Assessment of the worldwide burden of critical illness: the Intensive Care Over Nations (ICON) audit

*Jean-Louis Vincent, John C Marshall, Silvio A Ñamendys-Silva, Bruno François, Ignacio Martin-Loeches, Jeffrey Lipman, Konrad Reinhart, Massimo Antonelli, Peter Pickkers, Hassane Njimi, Edgar Jimenez, Yasser Sakr, on behalf of the ICON investigators**

Lancet Respir Med 2014; 2: 380–86

Published Online April 14, 2014 http://dx.doi.org/10.1016/S2213-2600(14)70061-X

See Comment page 343

*Details of ICON investigators are given in the appendix

Department of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium (Prof J-L Vincent MD, H Njimi PhD); Department of Surgery, Interdepartmental Division of Critical Care Medicine, University of Toronto, St Michael's Hospital, Toronto, ON, Canada (Prof J C Marshall MD); Department of Critical Care Medicine, Instituto Nacional de Cancerología, Mexico City, Mexico (S A Ñamendys-Silva MD); Service de Réanimation Polyvalente, CHU Dupuytren, Limoges cedex, France (Prof B François MD); Critical Care Centre, Corporació Sanitària I Universitaria Parc Taulí—Hospital De Sabadell, Institut Universitari Uab, Ciber Enfermedades Respiratorias, Sabadell, Barcelona, Spain (I Martin-Loeches MD); Department of Intensive Care Medicine, Royal Brisbane and Women's Hospital, University of Queensland, QLD, Australia (Prof J Lipman MD); Department of Anaesthesiology and Intensive Care and Centre for Sepsis Care and Control, Jena University Hospital, Jena, Germany (Prof K Reinhart MD, Y Sakr MD); Department of Anaesthesiology and Intensive Care, Catholic University—Policlinico A Gemelli University Hospital, Rome, Italy (Prof M Antonelli MD); Department of Intensive Care, Nijmegen Institute for Infection, Inflammation and Immunity, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands (P Pickkers MD); and Department of Critical Care, Orlando

Summary

Background Global epidemiological data regarding outcomes for patients in intensive care units (ICUs) are scarce, but are important in understanding the worldwide burden of critical illness. We, therefore, did an international audit of ICU patients worldwide and assessed variations between hospitals and countries in terms of ICU mortality.

Methods 730 participating centres in 84 countries prospectively collected data on all adult (>16 years) patients admitted to their ICU between May 8 and May 18, 2012, except those admitted for fewer than 24 h for routine postoperative monitoring. Participation was voluntary. Data were collected daily for a maximum of 28 days in the ICU and patients were followed up for outcome data until death or hospital discharge. In-hospital death was analysed using multilevel logistic regression with three levels: patient, hospital, and country.

Findings 10 069 patients were included from ICUs in Europe (5445 patients; 54·1%), Asia (1928; 19·2%), the Americas (1723; 17·1%), Oceania (439; 4·4%), the Middle East (393; 3·9%), and Africa (141; 1·4%). Overall, 2973 patients (29·5%) had sepsis on admission or during the ICU stay. ICU mortality rates were 16·2% (95% CI 15·5–16·9) across the whole population and 25·8% (24·2–27·4) in patients with sepsis. Hospital mortality rates were 22·4% (21·6–23·2) in the whole population and 35·3% (33·5–37·1) in patients with sepsis. Using a multilevel analysis, the unconditional model suggested significant between-country variations (var=0·19, p=0·002) and between-hospital variations (var=0·43, p<0·0001) in the individual risk of in-hospital death. There was a stepwise increase in the adjusted risk of in-hospital death according to decrease in global national income.

Interpretation This large database highlights that sepsis remains a major health problem worldwide, associated with high mortality rates in all countries. Our findings also show a significant association between the risk of death and the global national income and suggest that ICU organisation has an important effect on risk of death.

Funding None.

Introduction

Intensive care medicine has grown substantially over the past decades and now consumes a substantial part of the income of many countries worldwide (close to 1% of the gross domestic product [GDP] in the USA[1]). Previous studies have provided some epidemiological data regarding types of patients and treatments used in intensive care units (ICUs) and outcomes for patients in ICUs at a local and a national level, but there is much less information available at an international level.[2] A review in 2010 stressed that there is a "need to measure the global burden of critical illness and available critical-care resources, and develop both preventive and therapeutic interventions that are generalisable across countries".[2] The World Federation of Societies of Intensive and Critical Care Medicine, with a membership of more than 70 national societies of intensive and critical care medicine, provided a unique platform to initiate an audit of data from ICUs around the world to develop an international picture of the types of critically ill patients admitted to our ICUs, with a special emphasis on sepsis and organ failure. We provide a summary of the key findings of this major worldwide collaborative initiative, providing important insights into characteristics of intensive care patient populations and variations in mortality rates between different countries and regions of the globe.

Methods

Participating centres

Recruitment for participation in the Intensive Care Over Nations (ICON) audit was by open invitation, through national scientific societies, national and international meetings, and individual contacts. Participation was entirely voluntary, with no financial incentive. Institutional review board approval was obtained by the participating institutions in accordance with local ethical regulations.

Each participating centre (appendix) was asked to prospectively collect data on all adult patients (>16 years) admitted to their ICU between May 8 and May 18, 2012, except those who stayed in the ICU for fewer than 24 h for routine postoperative surveillance. Readmissions of previously included patients were excluded. Data were collected daily during the ICU stay for a maximum of 28 days. Patients were followed up for outcome data until death or hospital discharge.

Case report forms (CRFs; appendix) were electronically provided by the investigators using a secured internet-based website. Data collection on admission included

demographic data and comorbid diseases. Clinical and laboratory data for simplified acute physiology score (SAPS) II[3] and acute physiology and chronic health evaluation (APACHE) II[4] scores were reported as the worst values within 24 h after admission. Microbiological and clinical infections were reported daily as well as the antibiotics given. A daily assessment of organ function in accordance with the sequential organ failure assessment (SOFA) score[5] was done.

Definitions

Infection was defined in accordance with the definitions of the International Sepsis Forum.[6] Sepsis was defined as the presence of infection with the concomitant occurrence of at least one organ failure (defined as a SOFA score >2 for the organ in question).[7] Septic shock was defined as sepsis associated with cardiovascular failure (defined as a cardiovascular SOFA score >2).[7]

Surgical admissions referred to patients who had had surgery in the 4 weeks preceding admission. The presence of several comorbid disorders[3,4] was noted: chronic obstructive pulmonary disease (COPD), metastatic cancer (metastases proven by surgery, CT or MRI, or any other method), liver cirrhosis, heart failure (New York Heart Association classification [NYHA] III/IV), haematological malignancy (lymphoma, acute leukaemia, or multiple myeloma), acquired immunodeficiency syndrome, chronic renal failure (need for chronic renal support or history of chronic renal insufficiency with a serum creatinine greater than 3·6 mg/dL [300 µmol/L][5]), immunosuppression (steroid treatment given in the 6 months before ICU admission [at least 0·3 mg/kg per day prednisolone for at least 1 month], congenital immune-humoral, or cellular immune deficiency state), chemotherapy or radiotherapy (in the 6 months before ICU admission), severe malnutrition, and insulin-dependent diabetes mellitus.

Data management and quality control

Detailed instructions explaining the aim of the study, instructions for data collection, and definitions were available through a secured website for all participants before starting data collection and throughout the study period. Any additional queries were answered on a per-case basis by the coordinating centre during data collection. Validity checks were made concurrent with data entry on the electronic CRF including plausibility checks within each variable and between variables. Data were further reviewed by the coordinating centre for plausibility and availability of outcome parameter (death in the ICU), and any doubts were clarified with the centre in question. There was no on-site monitoring.

Statistical analysis

Data were processed and analysed in the department of intensive care of the University of Brussels, in collaboration with the Jena University Hospital (Jena, Germany). The appendix includes additional details of the statistical analysis.

For the purposes of this 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. Individual countries were also classified into three income groups in accordance with their 2011 gross national income (GNI) per person, using thresholds defined by the

Regional Medical Center, Orlando, FL, USA (E Jimenez MD)

Correspondence to:
Prof Jean-Louis Vincent, Department of Intensive Care, Erasme Hospital, Route de Lennik 808, 1070, Brussels
jlvincen@ulb.ac.be

See **Online** for appendix

	All patients, n=10 069	Low and lower-middle income, n=1209	Upper-middle income, n=2504	High income, n=6356
Number of patients per centre	10 (5–18)	10 (4–29)	8 (4–13)	11 (5–20)
Severity scores				
SAPS II score	40·2 (18·2)	33·4 (17·5)*†	40·7 (18·0)	41·2 (18·1)
APACHE II score	17·9 (9·4)	14·3 (8·9)*†	17·7 (9·4)*	18·7 (9·3)
SOFA score	6·3 (4·2)	4·6 (4·0)*†	6·0 (4·3)*	6·3 (4·4)
Type of admission				
Surgical (non-trauma)	3432 (36·0%)	317 (28·2%)*†	926 (39·3%)*	218 (36·2%)
Medical	5382 (56·5%)	728 (64·8%)*†	1216 (51·6%)	3438 (56·9%)
Trauma	643 (6·8%)	71 (6·3%)	189 (8·0%)*	383 (6·3%)
Other	66 (0·7%)	7 (0·6%)	24 (1·0%)	35 (0·6%)
Source of admission				
Emergency room or ambulance	3814 (37·9%)	438 (36·2%)	918 (36·7%)	2458 (38·7%)
Hospital floor	2625 (26·1%)	221 (18·3%)*†	773 (30·9%)*	1631 (25·7%)
Operating room or recovery room	1811 (18·0%)	147 (12·2%)*†	423 (16·9%)*	1241 (19·5%)
Other hospital	981 (9·7%)	165 (13·6%)*†	242 (9·7%)	574 (9·0%)
Other	838 (8·3%)	238 (19·7%)*†	148 (5·9%)	452 (7·1%)
Comorbidities				
COPD	1240 (12·3%)	72 (6·0%)*†	268 (10·7%)*	900 (14·2%)
Cancer (solid, non-metastatic)	888 (8·8%)	73 (6·0%)*	183 (7·3%)*	632 (9·9%)
Diabetes mellitus, insulin-dependent	972 (9·7%)	129 (10·7%)	219 (8·7%)	624 (9·8%)
Heart failure, NYHA III/IV	921 (9·1%)	64 (5·3%)*†	292 (11·7%)*	565 (8·9%)
Chronic renal failure	912 (9·1%)	80 (6·6%)*	188 (7·5%)*	644 (10·1%)
Immunosuppression	757 (7·5%)	63 (5·2%)*†	168 (6·7%)	526 (8·3%)
Cirrhosis	349 (3·5%)	27 (2·2%)*	78 (3·1%)	244 (3·8%)
Metastatic cancer	332 (3·3%)	33 (2·7%)	70 (2·8%)	229 (3·6%)
Haematological cancer	212 (2·1%)	11 (0·9%)*	38 (1·5%)*	163 (2·6%)
HIV infection	71 (0·7%)	3 (0·2%)	24 (1·0%)	44 (0·7%)
Number of comorbidities				
None	5512 (54·7%)	784 (64·8%)*†	1396 (55·8%)*	3332 (52·4%)
1	2917 (29·0%)	315 (26·1%)	755 (30·2%)	1847 (29·1%)
2	1252 (12·4%)	92 (7·6%)*†	289 (11·5%)*	871 (13·7%)
3	328 (3·3%)	16 (1·3%)*	61 (2·4%)*	251 (3·9%)
≥4	60 (0·6%)	2 (0·2%)	3 (0·1%)	55 (0·9%)
Infectious status				
Infection	2473 (24·6%)	186 (15·4%)*†	706 (28·2%)*	1581 (24·9%)
Sepsis	1808 (18·0%)	120 (9·9%) *†	497 (19·8%)	1191 (18·7%)
Septic shock	986 (9·8%)	60 (5·0%)†*	227 (9·1%)*	699 (11·0%)

