


ORIGINAL WORK



# Global Survey of Outcomes of Neurocritical Care Patients: Analysis of the PRINCE Study Part 2

Chethan P. Venkatasubba Rao<sup>1†</sup>, Jose I. Suarez<sup>2\*</sup> , Renee H. Martin<sup>3</sup>, Colleen Bauza<sup>4</sup>, Alexandros Georgiadis<sup>1</sup>, Eusebia Calvillo<sup>2</sup>, J. Claude Hemphill III<sup>5</sup>, Gene Sung<sup>6</sup>, Mauro Oddo<sup>7</sup>, Fabio Silvio Taccone<sup>8</sup> and Peter D. LeRoux<sup>9</sup> on behalf of PRINCE Study Investigators

© 2019 Springer Science+Business Media, LLC, part of Springer Nature and Neurocritical Care Society

## Abstract

**Background:** Neurocritical care is devoted to the care of critically ill patients with acute neurological or neurosurgical emergencies. There is limited information regarding epidemiological data, disease characteristics, variability of clinical care, and in-hospital mortality of neurocritically ill patients worldwide. We addressed these issues in the **Point PR**evalence **In Neurocritical CarE** (PRINCE) study, a prospective, cross-sectional, observational study.

**Methods:** We recruited patients from various intensive care units (ICUs) admitted on a pre-specified date, and the investigators recorded specific clinical care activities they performed on the subjects during their first 7 days of admission or discharge (whichever came first) from their ICUs and at hospital discharge. In this manuscript, we analyzed the final data set of the study that included patient admission characteristics, disease type and severity, ICU resources, ICU and hospital length of stay, and in-hospital mortality. We present descriptive statistics to summarize data from the case report form. We tested differences between geographically grouped data using parametric and nonparametric testing as appropriate. We used a multivariable logistic regression model to evaluate factors associated with in-hospital mortality.

**Results:** We analyzed data from 1545 patients admitted to 147 participating sites from 31 countries of which most were from North America (69%,  $N = 1063$ ). Globally, there was variability in patient characteristics, admission diagnosis, ICU treatment team and resource allocation, and in-hospital mortality. Seventy-three percent of the participating centers were academic, and the most common admitting diagnosis was subarachnoid hemorrhage (13%). The majority of patients were male (59%), a half of whom had at least two comorbidities, and median Glasgow Coma Scale (GCS) of 13. Factors associated with in-hospital mortality included age (OR 1.03; 95% CI, 1.02 to 1.04); lower GCS (OR 1.20; 95% CI, 1.14 to 1.16 for every point reduction in GCS); pupillary reactivity (OR 1.8; 95% CI, 1.09 to 3.23 for bilateral unreactive pupils); admission source (emergency room versus direct admission [OR 2.2; 95% CI, 1.3 to 3.75]; admission from a general ward versus direct admission [OR 5.85; 95% CI, 2.75 to 12.45; and admission from another ICU versus

\*Correspondence: jsuarez5@jhmi.edu

<sup>†</sup>Venkatasubba Rao and Suarez have contributed equally to this work.

<sup>2</sup> Division of Neurosciences Critical Care, Departments of Anesthesiology and Critical Care Medicine, Neurology, and Neurosurgery, Johns Hopkins University School of Medicine, 1800 Orleans Street, Zayed 3014C, Baltimore, MD 21287, USA

Full list of author information is available at the end of the article

See complete listing of the PRINCE Study Investigators in Appendix.

direct admission [OR 3.34; 95% CI, 1.27 to 8.8]); and the absence of a dedicated neurocritical care unit (NCCU) (OR 1.7; 95% CI, 1.04 to 2.47).

**Conclusion:** PRINCE is the first study to evaluate care patterns of neurocritical patients worldwide. The data suggest that there is a wide variability in clinical care resources and patient characteristics. Neurological severity of illness and the absence of a dedicated NCCU are independent predictors of in-patient mortality.

**Keywords:** Neurocritical care, Observational study, Outcomes, Critical care, Prospective

## Background and Significance

Neurocritical care (NCC) is dedicated to the treatment of patients who are critically ill with neurological or neurosurgical diseases. The practice of NCC aims to treat the primary insult to the nervous system and prevent or ameliorate secondary neurological injuries. Patients admitted to a neurocritical care unit (NCCU) benefit from care by a specialized multidisciplinary team comprised of physicians, nurses, respiratory therapists, physical and occupational therapists, pharmacists, nutritionists, social workers, and spiritual care providers. Provision of such care has been associated with reduced mortality, duration of hospitalization, and cost of care [1, 2]. Consequently, The Leapfrog Group, a premier nonprofit organization that promotes transparency in healthcare provision and advocates for patient outcomes in the USA, recognized neurointensivists as vital critical care providers in 2008; this helped establish NCC as an integral part of healthcare systems [3].

Patients admitted to NCCUs usually have diagnoses such as acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), traumatic brain and spinal cord injuries (TBI and TSI), neuromuscular weakness, status epilepticus, and hypoxic–ischemic injury that may require targeted temperature management. These diseases frequently are associated with significant morbidity. Clinical outcomes of neurocritically ill patients have mainly been documented in the setting of clinical trials or institutional databases. Recently, there have been attempts to collect patient characteristics and outcomes prospectively for several common disorders such as the Get With The Guidelines database from the American Heart Association for AIS [4], Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) [5], and Collaborative European Neuro Trauma Effectiveness Research in TBI (CENTER-TBI) [6].

Despite management advances and long-term follow-up of NCC patients, the overall impact of NCCU care on patient outcomes is difficult to define for multiple reasons. First, outcome reporting varies across studies as the differences in the definition of the variables and the timeline of collection can vary. Second, a majority of single-center studies tend to be descriptive and hence report outcomes of several pathologies while clinical

trials report outcomes for a single disorder. Third, multicenter studies may not truly represent global data since there are geographical limitations in enrollment and are concentrated in developed countries from large urban academic centers. For example, AIS is the leading cause of morbidity in the USA and about 1 in 8 thrombolysis patients require intensive care therapy [7]. However, it is not known whether the same applies to other geographic areas. Finally, availability and composition of NCCUs vary. NCCUs attached to trauma programs may treat severe TBI and TSI, while non-affiliated NCCUs may not.

It is important, therefore, to evaluate global patterns of care of neurocritically ill patients to help elucidate some areas for potential research: ascertain the global burden of neurocritical illnesses; delineate resource availability; and identify care patterns with potential global application to mitigate primary and secondary neurological injuries. We therefore designed a multicenter, international, point-prevalence, cross-sectional, prospective, observational study in NCC (PRINCE [Point Prevalence In Neurocritical Care] Study). We hypothesized that there is geographic variability in the scope of practice of neurointensivists and NCC delivery. In addition, we wanted to determine whether factors related to difference in care were associated with patient outcome.

## Methods

### Study Design

The PRINCE Study design has been described in detail in an accompanying manuscript, and we summarize it below [8]. The Institutional Review Board (IRB) of the Baylor College of Medicine (BCM) approved the study with a waiver of consent.

### Participating Sites

Participating centers were identified through the Neurocritical Care Research Network [9]. In addition, sites were recruited by emailing members of the neurointensive care section of the European Society of Intensive Care Medicine [10], the Latin American Brain Injury Consortium [11], the Clinical Trials Group of the Australian and New Zealand Intensive Care Society [12], the Canadian Critical Care Trials Group [13], Initiative of German Neurointensive Trial Engagement of the

---

German Neurointensive Care Society [14], the Chinese University of Hong Kong [15], and the Neurocritical Care Middle East and North Africa chapter of the International Pan Arab Critical Care Medicine Society [16]. Four months before study launch, participating sites registered and obtained IRB/ethics board clearance. The study day was set as 7/21/2014 when all patients admitted to registered intensive care units (ICUs) were enrolled in the study. Data were collected from patient care activities from enrollment day up to 7 days or ICU discharge (whichever came first). All data collected adhered to the National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements (CDE) project [17].

### Data Definition and Collection

PRINCE Study data were collected and managed using Research Electronic Data Capture (REDCap) [18] tools hosted at the BCM. The PRINCE database had a built-in audit trail that automatically logged all user activities and logged all pages viewed by every user, including contextual information (e.g., the project or record being accessed). In addition, the database implemented authentication to validate the identity of end users that logged into the system. We created six case report forms (CRFs) for investigators to fill out (See Appendix B—Part 1) [8]. CRF1 was completed upon registration. CRFs 2–5 were completed between days 1 and 7 of the data collection period. CRF 6 was completed at the time of hospital discharge. For the purpose of our study, we defined ICU resources as the work force required for patient care inclusive of physicians, nursing staff, dedicated pharmacists, respiratory therapists as well as physiotherapists. We also defined clinical care variability as the variability in the care providers (e.g., availability of dedicated NCC, availability and type of intensivist, nurse-to-patient ratios) and availability of components of ICU resources. We defined the need for monitoring as any monitoring that is required for the patient that pertains to that particular organ system that is not possible to perform in a regular floor or ward. For example, the use of pulse oximetry, mechanical ventilation, frequent pulmonary function status for respiratory system, continuous heart rate and/or frequent arterial blood pressure monitoring with pressure support for cardiac system, frequent clinical neurological monitoring, or the use of invasive monitoring devices for intracranial pressure for neurological system are some examples. In this manuscript, we describe data from the second part of the PRINCE Study, which included patient characteristics, ICU resources, disease type and severity, ICU and hospital length of stay, and in-hospital mortality.

### Training and Monitoring

PRINCE specific training videos and PowerPoint presentations were submitted electronically to all participating investigators. In addition, we held weekly teleconferences with participating sites in the month before the data collection start date. During these teleconferences, we reviewed the study protocol and addressed specific instructions for data collection and entry and concerns raised by the participating sites. We did not monitor data collection and entry. However, we evaluated incongruous data and outlier values and reconciled those with site investigators.

### Statistical Analysis

Investigators at the Department of Public Health Sciences at the Medical University of South Carolina (Charleston, SC) performed the data analysis. For the purpose of this study, we analyzed variables by grouping the participating centers into six geographic regions: North America, Latin America (including Mexico, Central, and South America), Europe, the Middle East and Africa, Asia, and Oceania. Since a majority of the patients in our study were from the USA, we also analyzed variables grouping those from the US sites and those from the remainder of the world. Variables also were analyzed according to each country's income in accordance with their 2013 gross national income (GNI) per person, using thresholds defined by the World Bank Atlas method. Individual countries were classified into three income groups: low and lower-middle income (GNI less than US\$4035); upper-middle income (GNI of \$4036–\$12,475); and high income (GNI greater than \$12,476) [19]. Data are summarized with means and SDs, medians and interquartile ranges (IQRs), or numbers and percentages as appropriate. Crude in-hospital mortality is presented as a percentage. Normality for continuous variables was assessed using statistical and graphical methods. Differences in practices among world regions were tested using ANOVA, Kruskal–Wallis test, Student's *t* test, Mann–Whitney test,  $\chi^2$  test, or Fisher's exact test, as appropriate. We used independent samples *t* test, Mann–Whitney test,  $\chi^2$  test, and Fisher's exact test to determine if there were differences in practice between the US sites and the remainder of the world.

