years, 25 to 49 years, 50 to 64 years, and 65 years of age or older.[16] Data were collected daily on the use of mechanical ventilation and extracorporeal membrane oxygenation. We calculated the duration of treatment in the ICU and the hospital, as well as the rates of occupancy of the ICU, for Australia and New Zealand and their constituent regions. We recorded outcomes of patients in the ICU and whether the patients had been discharged or were still in the hospital or the ICU as of September 7, 2009. To compare data from the current year with those from previous years, we obtained the number of patients who had been admitted to Australian or New Zealand ICUs with viral pneumonitis during the winters of 2004 through 2008, from the Australian and New Zealand Intensive Care (ANZIC) Society's Adult Patient Database.[17] This source of data does not categorize the cause of viral pneumonitis and may include some patients who had viral pneumonitis due to causes other than influenza A. To determine which groups were at increased risk of admission to an ICU with 2009 H1N1 influenza, we compared the proportions of patients with such an admission in each group of interest with the proportions of the general population of Australia[13] and New Zealand[14] that those admitted patients represented.

DATA MANAGEMENT

We collected data by means of electronic case report forms. The study coordinating center was the ANZIC Research Centre, Monash University, Melbourne, Australia.[18] Infection with the 2009 H1N1 virus is subject to mandatory reporting in both Australia and New Zealand, and all diagnoses were confirmed with the relevant state or territory's Department of Health. In addition, to confirm the completeness of case ascertainment, we contacted the 83 ICUs that had no reported cases at the end of the study period (August 31, 2009). Patients transferred between ICUs were counted as a single ICU admission. We made no assumptions regarding missing data; all proportions were calculated as percentages of the patients with available data.

STATISTICAL ANALYSIS

We performed statistical analysis using SAS software, version 9.1 (SAS Institute). We calculated descriptive statistics for all study variables. We report data for continuous variables as medians (with interquartile ranges) and for categorical variables as percentages (with 95% confidence intervals, where appropriate). We estimated the age-based population-admission rates.[13] We performed a univariate analysis for in-hospital mortality, using the chi-square test, Fisher's exact test, or Wilcoxon rank-sum test, as appropriate. We performed multivariate logistic-regression analysis to identify factors independently associated with in-hospital mortality, with the multivariate model constructed by using both stepwise-selection and backward-elimination techniques. We first included age, as a continuous variable. We then included in the model, as categorical variables,[16] the presence or absence of pregnancy, asthma or another chronic pulmonary disease, and chronic heart failure; BMI

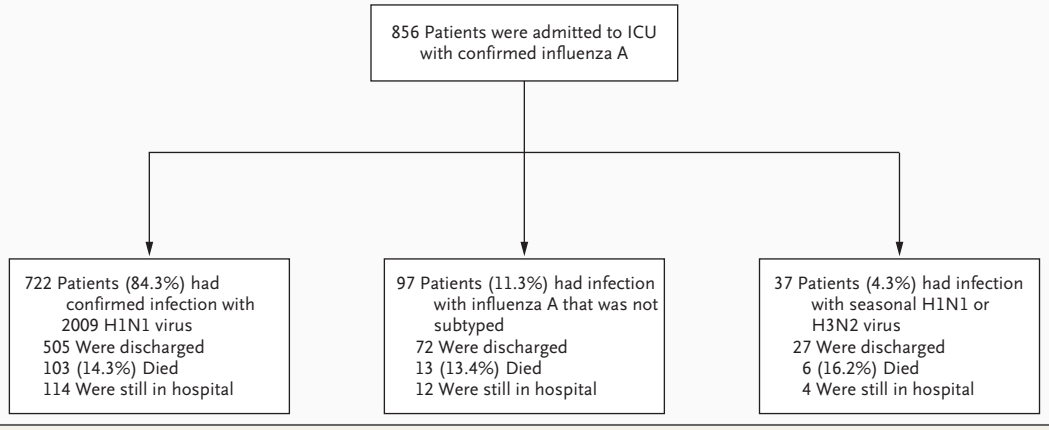


Figure 1. Enrollment and Follow-up of Patients with Influenza A Admitted to Intensive Care Units (ICUs) in Australia and New Zealand.

