Epidemiology, clinical characteristics and resource implications of pandemic (H1N1) 2009 in intensive care units in Ireland

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ABSTRACT

Objective: To describe the incidence, clinical characteristics and outcomes of critically ill patients in Ireland with pandemic (H1N1) 2009 infection, and to provide a dynamic assessment of the burden of such cases on Irish intensive care units.

Design, setting and participants: Multicentre prospective observational study of all adult patients admitted to any of the 30 ICUs in the Republic of Ireland between 15 July 2009 and 30 May 2010.

Main outcome measures: Patient demographics, clinical characteristics and ICU mortality; ICU admissions, bed-days, bed occupancy rates and distribution.

Results: Seventy-seven adult patients with pandemic (H1N1) 2009 infection were admitted to 27 of 30 Irish ICUs. The median age was 43 years (IQR, 30–56 years); 67 patients (88%) were aged under 65; 39 (51%) were male. Sixty-two patients (82%) had comorbid conditions, including obesity (36%), respiratory disease (34%) and malignancy or immunosuppression (20%). Eight (11%) were pregnant, and 27 (36%) were smokers. Sixty-seven patients were mechanically ventilated, 24 (32%) required renal replacement therapy, 39 (51%) received vasopressors and four (5%) received extracorporeal membrane oxygenation. Of 14 patients (18%) who died in the ICU, two had no pre-existing comorbidities. The ICU admission rate of patients with pandemic (H1N1) 2009 infection was 22.5/million population. A total of 1882 ICU bed-days (557.5 bed-days/million adult population) were consumed, equating to a 3.9% bed occupancy rate, with a peak of 14.0% in October 2009. Median length of stay was 12 days (IQR, 7–34 days).

Conclusion: The 2009 influenza A (H1N1) pandemic was a significant burden on Irish ICUs, predominantly affecting the tertiary centres. The demographics and clinical characteristics were similar to those described in the southern hemisphere, suggesting such data may inform future resource planning for similar threats.

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In April 2009, Mexican health authorities announced the outbreak of a novel H1N1 swine influenza virus,[1] and a global outbreak quickly followed, leading the World Health Organization to declare a Level 6 pandemic warning by June 2009.[2] This was the first pandemic since the Hong Kong influenza pandemic of 1968,[3] and the first worldwide health crisis since the SARS (severe acute respiratory syndrome) epidemic of 2002–2003. Reports of critical illness caused by pandemic (H1N1) 2009 infection during winter 2009 in the southern hemisphere[4,5] were useful in estimating surge capacity needed during winter 2009 in Ireland. These reinforced the need for a robust dataset to identify populations at risk of severe disease, to determine public health priorities and to inform future planning. The Enhanced Intensive Care Unit Surveillance dataset[6] was used to record the population admitted to Irish intensive care units during the pandemic, the distribution of cases across the entire tertiary and regional network of ICUs, and outcome data. This was a live dataset, updated daily, designed to identify those most at risk and allow redirection of resources to areas of greatest need as and when appropriate. This report describes the epidemiological characteristics, clinical features and outcomes of all adult ICU patients with pandemic (H1N1) 2009 infection in Ireland, and the number of ICU admissions, number of ICU bed-days used and ICU bed occupancy rates.

Methods

Study design

A multicentre prospective observational study was carried out involving all of the 30 ICUs in the Republic of Ireland. There are 289 adult critical care beds in Ireland, of which 201 are equipped for mechanical ventilation. Eighteen of these are designated specialty beds and 27 were closed, leaving 156 general ICU beds available (source: *Review of adult critical care services in the Republic of Ireland* [unpublished prospectus report, January 2009]).

The study was undertaken as part of a national program of enhanced surveillance of pandemic (H1N1) 2009. Written informed consent was not necessary, as H1N1 influenza

is subject to statutory notification in Ireland.[7] The study captured data for adult patients admitted to an Irish ICU with confirmed or probable pandemic (H1N1) 2009 infection between 15 July 2009 and 30 May 2010. The diagnosis was confirmed using a real-time rapid test polymerase chain reaction (RT-PCR) H1 and H3 subtyping assay for seasonal human H1 and H3 strains. Testing took place at the National Virus Reference Laboratory, Dublin, Cork University Hospital and Galway University Hospitals.