To determine the variables that were independently associated with in-hospital mortality, we built a multivariable logistic regression model with data from the patient/subject, hospital, and region of origin. A variable was considered as potential risk factor for in-hospital mortality if it was significant at the  $\alpha=0.10$  level. Backward selection using likelihood ratio test was used to obtain the final models that included significant risk

factors. Furthermore, age, Glasgow Coma Scale (GCS) at admission, history of comorbidities, pupillary reactivity at admission, admission source of the patient, geographical region, and the presence of dedicated NCC were included in the model. We report the fixed effects (measure of association) as odds ratio (OR) with their 95% confidence intervals (CI). Statistical covariates were calculated using the Wald test, defined P-values as 2-tailed, and deemed  $P < 0.05$  statistically significant. Statistical analyses were performed using SAS version 9.4.

## Results

Investigators from 257 institutions located in 47 countries registered for participation and completed Part 1 of PRINCE (Appendix). However, 147 institutions from 31 countries provided patient-level data (Table 1). Most participating institutions were in the USA (68; 46%), followed by Australia (9; 6%), India (8; 5%), and Belgium (6; 4%). According to geographic location, 71 (48%) sites were in North America, 30 (20%) in Europe, 16 (11%) in Asia, 4 (2.7%) in the Middle East, 16 (11%) in Latin America, and 10 (7%) in Oceania. In total, we collected data from 1545 patients and the level of missing data varied by variable but was  $< 5\%$  overall.

### Patient Characteristics

Most patients (59%) were male, with a mean age of  $56 \text{ years} \pm 0.5$ , and the majority were admitted to ICUs in North America (69%) (Table 1). Overall, the patients presented with a median admission GCS of 13 (IQR 7 to 15). Collectively, 7% of patients had no pupillary reactivity bilaterally, while 5% had unilateral and 88% had bilateral pupil reaction at admission. The most common primary reason for ICU admission was neurological monitoring (88%), and the majority of patients (42.6%) were admitted from the emergency department. The most frequent primary neurological diagnosis was SAH followed by ICH, subdural hematoma, and severe TBI. About a third of all patients had chronic hypertension at the time of diagnosis, and 14% of patients had more than four comorbidities. The median time for patients to be admitted to the ICU after hospital arrival was 2 h (IQR 0 to 7). Variation between the patient characteristics between the patients in the USA and the rest of the world is shown in Table 2.

Patients in the US centers who comprised the majority of our study population had several differences as compared to the rest of the world: The US patients tended to have lesser severity of illness as determined by GCS (median 14, IQR 8 to 15 versus median 10, IQR 5 to 14); lower proportion of the US patients had absent bilateral and unilateral pupillary reactivity (5% and 4%, 10% and 9%, respectively,  $p < 0.001$ ) upon admission; the US patients also tended to have more than 4 comorbidities

(17% vs. 7%,  $p < 0.0001$ ) and shorter admission time to the ICU (median 2 h, IQR 0 to 6 versus median 3 h, IQR 1 to 8,  $p > 0.0001$ ). Patients from the non-US sites required more respiratory and hemodynamic monitoring (63.9% vs. 44.9%, 69.3% vs. 51.1%, respectively,  $p < 0.0001$ ).

### Characteristics of Participating Institutions

Most participating sites were academic institutions and were located in large urban centers regardless of geographic region (Table 3). Participating institutions had a median overall ICU bed capacity of 54 (IQR 26 to 100). Two-thirds of facilities worldwide had dedicated NCCUs; this proportion was the highest in North America (83%) and lowest in Oceania (15%). The median NCCU bed capacity was 15 (IQR 10 to 20). The distribution of academic versus non-academic centers was uniform across the geographic distribution and more so when compared between the US and the non-US sites. The US sites, however, had a higher number of ICU beds (median 8, IQR 48 to 120 vs. median 32, IQR 18 to 78,  $p < 0.0001$ ) and a higher proportion of dedicated NCC (83% vs. 56%,  $p < 0.0001$ ) compared to the remainder of the world (see Table 2b).

### ICU Treatment Teams and Resource Allocation (Variability in Clinical Care)

The most common specialty of physicians working in the ICUs was pulmonary and critical care medicine (38%) (Tables 3, 4). However, on the day of patient data entry, in North America the most common specialty was NCC (29%), whereas in Europe it was anesthesiology and critical care (44%). ICU physicians were available on site or through telecommunication 24 h a day in most institutions (85%). Dedicated physiotherapists, pharmacists, and respiratory therapists were available in 62%, 68%, and 66% of participating centers, respectively. However, there were notable differences in the allocation of these healthcare professionals: Dedicated physiotherapists were available in all of ICUs in Oceania, compared to 50% in North America ( $p = 0.01$ ); dedicated pharmacists were available in 88% of North American ICUs compared to 30% in Latin America ( $p < 0.001$ ); dedicated respiratory therapists were available in more than 80% of North American ICUs, the Middle East, and Latin America, compared to none in Oceania ( $p < 0.001$ ); and advanced practice providers were mostly available in North America (72%) ( $p < 0.001$ ). Overall nurse-to-patient ratios were 1:2 in most ICUs during day and night shifts (75% and 69%, respectively). Nurse-to-patient ratios were 1:1 in all ICUs in Oceania compared to only 31% in North America and 10% in Latin America ( $p = 0.008$ ). North American sites had the highest proportion of 1:2

**Table 1 Baseline characteristics of the study cohort on admission to the ICU by geographic location**

	ALL patients (n = 1545)	North America (n = 1063)	Europe (n = 182)	Asia (n = 121)	Middle East (n = 25)	Latin America (n = 104)	Oceania (n = 50)	p-value
Severity scores on ICU admission (median, IQR)								
Glasgow Coma Score	13 (7,15)	14 (8, 15)	8 (3, 14)	10 (6.5, 14)	11 (8, 12)	11 (6, 15)	9 (3, 14)	< 0.0001
Pupillary reactivity, n (%)								
Both reactive	1300 (87.8)	921 (91.0)	144 (83.7)	92 (76.7)	18 (72.0)	85 (83.3)	40 (81.6)	< 0.0001
One reactive	79 (5.3)	38 (3.8)	14 (8.1)	15 (12.5)	4 (16.0)	5 (4.9)	3 (6.1)	
None	101 (6.8)	53 (5.2)	14 (8.1)	13 (10.8)	3 (12.0)	12 (11.8)	6 (12.2)	
ICU monitoring requirements <sup>a</sup> (% of patients)								
Neurological	1382 (87.8)	962 (90.5)	138 (75.8)	117 (96.7)	23 (92.0)	97 (93.3)	45 (90.0)	< 0.0001
Hemodynamic	883 (89.5)	547 (51.5)	124 (68.1)	88 (72.7)	21 (84.0)	67 (64.4)	36 (72.0)	< 0.0001
Respiratory	791 (51.2)	481 (45.3)	120 (65.9)	70 (58.9)	14 (56.0)	66 (63.5)	40 (80.0)	< 0.0001
Source of admission, n (%)								
Direct	352 (23.1)	286 (27.3)	27 (14.8)	20 (16.7)	3 (12.0)	5 (4.9)	11 (22.5)	< 0.0001
ED	650 (42.6)	438 (41.9)	69 (37.9)	61 (50.8)	11 (44.0)	49 (47.6)	22 (44.9)	
PACU	86 (5.6)	68 (6.5)	2 (1.1)	5 (4.2)	0 (0.0)	6 (5.8)	5 (10.2)	
OR	218 (14.3)	122 (11.7)	32 (17.6)	21 (17.5)	4 (16.0)	30 (29.1)	9 (18.4)	
Hospital ward	86 (5.6)	44 (4.2)	21 (11.5)	10 (8.3)	2 (8.0)	8 (7.8)	1 (2.0)	
Other ICU	37 (2.4)	21 (2.0)	13 (7.1)	1 (0.8)	0 (0.0)	2 (1.9)	0 (0.0)	
Other	96 (6.3)	67 (6.4)	18 (9.9)	2 (1.7)	5 (20.0)	3 (2.9)	1 (2.0)	
Primary diagnosis (5 most common), n (%)								
SAH: 178 (12.8)	Other: 146 (15.1)	SAH: 23 (14.0)	Severe TBI: 13 (12.6)	Severe TBI: 3 (18.8)	SAH: 13 (13.4)	SAH: 7 (15.9)		< 0.0001
Other: 169 (12.1)	SAH: 125 (12.9)	ICH spontaneous: 22 (13.4)	ICH spontaneous: 12 (11.7)	AIS: 3 (18.8)	Severe TBI: 12 (12.4)	ICH spontaneous: 5 (11.4)		
ICH spontaneous: 163 (11.7)	ICH spontaneous: 116 (12.0)	Severe TBI: 15 (9.2)	SAH: 9 (8.7)	SDH: 2 (12.5)	Other: 10 (10.3)	Other: 3 (6.8)		
SDH: 93 (6.7)	SDH: 75 (7.8)	Cardiac arrest 8 (4.9)	Severe TBI: 7 (6.8)	ICH spontaneous: 2 (12.5)	ICH spontaneous: 6 (6.2)	Head injury severe: 2 (4.6)		
Severe TBI: 79 (5.7) = 294	AIS: 34 (3.5)	SDH: 7 (4.3)	AIS: 5 (4.9)	SAH: 1 (6.3)	Malignant brain tumor: 6 (6.2)	AIS: 2 (4.6)		
Comorbidities [Five most common, (n, %)]								
HTN (501, 32.8%)	HTN (369, 34.8%)	HTN (47, 25.8%)	HTN (23, 19%)	HTN (5, 20%)	HTN (34, 32.7%)	HTN (22, 44%)		< 0.0001
Other (378, 24.5%)	Other (316, 29.8%)	Other (22, 11.5%)	DM (14, 8.3%)	DM (3, 12%)	Other (19, 18.3%)	Other (13, 26%)		
DM (191, 12.4%)	HChol (147, 13.9%)	HChol (18, 10.4%)	Other (7, 5.8%)	Other (2, 8%)	DM (11, 10.6%)	DM (10, 20%)		
HChol (181, 11.7%)	DM (144, 13.6%)	DM (14, 7.7%)	AFib (5, 4.1%)	Systemic hemorrhage (2, 8%)	Smoking (7, 6.7%)	HChol (6, 12%)		
CAD (82, 5.3%)	AFib (65, 6.1%)	AFib (10, 6%)	HChol (5, 4.1%)	HChol (1, 4%)	CAD (6, 6.1%)	CAD (5, 10%)		
Number of comorbidities, n (%)								
None	504	306 (28.8)	72 (40.0)	61 (50.4)	13 (52.0)	35 (33.7)	17 (34.0)	< 0.0001
1	366	244 (23.0)	42 (23.1)	33 (27.3)	8 (32.0)	29 (27.9)	10 (20.0)	
2	273	187 (17.6)	35 (19.2)	15 (12.4)	1 (4.0)	27 (26.0)	8 (16.0)	
3	189	145 (13.6)	14 (7.7)	12 (9.9)	2 (8.0)	7 (6.7)	9 (18.0)	
≥ 4	213	181 (17.0)	19 (10.4)	0 (0.0)	1 (4.0)	6 (5.8)	6 (12.0)	
Time from hospital arrival to ICU admission, in hours (median, IQR)	2 (0, 7)	2 (0, 7)	8 (3, 14)	2 (0, 7)	4.5 (0.5, 9)	6 (3, 12)	3 (1, 8)	< 0.0001