Follow-up data are as of September 7, 2009.

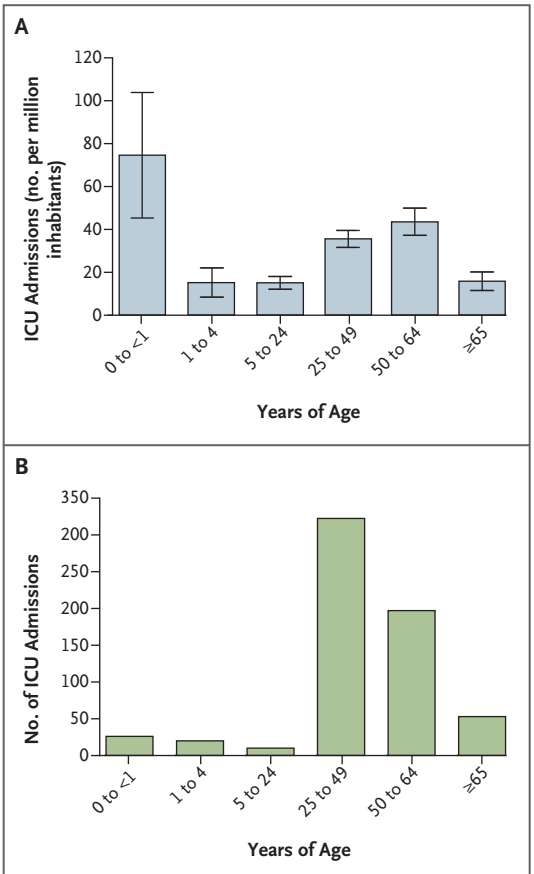


Figure 2. Incidence and Number of Admissions to the Intensive Care Unit (ICU), According to Age Group.

The incidence of ICU admission, expressed as the number per million residents, is shown in Panel A, and the number of ICU admissions is shown in Panel B. The age-specific incidence was calculated by dividing the number of admissions in each age group by the estimated number of persons in that age group in the population of Australia and New Zealand (which was 350,346 for 0 to 1 years, 1,324,185 for 1 to 4 years, 6,938,498 for 5 to 24 years, 9,111,600 for 25 to 49 years, 4,563,709 for 50 to 64 years, and 3,377,580 for 65 years or older). I bars indicate the 95% confidence intervals.

(the weight in kilograms divided by the square of the height in meters) greater than 35 versus 35 or less; race or ethnic group; and the presence or absence of any coexisting condition; and the type of influenza syndrome. Goodness of fit was determined with the use of the Hosmer–Lemeshow statistic. A two-sided P value of less than 0.05 was considered to indicate statistical significance, except in the multivariate model, where a P value of less than 0.01 was considered to indicate statistical significance.

RESULTS

We identified 856 patients with influenza A infection who were admitted to an ICU between June 1 and August 31, 2009. Of these, 722 (84.3%) had a confirmed infection with 2009 pandemic influenza A (H1N1) virus (Fig. 1). The 2009 H1N1 virus was diagnosed by means of PCR assay in 717 patients and serologic analysis in 5 patients. Among the 722 patients with 2009 H1N1 influenza, 626 were admitted to an ICU in Australia and 96 to an ICU in New Zealand. The numbers of patients with viral pneumonitis admitted to Australian or New Zealand ICUs from June 1 through August 31 were 57 in the year 2005, 33 in 2006, 69 in 2007, and 69 in 2008 (mean, 57 patients). During the winter of 2009, 37 patients were admitted to an ICU with confirmed seasonal subtypes of influenza A (H1N1) virus. The combined population of Australia and New Zealand was estimated at 25,180,770, giving an incidence of ICU admission for 2009 H1N1 influenza during winter 2009 of 28.7 (95% confidence interval [CI], 26.5 to 30.8) per million inhabitants.[13,14]

The number of admissions and the age-specific incidences varied substantially according to the age group (Fig. 2). The highest age-specific incidence of ICU admission was among infants (0 to 1 year of age) (Fig. 2A), whereas the highest number of ICU admissions was among patients 25 to 49 years of age (Fig. 2B). Additional demographic data and data on risk factors and type of critical illness among patients with 2009 H1N1 influenza are presented in Table 1.