Data management

Population data were provided by the Irish Central Statistics Office.[8] The dataset was devised by epidemiologists from the Health Protection Surveillance Centre (HPSC) working in collaboration with the Intensive Care Society of Ireland, the National Hospitals Office and the Office of Nursing Services (Health Service Executive). All hospitals with ICU capacity were enrolled in the study. Each hospital nominated a local coordinator to facilitate the exchange of information between its ICU and the HPSC. The data were reviewed centrally by a consultant intensivist coordinator, and any inconsistencies or queries were discussed with the local coordinator or treating clinicians as appropriate.

Data collection

Eligible patients included all adult patients with confirmed or probable pandemic (H1N1) 2009 infection admitted to Irish ICUs during the study period. Data were captured using a paper-based, two-part questionnaire at the time of admission and discharge. The admission questionnaire recorded standard demographic details, admission timelines and source, type and onset time of symptoms, and admission diagnoses. Severity of illness was assessed by the Sequential Organ Failure Assessment (SOFA)[9] score. Data relating to pre-existing comorbidities or predisposing conditions were collected. The discharge questionnaire recorded length of stay (LOS) in the ICU, clinical characteristics and disease course. Epidemiological characteristics, clinical features and ICU mortality were recorded for all patients. The number of ICU admissions, ICU LOS, total ICU bed-days used and bed occupancy rates were also recorded. Although the total number of admissions (including transfers between ICUs) was recorded, we looked at absolute patient numbers rather than admissions when analysing risk factors, in order to avoid duplication.

Analysis

Patients' demographic and clinical characteristics on admission to the ICU are described. Continuous variables are reported as median and interquartile range (IQR), and categorical data as proportions. Ninety-five per cent confidence intervals and *P* values are reported to reflect a two-tailed α level of 0.05. The mean of the SOFA scores on admission is presented.

Univariate analysis was used to study the effect of continuous variables on death, using the Student *t* test, Mann–Whitney *U* test or Kruskal–Wallis test as appropriate. The χ^2 test or Fisher exact test was used for categorical variables as appropriate. Multivariate analysis was performed using those variables that had a significant association with risk of death on univariate analysis ($P < 0.20$). Colinear variables were excluded from the analysis. Interaction between variables was assessed. The final model was built using a stepwise approach. The model was tested using receiver operating characteristic (ROC) analysis and calibrated using Windmeijer goodness-of-fit methodology. Linear regression was used to study the relationship between categorical variables and LOS. The natural logarithm of the LOS was used as the dependent variable. Analyses were conducted with Stata software version 9.0 (StataCorp LP, College Station, Tex, USA).

Results

Admissions

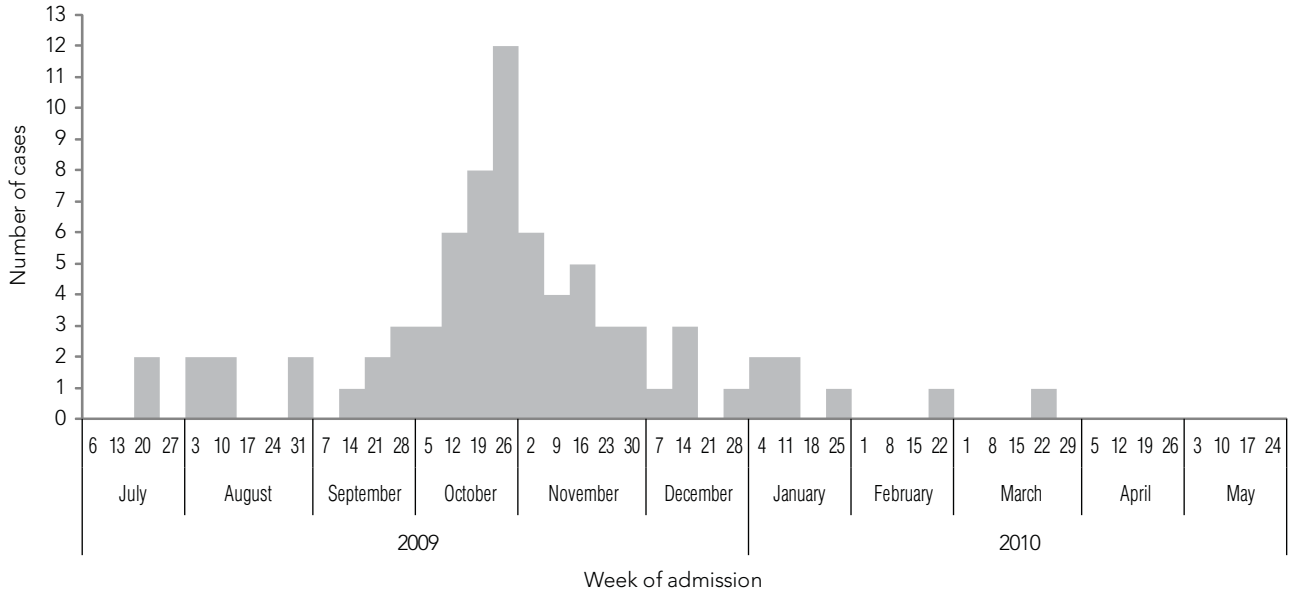
Seventy-seven critically ill patients with pandemic (H1N1) 2009 infection (76 confirmed and 1 probable — the probable case retained within the dataset after discussion between the central coordinator and treating clinicians) were admitted to 27 of 30 Irish ICUs during the study period. One patient stayed less than 12 hours and was omitted from the analysis. The first patient was admitted on 21 July 2009 and the last on 25 March 2010. Fifteen of the patients were transferred from regional to tertiary ICUs,* and three of these were returned to the referring ICU on completion of tertiary care. There were no readmissions to intensive care. Admission numbers are shown in Figure 1. The overall ICU admission rate was 22.5/million population. No patients were declined admission to the ICU for non-clinical reasons.

