CHEST

Decision-Making on Withholding or Withdrawing Life Support in the ICU

A Worldwide Perspective

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BACKGROUND: Many critically ill patients who die will do so after a decision has been made to withhold/withdraw life-sustaining therapy. The objective of this study was to document the characteristics of ICU patients with a decision to withhold/withdraw life-sustaining treatment, including the types of supportive treatments used, patterns of organ dysfunction, and international differences, including gross national income (GNI).

METHODS: In this observational cohort study conducted in 730 ICUs in 84 countries, all adult patients admitted between May 8, 2012, and May 18, 2012 (except admissions for routine postoperative surveillance), were included.

RESULTS: The analysis included 9,524 patients, with a hospital mortality of 24%. A decision to withhold/withdraw life-sustaining treatment was reported during the ICU stay in 1,259 patients (13%), including 820 (40%) nonsurvivors and 439 (5%) survivors. Hospital mortality in patients with a decision to withhold/withdraw life-sustaining treatment was 69%. The proportion of deaths in patients with a decision to withhold/withdraw life-sustaining treatment ranged from 10% in South Asia to 67% in Oceania. Decisions to withhold/withdraw life-sustaining treatment were less frequent in low/lower-middle GNI countries than in high GNI countries (6% vs 14%; $P < .001$). Greater disease severity, presence of ≥ 2 organ failures, severe comorbidities, medical and trauma admissions, and admission from the ED or hospital floor were independent predictors of a decision to withhold/withdraw life-sustaining treatment.

CONCLUSIONS: There is considerable worldwide variability in decisions to withhold/withdraw life-sustaining treatments. Interestingly, almost one-third of patients with a decision to withhold/withdraw life-sustaining treatment left the hospital alive. CHEST 2017; 152(2):321-329

KEY WORDS: decision-making; end-of-life; ethics

ABBREVIATIONS: eCRF = electronic case report form; GNI = gross national income; ICON = Intensive Care Over Nations; RRT = renal replacement therapy; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment

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FUNDING/SUPPORT: The authors have reported to *CHEST* that no funding was received for this study.

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DOI: http://dx.doi.org/10.1016/j.chest.2017.04.176

The progress of modern medicine has enabled organ function to be supported artificially in many patients who would otherwise die. Although it is well recognized that the majority of ICU deaths are preceded by a decision to limit life-sustaining treatment in North America and Europe,[1-3] these practices are less well defined in other parts of the world. A systematic review that included 56 studies from almost 1,000 ICUs in > 30 countries found substantial variability in the prevalence of withdrawal of life-sustaining treatment worldwide.[4] Decisions to limit life-sustaining treatment are influenced by many factors, including the severity and reversibility of the acute illness, the presence and severity of comorbidities, age, societal values, religious and cultural beliefs, legal concerns, and the subjective evaluation of the benefits and burdens of life support.[1,5-10]

We hypothesized that decisions to limit life-sustaining therapy would vary around the globe and would be more common in countries with a low gross national income (GNI) than in those with higher GNI. We therefore used a large prospective worldwide database to explore the characteristics of patients who received a decision to withhold/withdraw life-sustaining therapy during their ICU stay. The predictive factors for receiving such a decision were also evaluated.

Materials and Methods

This study was a preplanned secondary analysis of the international Intensive Care Over Nations (ICON) audit, which prospectively collected data on all adult (aged > 16 years) patients admitted to a participating ICU (see e-Appendix 1 for list of centers) between May 8, 2012, and May 18, 2012.[11] The ICON study was a worldwide audit, endorsed by the World Federation of Societies on Intensive and Critical Care. Recruitment for participation was by open invitation, through national scientific societies, national and international meetings, and individual contacts. Participation was voluntary. Institutional review board approval was obtained by the participating institutions according to local ethical regulations.

Electronic case report forms (eCRFs) were provided by the investigators using a secure Internet-based website. Patients admitted for < 24 h for routine postoperative surveillance and those readmitted to the ICU during the study period were excluded. Data were collected daily for a maximum of 28 days in the ICU, and patients were followed up for outcome data until death, hospital discharge, or for a maximum of 60 days. Validity checks were made concurrent with data entry on the eCRF, including plausibility checks within each variable and between variables.[11] Availability of outcome parameters was also verified by the coordinating center, and any doubts were clarified with the center in question. There was no on-site monitoring, and there was no attempt to assess interrater reliability or validity for the question about withholding/withdrawing life support.

Definitions are provided in the main study publication.[11] Clinical and laboratory data for Simplified Acute Physiology Score (SAPS) II were reported as the worst values within 24 h after admission.[12] Organ function was assessed daily using the Sequential Organ Failure Assessment (SOFA) score.[13] The follow-up section of the eCRF included the question "Was there a decision to withhold/withdraw a life-sustaining measure at any time during the ICU stay?" This question required a yes/no answer. Subjects with missing data regarding this question and those still in the ICU or hospital after 60 days (maximum observation period) were excluded from this analysis.

For the purposes of the present study, the world was divided into nine geographical regions: North America, South America, Western Europe, Eastern Europe, Middle East, South Asia, East and Southeast Asia, Oceania, and Africa (see e-Appendix 1 for list of countries in each region).[11] Individual countries were also classified into three groups according to their 2011 GNI per person, using thresholds defined by the World Bank Atlas method: GNI less than US $4,035 was defined as low and lower-middle income; $4,036 to $12,475 was defined as upper-middle income; and greater than $12,476 was defined as high income.

Data are shown as means with SDs, medians and interquartile ranges, or numbers and percentages. For continuous variables, normality assumption checking was performed by inspection of residual and normal plots. Differences between groups in the distribution of variables were assessed by using analysis of variance, Kruskal-Wallis test, the Student *t* test, Mann-Whitney test, chi-square test, or the Fisher exact test as appropriate. The least significant difference testing procedure was used for pairwise comparisons.

To identify independent risk factors for a decision to withhold/withdraw life-sustaining treatment and because of the hierarchical structure of the data, a multivariable analysis was performed, using a multilevel binary logistic model with three levels: patient (level 1: age, sex, SAPS II score, type of admission, source of admission, number of organ failures, treatment with mechanical ventilation or renal replacement therapy [RRT], presence of sepsis, and comorbidities), hospital (level 2: type of hospital, ICU specialty, ICU volume, and number of staffed ICU beds), and country (level 3: GNI). The dependent variable was decision to withhold/withdraw life-sustaining treatment.

For parameter testing, the likelihood ratio test was used. Colinearity between variables was checked by inspection of the correlation between them, by looking at the correlation matrix of the estimated parameters. The results of fixed effects (measures of association) are given as ORs with their 95% CIs. Random effects (measures of variation) measures included the variances and their SEs.

Data were analyzed using IBM SPSS Statistics software, version 22, for Windows (IBM SPSS Statistics, IBM Corporation) and MLwiN version 2.28. All reported *P* values are two-sided, and a *P* value < .05 was considered to indicate statistical significance.

Results

Of the 10,069 patients included in the ICON audit, 539 were excluded from this analysis because they were still in the ICU or hospital after 60 days and six because they had no answer to the question concerning a decision to withhold/withdraw life-sustaining treatment. The study cohort therefore included 9,524 patients, whose clinical data are shown in Table 1; 2,076 patients died. A decision to withhold/withdraw life-sustaining treatment was taken during the ICU stay in 1,259 (13%) patients, including in 820 (40%) of the hospital nonsurvivors and in 439 (5%) of the survivors.

At admission, patients who had a decision to withhold/withdraw life-sustaining treatment during their ICU stay were older, had higher SAPS II and SOFA scores, more organ failures, and were receiving more organ support, including mechanical ventilation and RRT. They were also more likely to have a central venous, arterial, or pulmonary artery catheter in situ; more likely to have been admitted for medical reasons; and more likely to have a diagnosis of infection or sepsis than patients without such a decision (Table 1). During the ICU stay, renal failure was particularly common in patients with a decision to withhold/withdraw life-sustaining treatment (e-Fig 1). The ICU length of stay was longer in the survivors with a decision to withhold/withdraw life-sustaining treatment than in those without (4.0 [2.0-8.0] days vs 3.0 [2.0-6.0] days; $P < .001$). ICU (56% vs 11%) and hospital (69% vs 17%) mortality rates were higher in patients with a decision to withhold/withdraw life-sustaining treatment than in those without (both $P < .001$).

Patients from ICUs in the Middle East had the highest severity scores and mortality rates, whereas those from North America and Asia had the lowest (e-Table 1). The proportion of patients who received a decision to withhold/withdraw life-sustaining treatment varied from 3% in South Asia to 30% in East and Southeast Asia; in the nonsurvivors, proportions varied from 10% in South Asia to > 65% in North America and Oceania (Fig 1).

Decisions to withhold/withdraw life-sustaining treatment were more frequently reported in high GNI countries than in low/lower-middle GNI countries (14% vs 6%; $P < .05$) (Table 2). For nonsurvivors, the frequency of a decision to withhold/withdraw life-sustaining treatment was significantly higher in high GNI countries (48%) than in upper-middle (27%) and low/lower-middle (20%) (both $P < 0.05$) GNI countries. Patients with a decision to withhold/withdraw life-sustaining treatment in high GNI countries were older, more severely ill, and had a longer duration of hospital stay than those in low/lower-middle GNI countries. Mechanical ventilation and RRT were used more frequently in patients with a decision to withhold/withdraw life-sustaining treatment in high GNI countries than in lower income countries (Fig 2).

In multivariable analysis, greater severity of disease, the presence of ≥ 2 organ failures, and the presence of solid or metastatic cancer, COPD, and heart failure (NYHA III/IV) were independent predictors of a decision to withhold/withdraw life-sustaining therapy (Table 3). A medical or trauma admission, the source of admission, and being admitted to a medical or mixed ICU rather than a surgical ICU were also independent predictors of a decision to withhold/withdraw life-sustaining therapy. After controlling for patient and hospital factors and GNI, between-hospital variation was about twice the between-country variation; both remained significant and could not be explained by the considered factors.

Discussion

This multicenter international study included a large number of countries and regions and reported variables that may independently affect end-of-life decisions in a worldwide perspective, including the GNI, which has rarely been evaluated in previous studies. The findings of this study can be summarized in five points. First, approximately 13% of all ICU patients, almost 40% of nonsurvivors, and 5% of survivors had a decision to withhold/withdraw life-sustaining measures at some time during the ICU stay. The percentage of hospital nonsurvivors with such a decision varied worldwide, from 10% to about 65%. Second, patients with a decision to withhold/withdraw life-sustaining treatment had high ICU and hospital mortality rates. Third, decisions were more common in patients admitted to upper-middle and high GNI countries compared with lower GNI countries (although these differences disappeared after adjusting for covariates). Fourth, variability in the prevalence of decisions on life-sustaining measures was higher for hospitals within countries than between countries. Finally, medical and trauma patients, patients with greater disease severity, those with major comorbidities, and those with ≥ 2 organ failures were more likely to receive a decision to withhold/withdraw life-sustaining treatment.

