# The Impact of Hospital and ICU Organizational Factors on Outcome in Critically III Patients: Results From the Extended Prevalence of Infection in Intensive Care Study\*

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### \*See also p. 695.

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Dr. Sakr conceived and designed the study. Drs. Sakr, Rhodes, Ferguson, Kleinpell, Pickkers, Kuiper, Lipman, and Vincent acquired the data. Drs. Sakr, Moreira, and Vincent analyzed and interpreted the data. Drs. Sakr and Moreira drafted the article. Drs. Sakr, Moreira, Rhodes, Ferguson, Kleinpell, Pickkers, Kuiper, Lipman, and Vincent critically revised the article for important intellectual content. Drs. Sakr and Vincent did statistical analysis. Dr. Vincent provided administrative, technical, or material support. Drs. Sakr and Vincent did study supervision.

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Dr. Rhodes consulted for Masimo and lectured for LiDCO and Edwards. Dr. Kleinpell is employed at Rush University Medical Center–Center for Clinical Research and Rush University College of Nursing, has reviewed medical legal cases and provided expert testimony, lectured (Agency for Healthcare Research & Policy grant), and received royalties from Springer Publishing (editor of book). Her institution received grant support from the Agency for Healthcare Research & Policy grant. Dr. Lipman served as

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a board member for Bayer European Society of Intensive Care Medicine Advisory Board; consulted for Merck Sharp Dohme (Aust) Pty, Pfizer Australia, and AstraZeneca; received grant support from AstraZeneca; and lectured for AstraZeneca and Pfizer Australia Pty. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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**Objective:** To investigate the impact of various facets of ICU organization on outcome in a large cohort of ICU patients from different geographic regions.

**Design:** International, multicenter, observational study.

**Setting:** All 1,265 ICUs in 75 countries that contributed to the 1-day point prevalence Extended Prevalence of Infection in Intensive Care study.

Patients: All adult patients present on a participating ICU on the study day.

Interventions: None.

Measurements and Main Results: The Extended Prevalence of Infection in Intensive Care study included data on 13,796 adult patients. Organizational characteristics of the participating hospitals and units varied across geographic areas. Participating North American hospitals had greater availability of microbiologic examination and more 24-hour emergency departments than did the participating European and Latin American units. Of the participating ICUs, 82.9% were closed format, with the lowest prevalence among North American units (62.7%) and the highest in ICUs in Oceania (92.6%). The proportion of participating ICUs with 24-hour intensivist coverage was lower in North America than in Latin America (86.8% vs 98.1%, p = 0.002). ICU volume was significantly lower in participating ICUs from Western Europe, Latin America, and Asia compared with North America. In multivariable logistic regression analysis, medical and mixed ICUs were independently associated with a greater risk of in-hospital death. A nurse:patient ratio of more than 1:1.5 on the study day was independently associated with a lower risk of in-hospital death.

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**Conclusions:** In this international large cohort of ICU patients, hospital and ICU characteristics varied worldwide. A high nurse:patient ratio was independently associated with a lower risk of in-hospital death. These exploratory data need to be confirmed in large prospective studies that consider additional country-specific ICU practice variations. (*Crit Care Med* 2015; 43:519–526) **Key Words:** 24-hour intensivist; international; mortality; nurse:patient ratio

utcomes following critical illness vary widely between ICUs (1, 2), in part because of differences in patient-related factors, including severity of illness, comorbid conditions, and disease-specific issues (2). Organizational issues can also impact on outcomes, including hospital and ICU volume (3–6), closed or open ICU format (7–9), availability of ICU specialists (10–12), and nurse staffing patterns (13–16). Identification of factors that may influence patient outcome at the institutional level is crucial for quality control purposes and benchmarking. In addition, variations in clinical practice and ICU organization may introduce a bias into the analysis of data from observational multicenter studies, if meticulous adjustment for these factors is not performed.

The possible impact of organizational issues on outcome from critical illness has been addressed in several observational studies (17, 18), studies using a before-and-after design (9, 10, 12) and/or including a limited number of ICUs at a national level (4, 7–9, 12). However, the generalizability of the data derived from single-center studies and those performed at national levels can be questioned. Furthermore, previous studies have just considered certain aspects of ICU organization and did not adjust for all possible confounders at the institutional level (4, 5, 7–9, 12, 19). As the focus of critical care worldwide is to improve care for critically ill patients, continued study of hospital and ICU organizational and structural factors to improve outcomes for patients is warranted.

The aim of this study was, therefore, to explore the impact of ICU organizational factors on outcomes in a large cohort of ICU patients from different geographic regions included in the international Extended Prevalence of Infection in Intensive Care (EPIC) study.