Bed occupancy and total ICU bed-days

ICU bed occupancy rates varied over the study period (Figure 2). In total, 1882 ICU bed-days were consumed by pandemic (H1N1) 2009. This equates to 3.9% of total ICU bed capacity over the study period. However, the impact varied by week and had a disproportionate impact on individual units. The overall peak occupancy rate (14.0%)

* Mater Misericordiae University Hospital, Dublin; St James's Hospital, Dublin; Beaumont Hospital, Dublin; St Vincent's University Hospital, Dublin; The Adelaide and Meath Hospital, Dublin; Cork University Hospital; Mid-Western Regional Hospital, Limerick; University College Hospital, Galway.

Figure 1. Number of patients with pandemic (H1N1) 2009 infection admitted to intensive care units in Ireland, by week of first ICU admission (*n* = 76)

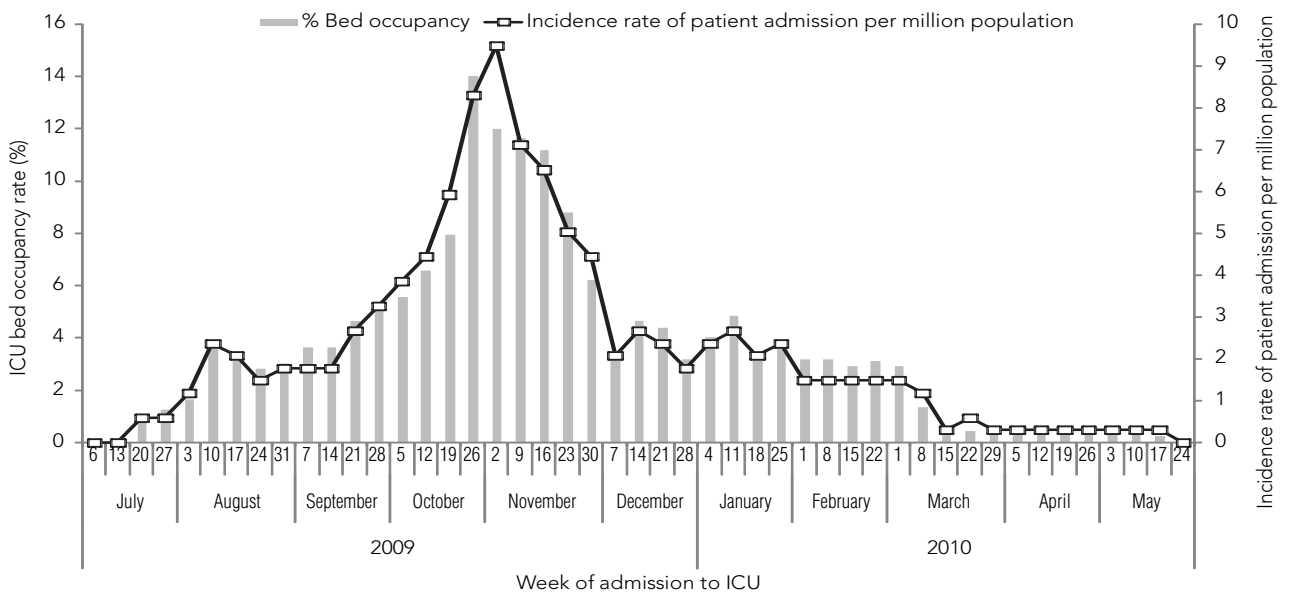


occurred during the week beginning 19 October 2009. During this week, the mean bed occupancy rate in tertiary centres was 22.7% (range, 6.0%–45.5%).

Patient characteristics

The median patient age was 43 years (range, 19–79; IQR, 30–56 years), and 39 patients (51%) were male (Table 1). The highest age-specific incidence (28.0/million population) was in patients aged 45–64 years (Figure 3). The mean SOFA score on admission was 5.9 (range, 0–15) (Figure 4). Comorbidities or predisposing conditions were present in 62 patients (82%). These included obesity (36%), smoking (36%), chronic obstructive pulmonary disease or asthma (34%), malignancy or immunosuppression (20%), preg-

Figure 2. Intensive care unit bed occupancy rates (%) and incidence rates of pandemic (H1N1) 2009 in patients admitted to ICUs in Ireland per million population, by week of admission (*n* = 76)



nancy (10%) and diabetes mellitus (8%) (Table 1). The incidence of these conditions in the general population is 8%, 29%, 17.7%, 1.2%, 1.4% and 5%, respectively.[10,11] Five of the eight pregnant patients had additional comorbidities.

Clinical course