Decisions to withhold/withdraw life-sustaining treatment were less frequently made during the ICU stay

TABLE 1] Characteristics of the Study Cohort on Admission to the ICU Stratified According to Whether a DLST Was Made

Parameter	All Patients	No Decision	Decision	*P*
No. of patients	9,524 (100)	8,265 (86.8)	1,259 (13.2)	
Age, y	60.1 ± 18.1	59.4 ± 18.0	64.4 ± 17.5	< .001
Male[a]	5,659 (60.1)	4,936 (60.4)	723 (58.2)	.13
Severity scores				
SAPS II score	40.1 ± 18.3	38.2 ± 17.4	52.1 ± 19.6	< .001
SOFA score at admission	6.0 ± 4.4	5.6 ± 4.2	8.3 ± 4.7	< .001
Max SOFA score	7.5 ± 4.9	7.1 ± 4.7	10.7 ± 5.2	< .001
Type of admission[b]				< .001
Surgical (nontrauma)	3,246 (36.0)	2,957 (37.7)	289 (24.8)	
Medical	5,107 (56.6)	4,323 (55.0)	784 (67.3)	
Trauma	608 (6.7)	522 (6.6)	86 (7.4)	
Other	57 (0.6)	51 (0.6)	6 (0.5)	
Source of admission				< .001
Other hospital	922 (9.7)	787 (9.5)	135 (10.7)	
ED/ambulance	3,632 (38.1)	3,084 (37.3)	548 (43.5)	
OR/recovery room	1,724 (18.1)	1,602 (19.4)	122 (9.7)	
Hospital floor	2,457 (25.8)	2,073 (25.1)	384 (30.5)	
Other	789 (8.3)	719 (8.7)	70 (5.6)	
Comorbidities				
COPD	1,171 (12.3)	963 (11.7)	208 (16.5)	< .001
Cancer	989 (10.4)	820 (9.9)	169 (13.4)	< .001
Metastatic cancer	318 (3.3)	240 (2.9)	78 (6.2)	< .001
Hematologic cancer	200 (2.1)	165 (2.0)	35 (2.8)	.07
Insulin	919 (9.6)	791 (9.6)	128 (10.2)	.5
Heart failure, NYHA functional class III/IV	878 (9.2)	704 (8.5)	174 (13.8)	< .001
Chronic renal failure	864 (9.1)	726 (8.8)	138 (11.0)	.01
HIV infection	66 (0.7)	56 (0.7)	10 (0.8)	.64
Cirrhosis	339 (3.6)	274 (3.3)	65 (5.2)	< .001
Immunosuppression	328 (3.4)	271 (3.3)	57 (4.5)	.02
Steroid therapy	331 (3.5)	272 (3.3)	59 (4.7)	.01
Chemotherapy	254 (2.7)	209 (2.5)	45 (3.6)	.03
Infectious status				< .001
Infection	3,428 (36.0)	2,825 (34.2)	603 (47.9)	
Sepsis	1,187 (12.5)	994 (12.0)	193 (15.3)	
Septic shock	1,539 (16.2)	1,184 (14.3)	355 (28.2)	
No. of organ failures				< .001
None	2,366 (24.8)	2,221 (26.9)	145 (11.5)	
1 organ	2,627 (27.6)	2,436 (29.5)	191 (15.2)	
2 organs	1,843 (19.4)	1,601 (19.4)	242 (19.2)	
3 organs	1,309 (13.7)	1,039 (12.6)	270 (21.4)	
> 3 organs	1,379 (14.5)	968 (11.7)	411 (32.6)	
Procedures				
Mechanical ventilation	5,058 (53.1)	4,166 (50.4)	892 (70.8)	< .001
Renal replacement therapy	1,135 (11.9)	908 (11.0)	227 (18.0)	< .001

(Continued)

TABLE 1] *(Continued)*

Parameter	All Patients	No Decision	Decision	*P*
Central venous catheter	5,471 (57.4)	4,613 (55.8)	858 (68.1)	< .001
Arterial catheter	5,276 (55.4)	4,478 (54.2)	798 (63.4)	< .001
Pulmonary artery catheter	1,155 (12.1)	968 (11.7)	187 (14.9)	< .01
ICU stay, median (IQR)[c]	3.0 [2.0-6.0]	3.0 [2.0-6.0]	4.0 [2.0-8.0]	< .001
Hospital stay, median (IQR)[c]	11.0 [6.0-21.0]	11.0 [6.0-21.0]	13.0 [6.0-28]	.02
ICU mortality[d]	1,566 (17.2)	884 (11.2)	682 (55.6)	< .001
Hospital mortality[e]	2,076 (23.8)	1,256 (16.7)	820 (68.7)	< .001

Data are presented as No. (%) or mean ± SD unless otherwise indicated. DLST = decision to withhold/withdraw life-sustaining treatment; NYHA = New York Heart Association; OR = operating room; SAPS = simplified acute physiology score; SOFA = sequential organ failure score.
[a]Missing data, n = 115 (percentages are calculated after excluding missing values).
[b]Missing data, n = 506 (percentages are calculated after excluding missing values).
[c]In survivors only.
[d]Missing data, n = 395 (percentages are calculated after excluding missing values).
[e]Missing data, n = 791 (percentages are calculated after excluding missing values).

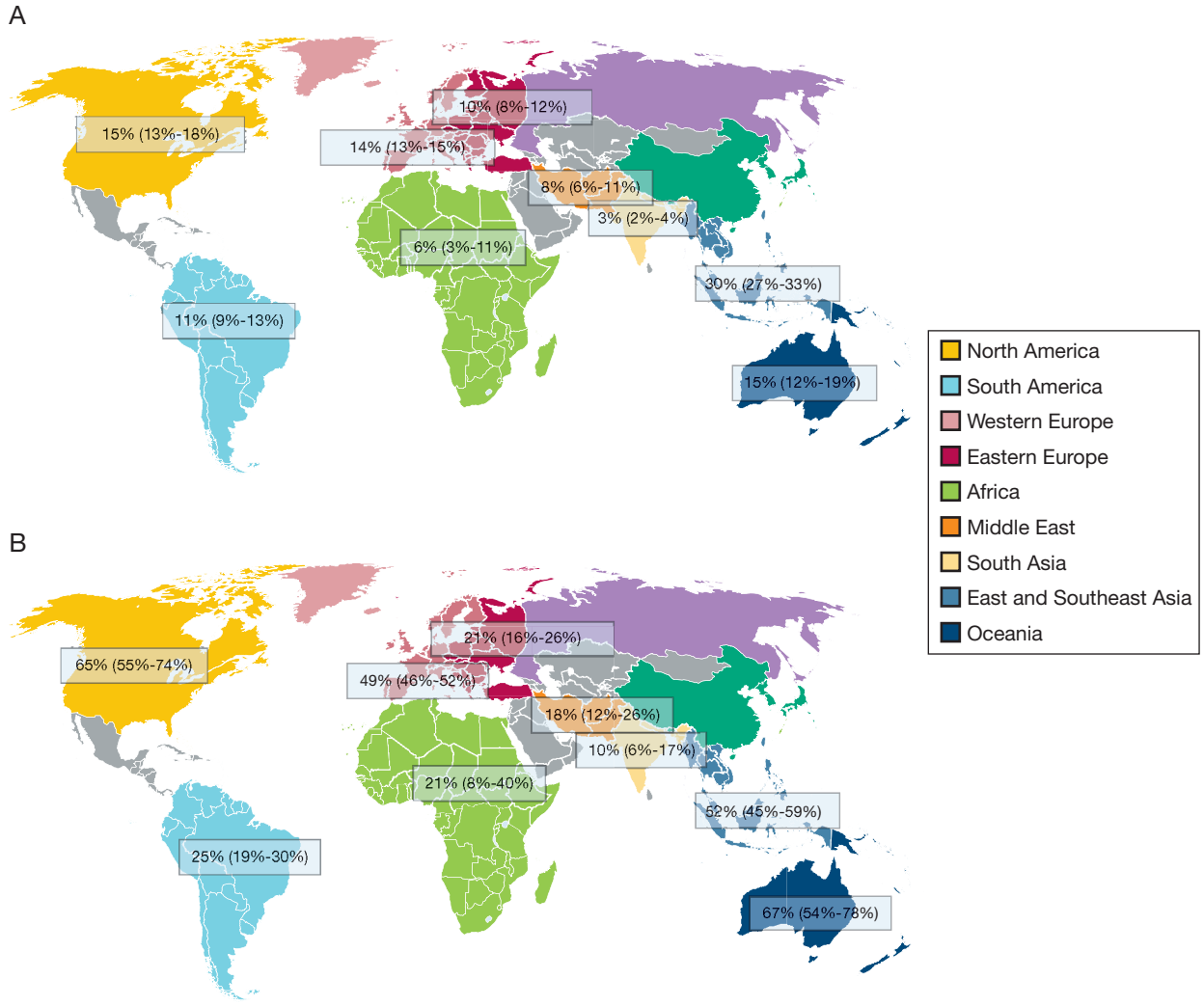


Figure 1 – *Proportion of patients (with 95% CIs) with a decision to limit or withdraw life-sustaining treatment in (A) the entire study population and (B) the hospital nonsurvivors according to geographical region.*

TABLE 2] Characteristics of the Patients With a DLST According to the GNI

Parameter	All Patients	High GNI	Upper-Middle GNI	Low/Lower-Middle GNI
Total No. of patients	9,524	6,004	2,355	1,165
DLST (%) in the whole cohort	1,259 (13.2)	816 (13.6)	374 (15.9)[a]	69 (5.9)[a]
DLST (%) in the hospital nonsurvivors	820 (39.5)	621 (48.4)	161 (26.6)[a]	38 (20.2)[a]
Age, y	64.4 ± 17.5	68.0 ± 15.1	57.7 ± 19.7[a]	58.9 ± 18.8[a]
Severity scores				
SAPS II score	52.1 ± 19.6	55.0 ± 19.1	46.9 ± 19.6[a]	45.7 ± 17.8[a]
SOFA score at admission	8.3 ± 4.7	8.8 ± 4.7	7.6 ± 4.5[a]	6.6 ± 4.2[a]
Septic shock	355 (28.2)	264 (32.4)	76 (20.3)[a]	15 (21.7)
Length of ICU stay, median (IQR), d	4.0 [2.0-8.0]	4.0 [1.0-8.0]	4.0 [2.0-8.0]	3.0 [1.0-6.0]
Length of hospital stay, median (IQR), d	6.0 [2.0-14.0]	6.0 [2.0-14.0]	7.0 [3.0-16.0][a]	3.0 [1.0-6.0][a]
ICU mortality	682 (55.6)	515 (63.7)	135 (38.4)[a]	32 (49.2)[a]
Hospital mortality	820 (68.7)	621 (77.2)	161 (49.2)[a]	38 (60.3)[a]

Data are presented as No. (%) or mean ± SD unless otherwise indicated. GNI = gross national income; IQR = interquartile range. See Table 1 legend for expansion of other abbreviations.
[a]Statistically significant vs high GNI at 5% level.

in hospital nonsurvivors in Eastern Europe (21%) than in Western Europe (49%). In the large Ethicus study[3] conducted in 1999 to 2000 in 17 European countries, a decision to limit life-sustaining treatment was made in 10% of all ICU admissions. At that time, decisions to withhold life-sustaining treatment were similarly distributed across European regions (34%-40%), but withdrawal was less frequently adopted in southern (18%) than in central (34%) and northern (47%) regions. We did not collect data separately for withholding and withdrawing decisions because the distinction between the two is not always clear; for example, a decision to withhold RRT in a patient who develops acute renal failure may be associated with a decision to withdraw mechanical ventilation, simultaneously or later, or even to increase the doses of sedative agents.

