Tabah, Alexis, Buetti, Niccolò, Staiquly, Quentin, Ruckly, Stéphane, Akova, Murat, Aslan, Abdullah Tarik, Leone, Marc, Conway Morris, Andrew, Bassetti, Matteo, Arvaniti, Kostoula, Lipman, Jeffrey, Ferrer, Ricard, Qiu, Haibo, Paiva, José-Artur, Povoa, Pedro, De Bus, Liesbet, De Waele, Jan, Zand, Farid, Gurjar, Mohan, Alsisi, Adel, Abidi, Khalid, Bracht, Hendrik, Hayashi, Yoshiro, Jeon, Kyeongman, Elhadi, Muhammed, Barbier, François, Timsit, Jean-François, Tabah, Alexis, Pollock, Hamish, Margetts, Ben, Young, Meredith, Bhadange, Neeraj, Tyler, Steven, Ledtischke, Anne, Finnis, Mackenzie, Ledtischke, Anne, Finnis, Mackenzie, Dwivedi, Jyotsna, Saxena, Manoj, Biradar, Vishwanath, Soar, Natalie, Sarode, Vineet, Brewster, David, Regli, Adrian, Weeda, Elizabeth, Ahmed, Samiul, Fourie, Cheryl, Laupland, Kevin, Ramanan, Mahesh, Walsham, James, Meyer, Jason, Litton, Edward, Palermo, Anna Maria, Yap, Timothy, Eroglu, Ege, Attokaran, Antony George, Jaramillo, CFhavala, Nafees, Khalid Mahmood Khan, Rashid, Nurhikmahtul Aqilah Haji Abd, Walid, Haji Adi Muhamad Ibnu, Mon, Tomas, Moorthi, P. Dhakshina, Sudhirchandra, Shah, Sridharan, Dhadappa Damodar, Haibo, Qiu, Jianfeng, Xie, Wei-Hua, Lu, Zhen, Wang, Qian, Chuanyun, Luo, Jili, Chen, Xiaomei, Wang, Hao, Zhao, Peng, Zhao, Juan, Wusi, Qiu, Mingmin, Chen, Xu, Lei, Yin, Chengfen, Wang, Ruilan, Wang, Jinfeng, Yin, Yongjie, Zhang, Min, Ye, Jilu, Hu, Chungfang, Zhou, Suming, Huang, Min, Yan, Jing, Wang, Yan, Qin, Bingyu, Ye, Ling, Weifeng, Xie, Peije, Li, Geng, Nan, Hayashi, Yoshiro, Karumai, Toshiyuki, Yamasaki, Masaki, Hashimoto, Satoru, Hosokawa, Koji, Makino, Jun, Matsuyoshi, Takeo, Kuriyama, Akira, Shigemitsu, Hidenobu, Mishima, Yuka, Nagashima, Michio, Yoshida, Hideki, Fujitani, Shigeki, Omori, Koichiro, Rinka, Hiroshi, Saito, Hiroki, Atobe, Kaori, Kato, Hideaki, Takaki, Shunsuke, Hasan, M. Shahnaz, Jamaluddin, Muhamad Fadhil Hadi, Pheng, Lee See, Visvalingam, Sheshendrasurian, Liew, Mun Thing, Wong, Siong Ling Danny, Fong, Kean Khang, Rahman, Hamizah Bt Abdul, Noor, Zuraini Md, Tong, Lee Kok, Azman, Abd. Hamid, Mazlan, Mohd Zulfakar, Ali, Saedah, Jeon, Kyeongman, Lee, Sang-Min, Park, Sunghoon, Park, Seung Yong, Lim, Sung Yoon, Goh, Qing Yuan, Ng, Shin Yi, Lie, Sui An, Kwa, Andrea Lay Hoon, Goh, Ken Junyang, Li, Andrew Yunkai, Ong, Caroline Yu Ming, Lim, Jia Yan, Quah, Jessica Lishan, Ng, Kangqi, Ng, Louis Xiang Long, Yeh, Yu Chang, Chou, Nai-Kuan, Cia, Cong-Tat, Hu, Ting-Yu, Kuo, Li-Kuo, Ku, Shih-Chi, Wongsurakiat, Phunsup, Apichatbutr, Yutthana, Chiewroongroj, Supattra, Nadeem, Rashid, Houfi, Ashraf El, Alsisi, Adel, Elhadidy, Amr, Barsoum, Mina, Osman, Nermin, Mostafa, Tarek, Elbahnasawy, Mohamed, Saber, Ahmed, Aldhalia, Amer, Elmandouh, Omar, Elsayed, Ahmed, Elbadawy, Merihan A., Awad, Ahmed K., Hemead, Hanan M., Zand, Farid, Ouhadian, Maryam, Borsi, Seyed Hamid, Mehraban, Zahra, Kashipazha, Davood, Ahmadi, Fatemeh, Savaie, Mohsen, Soltani, Farhad, Rashidi, Mahboobeh, Baghbanian, Reza, Javaherforoosh, Fatemeh, Amiri, Fereshteh, Kiani, Arash, Zargar, Mohammad Amin, Mahmoodpoor, Ata, Aalinezhad, Fatemeh, Dabiri, Gholamreza, Sabetian, Golnar, Sarshad, Hakimeh, Masjedi, Mansoor, Tajvidi, Ramin, Tabatabaei, Seyed Mohammad Nasirodin, Ahmed, Abdullah Khudhur, Singer, Pierre, Kagan, Ilya, Rigler, Merav, Belman, Daniel, Levin, Phillip, Harara, Belal, Diab, Adei, Abilama, Fayez, Ibrahim, Rebecca, Fares, Aya, Buimsaedah, Ahmad, Gamra, Marwa, Aqeelah, Ahmed, AliAli, Almajdoub Mohammed, Homaidan, Ahmed Gaber Sadik, Almiqlash, Bushray, Bilkhayr, Hala, Bouhuwaish, Ahmad, Taher, Ahmed Sa, [illegible]ed, Eman, Abousnina, Fathi A., Hdada, Aisha Khaled, Jobran, Rania, Hasan, Hayat Ben, Hasan, [illegible]aban Ben, Serghini, Issam, Seddiki, Rachid, Boukatta, Brahim, Kanjaa, Nabil, Mouhssine, [illegible], Wal[illegible] Maazouzi Ahmed, Dendane, Tarek, Zeggwagh, Amine Ali, Housni, Brahim, Younes, Oujidi, Hachimi, A[illegible]delhamid, Ghannam, A., Belkhadir, Z., Amro, Sarah, Jayyab, Mustafa Abu, Hssain, Ali Ait,