### **METHODS**

This was a post hoc analysis of data from the EPIC II study, an international 1-day point prevalence study, the primary aim of which was to provide an up-to-date global picture of the epidemiology of infection in ICU patients (2). All adult patients (> 18 yr old) present in participating ICUs between midnight on May 7, 2007, and midnight on May 8, 2007, were included in the study. The study was launched by open invitation, and participation in the study was entirely voluntary. Local ethics committees approved the study at each participating center and waived the need for consent due to the purely observational nature of the study.

A detailed description of the methodology used in the EPIC II study has been published elsewhere (2). Briefly, demographic, physiologic, bacteriological, and therapeutic data were collected from all patients present on a participating ICU on the study day. The Simplified Acute Physiology Score II (20) and Sequential Organ Failure Assessment (SOFA) (21) were calculated on the study day. Data were recorded using preprinted case report forms (CRF) and submitted via a dedicated website. Participants were asked to follow patients until hospital discharge or for 60 days (until July 9, 2007), and ICU and hospital outcomes were recorded.

# **Hospital and ICU Organizational Characteristics**

Prior to patient inclusion in the study, the participating centers reported a priori-defined data about their hospital and ICU structure and organization using an electronic CRF: 1) the type of hospital (university [including teaching and universityaffiliated hospitals] or nonuniversity); 2) hospital facilities, including bed capacity, the presence of 24 h/d microbiology and emergency departments, and the presence of an intermediate care unit; 3) ICU format (open [patients admitted to the ICU by any physician who continues to manage the patient during their ICU stay] or closed [patient care in the ICU is transferred to an intensivist, a physician with a qualification in critical care medicine according to local regulations]); 4) the reported number of admissions in the year preceding the study (2006); 5) the ICU (sub) specialty; and 6) the presence of 24 hr/d in-house intensivist coverage. The number of staffed ICU beds on the day of the study and the nurse:patient ratio at a predefined time point during the day (10:00-11:00 AM) and night (10:00–11:00 PM) of the study period were also recorded.

Hospital bed capacity was stratified into two categories according to the median capacity of the contributing centers. The ICUs were stratified into low volume (lowest quartile), medium volume (25–75% quartiles), and high volume (highest quartile) according to the reported number of admissions in the year preceding the study date (2006).

# **Definitions**

Infection was defined according to the definitions of the International Sepsis Forum (22) and adjudicated by the attending physician. Patients who had had surgery in the 4 weeks preceding admission were considered surgical admissions. Elective surgery was defined as surgery scheduled more than 24 hours in advance and emergency surgery as that scheduled within 24 hours of the operation. Trauma admissions were defined as ICU admissions directly related to, or occurring as a complication of, a traumatic event in the 30 days preceding admission. All other admissions were considered medical. The presence of the following comorbid conditions was noted: chronic obstructive pulmonary disease; metastatic cancer (metastases proven by surgery or imaging techniques); liver cirrhosis; heart failure (New York Heart Association III-IV); hematologic malignancy; HIV; chronic renal failure (need for chronic renal support or history of chronic renal insufficiency with a serum

TABLE 1. Characteristics of the Study Cohort (n = 13,796)

Characteristic	Count
Countries, n	75
Centers, n	1,265
Age, yr, mean ± sp	61±17
Male, n (%)	8,587 (62.3)
Severity scores on the study day, mean $\pm$ so	
Simplified Acute Physiology Score II	35±15
Sequential Organ Failure Assessment score	6±4
Type of admission, n (%)	
Medical	3,878 (28.2)
Surgical	
Elective	3,209 (23.3)
Emergency	5,298 (38.5)
Trauma	1,365 (9.9)
Source of admission, n (%)	
Emergency department/ambulance	4,010 (29.3)
Hospital floor	3,789 (27.7)
Operating room /recovery	3,510 (25.7)
Other hospital	1,921 (14.1)
Other	435 (3.2)
Comorbidities, n (%)	
Chronic obstructive pulmonary disease	2,303 (16.7)
Cancer	2,086 (15.1)
Heart failure (New York Heart Association III-IV)	1,342 (9.7)
Diabetes mellitus	1,336 (9.7)
Chronic renal failure	1,250 (9.1)
Immunosuppression	587 (4.3)
Cirrhosis	460 (3.3)
Hematologic cancer	282 (2)
HIV	96 (0.7)
Procedures on the day of inclusion, $n$ (%)	
Mechanical ventilation	7,694 (56.2)
Renal replacement therapy	1,247 (9.1)
ICU mortality, n (%)	2,370 (18.2)
Hospital mortality, n (%)	3,143 (24.2)
ICU length of stay, median (IQR)	9 (3-25)
Hospital length of stay, median (IQR)	20 (9-45)
Infection rate, n (%)	7,087 (51.4)
IOR = interquartile range	

IQR = interquartile range.

creatinine over 3.6 g/dL [300 µmol/L]); immunosuppression; and insulin-requiring diabetes mellitus.

For the purposes of this article, the world was divided into seven geographic regions: North America, Central and South America, Western Europe, Eastern Europe, Asia, Oceania, and Africa.

