The Extended Prevalence of Infection in the ICU Study:

EPIC II

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ABSTRACT

Context: Infection is a major cause of morbidity and mortality in intensive care units worldwide. However, there is still relatively little information about the global epidemiology of such infections.

Objective: To provide an up-to-date picture of the extent and patterns of infection in intensive care units around the world.

Design: One-day point prevalence study on May 8, 2007.

Setting: A total of 1265 intensive care units from 76 countries.

Patients: All patients present on one of the participating units on the study day.

Main outcome measures: Demographic, physiologic, bacteriological, and therapeutic data were collected, along with outcome data at intensive care unit and hospital discharge.

Results: On the day of the study, 51% of patients were considered to be infected. Seventy-one percent of all patients were receiving antibiotics. Sixty-four percent of infections were of respiratory origin, and 70% of infected patients had positive microbiological isolates; Gram-negative organisms were isolated from 62% of infectious episodes, Gram-positive organisms from 47%, and fungi from 19%. Gram-negative organisms were much less prevalent in North America, Europe and Oceania than in other regions. Patients who had longer intensive care unit stays prior to the study day had higher rates of infection, especially infections due to resistant staphylococci, *Acinetobacter*, *Pseudomonas* species and fungi. Intensive care unit (25 versus 11%) and hospital (33% versus 15%) mortality rates were more than double in infected than in non-infected patients (both $P<0.001$). In multivariable analysis, infection was independently

associated with an increased risk of hospital mortality (odds ratio 1.52 [1.37-1.69], $P<0.001$).

Conclusions: Infections are very common in contemporary intensive care unit patients, and risk of infection increases with duration of intensive care unit stay. In this large cohort, infection was independently associated with an increased risk of hospital death.

Introduction

Infection is a common problem for patients in intensive care units (ICUs), and is associated with considerable morbidity, mortality, and costs.[1-11] Infection and related sepsis are the leading cause of death in non-cardiac ICUs, with mortality rates that reach 60%, and account for approximately 40% of total ICU expenditure.[10,12] Importantly, the incidence of sepsis and, hence, the number of infection-related deaths is increasing.[5,13]

Most large epidemiological studies of infection and sepsis have been conducted in North America, Europe, and Australia [2,10,13-18], with limited data from other countries.[19,20] Differing definitions and different study populations make it difficult to compare study results. International data related to the prevalence, risk factors, causative microorganisms, and outcomes of infection are necessary to increase and maintain awareness of the impact of infection, to help in the development of local and international guidelines for diagnosis and treatment, to facilitate adequate and appropriate resource allocation, and to assist in the design of multicenter interventional studies.

The European Prevalence of Infection in intensive Care (EPIC) study,[21] conducted on April 29, 1992, included data from 1417 ICUs in 17 Western European countries and provided valuable information regarding the prevalence and epidemiology of infection in European critically ill patients. Fifteen years after that successful international collaboration, EPIC II, the *Extended* Prevalence of Infection in Intensive Care study, was conducted to provide an up-to-date picture of the extent and patterns of infection in ICUs around the world.

Methods

A international steering committee was established in 2006 and selected the study date, May 8, 2007. ICUs were invited to participate in a one-day, prospective, multicenter prevalence study of ICU infection. Methods for recruitment of participating institutions included direct mailings to members of the European Society of Intensive Care Medicine, announcements at international meetings and symposia, and mailings to contacts and collaborators of each steering committee member. Participation in the study was entirely voluntary and the study was not funded. Local ethical committee approval at each participating center was expedited or waived due to the purely observational nature of the study.

Demographic, physiologic, bacteriological, and therapeutic data were collected from all patients present on a participating ICU between midnight on May 7 and midnight on May 8, 2007. SAPS II[22] and sequential organ failure assessment (SOFA)[23] scores were calculated for the study day. Outcomes at ICU and hospital discharge, and any decision to withdraw/withhold therapy during the ICU stay were also recorded. Data were recorded using pre-printed case report forms (CRF) and were not monitored. A dedicated telephone hotline was available for any queries during the study follow-up period.

Infection was defined according to the definitions of the International Sepsis Forum[24] and adjudicated by the attending physician. Patients who had had surgery in the 4 weeks preceding admission were considered to be surgical admissions. Elective surgery was defined as surgery scheduled > 24 hours in advance and emergency surgery as that scheduled within 24 hours of operation. Trauma was defined as ICU admissions directly related to, or occurring as a complication of, a traumatic event in the 30 days preceding

admission. All other admissions were considered medical. The presence of the following comorbid conditions was noted: Chronic obstructive pulmonary disease (COPD); metastatic cancer (metastases proven by surgery, computed tomography or magnetic resonance scan, or any other method); liver cirrhosis; heart failure (NYHA III-IV); hematologic malignancy (lymphoma, acute leukemia, or multiple myeloma); human immunodeficiency virus (HIV) infection (HIV positive patients with clinical complications such as *Pneumocystis jirovecii*, Kaposi's sarcoma, lymphoma, tuberculosis, or toxoplasma infection); chronic renal failure (need for chronic renal support or history of chronic renal insufficiency with a serum creatinine > 3.6 gm/dL [300 μmol/L]); immunosuppression (administration in the 6 months prior to ICU admission of steroid treatment [at least 0.3 mg/kg/day prednisolone for at least one month], severe malnutrition, congenital immunohumoral or cellular immune deficiency state); chemotherapy/radiotherapy (in the 6 months prior to ICU admission); insulin-requiring diabetes mellitus (the need, prior to ICU admission, for insulin injections to control blood sugar levels).

For the purposes of the analysis, the world was divided into 7 geographical regions: North America, Central and South America, Western Europe, Eastern Europe, Asia, Oceania, and Africa. Data on health care expenditure in the various countries were obtained from the World Health Organization (http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf), generated using the WHO Statistical Information System and based on data from 2006.

Statistical analyses

All data were analyzed in the Department of Intensive Care of the University of Brussels, Belgium, in collaboration with the University of Jena, Germany. Statistical analyses were performed using SPSS for windows version 13.0 (SPSS Inc, Chicago, USA). The Kolmogorov-Smirnov test was used, and histograms and normal-quantile plots were examined to verify if there were significant deviations from the normality assumption of continuous variables. Non-parametric tests of comparison were used for variables evaluated as not normally distributed. Difference testing between groups was performed using ANOVA, Kruskal Wallis, Student's t-test, Mann-Whitney test, Chi square test and Fisher exact test as appropriate. A Bonferroni correction was made for multiple comparisons. Multivariable logistic regression analysis was used to determine risks factors for infection and hospital mortality. The following variables were investigated as independent risk factors: Type of admission, source of admission, comorbidities, age, sex, mechanical ventilation, hemofiltration or hemodialysis, infection, SAPS II score, type of microorganism. The odds ratios were adjusted for hospital- and organizational-related factors, including type of ICU (closed versus open, community versus university; surgical versus medical), number of ICU beds, number of nurses, number of physiotherapists, presence of 24h ICU physician, percentage of gross domestic product spent on healthcare (obtained from the World Health Organization [http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf], generated using the WHO Statistical Information System and based on data from 2006**)**, length of ICU stay prior to study day, and geographical region. Data are presented as mean ± SD, median value

(25th -75th interquartile ranges) or number (%) as appropriate. All statistics were two-tailed and a $p < 0.05$ was considered to be statistically significant.

Results

Characteristics of the study group

EPIC recruited 1265 ICUs in 76 countries (see Appendix for list of participating ICUs) . The greatest number of patients came from Western Europe, but the countries with more than 150 participating ICUs were Germany, Spain, Brazil, United Kingdom, United States, and Italy. University hospitals accounted for 60% of the total participating hospitals; 66% were mixed medical-surgical ICUs and 94% had 24-hour ICU physician cover. Characteristics of the ICUs are presented in Table 1.

On the study day, 14,414 patients were present on one of the participating ICUs; their demographic characteristics are presented in Table 2. Sixty-two percent of the patients were male, 61% were surgical admissions, and 50% of the patients had at least one comorbidity.

Prevalence and characteristics of infections

Of the 14,414 patients, 7330 (51%) were considered to be infected on the day of the study, and 71% of all patients were receiving antibiotics. Of the infected patients, 16% were being treated with antifungal agents. Infected patients were older, had more co-morbid conditions, and had higher SAPS II scores on admission than non-infected patients (Table 2). Greece and Portugal had the highest infection rates (65% each), and Switzerland (46%), Germany (43%), and the Netherlands (39%) had the lowest rates ($P<0.05$) (Table 3). The lungs were the most common site of infection, accounting for 64% of infections,

followed by abdominal (19%) and blood stream (15%) infections (Table 4). Seventy percent of infected patients had positive microbial isolates; 47% of infections were associated with Gram-positive isolates and 62% with Gram-negative isolates (Table 4). Nineteen percent of infected patients had isolates positive for fungi. In patients with positive isolates, the most commonly Gram-positive organism was *Staphylococcus aureus* (20%) and the most common Gram-negative organisms were *Pseudomonas* species (20%) and *Escherichia coli* (16%) (Table 5). There was considerable variation in the types of organisms isolated among the different geographical regions; for example, in Africa 21% of positive isolates were methicillin-resistant *S. aureus* (MRSA), while in Western Europe and Oceania the percentage was only 9 ($P<0.05$). The proportion of Gram-negative organisms was much greater in Asia, Western Europe and Latin America than in North America, Europe or Oceania.

Factors associated with higher risk of infections

The infection rate was related to disease severity as expressed by the SAPS II score and the degree of organ failure (Fig. 1). There was a relationship between the number of days spent in the ICU before the study day and the rate of infections: The infection rate increased from 32% for patients with a pre-study day ICU stay of 0-1 days to more than 70% for patients with a pre-study day ICU stay of more than 7 days ($r^2=0.89$, $p= 0.005$) (Fig. 2). This was particularly true for infections with MRSA, *Acinetobacter* spp, *Pseudomonas* spp and fungi. The rate of infection was related to health care expenditure, with countries which had a lower proportion of national product devoted to health care having higher rates of infection (Fig. 3).

In a multivariable logistic regression analysis, medical admission, admission after emergency surgery or trauma, referral from the hospital floor, emergency room (ER), or other hospital (with referral from the operating room [OR] as a reference), the presence of COPD, cancer, HIV, older age, mechanical ventilation and renal replacement therapy on the study day, and greater SAPS II scores were independently associated with a higher risk of infection (Table 6)

Mortality and morbidity

The ICU and hospital mortality rates for all patients were 17.9 and 23.7%, respectively, and were highest in ICUs from Central & South America and Eastern Europe and lowest in ICUs from Oceania (Table 7). Infected patients had higher ICU and hospital mortality rates (25.0 vs 10.5%, and 32.6 vs 14.5%, respectively, $p < 0.001$ for both) and lower ICU and hospital lengths of stay (4 [1-14] vs 16 [7-34] days and 13 [7-31] vs 29 [14-57], respectively, $p < 0.001$ for both) than those who did not have infections. Decisions to withhold or withdraw life-sustaining measures were made in 1269 patients (8.8%) and were more common in infected than non-infected patients (27.2 vs 14.2%, $P < 0.001$). There was also a significant relationship between the percentage of infected patients and the ICU and hospital mortality rates (Figure 4).

In a multivariable analysis of all patients, with hospital mortality as the dependent variable and adjusting for possible confounders, infection was independently associated with a greater risk of hospital mortality (OR: 1.52, 95% CI: 1.37-1.69, $P<0.001$). Other factors associated independently with a greater higher risk of in-hospital death are shown in Table 8. In patients with infections, factors independently associated with a greater risk

of hospital death included infection with *Pseudomonas* or *Acinetobacter* spp., cancer or cirrhosis as comorbidities, older age, and greater disease severity (Table 9).

Discussion

The data from this large international collaboration highlight the common occurrence of infections in contemporary ICUs, with 45-60% of ICU patients being classified by the attending physician as infected on the day of the study. Infected patients were older, had more comorbid conditions, and had higher SAPS II scores on admission.

As in other recent epidemiological studies,[1-9,19,25] the most common focus of infection in patients in our study was the lung, followed by the abdomen and blood stream. Interestingly, although studies have suggested an increasing incidence of Gram-positive organisms[26] and the SOAP study reported an equal frequency of Gram-positive and -negative organisms,[1] in the present study Gram-negative organisms were more commonly isolated than Gram-positive organisms, although these differences were most marked in Eastern Europe, Asia, and Central & South America. Patterns of infecting organisms were also similar to previous studies with predominant organisms being *S. aureus*, including MRSA, *Pseudomonas* spp, *Enterobacteriaceae* (mainly *E. coli*) and fungi.[1] Interestingly, *Acinetobacter* was involved in 9% of all infections, similar to the rate reported in the first EPIC study,[27] but considerably higher than the 3.6% reported in the more recent SOAP study.[1] In multivariable analysis, infection with *Acinetobacter* was associated with an increased risk of hospital death. Given the high level of resistance of *Acinetobacter* to many antibiotics, including carbapenems, and the high associated mortality,[28] this pathogen represents a continuing challenge in today's ICU. Infections

with *Pseudomonas* spp were also associated with an increased risk of in-hospital death as has been reported in the SOAP study.[1]

EPIC II was conducted 15 years after the original EPIC study,[21] which was limited to Western Europe and included just over 10,000 patients. In contrast to the EPIC study, we did not focus our analysis on nosocomial infections, as we were concerned that the distinction between community-acquired, hospital acquired and ICU-acquired infections may be difficult to achieve. As in the EPIC study,[21] and more recently the SOAP study,[1] there was a relationship between the prevalence of infection and mortality for the various countries. Importantly, this relationship was present overall, but also for countries of Western Europe, which represent a more homogeneous region, and contributed most patients to this study. We also noted a significant relationship between the time spent in the ICU prior to the study day and the development of infection, particularly for infections due to MRSA, *Acinetobacter*, *Pseudomonas species,* and fungi.