Pregnant women represent approximately 1% of the general population of Australia and New Zealand.[13,14] A total of 66 of the 722 patients (9.1%) admitted to the ICU with 2009 H1N1 influenza were pregnant women. Of the 601 adults for whom BMI data were available, 172 (28.6%) had a BMI greater than 35. The proportion of a representative adult Australian population with a BMI greater than 35 was 5.3% in 2003.[19] We estimate the proportion of patients with asthma or other chronic pulmonary disease in the general population to be around 13%.[20] Data on premorbid pulmonary disease were missing for 15 of the 722 patients with 2009 H1N1 influenza in our study; of the remaining 707 patients, 231 (32.7%) had asthma or another chronic pulmonary disease. Indigenous groups were relatively overrepresented in our study: aboriginal and Torres Strait

Table 1. Baseline Characteristics of Patients with Confirmed Critical Illness Related to 2009 H1N1 Influenza.*

Characteristic	Value
Age — yr	
Median	40
IQR	26–54
Female sex — no./total no. (%)	376/722 (52.1)
Pregnant — no./total no. (%)	66/722 (9.1)
Race or ethnic group — no./total no. (%)†	
White	483/683 (70.7)
Aboriginal or Torres Strait Islander	
All patients	61/683 (8.9)
Admitted to ICU in Australia	61/683 (8.9)
Maori	
All patients	31/683 (4.5)
Admitted to ICU in New Zealand	24/683 (3.5)
Pacific Islander	37/683 (5.4)
Asian	29/683 (4.2)
Other	42/683 (6.1)
Adults with BMI >35 — no./total no. (%)‡	172/601 (28.6)
Diabetes — no./total no. (%)	112/700 (16.0)
Asthma or chronic pulmonary disease — no./total no. (%)	231/707 (32.7)
Chronic heart failure — no./total no. (%)	74/703 (10.5)
Coexisting condition — no./total no. (%)§	192/687 (27.9)
No known predisposing factors — no./total no. (%)	229/722 (31.7)
Time from first symptoms to hospital admission — days¶	
Median	4
IQR	2–7
Influenza syndrome — no./total no. (%)	
Viral pneumonitis or ARDS	336/689 (48.8)
Secondary bacterial pneumonia	140/689 (20.3)
Exacerbation of airflow limitation	95/689 (13.9)
Intercurrent illness or other illness	118/689 (17.1)

* ARDS denotes the acute respiratory distress syndrome, ICU intensive care unit, and IQR interquartile range.
† Race or ethnic group was reported by patients or their next of kin or, for patients under 18 years of age, by a parent or guardian.
‡ The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.
§ Coexisting conditions for patients 16 years of age or older were any condition that is defined within the Chronic Health Evaluation component of the Acute Physiology, Age, and Chronic Health Evaluation (APACHE III),[15] and for patients under 16 years of age, defined as prematurity, immunodeficiency, cystic fibrosis, congenital heart disease, neuromuscular disorder, or chronic neurologic impairment.
¶ Time from first symptoms to hospital admission was known for 712 of the 722 patients.

Islanders account for 2.5% of the Australian population[13] but made up 9.7% of our patients with 2009 H1N1 influenza who were admitted to Australian ICUs. Maori represent 13.6% of the New Zealand population[14] but accounted for 25.0% of the patients with 2009 H1N1 influenza who were admitted to New Zealand ICUs. Overall, 229 patients (31.7%) had no known predisposing factor. Almost half of all patients (48.8%) had the acute respiratory distress syndrome or viral pneumonitis,