### **Outcome Variables**

The primary, a priori–defined outcome variable of this study was in-hospital mortality.

# **Statistical Analyses**

Statistical analyses were performed using SPSS Statistics 19 (IBM, Armonk, NY). Missing data on the type of hospital  $(n=13\ [1\%])$ , ICU specialty  $(n=25\ [2\%])$ , and ICU format  $(n=6\ [0.5\%])$  were completed after direct contact with the local investigators. For other missing data, we used a "mean substitution for subgroups" imputation approach (23). The Kolmogorov-Smirnov test was used, and histograms and normal-quantile plots were examined to verify if there were significant deviations from the normality assumption of continuous variables. Nonparametric tests of comparison were used for variables evaluated as not normally distributed. Difference testing between groups was performed using analysis of variance, Kruskal-Wallis, Student t test, Mann-Whitney test, chi-square test, and Fisher exact test, as appropriate. No adjustment was made for multiple comparisons (24).

A multilevel logistic regression model was used to explore the association between organizational factors and hospital mortality. A three-level model was considered with country as the highest (third) level, hospitals within the country as the second level, and patients within the hospital as the first level. Explanatory variables included the following:

- Patient level: age, sex, comorbidities, infection, and SOFA score
- Hospital level: type of ICU (closed vs open, university vs nonuniversity, and ICU speciality); number of ICU and hospital beds; nurse:patient ratio on the study day; presence of 24 hr/d in-house intensivist coverage; the presence of emergency and microbiology departments 24 hr/d; and the presence of an intermediate care unit
- Country level: gross domestic product (percentage of gross domestic product spent on healthcare generated using the World Health Organization Statistical Information System and based on data from 2006)

Bivariate correlations among variables were calculated to check for potential multicollinearity (25). All absolute values for Pearson correlations were less than 0.25 except that between the ICU volume and staffed ICU beds, which was 0.683; only ICU volume was considered in the analysis. Data are presented as mean  $\pm$  <sub>SD</sub>, median value (25th–75th interquartile ranges [IQRs]), number (%), or odds ratios (OR) (95% CI) as appropriate. All statistics were two-tailed, and a *p* value of less than 0.05 was considered to be statistically significant.

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TABLE 2. ICU and Hospital Organizational Issues in the Various Geographic Areas

Variable Variable	Total	North America	Africa
variable	IOLAI	NOTHI America	AIIICa
Type of hospital, <i>n</i> (%)			
University/academic	756 (59.8)	64 (77.1)	12 (70.6)
Nonuniversity	509 (40.2)	19 (22.9)	5 (29.4)
Hospital facilities, n (%)			
Microbiology (24 hr/d)	903 (71.4)	75 (90.4)	14 (82.4)
Emergency department (24 hr/d)	1,216 (96.1)	83 (100)	15 (88.2)ª
Intermediate care unit, n (%)	394 (31.1)	20 (24.1)	10 (58.8)ª
Hospital bed capacity, median (IQR)	485 (246-830)	520 (460-768)	470 (200–800)
Type of ICU, n (%)			
Closed	1,049 (82.9)	52 (62.7)	14 (82.4) <sup>a</sup>
Open	216 (17.1)	31 (37.4)	3 (17.7)
Staffed ICU beds, median (IQR)	10 (7-14)	14 (10-20)	8 (5-12)ª
ICU volume, admissions per year, median (IQR)	684 (412-1,078)	977 (684-1,431)	652 (412-1,131)ª
ICU specialty			
Surgical	238 (18.8)	28 (33.7)	4 (23.5)
Medical	132 (10.4)	24 (28.9)	2 (11.8)
Mixed	815 (64.4)	24 (29.9)	10 (58.8)
Others	80 (6.3)	7 (8.4)	1 (5.9)
In-house intensivist 24 hr/d	1,189 (94.0)	72 (86.8)	15 (88.2)
No. of patients per nurse, median (IQR)			
10:00-11:00 AM	1.5 (1.2)	1.5 (1.2-1.8)	1.6 (1.2)
10:00-11:00 PM	1.8 (1.4-2.5)	1.6 (1.2-1.5)	1.4 (1-2.5)
Collective	1.6 (1.05-2.2)	1.5 (1.2-1.8)	1.4 (0.8-2.0)

IQR = interquartile range.

# **RESULTS**

### **Characteristics of the Total Study Group**

Overall 1,265 ICUs contributed to the EPIC II study in 75 countries: 667 ICUs in Western Europe, 210 in Central and South America, 137 in Asia, 97 in Eastern Europe, 83 in North America, 54 in Oceania, and 17 in Africa (for a list of participating ICUs, see the **Appendix**, Supplemental Digital Content 1, http://links.lww.com/CCM/B131). On the study day, 14,414 patients were present in one of the participating ICUs; 13,796 were more than 18 years old, and their demographic characteristics are presented in **Table 1**. Sixty-two percent of the patients were male, 62% were surgical admissions, and 52% of the patients had at least one comorbidity. The overall ICU and hospital mortality rates were 18.2% and 24.2%, respectively, and the median ICU and hospital lengths of stay (LOS) were 9 days (3–25 d) and 20 days (9–45 d), respectively.