The study also revealed important differences in outcomes in various parts of the world. For example, mortality rates were lower in Oceania, both overall and in infected patients, than in other regions. The reasons for this are not entirely clear although differences in patient characteristics are likely to be at least in part responsible. It is also possible that a lead time bias may play a role, in that patients may be admitted earlier to the ICU in some regions than in others. The huge variability in critical care services among North American and European countries, with wide differences in both numbers of beds and volume of admissions, has also been recently highlighted[29] and is likely to be responsible for some of the regional differences in our data.

Interestingly, the rate of infection was related to the proportion of gross domestic product allocated to health care expenses, as countries with a lower health expenditure had higher rates of infection. Although our data do not allow us to offer a definitive explanation for this observation, it is interesting to speculate that countries with lower health care expenditure will have limitations on the number of ICU beds, which will therefore be occupied by more severely ill patients who are more likely to be infected. There are few data available on this topic. One recent report,[29] although reporting only a weak correlation between ICU beds per 100,000 population and healthcare spending per capita in 8 countries, did note an inverse correlation between the provision of ICU beds and the frequency of sepsis and hospital mortality using data from two large independent sources, the SOAP study[1] and the SAPS 3 database.[30]

Our study has advantages and limitations. An obvious strength is the international nature of the study collecting data on patterns of infection in a large and diverse group of patients across all geographical boundaries. A worldwide study has the advantage that differences in practice patterns can be used to probe independent influences of patient and management factors on epidemiology and outcome. The study was not funded, because we preferred to limit any possibility of industry influence. The size of this collaboration stresses the importance of the topic, and the desire to contribute to international projects without financial incentive. However, the voluntary nature of the study can be a potential source of bias. Moreover, the high proportion of university hospitals may have led to a patient case-mix that is not representative of all ICUs. Another disadvantage is that there was no data monitoring and results relied on the correct interpretation and use of the various definitions provided. A prevalence study has

the advantage of requiring a relatively limited data set while including a large number of patients; however, prevalence studies can overestimate the number of patients with diseases of long duration, such as sepsis. Finally, although the study dates was chosen to minimize as far as possible seasonal effects, in the northern and southern hemispheres, there is no way to be completely sure that such effects did not influence the results.

Conclusion

The EPIC II study demonstrates that, 15 years after the EPIC 1 study, infections remain a common problem in ICU patients. There is a strong relation between presence of infection, and length of ICU stay and mortality, and a significant inverse relation between the prevalence of infections and extent of government health care expenditure. There are major international differences in the prevalence of infections, in the type of microorganisms, and in mortality rates. These important data provide us with a picture of patterns of infection around the world, which can enhance our understanding of global and regional differences, and provide pointers to help optimize infection prophylaxis and management.

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Reference List

(1) Vincent JL, Sakr Y, Sprung CL et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med*. 2006;34(2):344-353.

(2) 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(4):580-588.

(3) van Gestel A, Bakker J, Veraart CP, van Hout BA. Prevalence and incidence of severe sepsis in Dutch intensive care units. *Crit Care*. 2004;8(4):R153-R162.

(4) Zahorec R, Firment J, Strakova J et al. Epidemiology of severe sepsis in intensive care units in the Slovak Republic. *Infection*. 2005;33(3):122-128.

(5) Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. *Crit Care*. 2006;10(2):R42.

(6) Esteban A, Frutos-Vivar F, Ferguson ND et al. Sepsis incidence and outcome: contrasting the intensive care unit with the hospital ward. *Crit Care Med*. 2007;35(5):1284-1289.

(7) Engel C, Brunkhorst FM, Bone HG et al. Epidemiology of sepsis in Germany: results from a national prospective multicenter study. *Intensive Care Med*. 2007;33(4):606-618.

(8) Karlsson S, Varpula M, Ruokonen E et al. Incidence, treatment, and outcome of severe sepsis in ICU-treated adults in Finland: the Finnsepsis study. *Intensive Care Med*. 2007;33:435-443.

(9) Sundararajan V, Macisaac CM, Presneill JJ, Cade JF, Visvanathan K. Epidemiology of sepsis in Victoria, Australia. *Crit Care Med*. 2005;33(1):71-80.

(10) Angus DC, Linde-Zwirble WT, Lidicker J et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med*. 2001;29(7):1303-1310.

(11) Wenzel RP, Edmond MB. Severe sepsis-national estimates. *Crit Care Med*. 2001;29(7):1472-1474.

(12) Vincent JL, Abraham E, Annane D et al. Reducing mortality in sepsis: new directions. *Crit Care*. 2002;6 Suppl 3:S1-18.

(13) Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med*. 2003;348(16):1546-1554.

(14) Alberti C, Brun-Buisson C, Burchardi H et al. Epidemiology of sepsis and infection in ICU patients from an international multicentre cohort study. *Intensive Care Med*. 2002;28(2):108-121.

(15) Padkin A, Goldfrad C, Brady AR et al. 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(9):2332-2338.

(16) Weycker D, Akhras KS, Edelsberg J, Angus DC, Oster G. Long-term mortality and medical care charges in patients with severe sepsis. *Crit Care Med*. 2003;31(9):2316-2323.

(17) Finfer S, Bellomo R, Lipman J et al. Adult-population incidence of severe sepsis in Australian and New Zealand intensive care units. *Intensive Care Med*. 2004;30(4):589-596.

(18) Moreno RP, Metnitz B, Adler L et al. Sepsis mortality prediction based on predisposition, infection and response. *Intensive Care Med*. 2008;34(3):496-504.

(19) Silva E, Pedro MA, Sogayar AC et al. Brazilian Sepsis Epidemiological Study (BASES study). *Crit Care*. 2004;8(4):R251-R260.

(20) Cheng B, Xie G, Yao S et al. Epidemiology of severe sepsis in critically ill surgical patients in ten university hospitals in China. *Crit Care Med*. 2007;35(11):2538-2546.

(21) Vincent JL, Bihari D, Suter PM et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) study. EPIC International Advisory Committee. *J A M A*. 1995;274:639-644.

(22) Le Gall J-R, Lemeshow S, Saulnier F. A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. *J A M A*. 1993;270:2957-2963.

(23) Vincent JL, Moreno R, Takala J et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med*. 1996;22:707-710.

(24) Calandra T, Cohen J. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. *Crit Care Med*. 2005;33(7):1538-1548.

(25) Martin CM, Priestap F, Fisher H et al. A prospective, observational registry of patients with severe sepsis: the Canadian Sepsis Treatment and Response Registry. *Crit Care Med*. 2009;37(1):81-88.

(26) Friedman G, Silva E, Vincent JL. Has the mortality of septic shock changed with time? *Crit Care Med*. 1998;26:2078-2086.

(27) Spencer RC. Predominant pathogens found in the European Prevalence of Infection in Intensive Care Study. *Eur J Clin Microbiol Infect Dis*. 1996;15(4):281-285.

(28) Falagas ME, Rafailidis PI. Attributable mortality of Acinetobacter baumannii: no longer a controversial issue. *Crit Care*. 2007;11(3):134.

(29) Wunsch H, Angus DC, Harrison DA et al. Variation in critical care services across North America and Western Europe. *Crit Care Med*. 2008;36(10):2787-2789.

(30) Metnitz PG, Moreno RP, Almeida E et al. SAPS 3--From evaluation of the patient to evaluation of the intensive care unit. Part 1: Objectives, methods and cohort description. *Intensive Care Med*. 2005;31(10):1336-1344.

Figure legends

Fig. 1. Relationship between rate of infection and disease severity and number of organs failing.

Fig. 2. Relationship between rate of infection and the duration of stay in the ICU before the study day for all infections (upper panel) and for infections with *Pseudomonas* species, MRSA, fungi, *Acinetobacter*, *Candida*, *Klebsiella* species, *E. coli* and *S. aureus* (lower panel). Spearman Rank Correlation Coefficient = 0.89, p-value = 0.005 (upper panel).

Fig. 3. Relationship between rate of infection and the total expenditure on health as % of Gross domestic product (GDP).

Fig. 4. Relationship between frequency of infection and hospital mortality for the countries contributing patients from more than 150 ICUs: Argentina (AR), Australia (AU), Austria (AT), Belgium (BE), Brazil (BR), Canada (CA), Colombia (CO), Czech Republic (CZ), France (FR), Germany (DE), Greece (GR), India (IN), Italy (IT), Netherlands (NL), Portugal (PT), Scandinavia (SCAN), Spain (ES), Switzerland (CH), Turkey (TR), United Kingdom (GB), United States (US).

Table 1. Characteristics of the contributing centers (n = 1265)

Characteristic	**Number (%)**
Type of hospital (%)	
University/academic	756 (60.4)
Non-university	496 (39.6)
Hospital bed capacity, median [IQ]	477 [240-830]
Population (%)	
Adult	957 (75.7)
Pediatric	34 (2.7)
Both	273 (21.6)
Type of ICU (%)	
Closed	1046 (83.8)
Open	211 (16.8)
ICU specialty (%)	
Surgical	214 (17.3)
Medical	133 (10.7)
Mixed	813 (65.6)
Others	80 (6.5)
Microbiology 24h/24h, n (%)	903 (71.6)
Emergency department 24h/24h, n (%)	1216 (96.2)
ICU physician 24h /24h, n (%)	1189 (94.1)
Number of ICU patients (2006), median [IQ]	684 [408-1100]
ICU mortality rate (2006), median [IQ]	12 [7-20]

Valid percentages are displayed after exclusion of missing values

Missing: Type of hospital=13, Population=1, Type of ICU=6, ICU specialty=25

Table 2. Basic characteristics of the study group

Characteristic	**All patients N=14141**	**Not infected N=6881**	**Infected N=7330**	***P* value**
Age, years, median [IQ]	(63 [47-74])	62 [47-73]	63 [48-74]	0.001
Age (adult patients only), years, median [IQ]	(64 [50-74])	63 [50-74]	64 [50-74]	0.166
Male, n (%)	8924 (61.9)	1678 (23.9)	2383 (32.6)	0.082
Severity scores on the study day, mean±SD (median [IQ])				
SAPS II score	34.8±15.5 (33 [24-43])	29 [21-38]	36 [27-48]	<0.001
SOFA score	6.3±4.0 (6 [3-9])	5 [2-7]	6 [4-10]	<0.001
Type of admission (%)				<0.001
Medical	4061 (28.3)	1678 (23.9)	2383 (32.6)	
Surgical: Elective	3355 (23.4)	2400 (34.2)	955 (13.1)	
Emergency	5455 (38)	2144 (30.5)	3311 (45.3)	
Trauma	1468 (10.2)	801 (11.4)	667 (9.1)	
Reason for ICU admission				<0.001
Respiratory	3269 (22.7)	916 (12.9)	2353 (32.1)	
Cardiovascular	3133 (21.7)	1605 (22.7)	1528 (20.8)	
Surveillance/monitoring	2726 (18.9)	2071 (29.2)	655 (8.9)	
Neurological	2102 (14.6)	1041 (14.7)	1061 (14.5)	
Digestive/liver	1329 (9.2)	492 (6.9)	837 (11.4)	
Trauma	1200 (8.3)	655 (9.2)	545 (7.4)	
Renal	326 (2.3)	120 (1.7)	206 (2.8)	
Others*	329 (2.3)	184 (2.6)	145 (2)	
Source of admission				<0.001
ER/ambulance	4152 (29.1)	2067 (29.7)	2085 (28.6)	
Hospital floor	3933 (27.6)	1579 (22.7)	2354 (32.3)	
OR/recovery	3651 (25.6)	2269 (32.6)	1382 (19)	

Other hospital	2073 (14.5)	838 (12)	1235 (17)	
Other	443 (3.1)	217 (3.1)	226 (3.1)	
Comorbidities, n (%)				
COPD	2313 (16)	877 (12.4)	1436 (19.6)	<0.001
Cancer	2110 (14.6)	985 (13.9)	1125 (15.3)	0.014
Heart Failure (NYHA III-IV)	1392 (9.7)	632 (8.9)	760 (10.4)	0.003
Diabetes mellitus	1340 (9.3)	609 (8.6)	731 (10)	0.005
Chronic renal failure	1253 (8.7)	496 (7)	757 (10.3)	<0.001
Cirrhosis	463 (3.2)	196 (2.8)	267 (3.6)	0.003
Hematologic cancer	290 (2)	74 (1)	216 (2.9)	<0.001
HIV	97 (0.7)	19 (0.3)	78 (1.1)	<0.001
Number of comorbidities, n (%)				<0.001
None	7176 (49.8)	3935 (55.5)	3241 (44.2)	
1	4530 (31.4)	2130 (30.1)	2400 (32.7)	
2	1855 (12.9)	730 (10.3)	1125 (15.3)	
3	629 (4.4)	230 (3.2)	399 (5.4)	
>3	224 (1.5)	59 (0.8)	165 (2.3)	

ER: emergency room; OR: operating room; COPD: chronic obstructive pulmonary disease; HIV: human immunodeficiency virus;