Elbuzidi, Abdurahaman, Karic, Edin, Lance, Marcus, Nissar, Shaikh, Sallam, Hend, Elrabi, Omar, Almekhlafi, Ghaleb A., Awad, Maher, Aljabbary, Ahmed, Chaaban, Mohammad Karam, Abu-Sayf, Natalia, Al-Jadaan, Mohammad, Bakr, Lubna, Bouaziz, Mounir, Turki, Olfa, Sellami, Walid, Centeno, Pablo, Morvillo, Lic Natalia, Acevedo, José Oscar, Lopez, Patricia Mabel, Fernández, Rubén, Segura, Matías, Aparicio, Dra Marta, Alonzo, Microbiologa Irene, Nuccetelli, Yanina, Montefiore, Pablo, Reyes, Luis Felipe, Reyes, Luis Felipe, Ñamendys-Silva, Silvio A., Romero-Gonzalez, Juan P., Hermosillo, Mariana, Castillo, Roberto Alejandro, Leal, Jesús Nicolás Pantoja, Aguilar, Candy Garcia, Herrera, Mara Ocotlan Gonzalez, Villafuerte, Missael Vladimir Espinoza, Lomeli-Teran, Manuel, Dominguez-Cherit, Jose G., Davalos-Alvarez, Adrian, Ñamendys-Silva, Silvio A., Sánchez-Hurtado, Luis, Tejeda-Huezo, Brigitte, Perez-Nieto, Orlando R., Tomas, Ernesto Deloya, De Bus, Liesbet, De Waele, Jan, Hollevoet, Isabelle, Denys, Wouter, Bourgeois, Marc, Vanderhaeghen, Sofie F. M., Mesland, Jean-Baptiste, Henin, Pierre, Haentjens, Lionel, Biston, Patrick, Noel, Cindérella, Layos, Nathalie, Misset, Benoît, De Schryver, Nicolas, Serck, Nicolas, Wittebole, Xavier, De Waele, Elisabeth, Opdenacker, Godelive, Kovacevic, Pedja, Zlojutro, Biljana, Custovic, Aida, Filipovic-Grcic, Ina, Radonic, Radovan, Brajkovic, Ana Vujaklija, Persec, Jasminka, Sakan, Sanja, Nikolic, Mario, Lasic, Hrvoje, Leone, Marc, Arbelot, Charlotte, Timsit, Jean-François, Patrier, Juliette, Zappela, N., Montravers, P., Dulac, Thierry, Castanera, Jérémy, Auchabie, Johann, Le Meur, Anthony, Marchalot, A., Beuzelin, M., Massri, Alexandre, Guesdon, Charlotte, Escudier, Etienne, Mateu, Philippe, Rosman, Jérémy, Leroy, Olivier, Alfandari, Serge, Nica, Alexandru, Souweine, Bertrand, Coupez, Elisabeth, Duburcq, Thibault, Kipnis, Eric, Bortolotti, Perrine, Le Souhaitier, Mathieu, Mira, Jean-Paul, Garcon, Pierre, Duprey, Matthieu, Thyrault, Martial, Paulet, Rémi, Philippart, François, Tran, Marc, Bruel, Cédric, Weiss, Emmanuel, Janny, Sylvie, Foucrier, Arnaud, Perrigault, Pierre-François, Djanikian, Flora, Barbier, François, Gainnier, Marc, Bourenne, Jérémy, Louis, Guillaume, Smonig, Roland, Argaud, Laurent, Baudry, Thomas, Dessap, Armand Mekonted, Razazi, Keyvan, Kalfon, Pierre, Badre, Gaëtan, Larcher, Romaric, Lefrant, Jean-Yves, Roger, Claire, Sarton, Benjamine, Silva, Stein, Demeret, Sophie, Le