Data are median (IQR), mean (SD), or n (%). Valid percentages are given after exclusion of missing values (data missing from 546 patients for type of admission). SAPS=simplified acute physiology score. APACHE=acute physiology and chronic health evaluation. SOFA=sequential organ failure score. COPD=chronic obstructive pulmonary disease. NYHA=New York Heart Association classification. Statistically significant at 5% with Bonferroni correction: *vs high. †vs upper middle.

Table 1: **Characteristics of the study cohort on admission to the ICU by GNI stratification**

World Bank Atlas method:[8] GNI less than US$4035 was defined as low and lower-middle income, $4036–$12 475 was defined as upper-middle income, and greater than $12 476 was defined as high income (appendix).

Data are summarised with means and SDs, medians and IQRs, or numbers and percentages. Crude mortality rates are given as percentages with Wald 95% CIs.[9] Single missing values of the SOFA score were imputed by linear interpolation. When first or last values were missing, the nearest value was carried backward or forward, respectively.

The Kolmogorov-Smirnov test was used, and histograms and quantile-quantile plots were examined to verify if there were significant deviations from the normality assumption of continuous variables. Difference testing between groups was done with ANOVA, Kruskal-Wallis test, Student's *t* test, Mann-Whitney test, χ^2 test, or Fisher's exact test, as appropriate. The least significant difference testing procedure was used for pairwise comparisons.

In-hospital death was analysed using multilevel logistic regression with three levels: patient, hospital, and country. The results of fixed effects (measures of association) are given as odds ratios (OR) with their 95% CIs and the 80% interval OR.[10–12] Random effects (measures of variation) measures included the variance (var) and its SE, the proportional change in variance,[12] and the median OR.[10–12] The statistical significance of covariates were calculated with the Wald test.[13]

Data were analysed with IBM SPSS statistics software, version 20 for windows, and MLwiN, version 2.28. All reported p values are two-sided and a p value of less than 0·05 was deemed to show statistical significance.

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

10 069 patients were included in the audit, most commonly from Europe (5445 patients; 54·1%), Asia (1928; 19·2%), and the Americas (1723; 17·1%). Table 1 lists the characteristics of the audit cohort on admission to the ICU according to GNI. Patients admitted to ICUs in countries with lower GNI were less severely ill than those admitted in higher income countries; they were more likely to be medical patients and less likely to have comorbid COPD or heart failure (table 1). Table 2 shows the organisational characteristics of the participating centres—most ICUs were located in university or academic hospitals. The highest hospital bed capacities were in centres from countries with higher GNI. There were no other major organisational differences between the centres according to GNI.

Patients from low-income countries were less likely to receive mechanical ventilation or renal replacement therapy during the ICU stay than patients in upper-middle or high income countries (all p<0·0001; table 3).

Almost a third of patients had sepsis during the ICU stay, but substantially lower occurrence rates were reported

	All centres, n=730	Low and lower-middle income, n=62	Upper-middle income, n=237	High income, n=431
Number of countries	84	17	27	40
Type of hospital				
University or academic	419 (57·4%)	26 (41·9%)*	148 (62·4%)†	245 (56·8%)
Non-university	247 (33·8%)	27 (43·5%)*	62 (26·2%)†	158 (36·7%)
Unknown	64 (8·8%)	9 (14·5%)	27 (11·4%)	28 (6·5%)
Hospital bed capacity	600 (320–982)	352 (200–600)*†	550 (200–1200)	642 (400–950)
ICU specialty				
Surgical	83 (11·4%)	7 (11·3%)	26 (11·0%)	50 (11·6%)
Medical	73 (10·0%)	4 (6·5%)	23 (9·7%)	46 (10·7%)
Mixed	479 (65·6%)	42 (67·7%)	152 (64·1%)	285 (66·1%)
Others	95 (13·0%)	9 (14·5%)	36 (15·2%)	50 (11·6%)
Number of ICU patients, 2011	700 (429–1100)	764 (466–1405)	624 (386–1200)	715 (441–1082)
ICU mortality rate, 2011	14 (8–21)	14 (9–26)	15 (8–22)	13 (8–19)
Number of staffed ICU beds, on the first day of the study	12 (8–18)	12 (10–20)	14 (10–18)†	12 (8–16)
ICU physician available 24 h/24 h	624 (94·5%)	49 (92·5%)	198 (95·2%)	377 (94·5%)
Physiotherapist available 24 h/24 h	454 (62·2%)	40 (64·5%)	128 (54%)†	286 (66·4%)
Pharmacist available 24 h/24 h	276 (37·8%)	23 (37·1%)	84 (35·4%)	169 (39·2%)
Technician available 24 h/24 h	286 (39·2%)	35 (56·5%)†	105 (44·3%)†	146 (33·9%)

Data are n (%) or median (IQR). Valid percentages are displayed after exclusion of missing values (data missing from 70 centres for ICU physician availability, 81 centres for number of ICU patients [2011], 89 centres for 2011 ICU mortality rates, 68 centres for number of staffed ICU beds, and 105 centres for hospital bed capacity). GNI=gross national income. ICU=intensive care unit. Statistically significant at 5% with Bonferroni correction: *vs upper middle. †vs high.

Table 2: **Characteristics of the participating centres by GNI**

	Number of centres	Number of patients (%)	Mean age, years (SD)	Mean SAPS II score (SD)	Mean APACHE II score (SD)	Number of cases of sepsis (%)	Mortality rate, % (95% CI)		Median length of stay, days (IQR)		Number of patients receiving mechanical ventilation (%)	Number of patients receiving RRT (%)
							ICU	In-hospital	ICU	In-hospital		
Total	730	10 069	60 (18)	40·2 (18·2)	17·9 (9·4)	2973 (29·5%)	16·2 (15·5–16·9)	22·4 (21·6–23·2)	3 (2–6)	10 (5–20)	5407 (53·7%)	1229 (12·2%)
Region												
Western Europe	317	4335 (43·1%)	63 (17)	41·7 (18·1)	18·8 (9·2)	1357 (31·3%)	15·5 (14·4–16·6)	22·6 (21·3–23·9)	3 (1–6)	11 (6–22)	2514 (58·0%)	553 (12·8%)
Eastern Europe	87	1110 (11·0%)	60 (17)	41·2 (18·2)	18·0 (9·4)	336 (30·3%)	21·9 (19·5–24·3)	27·2 (24·5–29·9)	3 (2–7)	10 (6–18)	651 (58·6%)	113 (10·2%)
South America	109	993 (9·9%)	59 (20)	40·8 (18·8)	17·1 (9·4)	303 (30·5%)	21·7 (19·0–24·4)	29·4 (26·2–32·6)	4 (2–7)	9 (5–20)	509 (51·3%)	127 (12·8%)
North America	23	730 (7·2%)	59 (18)	35·9 (16·5)	17·0 (8·4)	147 (20·1%)	9·3 (7·2–11·4)	13·1 (10·6–15·6)	2 (1–4)	6 (3–14)	267 (36·6%)	60 (8·2%)
East and southeast Asia	91	946 (9·4%)	60 (18)	43·2 (17·2)	19·8 (9·6)	372 (39·3%)	16·6 (14·2–19·0)	23·7 (20·9–26·5)	4 (2–7)	11 (5–25)	571 (60·4%)	150 (15·9%)
South Asia	36	982 (9·8%)	55 (17)	31·3 (16·8)	13·2 (8·4)	134 (13·6%)	10·9 (8·9–12·9)	14·4 (12·0–16·8)	2 (1–4)	6 (2–10)	317 (32·3%)	73 (7·4%)
Oceania	20	439 (4·4%)	58 (18)	41·2 (14·7)	18·5 (7·7)	135 (30·8%)	10·3 (7·5–13·1)	13·8 (10·6–17·0)	2 (1–5)	8 (4–17)	256 (58·3%)	45 (10·3%)
Middle East	36	393 (3·9%)	55 (20)	42·1 (20·8)	19·7 (11·2)	151 (38·4%)	26·2 (21·8–30·6)	34·1 (29·3–38·9)	4 (2–9)	10 (5–23)	252 (64·1%)	76 (19·3%)
Africa	11	141 (1·4%)	48 (19)	36·1 (17·4)	15·3 (9·2)	38 (27·0%)	16·9 (10·5–23·3)	20·7 (13·3–28·1)	2 (1–5)	8 (3–16)	70 (49·6%)	32 (22·7%)
GNI												
Low and lower-middle income	62	1209 (12·0%)	55 (17)	33·4 (17·5)	14·3 (8·9)	198 (16·4%)	14·1 (13·0–15·1)	18·2 (17·0–19·4)	2 (1–4)	6 (2–10)	432 (35·7%)	87 (7·2%)
Upper-middle income	237	2504 (24·9%)	58 (19)	40·7 (18·0)	17·7 (9·4)	790 (31·5%)	21·4 (20·3–22·2)	27·5 (26·6–28·5)	4 (2–7)	10 (5–19)	1377 (55·0%)	349 (13·9%)
High income	431	6356 (63·1%)	62 (18)	41·2 (18·1)	18·7 (9·3)	1985 (31·2%)	14·6 (13·8–15·5)	21·2 (20·7–21·8)	3 (1–6)	11 (5–21)	3598 (56·6%)	793 (12·5%)

ICU=intensive care unit. SAPS=simplified acute physiology score. APACHE=acute physiology and chronic health evaluation. RRT=renal replacement therapy. GNI=gross national income.