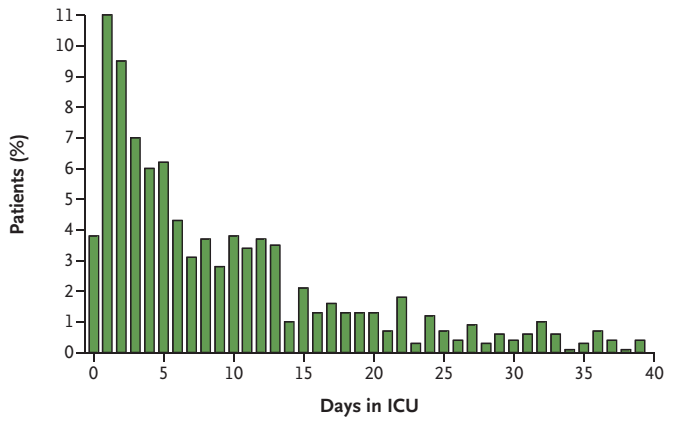


Figure 3. Length of Stay in the Intensive Care Unit (ICU) among Patients with 2009 H1N1 Influenza.

Figure 4 (facing page). Numbers of Patients with 2009 H1N1 Influenza Admitted to an ICU and Numbers of ICU Beds Occupied by Those Patients, According to Study Week and Region.

The panels on the left show the numbers of patients admitted to an ICU, and the panels on the right show the numbers of ICU beds occupied by those patients. All data are per million inhabitants. Data are shown for the Australian states of Victoria, New South Wales, and Queensland; for New Zealand; and for all regions of Australia and New Zealand combined.

and 20.3% of patients were clinically diagnosed with bacterial pneumonia (i.e., had unilateral or bilateral asymmetric lung infiltrates consistent with bacterial pneumonia, with bacterial infection proven or suspected) in association with confirmed infection with the 2009 H1N1 virus.

Data on the use of mechanical ventilation in the ICU were available for 706 patients; of these, 456 (64.6%) underwent mechanical ventilation for a median of 8 days (interquartile range, 4 to 16). The total number of days of ventilation was 5249, representing 208 days (95% CI, 203 to 214) per million inhabitants. Of the 456 patients undergoing mechanical ventilation, 53 (11.6%) were subsequently treated with extracorporeal membrane oxygenation, representing 2.1 patients (95% CI, 1.5 to 2.7) per million inhabitants. Available data on other cointerventions are given in the Supplementary Appendix (available with the full text of this article at NEJM.org).