Presenting symptoms included dyspnoea (59 patients [79%]), fever (53 patients [70%]), fatigue (54 patients [71%]) and gastrointestinal symptoms (35 patients [46%]). Admission sources were: inpatient medical ward (43 patients [56%]), emergency department (31 patients [41%]) and high-dependency unit (two patients [3%]). The median interval between onset of symptoms and hospital admission was 4 days (IQR, 2–6 days), and the median time from hospital ward to ICU admission was 3 days (IQR, 0–6 days). For the two patients admitted via the high-dependency unit, the corresponding intervals were 3 and 5 days, respectively.

Aspects of organ support, at admission and during ICU stay, are summarised in Table 1 and Table 2. At the time of ICU admission, 55 patients (72%) required mechanical ventilation and 8 (10%) required renal replacement therapy. Ultimately, 32% of patients required renal replacement therapy. Four patients (of which three were female) received extracorporeal membrane oxygenation (ECMO) — three in Ireland (for 14, 60 and 120 days, respectively) and one in Karolinska, Sweden (for 18 days). The mean age of ECMO patients was 30.5 years (range, 22–52 years). Their mean LOS in ICU before receiving ECMO was 17.3 days (range, 8–35 days). The mean PaO_2/FiO_2 ratio on commencement of ECMO was 6.6 kPa (range, 5–9 kPa), and the mean duration of ECMO was 53 days (range, 11–120 days). All four were weaned from ECMO, but one patient died on Day 8 after cessation of ECMO.

Length of stay and outcomes

The median LOS of all patients in the ICU was 12 days (IQR, 7–34 days). For patients who did not receive ECMO, the median LOS was 11 days (IQR, 7–30 days), and for those who did the median LOS was 96 days (IQR, 74–98 days). Non-pregnant women had a longer LOS in the ICU than men: 18 days (range, 10–36 days) versus 14 days (range, 5–38 days) ($P = 0.04$). Severely obese patients tended to have a longer LOS than non-obese patients (25 days [range, 8–32 days] v 10 days [range, 5–35 days]), although the difference was not statistically significant. Those with acute respiratory distress syndrome on admission were more likely to have a longer LOS. Sixty-two patients (82%) were discharged alive and 14 (18%) died in the ICU. Two of the patients who died had no pre-existing comorbidities.