# **Hospital and ICU Organizational Characteristics**

The hospital and ICU characteristics varied across the different geographic areas (Table 2). Almost 60% of the participating centers were university hospitals. Participating North American ICUs were more likely to have 24-hour microbiology availability than were participating European and Latin American ICUs, and more likely to have a 24-hour emergency department than were participating African and Eastern European ICUs (Table 2). In contrast, the participating North American centers were less likely to have an intermediate care unit (24.1%). The median hospital capacity was 485 beds (IQR, 246-830), and the median number of staffed ICU beds on the study day was 10 (IQR, 7-14). Hospital bed capacity was similar in participating Western European and North American centers. Participating centers in Asia and Eastern Europe had higher hospital bed capacity compared with North America, whereas participating centers in Latin America and Oceania had lower bed capacity. Of the participating ICUs, 82.9% were closed

<sup>&</sup>lt;sup>a</sup>p < 0.05% compared with North America.

Asia	Eastern Europe	Latin America	Oceania	Western Europe
76 (55.5) <sup>a</sup>	73 (75.3)	117 (55.7) <sup>a</sup>	43 (79.3)	371 (55.6) <sup>a</sup>
61 (44.5)	24 (24.7)	93 (44.3)	11 (20.4)	296 (44.4)
105 (76.6) <sup>a</sup>	44 (45.4) <sup>a</sup>	153 (72.9) <sup>a</sup>	51 (94.4)	461 (69.1) <sup>a</sup>
137 (100)	89 (91.8) <sup>a</sup>	203 (96.7)	51 (94.4) <sup>a</sup>	638 (95.7)
48 (35)	30 (30.9)	74 (35.2)	23 (42.6) <sup>a</sup>	189 (28.3)
650 (180-1,000)ª	563 (250-1,200)ª	199 (93–309)ª	425 (300-551) <sup>a</sup>	550 (320-950)
93 (67.9)	84 (86.6) <sup>a</sup>	165 (78.6) <sup>a</sup>	50 (92.6) <sup>a</sup>	591 (88.6)ª
44 (32.1)	13 (13.4)	45 (21.4)	4 (7.4)	76 (11.4)
12 (7-17)ª	10 (7-13) <sup>a</sup>	10 (7-14) <sup>a</sup>	10 (7-14) <sup>a</sup>	10 (7-14)ª
638 (400-1,074)ª	574 (328-1,196)ª	510 (348-813)ª	944 (736–1,227)	695 (423-1,080)ª
11 (8.0) <sup>a</sup>	26 (26.8)	15 (7.1) <sup>a</sup>	5 (9.3) <sup>a</sup>	149 (22.3)ª
14 (10.2)	19 (19.6)	13 (6.2)	0 (0.0)	60 (9.0)
104 (75.9)	40 (41.2)	176 (83.8)	46 (85.2)	415 (62.2)
8 (5.8)	12 (12.4)	6 (2.9)	3 (5.6)	43 (6.4)
131 (95.6)ª	94 (96.9) <sup>a</sup>	206 (98.1)ª	44 (81.5)	627 (94.0)ª
1 (0.7-1.6) <sup>a</sup>	1.3 (0.8–1.8)	1.7 (1-2.8)	1 (0.8-1.3) <sup>a</sup>	1.6 (1.1-2)
1.3 (0.9-2)	1.6 (1-2.3)	2 (1.1-3.2) <sup>a</sup>	1.1 (0.9-1.3) <sup>a</sup>	2 (1.3-2.7) <sup>a</sup>
1.1 (0.7-1.6) <sup>a</sup>	1.3 (0.8–2.0)	1.8 (1.0-2.6) <sup>a</sup>	1.1 (0.8-1.4) <sup>a</sup>	1.8 (1.2-2.3) <sup>a</sup>

units with the lowest prevalence in North America (62.7%). The highest proportions of closed ICUs were observed in Oceania (92.6%) and Western Europe (88.6%). The median nurse:patient ratio ranged between 1:1.1 (Oceania and Asia) and 1:1.8 (Latin America and Western Europe) and was consistently lower at nighttime than on day shifts. ICU volume was significantly lower in participating ICUs in Africa, Eastern Europe, Western Europe, Latin America, and Asia compared with North America.