*Metabolic/hematologic/obstetric and gynecology

Table 3. Characteristics of infected patients according to geographical region

	All	Western Europe	Eastern Europe	Central & South America	North America	Oceania	Africa	Asia
n (%)	7330 (50.9)	3752 (48.6)	473 (56.4)	1325 (60.1)	616 (48.2)	315 (45.5)	92 (43.8)	757 (51.6)
Age, mean ± SD	59.1±19.6	61.4 ±17.5	52.7 ±23.5*	59.1 ± 20.9*	56.9 ±18.8*	55.5 ± 22.9*	48.3 ±19.3*	55.9 ± 21.8*
Sex, male	4599 (65.6)	2460 (64.2)	291 (61.5)	773 (58.3)*	361 (59.1)*	190 (60.3)	58 (63.0)	466 (61.6)
SAPS II score, mean ±SD	38.5 ±15.7	38.4 ±15.3	36 ± 16.4*	41.4 ± 16.2*	37.8 ± 16	33.3 ± 13*	34 ±14.9*	38.8 ± 16.4
SOFA score, mean ± SD	7.2 ±4.2	7.2 ±4.2	6.8 ± 4.2	7.2 ± 4.4	7.8 ± 4.2	6.4 ± 3.8*	7.6 ±3.7	7.3 ± 4.1
ICU mortality, n (%)[a]	1724 (25)	810 (22.7)	136 (30.8)*	146 (34.6)*	110 (18.3)	43 (13.7)*	25 (28.1)	193 (27.5)*
Hospital mortality (%)[a]	2242 (32.6)	1086 (30.7)	162 (36.7)	509 (42.3)*	147 (24.5)*	64 (20.4)*	29 (32.6)	245 (34.9)
ICU length of stay, median [IQ]	16 [7 - 34]	19 [7-36]	19 [8-40]	17 [8-33]	11 [4-24]*	11 [5-20]*	12 [5-24]*	15 [7-33]*
Hospital LOS. median [IQ]	29 [14-57]	33 [17-62]	30 [14-62]	27 [13-56]*	19 [9-41]*	25 [12-49]*	21 [10-34]*	24 [12-51]*
Days in ICU before the study day, median [IQ]	6 [1 - 15]	7[2-17]	7[1-17]	6[1-15]	4[1-12]*	6[2-11]*	3[0-10]*	5[1-14]*

[a]446 missing; *$P < 0.05$ vs Western Europe

Table 4. Site of infection and major microbiologic isolates according to geographical region

	All	Western Europe	Eastern Europe	Central & South America	North America	Oceania	Africa	Asia
N	7330	3752	473	1325	616	315	92	757
Site of infection, n (%)								
Respiratory	4658 (63.5)	2371 (63.2)	335 (70.8)	879 (66.3)	350 (56.8)*	179 (56.8)	43 (46.7)*	501 (66.2)
Abdominal	1417 (19.3)	790 (21.1)	95 (20.1)	230 (17.4)*	102 (16.6)	54 (17.1)	16 (17.4)	130 (17.2)
Blood stream	1108 (15.1)	555 (14.8)	62 (13.1)	143 (10.8)*	159 (25.8)*	54 (17.1)	16 (17.4)	119 (15.7)
Renal/urinary tract	1028 (14)	415 (11.1)	85 (18)*	226 (17.1)*	138 (22.4)*	37 (11.7)	15 (16.3)	112 (14.8)*
Skin	485 (6.6)	248 (6.6)	39 (8.2)	73 (5.5)	28 (4.5)	33 (10.5)	8 (8.7)	56 (7.4)
Catheter-related	343 (4.7)	176 (4.7)	24 (5.1)	74 (5.6)	17 (2.8)	15 (4.8)	4 (4.3)	33 (4.4)
CNS	233 (3.2)	106 (2.8)	25 (5.3)*	43 (3.2)	15 (2.4)	17 (5.4)	4 (4.3)	23 (3)
Others	561 (7.7)	297 (7.9)	40 (8.5)	86 (6.5)	62 (10.1)	24 (7.6)	15 (16.3)	37 (4.9)*
Microorganisms, n (%)								
Positive isolates	5106 (69.6)	2728 (72.7)	384 (81.2)*	741 (55.9)*	465 (75.5)	225 (71.4)	57 (62)	505 (66.7)*
Gram-positive	2399 (47)	1345 (49.3)	195 (50.8)	286 (38.5)*	257 (55.3)	119 (52.9)	29 (50.9)	168 (33.3)*
Gram-negative	3165 (62)	1599 (58.6)	275 (71.6)*	522 (70.4)*	233 (50.1)*	127 (56.4)	33 (57.9)	376 (74.5)*
Anaerobes	225 (4.4)	145 (5.3)	12 (3.1)	10 (1.3)*	36 (7.7)	7 (3.1)	1 (1.8)	14 (2.8)
Fungi	945 (18.5)	548 (20.1)	74 (19.3)	104 (14)*	96 (20.6)	32 (14.2)	6 (10.5)	85 (16.8)
Viral/parasitic	135 (2.6)	36 (1.4)	9 (2.3)	13 (1.7)	15 (3.2)	4 (1.8)	0.0 (0.0)	13 (2.6)
Others	110 (2.2)	68 (2.5)	4(1)	12 (1.6)	11 (2.4)	5 (2.2)	2 (3.5)	8 (1.6)

*$P < 0.05$ vs Western Europe.

Table 5. Types of organisms in culture-positive infected patients according to geographical region

	All	**Western Europe**	**Eastern Europe**	**Central & South America**	**North America**	**Oceania**	**Africa**	**Asia**
Gram-positive								
Staphylococcus aureus	1024 (20.5)	536 (19.6)	85 (22.1)	143 (19.3)	127 (27.3)*	60 (26.7)	17 (29.8)	78 (15.4)
MRSA	524 (10.3)	237 (8.7)	42 (10.9)	83 (11.2)	81 (17.4)*	20 (8.9)	12 (21.1)*	49 (9.7)
S. epidermidis	557 (10.9)	312 (11.4)	45 (11.7)	72 (9.7)	57 (12.3)	18 (8)	8 (14)	45 (8.9)
S. pneumoniae	212 (4.2)	132 (4.8)	16 (4.2)	25 (3.4)	20 (4.3)	8 (3.6)	3 (5.3)	8 (1.6)*
Enterococcus	542 (10.6)	364 (13.3)	51 (13.3)	32 (4.3)*	46 (9.9)	21 (9.3)	1 (1.8)*	27 (5.3)*
others	336 (6.6)	187 (6.9)	15 (3.9)*	32 (4.3)*	50 (10.8)*	25 (11.1)*	4 (7)	23 (4.6)
Gram-negative								
E. coli	814 (15.9)	468 (17.2)	56 (14.6)	104 (14)	66 (14.2)	27 (12)	6 (10.5)	87 (17.2)
Enterobacter	353 (6.9)	189 (6.9)	29 (7.6)	62 (8.4)	38 (8.2)	8 (3.6)	4 (7)	23 (4.6)
Klebsiella spp	645 (12.6)	264 (9.7)	82 (21.4)*	121 (16.3)*	41 (8.8)	25 (11.1)	10 (17.5)	102 (20.2)*
Pseudomonas spp	1010 (19.8)	460 (16.9)	108 (28.1)*	194 (26.2)*	62 (13.3)	31 (13.8)	10 (17.5)	145 (28.7)*
Acinetobacter spp	454 (8.9)	152 (5.6)	67 (17.4)*	103 (13.9)*	18 (3.9)	9 (4)	9 (15.8)*	96 (19)*
others	862 (16.9)	495 (18.1)	57 (14.8)	124 (16.7)	52 (11.2)*	45 (20)	11 (19.3)	78 (15.4)
Anaerobes	225 (4.4)	145 (5.3)	12 (3.1)	10 (1.3)*	36 (7.7)	7 (3.1)	1 (1.8)	14 (2.8)
Other bacteria	82 (1.6)	34 (1.2)	10 (2.6)	14 (1.9)	4 (0.9)	4 (1.8)	3 (5.3)	13 (2.6)
Fungi								
Candida	859 (16.8)	502 (18.4)	69 (18)	93 (12.6)*	83 (17.8)	28 (12.4)	6 (10.5)	78 (15.4)

Aspergillus	71 (1.4)	44 (1.6)	1 (0.3)	5 (0.7)	12 (2.6)	3 (1.3)	0 (0)	6 (1.2)
others	50 (1)	22 (0.8)	5 (1.3)	7 (0.9)	10 (2.2)	2 (0.9)	0 (0)	4 (0.8)
Parasites	36 (0.7)	18 (0.7)	2 (0.5)	6 (0.8)	3 (0.6)	2 (0.9)	0 (0)	5 (1)
Other organisms	207 (4.1)	126 (4.6)	11 (2.9)	18 (2.4)*	22 (4.7)	12 (5.3)	2 (3.5)	16 (3.2)

MRSA: methicillin-resistant *S. aureus*; *$P < 0.05$ vs Western Europe

Table 6. Multivariable logistic regression analysis with infection as the dependent variable[a]

	OR (95% CI)	*P* value
Type of admission		
Elective surgery	Reference	NA
Medical admission	2.31 (2.01-2.65)	<0.001
Emergency surgery	2.94 (2.61-3.32)	<0.001
Trauma	1.70 (1.43-2.01)	<0.001
Source of admission		
OR/recovery	Reference	NA
ER/ambulance	0.86 (0.76-0.98)	0.023
Hospital floor	1.35 (1.20-1.52)	<0.001
Other hospital	1.17 (1.02-1.35)	0.029
Comorbidities		
COPD	1.51 (1.35-1.69)	<0.001
Cancer	1.26 (1.11-1.43)	<0.001
Heart failure (NYHA III-IV)	0.97 (0.84-1.11)	0.640
Diabetes mellitus	1.14 (1.00-1.31)	0.057
Chronic renal failure	1.14 (0.98-1.32)	0.092
Cirrhosis	0.94 (0.75-1.17)	0.567
Hematologic cancer	1.39 (1.01-1.92)	0.046
HIV	3.79 (2.04-7.05)	<0.001
Age (per year)	1.00 (0.99-1.00)	0.003
Male gender	1.08 (1.00-1.17)	0.062
Mechanical ventilation	1.70 (1.56-1.85)	<0.001
Hemodialysis/hemofiltration	1.49 (1.27-1.75)	<0.001
SAPS II (per point)	1.02 (1.02-1.02)	<0.001

[a]Adjusted for hospital and organizational factors and for geographic region.

Table 7. Severity scores, infection rates and outcome according to geographical region

	All	Western Europe	Eastern Europe	Central & South America	North America	Pacific	Africa	Asia
Centers, n	1265	667 (52.7)	97 (7.7)	209 (16.5)	83 (6.6)	54 (4.3)	17 (1.3)	138 (10.9)
Patients, n (%)	14414	7725 (53.6)	838 (5.8)	2204 (15.3)	1279 (8.9)	692 (4.8)	210 (1.5)	1466 (10.2)
Age, mean ± SD	58.4±20.2	60.9 ±18.3	53.0 ±23*	58.5 ± 20.9*	56.6 ±19.0*	53.0 ± 25.3*	46.2 ±21.3*	53.7 ± 22.3*
Sex, male	8924 (62.1)	4937 (64.2)	529 (63.1)	1252 (56.9)*	728 (57.3)*	417 (60.3)	143 (68.1)	918 (62.7)
Type of admission								
Medical	4061 (28.3)	1822 (23.7)	175 (20.9)	890 (40.5)*	478 (37.5)*	195 (28.3)	66 (31.4)	435 (29.8)*
Surgical								
Elective	3355 (23.4)	2036 (26.5)	235 (28.1)	347 (15.8)*	221 (17.4)*	190 (27.6)	37 (17.6)*	289 (19.8)*
Emergency	5455 (38)	3051 (39.8)	338 (40.4)	767 (34.9)*	397 (31.2)*	229 (33.2)*	81 (38.6)	592 (40.5)
Trauma	1468 (10.2)	763 (9.9)	88 (10.5)	195 (8.9)*	177 (13.9)	75 (10.9)	26 (12.4)	144 (9.9)
Mechanical ventilation	8056 (56.3)	4410 (57.6)	459 (55)	1231 (56.2)	689 (54.1)	381 (55.1)	105 (50.2)	781 (53.6)*
Hemodialysis/hemofiltration	1255(8.8)	684 (8.9)	44 (5.3)*	215 (9.8)	126 (9.9)	44 (6.4)	18 (8.6)	124 (8.5)
Infected	7330 (50.9)	3752 (48.6)	473 (56.4)*	1325 (60.1)*	616 (48.2)	315 (45.5)	92 (43.8)	757 (51.6)
Clinical infection	2225 (15.4)	1024 (13.3)	89 (10.6)	584 (26.5)*	151 (11.8)	90 (13)	35 (16.7)	252 (17.2)*
Infected + microorganisms	5105 (35.4)	2728 (35.3)	384 (45.8)*	741 (33.6)	465 (36.4)	225 (32.5)	57 (27.1)	505 (34.4)
SAPS II score, mean ± SD	34.8±15.5	35 ±15.1	33.6 ±16	37.3 ± 16.3*	34.1 ±15.6	30.7 ± 12.7*	32.1 ±16.8*	33.5 ± 16.5*
SOFA score, mean ± SD	6.3±4.0	6.3 ±4.0	6.1 ±3.9	6.3 ± 4.3	6.9 ±4.1*	5.9 ± 3.6	6.9 ±4.5	6.4 ± 4.0

ICU mortality, n (%)[a]	2430 (17.9)	1178 (16.2)	186 (23.9)*	536 (26.7)*	174 (13.9)	63 (9.2)*	39 (19.8)	254 (18.3)
Hospital mortality, n (%)[a]	3212 (23.7)	1610 (22.1)	221 (28.4)*	663 (33)*	240 (19.2)	101 (14.1)*	48 (24.4)	329 (23.7)
ICU LOS, median [IQ]	9 [3 - 25]	10[2-28]	10[3-29]*	11[4-28]*	6[2-18]*	7[2-17]*	7[2-21]	9[3-23]
Hospital LOS, median [IQ]	20 [9 - 45]	22[10-49]	22[10-45]	20[9-46]	14[6-33]*	17[8-40]*	14[6-31]*	17[8-41]*
Days in ICU before the study day, median [IQ]	3[0 - 11]	3[1-11]	4[0-13]	4[1-12]*	2[0-7]*	3[1-8]	1[0-8]*	3[0-8]

[a]834 missing; *$P < 0.05$ vs Western Europe.

