

Pandemic (H1N1) 2009 influenza (“swine flu”) in Australian and New Zealand intensive care

Steven A R Webb and Ian M Seppelt,
for the ANZIC Influenza Investigators

The influenza A virus undergoes periodic antigenic shifts leading to the emergence of new strains to which humanity has minimal immunity. These events are rare but, when they occur, can result in a pandemic.¹ Previous pandemics occurred in 1918 (caused by an H1N1 strain), 1957 (H2N2) and 1968 (H3N2), and resulted in substantial mortality. Another H1N1 pandemic (“swine flu”) began in 2009 and will be the first influenza pandemic to occur since intensive care became widely available.² The 2009 H1N1 pandemic is caused by a novel triple recombinant swine-origin influenza virus. Also termed pandemic (H1N1) 2009 influenza virus (H1N1 09), this was first identified in North America in April 2009.^{3,4} The virus has spread rapidly, and many intensivists in Australia and New Zealand have now cared for patients infected with H1N1 09 influenza.

Although the vast majority of infected individuals have a mild, self-limiting illness, in a small proportion of cases the infection is life-threatening. Three predominant syndromes are associated with life-threatening infection:

- acute viral pneumonitis with bilateral pulmonary infiltrates (“flu A”-associated acute respiratory distress syndrome [FLAAARDS]);
- secondary community-acquired bacterial pneumonia; and
- viral exacerbation of airflow limitation.

Of these, FLAAARDS — sometimes with associated multiple organ failure — is the most common syndrome and has the highest attributable mortality. Life-threatening infection appears to be more common in individuals with underlying comorbidities, including morbid obesity, type 2 diabetes mellitus, immunosuppression, malignancy, and chronic lung disease. Pregnant or postpartum women also appear to be at higher risk. Nevertheless, many patients with FLAAARDS are young and previously well.

It is not yet clear what the public health impact of H1N1 09 influenza will be. The total number of deaths, age distribution of those who die, and the impact of H1N1 09 influenza on ICUs may be quite different to what is seen as a consequence of seasonal influenza A. It has been estimated that in a “normal” year, about 3000 deaths occur in Australia due to influenza A.⁵ However, it is important to note that this is an estimate of unknown accuracy, based on modelling that imputes deaths as

being due to influenza A on the basis of the relationship between number of weekly laboratory confirmations of influenza A and number of weekly deaths. Two factors will ultimately determine the total mortality from H1N1 09 influenza: the attack rate (proportion of the population with symptomatic infection), and the case-fatality rate (proportion of patients with symptomatic infection who die). Predictions from the Australian Government are for an attack rate of 20% and a case-fatality rate of 0.14%, similar to that of seasonal flu.⁶ This implies about 6000 deaths in Australia due to H1N1 09. While the epidemic has not yet run its course, it now appears that both the attack rate and case-fatality rate will be substantially lower than this initial estimate. The availability of a vaccine in Australia in September or October is expected to minimise the attack rate.

A major difference between seasonal influenza A and H1N1 09 influenza is the age distribution of life-threatening cases and deaths. According to media reports, most deaths from H1N1 09 influenza are in young and middle-aged adults. In contrast, most deaths from seasonal influenza A occur in the elderly,⁷ and deaths of young people due to seasonal influenza are rare. In the United States, modelling indicates that the annual mortality from influenza A for individuals between the ages of 1 and 49 years is 0.2 per 100 000 person-years.⁷ If this were similar in Australia and New Zealand, it would translate to about 30 deaths per year in this age bracket. The true public health burden of H1N1 09 influenza should not be measured by the number of deaths but by the life-years lost.

The burden of ICU admissions caused by seasonal influenza A is not known. Some admissions due to community-acquired pneumonia and airflow limitation may be triggered by influenza A. Viral pneumonitis is a rare cause of ICU admission; about 100 cases are coded each year in Australia and New Zealand, presumably including some cases of influenza A (Graeme Hart, Adult Patient Database [APD], ANZICS Centre for Outcome and Resource Evaluation, Melbourne, VIC, personal communication). An important research objective will be to use APD data and existing modelling techniques for influenza A to estimate the burden of ICU admissions and resource

use that result from usual seasonal influenza. Unfortunately, this information has not been available to help plan ICU capacity for the current pandemic.