Guennec, Loïc, Siami, Shidasp, Aparicio, Christelle, Voiriot, Guillaume, Fartoukh, Muriel, Dahyot-Fizelier, Claire, Imzi, Nadia, Klouche, Kada, Bracht, Hendrik, Hoheisen, Sandra, Bloos, Frank, Thomas-Rueddel, Daniel, Petros, Sirak, Pasieka, Bastian, Dubler, Simon, Schmidt, Karsten, Gottschalk, Antje, Wempe, Carola, Lepper, Philippe, Metz, Carlos, Viderman, Dmitriy, Ymbetzhanov, Yerlan, Mugazov, Miras, Bazhykayeva, Yelena, Kaligozhin, Zhannur, Babashev, Baurzhan, Merenkov, Yevgeniy, Temirov, Talgat, Arvaniti, Kostoula, Smyrniotis, Dimitrios, Psallida, Vasiliki, Fildisis, Georgios, Soulountsi, Vasiliki, Kaimakamis, Evangelos, Iasonidou, Cristina, Papoti, Sofia, Renta, Foteini, Vasileiou, Maria, Romanou, Vasiliki, Koutsoukou, Vasiliki, Matei, Mariana Kristina, Moldovan, Leora, Karaiskos, Ilias, Paskalis, Harry, Marmanidou, Kyriaki, Papanikolaou, M., Kampolis, C., Oikonomou, Marina, Kogkopoulos, Evangelos, Nikolaou, Charikleia, Sakkalis, Anastasios, Chatzis, Marinos, Georgopoulou, Maria, Efthymiou, Anna, Chantziara, Vasiliki, Sakagianni, Aikaterini, Athanasa, Zoi, Papageorgiou, Eirini, Ali, Fadi, Dimopoulos, Georges, Almiroudi, Mariota Panagiota, Malliotakis, Polychronis, Marouli, Diamantina, Theodorou, Vasiliki, Retselas, Ioannis, Kouroulas, Vasilios, Papathanakos, Georgios, Montrucchio, Giorgia, Sales, Gabriele, De Pascale, Gennaro, Montini, Luca Maria, Carelli, Simone, Vargas, Joel, Di Gravio, Valentina, Giacobbe, Daniele Roberto, Gratarola, Angelo, Porcile, Elisa, Mirabella, Michele, Daroui, Ivan, Lodi, Giovanni, Zuccaro, Francesco, Schlevenin, Maria Grazia, Pelosi, Paolo, Battaglini, Denise, Cortegiani, Andrea, Ippolito, Mariachiara, Bellina, Davide, Di Guardo, Andrea, Pelagalli, Lorella, Covotta, Marco, Rocco, Monica, Fiorelli, Silvia, Cotoia, Antonella, Rizzo, Anna Chiara, Mikstacki, Adam, Tamowicz, Barbara, Komorowska, Irmina Kaptur, Szczesniak, Anna, Bojko, Jozef, Kotkowska, Anna, Walczak-Wieteska, Paulina, Wasowska, Dominika, Nowakowski, Tomasz, Broda, Hanna, Peichota, Mariusz, Pietraszek-Grzywaczewska, Iwona, Martin-Loeches, Ignacio, Bisanti, Alessandra, Cartoze, Nuno, Pereira, Tiago, Guimarães, Nádia, Alves, Madalena, Marques, Ana Josefina Pinheiro, Pinto, Ana Rios, Krystopchuk, Andriy, Teresa, Ana, de Figueiredo, António Manuel Pereira, Botelho, Isabel, Duarte, Tiago, Costa, Vasco, Cunha, Rui Pedro, Molinos, Elena, da Costa, Tito, Ledo, Sara, Queiró, Joana, Pascoalinho, Dulce, Nunes, Cristina, Moura, José Pedro, Pereira, Énio, Mendes, António Carvalho, Valeanu, Liana, Bubenek-Turconi, Serban, Grintescu, Ioana Marina, Cobilinschi, Cristian, Filipescu, Daniela Carmen, Predoi, Cornelia Elena, Tomescu, Dana, Popescu, Mihai, Marcu, Alexandra, Grigoras, Ioana, Lungu, Olguta, Gritsan, Alexey, Anderzhanova, Anastasia, Meleshkina, Yulia, Magomedov, Marat, Zubareva, Nadezhda, Tribulev, Maksim, Gaigolnik, Denis, Eremenko, Aleksandr, Vistovskaya, Natala, Chukina, Maria, Belskiy, Vladislav, Furman, Mikhail, Rocca, Ricard Ferrer, Martinez, Maria, Casares, Vanessa, Vera, Paula, Flores, Matias, Amerigo, Joaquin Amador, Arnillas, Maria Pilar Gracia, Bermudez, Rosana Munoz, Armestar, Fernando, Catalan,