AFib atrial fibrillation, AIS acute ischemic stroke, CAD coronary artery disease, DM diabetes mellitus type II, ED emergency department, HChol hypercholesterolemia/hyperlipidemia, Hemodyn hemodynamic, HTN chronic hypertension, ICH spontaneous intracerebral hemorrhage, ICU intensive care unit, IQR interquartile range, OR operating room, PACU post-anesthesia care unit, SAH subarachnoid hemorrhage, SDH subdural hematoma, TBI traumatic brain injury

<sup>a</sup> Could have multiple options chosen. Monitoring is defined as any monitoring that is required for the patient that pertains to that particular organ system that is not possible to perform in a regular floor or ward



**Table 2 Baseline characteristics of the study cohort on admission to the ICU: the USA versus remainder of the world**

	USA (n = 1033)	Remainder of the world (n = 512)	p-value
Severity scores on ICU admission (median ± IQR)			
Glasgow Coma Score	14 (8, 15)	10 (5, 14)	< 0.0001
Pupillary reactivity, n (%)			
Both reactive	894 (91.0)	406 (81.5)	< 0.0001
One reactive	36 (3.7)	43 (8.6)	
None	52 (5.3)	49 (9.8)	
ICU monitoring requirements <sup>a</sup> (% of patients)			
Neurological	933 (90.3)	449 (87.7)	0.1140
Hemodyn	528 (51.1)	355 (69.3)	< 0.0001
Respiratory	464 (44.9)	327 (63.9)	< 0.0001
Source of admission, n (%)			
Direct	284 (28.0)	68 (13.4)	< 0.0001
ED	428 (42.1)	222 (43.6)	
PACU	64 (6.3)	22 (4.3)	
OR	120 (11.8)	98 (19.3)	
Hospital floor	43 (4.2)	43 (8.5)	
Other ICU	14 (1.4)	23 (4.5)	
Other	63 (6.2)	33 (6.5)	
Primary diagnosis (5 most common), n (%)			
	Other 144 (15.3)	SAH 58 (12.8)	< 0.0001
	SAH 120 (12.8)	ICH spontaneous 53 (11.7)	
	ICH spontaneous 110 (11.7)	Severe TBI 38 (8.4)	
	SDH 73 (7.8)	Other 25 (5.5)	
	Stroke/AIS 50 (5.3)	SDH 20 (4.4)	
Number of comorbidities, n (%)			
None	299 (28.9)	205 (40.0)	< 0.0001
1	238 (23.0)	128 (25.0)	
2	187 (17.8)	89 (17.4)	
3	137 (13.3)	52 (10.2)	
≥ 4	175 (16.9)	38 (7.4)	
Time from hospital arrival to ICU admission, in hours (median, IQR)	2 (0, 6)	3 (1, 8)	< 0.0001

USA included Puerto Rico

AIS acute ischemic stroke, ED emergency department, Hemodyn hemodynamic, ICH spontaneous intracerebral hemorrhage, ICU intensive care unit, IQR interquartile range, PACU post-anesthesia care unit, OR operating room, SAH subarachnoid hemorrhage, SDH subdural hematoma, SOFA sequential organ failure assessment, USA The United States of America

<sup>a</sup> Could have multiple options chosen

nurse-to-patient staffing (89%,  $p < 0.0001$ ), while Latin America had highest proportion of 1:3 nurse-to-patient staffing ( $p < 0.0001$  for both). The US patients are generally treated in dedicated NCC (83% vs. 56%,  $p < 0.001$ ) by a higher proportion of pulmonary and critical care intensivists (38%,  $p = 0.002$ ) and receive a higher complement of physiotherapists, pharmacists, respiratory therapists and, advanced practice providers ( $p < 0.001$  for all) (Table 4).

### ICU Procedures

We collected data on ICU procedures, including mechanical ventilation, at the time of study entry. In addition, we identified procedures that were performed up to the time of hospital discharge. The procedures performed included: external ventricular drains (116 patients, 7.5%); other intracranial pressure monitors (28 patients, 1.8%); brain tissue oxygen monitoring (10 patients, 0.6%); jugular vein oxygen saturation monitors (1 patient, 0.1%); cerebral microdialysis (2 patients, 0.1%); arterial line (337 patients, 22%); central venous catheter (63 patients,

**Table 3 Characteristics of hospitals and ICUs by geographic location**

	ALL sites	North America	Europe	Asia	Middle East	Latin America	Oceania	p-value
Number of countries	31	2	10	7	1	9	2	
Type of hospital (% of sites)								0.0511
Academic Center	107 (72.6)	48 (70.2)	19 (77.8)	10 (67.7)	4 (100.0)	10 (67.6)	8 (85.7)	
Private, non-academic	20 (13.7)	13 (18.6)	0 (0.0)	3 (20.6)	0 (0.0)	2 (13.5)	1 (7.1)	
Public, non-academic	11 (7.6)	4 (6.5)	5 (15.6)	1 (2.9)	0 (0.0)	1 (8.1)	1 (7.1)	
Other	9 (6.1)	3 (4.8)	3 (6.7)	1 (2.9)	0 (0.0)	2 (10.8)	0 (0.0)	
City population (% sites responding)								0.0217
< 100,000	6 (4.2)	4 (6.5)	1 (2.2)	1 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	
100,000–250,000	17 (11.5)	7 (9.7)	7 (24.4)	3 (12.5)	0 (0.0)	2 (8.1)	0 (0.0)	
250,000–500,000	23 (15.7)	10 (15.3)	5 (20.0)	1 (9.4)	0 (0.0)	3 (21.6)	0 (0.0)	
500,000–750,000	16 (10.7)	9 (12.9)	5 (17.8)	0 (0.0)	0 (0.0)	1 (2.7)	2 (14.3)	
750,000–1,000,000	21 (14.2)	12 (17.7)	3 (13.3)	3 (12.5)	0 (0.0)	2 (8.1)	2 (14.3)	
> 1,000,000	64 (43.7)	26 (37.9)	6 (22.2)	7 (56.3)	4 (100.0)	7 (59.5)	6 (64.3)	
Number of ICU beds (median, IQR)	54 (26, 100)	77 (48, 120)	40 (21, 90)	39 (20, 96)	35 (22, 60)	20 (12, 44)	24 (21.5, 53)	< 0.0001
Presence of dedicated neuroICU, (% of sites responding)								< 0.0001
Yes	99 (67.4)	56 (83.1)	17 (64.4)	7 (57.6)	1 (37.5)	8 (54.1)	1 (14.3)	
Number of neuroICU beds (median ± IQR)	15 (10, 20)	18 (12.5, 22.5)	10 (8, 16)	17 (10, 26)	8 (7, 15)	8 (6, 10)	11.5 (10, 13)	< 0.0001
Specialty of physician caring for patients (%) <sup>b</sup>								0.0023
NCC	17 (19.8)	6 (28.6)	2 (12.5)	3 (20.0)	1 (20.0)	4 (23.5)	1 (8.3)	
PCCM	31 (38.4)	4 (19.1)	5 (37.5)	3 (20.0)	3 (60.0)	10 (58.8)	6 (58.3)	
ACC	13 (16.3)	0 (0.0)	7 (43.8)	5 (40.0)	0 (0.0)	1 (5.9)	0 (0.0)	
SCC	4 (4.7)	4 (19.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Neurosurgery	2 (3.5)	2 (9.5)	0 (0.0)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	
Other	14 (17.4)	5 (23.8)	1 (6.3)	2 (13.3)	1 (20.0)	2 (11.8)	4 (33.3)	
ICU physician availability 24 h (% of ICUs)								0.0243
Yes	127 (86.8)	53 (78.1)	26 (97.7)	14 (93.9)	4 (100.0)	13 (91.9)	9 (92.9)	
Dedicated physiotherapist availability (% of ICUs)								0.0128
Yes	91 (62.0)	34 (50.1)	20 (75.0)	10 (69.7)	4 (100.0)	10 (70.0)	9 (92.9)	
Dedicated pharmacist available (% of ICUs) †								< 0.001
Yes	100 (68.1)	60 (88.4)	13 (48.8)	7 (45.5)	3 (66.7)	6 (37.8)	8 (85.7)	
Dedicated respiratory therapists availability (% of ICUs)								< 0.001
Yes	96 (65.4)	58 (85.1)	7 (25.6)	6 (42.4)	3 (85.7)	312 (83.8)	1 (7.7)	
Dedicated advanced practice providers availability (% of ICUs)								< 0.001
Yes	61 (41.7)	49 (72.7)	3 (11.7)	3 (18.2)	0 (0.0)	2 (16.2)	1 (7.7)	
Daytime nurse-to-patient ratio (% of ICUs) <sup>a</sup>								
1:1	31 (21.1)	7 (10.7)	5 (18.2)	6 (39.4)	2 (57.1)	1 (8.1)	9 (92.9)	0.0081
1:2	98 (66.8)	59 (87.6)	17 (63.6)	7 (54.5)	2 (42.9)	6 (43.2)	0 (0.0)	< 0.0001
1:3	12 (8.6)	1 (0.8)	4 (13.6)	1 (3.0)	0 (0.0)	5 (35.1)	1 (7.1)	< 0.0001
1:4	3 (2.0)	0 (0.0)	1 (2.3)	1 (3.0)	0 (0.0)	2 (8.1)	0 (0.0)	0.1276
Other	2 (1.6)	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)	1 (5.4)	0 (0.0)	0.3759
Nighttime nurse-to-patient ratio (% of ICUs)								
1:1	24 (16.7)	7 (9.2)	4 (13.6)	3 (21.2)	2 (57.1)	1 (5.6)	10 (100.0)	0.0037
1:2	90 (61)	58 (85.0)	11 (38.6)	10 (66.7)	1 (14.3)	6 (36.1)	0 (0.0)	< 0.0001
1:3	22 (15)	2 (3.0)	9 (36.7)	2 (9.1)	1 (14.3)	5 (30)	0 (0.0)	< 0.0001
1:4	10 (6.3)	0 (0.0)	3 (11.4)	0 (0.0)	0 (0.0)	3 (25)	0 (0.0)	0.0029
Other	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A