The impact of H1N1 09 influenza on ICUs has already been enormous and clearly different from that of seasonal influenza A, with about 25% of intensive care beds occupied by patients with confirmed or suspected H1N1 09 infection (NSW Health Intensive Care Taskforce, personal communication). At least until the time of writing, the intensive care system has coped adequately with the surge in patients requiring ventilation and, in some cases, extracorporeal membrane oxygenation (ECMO). By the beginning of August, over 400 intensive care admissions had been documented, including at least 30 patients who required ECMO.⁸

State health departments are now in the “protect” phase of the pandemic,⁶ where it is impossible to document the overall community incidence of H1N1 09 infection. Consequently, ICUs are “the canary in the coal mine”. It is only by documenting the severe cases requiring intensive care that it is possible to get an idea of the overall impact of this new disease. In Australia and New Zealand, we are in the unique position of having both a clearly defined total population and a well-coordinated intensive care community. It should be possible to collect data on every intensive care case and every death due to H1N1 09 influenza, to describe accurately the epidemiology of the disease and inform the northern hemisphere as they move into winter in late 2009.

The Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG), in collaboration with the Australasian Society for Infectious Diseases (ASID) CTG, has established an influenza registry to collect a minimum dataset on all patients admitted to an ICU since 1 June 2009 who have confirmed influenza A.⁸ This project is being administered by the Australian and New Zealand Intensive Care Research Centre (ANZIC-RC) based at Monash University. The goal of identifying every case is realistic, and will be of immense immediate public health importance, as well as future research interest. We have full cooperation from Australian state health departments, the federal Department of Health and Ageing and the New Zealand Ministry of Health. We encourage all Australian and New Zealand intensivists to contribute their cases to this registry. The data are provided in real-time to state health departments and will facilitate the early provision of resources necessary for ICUs to manage H1N1 09-related critical illness.

A great concern has been the potential for occupational acquisition of infection by staff who care for patients in the ICU. Fortunately, this appears to have been rare. It is unclear whether this reflects the widespread and effective use of

personal protective equipment (PPE) or indicates that the virus has low transmissibility within an ICU environment. Decisions about duration of patient isolation, the risks associated with cohorting of patients with suspected or confirmed infection (where isolation capacity has been exceeded), and the required duration of use of PPE by staff are being made with limited evidence, largely extrapolated from experience of seasonal influenza in ambulant patients.

Another challenge has been decision-making about the care of individual patients with a new disease with no established evidence base. There is no information to guide the dose and duration of antiviral agents, or on their enteral absorption and clearance by haemofiltration. There has been a trend towards increased dosing but only limited evidence to support this practice. The role of corticosteroids is similarly unclear.^{9,10} The Australian and New Zealand intensive care community must produce a set of clinical guidelines describing diagnosis, treatment, and infection control policies. Inevitably, such guidelines will not be evidence-based, but will represent the consensus of experienced clinicians who have cared for patients with H1N1 09 infection. These guidelines are needed quickly to be of value locally and for colleagues in the northern hemisphere as their winter flu season approaches.

Planning of the public health response to H1N1 09 influenza has been difficult because of rapid evolution of the pandemic and the limited information available. The timing of the outbreak was unfortunate for countries in the southern hemisphere, but it is our impression that consultation between governments, public health planners and intensivists occurred later than would have been ideal. This pandemic, which at present is of moderate severity,² provides an opportunity for intensivists to ensure that they become more integral in the planning response to future public health threats that will involve intensive care management.

The high standards of intensive care in Australia and New Zealand should minimise morbidity and mortality from H1N1 09 infection. The collection of comprehensive information on cases treated and their outcomes will, we hope, be of major assistance to the rest of the world, which is yet to fully face the impact of the pandemic.

Author details

Steven AR Webb, Senior Staff Specialist,¹ and Clinical Associate Professor²

Ian M Seppelt, Senior Staff Specialist^{3,4}

For the Australian and New Zealand Intensive Care (ANZIC) Influenza Investigators^{5,6}

¹ Department of Intensive Care, Royal Perth Hospital, Perth, WA.

² School of Population Health, University of Western Australia, Perth, WA.

EDITORIALS

3 Department of Intensive Care Medicine, Nepean Hospital, Sydney, NSW.

4 Sydney Medical School, University of Sydney, Sydney, NSW.

5 ANZICS Clinical Trials Group, Melbourne, VIC.

6 ANZIC Research Centre, Monash University, Melbourne, VIC.

Correspondence: sarwebb@cylleneuwa.edu.au

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