Table 8. Multivariable logistic regression analysis with hospital mortality as the dependent variable[a]

	OR (95% CI)	*P* value
Type of admission		
Elective surgery	Reference	NA
Medical admission	1.20 (1.01-1.43)	0.038
Emergency surgery	1.61 (1.38-1.87)	<0.001
Trauma	1.34 (1.07-1.69)	0.012
Source of admission		
OR/recovery	Reference	NA
ER/ambulance	0.92 (0.79-1.08)	0.308
Hospital floor	1.38 (1.19-1.59)	<0.001
Other hospital	0.97 (0.82-1.16)	0.755
Comorbidities		
COPD	1.21 (1.07-1.37)	0.002
Cancer	1.35 (1.17-1.55)	<0.001
Heart Failure (NYHA III-IV)	1.44 (1.24-1.68)	<0.001
Diabetes mellitus	0.98 (0.84-1.15)	0.829
Chronic renal failure	1.04 (0.89-1.23)	0.598
Cirrhosis	2.15 (1.68-2.74)	<0.001
Hematologic cancer	1.17 (0.85-1.60)	0.330
HIV	0.97 (0.58-1.65)	0.921
Age (per year)	1.01 (1.01-1.01)	0.001
Male sex	0.99 (0.89-1.09)	0.781
Mechanical ventilation	1.91 (1.71-2.13)	<0.001
Hemodialysis/hemofiltration	1.62 (1.39-1.89)	<0.001
SAPS II (per point)	1.06 (1.05-1.06)	<0.001
Infection	1.52 (1.37-1.69)	<0.001

[a]Adjusted for hospital and organizational factors and for geographical region.

Table 9. Multivariable logistic regression analysis with hospital mortality as the dependent variable in infected patients[a]

	OR (95% CI)	*P* value
Type of admission		
Elective surgery	Reference	NA
Medical admission	0.93 (0.74-1.17)	0.534
Emergency surgery	1.20 (0.98-1.47)	0.075
Trauma	0.81 (0.59-1.11)	0.186
Source of admission		
OR/recovery	Reference	NA
Other	1.10 (0.76-1.59)	0.619
ER/ambulance	0.90 (0.73-1.10)	0.296
Hospital floor	1.33 (1.11-1.60)	0.002
Other hospital	0.90 (0.73-1.12)	0.360
Comorbidities		
COPD	1.15 (0.99-1.34)	0.072
Cancer	1.42 (1.19-1.7)	<0.001
Heart Failure (NYHA III-IV)	1.43 (1.18-1.73)	<0.001
Diabetes mellitus	1.00 (0.82-1.22)	0.996
Chronic renal failure	1.08 (0.89-1.32)	0.433
Cirrhosis	2.32 (1.71-3.15)	<0.001
Hematologic cancer	1.26 (0.88-1.81)	0.208
HIV	0.77 (0.43-1.40)	0.394
Age (per year)	1.01 (1.00-1.01)	<0.001
Male sex	1.00 (0.88-1.13)	0.998
Mechanical ventilation	1.72 (1.49-1.99)	<0.001
Hemodialysis/hemofiltration	1.60 (1.34-1.92)	<0.001
SAPS II (per point)	1.05 (1.04-1.06)	<0.001
Microorganisms		
S. aureus	0.81 (0.63-1.04)	0.095
MRSA	1.28 (0.93-1.77)	0.131

S. epidermidis	0.87 (0.69-1.09)	0.228
S. pneumoniae	0.74 (0.50-1.08)	0.121
Enterococcus	1.38 (1.10-1.73)	0.005
Gram +ve others	0.96 (0.71-1.30)	0.790
E. coli	0.91 (0.75-1.10)	0.330
Enterobacter	1.19 (0.90-1.57)	0.219
Klebsiella spp	1.01 (0.82-1.24)	0.919
Pseudomonas spp	1.42 (1.20-1.68)	<0.001
Acinetobacter spp	1.60 (1.26-2.02)	<0.001
Gram -ve others	1.15 (0.96-1.38)	0.130
Anaerobes	0.91 (0.64-1.28)	0.580
Other bacteria	1.24 (0.70-2.20)	0.462
Candida	1.1 (0.92-1.32)	0.308
Aspergillus	1.95 (1.07-3.54)	0.028
Fungi: others	2.04 (1.05-3.98)	0.037
Parasites	1.45 (0.60-3.52)	0.415
Other organisms	0.96 (0.66-1.39)	0.827

MRSA: methicillin-resistant *S. aureus*; [a]Adjusted for hospital and organizational factors and for geographical region.

Appendix: List of participating centers by country alphabetically

Andorra: Hospital Nostra Senyora de Meritxell (A Margarit); *Argentina:* Centro de Educación Médica E Investigaciones Clínicas (R Valentini); Clinica de Especialidades Villa Maria (Z Alan Javier); Clínica Modelo de Morón (C Bevilacqua); Clinica Y Maternidad Suizo (M Curone); CMIC (R Rabuffetti); Hospital Aleman (P Comignani); Hospital Argerich (M Torres Boden); Hospital Britanico (F Chertcoff); Hospital Central de San Isidro (G Cardonatti); Hospital de Niños Dr. Héctor Quintana (F Adén); Hospital del Niño Jesús (L Marcos); Hospital Dr Pedro Ecay (M Dónofrio); Hospital Español de Mendoza (R Fernández); Hospital Español Medical Plaza (R Lamberghini); Hospital Internacional General de Agudos "José de San Matín" (S Balasini); Hospital Interzonal Dr. O.Alende (J Teves); Hospital Italiano de Buenos Aires (M Las Heras, J Sinner); Hospital Juan A. Fernández (D Ceraso); Hospital Municipal de Chivilcoy (D Curcio); Hospital Profesor Alejandro Posadas (L Aguilar); Hospital Provincial de Rosario (C Weller); Hospital Provincial del Centenario (L Cardonnet); Hospital Regional Rio Gallegos (R Santa Cruz); Hospital Regional Ushuaia (E Manrique); Hospital Universitario Austral (D Bernardez, T Iolster); Hospital Universitario Universidad Abierta Interamericana (G Chiappero); Instituto Privado del Quemado Med-Inter (D Curcio); Nuevo Hospital El Milagro (P Ramos); Ramos Mejia Hospital (J Vergara); Sanatorio Agote (I Moine); Sanatorio de la Trinidad Mitre (S Ilutovich); Sanatorio de Los Arcos (G Jannello); Sanatorio Dupuytren (M Waschbusch); Sanatorio Frangioli de Salud 2000 Srl (G Rios Picaza); Sanatorio Mater Dei (A Raimondi); Sanatorio Otamendi Y Miroli (M Miriam); Sanatorio Parque (L Carlos); Sanatorio San José (D Curcio); *Armenia:* Centro Gallego de Buenos Aires (M Caridi); *Australia:* Alfred Hospital (T Leong); Barwon Health (N Orford); Blacktown Hospital (G Reece); Box Hill Hospital (D Ernest); Cabrini Hospital (F Hawker); Concord Repatriation General Hospital (J Tan); Epworth Eastern Private Hospital (C Giannellis); Epworth Hospital Richmond (B Ihle); Flinders Medical Centre (A Bersten); Frankston Hospital (J McInnes); Gold Coast Hospital (M Tallott); John Hunter Hospital (B Mcfadyen); Joondalup Health Campus (J Vibert); Liverpool Hospital, Sydney South West Area Health Service (M Parr); Logan Hospital (K Tran); Mater Health Services (J Sutton); Mount Hospital (S Webb); Nambour General Hospital (N Groves); Nepean Hospital, NSW (L Cole); Prince Charles Hospital (D Long); Prince of Wales Hospital (F Bass); Princess Margaret Hospital For Children (S Erickson); Royal Brisbane and Womens' Hospital (J Lipman); Royal Children's Hospital, Brisbane (D Long); Royal Children's Hospital, Melbourne (C Delzoppo); Royal Darwin Hospital (J Thomas); Royal Perth Hospital (G Dobb); Royal Prince Alfred Hospital (M Daley); Sir Charles Gairdner Hospital (B Roberts); St John of God Hospital, Subiaco (S Webb); St Vincent's Hospital, Melbourne (J Santamaria); Sydney Children's Hospital (J Young); The Children's Hospital at Westmead, Sydney (M Festa); The John Flynn Private Hospital (R Holland); The Prince Charles Hospital (D Mullany); The Queen Elizabeth Hospital (P Williams); The Townsville Hospital (M Corkeron); The Wollongong Hospital (M Gales); Westmead Hospital (A Banerjee); Women's and Children's Hospital, Adelaide (M Yung); *Austria:* University Hospital Innsbruck (N Mutz, M Hiesmayr); General Hospital (P Faybik); Hospital Hietzing (R Fitzgerald); Krankenhaus Barmherzige Brüder Linz (F Firlinger); Krankenhaus Der Barmherigen Brueder Wien (G Zasmeta); Krankenhaus Der Barmherzigen Brüder St. Veit (M Zink); Krankenhaus Der Barmherzigen Schwestern Linz (W Sieber); Krankenhaus Steyr (J Hildegard); Landeskrankenhaus Klagenfurt (R Bakondy); Landeskrankenhaus Stolzalpe (J Schlieber); Landeskrankenhaus Deutschlandsberg (G Filzwieser); Medical University Innsbruck (R Beer, M Joannidis); Medical University of Vienna (T Staudinger); Otto-Wagner Hospital (R Schuster); Unfallkrankenhaus Meidling Der Auva (W Scherzer); University Hospital (K Smolle); Wilhelminenspital (S Fitzal); *Bangladesh:* Central

Hospital Limited (R Manzoor); *Belgium:* A.I.T. (J Brunain); Ambroise Paré (D Alain); Asz-Aalst (G Huylenbroeck); Az Groeninge Kortrijk (M Van der Schueren); Az Maria Middelares (H 't kindt); Az Sint Jozef Malle (E Slock); Az Sint Lucas (D Rijckaert); Az St Augustinus (J Raemaekers); Az St Jan Av (M Bourgeois); Az Vesalius (I Van Cotthem); Az Damiaan Oostende (G Nackaerts); C.H.N.D.R.F. (D Gusu); Centre Hospitalier de Mouscron (G Philippe); CH Libramont (V Olivier); Chirec - Braine-L'Alleud (H Lignian); CHPLT Verviers (P Michel); CHR Citadelle (V Fraipont); CHR Haute Senne Soignies (M Vander Stappen); CHR St Joseph Mons-Warquignies (F Forêt); CHU Brugmann (D De Bels, J Devriendt, J Massaut); CHU Charleroi (B Patrick); CHU Saint-Pierre (A Roman); CHU Sart Tilman, Liège (B Lambermont); Clinique Sainte Elisabeth (A De Meulder); Clinique Notre Dame (V Frederic); Clinique Notre-Dame de Grâce (T Sottiaux); Clinique Saint Luc, Bouge (P Ruyffelaere); Cliniques de L'Europe, St-Michel (V Collin); Cliniques de L'Europe, Ste Elisabeth (S Anane); Hôpital Francais (P Kleiren); Hôpital Saint-Joseph (M Simon); Hornu (M Shahram); Imeldaziekenhuis (E Frans); Institut Jules Bordet (G Leroy, T Berghmans); Jan Yperman Hospital (R Joseph); Olv Ter Linden Ziekenhuis, Knokke (J Eerens); Saint Luc University Hospital (P Laterre); Sint Augustinus, Veurne (B Lagrou); St Vincent (R Rutsaert); St-Jozefkliniek Bornem-Willebroek (W Pisarek); UCL Mont-Godinne (A Dive); Universitair Ziekenhuis Gent (J De Waele); University Hospital Brussels (H Spapen); University Hospital of Liege (P Damas); Erasme University Hospital (JL Vincent); ZNA Stuivenberg (M Malbrain); *Belize:* Universal Health Services, Medical Center (J Hidalgo); *Brazil:* Bandeirantes Hospital (M Baptista); Barra Dor Hospital (D Salgado); Biocor Instituto (M Braga); Casa de Saude Sao Jose Caxias (C Avila); Centro Hospitalar Unimed (G Westphal); Centro Integrado de Atençaõ À Saúde -Unimed Vitória (E Caser); Clínica São Vicente da Gávea (A Alves); Complexo Hospitalar Santa Casa de Porto Alegre (G Friedman); Erasto Gaertner Hospital (M Luz); Federal University of Sao Paulo (M Assuncao); Fundacao Hospital de Clinicas Gaspar Vianna (H Reis); Fundação Hospitalar Do Estado de Minas Gerais - Fhemig (A Gomes); Fundação Pio Xii (U Silva); UNIFESP (W Nogueira Fh); Hopital das Clínicas - FMUSP (S El-Dash); Hospital Padre Albino-Faculdade de Medicina de Catanduva (J Valiatti); Hospital Alberto Cavalcanti (A Barbosa); Hospital Badim (C Coelho); Hospital Cardiotrauma Ipanema (M Knibel); Hospital Carlos Fernando Malzoni (C Minelli); Hospital Da Cidade de Passo Fundo (J Caovilla); Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (G Teixeira); Hospital das Clínicas, Universisty of São Paulo (A Hovnanian); Hospital das Nacoes (A Rea-Neto); Hospital de Base-Famerp (S Lobo); Hospital de Clínicas Mario Lioni (M Lugarinho); Hospital de Clínicas Niterói (P Souza); Hospital de Doenças Tropicais de Goiânia (D Ferreira); Hospital do Cancer / Uopeccan (P Duarte); Hospital do Trabalhador (M Oliveira); Hospital dos Servidores do Estado Rio de Janeiro (J Marques); Hospital E Maternidade São José (R Machado); Hospital Estadual Diadema (P Rehder); Hospital Estadual do Grajau-Unisa (S Mataloun); Hospital Evangelico (M Grilo); Hospital Evangelico do Rio de Janeiro (P Quesado); Hospital Geral de Pedreira (M Moock); Hospital Geral de São Mateus (F Ferreira); Hospital Geral Roberto Santos (J Teles); Hospital Israelita Albert Einstein (E Silva); Hospital Israelita Albert Sabin (C Coelho); Hospital Júlia Kubitschek (A Morais); Hospital Mater Dei (F Carvalho); Hospital Memorial Arthur Ramos (M Wanderley); Hospital Meridional (M Velasco); Hospital Moinhos de Vento (N Brandão da Silva); Hospital Municipal São José (J Feijó); Hospital Nossa Senhora Da Salete (P Duarte); Hospital Pasteur (V Souza Dantas); Hospital Português (J Teles); Hospital Pró-Cardíaco (R Costa Filho); Hospital Quinta D'Or (A Japiassu); Hospital Regional Antônio Dias (D Villela); Hospital Regional de Barbacena (C Santos); Hospital Salvador (R Passos); Hospital Samaritano (R Alheira-Rocha); Hospital Santa Izabel (R Silva); Hospital Santa Paula (J Houly); Hospital Sao Cristovao (J Aldrighi); Hospital São Lucas