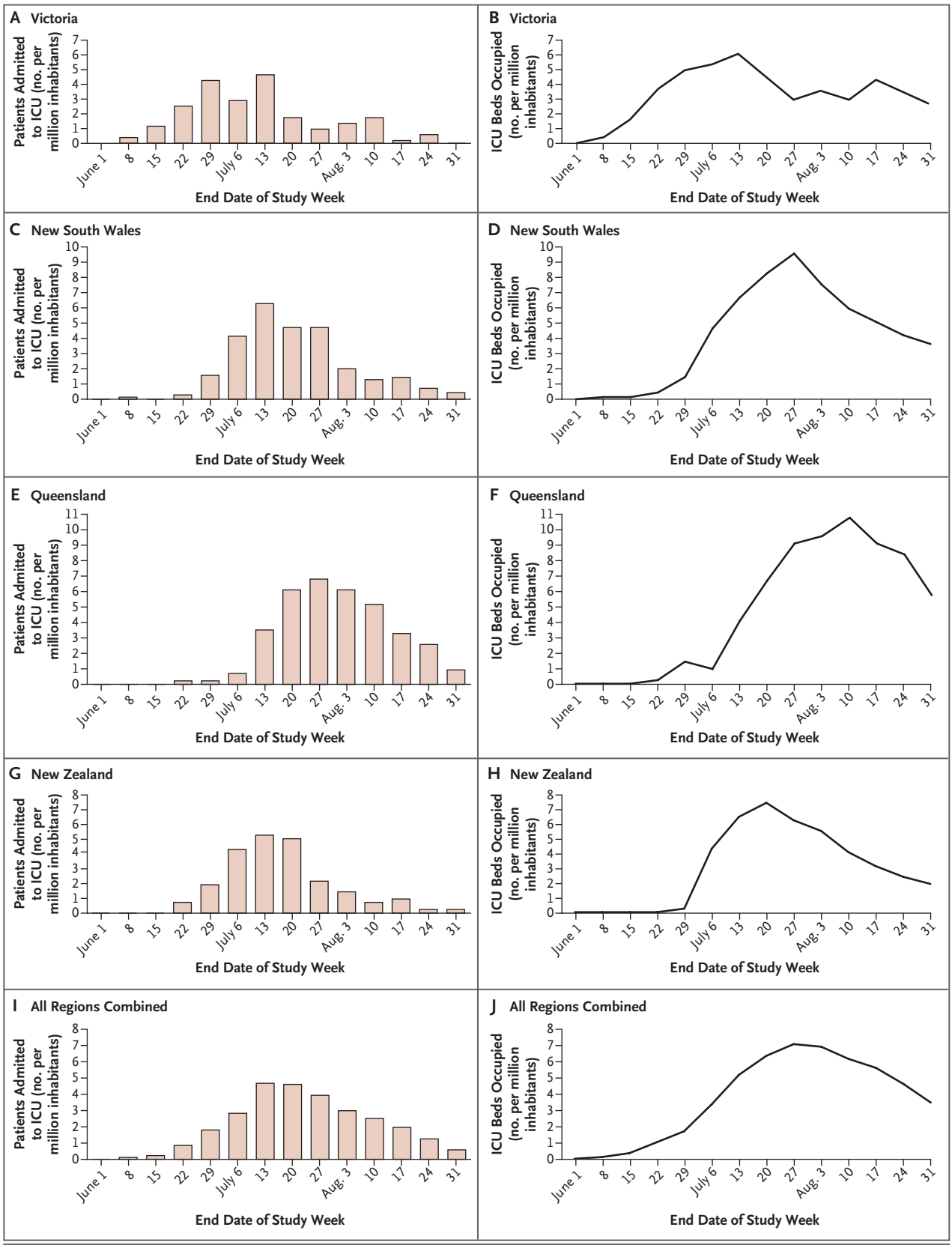
As of September 7, 2009, a total of 114 of the 722 patients (15.8%) were still in the hospital, of whom 37 (5.1%) were still in the ICU. Excluding these 114 patients still in the hospital or ICU and an additional 33 for whom data were not available (regarding duration of ICU treatment, for 3 patients, and duration of in-hospital treatment, for 30), we calculated the median duration of treatment in the ICU as 7.4 days (interquartile range, 3.0 to 16.0) (Fig. 3) and the median duration of treatment in the hospital as 12.3 days (interquartile range, 6.4 to 22.1).

The number of ICU admissions per million inhabitants varied over the study period, for Australia and New Zealand overall and for each of the main regions affected, as did the number of ICU beds occupied per million inhabitants (Fig. 4). Patients with 2009 H1N1 influenza occupied the ICU for a total of 8815 ICU bed-days, representing 350 bed-days (95% CI, 342 to 357) per million inhabitants. Across Australia and New Zealand, the maximum number of ICU beds occupied per million inhabitants was 7.4 (95% CI, 6.3 to 8.5) during the week ending July 27, 2009. The maximum number of beds occupied by region in the Australian states or New Zealand ranged between 6.3 and 10.6 per million inhabitants (Fig. 4). Over the 3-month study period, 5.2% of ICU bed-days were accounted for by patients with 2009 H1N1 influenza. The peak percentage of ICU beds occupied by patients with 2009 H1N1 influenza in Australian states and New Zealand ranged from 8.9 to 19.0%.

As of September 7, 2009, a total of 608 patients (84.2%) had been discharged from the hospital: 103 (16.9%) had died in the hospital and 505 (83.1%) had been discharged alive. For those who had died or been discharged alive, three factors were found, on multivariate logistic-regression analysis, to be independently associated with death in the hospital: requirement of invasive ventilation at ICU admission (odds ratio for in-hospital death, 5.51; 95% CI, 3.05 to 9.94; $P<0.001$), any coexisting condition (as defined in our study) (odds ratio, 2.56; 95% CI, 1.52 to 4.30; $P<0.001$), and older age (odds ratio per year of age, 1.02; 95% CI, 1.01 to 1.04; $P=0.002$). The data were well fitted by the model ($P=0.79$ by the Hosmer–Lemeshow test).