# **ICU** and Hospital Mortality

In a univariable logistic regression analysis with hospital outcome as the dependent variable, admission to a university/ academic center, the presence of a 24 hr/d emergency department, an open ICU format, and a medium/large ICU volume were associated with a lower risk of in-hospital death (**Table 3**). Medical and mixed ICUs were associated with a higher risk of in-hospital death than surgical ICUs. In multivariable

logistic regression analysis, medical and mixed ICUs remained associated with a higher risk of in-hospital death. A nurse:patient ratio of more than 1:1.5 was independently associated with a lower risk of in-hospital death, and availability of an in-house intensivist  $24\,\text{h/d}$  was associated with a trend toward a reduced risk of in-hospital death (OR, 0.69; 95% CI, 0.47–1.01; p=0.054).

# DISCUSSION

This worldwide prevalence study shows that ICU characteristics vary considerably among the participating ICUs from the different regions of the world. Within our study sample, admission to a medical or mixed ICU was associated with an increased risk of death compared with admission to a surgical unit after correcting for multiple potentially confounding variables, and a nurse:patient ratio greater than 1:1.5 on the study day was independently associated with a lower risk of in-hospital death.

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TABLE 3. Summary of Univariable and Multivariable Analyses With Hospital Mortality as the Dependent Variable