Results of a univariate analysis of demographics and clinical characteristics of survivors and non-survivors are

Table 1. Univariate analysis: patient demographics, comorbidities and admission characteristics — comparison of survivors and non-survivors

	All cases ($n = 76$)	Survivors ($n = 62$)	Non-survivors ($n = 14$)	Odds ratio (95% CIs)	P
Demographics					
Median age in years (IQR)	43 (30–56)	39 (30–55)	54 (43–64)		0.04
Male sex, *n* (%)	39 (51%)	31(50%)	8 (57%)	1.33 (0.41–4.30)	0.85
Non-Irish, *n* (%)	8 (10%)	7 (11%)	1 (7%)	0.60 (0.07–5.35)	1
Ever smoker (%)	38/67 (57%)	32/54 (59%)	6/13 (46%)	0.59 (0.17–1.99)	0.58
Comorbidities/predisposing conditions, *n* (%)					
Obesity (BMI $\geqslant 35$ kg/m^2)	27 (36%)	22 (35%)	5 (36%)	1.01 (0.30–3.39)	1
Asthma or chronic respiratory disease	26 (34%)	18 (29%)	8 (57%)	3.26 (0.99–10.74)	0.10
Chronic heart disease	18 (24%)	15 (24%)	3 (21%)	0.85 (0.21–3.47)	1
Malignancy or immunosuppression	15 (20%)	9(14%)	6 (43%)	4.42 (1.24–15.77)	0.05
Pregnancy	8 (10%)	8 (14%)	0	na	na
Chronic renal disease	5 (7%)	3 (5%)	2 (14%)	3.28 (0.49–21.78)	0.45
Diabetes mellitus	6 (8%)	6 (10%)	0	na	na
Chronic neurological disease	3 (4%)	2 (3%)	1 (7%)	2.31 (0.19–27.39)	0.92
Chronic liver disease	2 (3%)	1 (2%)	1 (7%)	4.69 (0.28–79.96)	0.67
Haemoglobinopathy	1 (1%)	1 (2%)	0	na	na
SOFA score at admission to ICU					
Mean (range)*	5.9 (0–15)	5.2 (0–14)	8.5 (3–15)		
Organ support at admission to ICU					
Mechanical ventilation, *n* (%)	55 (72%)	42 (68%)	13 (93%)	6.19 (0.76–50.67)	0.10
Renal replacement, *n* (%)	8 (10%)	5 (8%)	3 (21%)	3.11 (0.65–14.95)	0.32

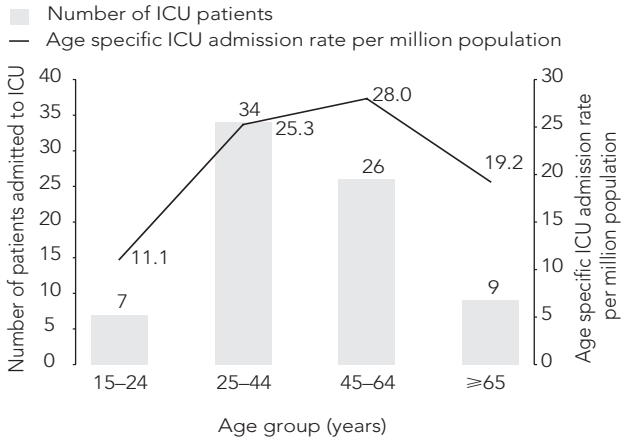
BMI = body mass index. IQR = interquartile range. na = not applicable. SOFA = Sequential Organ Failure Assessment. * Based on 75 of 76 patients.

shown in Table 1. On multivariate logistic regression analysis, variables independently associated with death were chronic respiratory disease and malignancy or immunosuppression (Table 3).

Discussion

The study identified 77 patients with pandemic (H1N1) 2009 infection admitted to Irish ICUs. Obesity, smoking and respiratory disease were the most common comorbidities. Chronic respiratory disease and malignancy or immunosuppression were independently associated with death. The ICU mortality rate was 18%. The ICU admission rate of patients with pandemic (H1N1) 2009 infection was 22.5/million population, with 1882 ICU bed-days consumed by the pandemic.