DISCUSSION

This cohort study identified all patients with confirmed 2009 H1N1 influenza who were admitted



to Australian or New Zealand ICUs during winter 2009 in the Southern Hemisphere. We identified 722 patients with the infection and estimated the winter population incidence of ICU admission: 28.7 per million inhabitants. The number of ICU admissions due to influenza A in 2009 was 15 times the number due to viral pneumonitis in recent years. We were able to document the use of ICU beds and patients' outcomes and estimate the number of ICU bed-days occupied: 350 per million inhabitants. We identified infants (0 to 1 year of age) and adults 25 to 64 years of age to be at particular risk. Pregnant women, adults with a BMI greater than 35, and indigenous Australian and New Zealand populations also appeared to have an increased risk. In-hospital mortality, estimated on the basis of data available at the time of this report, exceeded 16%.

Previously published reports have highlighted cases of severe viral pneumonia affecting patients younger than the expected age of patients affected during a normal influenza season[8,9] and have noted that pregnant women are at increased risk.[21] Our findings are consistent with these reports. The age-specific incidence rates were highest among infants and adults 25 to 64 years of age. Although the incidence of ICU admission varied across the age groups and was low for patients 65 years of age or older, the risk of death increased with increasing age. The proportion of patients who were admitted to an ICU and were pregnant, had chronic lung disease, had a BMI greater than 35, or were indigenous to Australia or New Zealand were all higher than the corresponding proportions in the general population. Finally, a third of our patients were young or middle-aged adults who neither were pregnant nor had a known coexisting condition.

Australia and New Zealand have 75 ICU beds per million inhabitants. The number of ICU beds varies greatly among developed countries,[22] and the capacity of countries to cope with a surge in demand for critical care services owing to infection with the 2009 pandemic influenza A (H1N1) virus will depend on the current numbers of ICU beds and the countries' ability to expand that capacity or restrain other demands on it.

Our data indicate that the greatest effect on ICU resources in a given region occurs approximately 4 to 6 weeks after the first confirmed winter ICU admission and that the extra workload lasts several weeks. Current recommendations are that patients with 2009 H1N1 influenza should receive treatment in isolation.[23] The requirement to treat many patients in isolation, combined with the need for interhospital transfer for optimal care, may further increase the strain on critical care resources.

The proportion of patients who died in the hospital in our study is no higher than that previously reported among patients with seasonal influenza A who were admitted to an ICU.[24] Patients admitted to an ICU with seasonal influenza A predominantly are elderly and have coexisting conditions.[24] Among patients admitted to ICU, older age, the presence of coexisting conditions, and a requirement for invasive ventilation were independently associated with increased risk of death, but because there were greater numbers of younger patients in our cohort, the majority of deaths occurred in younger patients.

The inferences that can be drawn from our data are subject to some limitations. First, to make this report available in time to assist planning in the Northern Hemisphere, we censored the hospital-outcome data, which may have introduced bias. Second, our data were gathered early during the pandemic in Australia and New Zealand. The findings may be different during future waves, owing to the timely deployment of an effective vaccine, to viral mutation, and to resistance to antiviral drugs. Third, the data regarding previous winters come not from an inception-cohort study but from our Australia–New Zealand database; therefore, they are not directly comparable to the data in the current study for winter 2009. Fourth, ascertainment of patients with 2009 H1N1 influenza who were admitted to an ICU may not have been complete, and we cannot rule out the possibility that a small number of cases were not reported to the registry. Finally, false negative diagnostic tests may well have led us to underestimate the true burden of 2009 H1N1 influenza in our patients. Among the patients with confirmed influenza A, there were 97 in whom the influenza virus was not subtyped, some of whom may have had false negative tests for the 2009 H1N1 virus. Nonetheless, with these caveats, knowledge of the rate of ICU admission and occupancy due to 2009 H1N1 influenza during the winter in Australia and New Zealand can inform the planning and assessment of critical care needs in countries yet to face the 2009 winter.