Hospital facilities           Microbiology 24 hr/d         0.91 (0.83−1)         0.056         0.89 (0.75−1.06)         0.15           Emergency department 24 hr/d         0.76 (0.61−0.95)         0.015         1.01 (0.7−1.46)         0.96           Intermediate care unit         0.98 (0.89−1.06)         0.566         1.02 (0.87−1.19)         0.84           Hospital bed capacity         Seference category         NA         Reference category         NA           > 485         0.95 (0.87−1.03)         0.174         1.15 (0.88−1.50)         0.30           Open vs closed ICU         0.84 (0.76−0.94)         0.001         0.99 (0.81−1.21)         0.91           ICU specialty         Surgical         Reference category         NA         Reference category         NA           Medical         2.48 (2.2 −2.8)         < 0.001         1.76 (1.47−2.12)         < 0.00           Mixed         2.31 (2.05−2.6)         < 0.001         1.54 (1.30−1.83)         < 0.00           Nurse:patient ratio*         Seference category         NA         Reference category         NA           1:1.5−1:1.99         0.97 (0.88−1.08)         0.600         0.84 (0.70−1.01)         0.06           1:1-1:1.49         1.08 (0.97−1.20)         0.166         0.71 (0.57−0.87)		Univariable Analysis		Multivariable Analysis <sup>a</sup>	Multivariable Analysis <sup>a</sup>	
Hospital facilities           Microbiology 24 hr/d         0.91 (0.83−1)         0.056         0.89 (0.75−1.06)         0.15           Emergency department 24 hr/d         0.76 (0.61−0.95)         0.015         1.01 (0.7−1.46)         0.96           Intermediate care unit         0.98 (0.89−1.06)         0.566         1.02 (0.87−1.19)         0.84           Hospital bed capacity         Seference category         NA         Reference category         NA           > 485         0.95 (0.87−1.03)         0.174         1.15 (0.88−1.50)         0.30           Open vs closed ICU         0.84 (0.76−0.94)         0.001         0.99 (0.81−1.21)         0.91           ICU specialty         Surgical         Reference category         NA         Reference category         NA           Medical         2.48 (2.2 −2.8)         < 0.001         1.76 (1.47−2.12)         < 0.00           Mixed         2.31 (2.05−2.6)         < 0.001         1.54 (1.30−1.83)         < 0.00           Nurse:patient ratio*         < 1:2         Reference category         NA         Reference category         NA           1:1.5−1:1.99         0.97 (0.88−1.08)         0.600         0.84 (0.70−1.01)         0.06           1:1-1:1.49         1.08 (0.97−1.20)         0.166	Variable	OR (95% CI)	p	OR (95% CI)	p	
Microbiology 24 hr/d         0.91 (0.83-1)         0.056         0.89 (0.75-1.06)         0.15           Emergency department 24 hr/d         0.76 (0.61-0.95)         0.015         1.01 (0.7-1.46)         0.96           Intermediate care unit         0.98 (0.89-1.06)         0.566         1.02 (0.87-1.19)         0.84           Hospital bed capacity         Separate         Separate         NA         Reference category         NA           ≥ 485         Reference category         NA         1.15 (0.88-1.50)         0.36           Open vs closed ICU         0.84 (0.76-0.94)         0.001         0.99 (0.81-1.21)         0.91           ICU specialty         Surgical         Reference category         NA         Reference category         NA           Medical         2.48 (2.2 - 2.8)         < 0.001	University/academic vs nonuniversity	0.91 (0.84-0.99)	0.029	1.19 (0.94–1.50)	0.146	
Emergency department 24hr/d       0.76 (0.61-0.95)       0.015       1.01 (0.7-1.46)       0.98         Intermediate care unit       0.98 (0.89-1.06)       0.566       1.02 (0.87-1.19)       0.84         Hospital bed capacity       Value	Hospital facilities					
Intermediate care unit         0.98 (0.89−1.06)         0.566         1.02 (0.87−1.19)         0.84           Hospital bed capacity         September 2485         Reference category         NA         Reference category         NA           > 485         0.95 (0.87−1.03)         0.174         1.15 (0.88−1.50)         0.30           Open vs closed ICU         0.84 (0.76−0.94)         0.001         0.99 (0.81−1.21)         0.91           ICU specialty         Surgical         Reference category         NA         Reference category         NA           Medical         2.48 (2.2 −2.8)         < 0.001	Microbiology 24 hr/d	0.91 (0.83-1)	0.056	0.89 (0.75-1.06)	0.192	
Hospital bed capacity  ≤ 485 Reference category NA Reference category NA  > 485 0.95 (0.87-1.03) 0.174 1.15 (0.88-1.50) 0.36  Open vs closed ICU 0.84 (0.76-0.94) 0.001 0.99 (0.81-1.21) 0.91  ICU specialty  Surgical Reference category NA Reference category NA  Medical 2.48 (2.2 - 2.8) < 0.001 1.76 (1.47-2.12) < 0.000  Mixed 2.31 (2.05-2.6) < 0.001 1.54 (1.30-1.83) < 0.000  Nurse:patient ratio <sup>6</sup> < 1:2 Reference category NA Reference category NA  1:1.5-1:1.99 0.97 (0.88-1.08) 0.600 0.84 (0.70-1.01) 0.060  1:1-1:1.49 1.08 (0.97-1.20) 0.166 0.71 (0.57-0.87) 0.060  > 1:1 1.08 (0.94-1.24) 0.296 0.69 (0.53-0.90) < 0.000  ICU volume  ≤ 412 Reference category NA Reference category NA  413-1,078 0.81 (0.72-0.91) < 0.001 1.01 (0.83-1.22) 0.950	Emergency department 24 hr/d	0.76 (0.61-0.95)	0.015	1.01 (0.7-1.46)	0.961	
≤ 485       Reference category       NA       Reference category       NA         > 485       0.95 (0.87−1.03)       0.174       1.15 (0.88−1.50)       0.30         Open vs closed ICU       0.84 (0.76−0.94)       0.001       0.99 (0.81−1.21)       0.91         ICU specialty       Surgical       Reference category       NA       Reference category       NA         Medical       2.48 (2.2 −2.8)       < 0.001	Intermediate care unit	0.98 (0.89-1.06)	0.566	1.02 (0.87-1.19)	0.848	
> 485       0.95 (0.87-1.03)       0.174       1.15 (0.88-1.50)       0.30         Open vs closed ICU       0.84 (0.76-0.94)       0.001       0.99 (0.81-1.21)       0.91         ICU specialty       Surgical       Reference category       NA       Reference category       NA         Medical       2.48 (2.2 - 2.8)       < 0.001	Hospital bed capacity					
Open vs closed ICU         0.84 (0.76−0.94)         0.001         0.99 (0.81−1.21)         0.91           ICU specialty         Surgical         Reference category         NA         Reference category         NA           Medical         2.48 (2.2 −2.8)         < 0.001	≤ 485	Reference category	NA	Reference category	NA	
ICU specialty         Surgical       Reference category       NA       Reference category       NA         Medical       2.48 (2.2 −2.8)       < 0.001	> 485	0.95 (0.87-1.03)	0.174	1.15 (0.88-1.50)	0.309	
Surgical       Reference category       NA       Reference category       NA         Medical $2.48 (2.2 - 2.8)$ < 0.001	Open vs closed ICU	0.84 (0.76-0.94)	0.001	0.99 (0.81-1.21)	0.916	
Medical $2.48$ ( $2.2 - 2.8$ )       < 0.001 $1.76$ ( $1.47 - 2.12$ )       < 0.001         Mixed $2.31$ ( $2.05 - 2.6$ )       < 0.001 $1.54$ ( $1.30 - 1.83$ )       < 0.001         Nurse:patient ratiob       Value	ICU specialty					
Mixed       2.31 (2.05-2.6)       < 0.001       1.54 (1.30-1.83)       < 0.001         Nurse:patient ratiob         1.22       Reference category       NA       Reference category       NA         1:1.5-1:1.99       0.97 (0.88-1.08)       0.600       0.84 (0.70-1.01)       0.060         1:1-1:1.49       1.08 (0.97-1.20)       0.166       0.71 (0.57-0.87)       0.00         > 1:1       1.08 (0.94-1.24)       0.296       0.69 (0.53-0.90)       < 0.00	Surgical	Reference category	NA	Reference category	NA	
Nurse:patient ratiob       Reference category       NA       Reference category       NA         1:1.5−1:1.99       0.97 (0.88−1.08)       0.600       0.84 (0.70−1.01)       0.06         1:1−1:1.49       1.08 (0.97−1.20)       0.166       0.71 (0.57−0.87)       0.00         > 1:1       1.08 (0.94−1.24)       0.296       0.69 (0.53−0.90)       < 0.00	Medical	2.48 (2.2 -2.8)	< 0.001	1.76 (1.47-2.12)	< 0.001	
< 1:2	Mixed	2.31 (2.05-2.6)	< 0.001	1.54 (1.30-1.83)	< 0.001	
1:1.5-1:1.99 $0.97 (0.88-1.08)$ $0.600$ $0.84 (0.70-1.01)$ $0.006$ 1:1-1:1.49 $1.08 (0.97-1.20)$ $0.166$ $0.71 (0.57-0.87)$ $0.006$ > 1:1 $1.08 (0.94-1.24)$ $0.296$ $0.69 (0.53-0.90)$ $< 0.006$ ICU volume $\leq 412$ Reference category       NA       Reference category       NA $413-1,078$ $0.81 (0.72-0.91)$ $< 0.001$ $1.01 (0.83-1.22)$ $0.98$	Nurse:patient ratio <sup>b</sup>					
1:1-1:1.49       1.08 (0.97-1.20)       0.166       0.71 (0.57-0.87)       0.00         > 1:1       1.08 (0.94-1.24)       0.296       0.69 (0.53-0.90)       < 0.00	< 1:2	Reference category	NA	Reference category	NA	
> 1:1       1.08 (0.94−1.24)       0.296       0.69 (0.53−0.90)       < 0.001         ICU volume       ≤ 412       Reference category       NA       Reference category       NA         413−1,078       0.81 (0.72−0.91)       < 0.001	1:1.5-1:1.99	0.97 (0.88-1.08)	0.600	0.84 (0.70-1.01)	0.067	
ICU volume  ≤ 412 Reference category NA Reference category NA 413-1,078 0.81 (0.72-0.91) < 0.001 1.01 (0.83-1.22) 0.95	1:1-1:1.49	1.08 (0.97-1.20)	0.166	0.71 (0.57-0.87)	0.001	
≤ 412       Reference category       NA       Reference category       NA         413-1,078       0.81 (0.72-0.91)       < 0.001	> 1:1	1.08 (0.94-1.24)	0.296	0.69 (0.53-0.90)	< 0.001	
413-1,078 0.81 (0.72-0.91) < 0.001 1.01 (0.83-1.22) 0.95	ICU volume					
	≤ 412	Reference category	NA	Reference category	NA	
	413-1,078	0.81 (0.72-0.91)	< 0.001	1.01 (0.83-1.22)	0.955	
> 1,078 0.59 (0.52-0.67) < 0.001 0.94 (0.75-1.18) 0.61	> 1,078	0.59 (0.52-0.67)	< 0.001	0.94 (0.75-1.18)	0.611	
In-house intensivist 24 hr/d 1.15 (0.94–1.4) 0.188 0.69 (0.47–1.01) 0.05	In-house intensivist 24 hr/d	1.15 (0.94–1.4)	0.188	0.69 (0.47-1.01)	0.054	