(R Hatum); Hospital São Lucas da PUCRS (F Suparregui Dias); Hospital São Luiz - Unidade Itaim (L Ferreira); Hospital São Rafael (L Ferro); Hospital São Vicente de Paulo (J Gomez); Hospital Universitário Clementindo Fraga Filho - Ufrj (R Fleury); Hospital Universitario da Universidade Federal do Rio de Janeiro (C David); Hospital Universitário de Santa Maria (T Resener); Hospital Universitário do Oeste do Paraná (P Duarte); Hospital Universitário Lauro Wanderley - UTI Adulto (C Mendes); Hospital Universitario Regional de Maringa (A Germano); Hospital Vita Curitiba (M Oliveira); Hospital Vivalle (F De marco); Instituto de Espquisa Clinica Evandro Chagas (A Japiassu); Instituto Do Coração - HC-FMUSP (S Lage); Instituto Nacional de Cancer (J Salluh); Irmandade Santa Casa de Misericordia de Porto Alegre (A Torelly); Luxemburgo Hospital (R Sad); Mternidade Odete Valadares (A Barbosa); Prontocor Lagoa (G Oliveira); Samaritano Hospital (R Lima); Santa Casa Da Misericórdia de São João del Rei (J Paranhos); Santa Casa de Misericordia de Passos (M Oliveira); Santa Casa de Porto Alegre (M Rocha); Sao Sebastiao Hospital (W Bitencourt); São Sebastião Hospital (W Bitencourt); Universidade Federal Do Parana (A Rea-Neto); University of Londrina (C Grion); University of Sao Paulo (D Forte); Uti Da Disciplina de Clínica Médica-Unifesp (H Guimarães); Vitória Apart Hospital (C Piras); *Bulgaria:* Mbal Ruse (L Stephanova); Multiprofile Hospital of Active Treatment, Ruse (L Lyubenov); Uh St. Ekaterina (G Tsarianski); Univerisity Hospital (G Dimov); *Canada:* Capital Health-Queen Elizabeth II Health Sciences Centre (R Green); Centre Hospitalier Régional de Lanaudière (J Levasseur); Children's Hospital of Eastern Ontario (R Ward); CHU Sherbrooke (O Lesur); Hôpital Charles Lemoyne (G Poirier); Mount Sinai Hospital (R Wax); Royal Jubilee Hospital (G Wood); St. Joseph's Healthcare (D Cook); St. Michael's Hospital (J Marshall); Toronto General Hospital (M Herridge); Toronto Western Hospital (N Ferguson); Victoria General Hospital (G Wood); *Chile:* Clinica Alemana de Santiago (M Espinoza); Clinica las Condes (S Valdés jimenez); Hospital Clínico de la Pontificia Universidad Católica de Chile (A Bruhn); Hospital del Trabajador (J Micolich); Hospital Dr G. Fricke (S Galvez); Hospital El Pino (I Escamilla Leon); *China:* Beijing Chaoyang Hospital (Q Zhan); Beijing Tongren Hospital (Y Xu); Chinense Pla General Hospital (Y Zhao); Fuxing Hospital, Capital Medical University (L Zhang); Guangdong Provincial People's Hospital (T Qin); Peking Union Medical College Hospital (B Du); Peking University People's Hospital (M Li); Ren Ji Hospital,Shanghai Jiao Tong University (X Wang); The Affiliated Hospital of Ningxia Medical College of China (Y Jing); The First Affiliate Hospital of China Medical University (Z Zhang); The First Affiliated Hospital of Dalian Medical University (W Xianyao); The First People's Hospital of Nantong, Jiangsu (F Li); Zhong-Da Hospital and School of Clinical Medicine, Southeast University (Y Congshan); *Colombia:* Clinica General del Norte (C Rebolledo); Clinica Central del Quindio (D Diaz); Clinica Medellin (R Murillo Arboleda); Clinica Saludcoop (C Rebolledo); Clinica Santa Isabel de Valledupar. (A Arias Antun); Fundación Hospital San Carlos (G Montenegro); Fundacion Valle del Lili (M Granados); Hospital Bocagrande de Cartagena ( ); Hospital Departamental de Villavicencio (N Perez); Hospital El Tunal (G Libreros Duque); Hospital San Jose de Bogota (M Coral); Hospital Santa Clara (G Ortiz); *Costa Rica:* Hospital Calderón Guardia CCSS (D Rodriguez); *Croatia:* Hospital for Infectious Diseases (B Barsic); Sveti Duh General Hospital, School of Medicine, Zagreb (M Cubrilo-Turek); University Hospital Centre (I Gornik); University Hospital Zagreb (M Grljusic); *Cuba:* Hospital Universitario Arnaldo Milian Castro (A Caballero lopez); Hospital Universitario Dr. Gustavo Aldereguía Lima (M Iraola ferrer); *Czech Republic:* Centre of Cardivascular and Transplant Surgery (P Pavlik); Charles University Teaching Hospital, Hradec Kralove (J Manak); Charles University Medical School and Teaching Hospital (J Radej); Faculty General Hospital, Charles University Prague (J Belohlavek); Faculty Hospital Brno (P Sevcik); Faculty Hospital Olomouc

(L Blahut); General Teaching Hospital of 1St Faculty and Charles University (D Tyl); Horovice Hospital (J Steinbach); Klaudians Hospital (I Herold); Krajska Nemocnice Liberec (I Zykova); Nemocnice V Usti Nad Orlici (D Prchal); St. Anne's University Hospital Brno (T Bartosik); University Hospital Brno (M Kolarova); University Hospital Olomouc (R Hájek, J Kohoutová, O Marek); University Hospital Ostrava (P Hon); University Hospital Plzen (I Chytra); *Denmark:* Århus University Hospital (H Betsch); Næstved Hospital (B Fogh); Rigshospitalet (K Espersen); Sygehus Fyn (K Jacobsen); Vejle Sygehus (P Berezowicz); *Ecuador:* Carlos Andrade Marín Hospital (F Guerrero); Clinica La Merced (E Salgado); Hospital Eugenio Espejo (D Barahona); Hospital General de Las Fuerzas Armadas del Ecuador Hg-1 (H Del pozo sanchez); Hospital Metropolitano (M Jibaja); *Egypt:* Dar Alfouad Hospital (A Alansary); *Estonia:* East Tallinn Central Hospital (A Reintam); Tartu University Hospital (J Starkopf); *Finland:* Helsinki University Central Hospital (V Harjola); *France:* AP-HP, CHU Jean Verdier (L Tual); Assistance Publique-Hôpitaux de Marseille, CHU Nord (M Leone); Centre Hospitalier Dunkerque (M Serge); Centre Hospitalier Universitaire (P Michel); Centre Hospitalier (O Leroy); Centre Hospitalier D'Auch (L Mallet); Centre Hospitalier de Blois (B Marc); Centre Hospitalier de Fougères (D Dormoy); Centre Hospitalier de Niort (H Pascal); Centre Hospitalier Dr Schaffner (L Tronchon); Centre Hospitalier du Pays D'Aix (B Garrigues); Centre Hospitalier Region Annecy (C Santré); Centre Hospitalier Universitaire Amiens (H Dupont); Centre Hospitalier Universitaire de Bicêtre (J Duranteau); Centre Hospitalier Universitaire Reims (A Leon); CH Colmar (L Henry); CHG Armentieres (C Canevet); CHU Angers (L Dube); CHU Angers (H Julien); CHU Bicetre (A Nadia); CHU Brest (B Francois); CHU de Bordeaux (J Gérard); CHU Dijon Hopital Général (M Freysz); CHU Hôtel Dieu - APHP (G Remy); CHU Nantes (Y Blanloeil); Clinique Ambroise Paré (P Squara); General Hospital (J Korach); Grenoble University Hospital (M Durand); Groupe Hospitalier du Havre (C Gabriel); Hia Laveran (P Eric); Hopital Antoine Béclère APHP (F Jacobs); Hopital Bichat (R Bronchard); Hôpital Claude Huriez, Centre Hospitalier Régional Universitaire de Lille (E Kipnis); Hopital Cochin Paris (M Moussa); Hôpital de Hautepierre (A Launoy); Hopital de la Croix Rousse (C Guérin); Hôpital Edouard Herriot (P Vanhems); Hôpital Maison Blanche (A Wynckel); Hôpital Raymond Poincaré (B Clair); Hôpital Saint-Louis (E Azoulay); Hôpital Tenon (J Fulgencio); Hôpitaux Civils de Colmar (Y Gottwalles); Hôpitaux Universitaires de Strasbourg (T Krummel); Hospices Civils de Lyon (A Lepape); La Rochelle Hospital (O Lesieur); Lariboisiere University Hospital (D Payen); Poissy Hospital (O Hérvé); Polyclinique Saint André (J Farkas); Rangueil Hospital (P Cougot); Réanimation Chirurgicale (Y Malledant); University Hospital of Bordeaux Haut-Lèvéque (O Joannes-Boyau); *Germany:* Academic Hospital Solingen (T Standl); Ameos Klinikum St.Salvator Halberstadt GMBH (U Sierig); Asklepios Fachkliniken München-Gauting (J Geiseler); Asklepios Klinik Langen (H Hopf); Behandlungszentrum Vogtareuth (M Burgau); Bergmannsheil Bochum (E Conrad-Opel); Bethanien-Krankenhaus (C Hermann); Bundeswehrkrankenhaus Ulm (M Ventzke); Charite/Campus Virchow-Klinikum (T Henneberg); Charite Berlin-Buch (H Loeser); Charité Campus, Mitte (C Spies); Charité Campus, Virchow Klinikum (C Spies); Charite Campus, Virchow (F Esposito); Charité Universitätsmedizin Berlin (H Zuckermann-becker); Clemenshospitl (R Scherer); Dominikus Krankenhaus (A Pauer); Drk-Kliniken Mark Brandenburg (S Kljucar); Drk-Krankenhaus Ratzeburg (K Delfs); Elisabeth-Krankenhaus Essen (E Blank); Ev. Kliniken Bonn Betriebsstätte Waldkrankenhaus (J Busch); Ev.-Freikirchliches Krankenhaus Rüdersdorf (K Wendt); Evang. Krankenhaus Mülheim (J Leßmann); Evangelische Kliniken Bonn Wadkrankenhaus (J Busch); Evangelisches Krankenhaus Bielefeld (F Bach); Friedrich Schiller University, Jena (Y Sakr); Gemeinschaftskrankenhaus Herdecke (T Berlet); Georg-August University of Göttingen (A Kernchen); Georg-August-