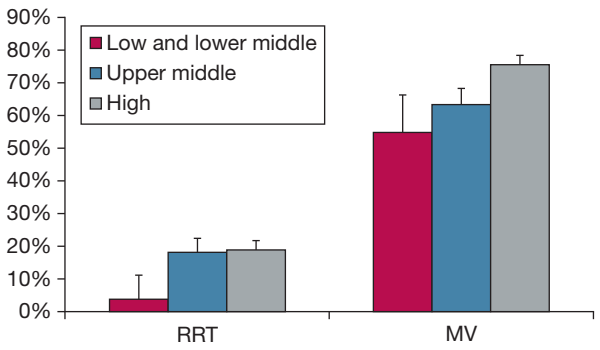


Figure 2 – *Prevalence of MV and RRT in patients with decision to withhold or withdraw life-sustaining treatment according to GNI. GNI = gross national income; MV = mechanical ventilation; RRT = renal replacement therapy.*

The percentage of ICU nonsurvivors from North American ICUs in whom a decision was made during the ICU stay to limit life-sustaining treatment was 76%. In 1998, a study in 110 US institutions reported that 10% of 5,910 patients who died in the ICU had life support withheld and 38% had life support withdrawn.[14] This observation suggests that the proportion of ICU patients who die after a decision to limit life-sustaining therapy may have increased in North America in recent years.

In Asia, decisions to withhold/withdraw life-sustaining treatment are less commonly made in South Asia than in East and Southeast Asia, which may be related to economic and cultural factors. In the Asian Collaboration for Medical Ethics (ACME) Study (a survey conducted in 16 Asian countries), 70.2% of the respondents reported that they commonly withheld life-supporting treatment, and 20.7% reported that they commonly withdrew treatment.[15] Interestingly, in a questionnaire survey, Chinese physicians from Hong Kong, with its unique colonial history and western influence on education, had attitudes more similar to those reported in Europe,[10] with 99% reporting withholding and 89% withdrawing in Hong Kong compared with only 54% and 32%, respectively, in the rest of China.[16]

TABLE 3] Multivariable Analysis of Factors Associated With a DLST

Variables	OR (95% CI)	*P*
Fixed-effects, varying within clusters		
Age	1.01 (0.99-1.02)	.106
Male sex	0.95 (0.84-1.07)	.416
SAPS II	1.03 (1.02-1.04)	< .001
Type of admission (%)		
Surgical	Ref	NA
Medical	1.44 (1.17-1.76)	< .001
Trauma	2.40 (1.71-3.38)	< .001
Other	1.52 (0.67-3.46)	.320
Source of admission		
OR/recovery	Ref	NA
Other hospital	1.92 (1.32-2.78)	.001
ED/ambulance	1.60 (1.11-2.31)	.012
Hospital floor	1.73 (1.26-2.38)	.001
Other	1.29 (0.92-1.83)	.143
No. of organ failure		
None	Ref	NA
1	1.20 (0.98-1.46)	.081
2	1.78 (1.38-2.29)	< .001
3	1.69 (1.31-2.18)	< .001
≥ 4	1.65 (1.13-2.42)	.010
Procedures		
Mechanical ventilation	1.17 (0.95-1.45)	.149
Renal replacement therapy	0.82 (0.65-1.03)	.092
Sepsis	1.04 (0.87-1.23)	.694
Comorbidities		
COPD	1.22 (1.02-1.47)	.031
Cancer	1.57 (1.28-1.92)	< .001
Metastatic cancer	1.92 (1.41-2.60)	< .001
Hematologic cancer	0.77 (0.54-1.10)	.147
Insulin	1.10 (0.86-1.41)	.456
Heart failure, NYHA functional class III/IV	1.45 (1.18-1.77)	< .001
Chronic renal failure	1.00 (0.83-1.19)	.978
HIV infection	0.57 (0.25-1.30)	.178
Cirrhosis	1.19 (0.82-1.71)	.364
Immunosuppression	1.21 (0.93-1.57)	.148
Fixed effects, constant within clusters		
Type of hospital		
Nonuniversity	Ref	NA
University/academic	0.96 (0.73-1.26)	.756
ICU volume		
< 250	Ref	NA
250-499	0.77 (0.39-1.54)	.463
500-749	0.93 (0.47-1.86)	.837
≥ 750	0.82 (0.41-1.63)	.562
ICU speciality		
Surgical	Ref	NA
Medical	2.14 (1.14-4.04)	.018
Mixed	1.68 (1.15-2.43)	.007
Others	2.29 (1.09-4.81)	.029
Staffed ICU beds		
< 15	Ref	NA
≥ 15	0.81 (0.65-1.00)	.051
GNI		
High	Ref	NA
Low and lower-middle	0.86 (0.35-2.11)	.742
Upper-middle	1.03 (0.48-2.21)	.941
Random effects		
Country		
Variance (SE)	0.44 (0.14)	
P	.002	
Hospital within country		
Variance (SE)	1.09 (0.13)	
P	< .001	

NA = not applicable. See Table 1 and 2 legends for expansion of other abbreviations.

In 2002, the SAPS III database evaluated practices in 14,488 patients from 282 ICUs in seven world regions and reported that 36% of the deaths occurred after a decision was made to limit life-supporting treatment, also noting wide variations in the incidence and characteristics of these decisions.[2] In a systematic review of 53 studies, Mark et al[4] reported variability among countries, among different ICUs within a country, and among different intensivists within one ICU. In nonsurvivors, death was preceded by withdrawal of life-supporting treatment in 42% of cases (range, 0%-84%), by withholding of life-supporting treatment in 27% (range, 5%-67%), and by both in 52% (range, 10%-82%). The marked international variability in decisions to withhold/withdraw life-sustaining therapy can be explained, in part, by multidimensional differences among countries, including physician and patient culture and religion, and medicolegal factors. Our finding that the variability in decisions was higher

for hospitals within a country than between countries suggests that the variance is due as much to variability in the approach or culture at the local hospital level as to that of different countries.

Interestingly, and in contrast to our hypothesis, decisions on withholding/withdrawing life-sustaining treatment were lower in nonsurvivors in low/lower-middle GNI countries than in those from higher GNI countries. A possible reason for this observation is that end-of-life decisions may be less explicit in low-income countries. Alternatively, there may be other barriers to making such decisions, such as lack of policies to support the provision of withholding/withdrawing care, incertitude regarding legislative support, and fewer opportunities for staff training. Interestingly, patients from ICUs in a high GNI country who had a decision to limit life-sustaining treatment were significantly older and more severely ill on admission than those from ICUs in lower GNI countries, potentially explaining the greater use of mechanical ventilation and RRT in these patients. It is also likely that therapeutic efforts are stopped earlier in low-income countries.

Patients with a decision to withhold/withdraw life-sustaining treatment were older than patients without a decision, but age was not an independent predictive factor for such decisions, in contrast with reports in other studies.[17,18] Older age, pre-existing severe comorbidities, emergency surgery, and medical admission were independent predictors of withdrawal of treatment in a cohort study of 118,199 patients in the United Kingdom, along with cardiopulmonary resuscitation in the 24 h prior to admission.[17] In another study that included 269,000 patients in the United States, patients aged ≥ 65 years and female patients were more likely to receive a decision to forgo life-supporting treatment, and those of black ethnicity were less likely.[18]

Azoulay et al[2] reported that, among other variables, medical admission, presence of comorbidities, cancer, and chronic heart failure (New York Heart Association functional class IV) were predictive of a decision to forgo life-sustaining therapies, whereas availability of an ED in the same hospital, presence of a full-time specialist, and physician's presence during nights and weekends decreased the incidence of a decision to forgo life-sustaining therapies. In a consensus paper, Joynt et al[19] reported that the following factors were considered important for triggering a decision to withhold/withdraw life-sustaining treatment: survival expected to be < 1 to 3 months, multiple organ failure (≥ 3 organs for ≥ 7 days, despite therapy), very severe brain injury, and the health-care team's opinion that the patient is receiving nonbeneficial therapy or the patient has a nonsurvivable injury. In our study, medical and, in particular, trauma admissions, the presence of ≥ 2 organ failures, the presence of solid or metastatic cancer, COPD, and heart failure (NYHA III/IV) were independent predictors of a decision to withhold/withdraw life-sustaining therapy.

The aim of withholding or withdrawing life-sustaining treatments is to remove treatments that no longer provide benefit and only prolong the dying process in terminally ill patients. For these patients, an important goal is to achieve the most comfortable death. Our study shows that having a decision to withhold/withdraw life-sustaining treatment does not necessarily mean that death is imminent or speed the dying process. ICU and hospital mortality rates were 56% and 69%, respectively, in patients with a decision to withhold/withdraw life-sustaining treatment. Likewise, in a cohort of 187,401 patients from the Australia and New Zealand Intensive Care Society database, 30% of patients with treatment limitations were ultimately discharged home.[20]

The present study has numerous strengths, including the prospective design, inclusion of consecutive admissions to a large number of ICUs, regions and countries, and collection of data that allowed multilevel analysis regarding patient, hospital, and country characteristics. This study also has several limitations. First, although the audit included many ICUs, the voluntary nature of participation and exclusion of patients admitted for < 24 h, readmitted to the ICU during the study period, or with a length of hospital stay > 60 days might have created some reporting bias. Second, patients were included over a 10-day period and may not reflect all ICU admissions. Third, country income was analyzed according to GNI, rather than according to the percentage of gross domestic product allocated specifically to health care. Fourth, in this post hoc analysis, important data that may influence variability in practice, such as religious beliefs, differences in legal regulations, and when the decision was made, were not available. Finally, the presence of an end-of-life decision was evaluated as a single event, not separated according to separate withhold or withdraw decisions, thus limiting direct comparison with some older studies.