Table 3: **Epidemiology, major ICU interventions and sepsis occurrence on admission or during ICU stay, and mortality rates**

in south Asia and the highest rates were reported in east and southeast Asia and the Middle East (table 3). Of the patients with sepsis, 1808 (60·8%) already had sepsis on admission to the ICU, and 1681 (56·5%) had septic shock.

ICU and hospital mortality rates varied widely by geographical region (table 3). Crude ICU and hospital mortality rates were higher in patients admitted to ICUs in upper-middle income countries than to ICUs in low and lower-middle or high-income countries (all p<0·0001). The highest crude ICU and hospital mortality rates were recorded in patients admitted to ICUs in countries with upper-middle GNI (table 3). Hospital mortality rates per country according to GNI are shown in the appendix.

ICU and hospital mortality rates in patients with sepsis were 25·8% (24·2–27·4) and 35·3% (33·5–37·1), respectively, and varied between 11·9% and 19·3% (Oceania) to 39·5% and 47·2% (Africa), respectively.

The unconditional model suggested significant between-country variations (var=0·19, p=0·002) and between-hospital variations (var=0·43, p<0·0001) in the individual risk of in-hospital death (appendix). Between-hospital variations seemed to be greater than between-country variations, as shown by the median OR (1·86 *vs* 1·51).

After controlling for patient and hospital factors and GNI (country factor), the differences across hospitals decreased by 49% but remained significant (var=0·34, p<0·0001); by contrast, the differences across countries disappeared after adjustment (82% decrease, var=0·03, p=0·18). There was a stepwise increase in the adjusted risk of in-hospital death with decreasing GNI (figure, appendix) such that, compared with patients from high income countries, those from upper-middle income countries (OR 1·74, 95% CI 1·38–2·20) and low and lower-middle income countries (OR 2·10, 1·46–3·03) had a greater risk of in-hospital death.

Patients with sepsis were more at risk of in-hospital death than those without (OR 1·29, 1·13–1·48). Other independent risk factors for in-hospital death included older age, higher SAPS II score, medical or trauma admission (compared with the surgical admission group), admissions from the hospital floor (compared with admissions from the emergency room or ambulance), comorbid cancer, chronic heart failure (NYHA III/IV),

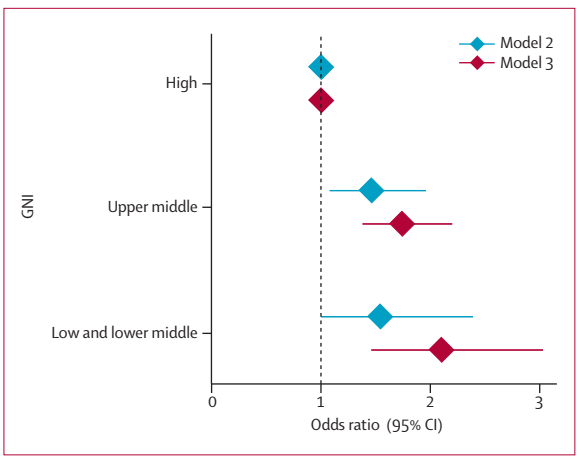


Figure: **Adjusted odds ratios of in-hospital death**
Odds ratios are according to the GNI in the whole cohort, with patients admitted to intensive care units in countries with high GNI as the reference category. Model 2 includes adjustment for hospital-level variables. Model 3 includes adjustment for patient-level and hospital-level variables. GNI=gross national income.

immunosuppression, cirrhosis, and the need for mechanical ventilation or renal replacement therapy (appendix).

Discussion

Our study shows important aspects related to the burden of intensive care worldwide. Notably, after adjustment for possible confounders in a multivariable analysis, there was a stepwise increase in the risk of in-hospital death according to decreasing GNI. There are many possible reasons for this finding, including potential issues related to differences in availability of trained staff and treatments or in quality of care. There are few data available concerning intensive care facilities in lower income countries (panel).[14] A recent study from Tanzania reported that although sufficient equipment and drugs seemed to be available for emergency and critical care, the infrastructure, training, and process of care were inadequate.[16] Similar findings have been reported from other low income countries.[17–20]

Using multilevel modelling to assess the reasons involved in the individual risk of in-hospital death, our findings suggest that the centre effect might be more important than the effect of GNI, suggesting that differences in ICU organisation among centres within any one country have a key role in determining patient outcomes. Various organisational issues have been shown to affect ICU patient outcomes in different countries.[21–23] In a study of 24 ICUs in one US county,[24] patients with acute lung injury had better outcomes if cared for in a closed-format (units that transferred all patients to an intensive care team or where a consultation with an intensivist who then shared responsibility for patient management with the admitting physician was mandatory) than in an open-format (units where any attending physician with ICU admitting privileges could be responsible for patient management) ICU. In a recent study of 69 ICUs across the USA,[23] daily care review and a lower bed-to-nurse ratio were associated with a lower annual ICU mortality, but not closed ICU format or 24-h presence of an intensivist. In an analysis of the large EPIC II database, a high nurse-to-patient ratio was noted to be independently associated with a lower risk of in-hospital death (Sakr Y, unpublished). Availability of a consultant-level intensivist and use of multidisciplinary clinical wardrounds are known to be associated with a high level of quality of care.[25] The effect of ICU infrastructure, staff training and availability, and process of care on patient outcomes clearly needs further study so that intensive care provision can be optimised across centres and resources can be targeted most appropriately on a global basis.

Our study has several limitations that should be considered when interpreting the data. First, although the audit included many ICUs, the voluntary nature of the participation might have affected the number and types of centres participating, perhaps particularly in the low and lower-middle income countries. This might have led to an underestimation of the burden of critical illness in these areas. Moreover, we are unable to assess how representative the participating hospitals are of their region. For example, a high percentage of the ICUs from low and lower-middle income countries reported 24-h intensivist cover and many reported high availability of ancillary staff, which seems to conflict with some other reports from these countries.[14] Some patient characteristics also seem to conflict with other data from these regions—eg, the rate of HIV infection was lowest in the low and lower-middle income countries, although in general the prevalence of HIV in these countries, many of which are located in sub-Saharan Africa, is particularly high.[14] The reasons for these apparent differences are not clear but probably relate to, at least partly, some degree of sample bias. The lower prevalence of reported comorbidities (COPD and heart failure) in low and lower-middle income countries versus high income countries might have been related to reporting bias. With the likely lower access to medical facilities in low and lower-income countries, it is possible that patients are less likely to have been diagnosed with a chronic disease. Nonetheless, our cohort provides large-scale comparative data in critically ill patients across multiple geographical areas and should be regarded as a unique initiative that can encourage future international collaboration in this field.

Second, data collection was not monitored and only incongruous data were verified. Third, missing SOFA scores were imputed by linear interpolation or carrying values backward or forward, which might potentially affect our estimations; however, the percentage of imputed data was small (about 3%) so it is unlikely that this will have had a major influence. Fourth, we analysed countries according to GNI, rather than the percentage of GDP allocated to health care specifically, but these data are difficult to obtain and less comparable because their

Panel: Research in context

Systematic review

We searched PubMed for reports published before Dec 1, 2013, with the search terms "critical illness", "intensive care medicine", "burden", "outcome", and "global". The search was limited to reports in English. We also checked the reference lists of reports identified in the search. Global comparative cohorts investigating intensive care practice, outcome, and the burden of critical illness are lacking. Several recent papers have highlighted the lack of information on the global burden of critical illness and availability of intensive care and called for studies to broaden knowledge in this field.[2,14,15]

Interpretation

To our knowledge, our study provides the largest available report of information related to provision of intensive care worldwide. The results of the present audit show a strong relation between the risk of death and the global national income, and suggest that differences in ICU organisation among centres play an important part in determining risk of death. Our data also show that sepsis remains a major health problem worldwide, associated with high mortality rates in all countries.

definition varies among countries. Fifth, because of the study design, data were collected over a short period of time and it is possible that this period was not representative of the average annual situation in each centre. Finally, the results of the multilevel analysis might not have accounted for unmeasured variables, but we adjusted for a large number of variables that might affect outcome.

The frequency of sepsis in our cohort was similar to that reported in the SOAP study (37·4%).[26] Other studies[27–29] have reported lower incidences of sepsis, but our study did not include routine postoperative patients.

Although study entry was entirely voluntary, the large amount of data collected on more than 10 000 patients from more than 80 countries shows the perceived need for such an international audit. International epidemiological data such as these provide a valuable insight into the global burden of critical illness worldwide. Indeed, several recent reports have highlighted the lack of information on the global burden of critical illness and availability of intensive care and called for studies to broaden knowledge in this field.[2,14,15] The results of the present audit, bearing in mind the limitations of the study design as discussed, show a strong relation between the risk of death and the GNI, and suggest that differences in ICU organisation among centres might have an important role in determining risk of death, although our data are insufficient to capture which specific aspects might be involved. Further study is needed to better define those aspects of ICU organisation that have the greatest effect.

Our data also show that sepsis remains a major health problem worldwide, associated with high mortality rates in all countries, supporting the need for continued emphasis to be placed on the epidemiology, prevention, and treatment of this important societal problem.

Contributors

J-LV conceived the study. J-LV, JCM, KR, MA, HN, EJ, and YS designed the study. SAN-S, BF, IM-L, JL, and PP were involved in acquiring data. HN and YS were responsible for the statistical analysis. HN, YS, and J-LV interpreted the data. YS and J-LV wrote the first draft of the report. JCM, SAN-S, BF, IM-L, JL, KR, MA, PP, HN, and EJ revised the report critically for important intellectual content. All authors approved the final version of the manuscript.

Declaration of interests

We declare that we have no competing interests.

References

1 Halpern NA, Pastores SM. Critical care medicine in the United States 2000–2005: an analysis of bed numbers, occupancy rates, payer mix, and costs. *Crit Care Med* 2010; **38:** 65–71.

2 Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. *Lancet* 2010; **376:** 1339–46.

3 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:** 2957–63.

4 Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985; **13:** 818–29.

5 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:** 707–10.

6 Calandra T, Cohen J. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. *Crit Care Med* 2005; **33:** 1538–48.

7 Vincent JL, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for change. *Lancet* 2013; **381:** 774–75.

8 World Bank. GNI per capita, Atlas method (current US$). http://data.worldbank.org/indicator/NY.GNP.PCAP.CD (accessed March 10, 2014).