University of Göttingen (M Quintel); Hanse-Klinikum Wismar (D Holst); Heart clinic of the University of Munich (E Kilger); Helfenstein Klinik (T Holubarsch); Helios Klinik Lengerich (C Raufhake); Helios-Klinikum Berlin-Buch (R, Kuhlen, C Stolt); Helios Klinikum Emil Von Behring (A Lubasch); Helios Klinikum Erfurt Gmbh (A Meier-Hellmann); Helios Klinikum Wuppertal Barmen (G Woebker); Henriettenstift (C Scharnofske); Herz-Jesu-Krankenhaus (M Breyer); Hochtaunus Kliniken Bad Homburg (T Risch); Hospital Links Der Weser (C Manhold); Icu In Drk Kliniken Mark Brandenburg (S Kljucar); J.W. Goethe - University Medical School Frankfurt Am Main (D Meininger); Johanniter Krankenhaus Bonn (C Greive); Johanniter Krankenhaus Stendal Ggmbh (J Rau); Jung-Stilling-Krankenhaus (A Seibel); Katharinenhospital (A Henn-beilharz); Katholisches Krankenhaus Hagen (R Wolbert); Krankenhaus Prignitz Gemmeinnützige GMBH (T Scherke); Klinik Am Eichert (J Martin); Klinik Für Herzchirurgie (M Rudolph); Klinik Füranästhesie, Operative Intensivmedizin U. Schmerztherapie (J Gleißner); Kliniken Ludwigsburg-Bietigheim GMBH (M Wolf); Kliniken Maria Hilf (F Schleibach); Klinikum Augsburg (U Jaschinski); Klinikum Bad Salzungen (A Lunkeit); Klinikum Darmstadt (M Welte); Klinikum Der J.W. Goethe-Universität (T Bingold); Klinikum Der Stedt Wolfsburg ( ); Klinikum Emden (K Kogelmann); Klinikum Forchheim (F Fischer); Klinikum Fuerth (B Fischer, M Schmid); Klinikum Grosshadern, Universität München (M Klein); Klinikum Harlaching Städtisches Klinikum Muenchen (A Bechtold); Klinikum Hildesheim (K Bodmann); Klinikum Kaufbeuren (J Klasen); Klinikum Landsberg (H Meyrl); Klinikum Lippe - Detmold (J Goetz); Klinikum Ludwigsburg (G Geldner); Klinikum Luedenscheid (T Helmes); Klinikum Meiningen GMBH (N Jensen); Klinikum Minden (H Eickmeyer, W Lengfelder); Klinikum Nürnberg (B Langenstein); Klinikum Rechts Der Isar (R Bogdanski); Klinikum Rechts Der Isar Der Technischen Universität München (S Jelen-Esselborn, A Umgelter); Klinikum Region Hannover (F Dörr); Klinikum Region Hannover Krankenhaus Großburgwedel (K Lüttje); Klinikum Region Hannover, Krankenhaus Oststadt-Heidehaus (D Heinemeyer); Klinikum Starnberg (M Uhl); Klinikum Stuttgart - Olgahospital (P Schirle); Klinikum Suedstadt (H Benad); Klinikum Traunstein (M Glaser); Klinikum Uelzen (W Panzer); Klinikum Worms (E Huettemann); Klinikverbund St. Ansgar, Krankenhaus Bassum (R Stierwaldt); Klinikverbund Süd-West (M Schappacher); Knappschaftskrankenhaus Bochum-Langendreer (E Müller); Krankenhaus Freyung (Rural Hospital) (W Stadlmeyer); Krankenhaus Lübbecke (M Fantini); Krankenhaus Mol GMBH Strausberg (B Dummer); Krankenhaus Nordwest (M Thörner); Krankenhaus Nordwest (V Jost); Krankenhaus Reinbek (T Loerbroks); Kreisklinik Trostberg (T Glück); Kreiskrankenhaus Bergstrasse (R Zimmermann); Kreiskrankenhaus Calw (R Clement); Kreiskrankenhaus Mechernich GMBH (R Hering); Kreiskrankenhaus Nagold (T Klinger); Kreiskrankenhaus Rottweil (J Mehl); Kreiskrankenhaus St. Marienberg Helmstedt (H Polozek); Leopoldina-Krankenhaus (A Rothhammer); Ludmillenstift (R Seidler); Lukas-Krankenhaus Bünde (P Lorenz); Lungenfachklinik Amsee Waren Mueritz (M Lutze); Marienhospital Bruehl (M Euler); Marienkrankenhaus Schwerte (M Heintz); Martin Luther Universität Halle (M Winkler); Medizinische Klinik (M Angstwurm); Mlu Halle-Wittenberg (K Krohe); Mueritz-Klinikum Waren (T Treu); Neurological Intensive Care Unit (T Steiner); Oberschwabenklinik Wangen (S Locher); Orthopädische Klinik Markgröningen (A Walz); Ostalb-Klinikum Aalen (P Zahn); Otto-Von-Guericke Universität Magdeburg (W Brandt); Scivias-Krankenhaus St. Josef (M Marks); Ska-Bileelfeld-Mitte (F Henning); St. Antonius Hospital (U Janssens); St. Hildegardis Krankenhaus Mainz (M Luethgens); St. Johannes Krankenhaus (W Theelen); St. Johannes-Hospital (M Sydow); St. Johannes-Hospital (M Weber); St. Josef-Hospital, Ruhr-Universität Bochum (A Meiser); St. Josefs-Hospital (C Deutschmann); St. Joseph Krankenhaus (C Buttner); St.-Marien Hospital Lünen (M Jokiel); St. Marienhospital Hamm (C Bozzetti); St.

Vincentius Kliniken (B Jürgen); St.-Elisabeth Krankenhaus Köln-Hohenlind (F Fiedler); St.-Vincentius-Krankenhaus Speyer (K Wresch); Städtischen Kliniken Neuss - Lukaskrankenhaus (A Kremer); Städtisches Klinikum Karlsruhe (H Bleier); Städtisches Klinikum Wiesbaden, Dr.-Horst-Schmidt-Kliniken Hsk (M Rueckert); Staedtisches Klinikum Guetersloh (H Ditter); Staedtisches Klinikum Muenchen Gmbh - Klinikum Harlaching (C Peckelsen); Staedtisches Klinikum Muenchen Gmbh/Klinikum Bogenhausen (P Friederich); Staedtisches Klinikum München - Klinikum Neuperlach (K Weber); Tübingen University Hospital (W Krueger); Ubbo-Emmius-Klinik Aurich (R Lowack); Überlingen Hospital (A Michalsen); Uniklinikum Dresden (M Ragaller); Universitaetsklinikum des Saarlandes (A Groeschel); Universitaetsklinikum Mannheim (T Friedrich); Universität Rostock (M Hinz); Universitätsklinikum Der Martin-Luther-Universität Halle-Wittenberg (A Christel); Universitätsklinikum Dresden Carl Gustav Carus (M Ragaller); Universitätsklinikum Leipzig Aör (T Hartwig); Universitätsmedizin Berlin Charité Campus Benjamin Franklin (S Vögeler); University (M Weiss); University Childrens Hospital Hauner (K Reiter); University Hospital (T Schwab); University Hospital Cologne (U Trieschmann); University Hospital Dusseldorf (D Kindgen-milles); University Hospital Giessen and Marburg Gmbh - Giessen (J Engel); University Hospital Lübeck (B Sedemund-adib); University Hospital Mainz (M Lauterbach); University Hospital Marburg (M Max); University Hospital Muenster (T Volkert); University Hospital of Essen (C Waydhas); University Hospital of Mannheim (S Hien); University Hospital of Munich, LMU (J Briegel); University Hospital of Regensburg (V Guralnik); University Hospital Rwth Aachen (N Zoremba); University Hospital Tübingen (R Riessen); University Hospital Würzburg (W Müllges); University Medical Center Hamburg-Eppendorf (A Nierhaus); University of Erlangen (R Strauss); University of Freiburg (S Utzolino); University of Giessen (J Thul); University of Greifswald (P Abel, M Gründling, W Keßler); University of Heidelberg (K Scheuren); University of Leipzig (E Lothar, U Kaisers, D Schmitt, D Schneider); University of Rostock (D Vagts); University of Saarland (H Rensing); University Hospital Essen (B Schoch); Universty Hospital (K Kopp); Vivantes - Klinikum Neukoelln (H Gerlach); Vivantes Klinikum Prenzlauer Berg (M Corea); Vivantes-Klinikum Am Urban (A Uhrig); Westkuestenklinikum Heide (S Schroeder); Westküstenklinikum Heide (F Jordan); Westpfalz-Klinikum Kaiserslautern (T Huber); Zentralöklinikum Augsburg (M Bittinger) *Greece:* Ahepa University Hospital (E Sofianos); Athens University Medical School (A Armaganidis); Evangelismos Hospital (C Routsi); G.Papanikolaou (M Bitzani); General Hospital of Rethymno (A Chalkiadaki); Henry Dunant Hospital (A Michalopoulos); Hippokrateion Hospital Thessaloniki (E Mouloudi); Kat General Hospital (E Ioannidou); Kat Hospital (P Myrianthefs); Kat Hospital, Athens (D Koulenti); Konstantopoulio General Hospital (I Karampela); Lamia General Hospital (G Kyriazopoulos); Red Cross Hospital of Athens (K Mandragos); Thriassio Hospital of Eleusis (P Clouva-molyvdas); University Hospital of Ioannina (A Moraiti); University Hospital of Alexandroupolis (I Pneumatikos); University Hospital of Rion, Patras (K Filos); University Hospital of Thessaly (Larissa) (E Zakynthinos); University of Athens, Medical Shcool (A Kotanidou); Xanthi General Hospital (A Vakalos) *Hong Kong:* Northern District Hospital (A Cheng); Princess Margaret Hospital and Yan Chai Hospital (T Buckley); The Chinese University of Hong Kong (C Gomersall) *Hungary:* National Institute of Neurosurgery (K Kiss); Péterfy Hospital Budapest (P Tamási); Saint George Hospital Hungary (A Sarkany); Semmelweis University (A Csomos); University of Szeged (É Zöllei) *India:* Advanced Medicare Research Institute (S Todi); B.D.Petit Parsee General Hospital (F Udwadia); Bhailal Amin General Hospital (R Shah); Bombay Hospital (P Amin); Breach Candy Hospital Trust (F Udwadia); Care Hospitals (S Samavedam); Christian Medical College (A Mathai); Cumballa Hill Hospital & Heart Institute (M Patil); Deenanath Mangeshkar Hospital (S Jog); Dr.

S. N. Medical College (M Gurjar); Escorts Heart Institute & Research Centre (M Vats); Fortis Healthcare (A Varma); Global Hospitals (P Gopal); Hinduja Hospital & Medical Research Center (F Kapadia); Indraprastha Apoolo Hospitals (R Chawla); Jehangir Hospital (S Iyer); Kalinga Hospital (S Sahu); Kasturba Hospital (C Bakshi); Lokmanya Care Hospital (D Ambike); Max Super Speciality Hospital (D Govil); Medical Trust Hospital, Cochin (V Karipparambath); Nh Hospital (J Chacko); Ruby Hall Clinic (P Sathe); Rungta Hospital (N Rungta); Saifee Hospital (C Jani); Seth Ramdas Shah Memorial Hospital & Research Centre (A Bhome); Shree Medical Foundation (S Prayag); Sir Ganga Ram Hospital (S Ray); Sundaram Medical Foundation (R Rajagopalan); Tata Memorial Hospital (J Divatia); Wockhardt Hospital (R Da costa); Wockhrdt Hospital (T Shyam Sunder) *Indonesia:* Bintaro International Hospital (P Wibowo); Hasan Sadikin Hospital (T Maskoen); Pantai Indah Kapuk Hospital (T Sugiman) *Islamic Republic of Iran*: Imamreza Hospital (S Nowruzinia); Laleh Hospital (A Lotfi); Tehran University of Medical Sciences (A Mahmoodpoor) *Ireland:* Amnch (M Donnelly); Cork University Hospital (D Breen); Mater Misercordiae University Hospital (S Ng); University Hospital Galway (J Bates) *Israel:* Hadassah Medical Center (C Sprung); Haemek Medical Center (A Lev); Kaplan Medical Center (E Kishinevsky); Rabin Medical Center (J Cohen); Soroka Medical Center (S Sofer) *Italy:* A.O Niguarda (S Vesconi); A.O. Ospedale Di Circolo Di Busto Arsizio (S Greco); A.O. Treviglio-Caravaggio (M Borelli); Anestesia E Rianimazione 2 Prof.De Gaudio (P Cecilia); Arnas Ospedale Civico (M Sapuppo); ASL 10 (A Lazzero); ASL 10 Florence Hospital San Giovanni Di Dio (V Mangani); Azienda Ospedaliera Desenzano (N Petrucci); Azienda Ospedaliera Di Melegnano (M Minerva); Azienda Ospedaliera G. Rummo (E De blasio); Azienda Ospedaliera Polo Universitario San Paolo (S Marzorati); Azienda Ospedaliera Santa Maria Alle Scotte (R Rosi); Azienda Ospedaliera Universitaria P.Giaccone Policlinico (A Giarratano); Azienda Ospedaliera-Universitaria Udine (O Margarit); Azienda Ospedaliero -Universitaria (A Guberti); Azienda Ospedaliero-Universitaria S.M.Misericordia (S Scolz); Clinica San Gaudenzio (E Stelian); Fondazione IRCCS Policlinico San Matteo (V Emmi); Fondazione Ospedale Maggiore Policlinico, Mangiagalli Regina Elena (M Caspani); Fondazione Poliambulanza (A Rosano); H San Gerardo (C Abbruzzese); Hospital Panico Tricase (S Colonna); Humanitas Gavazzeni (R Ceriani); II Faculty of Medicne I University of Rome- Osp. S.Andrea (R De Blasi); S. Salvatore Hospital (L Panella); IRCCS Casa Sollievo Della Sofferenza (F Borrelli); Istituto Nazionale Tumori Regina Elena (P Lorella); KH Brixen (H Ruatti); Osepdali Riuniti Di Ancona (C Munch); Ospedale "Ca Foncello" - Treviso (Italia) (C Sorbara); Ospedale "Santa Croce" - ASL 8 (G Fiore); Ospedale Bufalini-Cesena (A Chieregato); Ospedale Di Circolo E Fondazione Macchi (V Conti); Ospedale Di Massa (A Guadagnucci); Ospedale Di Piacenza (P Mario); Ospedale Ferrarotto (M Locicero); Ospedale Maggiore Ausl Bologna (I Marri); Ospedale Maggiore Policlinico Milano (A Sicignano); Ospedale Maggiore Policlinico, Mangiagalli E Regina Elena, IRCCS Milano (V Conte); Ospedale Mugello Azienda Sanitaria Firenze (R Oggioni); Ospedale Niguarda Ca Granda, Milano (A De Gasperi); Ospedale Oncologico Regionale - Centro Di Riferimento Oncologico Della Basilicata (P De negri); Ospedale Provinciale Pistoia (G Santagostino); Ospedale S. Gerardo (F Roberto); Ospedale San Raffaele (G Marino); Ospedele Vittorio Emanuele (G Castiglione); P.O. San Severo Asl Fg (D Sforza); S. Camillo Hospitql (N Giuseppe); San Martino Hospital (M Bassetti); Seconda Università Degli Studi Di Napoli (F Ferraro); Sesto San Giovanni Hospital (S Clementi); Teaching Hospital Careggi (D Alessandro); Terapia Intensiva - Aso S. Giovanni Battista Di Torino - Ospedale Molinette (P Cotogni, MV Ranieri); Università Cattolica (M Antonelli); Universita' Cattolica Del S. Cuore (L Martinelli); University-Hospital Careggi, Florence, (L Gianesello); University Hospital Policlinico Di Catania (A Gullo); University of Rome "La Sapienza" (A Morelli); UTI Trapianti (G