OR = odds ratio, NA = not applicable.

Although admission to a high-volume ICU was associated with a lower risk of in-hospital death in univariable analysis, these differences were not retained after adjustment for possible confounders. Previous studies have suggested that high-volume ICUs may be independently associated with a lower risk of in-hospital death (3–6). However, in a recent literature review, Abbenbroek et al (26) reported that the association of high-volume ICUs with improved outcomes was not consistent across all diagnoses and there appeared to be a high-volume threshold above which any mortality benefit was lost (26). A potential bias when interpreting this relationship is that physicians (and hospitals) achieving better outcomes receive more referrals or have differential admission thresholds and thus acquire larger volumes (selective referral) (27, 28).

We observed a stepwise decrease in the risk of in-hospital death related to increasing nurse:patient ratios on the study day. The provision of adequate quality of care conceptually requires sufficient numbers of nursing staff who can spend more time with each patient. It is widely acknowledged by critical care nursing organizations worldwide that staffing and workforce issues are important to ICU patient outcomes (29). Time constraints related to a reduced nurse:patient ratio may increase the likelihood of mistakes by creating a stressful environment with distractions and interruptions that adversely affect quality of care (14). Although several studies have previously reported the correlation between adequate numbers of nursing staff and outcome from critical illness, they were limited by their retrospective design (14, 19, 30) and were restricted to a specific geographic area. Nurse staffing practices vary considerably

<sup>&</sup>lt;sup>a</sup>Adjusted for geographic region, Sequential Organ Failure Assessment score, age, sex, and comorbidities.