Conclusions

These data confirm that many deaths in the hospital are preceded by a decision to withhold or withdraw life-sustaining therapy during the ICU stay, although there are considerable variations around the world. Decisions to limit life-sustaining treatment are more frequent in patients admitted to ICUs in countries with higher GNI. Global data on end-of-life decision-making, such as provided in this study, will help stimulate more open discussion of these issues.

Acknowledgments

Author contributions: S. M. L. acts as guarantor for the paper. S. M. L. and F. H. B. D. S. designed the study, analyzed the data, and drafted the article. S. M. L., S. M. J., A. E., S. V., A. B., I. M. L., Y. S., and J. L. V. participated in the original ICON study and revised the article for critical content. All authors read and approved the final manuscript.

Financial/nonfinancial disclosures: None declared.

Other contributions: The authors thank Hassane Njimi, PhD, for his help with the statistical analyses.

Additional information: The e-Appendix, e-Figure, and e-Table can be found in the Supplemental Materials section of the online article.

References

1. Cook D, Rocker G. Dying with dignity in the intensive care unit. *N Engl J Med*. 2014;370(26):2506-2514.
2. Azoulay E, Metnitz B, Sprung CL, et al. End-of-life practices in 282 intensive care units: data from the SAPS 3 database. *Intensive Care Med*. 2009;35(4):623-630.
3. Sprung CL, Cohen SL, Sjokvist P, et al. End-of-life practices in European intensive care units: the Ethicus Study. *JAMA*. 2003;290(6):790-797.
4. Mark NM, Rayner SG, Lee NJ, Curtis JR. Global variability in withholding and withdrawal of life-sustaining treatment in the intensive care unit: a systematic review. *Intensive Care Med*. 2015;41(9):1572-1585.
5. Ferrand E, Robert R, Ingrand P, Lemaire F. Withholding and withdrawal of life support in intensive-care units in France: a prospective survey. French LATAREA Group. *Lancet*. 2001;357(9249):9-14.
6. Gibbins J, McCoubrie R, Forbes K. Why are newly qualified doctors unprepared to care for patients at the end of life? *Med Educ*. 2011;45(4):389-399.
7. Price S, Schofield S. How do junior doctors in the UK learn to provide end of life care: a qualitative evaluation of postgraduate education. *BMC Palliat Care*. 2015;14:45.
8. Curtis JR, Vincent JL. Ethics and end-of-life care for adults in the intensive care unit. *Lancet*. 2010;376(9749):1347-1353.
9. Sprung CL, Maia P, Bulow HH, et al. The importance of religious affiliation and culture on end-of-life decisions in European intensive care units. *Intensive Care Med*. 2007;33(10):1732-1739.
10. Vincent JL. Forgoing life support in western European intensive care units: the results of an ethical questionnaire. *Crit Care Med*. 1999;27(8):1626-1633.
11. 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):380-386.
12. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA*. 1993;270(24):2957-2963.
13. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med*. 1996;22(7):707-710.
14. Prendergast TJ, Claessens MT, Luce JM. A national survey of end-of-life care for critically ill patients. *Am J Respir Crit Care Med*. 1998;158(4):1163-1167.
15. Phua J, Joynt GM, Nishimura M, et al. Withholding and withdrawal of life-sustaining treatments in intensive care units in Asia. *JAMA Intern Med*. 2015;175(3):363-371.
16. Weng L, Joynt GM, Lee A, et al. Attitudes towards ethical problems in critical care medicine: the Chinese perspective. *Intensive Care Med*. 2011;37(4):655-664.
17. Wunsch H, Harrison DA, Harvey S, Rowan K. End-of-life decisions: a cohort study of the withdrawal of all active treatment in intensive care units in the United Kingdom. *Intensive Care Med*. 2005;31(6):823-831.
18. Quill CM, Ratcliffe SJ, Harhay MO, Halpern SD. Variation in decisions to forgo life-sustaining therapies in US ICUs. *Chest*. 2014;146(3):573-582.
19. Joynt GM, Lipman J, Hartog C, et al. The Durban World Congress Ethics Round Table IV: health care professional end-of-life decision making. *J Crit Care*. 2015;30(2):224-230.
20. Godfrey G, Pilcher D, Hilton A, Bailey M, Hodgson CL, Bellomo R. Treatment limitations at admission to intensive care units in Australia and New Zealand: prevalence, outcomes, and resource use. *Crit Care Med*. 2012;40(7):2082-2089.

e-Appendix 1. Alphabetical list of participating centers by region and country

Africa

Angola: Clinica Sagrada Esperança (E Tomas)

Democratic Republic of Congo: Cliniques Universitaires De Kinshasa (E Amisi Bibonge)

Morocco: Chu Ibn Rochd Casablanca (B Charra); Ibn Sina Hospital (M Faroudy)

South Africa: Chris Hani Baragwanath Academic Hospital (L Doedens); Grey's Hospital (Z Farina); Sandton Medi Clinic (D Adler); Tygerberg Hospital (C Balkema); Union hospital Alberton (A Kok)

Tunisia: Bizerte Hospital (S Alaya); Military Hospital of Tunis (H Gharsallah)

East Europe

Albania: National Trauma Centre and Military Hospital, Tirana (D Muzha)

Bulgaria: Alexandrovska University Hospital (A Temelkov); Emergency University Hospital 'Pirogov' (G Georgiev); Tokuda Hospital Sofia (G Simeonov); Uh St Ekaterina Sofia (G Tsaryanski); University Hospital for Obstetrics and Gynaecology (S Georgiev); University Hospital Sveta Marina - Varna (A Seliman)

Croatia: General Hosp. Sibenik (S Vrankovic); University Hospital Centre "Sestre Milosrdnice" (Z Vucicevic); University Hospital Centre Zagreb (I Gornik); University Hospital for Infectious Diseases (B Barsic); University Hospital Dubrava (I Husedzinovic)

Czech Republic: Centre of Cardiovascular and Transplant Surgery (P Pavlik); Charles University Hospital (J Manak); IKEM, Prague (E Kieslichova); KNTB Zlín A.S. (R Turek); Krajska Nemocnice Liberec (M Fischer); Masarykova Nemocnice V Usti Nad Labem (R Valkova); St. Anne's University Hospital Brno (L Dadak); University Hospital Haradec Králové (P Dostal); University Hospital Brno (J Malaska); University Hospital Olomouc (R Hajek); University Hospital Plzen (A Židková); Charles University Hospital Plzen (P Lavicka)

Estonia: Tartu University Hospital (J Starkopf)

Georgia: Critical Care Medicine Institute (Z Kheladze); Jo Ann Medical Centre (M Chkhaidze); Kipshidze Central University Hospital (V Kaloiani)

Hungary: Dr. Kenessey Albert Hospital (L Medve); Fejér County St George Teaching Hospital (A Sarkany); Flor Ferenc County Hospital (I Kremer); Jávorszky Ödön Hospital (Z Marjanek); Peterfy Hospital Budapest (P Tamasi)

Latvia: Infectology Centre of Latvia (I Krupnova); Paul Stradins Clinical University Hospital (I Vanags); Riga East Clinical University Hospital (V Liguts)

Lithuania: Hospital of Lithuanian University of Health Sciences Kauno Klinikos (V Pilvinis); Vilnius University Hospital (S Vosylius); Vilnius University Hospital "Santariskiu Clinics", HSICU (G Kekstas); Vilnius University Hospital Santariskiu Clinics, CICU (M Balciunas)

Poland: Csk Mswia (J Kolbusz); Medical University (A Kübler); Medical University Of Wroclaw (B

Mielczarek); Medical University Warsaw (M Mikaszewska-Sokolewicz); Pomeranian Medical University (K Kotfis); Regional Hospital in Poznan (B Tamowicz); Szpital Powiatowy W Ostrowi Mazowieckiej (W Sulkowski); University Hospital, Poznam (P Smuszkiewicz); Wojewódzki Szpital Zakazny (A Pihowicz); Wojewódzkie Centrum Medyczne (E Trejnowska)
Romania: Emergency County Hospital Cluj (N Hagau); Emergency Institute for Cardiovascular Diseases (D Filipescu); Fundeni Clinical Institute (G Droc); Galati Hospital (M Lupu); Inbi "Prof. Dr. Matei Bals" (A Nica); Institute of Pulmonology Marius Nasta (R Stoica); Institutul Clinic Fundeni (D Tomescu); Sfantul Pantelimon Hospital (D Constantinescu); Spitalul Cf 2 Bucuresti (G Valcoreanu Zbaganu); "Luliu Hatieganu" University of Medicine and Pharmacy, Teaching Hospital of Infectious Diseases, Cluj-Napoca (A Slavcovici)
Russia: City Clinical Hospital No 40 (V Bagin); City Hospital No 40 (D Belsky); Clinical Hospital N.A. N.V.Solovyev (S Palyutin); Emergency Research Institute N.A. Djanelidze (S Shlyapnikov); Federal Research Centre Paediatric Haematology, Oncology and Immunology (D Bikkulova); Krasnoyarsk State Medical University, Krasnoyarsk Regional Hospital (A Gritsan); Medical Association "Novaya Bolnitsa" (G Natalia); Military Medical Academy (E Makarenko); Novosibirsk Medical University (V Kokhno); Omsk Regional Clinical Hospital (A Tolkach); Railway Hospital of Khabarovsk (E Kokarev); St Alexy Hospital (B Belotserkovskiy); State District Hospital (K Zolotukhin); Vishnevsky Institute of Surgery (V Kulabukhov)
Serbia: Clinic for Cardiac Surgery, Clinical Centre of Serbia (L Soskic); Clinic for Digestive Surgery, Clinical Centre Serbia (I Palibrk); Clinic for Vascular Surgery, Clinical Centre Nis (R Jankovic); Clinical Centre of Serbia (B Jovanovic); Clinical Centre of Serbia (M Pandurovic); Emergency Centre, Clinical Centre of Belgrade (V Bumbasirevic); General University Hospital (B Uljarevic); Military Medical Academy (M Surbatovic); Urology Hospital (N Ladjevic)
Slovakia: District Hospital (G Slobodianiuk); Faculty Hospital (V Sobona); University Hospital Bratislava-Hospital Ruzinov ICU (A Cikova); University Hospital Ruzinov Bratislava (A Gebhardtova)

East & Southeast Asia

China: A Tertiary Hospital (C Jun); Affiliated Hospital of Medical College Qingdao Universty (S Yunbo); Beijing Cancer Hospital ,Beijing Institute for Cancer Research (J Dong); Beijing Chaoyang Hospital (S Feng); Beijing Friendship Hospital (M Duan); Beijing Tongren Hospital Affiliate of Capital Medical University (Y Xu); Beijing University People's Hospital (X Xue); Beijing Luhe Hospital (T Gao); Cancer Hospital, Chinese Academy of Medical Sciences (X Xing); China Academy of Chinese Medical Sciences Guang 'An Men Hospital (X Zhao); Chuxiong, Yunnan Province, People's Hospital (C Li); Donge County People's Hospital of Shandong Province (G Gengxihua); Fu Wai Hospital, Chinese Academy of Medical Sciences (H Tan); Fujian Provincial Hospital (J Xu);