Figure 3. Number of patients admitted to the intensive care unit by age group, and age-specific ICU admission rates per million population



Accurate information is essential to describe the impact of an event such as pandemic influenza. It is important to quantify the morbidity and mortality associated with the event, to identify individuals and populations who are most at risk, and to ensure that measures adopted to protect health and wellbeing (including vaccination campaigns) are not only effective but are also implemented effectively. It is important to quantify use of health care resources, access to health care and health outcomes, in order to plan for such threats in the future. Surge capacity planning in Ireland was based on the European Centre for Disease Prevention and Control modelling of 16 September 2009,[12] and ICU expanded-capacity resource to meet a potential doubling of ICU care capacity extended into non-ICU areas. This was further informed by the Australian and New Zealand Intensive Care Society (ANZICS) Influenza Investigators report[4] and the evolving expertise with ECMO.[5,13]

Results from Ireland show many similarities to those of the ANZICS study. The overall bed occupancy over the period of our study was 557.5 bed-days/million population, compared with 350 bed-days/million reported from Australia and New Zealand, with Ireland having a maximum critical care bed resource of 46.2 beds per million Irish adults. Tertiary centres carried the burden of care, with 73 of 76 patients looked after in tertiary centres, and the

Figure 4. SOFA (Sequential Organ Failure Assessment) score at time of admission, with survivor and non-survivor breakdown

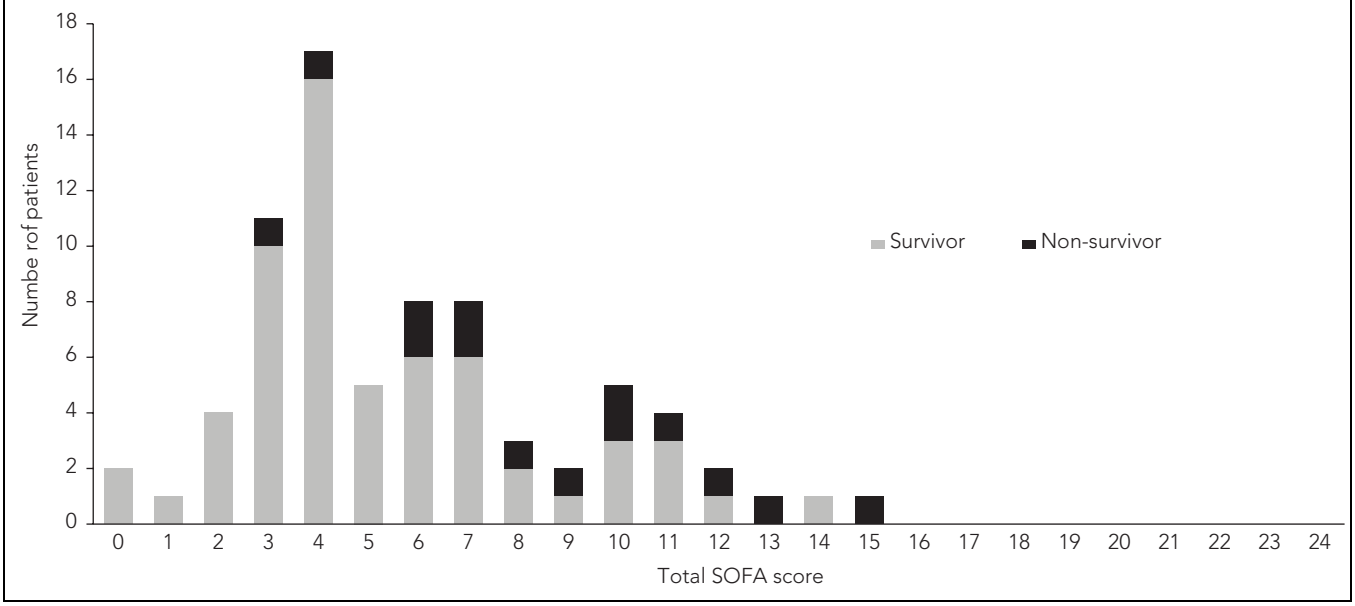


Table 2. Type, incidence and duration of organ support or disease process

Organ support or disease process	Incidence, n (%)	Median duration in days (IQR) [available data]
Mechanical ventilation	67 (88%)	
Non-invasive (total)	45 (59%)	3.5 (1–8) [n = 38/45]
Non-invasive only	17 (22%)	6 (3–9) [n = 13/17]
Invasive ventilation	50 (66%)	10 (5–23) [n = 46/50]
HFOV	17 (22%)	7 (4–11) [n = 76]
Conventional ventilation prior to HFOV	17 (100%)	10 (5–24) [n = 15/17]
Renal replacement therapy		
Intermittent HD	5 (7%)	15 (8–18) [n = 76]
Intermittent HD only	0	
CRRT	24 (32%)	10 (7–21) [n = 76]
Vasopressor support	39 (51%)	n/a
ECMO	4 (5%)	53 (mean) (range, 14–120)
ARDS	47 (62%)	NA
Secondary bacterial pneumonia	41 (54%)	n/a
Sepsis/MOF	38 (50%)	n/a

ARDS = acute respiratory distress syndrome. CRRT = continuous renal replacement therapy. ECMO = extracorporeal membrane oxygenation. HD = haemodialysis. HFOV = high-frequency oscillatory ventilation. IQR = interquartile range. MOF = multiorgan failure. n/a = not available (not defined in dataset). NA = not applicable.