<sup>&</sup>lt;sup>b</sup>For the 24-hour study day.

across countries, depending on local regulations, nurse availability and roles, but also the presence, notably in the United States, of respiratory therapists who assist in the management of ventilated patients (31). Nonetheless, in a meta-analysis by Kane et al (16), high nurse staffing numbers were associated with lower hospital-related mortality in ICUs. Likewise, a recent review of the literature (13) showed that reduced numbers of nurses were associated with adverse outcomes in ICU patients, including increased risk of infection and respiratory failure, unplanned extubation, greater 30-day mortality, and higher risk of decubitus ulcers. Finally, in a recent survey of 69 U.S. ICUs, ICUs with a lower bed-to-nurse ratio had lower annual mortality rates after adjusting for disease severity and other potential process and organizational confounders (1.8% lower when the ratio decreased from 2:1 to 1.5:1 [95% CI, 0.25-3.4%]) (32). As the nursing workforce represents the largest groups of caregivers in all healthcare settings, including the ICU, determining the optimal nurse:patient ratios to promote best outcomes for critically ill patients remains a priority.

The availability of a 24 hr/d in-house intensivist in our study was associated with a trend to a decreased risk of in-hospital death. Several single-center studies have reported that changing from on-demand to mandatory 24 hr/d critical care specialist presence may reduce nonadherence to evidence-based care processes (12) and the rate of complications (12) and may shorten ICU (10) and hospital (12) LOS and total hospital cost estimates (10). These studies (10, 12) were limited, however, by the before-and-after study design and the relatively small sample size. In a meta-analysis by Pronovost et al (11), highintensity intensivist staffing was associated with lower ICU and hospital mortality rates and reduced ICU and hospital LOS. In a recent study by Wallace et al (33), nighttime intensivist staffing was associated with a reduction in risk-adjusted inhospital mortality in ICUs with low-intensity daytime staffing. However, among ICUs with high-intensity daytime staffing, nighttime intensivist staffing conferred no benefit with respect to risk-adjusted in-hospital mortality. Nonetheless, our data do not allow direct comparison with this study (33) as we did not collect data on the intensity and day versus nighttime intensivist coverage.

After adjustment for confounders, there was no correlation between admission to university/academic centers and outcome. Teaching hospitals have been shown to achieve better-quality care than nonteaching hospitals (34, 35), and several studies have reported lower risk-adjusted mortality in major teaching hospitals compared with minor teaching or nonteaching hospitals (36-38). However, these observations were not confirmed in a systematic review (39). Nevertheless, possible differences for specific diseases cannot be excluded. Polanczyk et al (40) found that major teaching hospital status was an important determinant of outcomes in patients hospitalized with myocardial infarction, heart failure, or stroke. Likewise, in a large cohort of 114,411 patients with acute myocardial infarction, admission to a teaching hospital was associated with better quality of care and lower mortality (37).

ICU format also did not influence the adjusted risk of in-hospital death. This observation is in apparent contrast to the results of several previous studies (7–9, 41, 42) in which a closed ICU format was associated with a more favorable outcome than an open format, although the survey by Checkley et al (32) of 69 U.S. ICUs also reported that closed ICU status was not associated with lower annual ICU mortality. In closed ICUs, specifically trained and dedicated intensive care physicians are responsible for patient management decisions, potentially making it easier to maintain a coherent management strategy and provide appropriate and timely responses to complications (9). Our data should be interpreted with caution because the vast majority of the ICUs in our study (83%) were closed ICUs, and the relatively small number of open ICUs may not have been sufficient to demonstrate possible differences in outcome according to ICU format.

Our study has several advantages and limitations. An obvious strength is the international nature and the large number of contributing ICUs worldwide. However, the voluntary nature of participation in the study may have introduced a degree of selection bias and limits the representativeness of the data across countries and geographic regions. We did not use any prespecified sampling strategy to provide accurate estimates of the epidemiology of the organizational factors in our study. Descriptive comparisons between geographic regions should, therefore, be interpreted with some caution. Similarly, we are unable to confirm that the patients present on each ICU on the study day were representative of the type of patient generally admitted to that ICU. Nevertheless, the apparent differences in practice patterns identified from our data after adjustment for multiple potentially confounding factors can be used to explore independent influences of patient and management factors on epidemiology and outcome. Another limitation relates to the 1-day point prevalence study design, such that the collected severity scores relate to patients at different periods in the course of their disease. Finally, although we adjusted for a large number of important variables related to patient case-mix and organizational issues at the hospital and ICU level, the multivariable analysis may not have taken into account other unmeasured factors, such as adherence to evidence-based medicine guidelines, quality of care, differences in nurse staffing ratios based on countryspecific practices, levels of staff training and expertise, and disease-specific outcomes.

### CONCLUSIONS

In this large international cohort of ICU patients, hospital and ICU characteristics varied worldwide and nurse:patient ratios greater than 1:1.5 were independently associated with a lower risk of in-hospital death. Because of limitations associated with the potential lack of representativeness of our patients within hospitals and countries, these data must be considered as exploratory and need to be confirmed in large prospective studies that consider additional country-specific ICU practice variations.

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