Fuxing Hospital, Capital Medicine University (L Jiang); Guangdong General Hospital (Q Tiehe); Henan Provincial People's Hospital (Q Bingyu); Xian Jiaotong University College of Medicine (Q Shi); Kunming Third People's Hospital (Z Lv); Lanzhou University Second Hospital (L Zhang); No 309th Hospital (L Jingtao); No.1 Hospital of China Medical University (Z Zhen); Peking University Shougang Hospital (Z Wang); Peking University Third Hospital (T Wang); Pla Navy General Hospital (L Yuhong); Qilu Hospital Shandong University (Q Zhai); Ruijin Hospital Affiliated Medical School of Jiaotong University, Shanghai (Y Chen); Shandong Provincial Hospital (C Wang); Shanghai 10th People's Hospital (W Jiang); Shanghai First People's Hospital (W Ruilan); Sichuan Provincial People's Hospital (Y Chen); Sichuan Provincial People's Hospital (H Xiaobo); Sir Run Run Shaw Hospital (H Ge); The Affiliated of Guiyang Medical College (T Yan); The Fifth People's Hospital of Shanghai, Fudan University (C Yuhui); The First Affiliated Hospital of Dalian Medical University (J Zhang); The First Affiliated Hospital of Suzhou University (F Jian-Hong); The First Affiliated Hospital of Xinjiang Medical University (H Zhu); The First Hospital of Jilin University (F Huo); The First Hospital of Jilin University (Y Wang); The First People's Hospital of Kunming (C Li); The General Hospital of Shenyang Military Region ,China (M Zhuang); The People's Hospital of Cangzhou (Z Ma); The Second Hospital of Jilin University (J Sun); The Second People's Hospital of Liaocheng City Shandong Province (L Liuqingyue); The Third Xiangya Hospital (M Yang); Tongde Hospital of Zhejiang Province (J Meng); Tongji University Shanghai East Hospital (S Ma); West China Hospital, Scu (Y Kang); Wuhan Centre Hospital (L Yu); Xiangya Hospital, Changsha, Hunan Province, China (Q Peng); Yantai Yuhuangding Hospital (Y Wei); Yantaishan Hospital, Shandong Province (W Zhang); Zhejiang Provincial People's Hospital (R Sun)

Hong Kong (China): Pamela Youde Nethersole Eastern Hospital (A Yeung); Princess Margaret Hospital (W Wan); Queen Elizabeth Hospital (K Sin); United Christian Hospital of Hong Kong SAR (K Lee)

Indonesia: Anestesi (M Wijanti); Pku Muhammadiyah Bantul, Yogyakarta (U Widodo); Rd Mattaher Hospital Jambi (H Samsirun); Rumah Sakit Pantai Indah Kapuk (T Sugiman); Sardjito Hospital (C Wisudarti); School of Medicine Unpad - Hasan Sadikin Hospital (T Maskoen)

Japan: Chiba Hokusoh Hospital, Nippon Medical School (N Hata); Chiba University Hospital (Y Kobe); Fujita Health University School of Medicine (O Nishida); Japanese Red Cross Maebashi Hospital (D Miyazaki); Jichi Medical University Hospital (S Nunomiya); Jikei University School of Medicine (S Uchino); Kimitsu Chuo Hospital (N Kitamura); Kochi Medical School (K Yamashita); Kyoto Prefectural University of Medicine (S Hashimoto); Nara Medical University Hospital (H Fukushima)

Malaysia: Hospital Sultanah Nur Zahirah, Kuala Terengganu, Terengganu, (N Nik Adib); Kuala Lumpur Hospital (L Tai); Queen Elizabeth Hospital 2 (B Tony)

Philippines: Cebu Velez General Hospital (R Bigornia); Chong Hua Hospital (R Bigornia); Perpetual

Succour Hospital (R Bigornia); The Medical City (J Palo)
Singapore: Alexandra Hospital (S Chatterjee); National University Health System (B Tan); Singapore General Hospital (A Kong); Tan Tock Seng Hospital (S Goh)
Taiwan: National Taiwan University Hospital (C Lee)
Thailand: Maharaj Nakorn Chiangmai Hospital, Chiaingmai University (C Pothirat); Prince of Songkla University (B Khwannimit); Ramathibodi Hospital (P Theerawit); Ramathibodi Hospital, Somdech Phra Debaratana Medical Centre (P Pornsuriyasak); Siriraj Hospital, Mahidol University (A Piriyapatsom)

Middle East
Egypt: Cairo University (A Mukhtar); Demerdash Surgical Intensive Care Unit (Dsicu); Ain Shams Faculty of Medicine (A Nabil Hamdy); Zaitoun Specialized Hospital (H Hosny)
Iran: Gums (A Ashraf); Imam Hossein Hospital, Sbums (M Mokhtari); Imamreza Hospital (S Nowruzinia); Laleh Hospital (A Lotfi); Shiraz University of Medical Sciences, SACRC (F Zand); Shiraz University of Medical Sciences (R Nikandish); Tehran Medical Sciences University (O Moradi Moghaddam)
Israel: Rabin Medical Centre (J Cohen); Sourasky Tel Aviv Medical Centre (O Sold)
Lebanon: Centre Hospitalier Du Nord (T Sfeir)
Oman: Sohar Hospital (A Hasan)
Palestinian Territories: Specialized Arab Hospital (D Abugaber)
Saudi Arabia: Almana General Hospital (H Ahmad); KFSHRC, Riyadh (T Tantawy); King Abdulaziz Medical City Riyadh (S Baharoom); King Abdulaziz University (H Algethamy); King Saud Medical City (A Amr); Riyadh Military Hospital (G Almekhlafi)
Turkey: Erciyes University Medical Faculty (R Coskun); Erciyes University Medical School (M Sungur); Gülhane Military Medical Academy (A Cosar); International Hospital, Istanbul (B Güçyetmez); Istanbul University Cerrahpasa Medical School Hospital (O Demirkiran); Istanbul University Istanbul Medical Faculty (E Senturk); Karadeniz Technical University, Medical Faculty (H Ulusoy); Memorial Atasehir Hospital (H Atalan); Pamukkale Universty (S Serin); Yuzuncu Yil Universitesy Medical Faculty (I Kati)
United Arab Emirates: Dubai Hospital (Z Alnassrawi); Mafraq Hospital (A Almemari); Sheikh Khalifa Medical City (K Krishnareddy); Tawam Hospital (S Kashef); The City Hospital (A Alsabbah)

North America
Canada: Hôpital Charles Lemoyne (G Poirier); St. Michael's Hospital (J Marshall); Toronto General Hospital (M Herridge); Toronto Western Hospital (M Herridge)
Puerto Rico: San Juan Hospital (R Fernandez-Medero)

United States: Christiana Care Health System (G Fulda); Cincinnati Children's Hospital Medical Centre (S Banschbach); El Camino Hospital (J Quintero); George Washington Hospital (E Schroeder); Hospital of The University of Pennsylvania (C Sicoutris); John H Stroger Hospital of Cook County (R Gueret); Mayo Clinic, CCM (R Kashyap); Mayo Clinic, PCC (P Bauer); Medical College of Wisconsin (R Nanchal); Northwestern Memorial Hospital (R Wunderink); Orlando Regional Medical Centre (E Jimenez); Washington Hospital Centre (A Ryan); Washington Hospital Centre,2H (A Ryan); Washington Hospital Centre, 2G (A Ryan); Washington Hospital Centre, 3H (A Ryan); Washington Hospital Centre, 3G (A Ryan); Washington Hospital Centre, 4H (A Ryan); Washington Hospital Centre, CVRR (A Ryan)

Oceania

Australia: Armadale Health Service (D Prince); Bendigo Hospital (J Edington); Canberra Hospital (F Van Haren); Flinders Medical Centre (A Bersten); Joondalup Health Campus (DJ Hawkins); Lismore Base Hospital (M Kilminster); Mater Adult Hospital (D Sturgess); Prince Charles Hospital, Brisbane (M Ziegenfuss); Royal Adelaide Hospital (S O' Connor); Royal Brisbane and Womens' Hospital (J Lipman); Royal Darwin Hospital (L Campbell); Royal Hobart Hospital (R Mcallister); Sir Charles Gairdner Hospital (B Roberts); The Queen Elizabeth Hospital (P Williams)
New Zealand: Auckland District Health Board (R Parke); Christchurch Hospital (P Seigne); Hawke's Bay Hospital (R Freebairn); Midcentral Health, Palmerston North Hospital (D Nistor); Middlemore Hospital (C Oxley); Wellington Hospital (P Young)

South America

Argentina: Cemic (Centro De Educación Médica E Investigaciones Clínicas) (R Valentini); Fleni (N Wainsztein); Hospital Aleman (P Comignani); Hospital Central San Isidro (M Casaretto); Hospital Fernandez (G Sutton); Hospital Francisco Lopez Lima Area Programa General Roca (P Villegas); Sanatorio Allende (C Galletti); Sanatorio De La Trinidad Palermo (J Neira); Sanatorio Julio Corzo Rosario (D Rovira)
Belize: Karl Heusner Memorial Hospital and Belize Healthcare Partner (J Hidalgo)
Bolivia: Hospital Obrero No1 (F Sandi)
Brazil: Cias -Unimed Vitória (E Caser); Evangelical Hospital of Cachoeiro De Itapemirim (M Thompson); Hospital 9 De Julho (M D'agostino Dias); Hospital Alcides Carneiro (L Fontes); Hospital Das Clínicas Luzia De Pinho Melo (M Lunardi); Hospital Das Nações De Curitiba (N Youssef); Hospital De Base Famerp (S Lobo); Hospital De Clínicas De Niterói (R Silva); Hospital De Clínicas Padre Miguel (J Sales Jr); Hospital De Terapia Intensiva (L Madeira Campos Melo); Hospital Do Trabalhador (M Oliveira); Hospital Esperanca (M Fonte); Hospital Evangelico De Londrina (C Grion); Hospital Geral De Fortaleza (C Feijo); Hospital Geral De Roraima (V Rezende);