Epidemiology and outcomes of hospital-acquired bloodstream infections in intensive care unit patients: the EUROBACT-2 international cohort study.

Alexis Tabah, Niccolò Buetti, Quentin Staiquly, Stéphane Ruckly, Murat Akova, Abdullah Tarik Aslan, Marc Leone, Andrew Conway Morris, Matteo Bassetti, Kostoula Arvaniti, Jeffrey Lipman, Ricard Ferrer, Haibo Qiu, Jose Artur Paiva, Pedro Povoa, Liesbet De Bus, Jan de Waele, Farid Zand, Mohan Gurjar, Adel Alsisi, Khalid Abidi, Hendrik Bracht, Yoshiro Hayashi, Kyeongman Jeon, Muhammed Elhadi, François Barbier and Jean-François Timsit for the Eurobact-2 study group, on behalf of the ESICM, ESGCIP, and the OUTCOMEREA network.

This is a copy of the manuscript as accepted for publication – the online version can be found on https://doi.org/10.1007/s00134-022-06944-2

Corresponding Author: Alexis Tabah

Intensive care Unit, Redcliffe Hospital, Brisbane, Australia. Email: a.tabah@uq.edu.au

Tel +61 (0)7 3883 7777

Alexis Tabah
1: Intensive Care Unit, Redcliffe Hospital, Metro North Hospital and Health services, Queensland, Australia.
2: Queensland University of Technology, Brisbane, Queensland.
3: Faculty of Medicine, The University of Queensland, Brisbane, Queensland.
ORCID: 0003-3513-2778

Niccolò Buetti
1: Infection Control Program and WHO Collaborating Centre on Patient Safety, Geneva University Hospitals and Faculty of Medicine, Rue Gabrielle-Perret-Gentil 4, 1205 Geneva, Switzerland.
2: Université de Paris, INSERM, IAME UMR 1137, F-75018 Paris, France.