ACC anesthesiology and critical care, ICU intensive care unit, IQR interquartile range, NCC neurocritical care, PCCM pulmonary critical care medicine, SCC surgical critical care

<sup>a</sup> May have more than one response per site

<sup>b</sup> Physicians caring for patients whose data were entered into the study

**Table 4 Characteristics of hospitals and ICUs by geographic location: the USA versus remainder of the world**

	USA	Remainder of world	p-value
Type of hospital (% of sites)			0.1070
Academic Center	47 (69.0)	61 (76.4)	
Private, non-academic	13 (19.8)	7 (9.3)	
Public, non-academic	5 (6.9)	6 (7.9)	
Other	3 (4.3)	5 (6.4)	
City population (% sites)			0.0766
< 100,000	4 (6.0)	2 (2.2)	
100,000–250,000	7 (10.3)	10 (13.0)	
250,000–500,000	10 (15.5)	12 (15.9)	
500,000–750,000	9 (13.8)	7 (8.7)	
750,000–1,000,000	14 (19.0)	9 (10.9)	
> 1,000,000	24 (35.3)	39 (49.3)	
Number of ICU beds (median, IQR)	80 (48, 120)	32 (18, 78)	< 0.0001
Presence of dedicated neuroICU, (% of sites)			< 0.0001
Yes	56 (82.8)	44 (55.8)	
Number of neuroICU beds (median $\pm$ IQR)	18 (13, 23.5)	10 (8, 16)	< 0.0001
Specialty of physician caring for patients (%) <sup>b</sup>			0.0023
NCC	14 (21.0)	22 (28.6)	
PCCM	26 (38.3)	16 (19.1)	
ACC	12 (16.1)	23.9 (19.0)	
SCC	3 (4.9)	15 (19.0)	
Neurosurgery	2 (2.5)	7 (9.5)	
Other	11 (17.3)	3 (5.0)	
ICU physician available 24 h (% of ICUs)			0.0007
Yes	51 (75.8)	75 (94.8)	
Dedicated physiotherapist available (% of ICUs)			< 0.0001
Yes	33 (48.9)	62 (79.2)	
Dedicated pharmacist available (% of ICUs)			< 0.001
Yes	61 (89.3)	32 (40.3)	
Dedicated respiratory therapist available (% of ICUs)			< 0.001
Yes	55 (81.7)	37 (47.4)	
Dedicated advanced practice providers available, (% of ICUs)			< 0.001
Yes	55 (81.7)	11 (14.5)	
Daytime nurse-to-patient ratio (% of ICUs) <sup>a</sup>			
1:1	20 (30.2)	20 (26.0)	0.5390
1:2	62 (90.6)	44 (55.8)	< 0.0001
1:3	1 (1.0)	13 (16.9)	0.0001
1:4	0 (0.0)	4 (5.2)	0.0375
Other	0 (0.0)	2 (2.6)	0.1967
Nighttime nurse-to-patient ratio (% of ICUs) <sup>a</sup>			
1:1	18 (27.1)	14 (18.2)	0.1676
1:2	60 (88.5)	35 (44.2)	< 0.0001
1:3	2 (3.1)	21 (27.3)	< 0.0001
1:4	0 (0.0)	9 (11.7)	0.0005
Other	0 (0.0)	0 (0.0)	N/A

ACC anesthesiology and critical care, ICU intensive care unit, IQR interquartile range, NCC neurocritical care PCCM pulmonary critical care medicine, SCC surgical critical care, USA The United States of America

<sup>a</sup> Could have multiple options chosen

<sup>b</sup> Specialty of physicians caring for patients not within an ICU



**Table 5 Patient characteristics, length of stay, mortality rates, and interventions by region**

	ALL patients	North America	Europe	Asia	Middle East	Latin America	Oceania	p-value
Age, median (IQR)	58 (44, 70)	59 (47, 70)	61 (48, 73)	46.5 (29, 60.5)	41 (26, 59)	55 (36, 69)	58 (46, 68)	<0.0001
Gender, n (%)								0.0105
Male	908 (59.0)	596 (56.2)	119 (65.4)	78 (65.0)	17 (68.0)	72 (69.9)	26 (53.1)	
Female	632 (41.0)	465 (43.8)	63 (34.6)	42 (35.0)	8 (32.0)	31 (30.1)	23 (46.9)	
ICU LOS (in days), median (IQR)	7 (3, 16)	7 (3, 15)	11.5 (6, 25)	5 (3, 9)	16 (12, 20)	16 (12, 20)	6.5 (3, 14)	<0.0001
Hospital LOS (in days), median (IQR)	13 (6, 24)	12 (5, 21)	25 (11, 39)	14.5 (9.5, 24.5)	25 (22, 34)	13 (7, 23)	11 (6, 23)	<0.0001
In-hospital death rate, n (%)	192 (12.4)	111 (10.4)	31 (17.0)	12 (9.9)	3 (12.0)	28 (26.9)	7 (14.0)	<0.0001
DNR order initiated, n (%)								0.1549
Yes	195 (14.6)	142 (15.3)	25 (15.3)	5 (5.4)	1 (11.1)	13 (13.5)	9 (20.0)	
Comfort care instituted, n (%)								0.0202
Yes	148 (11.2)	110 (11.9)	14 (8.5)	2 (2.3)	0 (0.0)	16 (17.0)	6 (13.6)	
Palliative care consultation, n (%)								0.0388
Yes	86 (6.6)	68 (7.5)	14 (8.6)	1 (1.1)	0 (0.0)	2 (2.1)	1 (2.3)	

DNR do-not-resuscitate, ICU intensive care unit, IQR interquartile range, LOS length of stay

**Table 6 Patient characteristics, length of stay, mortality rates, and interventions by region (the USA vs. remainder of the world)**

	USA	Remainder of world	p-value
Age, median (IQR)	59 (47, 70)	56 (39, 70)	0.0006
Gender, n (%)			0.0015
Male	579 (56.2)	329 (64.6)	
Female	452 (43.8)	180 (35.4)	
ICU LOS (in days), median (IQR)	7 (3, 15)	8 (4, 18)	<0.0001
Hospital LOS (in days), median (IQR)	12 (5, 21)	17 (8, 32)	<0.0001
In-hospital death rate, n (%)	108 (10.5)	84 (16.4)	0.0008
DNR order initiated, n (%)			0.3239
Yes	137 (15.3)	58 (13.3)	
Comfort care instituted, n (%)			0.0952
Yes	109 (12.2)	39 (9.1)	
<b>Palliative care consultation, n (%)</b>			0.0071
Yes	69 (7.9)	17 (3.9)	

DNR do-not-resuscitate, ICU intensive care unit, IQR interquartile range, LOS length of stay

4%); mechanical ventilation (288 patients, 19%); tracheostomies (288 patients, 19%); and gastrostomy tube placements (316 patients, 20.5%). There was geographic variation in the number of procedures performed with more being performed in North America including 63% of mechanical ventilation and 85% of external ventricular drains. Brain tissue oxygenation, jugular vein oxygen saturation monitoring, and cerebral microdialysis were only performed in North America and Europe.

#### In-Hospital Length of Stay and Mortality

Median length of ICU and hospital stay was 7 days and 13 days, respectively (Table 5). European centers

reported having the longest lengths of ICU and hospital stay (12 and 25 days, respectively) and the USA the shortest (7 and 12 days) (Table 6).

One hundred and ninety-two patients died before hospital discharge. Median hospital mortality (described as crude mortality rates) was 12.4% and varied by geographical regions; it was the highest in Latin America (27%) and the lowest in Oceania (11%) (Table 5). Palliative care consultation does not resuscitate (DNR) orders, and comfort care measures were most frequently reported in North American sites. Worldwide 1 in 10 patients had comfort care measures. Patients admitted in the USA had lower length

**Table 7 Patient characteristics, length of stay, mortality rates, and interventions by gross national income**

	Lower	Upper	High	p-value
Age, median (IQR)	45 (28, 60)	44 (32, 62)	59 (46, 70)	<0.0001
Gender, n (%)				0.0399
Male	36 (58.1)	60 (72.3)	812 (58.2)	
Female	26 (41.9)	23 (27.7)	583 (41.8)	
ICU LOS (in days), median (IQR)	7 (3.5, 13.5)	7 (4, 17)	7 (3, 16)	0.9502
Hospital LOS (in days), median (IQR)	14 (6, 28)	15 (10, 23)	12 (6, 24)	0.2620
In-hospital death rate, n (%)	8 (12.7)	20 (24.1)	164 (11.7)	0.0040
DNR order initiated, n (%)				0.0569
Yes	2 (3.6)	9 (15.0)	184 (15.1)	
Comfort care instituted, n (%)				0.0613
Yes	2 (4.1)	11 (18.3)	135 (11.1)	
Palliative care consultation, n (%)				0.0361
Yes	0 (0.0)	1 (1.8)	85 (7.1)	

DNR do-not-resuscitate; ICU intensive care unit; IQR interquartile range; LOS length of stay

of ICU (median 7, IQR 3 to 15 vs. median 8, IQR 4 to 18,  $p < 0.0001$ ) and hospital stay, (median 12, IQR 5 to 21 vs. median 17, IQR 8 to 32,  $p < 0.0001$ ), and in-hospital deaths (10.5% vs. 16.4%,  $p = 0.0008$ ) and received higher rates of palliative care consultations (Table 6). We noticed that patients from upper- and high-GNI nations had higher mortality and received higher proportion of comfort care measures and palliative care consultations. The proportion of patients who received DNR orders and comfort care measures did not differ ( $p = 0.15$ ) (Table 7).