Hospital Israelita Albert Einstein (M Assuncao); Hospital Mater Dei (A Neves); Hospital Meridional (P Gusman); Hospital Meridional (D Dalcomune); Hospital Moinhos De Vento (C Teixeira); Hospital Municipal Ruth Cardoso (K Kaefer); Hospital Nereu Ramos (I Maia); Hospital Pasteur (V Souza Dantas); Hospital Pro Cardiaco (R Costa Filho); Hospital Regional De Samambaia (F Amorim); Hospital Regional Hans Dieter Schmidt (M Assef); Hospital Santa Casa - Campo Mourão (P Schiavetto); Hospital Santa Paula (J Houly); Hospital Santapaula (J Houly); Hospital São José Do Avaí (F Bianchi); Hospital São Lucas Da Pucrs (F Dias); Hospital Sao Vicente De Paula (C Avila); Hospital São Vicente De Paulo (J Gomez); Hospital Saude Da Mulher (L Rego); Hospital Tacchini (P Castro); Hospital Unimed Costa Do Sol-Macae-Rj (J Passos); Hospital Universitário - Ufpb - João Pessoa (C Mendes); Hospital Universitário De Londrina (C Grion); Hospital Universitário São Francisco (G Colozza Mecatti); Santa Casa De Caridade De Diamantina (M Ferrreira); Santa Casa De Misericordia De Tatui (V Irineu); São Francisco De Paula Hospital (M Guerreiro)

Chile: Clinica Indisa (S Ugarte); Clinica Las Lilas (V Tomicic); Hospital Carlos Van Buren (C Godoy); Hospital Del Trabajador De Santiago (W Samaniego); Hospital El Pino (I Escamilla); Hospital Mutual De Seguridad (I Escamilla)

Colombia: Centro Medico Imbanaco (L Castro Castro); Clinica Colombia Cali (G Libreros Duque); Clínica Del Café (D Diaz-Guio); Clínica La Estancia S.A. (F Benítez); Clinica Medellin (A Guerra Urrego); Fundacion Clinica Shaio (R Buitrago); Hospital Santa Clara (G Ortiz); Hospital Universitario Fundación Santa Fe De Bogota (M Villalba Gaviria)

Costa Rica: Calderón Guardia Hospital (D Salas); Hospital Dr Rafael Angel Varlderon Guardia Ccss (J Ramirez-Arce)

Ecuador: Clinica La Merced (E Salgado); Hospital Eugenio Espejo (D Morocho); Hospital Luis Vernaza (J Vergara); Shdug Sistema Hospitalario Docente De La Universidad De Guayaquil (M Chung Sang)

El Salvador: General Hospital (C Orellana-Jimenez)

Guatemala: Hospital Centro Medico (L Garrido)

Honduras: Instituto Hondureño Del Seguro Social (O Diaz)

Martinique: Centre Hospitalier Universitaire De Fort-De-France (D Resiere)

Mexico: Centro Estatal De Cuidados Críticos (C Osorio); Centro Médico Nacional "20 De Noviembre" Issste (A De La Vega); Fundacion Clinica Medica Sur (R Carrillo); Hospital San Jose TEC Monterrey (V Sanchez); Hospital 1o De Octubre, Issste (A Villagomez); Hospital Español De Mexico (R Martinez Zubieta); Hospital General Ajusco Medio (M Sandia); Hospital General Guadalupe Victoria (M Zalatiel); Hospital Juarez De Mexico (M Poblano); Hospitalcivil De Guadalajara, Hspitaljuan I Menchaca (D Rodriguez Gonzalez); Instituto Mexicano Del Seguro Social (F Arrazola); Instituto Mexicano Del Seguro Social (L Juan Francisco); Instituto Nacional de Cancerología, México (SA Ñamendys-Silva); ISSSTE Guerra Moya); Medical Centre ISSEMYM

Toluca (M Hernandez); Mixta (D Rodriguez Cadena); Secretaria De Salud Del Distrito Federal (I Lopez Islas)
Panama: Hospital Santo Tomás (C Ballesteros Zarzavilla); Social Security Hospital (A Matos)
Peru: Clinica Anglo Americana (I Oyanguren); Essalud (J Cerna); Hospital Nacional Dos De Mayo (R Quispe Sierra); Hospital Rebagliati (R Jimenez); Instituto Nacional De Enfermedades Neoplasicas (L Castillo)
Turks And Caicos Islands: Gulhane Medical Faculty (R Ocal); Izmir Atatürk Educational And Research Hosp. (A Sencan)
Uruguay: CAMS (S Mareque Gianoni); CASMU (A Deicas); Hospital Español Asse (J Hurtado); Hospital Maciel (G Burghi)
Venezuela: Centro Medico De Caracas (A Martinelli); Hospital Miguel Perez Carreño (I Von Der Osten)

South Asia

Afghanistan: MSF Trauma Hospital Kunduz (C Du Maine)
India: Amri Hospitals (M Bhattacharyya); Amri Hospitals Salt Lake (S Bandyopadhyay); Apollo Hospital (S Yanamala); Apollo Hospitals (P Gopal); Apollo Hospitals, Bhubaneswar (S Sahu); Apollo Speciality Hospital (M Ibrahim); Asian Heart Institute (D Rathod); Baby Memorial Hospital Ltd, Calicut, Kerala (N Mukundan); Batra Hospital & Mrc, New Delhi 110062 (A Dewan); Bombay Hospital Institute of Medical Sciences (P Amin); Care Hospital (S Samavedam); Cims Hospital (B Shah); Columbiaasia Hospital, Mysore (D Gurupal); Dispur Hospitals (B Lahkar); Fortis Hospital (A Mandal); Fortis Hospital (Noida) (M Sircar); Fortis-Escorts Hospital, Faridabad, India (S Ghosh); Ganga Medical Centre & Hospital P Ltd. (V Balasubramani); Hinduja Hospital (F Kapadia); KDAH (S Vadi); Kerala Institute of Medical Sciences (KIMS, RMCC) (K Nair); Kalinga Institute of Medical Sciences (KIMS, DTEM) (S Tripathy); Kovai Medical Centre and Hospital (S Nandakumar); Medanta The Medicity, Gurgaon (J Sharma); Medica Superspecialty Hospitals (A Kar); Metro Heart Institute with Multispeciality (S Jha); Ruby Hall Pune (K Zirpe/Gurav); Saifee Hospital (M Patel); Spandan Multispeciality Hospital (A Bhavsar); Tata Main Hospital (D Samaddar); Tata Memorial Hospital (A Kulkarni)
Pakistan: Aga Khan University (M Hashmi); Hearts International Hospital (W Ali); Liaquat National Hospital (S Nadeem)
Sri Lanka: Sri Jayewardenepura General Hospital (K Indraratna)

West Europe

Andorra: Hospital Nostra Senyora De Meritxell (A Margarit)
Austria: Akh Wien (P Urbanek); Allgemeines Und Orthopädisches Landeskrankenhaus Stolzalpe (J

Schlieber); Barmherzige Schwestern Linz (J Reisinger); General Hospital Braunau (J Auer); Krankenhaus D. Barmherzigen Schwestern Ried I.I. (A Hartjes); Krankenhaus Floridsdorf (A Lerche); LK Gmünd-Waidhofen/Thaya-Zwettl, Standort Zwettl (T Janous); LKH Hörgas-Enzenbach (E Kink); LKH West (W Krahulec); University Hospital (K Smolle)
Belgium: AZ Groeninge Kortrijk (M Van Der Schueren); AZ Jan Palfijn Gent (P Thibo); AZ Turnhout (M Vanhoof); Bracops Anderlecht (I Ahmet); Centre Hospitalier Mouscron (G Philippe); CH Peltzer La Tourelle (P Dufaye); Chirec Edith Cavell (O Jacobs); CHR Citadelle (V Fraipont); CHU Charleroi (P Biston); Chu Mont-Godinne (A Dive); CHU Tivoli (Y Bouckaert); Chwapi (E Gilbert); Clinique Saint-Pierre Ottignies (B Gressens); Clinique-Maternité Sainte Elisabeth (E Pinck); Cliniques De L'Europe - St-Michel (V Collin); Erasme University Hospital (JL Vincent); Ghent University Hospital (J De Waele); Moliere Hospital (R Rimachi); Notre Dame (D Gusu); Onze Lieve Vrouw Ziekenhuis, Aalst (K De Decker); Ixelles Hospital (K Mandianga); Sint-Augustinus (L Heytens); St Luc University Hospital (UCL) (X Wittebole); UZ Brussel (S Herbert); Vivalia Site De Libramont (V Olivier); VZW Gezondheidszorg Oostkust Knokke-Heist (W Vandenheede); ZNA Middelheim (P Rogiers)
Denmark: Herning Hospital (P Kolodzeike); Hjoerring Hospital (M Kruse); Vejle Hospital (T Andersen)
Finland: Helsinki University Central Hospital (V Harjola); Seinäjoki Central Hospital (K Saarinen)
France: Aix Marseille Univ, Hôpital Nord (M Leone); Calmette Hospital, Lille (A Durocher); Centre Hospitalier de Dunkerque (S Moulront); Centre Hospitalier Lyon Sud (A Lepape); Centre Hospitalo-Universitaire Nancy-Brabois (M Losser); CH Saint Philibert, Ghicl, Lille (P Cabaret); CHR De Dax (E Kalaitzis); CHU Amiens (E Zogheib); CHU Dijon (P Charve); CHU Dupuytren (B Francois); CHU Nîmes (JY Lefrant); Centre Hospitalier De Troyes (B Beilouny); Groupe Hospitalier Est Francilien-Centre Hospitalier De Meaux (X Forceville); Groupe Hospitalier Paris Saint Joseph (B Misset); Hopital Antoine Béclère (F Jacobs); Hopital Edouard Herriot (F Bernard); Hôpital Lariboisère, APHP, Paris France (D Payen); Hopital Maison Blanche, Reims (A Wynckel); Hopitaux Universitaires de Strasbourg (V Castelain); Hospices Civils de Lyon (A Faure); CHU-Grenoble (P Lavagne); CHU-Nantes (L Thierry); Réanimation Chirurgical Cardiovasculaire, CHRU Lille (M Moussa); University Hospital Ambroise Paré (A Vieillard-Baron); University Hospital Grenoble (M Durand); University Hospital of Marseille (M Gainnier); University of Nice (C Ichai)
Germany: Alexianer Krefeld Gmbh (S Arens); Charite Hochschulmedizin Berlin (C Hoffmann); Charite-University-Hospital, Berlin (M Kaffarnik); Diakoniekrankenhaus Henriettenstiftung Gmbh (C Scharnofske); Elisabeth-Krankenhaus Essen (I Voigt); Harlaching Hospital, Munich Municipal Hospital Group (C Peckelsen); Helios St. Johannes Klinik (M Weber); Hospital St. Georg Leipzig (J Gille); Klinik Hennigsdorf Der Oberhavel Kliniken Gmbh (A Lange); Klinik Tettnang (G Schoser); Klinikum "St. Georg" Leipzig (A Sablotzki); Klinikum Augsburg (U Jaschinski); Klinikum Augsburg