9 Agresti A, Coull BA. Approximate Is better than "exact" for interval estimation of binomial proportions. *Am Stat* 1998; **52:** 119–26.

10 Larsen K, Petersen JH, Budtz-Jorgensen E, Endahl L. Interpreting parameters in the logistic regression model with random effects. *Biometrics* 2000; **56:** 909–14.

11 Larsen K, Merlo J. Appropriate assessment of neighborhood effects on individual health: integrating random and fixed effects in multilevel logistic regression. *Am J Epidemiol* 2005; **161:** 81–88.

12 Merlo J, Chaix B, Ohlsson H, et al. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. *J Epidemiol Community Health* 2006; **60:** 290–97.

13 Rasbash J, Steele F, Browne W, Goldstein H. A user's guide to MLwiN. Bristol: University of Bristol, 2012.

14 Dunser MW, Baelani I, Ganbold L. A review and analysis of intensive care medicine in the least developed countries. *Crit Care Med* 2006; **34:** 1234–42.

15 Fowler RA, Adhikari NK, Bhagwanjee S. Clinical review: critical care in the global context—disparities in burden of illness, access, and economics. *Crit Care* 2008; **12:** 225.

16 Baker T, Lugazia E, Eriksen J, Mwafongo V, Irestedt L, Konrad D. Emergency and critical care services in Tanzania: a survey of ten hospitals. *BMC Health Serv Res* 2013; **13:** 140.

17 Hsia RY, Mbembati NA, Macfarlane S, Kruk ME. Access to emergency and surgical care in sub-Saharan Africa: the infrastructure gap. *Health Policy Plan* 2012; **27:** 234–44.

18 Jochberger S, Ismailova F, Lederer W, et al. Anesthesia and its allied disciplines in the developing world: a nationwide survey of the Republic of Zambia. *Anesth Analg* 2008; **106:** 942–48.

19 Baelani I, Jochberger S, Laimer T, et al. Availability of critical care resources to treat patients with severe sepsis or septic shock in Africa: a self-reported, continent-wide survey of anaesthesia providers. *Crit Care* 2011; **15:** R10.

20 Bataar O, Lundeg G, Tsenddorj G, et al. Nationwide survey on resource availability for implementing current sepsis guidelines in Mongolia. *Bull World Health Organ* 2010; **88:** 839–46.

21 Durairaj L, Torner JC, Chrischilles EA, Vaughan Sarrazin MS, Yankey J, Rosenthal GE. Hospital volume-outcome relationships among medical admissions to ICUs. *Chest* 2005; **128:** 1682–89.

22 van der Sluis FJ, Slagt C, Liebman B, Beute J, Mulder JW, Engel AF. The impact of open versus closed format ICU admission practices on the outcome of high risk surgical patients: a cohort analysis. *BMC Surg* 2011; **11:** 18.

23 Checkley W, Martin GS, Brown SM, et al. Structure, process, and annual ICU mortality across 69 centers: United States Critical Illness and Injury Trials Group Critical Illness Outcomes Study. *Crit Care Med* 2014; **42:** 344–56.

24 Treggiari MM, Martin DP, Yanez ND, Caldwell E, Hudson LD, Rubenfeld GD. Effect of intensive care unit organizational model and structure on outcomes in patients with acute lung injury. *Am J Respir Crit Care Med* 2007; **176:** 685–90.

25 Rhodes A, Moreno RP, Azoulay E, et al. Prospectively defined indicators to improve the safety and quality of care for critically ill patients: a report from the Task Force on Safety and Quality of the European Society of Intensive Care Medicine (ESICM). *Intensive Care Med* 2012; **38:** 598–605.

26 Vincent JL, Sakr Y, Sprung CL, et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006; **34:** 344–53.

27 Brun-Buisson C, Meshaka P, Pinton P, Vallet B. EPISEPSIS: a reappraisal of the epidemiology and outcome of severe sepsis in French intensive care units. *Intensive Care Med* 2004; **30:** 580–88.

28 Padkin A, Goldfrad C, Brady AR, Young D, Black N, Rowan K. Epidemiology of severe sepsis occurring in the first 24 hrs in intensive care units in England, Wales, and Northern Ireland. *Crit Care Med* 2003; **31:** 2332–38.

29 Sakr Y, Elia C, Mascia L, et al. Epidemiology and outcome of sepsis syndromes in Italian ICUs: a regional multicenter observational cohort. *Minerva Anestesiol* 2013; **79:** 993–1002.

THE LANCET Respiratory Medicine

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Vincent J-L, Marshall JC, Ñamendys-Silva SA, et al, on behalf of the ICON investigators. Assessment of the worldwide burden of critical illness: the Intensive Care Over Nations (ICON) audit. *Lancet Infect Dis* 2014; published online April 14. http://dx.doi.org/10.1016/S2213-2600(14)70061-X.

Appendix 1. Alphabetical list of participating centres by region & 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); University of Medicine and Pharmacy Iuliu Hatieganu Cluj-Napoca (S Adriana)

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); United Christian Hospital of Hong Kong Sar (K Lee); 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)
Indonesia: Anestesi (M Wijanti); Pku Muhammadiyah Bantul, Yogyakarta, Indonesia (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 (Y Shimomura); 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 (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)
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 (B Richards); 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); Has-Tec (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, Mexíco (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); Kerala 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 (J 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 (Q Brigida); Hospital Universitario De Alava, Santiago (A Quintano); Hospital Universitario De Basurto, Bilbao (M Tebar); Hospital Universitario de Getafe (F Frutos-Vivar); 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 (K Williams); 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)

The Intensive Care Over Nations (ICON) Audit
Electronic Supplementary Data

Statistical analysis

Data were processed and analyzed in the Dept of Intensive Care of the University of Brussels, in collaboration with the Jena University Hospital, Jena, Germany.

Data are summarized using means with standard deviation, medians and interquartile ranges, or numbers and percentages. Crude mortality rates are given as percentages with Wald 95% confidence intervals (CI).[1] Single missing values of the SOFA score were imputed by linear interpolation. When first or last values were missing, the nearest value was carried backward or forward respectively. Missing data represented 6.1% of the collected data; 3.2% of the missing data were replaced as described.

For the purposes of this study, the world was divided into 9 geographic regions: North America, South America, Western Europe, Eastern Europe, Middle East, South Asia, East and South-East Asia, Oceania and Africa. Individual countries were also classified into three income groups according to the 2011 gross national income (GNI) per capita, using thresholds defined by the World Bank Atlas method[2]: GNI < $4,035 = low and lower middle income; GNI $4,036–12,475 = upper middle income; and GNI >$12,476 = high income.

The Kolmogorov-Smirnov test was used, and histograms and normal quantile-quantile plots were examined to verify if there were significant deviations from the normality assumption of continuous variables. Difference testing between groups was performed using analysis of variance (ANOVA), Kruskal Wallis test, Student's t-test, Mann-Whitney test, chi-square test or Fisher's exact test, as appropriate. The least significant difference testing procedure was used for pairwise comparisons.

For the binary outcome of in-hospital death and because of the hierarchical structure of the data, we used a three-level multilevel technique, with the structure of a patient (level 1) admitted to a hospital (level 2) within a country (level 3). The explanatory variables considered in the model were:

- Individual-level factors: age, sex, SAPS II score, type of admission, source of admission, mechanical ventilation, renal replacement therapy, comorbidities and presence of infection.
- Hospital-level factors: type of hospital; ICU specialty; total number of ICU patients in 2011; number of staffed ICU beds.
- Country-level factors: GNI.

Three models were constructed: The first model, an unconditional model with no exposure factors, was used to discern the amount of variance that existed between hospital and country levels; the second model contained hospital-level and country-level variables; the third model was extended to include patient-level characteristics. The results of fixed effects (measures of association) are given as odds ratios (OR) with their 95% confidence intervals and the 80% interval OR (IOR-80).[3-5] Random effects (measures of variation) measures included the variance (var) and its standard error (se), the proportional change in variance (PCV)[5] and the median odds ratio (MOR).[3-5] A second order penalized quasi-likelihood (PQL) estimation method was used, because this method approximates well compared to other methods.[6] The statistical significance of covariates were calculated using the Wald test.[7]

Data were analyzed using IBM® SPSS® Statistics software, version 20 for windows, and MLwiN v.2.28. All reported p-values are two-sided and a p-value of less than 0.05 was considered to indicate statistical significance.

Table E1. The list of countries by the category of income according to the World Bank Atlas method[2]

Low and lower middle Income	**Upper middle Income**	**High Income**
Afghanistan	Angola	Andorra
Albania	Argentina	Australia
Belize	Brazil	Austria
Bolivia	Bulgaria	Belgium
Democratic Republic of the Congo	Chile	Canada
Egypt	China	Croatia
El Salvador	Colombia	Czech Republic
Georgia	Costa Rica	Denmark
Guatemala	Ecuador	Estonia
Honduras	Iran	Finland
India	Latvia	France
Indonesia	Lebanon	Germany
Morocco	Lithuania	Greece
Pakistan	Malaysia	Hong Kong (China)
Palestinian territories	Mexico	Hungary
Philippines	Panama	Iceland
Sri Lanka	Peru	Ireland
	Romania	Israel
	Russia	Italy
	Serbia	Japan
	South Africa	Malta
	Taiwan	Martinique
	Thailand	Netherlands
	Tunisia	New Zealand
	Turkey	Norway
	Uruguay	Oman
	Venezuela	Poland
		Portugal
		Puerto Rico
		Saudi Arabia
		Singapore
		Slovakia
		Slovenia
		Spain
		Sweden
		Switzerland
		Turks and Caicos Islands
		United Arab Emirates
		United Kingdom
		United States