Independent predictors of increased in-hospital mortality included the following: age; admission GCS score; admission pupillary response; admission source (e.g., emergency room, transfer from another hospital or from elsewhere in the hospital); geographic location; and the absence of a dedicated NCCU (Table 8).

## Discussion

The PRINCE Study is the first to evaluate the provision of NCC around the world. We demonstrate a wide variability in several aspects, including disease burden, patient characteristics, NCCU treatment teams and resource allocations, and mortality in the NCCU patient population.

## Study Strengths and Limitations

The PRINCE Study has several strengths. First, PRINCE is the first study to evaluate prospectively a day in the life of a NCCU and of a neurointensivist around the world. Second, the majority of world regions, except for the African continent, are represented in the study. Third, we used NINDS-recommended CDE, when available, and

**Table 8 Predictors of in-hospital mortality**

Predictors	Odds ratio	95% Wald CI
Patient age	1.03	1.02, 1.04
Total Glasgow Coma Scale <sup>a</sup>	0.81	0.77, 0.85
Pupillary reactivity at admission		
One reactive vs both reactive	1.64	0.85, 3.17
None reactive vs both reactive	2.07	1.19, 3.17
Admission source of the patient		
ED versus direct	2.20	1.30, 3.75
OR (PACU and OR) versus direct	1.44	0.75, 2.76
General hospital ward versus direct	5.85	2.75, 12.35
Other ICU versus direct	3.34	1.27, 8.80
Other versus direct	1.35	0.52, 3.51
Region		
Asia versus North America	0.53	0.24, 1.16
Europe versus North America	0.79	0.47, 1.32
Latin America versus North America	2.29	1.28, 4.12
The Middle East versus North America	2.2	0.44, 11.08
Oceania versus North America	0.66	0.25, 1.69
Dedicated NeuroICU		
No versus yes	1.71	1.05, 2.45

The following variables were included in the model: patient age ( $p < 0.0001$ ), total Glasgow Coma Scale at admission ( $p$ -value  $< 0.0001$ ), history of comorbidities ( $p$ -value = 0.1004), pupillary reactivity at admission ( $p$ -value = 0.0219), admission source of the patient ( $p$ -value = 0.0002), region ( $p$ -value = 0.0051), and whether the hospital has a dedicated NCC ( $p$ -value = 0.0311)

ED emergency department; ICU intensive care unit; PACU post-anesthesia care unit

<sup>a</sup> For every unit increase in Glasgow Coma Scale, mortality decreases by 17%

trained the investigators in data collection. However, the PRINCE Study has several potential limitations. First, the study was not funded, and hence, the participation was

---

voluntary and uncompensated. This may have potentially limited sites from participating in PRINCE. In addition, this meant the data were only evaluated in the setting of incongruence or for outliers, since site monitoring was not feasible. Second, nearly half of the sites were from North America (comprising about two-thirds of the patients), and nearly three quarters were from academic centers in large cities. This may not completely represent neurocritical patient care in other hospital settings. Third, there were challenges associated with data user agreements and institutional board regulations, which may have limited some sites from participating. Fourth, the sample size is limited by the study design and a short collection period; this may not fully represent the actual annual disease distribution in each region. Fifth, we did not collect long-term outcomes and quality of life measures. Finally, we used multiple logistic regression modeling to evaluate mortality, which inherently cannot account for unmeasured variables. Despite these limitations, we believe PRINCE provides robust data to help define global NCC.

#### Implications of the PRINCE Study

There are several important observations that result from the PRINCE Study. Based on the data presented, an average NCCU patient as per our study can be described as a sexagenarian with at least one comorbidity, who presents with a GCS of 13, is likely to stay in the NCCU for about a week and has a 2 out of 3 chance for mechanical ventilation, 1 in 5 chance for gastrostomy and tracheostomy, and a 13% risk of in-hospital mortality. We observed variability in the healthcare resources available worldwide; this is similar to general critical care. Dedicated NCCUs were far more likely in North America. However, worldwide neurointensivists cared for only a fifth of NCCU patients. Furthermore, depending on the geographic area, a non-intensivist as the primary provider cared for 1 in 10 to 1 in 3 of patients. Similar observations are described in general critical care studies where about half of the patients did not have a critical care physician as the primary provider [20]. Similar to general critical care studies, the PRINCE Study also showed variability in the physical therapist [21], pharmacist [22], respiratory therapist, and advanced practice provider staffing or availability and the nurse-to-patient ratio [21]. Staffing ICUs with appropriately trained intensivists can reduce mortality and ICU length of stay in both general medical ICUs and NCCUs [23–25]. Relative to the non-US sites, we observed a higher number of ICU beds, NCC beds, in the US sites. In relation to manpower, the US sites had a lower proportion of physicians available around the clock, with a third of them representing pulmonary and critical care intensivists. In addition, the US sites were

less supported by physical therapists, while had better pharmacist and respiratory therapist support.

The characteristics of NCCU patients and care have several similarities with general critical care including: median age and gender distribution [26, 27]. However, there are several differences between NCC and general critical care. First, nearly 20% of NCCU patients had a tracheostomy and gastrostomy compared to 2–11% of patients in general critical care [28, 29]. This may have to do more with airway control than respiratory function in the NCCU patients. Second, the proportion of NCCU patients with >4 comorbidities (14%) was greater than that observed in general critical care patients described in the ICON patient cohort [27]. Third, the most common diagnosis for NCCU admission was SAH, which is one of the neurological emergencies in need of further research to help improve long-term clinical outcomes [30]. Fourth, PRINCE Study patients had a longer length of ICU stay (13 days) compared to general ICU patients (4 days) [31]. Possible explanations for this difference include the underlying pathology, more comorbidities, lack of trained intensivists, and variable treatment teams.

The in-hospital mortality of PRINCE patients was 12%. Patient characteristics that were associated with higher mortality included: age, lower GCS score, and the absence of pupillary response bilaterally [32, 33]. Several hospital- and resource-associated factors also were associated with mortality. First, admission from the emergency room or from the general ward or other ICU influenced mortality. We speculate that the presence of a neurological disorder superimposed on a different illness for which the patients were treated on a regular ward may aggravate outcome. This second disorder was not present in patients who were directly admitted to the ICU. Second, the absence of a dedicated NCCU was associated with a near twofold increase in mortality. This is consistent with previous observations that suggest the presence of critical or NCC teams is associated with reduced mortality and length of ICU stay [23–25]. Together, these findings suggest that specialized NCCUs may help improve patient outcomes. Third, there were geographic differences in mortality. For example, patients admitted to ICUs in Latin America had a several-fold greater mortality than those admitted to North American ICUs. Similar observations have been made in general critical care and may be explained by availability of treatment teams and their allocations [27]. However, in the PRINCE Study patients admitted to ICUs in Latin America often appeared to be sicker than those admitted in other geographic regions and had lower median GCS and more frequently had bilateral absent pupillary reflexes and had higher rates of comfort care initiation.

The majority population in our study, from the USA, had a lower mortality relative to the rest of the world. Several factors can explain this observation. As noted earlier, the US patients had higher GCS scores, sequential organ failure assessment scores, more favorable pupillary reflexes, and lesser requirement for pulmonary and hemodynamic monitoring. Furthermore, a lower proportion of the US patients were admitted from regular hospital ward and other ICUs. Surprisingly, despite comparable use of DNR orders, the US patients had more comfort care institutions and more palliative consultations. We can only speculate that these patients might have been transferred to a hospice facility. This may have artificially reduced the ICU mortality in addition to reducing the lengths of stay in the ICU and hospital.

In general critical care, hospital mortality is reported to be 10–29% and ICU mortality about 3%, based on patients' age and underlying severity of illness [34, 35]. However, mortality varies with pathology and can be as much as 45% for sepsis [26]. In part, the in-hospital mortality observed in NCC may be explained by the more frequent use of DNR and palliative care rather than allowing patients with devastating neurological disorders survive with severe disability. In PRINCE, we observed that DNR, comfort measures, and palliative care were initiated in 15%, 11%, and 7% of patients, respectively. In a study by Hua et al. [36], evaluating patients in general ICU, DNR was initiated in 8% of adults >65 years and 4% of adults <65 years. In the same study, about 1 in 7 patients were eligible for palliative care in a general ICU. However, whether these findings can be generalizable worldwide remains to be determined. Similar to general critical care, we observed that comfort care and DNR status were more frequent in countries with higher GNI [37].

### Future Directions

The PRINCE Study provides the first detailed information about the care of neurocritically ill patients worldwide. There still are several important questions that need to be addressed including: the influence on mortality relative to the percentage of a nation's gross domestic product (GDP) assigned to healthcare; the impact of protocol-based management on patient mortality; variability of care within and across regions; type of neuroimaging and whether it is available 24 h a day; patterns of care to treat individual diagnoses; and long-term mortality and quality of life of survivors. We anticipate that the PRINCE Study can create a platform and serve as the springboard to address such issues in the future.

## Conclusion

The PRINCE Study provides valuable data on care for NCC patients globally. Mortality of neurocritical patients appears to be associated with the severity of neurological injury and the absence of a dedicated NCCU.

### Author details

<sup>1</sup> Division of Vascular Neurology and Neurocritical Care, Baylor College of Medicine and CHI Baylor St Luke's Medical Center, Houston, TX, USA.

<sup>2</sup> Division of Neurosciences Critical Care, Departments of Anesthesiology and Critical Care Medicine, Neurology, and Neurosurgery, Johns Hopkins University School of Medicine, 1800 Orleans Street, Zayed 3014C, Baltimore, MD 21287, USA. <sup>3</sup> Medical University of South Carolina, Charleston, SC, USA.

<sup>4</sup> Department of Health Informatics, Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA. <sup>5</sup> University of California San Francisco, San Francisco, CA, USA. <sup>6</sup> University of Southern California, Los Angeles, CA, USA. <sup>7</sup> CHUV Lausanne University Hospital, Lausanne, Switzerland. <sup>8</sup> Erasme Hospital and Free University of Brussels, Brussels, Belgium. <sup>9</sup> Main Line Health Care Wynnewood, Wynnewood, PA, USA.