(A Bluethgen); Klinikum Bremen-Mitte (F Vogel); Klinikum Bremen-Ost (A Tscheu); Klinikum Heidenheim (T Fuchs); Klinikum Links Der Weser Gmbh (M Wattenberg); Klinikum Luedenscheid (T Helmes); Krankenhaus Neuwerk (S Scieszka); Marienkrankenhaus Schwerte (M Heintz); Medical Centre Cologne Merheim (S Sakka); Schwarzwald-Baar Klinikum Villingen-Schwenningen (J Kohler); St. Elisabeth Krankenhaus Köln-Hohenlind (F Fiedler); St. Martinus Hospital Olpe (M Danz); Uniklinikum Jena (Y Sakr); Universitätsklinikum Tübingen (R Riessen); Universitätsmedizin Mainz (T Kerz); University Hospital Aachen, CPACC (A Kersten); University Hospital Aachen, DMIII (F Tacke); University Hospital Aachen, OIC (G Marx); University Hospital Muenster (T Volkert); University Medical Centre Freiburg (A Schmutz); University Medical Centre Hamburg-Eppendorf (A Nierhaus); University Medical Centre Hamburg-Eppendorf (S Kluge); University Medicine Greifswald (P Abel); University of Duisburg-Essen (R Janosi); University of Freiburg (S Utzolino); University clinic Ulm (H Bracht); Vivantes Klinikum Neukoelln (S Toussaint)

Greece: Ahepa University Hospital (M Giannakou Peftoulidou); Athens University (P Myrianthefs); Athens University Medical School (A Armaganidis); Evangelismos Hospital (C Routsi); General Hospital of Chania, Crete (A Xini); Hippokration General Hospital, Thessaloniki (E Mouloudi); General hospital of Velos (I Kokoris); Lamia General Hospital (G Kyriazopoulos); Naval and Veterans Hospital (S Vlachos); Papanikolaou General Hospital (A Lavrentieva); University Hospital Alexandroupolis (P Partala); University of Ioannina (G Nakos)

Iceland: Landspitali University Hospital (A Moller); Landspitali University Hospital Fossvogur (S Stefansson)

Ireland: Cork University Hospital (J Barry); Mercy University Hospital (R O'Leary); Mid Western Regional Hospital Complex (C Motherway); Midland Regional Hospital Mullingar, Co Westmeath (M Faheem); St. Vincent's University Hospital (E Dunne); Tallaght Hospital (M Donnelly); University Hospital Galway (T Konrad)

Italy: Anesthesiology and Intensive Care (E Bonora); AO Ospedale Niguarda Ca' Granda (C Achilli); Azienda Ospedaliera Di Padova (S Rossi); Azienda Ospedaliero Universitaria Policlinico Vittorio Emanuele (G Castiglione); Careggi Teaching Hospital (A Peris); Clinicized Hospital Ss Annunziata - Chieti (D Albanese); Fondazione Irccs Ca' Granda Ospedale Maggiore Policlinico, Milano; University of Milan (N Stocchetti); H San Gerardo - Monza (G Citerio); Icu "Ceccarini" Hospital Riccione (L Mozzoni); Irccs Centro Cardiologico Monzino (E Sisillo); Irccs Centro Di Riferimento Oncologico Della Basilicata (P De Negri); Irccs Fondazione Ca' Granda - Ospedale Maggiore Policlinico (M Savioli); Ospedale Belcolle Viterbo (P Vecchiarelli); Ospedale Civile Maggiore - A.O.U.I Verona (F Puflea); Ospedale Civile Maggiore - A.O.U.I Verona (V Stankovic); Ospedale Di Circolo E Fondazione Macchi - Varese (G Minoja); Ospedale Di Trento - Azienda Provinciale Per I Servizi Sanitari Della Provincia Autonoma Di Trento (S Montibeller); Ospedale Orlandi (P Calligaro); Ospedale Regionale U.Parini-Aosta (R Sorrentino); Ospedale San Donato

Arezzo (M Feri); Ospedale San Raffaele (M Zambon); Policlinico G.B. Rossi - A.O.U.I Verona (E Colombaroli); Policlinico University of Palermo (A Giarratano); Santa Maria Degli Angeli Hospital (T Pellis); Saronno Hospital (C Capra); Università Cattolica Del Sacro Cuore (M Antonelli); University Catania, Italy (A Gullo); University of Florence, Florence (C Chelazzi); University of Foggia (A De Capraris); University of Milano-Bicocca, San Gerardo Hospital (N Patroniti); University of Modena (M Girardis); University of Siena (F Franchi); University of Trieste (G Berlot)

Malta: Mater Dei Hospital (M Buttigieg)

Netherlands: Albert Schweitzer Hospital (H Ponssen); Antoni Van Leeuwenhoek Ziekenhuis (J Ten Cate); Atrium Medisch Centrum Parkstad (L Bormans); Bovenij Hospital (S Husada); Catharina Hospital Eindhoven (M Buise); Erasmus University Medical Centre (B Van Der Hoven); Martiniziekenhuis Groningen (A Reidinga); Medical Centre Leeuwarden (M Kuiper); Radboud University Nijmegen Medical Centre (P Pickkers); Slotervaart Ziekenhuis Amsterdam (G Kluge); Spaarne Ziekenhuis (S Den Boer); University Medical Centre Utrecht (J Kesecioglu); Ziekenhuis Rijnstate (H Van Leeuwen)

Norway: Haukeland University Hospital (H Flaatten); St Olavs Hospital, Trondheim University Hospital (S Mo)

Portugal: Centro Hospitalar Cova Da Beira (V Branco); Centro Hospitalar Do Porto (F Rua); Centro Hospitalar Do Tâmega E Sousa (E Lafuente); Centro Hospitalar Gaia/Espinho, Epe (M Sousa); Centro Hospitalar Médio Tejo (N Catorze); Centro Hospitalar Tondela-Viseu (M Barros); Faro Hospital (L Pereira); Hospital Curry Cabral (A Vintém De Oliveira); Hospital Da Luz (J Gomes); Hospital De Egas Moniz - Chlo (I Gaspar); Hospital De Santo António, Centro Hospitalar Do Porto (M Pereira); Hospital Divino Espírito Santo, Epe (M Cymbron); Hospital Espirito Santo - Évora Epe (A Dias); Hospital Garcia Orta (E Almeida); Hospital Geral Centro Hospitalar E Universitario Coimbra (S Beirao); Hospital Prof. Doutor Fernando Fonseca Epe (I Serra); Hospital São Bernardo (R Ribeiro); Hospital Sao Francisco Xavier, Chlo (P Povoa); Instituto Portugues De Oncologia Francisco Gentil, Porto (F Faria); Santa Maria Hospital (Z Costa-E-Silva); Serviço De Saúde Da Região Autonóma Da Madeira (J Nóbrega); UCIP (F Fernandes); ULS - Castelo Branco (J Gabriel)

Slovenia: General Hospital Celje (G Voga); General Hospital Izola (E Rupnik); General Hospital Novo Mesto (L Kosec); Oncological Institute (M Kerin Povšic); Ukc Maribor (I Osojnik); University Clinic of Respiratory and Allergic Diseases (V Tomic); University Clinical Centre Maribor (A Sinkovic)

Spain: CH Salamanca (J González); Clinic Hospital (E Zavala); Complejo Hospitalario De Jaén (J Pérez Valenzuela); Complejo Hospitalario De Toledo (L Marina); Complexo Hospitalario Universitario De Ourense (P Vidal-Cortés); Complexo Hospitalario Universitario De Vigo (P Posada); Corporación Sanitaria Parc Tauli (A Ignacio Martin-Loeches); Cruz Roja Hospital (N Muñoz Guillén); H Vall Hebron (M Palomar); HGGC Dr Negrín (J Sole-Violan); Hospital Clinic (A

Torres); Hospital Clinico San Carlos (M Gonzalez Gallego); Hospital Clínico Universitario De Valencia (G Aguilar); Hospital Clínico Universitario Lozano Blesa (R Montoiro Allué); Hospital Clinico Valencia (M Argüeso); Hospital De La Ribera (M Parejo); Hospital De Sagunto (M Palomo Navarro); Hospital De San Juan De Alicante (A Jose); Hospital De Torrejon De Ardoz (N Nin); Hospital Del Mar (F Alvarez Lerma); Hospital Del Tajo (O Martinez); Hospital General Universitario De Elche (E Tenza Lozano); Hospital General Universitario Gregorio Marañon (S Arenal López); Hospital General Universitario Gregorio Marañon (M Perez Granda); Hospital General Universitario Santa Lucía (S Moreno); Hospital Germans Trias I Pujol (C Llubia); Hospital Infanta Margarita (C De La Fuente Martos); Hospital Infanta Sofia (P Gonzalez-Arenas); Hospital J.M. Morales Meseguer (N Llamas Fernández); Hospital J.M. Morales Meseguer (B Gil Rueda); Hospital Marina Salu. Denia. Alicante. (I Estruch Pons); Hospital Nuestra Señora Del Prado, Talavera De La Reina, Toledo. España (N Cruza); Hospital San Juan De Dios Aljarafe (F Maroto); Hospital Sas of Jerez (A Estella); Hospital Son Llatzer (A Ferrer); Hospital Universitario Central De Asturias (L Iglesias Fraile); Hospital Universitario Central De Asturias (B Quindos); Hospital Universitario De Alava, Santiago (A Quintano); Hospital Universitario De Basurto, Bilbao (M Tebar); Hospital Universitario de Getafe (P Cardinal); Hospital Universitario De La Princesa (A Reyes); Hospital Universitario de Tarragona Joan Xxiii (A Rodríguez); Hospital Universitario Del Henares (A Abella); Hospital Universitario Fundación Alcorcón (S García Del Valle); Hospital Universitario La Paz (S Yus); Hospital Universitario La Paz (E Maseda); Hospital Universitario Rio Hortega (J Berezo); Hospital Universitario San Cecilio (Granada) (A Tejero Pedregosa); Hospital Virgen Del Camino (C Laplaza); Mutua Terrassa University Hospital (R Ferrer); Rão Hortega University Hospital (J Rico-Feijoo); Servicio Andaluz De Salud. Spain. (M Rodríguez); University Opf Navarra (P Monedero)