Biancofiore); University of Udine (G Della Rocca) *Japan:* Kyoto Prefectural University of Medicine (S Hashimoto); Nagoya University Hospital (M Onodera); Oosaka-Fu Saiseikai Suita Hospital (A Kobayashi); Sanai Hospital (T Shinozuka); Tokushima University School of Medicine (H Imanaka); Tokyo Medical University, Hachioji Medical Center (T Ikeda); Tokyo Women's Medical University (A Yaguchi) *Latvia:* Hospital of Traumatology and Orthopedics (I Misane); 7th Hospital of Riga (A Piebalga) *Lebanon:* Lebanese Canadian Hospital (A Moughaghab) *Lithuania:* Medicine University of Kaunas (V Pilvinis); Vilnius University Emergency Hospital (S Vosylius); Vilnius University Hospital Santariskiu Clinics (M Balciunas, G Kekstas) *Luxembourg:* Centre Hospitalier de Luxembourg (H Margaret); Clinique Ste Thérèse (M Klop) *Macedonia*: Clinic For Infectious Diseases (K Grozdanovski); General Hospital Stip (B Eftimova) *Malaysia:* Faculty of Medicine, Universiti Kebangsaan Malaysia (S Wafa); Hospital Pulau Pinang (C Lim); Hospital Tengku Ampuan Afzan, Kuantan, Pahang (M Mat nor); Kuala Lumpur Hospital (L Tai); National Heart Institute (S Syed Mohd Tahir); Sarawak General Hospital (N Idris); Sultanah Aminah Hospital (C Tan) *Malta:* St Luke's Hospital (M Borg); *Mexico:* Angeles Metropolitano Hospital (E Manzo); Centro Medico Lic.Adolfo Lopez Mateos (H Gutierrez Morales); Hgr 25 Imss Zaragoza (P Miguel); Hospital Angeles Clinica Londres (A Villagomez); Hospital Angeles del Carmen (A Bassols); Hospital Civil de Guadalajara "Fray Antonio Alcalde" (G Aguirre); Hospital Español de México (U Cerón); Hospital General Bernardo J. Gastelum (J Lopez ramos); Hospital General del Estado "Dr Ernesto Ramos Bours", Hermosillo Sonora Mexico (J Monjardín); Hospital General Regional de Leon (E Bermudez Aceves); Hospital General Reynosa (F Gonzalez Salazar); Hospital Juan I.Menchaca Hospital Civil de Guadalajara (D Rodriguez Gonzalez); Hospital Juárez de México (M Poblano-Morales); Hospital Mèdica Sur (F Ramirez); Hospital O´horan (M Cetina); Hospital Privado de Hermosillo (J Navarro); Hospital Regional 1° Octubre, Issste (A Villagomez Ortiz); Hospital San Jose Tec Monterrey (V Sanchez); Hospital Universitario "Dr. Jose E. Gonzalez" (U Chavarria); IMSS (O Fernandez-Ponce); Iner (H Serna secundino); Instituto de Salud del Estado de Aguascalientes (O Leonardo); Instituto Mexicano del Seguro Social (R Diego Manuel, J Mijangos); Issemym Medical Center (G Vazquez de Anda); Mexican Red Cross (E Martin); Ocq Hospital (P Gutierrez); Secretaria de Salud del Gobierno del Distrito Federal (I López Islas); Servicios de Salud En Yucatan (L Soberanes) *Montenegro*: Clinical Center of Montenegro (P Ljubica) *Morocco:* Chu Ibn Sina (A Sbihi); Polyclinique CNSS Derb Ghallef (B Ouahid); Réanimation Médicale, Hôpital Ibn Sina (M Naoufel) *Netherlands:* Academic Medical Center (A De Pont); Amphia Hospital (P Rosseel); Antoni Van Leeuwenhoek Ziekenhuis (J Ten Cate); Beatrix Zienhuis Rivas Zorggroep (G Van Berkel); Canisius Wilhelmina Ziekenhuis (S Corsten); Erasmus Mc University Medical Center (J Bakker); Hagaziekenhuis (J Vogelaar); Hofpoort Hospital Woerden (H Blom); Isala Clinics (H Kieft); Medical Center Leeuwarden (M Kuiper); Medisch Spectrum Twente (A Gille); Radboud University Nijmegen Medical Centre (P Pickkers); Rode Kruis Ziekenhuis (J Vet); Slingeland Ziekenhuis (J Ammann); Spaarneziekenhuis (S Den Boer); St. Antonius Ziekenhuis (R Wesselink); St.Elisabeth Hospital (B Speelberg); Twenteborg Hospital Almelo (C Pham); University Hospital Groningen (M Rodgers); University Hospital Maastricht (D Bergmans); Vu University Medical Center (J Groeneveld) *New Zealand:* Auckland City Hospital (C Mcarthur); Auckland City Hospital (M Rachael); Christchurch (J Mehrtens); Dunedin Hospital (L Celi); Hawkes Bay Hospital (R Freebairn); Middlemore Hospital (N Rankin); Nelson Marlborough District Health Board (C Heffernan); Palmerston North Hospital (G McHugh); Starship Children's Hospital (J Beca); Waikato Hospital (F Van haren); Wellington Public Hospital (B Barry); Whangarei Base Hospital (M Kalkoff) *Norway:* Aker University Hospital (R Loevstad); St Olavs University

Hospital (P Klepstad); Sykehuset Asker Og Bærum Hf (P Erno); Sykehuset I Vestfold Hf , Toensberg (A Junker) *Pakistan:* Armed Forces Institute of Cardiology (S Naqvi); Jinnah Hospital Lahore Pakistan (I Javed) *Panama*: Complejo Hospitalario Metropolitano (J Sinclair) *Peru:* Hipolito Unanue Hospital (R Rivera); Hospital Regional Honorio Delgado (C Chavez); Hospital Alberto Sabogal Sologuren (Z Donayre Taber); Hospital Dos De Mayo (R Quispe Sierra); Hospital Edgardo Rebagliati Martins (J Muñoz); Hospital Maria Auxiliadora (J Galvez Ruiz); Hospital Nacional Almanzor Aguinaga Asenjo Essalud Chiclayo (J Fang Li); Hospital Nacional Arzobispo Loayza (M Candiotti Herrera); Hospital Víctor Lazarte Echegaray (A Arroyo); Instituto de Salud del Niño (R Becerra); Navy Hospital (J Meza); Peruvian Air Force Central Hospital (M Mayorga) *Poland:* 4th Military Clinical Hospital (P Garba); Academic Centre for Maritime and Tropical Medicine AMG (J Kot); Barlicki University Hospital, University of Medical Science, Lodz, (T Gaszynski); Boleslaw Szarecki Teaching Hospital No. 5 of The Medical University In Lodz (M Piechota); Clinical Hospital No 2 (S Renata); Collegium Medicum Jagiellonian University (P Müller); Institute of Cardiology (J Stepinska); J. Brudzinski's Hospital In Gdynia (K Jacek); Jagiellonian University (T Cieniawa); Karol Marcinkowski University of Medical Sciences (A Mikstacki, B Tamowicz); Poznan University of Medical Sciences (A Bartkowska-Sniatkowska); Silesian University of Medicine (E Karpel); University Hospital Bydgoszcz Cm Umk (K Kusza); University Hospital No 2 (P Smuszkiewicz); University Hospital Warsaw (M Mikaszewska-Sokolewicz); Wojewodzki Szpital Specjalistyczny (R Goraj); Wroclaw Medical University (A Kubler) *Portugal:* Centro Hospitalar Alto Ave (A Bártolo); Centro Hospitalar Cova Da Beira (M Castelo-Branco Sousa); Centro Hospitalar Tras Os Montes E Alto Douro (F Esteves); Chlo-Hospital S Francisco Xavier (A Martins); H S Joao (T Oliveira); Hospital Cuf Infante Santo (P Ponce); Hospital Curry Cabral (L Mourão); Hospital Da Luz (C Febra); Hospital de Egas Moniz (E Carmo); Hospital de S. José (V Lopes); Hospital de São Francisco Xavier (P Póvoa); Hospital de São José (A Rezende); Hospital Divino Espirito Santo (H Costa); Hospital Do Litoral Alentejano (P Moreira); Hospital Dr. José Maria Grande, Portalegre (F Pádua); Hospital Fernando Fonseca (A Leite); Hospital Garcia Orta (E Almeida); Hospital Geral de Santo António (M Alves); Hospital Pulido Valente (A Sousa, L Telo); Hospital S. Joao (C Dias, J Paiva); Hospital Sao Bernardo (R Ribeiro); Hospital São Sebastião, Epe (P Amaro); Hospital Sto Antonio (A Carneiro); Hospital de St. Antonio Dos Cqpuchos (R Moreno); Instituto Português de Oncologia de Lisboa (M Bouw); University Hospital St Maria (C Franca) *Qatar:* Alkhor Hospital (A Ibrahim); Romania: "Maria Sklodowska Curie" Children's Emergency Hospital, Bucharest (R Tabacaru); Department Public Hospital (V Ionita); Fundeni Institute (D Tulbure); Institute of Cardiovascular Disease (D Filipescu); Institutul de Boli Cardiovasculare Si Transplant Tg. Mures (S Pascanu); Spitalul "Sf. Spiridon" (I Grigoras); University Emergency County Hospital (S Copotoiu) *Russia:* Bakoulev Scientific Center For Cardiovascular Surgery (D Popov); City Clinical Hospital (E Lebedev); City Hospital (I Olga); City Hospital #7 (A Yaroshetskiy); Clinical Hospital N°40 (T Lugovkina); Ekaterinburg. University Hospital N°40 (B Dmitry); Izhevsk State Medical Academy (O Malinin); Moscow Children's Surgery Institut (A Lekmanov) *Saudi Arabia:* Alawi Tunsi Hospital (M Abulmagd); King Abdulaziz Medical City (Y Arabi); King Abdulaziz University Hospital (J Alhashemi); King Fahad Specialist Hospital Dammam (A Ali); King Faisal Specialist Hospital (K Maghrabi); Kingdom Hospital (A Debek); Riyadh Millitary Hospital (M Malik) *Serbia:* Clinical Center Nis (R Jankovic); Clinical Centre of Serbia (I Palibrk); Dedinje Cardiovascular Institute (V Maravic-stojkovic); KBC Bezanijka Kosa (V Malenkovic); Military Medical Academy, Belgrade (M Surbatovic); Unuiversity of Belgrade (V Bumbasirevic) *Singapore:* Changi General Hospital (N Lim); Kk Hospital (T Loh); Tan Tock

Seng Hospital (H Tan) *Slovakia:* Fakultna Nemocnica Nitra (H Sekeresova); FNSP Bratislava-Hospital Ruzinov (J Koutun); Madical Faculty Hospital Kosice (J Firment); Nusch Bratislava (P Malik); Reiman Hospital (S Trenkler) *Slovenia:* Clinic Center Ljubljana (I Muzlovic); General Hospital Novo Mesto (L Kosec, B Ozek); General Hospital Slovenj Gradec (D Kasnik); University Clinic of Respiratory and Allergic Diseases (V Tomic); University Clinical Center Ljubljana (R Knafelj); University Medical Center Ljubljana (V Svigelj) *South Africa:* 1 Military Hospital (H Du Plessis); Groote Schuur Hospital (R Raine); Johannesburg Hospital (S Bhagwanjee, G Richards); Johannesburg Hospital (S Bhagwanjee); Johannesburg Hospital Trauma Unit (J Goosen); Unitas Hospital (J De Jager); Wits Donald Gordon Medical Center (G Schleicher) *Spain:* Althaia (O Rubio); Bellvitge University Hospital (R Mañez); Centro Medico Delfos (M Burgueño Campiñez); Clinica Moncloa (M Alvarez); Clinica Rotger (R Jorda); Clinica Santa Elena (E Naveira-Abeigón); Clinica Universitaria de Navarra (P Monedero); Complejo Hospitalario de Pontevedra (E Alemparte-Pardavila); Fundacion Hospital Alcorcon (S Garcia del Valle); Fundacion Jimenez Diaz (C Perez Calvo); H Vall Hebron (M Palomar); H.U. Virgen de Las Nieves- H. Traumatología Y Rehabilitación (F Guerrero); Hospital "Virgen de La Concha" - Zamora (A Caballero Zirena); Hospital Arnau de Vilanova (M Arribas); Hospital Can Misses (E Bustamante Munguira); Hospital Casa de Salud (J Ruiz); Hospital Central de Asturias (L Iglesias); Hospital Clinic (E Zavala); Hospital Clinic de Barcelona (M Valencia); Hospital Clinico San Carlos (A Blesa Malpica); Hospital Clinico San Carlos (F Martinez-Sagasti, M Nieto); Hospital Clinico Universitario (G Aguilar); Hospital Clinico Universitario de Santiago (F Martinon-Torres); Hospital Comarcal Vinaros (C Lorente); Hospital de Navarra (J Insausti); Hospital de Antequera (R Vegas Pinto); Hospital de Basurto (I Santos); Hospital de Fuenlabrada (A Escriba); Hospital de Galdakao (P Olaechea); Hospital de La Merced (E Muñoz); Hospital de Manacor (E Antón Caraballo); Hospital de Mostoles (P Galdos-Anuncibay); Hospital de Sagunto (V Lopez Camps); Hospital de Tortosa Verge de La Cinta (F Esteban-Reboll); Hospital del Sas de Jerez (E Angel); Hospital Donostia (L Bocero); Hospital Dr Peset (A Ibañez); Hospital G. Yagüe (L Pueyo); Hospital General (L María Jesús); Hospital General de Asturias (L Iglesias); Hospital General de Ciudad Real (J Silva); Hospital General de Granollers (P Garro); Hospital General de La Palma (L Ramos-gómez); Hospital General de L'Hospitalet (A Rovira); Hospital General de Vic (M Martin Delgado); Hospital General Salud "Obispo Polanco" (J Monton Dito); Hospital General Universitario de Albacete (F Garcia); Hospital General Universitario de Alicante (J Navarro); Hospital General Universitario de Elche (J Latour-Perez); Hospital General Universitario de Guadalajara (A Albaya); Hospital General Universitario Gregorio Marañon (A Bustinza); Hospital Gran Canaria "Dr Negrín" (J Sole-violán); Hospital Marques de Valdecilla (P Ugarte Peña); Hospital Maz (I Yuste); Hospital Parque San Antonio (J De Rojas Román); Hospital Sabadell (J Vallés); Hospital Sant Joan de Déu (E Esteban); Hospital Sant Pau (E Quintana Tort-Martorell); Hospital Santa María del Rosell (M Moreno); Hospital Santa Maria Madre-Complejo Hospitalario de Ourense (V López Ciudad); Hospital Santiago Apostol (A Manzano Ramirez); Hospital Sevilla-Aljarafe (J Sánchez-Olmedo); Hospital Son Llàtzer (M Borges); Hospital Terrassa (J Amador Amerigo); Hospital Torrecardenas (F Guerrero Gomez); Hospital Universitaio 12 de Octubre (J Montejo González); Hospital Universitari de Girona Doctor Josep Trueta (J Sirvent); Hospital Universitari Germans Trias I Pujol (E Mesalles Sanjuan); Hospital Universitario Arnau de Vilanova (F Barcenilla-Gaite); Hospital Universitario de Canarias (N Serrano); Hospital Universitario de Getafe (E Cerdá); Hospital Universitario de Valme (A Lesmes Serrano); Hospital Universitario Doce de Octubre (C Garcia-Fuentes); Hospital Universitario Infanta Crsitina (J Macias Pingarrón); Hospital Universitario Nªsra de Candelaria (E Espinosa); Hospital Universitario Principe de Asturias (M Sanchez Garcia);