### Acknowledgements

We thank the following individuals for their great support and help with the PRINCE Study: Amanda Simons from the BCM IT Department for her help in setting up the electronic database; Kimberly Weiderhold from the BCM legal department for assisting with Data Use Agreements; Jean Louis Vincent from the Free University of Brussels for providing us with copies of CRFs from the ICON Study; Ian Seppelt from the University of Sydney for helping us with the ANZICS-CTG sites; Katja Wartenberg from Martin Luther University, Germany, for facilitating interactions with IGNITE and MENA

### Authors' contributions

Jose I Suarez was involved in protocol development, data collection, data analysis, and manuscript writing/editing; Renee H Martin contributed to data collection, data management, data analysis, and manuscript writing/editing; Colleen Bauza took part in data collection, data management, data analysis, and manuscript writing/editing; Alexandros Georgiadis was involved in protocol development, data collection, data analysis, and manuscript writing/editing; Chethan P Venkatasubba Rao contributed to protocol development, data collection, data analysis, and manuscript writing/editing; Eusebia Calvillo took part in protocol development, data collection, data analysis, and manuscript writing/editing; J Claude Hemphill was involved in protocol development, data collection, data analysis, and manuscript writing/editing; Mauro Oddo contributed to protocol development, and manuscript writing/editing; Fabio Silvio Taccone took part in protocol development, and manuscript writing/editing; Peter D LeRoux was involved in protocol development, and manuscript writing/editing. The corresponding author confirms that authorship requirements have been met, the final manuscript was approved by ALL authors, and that this manuscript has not been published elsewhere and is not under consideration by another journal. There was no support for this work. The PRINCE Study adhered to ethical guidelines, and the IRB at the Baylor College of Medicine approved it with a waiver of consent. We used the STROBE reporting checklist for observational studies.

### Source of Support

The PRINCE Study recieved no funding.

### Compliance with ethical standards

### Conflict of interest

Dr Suarez reports being the President of the Neurocritical Care Society, a member of the Editorial Board of Stroke Journal, and Chair of the DSMB for the INTREPID Study sponsored by BARD, outside of the submitted work. Dr LeRoux, Dr Bauza, Dr Sung, Dr Hemphill, Dr Oddo, Dr Martin, Dr Taccone, Dr Georgiadis, Dr Venkatasubba Rao, and Ms Calvillo have nothing to disclose.

---

### Ethical approval

The Institutional Review Board of the Baylor College of Medicine approved the study with a waiver of consent. PRINCE Study investigators adhered to ethical standards.

## Appendix

### PRINCE Study Investigators

*Argentina:* Gustavo Domeniconi, MD, Sanatorio de la Trinidad San Isidro, Gran Buenos Aires; Luis Alberto Computaro, Sanatorio San Jose, Buenos Aires; Milton Villalobos, Hospital Municipal San Miguel, Buenos Aires; Mariela Allasia, Hospital de Ninos O Allasia, Santa Fe; Fernando D Goldenberg, MD, Mario D Teran, MD, Foda Rosciani, MD, Hospital Italiano, Buenos Aires; Hector Alvarez, Hospital Escuela General San Martin, Buenos Aires; Marcelo Costilla, MD, Walter Videtta, MD, Hospital Nacional Alejandro Posadas, Buenos Aires; Diego Perez, Hospital de Trauma y Emergencia Dr. Federico Abete, Buenos Aires; Pablo Raffa, Hospital Interzonal General de Agudos, Buenos Aires; Walter Videtta, Hospital Eva Peron de Merlo, Buenos Aires. *Australia:* Ian Sepelt, Nepean Hospital, Sydney; Helen Rodgers, Canberra Hospital, Canberra; Jody Paxton, Gold Coast University Hospital, Southport; Deepak Bhonagiri, Macquarie University Hospital, Sydney; Anders Aneman, Liverpool Hospital, Liverpool; Elizabeth Jenkinson, Royal Perth Hospital, Perth; Celia Bradford, B Med, Simon Finfer, MBBS; Elizabeth Yarad, RN, BN, Frances Bass, RN, BN, Naomi Hammond, RN, BN, Anne O'Connor, RN, Simon Bird, RN, Royal North Shore Hospital, Sydney; Roger Smith, St Vincent's Hospital, Melbourne; Deborah Barge, The Royal Melbourne Hospital, Melbourne; Jane Shilkin, WPD Woods, MD, Brigit Roberts, Sir Charles Gairdner Hospital, Nedlands; Michael O'Leary, Royal Prince Alfred Hospital, Camperdown; Shirley Vallance, Alfred Hospital, Melbourne. *Austria:* Raimund Helbok, MD, Ronny Beer, MD, Bettina Pfaulser, MD, Alois Schiefecker, MD, Innsbruck Medical University, Innsbruck. *Bahrain:* Ayesha Almamari, Mafrq Hospital; Sajid Mukaddam, Salmaniya Medical Complex. *Belgium:* Fabio S Taccone, MD, Hopital Erasme, Brussels; Xavier Wittebole, MD, Caroline Berghe, RN, Marie-France Dujardin, RN, Suzanne Renard, RN, Philippe Hantson, MD, Cliniques Universitaires Saint Luc, Louvain; Patrick Biston, CHU de Charleroi, Charleroi; Geert Meyfroidt, University Hospitals, Leuven. *Brazil:* Ivan Rocha Ferreira da Silva, MD, Janaina de Oliveira, MD, Hospital Copa D'Or, Rio de Janeiro; Alvaro Reao Neto, Instituto de Neurologia de Curitiba, Curitiba; Joao Roberto Sala Domingues, Hospital Samaritano, Sao Paulo; Pedro Mendes de Azambuja Rodrigues, São Lucas Copacabana Hospital, Rio de Janeiro. *Canada:* Jeanne Teitelbaum, MD, Montreal Neurological Institute, Montreal; Martin Chapman, MD,

Vicki McCredie, MD, Nicole Marinoff, Adic Perez, Sunnybrook Health Sciences Unit, Toronto; Demetrios Jim Kutsogiannis, MD, University of Alberta Hospital, Edmonton; Francis Bernard, MD, Hopital Sacre-Coeur, Montreal; Andreas Kramer, MD, University of Calgary, Calgary. *Chile:* Jose I Moretti, MD, Hospital del Trabajador, Santiago; Sergio Aguilera, MD, Hospital Regional de Iquique, Iquique; Eugenio J. Poch, MD, Instituto de Neurocirugia Alfonso Asenjo, Santiago; Carlos Romero, MD, Hospital Clinico Universidad de Chile, Santiago. *China:* George K.C. Wong, MD, Chinese University of Hong Kong, Hong Kong; Jian Song, MD, Guozheng Xu, MD, Wuhan General Hospital, Wuhan. *Colombia:* Jorge H. Mejia-Mantilla, Humberto Madrinan-Navia, MD, Jorge E Martinez, MD, Maria Elena Ochoa, MD, Diego Bautista, MD, Monica Varga, MD, Monica Gomez, MD, Fundacion Valle del Lili, Cali; Juan Diego Ciro, MD, Bladimir Gil, MD, Rodrigo Murillo, MD, Clinica Las Americas, Medellin; Olga Hernandez, MD, Instituto Neurologico de Colombia, Medellin. *Costa Rica:* Jorge Ramirez-Arce, MD, Surgical Intensive Care Unit, CCSS, San Jose. *Croatia:* Tomislav Breitenfeld, KBC Sestre milosrdnice, Zagreb. *Cuba:* Angel J. Lacerda Gallardo, Hospital General Roberto Rodriguez, Moron. *Dominican Republic:* Hubiel J Lopez Delgado, MD, Jose Rafael Yunen Gonzalez, MD, Manuel Hache-Marliere, CEDIMAT, Santo Domingo. *Ecuador:* Diego Barahona Pinto, Hospital de Los Valles, Quito; Miguel Llano, MD, Hospital de Especialidades de la FF.AA., Quito; Estuardo Salgado, Clinica La Merced, Quito; Manuel Jibaja, MD, Hospital Eugenio Espejo, Quito. *England:* Judith C Wright, James Cook University Hospital, Middlesbrough; Daniel Harvey, Nottingham University Hospitals, Nottingham; Vishwajit Verma, Royal London Hospital, London; Philip Hopkins, MD, Alexander Chan, King's College Hospital, London; Jessie Welbourne, Derriford Hospital, Plymouth; Susan Dowling, Whiston Hospital, Merseyside. *Finland:* Ari Katila, Turku University Hospital, Turku. *France:* Sigismond Lasocki, CHU-Angers, Angers. *Germany:* Katja Wartenberg, MD, Martin-Luther-University Halle-Wittenberg; Carsten Hobohm, MD, University of Leipzig, Leipzig; Sven Poli, MD, University of Tuebingen, Tubingen; Ingo Schirotzek, UKGM, Giessen; Julian Bosel, MD, Silvia Schoenenberger, Susanne Francken, Simon Shieber, Alexander Kern, University of Heidelberg, Heidelberg. *Guatemala:* Joel Falla and Edgar Avalos Herrera, Hospital General San Juan de Dios, Guatemala City. *India:* P. C. Gilvaz, Jubilee Mission Medical College, Thrissur; Keshav Goyal, MD, Navdeep Sokhal, MD, Jyoti Sohal, MD, All India Institute of Medical Sciences, New Delhi; Deepesh G. Aggarwal, Saifee Hospital, Mumbai; Banambar Ray, MD, Saroj Pattnaik, MD, Apollo Hospitals, Bhubaneswar; Sanchita Garg, Fortis Hospital, Mohali; Subhal Dixit,