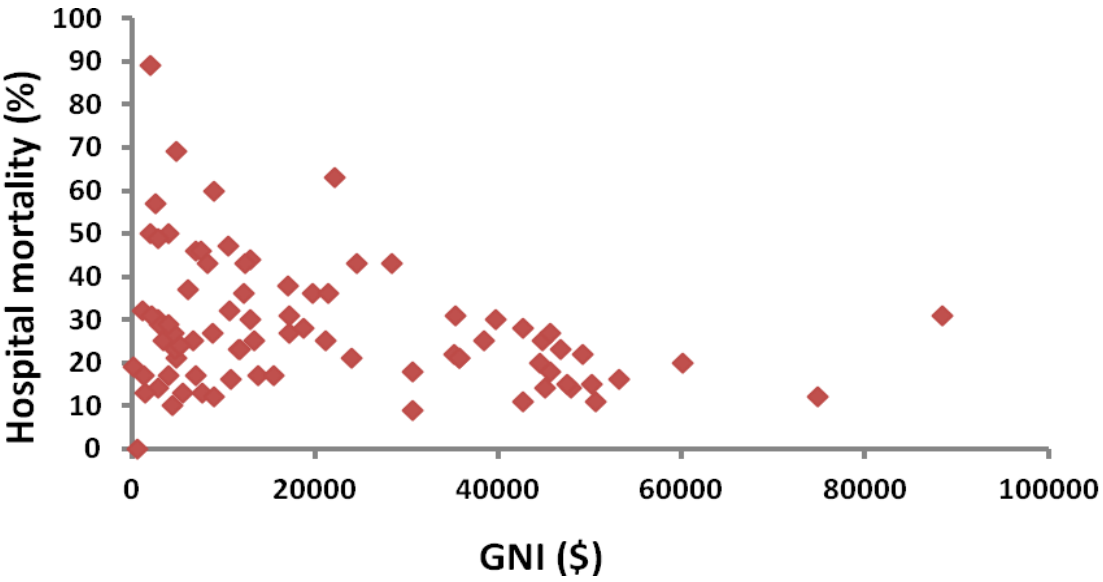
Table E2. Summary of multilevel analysis* with in-hospital mortality as the dependent variable in the whole cohort

	Model 1[a]	**Model 2[b]**			**Model 3[c]**		
Variables	OR (95%CI)	OR (95%CI)	p-value	IOR-80	OR (95%CI)	p-value	IOR-80
Level 1: patient							
Age (year)	-	-		-	1.01 (1.00-1.01)	<0.0001	-
Sex, Male	-	-		-	1.01 (0.89-1.15)	0.88	-
SAPSII	-	-		-	1.06 (1.06-1.07)	<0.0001	-
Type of admission (%)							
Surgical	-	-		-			-
Medical	-	-		-	1.60 (1.33-1.92)	<0.0001	-
Trauma	-	-		-	1.94 (1.42-2.66)	<0.0001	-
Other	-	-		-	2.12 (1.03-4.36)	0.04	-
Source of admission							
ER/ambulance	-	-		-			-
Hospital floor	-	-		-	1.40 (1.19-1.65)	<0.0001	-
OR/recovery	-	-		-	0.84 (0.65-1.07)	0.16	-
Other hospital	-	-		-	1.17 (0.93-1.47)	0.18	-
Other	-	-		-	1.08 (0.83-1.42)	0.56	-
Comorbidities							
COPD	-	-		-	0.99 (0.83-1.20)	0.95	-
Cancer (solid, non-metastatic)	-	-		-	1.56 (1.26-1.94)	<0.0001	-
Diabetes melitus	-	-		-	0.99 (0.80-1.22)	0.93	-
Heart failure, NYHA III/IV	-	-		-	1.45 (1.19-1.78)	0.0003	-
Chronic renal failure	-	-		-	1.06 (0.86-1.31)	0.59	-
Immunosuppression	-	-		-	1.26 (1.01-1.58)	0.04	-
Cirrhosis	-	-		-	2.22 (1.64-2.99)	<0.0001	-
Metastatic cancer	-	-		-	1.82 (1.33-2.48)	0.0002	-
Hematologic cancer	-	-		-	1.51 (1.04-2.19)	0.03	-
HIV infection	-	-		-	1.03 (0.55-1.95)	0.92	-
Procedures							
Mechanical ventilation	-	-		-	2.47 (2.10-2.91)	<0.0001	-
Renal replacement therapy	-	-		-	1.27 (1.06-1.51)	0.008	-
Sepsis	-	-		-	1.29 (1.13-1.48)	0.0002	-
Level 2: hospital							
Type of Hospital							
Non-university		Ref	na	na	Ref	na	na
Univesity/academic	-	1.09 (0.90-1.32)	0.38	(0.35-3.40)	1.05 (0.87-1.28)	0.6	(0.37-3.02)
Number of treated patients in ICU in 2011							
<250	-	Ref	na	na	Ref	na	na
250-499	-	1.57 (1.15-2.16)	0.005	(0.50-4.91)	1.47 (1.06-2.04)	0.02	(0.51-4.21)
500-749	-	1.70 (1.25-2.30)	<0.0006	(0.54-5.29)	1.48 (1.08-2.03)	0.02	(0.52-4.24)
750+	-	1.92 (1.40-2.62)	<0.0001	(0.61-5.98)	1.50 (1.09-2.06)	0.01	(0.52-4.29)
ICU speciality							
Mixed	-	Ref	na	na	Ref	na	na

Surgical	-	0.82 (0.62-1.10)	0.19	(0.26-2.57)	1.07 (0.79-1.43)	0.68	(0.37-3.05)
Medical	-	0.96 (0.73-1.26)	0.76	(0.31-2.99)	0.93 (0.70-1.24)	0.63	(0.33-2.67)
Others	-	1.20 (0.81-1.78)	0.36	(0.38-3.75)	1.28 (0.83-1.96)	0.26	(0.45-3.66)
Staffed ICU beds							
<15	-	Ref	na	na	Ref	na	na
15+	-	0.87 (0.72-1.03)	0.11	(0.28-2.70)	0.93 (0.77-1.12)	0.43	(0.32-2.66)
Level 3: country							
Income							
High	-	Ref	na	na	Ref	na	na
Low and lower middle	-	1.54 (1.00-2.39)	0.05	(0.76-3.12)	2.10 (1.46-3.03)	<0.0001	(1.51-2.94)
Upper middle	-	1.46 (1.08-1.96)	0.01	(0.72-2.95)	1.74 (1.38-2.20)	<0.0001	(1.25-2.43)
Random-effects							
Country: Variance (se)	0.19 (0.06)	0.15 (0.05)			0.03 (0.03)		
p-value	0.002	0.003			0.18		
MOR	1.51	1.45			1.19		
PCV		19%			82%		
Hospital: Variance (se)	0.43 (0.06)	0.40 (0.05)			0.34 (0.06)		
p-value	<0.0001	<0.0001			<0.0001		
MOR	1.86	1.82			1.74		
PCV	-	18%			49%		

PCV: proportional change in variance; OR: odds ratio; MOR: median odds ratio; IOR-80: 80% interval odds ratio; se: standard error. a: the unconditional model without any exposure variables. b: with adjustment by hospital-level and country-level variables. c: with adjustment by patient-level, hospital-level and country-level variables.

Figure E1. Hospital mortality rates per country according to GNI



References

1 Agresti A, Coull BA. Approximate Is better than "exact" for interval estimation of binomial proportions. *Am Stat* 1998; **52**: 119-26.

2 The World Bank. GNI per capita, Atlas method (current US$). http://data.worldbank.org/indicator/NY.GNP.PCAP.CD . 2013.
Ref Type: Internet Communication

3 Larsen K, Petersen JH, Budtz-Jorgensen E, Endahl L. Interpreting parameters in the logistic regression model with random effects. *Biometrics* 2000; **56**: 909-14.

4 Larsen K, Merlo J. Appropriate assessment of neighborhood effects on individual health: integrating random and fixed effects in multilevel logistic regression. *Am J Epidemiol* 2005; **161**: 81-8.

5 Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, Rastam L, Larsen K. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. *J Epidemiol Community Health* 2006; **60**: 290-7.

6 Goldstein H. Multilevel Statistical Models. London: Hodder Arnold; 2003.

7 Rasbash J, Steele F, Browne W, Goldstein H. A User's Guide to MLwiN. Bristol: 2012.

ICON

Form 1: Center Inclusion

Center | | | | |

Institution: .....

Type of hospital: ☐ University/academic ☐ Non-university

Hospital capacity: _ _ _ _ Beds

ICU speciality: ***Surgical -*** Cardiac ☐ Non-cardiac ☐ Trauma ☐ Mixed ☐

Medical - Coronary ☐ Neurologic ☐ Respiratory ☐ Mixed ☐

Mixed Medical/surgical ☐

Other, please specify .....

How many patients were treated in your ICU in 2011? _ _ _ patients

What was the mortality rate in your ICU in 2011? _ _ %

Is a physician available in your ICU 24 hours/day? ☐ Yes ☐ No

Total No of staffed ICU beds (on the first day of the study)**:** _ _ _ _ ICU Beds

(+ _ _ _ _ middle care beds)

Global nurse/patient ratio (No of nurses / No of staffed beds)**:** _ _ _ _

Other personnel available in your ICU:

(FTE: full-time equivalent, on the first day of the study)

Physiotherapist .....FTE

Pharmacist .....FTE

Technician.....FTE

ICON

Form 2: Enrollment/Completion

Center | | | | | **Patient** | | |

Date of hospital admission _ _ / _ _ / 2012

Date of ICU admission _ _ / 05 / 2012 (dd mm yyyy) _ _ : _ _ (24 h Clock) (hh mm)

Age[1] _ _ yrs **Sex** ☐ Male ☐ Female **Weight** _ _ Kg **Height** _ _ cm

---

Type of admission[2]**:** ☐ Medical

☐ Surgical Date of initial surgery _ _ / _ _ / 2012

Site of initial surgery _ _ _ /_ _ _ / _ _ _

□ Elective □ Emergency

☐ Trauma

Admission source: ☐ Other hospital ☐ ER/ambulance ☐ OR/Recovery

☐ Hospital floor ☐ Other, please specify ……..

Primary diagnosis _ _ _ **Secondary diagnoses** _ _ _ /_ _ _ / _ _ _

_ _ _ /_ _ _ / _ _ _

Comorbidities

□ COPD □ Cancer □ Metastatic cancer

□ Hematologic cancer □ Insulin dependent diabetes mellitus □ Heart failure (NYHA III-IV)

□ Chronic renal failure □ HIV infection □ Cirrhosis □ Immunosuppression

□ Steroid therapy □ Chemotherapy

Follow up

Was there a decision to withhold/withdraw a life sustaining measure at any time during the ICU stay? □ Yes □ No

ICU outcome

Date of ICU discharge _ _ / _ _ (Day / month) _ _ : _ _ (24 h Clock) (hh mm)

Discharged to:

□ Intermediate unit □ Other ICU □ Hospital floor

□ Other hospital/ Long term facility □ Other …… □ Dead

Hospital Outcome

Date of hospital discharge _ _ / _ _ (Day / month) ☐ Alive ☐ Dead

Tick here if the patient is still in the ICU or hospital on July 17 ☐

---

[1] Over 16 years.

[2] Planned ICU admissions for routine postoperative surveillance for less than 24 hours after uncomplicated surgery should not be included.