Hospital Universitario Reina Sofía, Murcia (F Felices); Hospital Universitario Virgen de La Victoria (M de la Torre-Prados); Hospital Univesitario Puerto Real (H Maria Jesus); Hospital Valle del Nalon (V Luis); Hospital Virgen Arrixaca (R Jara); Hospital Xanit Internacional (M Briones Lopez); Hospital Xeral Cies (P Posada); Hu La Paz (B Galvan); Hu La Paz (F Mariscal); Joan Xxiii University Hospital (J Rello); Morales Meseguer (B Gil); Puerta del Mar Universitary Hospital (R Sierra); Rio Hortega University Hospital (J Rico-Feijoo); San Pedro de Alcantara Hospital (C Corcobado Márquez); Servicio Navarro de Salud.Hospital Virgen del Camino (J Izura); Uci H. U. Salamanca (J González); Universitary Hospital Dr. Peset (J Soto Ibáñez) *Sudan:* Soba University Hospital (H Agabani) *Sweden:* Anestesikliniken (P Petersen); Centralsjukhuset Karlstad (L Johansson); University Hospital, Linköping (H Blomqvist, B Peterzén, N Wyon); Göteborg (I Lindström); Kärnsjukhuset Skövde (A Paulsson); Karolinska University Hospital Huddinge (C Agvald-Ohman); Karolinska University Hospital, Solna (J Petersson); Lund University Hospital (H Friberg); Malmoe University Hospital (V Einar); Op/ Iva Kliniken (F Hammarskjöld); Ostersund Hospital (M Schindele); Ostra Hospital, Göteborg (S Arvidsson); Sahlgrenska University Hospital (J Sellgren); Söder Hospital (Södersjukhuset) (J Hulting); Sodersjukhuset (J Häggqvist); Sollefteå Hospital (J Rudenstam); Sunderby Hospital (D Lind); The Queen Silvia Children's Hospital (E Kokinsky); Thoracic Intensive Care, Karolinska Hospital (A Owall); Umeå University Hospital (S Jacobson); University Hospital (H Stiernstrom); University Hospital of Örebro (A Nydahl) *Switzerland:* CHUV, Lausanne (P Eggimann); University of Geneva (R Stocker); Hirslanden Klinik Beau-Site (G Loderer); Kantonsspital Liestal (R Loetscher); Kantonsspital Luzern (A Mehlig); Lindenhofspital (K Heer); Neuchâtel (H Zender); Ospedale Civico Di Lugano (S Cottini); Regional Hospital Mendrisio (A Pagnamenta); Stadtspital Triemli (G Eich); Swiss Paraplegic Centre (P Felleiter); University Hospital Zurich (M Marco); University Hospitals of Geneva (J Pugin) *Taiwan:* Changhua Christian Hospital (W Shu-Hui); Kaohsiung Veterans General Hospital (K Hsieh) *Thailand:* Faculty of Medicine Siriraj Hospital (P Toomtong); Prince of Songkla University (B Khwannimit); The Bnh Hospital (P Kietdumrongwong) *Tunisia:* Children's Hospital of Tunis (A Khaldi); Hopital Aziza Othmana (A Messadi); Military Hospital of Tunis (I Labbene); Mongi Slim Hospital (N Frikha) *Turkey:* Acibadem Kadikoy Hospital (K Atalan); Acibadem Bakirkoy Hospital (C Ates); Acibadem Bursa Hospital (A Kahveci); Acibadem Kozyatagi Hospital (H Fistikci); Ankara Univercity (A Kaya); Ankara University Medical Faculty, Ibni Sina Hospital (E Ozgencil); Ataturk University Medical Faculty (M Kizilkaya); Dicle University Medical School (M Bosnak); Dokuz Eylul University (H Bodur); Dokuz Eylul University School of Medicine (M Akan); Erciyes University Medical Faculty (M Guven); Gazi University School of Medicine (M Turkoglu); Hacettepe University Hospital (A Topeli); Inonu University Medical Faculty (T Togal); Istanbul Faculty of Medicine (N Uzel); Istanbul Medical Faculty (I Akinci, N Cakar, S Tugrul); Istanbul University Cerrahpasa Medical School (O Demirkiran); Izmir Ataturk Training and Resarch Hospital (T Adanir); Memorial Hospital (K Dogruer); Okmeydani Teaching & Research Hospital (A Turkmen); Okmeydani Teaching & Research Hospital (H Guven); Ondokuz Mayis University, Medical Faculty (F Ulger); Selcuk University Meram Faculty of Medicine (S Kocak) *Ukraine:* Lugansk City Hospital No. 7 (Y Nalapko); Lugansk District Hospital (Y Nalapko) *United Arab Emirates*: Al-Mafraq Hospital (S Rady); Department of Health & Medical Services (A Alsabbah); Dohms (N Elahi); Dubai Hospital (H Al rahma); Tawam Hospital (M Rahman, S Kashef) *United Kingdom:* Aberdeen Royal Infirmary (B Cuthbertson); Addenbrookes Hospital (K Gunning); Barnsley Hospital (Y Myint); Bristol Royal Infirmary (J Bewley); Cambridge University Teaching Hospitals (R Burnstein); Christie Hospital (P Haji-Michael); Dumfries and Galloway Royal Infirmary (D Wrathall); Kent and Canterbury

Hospital (L Folan); Freeman Hospital (I Nesbitt); Friarage Hospital Northallerton (A Ratnaparkhi); Frimley Park Hospital (S Pambakian); Glasgow Royal Infirmary (M Booth); Great Western Hospital Swindon (M Watters); Guys and St Thomas' NHS Foundation Trust (T Sherry); Huddersfield Royal Infirmary (U Buehner); Hurstwood Park Neurosurgical Centre (C Barrera Groba); James Paget University Hospital (P Bothma); John Radcliffe Hospital (N George, J Millo; Kettering General Hospital (L Hollos); Lothian University Hospitals Trust (S Mclellan); Macclesfield District General Hospital (J Hunter); Manchester Royal Infirmary (M Garrioch, N O'Keeffe); Medway NHS Trust (N Divekar); Morriston Hospital (S Eggert); New Cross Hospital,Wolverhampton. (S Smith); Newcastle General Hospital (A Vincent); Newham University Hospital Trust (P Withington); NHS Tayside (C Macmillan); Northampton General Hospital (R Webster); Papworth Hospital (A Vuylsteke); Peterborough Hospitals (B Appadu); Princess Royal Hospital (C Barrera groba); Queen Alexandra Hospital, Portsmouth (P McQuillan); Queen Elizabeth Hospital (M Blunt); Queen Elizabeth Medical Center, Birmingham (N Parekh); Rotherham DGH (D William); Royal Berkshire Hospital (C Jones); Royal Blackburn Hospital (A Krige); Royal Bournemouth NHS Foundation Trust (M Schuster-Bruce); Royal Cornwall Hospital (J Boyden); Royal Devon & Exeter NHS Foundation Trust (C Boulanger); Royal Infirmary of Edinburgh (D Swann); Royal Liverpool University Hospital (J Walker); Royal Marsden Hospital (T Wigmore); Royal Shrewsbury Hospital (R Law); Royal Sussex County Hospital (F Baldwin); South Tyneside Hospital (C Muench); Southmead Hospital (S Robinson); St George's Hospital (A Crerar-Gilbert, A Rhodes); St Helens and Knowsley Hospital (T Mahambrey); St John's Hospital (L Cameron); St. James's University Hospital (J Thornton); St. Mary's Hospital (M Stotz); St. Peters Hospital (M Russell); Stirling Royal Infirmary (A Longmate); Tameside General Hospital (R Kitson); Taunton & Somerset NHS Trust (B Browne); The Hillingdon Hospital (A Thorniley); The James Cook University Hospital (I Gonzalez); Torbay Hospital (M Swart); University College Hospital (M Singer); University Hospital Birmingham (N Gautam); University Hospital of South Manchester (V Prasad); University Hospitals Coventry & Warwickshire Nhs Trust (D Watson); West Middlesex University Hospital (T Szakmany); West Suffolk Hospital (J Cardy); Western Infirmary Glasgow (A Binning); Wexham Park Hospital (R Loveland); Wirral Hospitals Nhs Trust (J Gannon); Wolverhampton Hospital (G Martinelli); Wythenshawe Hospital (P Nightingale); Yeovil District Hospital (J Howes) *United States:* Baystate Medical Center (J Steingrub); Denver Health Medical Center (L Ammons); Emory University Hospital - Micu (M Fisher); Englewood Hopital Medical Center (N Gandhi); Grady Memorial Hospital-Emory University (G Martin); Hospital of The University of Pennsylvania (C Deutschman); Ihc Health Services Inc, Dba Lds Hospital (N Dean); Inova Fairfax Hospital (C Michetti); Los Angeles County+University of Southern California Medical Center (H Belzberg); Lsuhsc Shreveport (K Hutchinson); Maine Medical Center (T Van der kloot); Mayo Clinic (B Afessa); Mount Sinai School of Medicine (D Kaufman); Nassau University Medical Center (J Iqbal); New York University (D Ost); Northwestern University (M West, R Wunderink); Northwestern University Feinberg School of Medicine Critical Care (S Afifi); Olive View Ucla Medical Center (S Stein); Oregon Health & Science University (D Hagg); Orlando Regional Medical Center (E Jimenez); Penn State Hershey Medical Center (S Blosser); Rochester General Hospital (S Chhangani); Rush University Medical Center (R Kleinpell); Rutland Regional Medical Center (H Reich); Scott and White Hospital (E Fileds); Sharp Memorial Hospital (D Willms); South Texas Veterans Health Care System (P Castellanos-Mateus); St. Joseph Medical Center Fhs (L Melnik); Texas Tech University Health Sciences Center (L Oud); The Methodist Hospital (E Chi); The Methodist Hospital (R Halfon); The University of Mississippi Medical Center (A Badr); The University of Texas Health Science

Center At San Antonio (P Castellanos-mateus); University of Chicago (A Pohlman); University of Cincinnati (R Branson); University of Kansas Hospital (S Simpson); University of Miami School of Medicine (D Kett); University of Michigan (T Jacobs, P Park, W Wahl); University of Texas Health Science Center at San Antonio (C Patricia); University of Toledo Medical Center (J Hammersley, T Papadimos); University of Virginia (R Sawyer); Uthsc At Memphis - Regional Medical Center (Site) (A Freire); Veterans Caribbean Healthcare System (W Rodriguez); Washington Hospital Center (A Ryan); West Suburban Medical Center (B Margolis); Winthrop University Hospital (M Groth) *Uruguay:* Amecom (H Escanda); Comta (J Baraibar); Hopital Policial (D Paciel); Hospital Maciel (H Bagnulo); Hospital Tacuarembo (F Hitta); Médica Uruguaya Corporación de Asistencia Médica (P Nadales); Sanatorio Americano - Femi (H Albornoz) *Venezuela:* Hospital Dr Luis Ortega (Z Salmen); Hospital Unversitario de Caracas (C Pacheco) *Vietnam:* Bach Mai Hospital (T Bui); Franco Vietnamese Hospital (F Potie); Ninh Thuan Hospital (C Nguyen Huu)