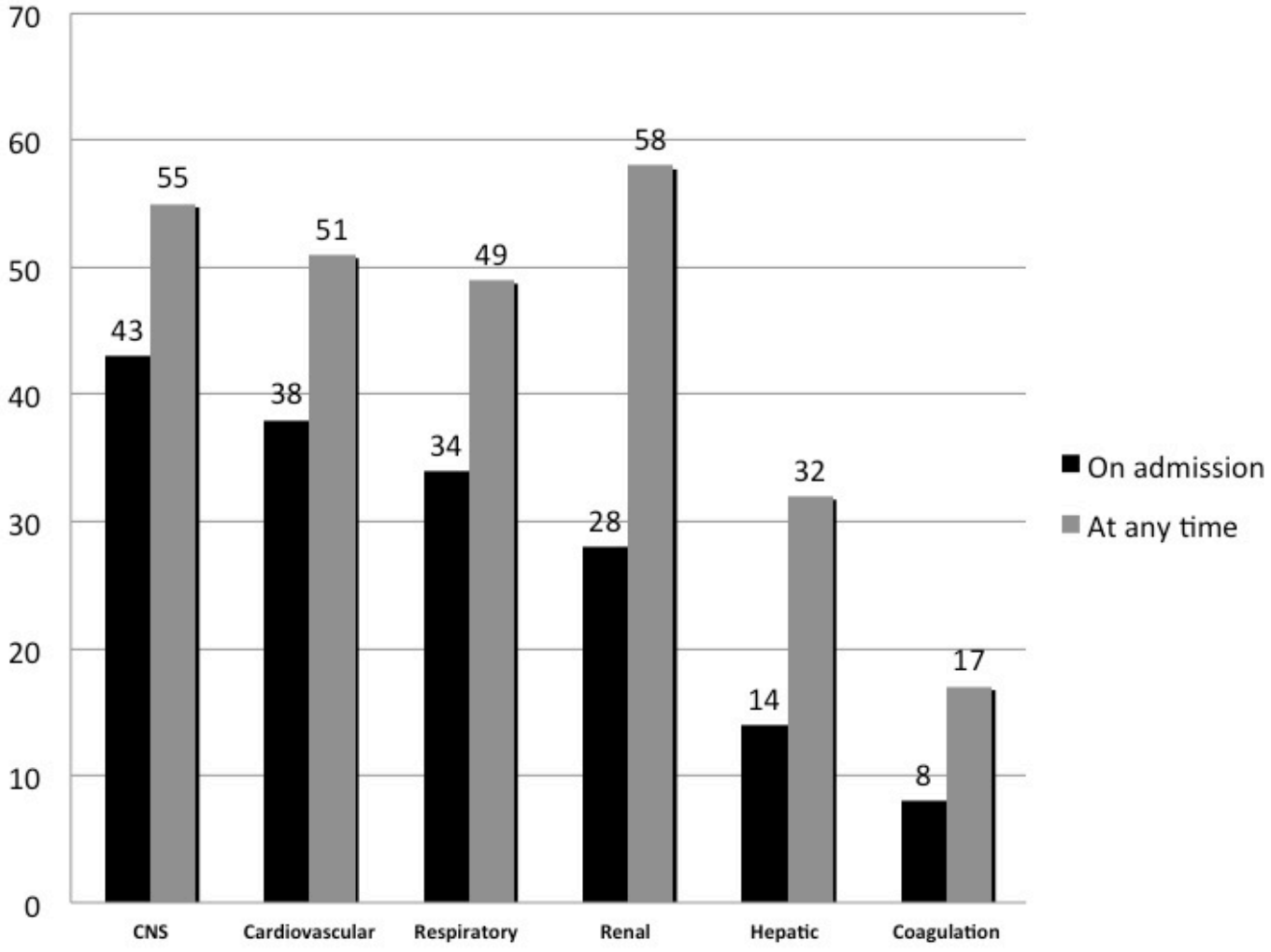
Sweden: Karolinska University Hospital And Karolinska Institute (K Eriksson); Sunderby Hospital, Luleå (D Lind)

Switzerland: Hôpital Intercantonal De La Broye (D Chabanel); Hôpital Neuchâtelois - La Chaux-De-Fonds (H Zender); Lindenhofspital (K Heer); Regionalspital Surselva Ilanz (Gr) Schweiz (B Frankenberger); University Hospital Bern (S Jakob); Zentrum Für Intensivmedizin (A Haller)

United Kingdom: Alexandra Hospital Redditch (S Mathew); Blackpool Teaching Hospitals (R Downes); Brighton And Sussex University Hospitals (C Barrera Groba); Cambridge University Hospitals NHS Foundation Trust (A Johnston); Charing Cross Hospital (R Meacher); Chelsea & Westminster Hospital (R Keays); Christie Foundation Trust (P Haji-Michael); County Hospital, Lincoln (C Tyler); Craigavon Area Hospital (A Ferguson); Cumberland Infirmary (S Jones); Darent Valley Hospital (D Tyl); Dorset County Hospital (A Ball); Ealing Hospital NHS Trust (J Vogel); Glasgow Royal Infirmary (M Booth); Gloucester Royal Hospital (P Downie); The Great Western Hospital, Swindon (M Watters); Imperial College Healthcare NHS Trust (S Brett); Ipswich Hospital Nhs Trust (M Garfield); James Paget University Hospital NHS Foundation Trust (L Everett); King's

College Hospital (S Heenen); King's Mill Hospital (S Dhir); Leeds Teaching Hospitals NHS Trust (Z Beardow); Lewisham Healthcare NHS Trust (M Mostert); Luton and Dunstable Hospital NHS Trust (S Brosnan); Medway Maritime Hospital (N Pinto); Musgrove Park Hospital (S Harris); Nevill Hall Hospital (A Summors); Pilgrim Hospital (N Andrew); Pinderfields Hospital, Mid Yorkshire NHS Trust (A Rose); Plymouth Hospitals Nhs Trust (R Appelboam); Princess Royal Hospital Telford (O Davies); Royal Bournemouth Hospital (E Vickers); Royal Free Hampstead NHS Foundation Trust (B Agarwal); Royal Glamorgan Hospital (T Szakmany); Royal Hampshire County Hospital (S Wimbush); Royal Liverpool University Hospital (I Welters); Royal London Hospital, Barts Health NHS Trust (R Pearse); Royal Shrewsbury Hospital (R Hollands); Royal Surrey County Hospital (J Kirk-Bayley); St Georges Healthcare (N Fletcher); Surrey & Sussex Healthcare Trust (B Bray); University College Hospital (D Brealey)

e-Figure 1. Distribution of organ failure (%) on admission and at any time in patients with a decision to withhold or withdraw life-supporting treatment



e-Table 1. Characteristics of patients with a decision to withhold/withdraw life-sustaining treatment (DLST) according to geographical region

	All patients	Western Europe	Eastern Europe	South America	North America	East & southeast Asia	South Asia	Oceania	Middle East	Africa
Total number of patients, n	9524	4130	1046	908	715	854	973	416	354	128
DLST in the whole cohort, n (%)	1259 (13.2)	572 (13.8)	100 (9.6)*	96 (10.6)*	109 (15.2)	255 (29.9)	28 (2.9)*	62 (14.9)	29 (8.2)*	8 (6.3)*
DLST in the hospital non-survivors, n (%)	820 (39.5)	455 (49.2)	60 (20.8)*	58 (24.6)*	60 (65.2)*	107 (51.9)	12 (10.2)*	40 (66.7)*	23 (18.3)*	5 (20.8)*
DLST in the ICU non-survivors, n (%)	682 (43.6)	374 (57.4)	55 (22.9)*	48 (25.1)*	50 (75.8)*	85 (55.9)	11 (11.3)*	34 (75.6)*	20 (19.8)*	5 (22.7)*
Age, years, mean ± SD	64.4±17.5	68.7±14.6	61.7±17.7*	62.0±19.2*	65.9±16.8	56.7±19.4*	58.2±19.9*	68.1±14.2	60.9±22.4*	56.1±18.1*
Male, n (%)	723 (58.2)	346 (61.2)	60 (61.2)	46 (48.9)*	51 (47.2)*	144 (57.1)	17 (60.7)	39 (63.9)	13 (44.8)	7 (87.5)
Severity scores, mean ± SD										
SAPS II score	52.1±19.6	55.8±18.8	49.8±22.4*	50.1±19.5*	46.9 ±20.7*	47.0 ±18.0*	42.5 ±20.0*	53.0 ±14.3	64.6±23.4*	50.1±13.2
SOFA score at admission	8.3 ±4.7	8.7±4.6	8.2 ±4.6	7.0±4.5*	7.3 ±5.2*	7.9 ±4.6*	6.1 ±4.6*	9.7 ±3.9	10.8±4.1*	10.1±3.6
Procedures, n (%)										
Mechanical ventilation	892 (70.8)	460 (80.4)	68 (68.0)*	66 (68.8)*	55 (50.5)*	164 (64.3)*	11 (39.3)*	40 (64.5)*	23 (79.3)	5 (62.5)
Renal replacement therapy	227 (18.0)	110 (19.2)	11 (11.0)*	19 (19.8)	10 (9.2)*	51 (20.0)	1 (3.6)*	13 (21.0)	10 (34.5)*	2 (25.0)
ICU stay, median (IQR)	4.0 [2.0-8.0]	4.0 [2.0-9.0]	3.5 [2.0-9.5]	4.0 [2.0-9.0]	2.0 [1.0-6.0]	4.0 [2.0-8.0]	2.0 [1.0-5.0]	3.0 [2.0-5.0]*	5.0 [2.0-15.0]*	7.0 [3.0-16.0]
Hospital stay, median(IQR)	6.0 [2.0-14.0]	6.0 [2.0-15.0]	7.0 [3.0-14.0]	5.0 [3.0-15.0]	5.0 [2.0-11.0]	7.0 [3.0-17.0]	3.0 [1.0-6.0]*	5.0 [2.0-12.0]	7.5 [3.5-13.0]	6.0 [3.0-16.0]
ICU stay, days #	4.0 [1.0-9.0]	4.0 [1.0-9.0]	4.0 [1.0-9.0]	4.0 [2.0-8.0]	3.0 [1.0-9.0]	3.0 [1.0-8.0]	3.0 [1.0-6.0]	3.0 [1.0-7.5]	5.0 [2.0-12.0]*	2.0 [1.0-6.0]
Hospital stay, days #	5.0 [2.0-13.0]	6.0 [2.0-15.0]	5.0 [1.0-12.0]	5.0 [2.0-12.0]	5.0 [1.5-11.5]	4.0 [1.0-11.0]	3.0 [1.0-8.0]*	4.0 [2.0-11.5]	7.0 [3.0-17.0]	2.0 [1.0-11.0]
ICU mortality, n (%)	682 (55.6)	374 (65.8)	55 (55.6)*	48 (56.5)	50 (46.7)*	85 (34.7)*	11 (44.0)*	34 (54.8)	20 (74.1)	5 (62.5)
Hospital mortality, n (%)	820 (68.7)	455 (80.5)	60 (60.6)*	58 (73.4)	60 (56.1)*	107 (47.3)*	12 (48.0)*	40 (65.6)*	23 (92.0)	5 (71.4)

*: statistically significant vs Western Europe at 5% level.
Data are mean (SD), median [IQR], or n (%). DLST = Decision on life-supporting treatment. SAPS=simplified acute physiology score. SOFA=sequential organ failure score. #: Considering only surviving patients.