ICON

Form 3*: APACHE II

Center | | | | | Patient | | | |

Core body temperature	**(min)**	_ _ . _	**(max)**	_ _ . _ °C
Heart rate	**(min)**	_ _ _	**(max)**	_ _ _ bpm
Systolic blood pressure	**(min)**	_ _ _	**(max)**	_ _ _ □ mmHg □ KPa
Mean arterial pressure	**(min)**	_ _ _	**(max)**	_ _ _ □ mmHg □ KPa
Respiratory rate	**(min)**	_ _	**(max)**	_ _ bpm
FiO2	**(min)**	_ _	**(max)**	_ _ (%)
PaO2	**(min)**	_ _ _	**(max)**	_ _ _ □ mmHg □ KPa
PaCO2	**(min)**	_ _ _	**(max)**	_ _ _ □ mmHg □ KPa
Serum HCO3 (if no ABGs)	**(min)**	_ _ . _	**(max)**	_ _ _ . _ mmol/L
Arterial pH	**(min)**	_ _ _	**(max)**	_ _ _
Serum creatinine	**(min)**	_ . _	**(max)**	_ . _ □ mg/dL □ µmol/L
Blood urea	**(max)**	_ _ _ . _	□ mg/dL □ mmol/L	
Urine output		_ _ _	mL/24hours	
White Blood Count	**(min)**	_ _ _	**(max)**	_ _ _ $10^3/mm^3$
Serum potassium	**(min)**	_ . _	**(max)**	_ . _ mmol/L
Serum sodium	**(min)**	_ _ _	**(max)**	_ _ _ mmol/L
Hematocrit	**(min)**	_ _ . _	**(max)**	_ _ . _ (%)
Total bilirubin	**(max)**	_ _ _ . _	□ mg/dL □ µmol/L	
Glasgow coma score	**(min)**	_ _		

* Data collected during the first 24 hours after ICU admission

Form 4: Clinical information

Center | | | | | Patient | | |

	Day 0[3]	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	
Number of hours	_ _ h	24h	24h	24h	24h	24h	24h	
Temperature (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	° C
Temperature (max)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	° C
WBC count (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	1000/mm3
WBC count (max)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	1000/mm3
Heart rate (max)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	beats/min
Respiratory rate (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	Breaths/min
Respiratory PaO2/FiO2 (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	□ mmHg/ □ KPa
Artificial airway	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Mechanical ventilation	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Bilateral infiltrates	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Plateau pressure (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	cm H2O
Tidal volume (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	cc
PEEP/CPAP (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	cm H2O
Cardiovascular MAP (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	□ mmHg/□ KPa
Central venous catheter	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Arterial catheter	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
PA catheter	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Norepinephrine (max)	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	µg/kg/min
Dopamine (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	µg/kg/min
Dobutamine (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	µg/kg/min
Epinephrine (max)	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	µg/kg/min
Vasopressin (max)	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	U/min
Others (specify)								
(dose, max)								
Lactate (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	mmol/L
Neurological GCS (min)[4]	_ _	_ _	_ _	_ _	_ _	_ _	_ _	
Hematological Platelet count (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	X 10^3/µL
Hemoglobin (min)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	□ g/dL □ mmol/L
(max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	□ g/dL □ mmol/L
Hepatic Bilirubin (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	□ mg/dL/ □ µmol/L
Renal Creatinine (max)	_ _ _ . _	_ _ _ . _	_ _ _ . _	_ _ _ . _	_ _ _ . _	_ _ _ . _	_ _ _ . _	□ mg/dL □ µmol/L
Hemodialysis	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Hemofiltration	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Fluid balance Urine Output	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Other losses	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
HES	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Gelatins	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Dextrans	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Albumin (4%-5%)	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Albumin (20%-25%)	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Crystalloids	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
RBC	_ _	_ _	_ _	_ _	_ _	_ _	_ _	Units
Enteral	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml

[3] From the time of admission till the start of the next ICU day
[4] In sedated patients, use the assumed Glasgow Coma Score that the patient would have in absence of sedation

ICON

Form 4: Clinical Information

Center | | | | | Patient | | | |

	Day _	Day _	Day _	Day _	Day _	Day _	Day _	
Number of hours	24h	24h	24h	24h	24h	24h	24h	
Temperature (min)								° C
Temperature (max)								° C
WBC count (min)								1000/mm3
WBC count (max)								1000/mm3
Heart rate (max)								beats/min
Respiratory rate (max)								Breaths/min
Respiratory PaO2/FiO2 (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	□ mmHg/ □ KPa
Artificial airway	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Mechanical ventilation	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Bilateral infiltrates	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Plateau pressure (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	cm H2O
Tidal volume (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	cc
PEEP/CPAP (max)	_ _	_ _	_ _	_ _	_ _	_ _	_ _	cm H2O
Cardiovascular MAP (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	□ mmHg/□ KPa
Central venous catheter	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Arterial catheter	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
PA catheter	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Norepinephrine (max)	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	µg/kg/min
Dopamine (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	µg/kg/min
Dobutamine (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	µg/kg/min
Epinephrine (max)	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	µg/kg/min
Vasopressin (max)	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	_ . _ _	U/min
Others (specify)								
(dose, max)								
Lactate (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	mmol/L
Neurological GCS (min)[5]	_ _	_ _	_ _	_ _	_ _	_ _	_ _	
Hematological Platelet count (min)	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	_ _ _	X 10^3/µL
Hemoglobin (min)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	□ g/dL □ mmol/L
(max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	□ g/dL □ mmol/L
Hepatic Bilirubin (max)	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	_ _ . _	□ mg/dL/ □ µmol/L
Renal Creatinine (max)	_ _ _ .	_ _ _ .	_ _ _ .	_ _ _ .	_ _ _ .	_ _ _ .	_ _ _ .	□ mg/dL □ µmol/L
Hemodialysis	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Hemofiltration	Y N	Y N	Y N	Y N	Y N	Y N	Y N	
Fluid balance Urine Output	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Other losses	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
HES	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Gelatins	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Dextrans	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Albumin (4%-5%)	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Albumin (20%-25%)	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
Crystalloids	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml
RBC	_ _	_ _	_ _	_ _	_ _	_ _	_ _	Units
Enteral	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	_ _ _ _ _	ml

[5] In sedated patients, use the assumed Glasgow Coma Score that the patient would have in absence of sedation

Form 5: Microbiology and Clinical Infection

Center | | | | | Patient | | | |

	Day 0[6]	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Number of hours	__ h	24h	24h	24h	24h	24h	24h
Microbiological sampling	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Respiratory Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Abdominal Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Urinary							
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Skin/Wound Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Catheter Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Blood							
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Others (specify)							
Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Others (specify)							
Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Unknown source	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Antibiotics	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___

[6] From the time of admission till the start of the next ICU day

Form 5: Microbiology and Clinical Infection

Center | | | | | **Patient** | | |

	Day _	Day _	Day _	Day _	Day _	Day _	Day _
Number of hours	24h	24h	24h	24h	24h	24h	24h
Microbiological sampling	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Respiratory Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Abdominal Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Urinary							
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Skin/Wound Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Catheter Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Blood							
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Others (specify)							
Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Others (specify)							
Clinical diagnosis	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Microorganism	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___	___/___ ___/___
Unknown source	Y N	Y N	Y N	Y N	Y N	Y N	Y N
Antibiotics	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___	___/___ ___/___ ___/___

Codes

I. Site of surgery

000 No surgery during the current hospital stay

Head (non-trauma)
101 Cerebrovascular accident, or other non-traumatic accident (hemorrhage, aneurysm)
102 Intracranial tumor
103 Spinal surgery
104 Maxillo-facial surgery or Ear, nose and throat surgery
105 Other

Thoracic
201 Pneumonectomy, lobectomy
202 Pleural
203 Lung transplantation
204 Other

Cardiovascular
301 Valvular, without CABG
302 Valvular with CABG
303 CABG without vale repair
304 Other: pericardial, congenital anomaly, ventricular aneurysm…
305 Heart or heart & lung transplantation
306 Major aortic surgery: includes all surgery on aorta for dissection, atheroma, aneurysm.
307 Other major vascular surgery
308 Other

Renal-urinary or genital tract
401 Renal surgery
402 Urological surgery
403 Obstetric surgery: Cesarean section, peri or post partum hemorrhage...
404 Gynecological surgery
405 Other

Digestive
501 Upper gastro-intestinal surgery (up to and including the jejunum)
502 Lower gastrointestinal surgery
503 Bilio-pancreatic
504 Liver: partial hepatectomy
505 Liver transplantation

Endocrine
601 Thyroid, adrenal, pancreas, etc

Trauma
701 Brain (subdural, epidural, intracerebral hematoma, skull fracture…)
702 Spine
703 Thorax (cardiac, respiratory or digestive tract, vessels)
704 Abdomen
705 Limb(s)

800 Other

II. Diagnosis

Neurological (non-trauma)
101 Post-anoxic coma
102 Coma, non post-anoxic
103 Seizures
104 Cerebrovascular accident
105 Intracranial tumor
106 Degenerative disease: Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease…
107 Polymyopathy incl. Myopathia, myositis…
108 Spinal cord injury (any type)
109 Delirium
110 Other

Respiratory
201 ARDS
202 Severe lung infection (previously healthy lungs)
203 Acute on chronic pulmonary disease (decompensated COPD, etc)
204 Asthma, severe bronchospasm
205 Pulmonary embolism
206 Large pleural effusion
207 Upper airway obstruction
208 Tumor
209 Other

Cardiovascular
301 S/P cardiac arrest (CPR prior to admission to ICU)
302 Septic shock
303 Cardiogenic shock
304 Hypovolemic shock
305 Obstructive shock
306 Anaphylactic shock
307 Shock, unknown type
308 Acute coronary syndrome
309 Cardiac failure without shock (left, right or global)
310 Hypertensive crisis
311 Major arrhythmia
312 Other

Renal/Ob-gyn
401 Organic acute renal failure
402 Obstructive ARF
403 Pre-renal ARF
404 Acute on chronic renal failure
405 Special diagnoses (tumor, glomerularephisis, vasculitis,etc)
406 Gynecological diseases
407 Eclampsia, preeclampsia
408 HELLP syndrome
409 Delivery hemorrhage
410 Other

Hematological
501 Hemorrhagic syndrome (with or without coagulopathy)
502 Febrile leukopenia
503 Severe anemia (without acute bleeding)
504 Hematologic cancer (lymphoma, acute leukemia, multiple myeloma, etc)
505 Other