---

Sanjeevan Hospital, Pune; Raj Rawal, Hope Neuro Care Hospital, Ahmadabad; Srinivas Samavedam, Madhu Madhusudan, Care Hospitals, Hyderabad; Gunchan Paul, Dayanand Medical College, Pohir; Sanghamitra Mishra, IMS & SUM Hospital, Bhubaneswar; Patil Shushma, Ruby Hall Clinic, Pune; Urvi Shukla, Aditya Birla Memorial Hospital, Pune; Vandana Sinha, GNRC Hospitals, Dispur; Ponniah Vanamoorthy, Global Health City, Chennai; Sonali Vadi, Global Hospital, Mumbai; *Iran*: Majid Mokhtari, IHH, SBUMS, Tehran. *Italy*: Frank Rasulo, Spedali Civili Hospital, Brescia; Marianna Pegoli, Ospedale Bellaria IRCCS delle Scienze Neurologiche, Bologna; Federico Bilotta, Ospedale Policlinico Umberto I, Rome. *Japan*: Masao Nagayama, MD, PhD, International University of Health and Welfare Atami Hospital, Atami; Hitoshi Kobata, Osaka Mishima Emergency Critical Care Center, Osaka. *Lithuania*: Saulius Vosylius, Vilnius University Hospital, Vilnius. *Malaysia*: Jafri Malin Abdullah, Center for Neuroscience Services and Research, Universiti Sains Malaysia-P3Neuro, Kubang Kerian. *Mexico*: Juvenal Franco Granillo, Centro Medico ABC, Mexico City; Julio Cesar Mijangos-Mendez, Hospital Civil De Guadalajara, Guadalajara. *The Netherlands*: Janneke Horn, Academic Medical Center, Amsterdam; Marcella C A Muller, MD, PhD, Medisch Centrum Haaglanden, The Hague; Michael Kuiper, Medical Center Leeuwarden, Leeuwarden; Wilson F Abdo, MD, PhD, Radboud UMC, Nijmegen. *New Zealand*: Colin McArthur, MD, Lynette Newby, Auckland City Hospital, Auckland. *Pakistan*: Madiha Hashmi, Aga Khan University, Karachi; Seemin Afshan Shiraz, Sheikh Khalifa General Hospital, Lahore. *Panama*: Guadalupe Castillo Abrego MD, Caja de Seguro Social Hospital, Panama City. *Peru*: Ermitaño Bautista Coronel, Hospital Nacional Hipolito Unanue, Lima; Oscar Saldarriaga Rivera, Hospital Guillermo Almenara Irigoyen, Lima; Juan Luis Cam Paucar, Instituto Nacional de Ciencias Neurológicas, Lima; Oscar Gomez, Hospital Nacional Dos de Mayo, Lima. *Philippines*: Jose Emmanuel Palo, The Medical City, Manila; Johnny Lokin, University of Santo Tomas Hospital, Manila. *Poland*: **Agnieszka Misiewska-Kaczur, MD, PhD**, ZPZOZ Silesian Hospital, Cieszyn. *Portugal*: Celeste Dias, Hospital Sao Joao, Porto; Pedro Amorim, Sonia Andre, Hospital de Santo Antonio, Porto. *Puerto Rico*: Gloria Rodriguez-Vega, MD, HIMA San Pablo, Caguas. *Russia*: Alexey Gritsan, Krasnoyarsk Regional Hospital, Krasnoyarsk; Yulia Titova, Sklifosovsky Research Institute for Emergency Medicine, Moscow. *Saudi Arabia*: Ahmed Al Jabbary, MD, Amer Rashed Al Zahrani, MD, Lucie Pelunkova, RN, Hebaa Zraiki, RN, Ahmad M Deeb, King Abdulaziz Medical City, Riyadh; Ali Al Bshabshe, Aseer Central Hospital, Abha; Hosam Al-Jehani, King Fahad University Hospital, Dammam;

Faisal Al-Suwaidan, MD, King Fahad Medical City, Riyadh. *Slovenia*: Viktor Svirgelj, MD, University Medical Centre, Ljubljana. *Spain*: Luis A Ramos-Gomez, MD, Hospital General de La Palma, Santa Cruz de Tenerife; Gerardo Aguilar, Rafael Badenes, Hospital Clinico Universitario de Valencia, Valencia; Juan Antonio Llopart Pou, Hospital Universitari Son Espases, Palma de Mallorca; Elizabeth Zavala, Hospital Clinic, Barcelona; Francisco Bernal Julian, Laura Galarza Barrachina, Barbara Vidal Tegedor, Susana Altaba Tena, Hospital General Universitario de Castello, Castello; Oliva Romero Krauchi, Hospital Son Espases, Palma de Mallorca; Gonzalo Tamayo, Cruces University Hospital, Barakaldo; Baltasar Sanchez, Hospital Universitari Mutua Terrassa, Barcelona; Raul-Ismael Gonzalez Luengo, Complejo Hospitalario de Leon, Leon. *Sri Lanka*: S. Puvanendiran, General Teaching Hospital. *Switzerland*: Paolo Merlani, Ospedale Regionale, Lugano. *Thailand*: Denchai Laiwatana, Bangkok hospital Trat, Bangkok; Panuwat Promsin, Siriraj Hospital, Bangkok. *Turkey*: Bijen Nazliel, Gazi University Faculty of Medicine, Ankara. *USA*: Evert Eriksson, MD, Julio Chalela, MD, MUSC, Charleston, SC; David W Miller, MD, University of Alabama at Birmingham; Raul Guisado, MD, San Jose Regional Medical Center, San Jose, CA; Errol Gordon, MD, Mt Sinai Medical Center, NYC, NY; Harrish H K Murthy, MD, Audrey Paulson, Good Samaritan Hospital, San Jose, CA; Venkatakrishna Rajajee, MD, Kyle Sheehan, MD, Craig Williamson, MD, Ron Ball, University of Michigan, Ann Arbor, MI; Patrick Allan, MD, Good Samaritan Hospital, Dayton, OH; Jennifer Berkeley, Sinai Hospital of Baltimore, MD; Susanne Muehlschlegel, MD, Raphael Carandang, Willey Hall, University of Massachusetts Medical School (UMASS), Worcester, MA; Aarti Sarwal, Wake Forest Baptist Medical Center, Winston-Salem, NC; Jose I Suarez, MD, Chethan P Venkatasubba Rao, MD, Alexandros Georgiadis, MD, Eusebia Calvillo, RN, Rahul Damani, MD, Nelson Maldonado, MD, Benedict Tan, MD, Pramod Gupta, MD, Christos Lazaridis, MD, Eric M Bershad, MD, Baylor College of Medicine, Houston, TX; Safdar Ansari, MD, Julie Martinez, University of Utah, Salt lake City, UT; Eduardo Smith Singares, MD, Advocate Christ Medical Center, Oak Lawn, IL; Edward Manno, MD, J Javier Provencio, MD, Burhan Chaudhry, MD, Moneen McBride, Cleveland Clinic Foundation, Cleveland, OH; Raj Dhar, MD, Debra Roberts, MD, PhD, Michelle Allen, RN, Barnes-Jewish Hospital, St Louis MO; Hermann C Schumacher, Lehigh Valley Health Network, Allentown, PA; Wassim Habre, MD, Corzer Chester Medical Center, Chester, PA; Kevin Sheth, MD, David Greer, MD, Kimberley Kunze, Yale University School of Medicine, New Haven, CT; Panayiotis Varelas, MD, PhD, Lauren Tack, Henry Ford Hospital, Detroit, MI; N



---

Stevenson Porter, Rhode Island Hospital, Providence, RI; Christopher Junker, George Washington University, Washington, DC; Michael Rodricks, MD, Misti Tuppeny, MSN, RN, Cherlynn Basignani BSN, RN, Sarah Napolitano, MS, CHES, Gabriella Anderson, BA, Karin Donaldson, LPN, Florida Hospital, Orlando, FL; Rhonda Davis, Shannon Sternberg, Greenville Health System, Greenville, SC; Elias A Giraldo, Drexel University, Philadelphia, PA; Huy Tran, MD, University of New Mexico, Albuquerque, NM; William M Coplin, MD, St Anthony Hospital, Denver, CO; Neeraj Badjatia, MD, University of Maryland, Baltimore, MD; Ahmed Fathy, Miami Valley Hospital, Dayton, OH; Rwoof A Reshi, MD, University of Minnesota, Minneapolis, MN; Jordan Bonomo, MD, University of Cincinnati, Cincinnati, OH; David Seder, MD, Lauren S Connolly, RN, BSN, Barbara McCrum, RN, BSN, Maine Medical Center, Portland, ME; Teresa Carter, Sutter Roseville Medical Center, Roseville, CA; Miriam Treggiari, MD, University of Washington, Seattle, WA; Matthew Dickinson, MD, Centura St Anthony Hospital, Lakewood, CO; Richard A Rison, PIH Health, Whittier, CA; Marek Mirski, MD, PhD, Johns Hopkins University, Baltimore, MD; Sayona John, Thomas P Bleck, MD, Rush University Medical Center, Chicago, IL; Ali Malek, MD, Tiffany Trim, RN, Murline Smith, RN, St Mary's Medical Center, West Palm Beach, FL; M Kamran Athar, MD, Fred Rincon, MD, Thomas Jefferson University Hospital, Philadelphia, PA; Laith Altaweel, Inova Fairfax, Falls Church, VA; Paul Vespa, MD, PhD, UCLA Medical Center, Los Angeles, CA; Gene Sung, MD, Benjamin Emanuel, DO, University of Southern California, Los Angeles, CA; Eric Eskiogly, MD, Physicians Regional Healthcare System, Naples, FL; Molly McNett, PhD, RN, CNRN, Metro Health Medical Center, Cleveland, OH; Anakara V Sukumaran, MD, Houston Methodist Hospital, Houston, TX; Lori Shutter, MD, University of Pittsburgh/UPMC, Pittsburgh, PA; Dave Milzman, MD, Georgetown University, Washington, DC; Stuart Glassner, University of Florida, Jacksonville, FL; Kristine O'Phelan, MD, University of Miami, Miami, FL; Eric Rosenthal, MD, Massachusetts General Hospital, Boston, MA; J C Hemphill III, MD, PhD, Mohan Kottapally, MD, Wade S Smith, MD, PhD, Nerissa Ko, MD, Scott A Josephson, MD, Anthony Kim, MD, Neel S Singhal, MD, PhD, Ahmad Ahmad, MD, Michele Meeker, University of California San Francisco, CA; Karen G Hirsch, MD, Stanford University, Palo Alto, CA; Mohan Kottapally, MD, San Francisco General Hospital, San Francisco, CA; Deepak Nair, MD, OSF Saint Francis Medical Center, Peoria, IL; Sherry Chou, MD, Gabriela Santos, Sarah Clark, Steven Feske, MD, Galen Henderson, MD, Farzaneh Sorond, MD, Henrikas Vaitkevicius, MD, David Chung, MD, Jennifer Kim, MD, Mary Amatangelo, RN,