Quentin Staiquly
1: ICUREsearch, Biometry, 38600 Fontaine, France

Stéphane Ruckly
1: Université de Paris, INSERM, IAME UMR 1137, F-75018 Paris, France.
2: ICUREsearch, Biometry, 38600 Fontaine, France

Murat Akova
1: Department of Infectious Diseases, Hacettepe University School of Medicine, Ankara, Turkey.

Abdullah Tarik Aslan
1: Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey

Marc Leone
1: Department of Anesthesiology and Intensive Care Unit, Hospital Nord, Aix Marseille University, Assistance Publique Hôpitaux Universitaires de Marseille, Marseille, France.

Andrew Conway Morris
1: Division of Anaesthesia, Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 0QQ, United Kingdom
2: Division of Immunology, Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge, Cb2 1QP, United Kingdom
3: JVF Intensive Care Unit, Addenbrooke's Hospital, Cambridge, Hills Road, Cambridge, CB2 0QQ, United Kingdom
ORCID-ID: 0000-0002-3211-3216

Matteo Bassetti
1: Infectious diseases Clinic, department of Health Sciences University of Genoa and Ospedale Policlinico San Martino, Genoa, Italy

Kostoula Arvaniti
1: Intensive Care Unit, Papageorgiou University Affiliated Hospital, Thessaloníki, Greece.

Jeffrey Lipman
1: Faculty of Medicine, The University of Queensland, Brisbane, Queensland.
2: Nimes University Hospital, University of Montpellier, Nimes, France.
3: Jamieson Trauma Institute, Royal Brisbane and Women's Hospital.

Ricard Ferrer
1: Intensive Care Department. SODIR-VHIR Research Group. Vall d'Hebron University Hospital.

Haibo Qiu
1: Jiangsu Provincial Key Laboratory of Critical Care Medicine, Department of Critical Care Medicine, Nanjing Zhongda Hospital, Southeast University, Nanjing 210009,China.

José Artur Paiva
1: Intensive Care Medicine Department, Centro Hospitalar Universitário Sao Joao; Department of Medicine, Faculty of Medicine, University of Porto; Infection and Sepsis ID Group, Porto, Portugal

Pedro Povoa
1: NOVA Medical School, New University of Lisbon, Portugal
2: Center for Clinical Epidemiology and Research Unit of Clinical Epidemiology, OUH Odense University Hospital, Denmark
3: Polyvalent Intensive Care Unit, Hospital de São Francisco Xavier, CHLO, Lisbon, Portugal

Liesbet De Bus
1: Department of Critical Care Medicine, Ghent University Hospital, Ghent, Belgium

Jan de Waele
1: Department of Internal Medicine and Pediatrics, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium.
2: Department of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium.
ORCID-ID: 0000-0003-1017-9748

Farid Zand
1: Anesthesiology and Critical Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Mohan Gurjar
1: Department of Critical Care Medicine, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, India. ORCID: 0000-0002-8489-0324

Adel Alsisi
1: ICU Department, Prime Hospital, Dubai, United Arab Emirates.
2: Critical Care Department, Faculty of Medicine. Cairo University, Cairo, Egypt.

Khalid Abidi
1: Medical ICU, Ibn Sina University Hospital, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco

Hendrik Bracht
1: Central Interdisciplinary Emergency Medicine; University Hospital Ulm, Germany

Yoshiro Hayashi
1: Department of Intensive Care Medicine, Kameda General Hospital, Kamogawa, Japan.

Kyeongman Jeon
1: Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea.

Muhammed Elhadi
1: Faculty of Medicine, University of Tripoli, Tripoli, Libya

François Barbier
1: Service de Médecine Intensive-Réanimation, Centre Hospitalier Régional d'Orléans, 14, avenue de l'Hôpital, 45100, Orléans, France.

Jean-François Timsit
1: Université de Paris, INSERM, IAME UMR 1137, F-75018 Paris, France.
2: Medical and Infectious Diseases Intensive Care Unit, AP-HP, Bichat-Claude Bernard University Hospital, 46 Omdurman maternity hospitalrue Henri Huchard, 75877, Paris Cedex, France.

Abstract

Purpose: In the critically ill, hospital-acquired bloodstream infections (HA-BSI) are associated with significant mortality. Granular data are required for optimizing management, developing guidelines and clinical trials.

Methods: Prospective international cohort study of adult patients (≥18 years of age) with HA-BSI treated in Intensive care units (ICUs) between June 2019 and February 2021.