Digestive/Liver
601 Gastrointestinal bleeding
602 Acute abdomen
603 Severe pancreatitis
604 Cirrhosis, liver failure
605 Cholecystitis, cholangitis.
606 Acute hepatitis
607 Neoplasia of the upper digestive tract (esophageal, gastric or duodenal).
608 Neoplasia of the lower digestive tract (colon and rectum)
609 Other

Metabolic
701 Major electrolyte disturbance
702 Hypothermia
703 Drug overdose
704 Other intoxication, acute: (alcohol, CO inhalation, industrial, domestic, etc)
705 Adverse effects of medication (Lyell syndrome, neuroleptic malignant syndrome…)
706 Diabetic ketoacidosis
707 Hyperosmolar diabetic coma
708 Hypoglycemia
709 Endocrinopathy: thyroid, pituitary gland, adrenal cortex, parathyroid…
710 Other

Trauma
801 lsolated brain trauma
802 Monotrauma, without brain trauma
803 Polytrauma, without brain trauma
804 Polytrauma, with brain trauma
805 Burn
806 Near-drowning
807 Other

900 Other diseases

ICON

III. Microorganisms

Gram positive
101 Staphylococcus aureus sensitive to methicillin
102 Staphylococcus aureus resistant to methicillin
103 Staphylococcus coagulase negative (epidermidis, haemolyticus, …)
104 Streptococcus D group (Enterococcus faecalis, faecium)
105 Streptococcus pneumoniae
106 Streptococcus, other
107 Cocci Gram +ve, other
108 Listeria
109 Bacillus Gram +ve, others (Bacillus cereus, Bacillus spp, Corynebacterium spp, Lactobacillus, Rhodococcus equi, Nocardia spp, other)

Gram negative
201 Escherichia coli
202 Enterobacter
203 Klebsiella
204 Acinetobacter
205 Proteus (incl. Morganella and Providencia)
206 Salmonella
207 Serratia (Serratia marcescens, Serratia spp)
208 Citrobacter (Citrobacter freundii, Citrobacter spp)
209 Pseudomonas aeruginosa
210 Pseudomonas, other
211 Stenotrophomonas maltophilia
212 Haemophilus (influenzae or other)
213 Enterobacteria, other (incl. Yersinia or Shigella)
214 Bacillus Gram -ve, other
215 Cocci (Neisseria meningitidis, Moraxella…)

Anaerobes
301 Clostridium difficile
302 Clostridium, other
303 Anaerobe, other

Other organisms
401 Mycobacteria (tuberculosis or other)
402 Chlamydia, Rickettsia
403 Mycoplasma
404 Legionella

Fungi
501 Candida albicans
502 Candida non-albicans
503 Aspergillus
504 Fungi, other (Cryptoccus neoformans, Histoplasma spp…)

Viruses
601 Herpes simplex, zoster
602 respiratory virus (RSV, influenza, …)
603 CMV
603 Others

Others
701 Plasmodium falciparum
702 Pneumocystis jiroveci
703 others

IV. Antibiotics

Cephalosporins
11 Cefuroxime
12 Ceftriaxone
13 Cefotaxime
14 Ceftazidime
15 Cefepime/cefpirome
16 Other cephalosporin

Penicillins
21 Benzyl penicillin
22 Ampicillin/amoxy + clavulanate
23 Carbeni/pipera/ticarcillin + enzyme inhibitor
24 Oxa/cloxa/flucloxacillin
25 Other penicillin

Other beta-lactams
31 Temocillin
32 Penem (imi-, mero-, dori-)
33 Aztreonam
34 Other

Aminoglycoside
41 Amikacin
42 Tobramycin
43 Other

Quinolone
51 Ciprofloxacin
52 Other

Glycopeptides
61 Vancomycin
62 Other

Macrolides
71 Erythromycin
72 Clindamycin
73 Other (clarithromycin, etc)

Other antibiotics
81 Metronidazole/tinidazole
82 Cotrimoxazole
83 Colistin/polymyxin B
84 Oxazolidinone (Linezolid)
85 Lipopeptide (Daptomycin)
86 Tetracyclines
87 Fosfomicin
88 Tigecycline
89 Other

Antifungal
91 Fluconazole
92 Caspofungin
93 Voriconazole
94 Anidulafungin
95 Micafungin
96 Amphotericin B

97 Ampho lipid formulation
98 Other

Antiviral
101 Ganciclovir
102 Other

V. Infection diagnosis

1.Pneumonia

***Microbiologically confirmed*:** The patient must have a new or progressive radiographic infiltrate, along with a high clinical suspicion of pneumonia plus a definite cause established by the recovery of a probable etiologic agent from a) an uncontaminated specimen (blood, pleural fluid, transtracheal aspirate, or transthoracic aspirate); b) the recovery from respiratory secretions of a likely pathogen that does not colonize the upper airways (e.g., *Mycobacterium tuberculosis*, *Legionella* species, influenza virus, or *Pneumocystis jiroveci (carinii*); c) recovery of a likely/possible respiratory pathogen in high concentrations using quantitative cultures of a lower respiratory tract sample (endotracheal aspirate, BAL, or protected specimen brush); or d) positive serology.

***Probable*:** The patient must have a new or progressive radiographic infiltrate along with a high clinical suspicion of pneumonia plus detection (by staining or culture) of a likely pulmonary pathogen in respiratory secretions (expectorated sputum, endotracheal or bronchoscopic aspirate, or quantitatively cultured bronchoscopic BAL fluid or brush catheter specimen), but in concentrations below the diagnostic threshold, or the presence of a negative lower respiratory tract culture if collected within 72 hrs after starting a new antibiotic regimen.

***Possible*:** Abnormal chest radiograph of uncertain cause, in a patient with a low or moderate clinical suspicion of pneumonia, but with microbiological or serological evidence of definite or probable pneumonia (as defined above).

2. Bloodstream infection (BSI) of unknown origin (i.e., primary BSI)

Patient must meet the following two criteria: Patient has a recognized pathogen (defined as a microorganism not usually regarded as a common skin contaminant, i.e., diphtheroids, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci, or micrococci) cultured from one or more blood cultures **or** a common skin contaminant (e.g., diphtheroids, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci, or micrococci) cultured from two or more blood cultures drawn on separate occasions (including one drawn by venipuncture) **and** the organism cultured from blood is not related to an infection at another site, including intravascular-access devices

3. Secondary bloodstream infection (BSI) (other than catheter-related BSI)

Patient must meet the following two criteria: Patient has a recognized pathogen defined as a microorganism not usually regarded as a common skin contaminant (i.e., diphtheroids, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci, or micrococci) cultured

from one or more blood cultures the organism cultured from the blood is related to an infection with the same organism at another site

4. Catheter-related infection with bacteriologic confirmation

Definite catheter-related infection with bacteriologic confirmation is defined as at least one peripheral positive blood culture **and** one of the following: 1) A positive semiquantitative (≥15 colony-forming units [cfu]/catheter segment) or quantitative (≥103 cfu/catheter segment) catheter tip culture (i.e., catheter colonization), whereby the same microorganism (species and antibiogram) is isolated from the catheter segment and peripheral blood, 2) A positive hub or exit site culture growing the same microorganism as peripheral blood **or** positive paired central and peripheral blood cultures growing the same organism, where the central blood culture is positive ≥2 hrs earlier than the peripheral blood culture or has five times the growth of the peripheral blood culture

5. Primary peritonitis

Primary peritonitis (also referred to as spontaneous bacterial peritonitis) is defined as a microbial infection of the peritoneal fluid in the absence of a gastrointestinal perforation, abscess, or other localized infection within the gastrointestinal tract

***Microbiologically confirmed*:** the presence of a clinically compatible presentation of primary peritonitis with the isolation of microbial pathogens (inperitoneal fluid or blood) along with evidence of an acute inflammatory reaction within the peritoneal fluid (i.e., ≥500 leukocytes/mL) with a neutrophilic predominance, an ascitic fluid pH of ≤7.35 (arterial to ascitic pH difference of ≥0.1), or a lactate concentration of ≥2.5 mg/L.

***Probable*:** Clinically appropriate setting with evidence of an inflammatory ascitic fluid (≥500 leukocytes/mL with a neutrophil predominance) in the presence of a positive Gram stain but negative peritoneal fluid cultures or in the presence of a positive blood culture for a pathologic organism with inflammatory cells in ascitic fluid.

***Possible*:** A compatible clinical illness with an inflammatory peritoneal fluid (≥500 leukocytes/mL) in the absence of a positive culture (in peritoneal fluid or blood) or Gram stain.

6. Secondary peritonitis

Secondary peritonitis is a microbial infection of the peritoneal space following perforation, abscess formation, ischemic necrosis, or penetrating injury of the intra-abdominal contents

Microbiologically confirmed: Isolation of one or more microbial pathogens found in the peritoneum or the blood ≥24 hrs after a gastrointestinal perforation of the stomach, esophagus or duodenum, or any perforation of the small bowel distal to the ligament of Treitz. Spillage of luminal contents during an operative procedure is not sufficient evidence of perforation that

allows for definitive diagnosis of peritonitis. A penetrating abdominal wound or documented perforation that is surgically repaired within 12 hrs of its occurrence is not sufficient evidence to support diagnosis of secondary bacterial peritonitis.

***Probable*:** Compatible clinical illness associated with documented evidence of perforation (free air in the abdomen on radiographic studies or surgical confirmation of peritoneal inflammation following luminal perforation in the absence of microbiologically confirmed peritonitis). A Gram stain in the absence of a positive culture from the peritoneum would be considered probable secondary bacterial peritonitis.

***Possible*:** Upper gastrointestinal perforation or penetrating abdominal trauma that is surgically repaired without further evidence of microbiologic confirmation or clinical signs or symptoms supportive of a diagnosis of bacterial or fungal peritonitis. An inflammatory peritoneal fluid in the presence of a documented but localized intra-abdominal abscess in the absence of culture confirmation would also be considered possible secondary bacterial peritonitis.

7. Tertiary peritonitis

Tertiary peritonitis is defined as persistent intra-abdominal inflammation and clinical signs of peritoneal irritation following secondary peritonitis from nosocomial pathogens.

***Microbiologically confirmed*:** Isolation of one or more nosocomial pathogens from peritoneal fluid or blood in an appropriate clinical situation ($\geq$48 hrs after treatment for primary or secondary peritonitis).

***Probable*:** Compatible clinical illness with documented secondary peritonitis with persistent peritoneal inflammation ($\geq$500 leukocytes/mL peritoneal fluid) in the absence of microbiologically confirmed microbial persistence in the peritoneal space.

***Possible*:** Compatible clinical illness with persistent signs of systemic inflammation but without clear documented evidence of persistent inflammation within the peritoneal space following secondary bacterial peritonitis.