NP, Brigham and Women's Hospital, Boston, MA; Gregory Kapinos, MD, MS, North Shore – LIJ Health System, Long Island, NY; Michel Torbey, MD, Wexner Medical Center at The Ohio State University, Columbus, OH; D Ethan Kahn, Christiana Care Health System, Wilmington, DE; Cherylee Chang, MD, Matthew Koenig, MD, The Queen's Medical Center, Honolulu, HI; Mark Gorman, MD, Fletcher Allen Health Care, Burlington, VT; James R Langdon, MD, University of Tennessee Medical Center, Knoxville, TN; Jonathan Dissin, MD, Einstein Medical Center, Philadelphia, PA; Laura Cross, Harry Peled, MD, St Jude Medical Center, Fullerton, CA; Jan Claassen, MD, PhD, Columbia University, NYC, NY; Abbas Ali, MD, AJ Layon, MD, Angela Miller, MBA, SSBB, The Geisinger Medical Center, Danville, PA; Eileen Maloney Wilensky, Monisha Kumar, MD, Joshua M Levine, MD, University of Pennsylvania, Philadelphia, PA; Ivan L Maldonado, Ministry St Joseph's Hospital, Marshfield, WI; Michael Schneck, MD, Loyola University, Chicago, IL; Abhijit Lele, MD, University of Kansas Medical Center, Kansas City, KS; Anand K Sarma, MD, Medical College of Virginia, Richmond, VA; Moussa F. Yazbeck, MD, John Muir Health, Walnut Creek, CA; Greg Johnston, Emory University Hospital, Atlanta; Adrian A Jarquin-Valdivia, TriStar Centennial Medical Center, Nashville, TN; Lindsey Johnson MD, Halifax Health, Port Orange, FL; Lauren Kuisle, Swedish Medical Center, Aurora, CO; Rehan Sajjad, Aurora St Luke's Medical Center, Milwaukee, WI; Scott Glickman, Six Points Neuroscience; Rachel Garvin, Augusto Parra, MD, University of Texas Health Science Center San Antonio; Michele DeFilippis, Morristown Medical Center, Morristown; Jeffrey J Fletcher, Bronson Methodist Hospital, Kalamazoo, MI; W David Freeman, MD, Mayo Clinic, Jacksonville, FL; Vivek A. Rao, MD, Redwood City Medical Center, Redwood City, CA; Huitzilil Mauricio Olmecah, Loma Linda University Medical Center, Loma Linda, CA; Guy Dugan, MD, Alexian Brothers Medical Center, Elk Grove Village, IL; Irene B Medary, MD, Orlando Health, Orlando, FL; Robert Hoesch, MD, PhD, Intermountain Medical Center, Salt Lake City, UT; Scott S Brehaut, MD, Faxton St. Luke's Healthcare, Utica, NY; Arash Afshinnik, MD, Ochsner Health System, New Orleans, LA; Melissa Moreda, Carmelo Graffagnino, MD, Daniel T Laskowitz, MD, Duke University Medical Center, Durham, NC; Andrew Naidech, MD, Brandon Francis, MD, Michael Berman, BA, Northwestern University, Chicago, IL; Eljim Tesoro, MD, University of Illinois at Chicago, IL; Joshua Medow, MD, University of Wisconsin, Madison, WI; Dedrick Jordan, MD, PhD, University of North Carolina at Chapel Hill, NC; Venkatesh Aiyagari, MD, The University of Texas Southwestern Medical Center, Dallas, TX; Axel Rosengart, MD, NYPH-Weill Cornell Medical

College, New York, NY; Michael De Georgia, MD, University Hospitals Case Medical Center, Cleveland, OH; Susana Bowling, MD, Summa Health System, Akron, OH; Mohamed Sharaby, Barnett Nathan, MD, The University of Virginia Health System, Charlottesville, VA; Ryan Landry, RN, Cullen Hebert, MD, Our Lady of the Lake RMC, Baton Rouge, LA; Kathleen E Hubner, St Vincent's Hospital, Indianapolis, IN; Navaz Karanjia, MD, University of California at San Diego, CA; Bradley Hightower, MD, Kathie Cummings, Jennifer Kirkwood, University of Oklahoma Health Sciences Center, Oklahoma City, OK; Jeffrey I Frank, MD, University of Chicago, Chicago, IL; Ameer Hassan, MD, Olive Sanchez, Valley Baptist Hospital, Harlingen, TX; Steve Cordina, MD, University of South Alabama, Mobile, AL. *Venezuela:* Jacobo Elias Mora, Hospital Universitario Luis Razetti, Puerto La Cruz. *Vietnam:* Tuan Van Bui, Cho Ray Hospital, Ho Chi Minh City.

## Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Published online: 04 September 2019

## References

- Kramer AH, Zygun DA. Do neurocritical care units save lives? Measuring the impact of specialized ICUs. *Neurocrit Care*. 2011;14(3):329–33.
- Suarez JL. Outcome in neurocritical care: advances in monitoring and treatment and effect of a specialized neurocritical care team. *Crit Care Med*. 2006;34(9 Suppl):S232–8.
- Markandaya M, Thomas KP, Jahromi B, et al. The role of neurocritical care: a brief report on the survey results of neurosciences and critical care specialists. *Neurocrit Care*. 2012;16(1):72–81.
- Xian Y, Fonarow GC, Reeves MJ, et al. Data quality in the American Heart Association Get With The Guidelines-Stroke (GWTG-Stroke): results from a national data validation audit. *Am Heart J*. 2012;163(3):392–8.
- Yue JK, Vassar MJ, Lingsma HF, et al. Transforming research and clinical knowledge in traumatic brain injury pilot: multicenter implementation of the common data elements for traumatic brain injury. *J Neurotrauma*. 2013;30(22):1831–44.
- Maas AI, Menon DK, Steyerberg EW, et al. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI): a prospective longitudinal observational study. *Neurosurgery*. 2015;76(1):67–80.
- Faigle R, Marsh EB, Llinas RH, Urrutia VC, Gottesman RF. ICAT: a simple score predicting critical care needs after thrombolysis in stroke patients. *Crit Care*. 2016;20:26.
- Suarez JL, Martin RH, Bauza C, Georgiadis A, Venkatasubba Rao CP, Calvillo E, Hemphill JC III, Sung G, Oddo M, Taccone FS, LeRoux PD. Worldwide organization of neurocritical care: results from the PRINCE Study Part 1. *Neurocrit Care*. 2019. <https://doi.org/10.1007/s12028-019-00750-3>.
- Suarez JL, Geocadin R, Hall C, et al. The neurocritical care research network: NCRN. *Neurocrit Care*. 2012;16(1):29–34.
- (ESICM) ESICM. <https://www.esicm.org/>. Accessed 31st Jan 2019.
- (LABIC) LABIC. <http://www.internationalbrain.org/articles/latin-american-brain-injury-consortium-labic/>. Accessed 31 Jan 2019.
- (ANZICS-CTG) CTGotAaNZICS.
- (CCCTG) CCCTG. <https://www.ccctg.ca/>. Accessed 31st Jan 2019.
- (IGNITE) loGNTe. <https://www.dgni.de/forschung/84-ignite-initiative-of-german-neurointensive-trial-engagement.html>. Accessed 31st Jan 2019.
- (CUHK) CUoHK. <http://www.cuhk.edu.hk/english/index.html>. Accessed 31st Jan 2019.
- Society IPACCM. <https://currents.neurocriticalcare.org/blogs/currents-editor/2018/09/18/1st-regional-neurocritical-care-meeting-in-the->
- NINDS. 2018. <https://www.commondataelements.ninds.nih.gov/#page=Default>. Accessed 28 Dec 2018.
- REDCAP. <https://www.project-redcap.org/>.
- Bank TW. GNI per capita, Atlas Method.
- Angus DC, Shorr AF, White A, et al. Critical care delivery in the United States: distribution of services and compliance with Leapfrog recommendations. *Crit Care Med*. 2006;34(4):1016–24.
- Bakhru RN, McWilliams DJ, Wiebe DJ, Spuhler VJ, Schweickert WD. Intensive care unit structure variation and implications for early mobilization practices. An international survey. *Ann Am Thorac Soc*. 2016;13(9):1527–37.
- Devlin JW, McKenzie C. Expanding the reach of critical care pharmacists globally. *Crit Care Med*. 2018;46(2):328–30.
- Suarez JL, Zaidat OO, Suri MF, et al. Length of stay and mortality in neurocritically ill patients: impact of a specialized neurocritical care team. *Crit Care Med*. 2004;32(11):2311–7.
- Pronovost PJ, Angus DC, Dorman T, Robinson KA, Dremsizov TT, Young TL. Physician staffing patterns and clinical outcomes in critically ill patients: a systematic review. *JAMA*. 2002;288(17):2151–62.
- Varela PN, Conti MM, Spanaki MV, et al. The impact of a neurointensivist-led team on a semiclosed neurosciences intensive care unit. *Crit Care Med*. 2004;32(11):2191–8.
- Sakr Y, Jaschinski U, Wittebole X, et al. Sepsis in intensive care unit patients: worldwide data from the intensive care over nations audit. *Open Forum Infect Dis*. 2018;5(12):ofy313.
- Vincent JL, Marshall JC, Namendys-Silva SA, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med*. 2014;2(5):380–6.
- Abe T, Madotto F, Pham T, et al. Epidemiology and patterns of tracheostomy practice in patients with acute respiratory distress syndrome in ICUs across 50 countries. *Crit Care*. 2018;22(1):195.
- Durbin CG Jr. Tracheostomy: why, when, and how? *Respir Care*. 2010;55(8):1056–68.
- Suarez JL, Tarr RW, Selman WR. Aneurysmal subarachnoid hemorrhage. *N Engl J Med*. 2006;354(4):387–96.
- Gruenberg DA, Shelton W, Rose SL, Rutter AE, Socaris S, McGee G. Factors influencing length of stay in the intensive care unit. *Am J Crit Care Offic Publ Am Assoc Crit Care Nurses*. 2006;15(5):502–9.
- Balestreri M, Czosnyka M, Chatfield DA, et al. Predictive value of Glasgow Coma Scale after brain trauma: change in trend over the past ten years. *J Neurol Neurosurg Psychiatry*. 2004;75(1):161–2.
- Hoffmann M, Lefering R, Rueger JM, et al. Pupil evaluation in addition to Glasgow Coma Scale components in prediction of traumatic brain injury and mortality. *Br J Surg*. 2012;99(Suppl 1):122–30.
- Elias KM, Moromizato T, Gibbons FK, Christopher KB. Derivation and validation of the acute organ failure score to predict outcome in critically ill patients: a cohort study. *Crit Care Med*. 2015;43(4):856–64.
- Wunsch H, Guerra C, Barnato AE, Angus DC, Li G, Linde-Zwirble WT. Three-year outcomes for medicare beneficiaries who survive intensive care. *JAMA*. 2010;303(9):849–56.
- Hua MS, Li G, Blinderman CD, Wunsch H. Estimates of the need for palliative care consultation across united states intensive care units using a trigger-based model. *Am J Respir Crit Care Med*. 2014;189(4):428–36.
- Cao L, Song W. Do-not-resuscitate orders in critical care elderly: no age discrimination against elderly in a community hospital. *Arch Intern Med*. 1998;158(10):1154.