Results: 2600 patients from 333 ICUs in 52 countries were included. 78% HA-BSI were ICU-acquired. Median SOFA score was 8 [IQR 5; 11] at HA-BSI diagnosis. Most frequent sources of infection included pneumonia (26.7%) and intravascular catheters (26.4%). Most frequent pathogens were Gram-negative bacteria (59.0%), predominantly *Klebsiella spp*. (27.9%), *Acinetobacter spp.* (20.3%), *Escherichia coli* (15.8%), and *Pseudomonas spp.* (14.3%). Carbapenem resistance was present in 37.8%, 84.6%, 7.4%, and 33.2%, respectively. Difficult-to-treat resistance (DTR) present in 23.5% and pan-drug resistance in 1.5%. Antimicrobial therapy was deemed adequate within 24 hours for 51.5%. Antimicrobial resistance was associated with longer delays to adequate antimicrobial therapy. Source control was needed in 52.5% but not achieved in 18.2%. Mortality was 37.1%, and only 16.1% had been discharged from hospital by day-28.

Interpretation: HA-BSI was frequently caused by Gram-negative, carbapenem resistant and DTR pathogens. Antimicrobial resistance led to delays in adequate antimicrobial therapy. Mortality was high, and at day-28 only a minority of the patients were discharged alive from the hospital. Prevention of antimicrobial resistance and focusing on adequate antimicrobial therapy and source control are important to optimize patient management and outcomes.

Take Home message – key points

Hospital-acquired bloodstream infections were frequently caused by Gram-negative, carbapenem resistant or with difficult to treat resistance pathogens. Antibiotic resistance was associated with delays to antimicrobial therapy. Mortality was 37% at day-28.

Introduction

Hospital-acquired bloodstream infections (HA-BSI) are the healthcare associated infection causing the highest burden in disability-adjusted life years [1]. They are relatively frequent in Intensive Care Unit (ICU) patients and are associated with 36% to 42% mortality [2-5]. In 2012, the Eurobact-1

international cohort study highlighted the prevalence of multidrug-resistant organisms and its association with higher risk of death in intensive care unit (ICU) patients with HA-BSI. In recent years, worrisome increases in antimicrobial resistance have been highlighted by agencies and scientific societies worldwide [6-8]. Indeed, antimicrobial resistance is associated with delays to adequate antimicrobial therapy, increased mortality, resource utilisation and costs [2, 9, 10]. It leads to considerable increases in the use of broad-spectrum antimicrobials which in turn exacerbates the problem by selecting antimicrobial resistant micro-organisms. Given the frequency of sepsis, septic shock, and the high mortality in ICU patients with HA-BSI, large international studies are essential to identify potentially modifiable factors of poor prognosis. These data may inform patient care, the development of guidelines, and the design of clinical trials.

The Eurobact 2 study was designed to update the epidemiology and main factors associated with day-28 mortality in ICU patients with HA-BSI by prospectively collecting granular center, patient, pathogen, treatment, and outcome data from ICUs worldwide.

Methods

Study design

Eurobact 2 was a prospective international cohort study, registered with ClinicalTrials.org (NCT03937245) and reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [11]. The study was conducted across the first year of the COVID-19 pandemic. We reported the differences in the epidemiology of HA-BSI in patients with COVID-19 separately [12]. Initial ethical approval as a low-risk research project with waiver of individual consent was granted by the Human Research Ethics Committee of the Royal Brisbane & Women's Hospital, Queensland, Australia (LNR/2019/QRBW/48376). Each study site then obtained ethical and governance approvals according to national and/or local regulations.

Setting

Endorsement, financial, and logistical support were obtained from the European Society of Intensive Care Medicine (ESICM) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) study Group for Infections in Critically Ill Patients (ESGCIP). The operational committee (AT, NB, FB, SR, QS, CD, JFT) oversaw study operations under the responsibility of the primary investigator (AT). Logistics were provided by the OUTCOMEREA non-profit research group (Paris, France). National coordinators recruited participating ICUs, applied for ethical and regulatory approvals, and facilitated communication within their country.

Participants

We included adult (≥18 years of age) patients with a HA-BSI treated in the ICU.