Table 3. Multivariate analysis: factors associated with death in the intensive care unit

Patient characteristics/comorbid conditions	OR (95% CI)
Sex (male/female)	0.7 (0.1–3.2)
Immunocompromise or malignancy	4.7 (1.0–21.9)
Chronic respiratory disease or asthma	3.9 (0.9–16.5)

OR = odds ratio.

majority presenting directly to these centres. As a consequence, bed occupancy in the eight tertiary centres peaked at 46.4% (range, 12.5%–46.4%), with five centres having peak occupancy in excess of 30%. These results suggest that any extra resources may have been best directed mainly to tertiary centres, to meet evolving need.

The short period of hospitalisation prior to ICU referral is consistent with international experience, as was the presence of co-morbidities, particularly increased body mass index (BMI), asthma, and immunocompromised status.[4,14] Eight pregnant patients were admitted to the ICU, all of whom survived. Increased BMI, although a risk factor for severe disease, was not associated with increased mortality. The age demographic also mirrored experiences elsewhere,[4,14] with a disproportionate number of patients under 65 years of age requiring ICU admission. Similarly, duration of ICU stay and the proportion of patients requiring mechanical ventilation reflected the results of other published studies. The prevalence of acute kidney injury requiring dialysis was 32%, similar to the preliminary Swine Flu Triage (SwiFT) study data (25%),[15] but notably higher than in the ANZICS study (5%).[4]

ECMO, which is available in one centre in Ireland, was used in four patients. This represents an incidence of 1.2 ECMO cases per million adults, about half of the corresponding figure reported in the ANZICS study.[4] Of note, PaO_2/FiO_2 ratios on commencement of ECMO were similar in the two studies, but the median duration of mechanical ventilation prior to ECMO was longer in our study: 17.2 days (range, 8–35 days) versus 2 days (range, 1–5 days) in the ANZICS study. The duration of ECMO in two of the four Irish patients (60 and 120 days) was much longer than the median ECMO duration of 10 days (IQR, 7–15 days) in the ANZICS study. Although the numbers are small, the outcome data are comparable: 3/4 patients (75%) survived to ICU discharge compared with 48/68 patients (71%) in the ANZICS cohort.

Five patients with a SOFA score > 11 were admitted to intensive care, two of whom survived. Although these numbers are small, it raises significant questions about the role of triage protocols and their need for validation before use.[16,17] The Irish Council for Bioethics was asked to contribute to discussion on this issue at the time of planning for the pandemic. Given the difficulties in developing such a framework, regional critical care leaders supported a recommendation that all cases be assessed individually by the consultant intensivist on duty, with those intensivists informed by the triage concepts to date[18] and evolving clinical experience with influenza A (H1N1) in critically ill patients.[19]

Our study has limitations. The outcome data relate only to the time of ICU discharge, and as yet include no long-term follow-up. The dataset itself is somewhat limited. It is less detailed than other registries such as the European Society of Intensive Care Medicine Flu Registry dataset[20] and the Intensive Care National Audit and Research Centre SwiFT registry.[15] However, it was established to ensure the ability of all centres to fulfil the audit requirement, particu-

larly given the lack of administrative support in most Irish ICUs. The lack of agreed criteria for entry to renal replacement therapy is a limitation to further analysis of our data.

The similarity in demographics, admission rates and bed occupancy between our study and that of the ANZIC Influenza Investigators clearly highlights the usefulness of the ANZICS study to northern hemisphere countries in estimating surge capacity needed for our winter. The potential benefit of future studies in similar circumstances is also clear. Although the overall ICU bed occupancy in Ireland was 14.0% at its peak, with a bias towards tertiary ICUs, the system was not overwhelmed. However, the process of critical care emergency planning is now better informed and more robust.

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