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APPENDIX

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REFERENCES

1. 2009 H1N1 flu: international situation update. Atlanta: Centers for Disease Control and Prevention. (Accessed October 19, 2009, at http://www.cdc.gov/h1n1flu/updates/international/.)
2. flucount.org. Worldwide H1N1 (swine flu) infection data. (Accessed October 19, 2009, at http://www.flucount.org/.)
3. Hospitalized patients with novel influenza A (H1N1) virus infection — California, April–May, 2009. MMWR Morb Mortal Wkly Rep 2009;58:536-41.
4. Intensive-care patients with severe novel influenza A (H1N1) virus infection — Michigan, June 2009. MMWR Morb Mortal Wkly Rep 2009;58:749-52.
5. Gatherer D. The 2009 H1N1 influenza outbreak in its historical context. J Clin Virol 2009;45:174-8.
6. Miller MA, Viboud C, Balinska M, Simonsen L. The signature features of influenza pandemics — implications for policy. N Engl J Med 2009;360:2595-8.
7. Cutler J, Schleihauf E, Hatchette TF, et al. Investigation of the first cases of human-to-human infection with the new swine-origin influenza A (H1N1) virus in Canada. CMAJ 2009;181:159-63.
8. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med 2009;360:2605-15. [Erratum, N Engl J Med 2009;361:102.]
9. Chowell G, Bertozzi SM, Colchero MA, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. N Engl J Med 2009;361:674-9.
10. Clark TW, Pareek M, Hoschler K, et al. Trial of influenza A (H1N1) 2009 monovalent MF59-adjuvanted vaccine — preliminary report. N Engl J Med 2009;361. DOI: 10.1056/NEJMoa0907650.
11. Greenberg ME, Lai MH, Hartel GF, et al. Response after one dose of a monovalent influenza A (H1N1) 2009 vaccine — preliminary report. N Engl J Med 2009;361. DOI: 10.1056/NEJMoa0907413.
12. Drennan K, Hart GK, Hicks P. Intensive care resources & activity: Australia & New Zealand 2006/2007. Melbourne, Australia: ANZICS, 2008.
13. Australian Bureau of Statistics. 3201.0 — population by age and sex, Australian states and territories, June 2008. (Accessed October 19, 2009, at http://www.abs.gov.au/AUSSTATS/abs@.nsf/MF/3201.0.)
14. Statistics New Zealand. National population estimates. (Accessed October 19, 2009, at http://search.stats.govt.nz/search?w=national%20population%20estimates.)
15. Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system: risk prediction of hospital mortality for critically ill hospitalized adults. Chest 1991;100:1619-36.
16. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. JAMA 2003;289:179-86.
17. Stow PJ, Hart GK, Higlett T, et al. Development and implementation of a high-quality clinical database: the Australian and New Zealand Intensive Care Society Adult Patient Database. J Crit Care 2006;21:133-41.
18. Webb SA, Seppelt IM. Pandemic (H1N1) 2009 influenza ("swine flu") in Australian and New Zealand intensive care. Crit Care Resusc 2009;11:170-2.
19. Dal Grande E, Gill T, Taylor AW, Chittleborough C, Carter P. Obesity in South Australian adults — prevalence, projections and generational assessment over 13 years. Aust N Z J Public Health 2005;29:343-8.
20. Australia's health 2008. Canberra: Australian Institute of Health and Welfare, 2008.
21. Jamieson DJ, Honein MA, Rasmussen SA, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet 2009;374:451-8.
22. Wunsch H, Angus DC, Harrison DA, et al. Variation in critical care services across North America and Western Europe. Crit Care Med 2008;36:2787-93.
23. Interim guidance for infection control for care of patients with confirmed or suspected swine influenza A (H1N1) virus infection in a healthcare setting. Atlanta: Centers for Disease Control and Prevention. (Accessed October 19, 2009, at http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm.)
24. Li G, Yilmaz M, Kojicic M, et al. Outcome of critically ill patients with influenza virus infection. J Clin Virol 2009 August 19 (Epub ahead of print).