8. Peritoneal dialysis-related peritonitis

***Microbiologically confirmed*:** In a patient receiving peritoneal dialysis, an acute inflammatory process within the peritoneum ($\geq$100 leukocytes/mL) with a predominance of neutrophils in the presence of culture documentation in peritoneal fluid or blood of a pathogenic microorganism.

***Probable*:** An inflammatory process ($\geq$100 leukocytes/mL with a neutrophil predominance) of the peritoneum during the course of peritoneal dialysis, with Gram stain evidence of an infection but without culture documentation from blood or the peritoneal space.

***Possible*:** Abnormal accumulation of inflammatory cells in the peritoneum ($\geq$100 leukocytes/mL) with a predominance of neutrophils in the absence of Gram strain and culture evidence of infection.

9. Intra-abdominal abscess

***Microbiologically confirmed*:** Clinical, radiographic, and direct surgical confirmation of an inflammatory collection within the peritoneal space or surrounding structures with isolation of one or multiple microbial pathogens from the fluid collection. Microbiologic confirmation will require specimen collection from percutaneous aspirations under sterile technique or direct surgical observation with acquisition of culture material directly from the abscess cavity or the blood.

***Probable*:** The presence of an abnormal collection of fluid in the intra-abdominal contents or surrounding structures with evidence of inflammatory cells and/or positive Gram stain but with negative cultures from that fluid accumulation or blood.

***Possible*:** Clinical or radiographic evidence of an abnormal fluid accumulation within the abdominal contents or surrounding structures but without microbiologic or surgical confirmation.

10. Biliary tract infection

***Microbiologically confirmed*:** An acute inflammatory process of the biliary tract or surrounding structures with the isolation of pathogenic microorganisms obtained via percutaneous or direct surgical collection of samples in the lumen of the gall bladder or the biliary tract or the blood.

***Probable*:** An appropriate clinical syndrome with evidence of microbial infection verified by Gram stain from the biliary system but with negative cultures from the biliary system or blood for enteric microbial pathogens.

***Possible*:** This includes patients with clinical evidence of biliary tract infection with surgical or radiographic evidence of suppurative complications but in the absence of microbiologic verification, positive blood cultures, or a Gram stain evidence of active infection. In the presence of ascending cholangitis, a positive blood culture is sufficient to make the diagnosis of microbiologically confirmed, ascending cholangitis ($\geq$50% of patients will be bacteremic with this biliary tract infection). A positive culture from the biliary tract in the absence of clinical symptoms (bactobilia) is not sufficient to make a diagnosis. Positive culture from a T-tube drainage from the common bile duct is not sufficient evidence to make a diagnosis of biliary tract infection if the tube has been in place for $\geq$24 hrs.

11. Pancreatic infection

***Microbiologically confirmed*:** This requires direct confirmation of positive microbial cultures from the pancreas or surrounding structures by percutaneous aspiration or direct visualization and culture at the time of surgery or from the bloodstream.

***Probable*:** The presence of surgical or radiographic evidence of an abnormal collection of an inflammatory focus within the substance of the pancreas or surrounding structures with a positive Gram stain from the pancreatic collection in the absence of culture documentation.

Possible: Radiographic or direct surgical inspection with evidence suggestive of pancreatic abscess or other type of infection.

12. Typhlitis

Typhlitis is defined as transmural inflammation and variable degrees of necrosis and infection of the cecum and colon found in immunocompromised hosts (primarily in neutropenic patients and HIV-infected patients).

Microbiologically confirmed: Detection of microbial pathogens within the submucosa of the bowel wall of the cecum following surgical excision.

Probable: The presence of a pathogenic microorganism in the systemic circulation or peritoneum in the appropriate clinical situation with radiographic evidence of air in the bowel wall, thickening, or hemorrhagic necrosis on abdominal computed tomography scan or direct surgical inspection of the cecum.

Possible: A compatible clinical presentation with radiographic evidence of bowel wall edema and/or gas and/or hemorrhagic necrosis within the bowel wall of the cecum without microbiologic or surgical confirmation.

13. Toxic megacolon

Toxic megacolon is defined as an acute dilation of the colon due to diffuse inflammation or necrosis of the bowel wall in the absence of mechanical obstruction.

***Microbiologically confirmed*:** The isolation of pathogenic microorganisms within the peritoneum, blood, or bowel wall from surgically resected tissues in patients presenting with the clinical picture of toxic megacolon with radiographic evidence of dilatation of the lumen of the large bowel > 6 cm.

***Probable*:** Radiographic evidence of acute dilation of the lumen of the large bowel >6 cm in the appropriate clinical situation with evidence of peritoneal inflammation and/or positive Gram stain but without pathologic evidence of microbial invasion of the bowel wall and/or submucosal necrosis.

Possible: A clinical presentation compatible with toxic megacolon and radiographic evidence of acute dilatation of the lumen of the large bowel > 6 cm without microbiologic or pathologic confirmation.

14. Urosepsis in noncatheterized patients

1. Lower urinary tract infection

Is usually not considered as a possible source of severe sepsis/septic shock, but if required the conventional microbiological definition of >105 cfu/ mL can be used.

2. Upper urinary tract infection (kidney, ureter, or tissue surrounding the retroperitoneal or perinephric space)

Must meet one of the following criteria: 1) Organism isolated from culture of fluid (other than urine) or tissue from the affected site. 2) An abscess or other evidence of infection seen on direct examination, during surgery, or by histopathologic examination **or** two of the following: Fever (>38°C); urgency; localized pain or tenderness at involved site; and any one of the following: microscopic examination (urinalysis or Gram stain) showing pyuria or >105 cfu/mL; purulent drainage from the affected site; pyuria; hematuria; organism isolated from urine culture; positive Gram stain; radiographic evidence of infection (e.g., ultrasound, computed tomography, magnetic resonance imaging, radiolabeled scan).

15. Urosepsis in catheterized patients (urinary catheter is present or has been removed within the past 6 days)

1. Lower urinary tract infection : The presence of suggestive signs and symptoms including fever (>38°C), urgency, frequency, dysuria, pyuria, hematuria, positive Gram stain, pus, suggestive imaging **and** Positive dipstick for leukocyte esterase and/or nitrate **or** pyuria (>10 white blood cells/µL or >3 white blood cells/high-power field of unspun urine) **or** organisms seen on Gram stain of unspun urine **or** frank pus expressed around the urinary catheter **or** >103 cfu/mL **or** if the patient can report symptoms.
2. Upper urinary tract infection (kidney, ureter, bladder, urethra, or tissue surrounding the retroperitoneal or perinephric space)
Must meet **one** of the following criteria: Organism isolated from culture of fluid (other than urine) or tissue from the affected site; an abscess or other evidence of infection seen on direct examination, during surgery, or by histopathologic examination
or two of the following: Fever (>38°C), urgency, localized pain or tenderness at involved site, and any of the following: purulent drainage from the affected site, pyuria, hematuria, organism isolated from culture, positive Gram stain, radiographic evidence of infection (e.g., ultrasound, computed tomography, magnetic resonance imaging, radiolabeled scan).

16. Candiduria

A. In catheterized patients
Candiduria >103 cfu/mL represents asymptomatic candiduria
B. In noncatheterized patients*a*
Candiduria >104 cfu/mL represents asymptomatic candiduria
Patients who satisfy either of the above criteria **and** have clinical signs and/or symptoms of urinary tract infection based on CDC criteria*b* can be designated as having clinically significant *Candida* urinary tract infection
C. Upper urinary tract infection
Same criteria as upper urinary tract bacterial infection (see # 15)

17. Skin and soft tissue infections

1. Surgical site infections

Surgical site infection is defined as an infection that arises within 30 days of an operative procedure and at the site of surgical intervention.

Symptoms and signs suggestive of a surgical site infection include wound erythema and blanching, tenderness, pain, purulent discharge, fever (temperature >38.0℃), and leukocytosis. A superficial surgical site infection involves the skin or subcutaneous tissues alone, whereas a deep surgical site infection involves the fascia or muscle layers, and an organ space surgical site infection involves the deeper anatomic areas opened during the surgical procedure.

2. Nonsurgical site infections

Cellulitis is defined as an acute spreading infection of the skin and underlying soft tissue suggested by the presence of a rapidly expanding erythema, local tenderness, pain, swelling, lymphangitis, and lymphadenopathy, which is frequently accompanied by systemic signs and symptoms including malaise, fever (temperature _38.0℃), and chills.

Necrotizing cellulitis and fasciitis are defined as acute, rapidly progressing, and life-threatening destructive (i.e., necrotizing) infections of the subcutaneous tissues dissecting along tissue planes. Although these two clinical entities exhibit some distinctive clinical and microbial characteristics, they share common features. The symptoms and signs suggestive of necrotizing cellulitis or fasciitis are intense local pain (a cardinal feature), exquisite tenderness, erythema (initially discrete but evolving to red-purple and then blue-gray cutaneous lesions often with hemorrhagic bullae), swelling, edema, crepitations (in the case of necrotizing cellulitis), and extensive tissue necrosis, which are associated with prominent systemic toxicity (toxic shock syndrome, severe sepsis, or septic shock).

Appendix

A) The Glasgow Coma Scale

Eyes	Open	Spontaneously	4
		To verbal stimulus	3
		To pain	2
		No response	1
Best motor response	To verbal commands	Obeys	6
	To painful stimulus	Localizes pain	5
		Semi-purposeful	4
		Decorticates (flexion)	3
		Decerebrates (extension)	2
		No response	1
Best verbal response		Oriented and converses	5
		Disoriented and converses	4
		Inappropriate words	3
		Incomprehensible sounds	2
		No response	1
Total		3-15	

Glasgow coma score should be assumed (i.e. a patient who is in deep coma only because he is being treated with high doses of sedative agents should be considered to have a Glasgow coma score of 15). The lowest score during the day is recorded.

B) Conversion tables

1 Estimating PaO_2 from a given SO_2

SO_2 (%)	PaO_2 (mmHg)
80	44
81	45
82	46
83	47
84	49
85	50
86	52
87	53
88	55
89	57
90	60
91	62
92	65
93	69
94	73
95	79
96	86
97	96
98	112
99	145

2 Estimating FiO_2

Method	O_2 flow (l/min)	Estimated FiO2 (%)
Nasal cannula	1	24
	2	28
	3	32
	4	36
	5	40
	6	44
Nasopharyngeal catheter	4	40
	5	50
	6	60
Face mask	5	40
	6-7	50
	7-8	60
Face mask with reservoir	6	60
	7	70
	8	80
	9	90
	10	95