HA-BSI was defined as a positive blood culture sampled more than 48 hours after hospital admission. Treatment in the ICU was defined as the blood culture having been either sampled in the ICU or the patient having been transferred to the ICU for the treatment of the HA-BSI. Detailed definitions are available in the electronic supplemental material (ESM).

For usually considered as common contaminants (list provided in the ESM), at least 2 blood cultures with the same antimicrobial susceptibility profile, or strong clinical grounds that it was not a contaminant (*e.g.*, intravascular catheters or other infected material proven as a source for the HA-BSI) were mandatory. All possible contaminants were carefully reviewed for eligibility by the operational committee in collaboration with the local investigators and excluded if the above criteria were not met.

Data collection

Centers prospectively recruited patients between the 1st of June 2019 and the 30th of January 2021, with a minimum of 10 consecutive patients or for a 3-month period, which on request could be extended. Hospital and ICU characteristics were recorded. Patient data were retrieved from the

hospital charts without additional tests or interventions. Demographic data, the main diagnosis at ICU admission, and comorbidities were collected. Geographical regions and income categories were defined using the United Nations M49 standard [13]. Severity of illness was assessed at ICU admission by the Simplified Acute Physiology Score II (SAPS II) [14], and at HA-BSI diagnosis by the Sequential Organ Failure Assessment (SOFA) score [15]. Given all included patients had an infection, sepsis was defined at HA-BSI diagnosis according to Sepsis III criteria by a SOFA score ≥2, and septic shock as sepsis plus vasopressor use plus lactate >2 mmol/L [16]. We focused on each patient's first episode of HA-BSI, collected pathogen with antibiogram, date and time of blood culture sampling and followed patients for 28 days, until hospital discharge, or death. Blood culture sampling represented the time zero of the study from which all timings were calculated (e.g., time to adequate antimicrobial therapy). Sources of HA-BSI were recorded in order of clinical likelihood according to the treating clinician. Primary HA-BSI was defined as no clear portal of entry or source of infection. Antimicrobials were collected from 2 days prior to HA-BSI to ICU discharge or day-28 follow-up. Carbapenem resistance for *Enterobacterales* was defined as resistance to at least one carbapenem [17]. Difficult-to-treat resistance (DTR) was defined as resistance to all first line antimicrobials [18], and pan-drug-resistance (PDR) as resistance to all tested antimicrobials. To avoid over-reporting DTR and PDR for pathogens with incompletely reported antibiograms, the assessment required availability of antimicrobial susceptibility testing for at least one fluoroquinolone, one cephalosporin, one carbapenem, plus polymyxins for PDR. DTR and PDR were assessed for *Enterobacterales*, *Pseudomonas spp.,* and *Acinetobacter spp.* Adequate antimicrobial therapy was defined as receiving at least 1 antimicrobial with in-vitro activity for the pathogen at the considered timepoint, with adequacy of antimicrobial selection, dosing and administration manually reviewed for all infections and sources of HA-BSI. Time to adequate antimicrobial therapy was defined as the time between sampling of the first positive blood culture and receipt of at least one adequate antibiotic for each pathogen. Source control was reported according to the source and intervention, with adequacy assessed by the investigator.

Statistical analysis

As detailed in the ESM, and to ensure consistency, database lock was made on the 12/08/2021 after answering of all queries by the investigators, crosschecking with electronic controls, and careful reading of all the case-report forms by the operational committee.

Linearity to the logit for continuous variables was checked with generalized additive models. Non-linear variables were discretised into categorical variables based on quartiles. Continuous variables were expressed as medians (interquartile range [IQR]) and categorical variables as absolute frequencies and percentage. Differences were tested by the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables.

To identify factors associated with day-28 death, we built a three-tiered hierarchical logistic mixed model and a subdistribution hazard frailty model that considered ICU discharge as a competing risk, as suggested by Fine and Gray [19]. Both are presented in the ESM as exploratory analyses, alongside sensitivity analysis excluding COVID-19 patients and investigating the role of carbapenem resistance in place of DTR. All analyses were two-sided with p-values less than 0.05 deemed statistically significant. Statistical analysis was done using SAS 9.4 statistical software (SAS Institute Inc., Cary, NC, USA) and R project version 4.04.

Results

Study Population

We enrolled 2600 patients from 333 ICUs in 52 countries or territories (ESM eFigures 1 – 2, Table 1 and eTables 2-3). Most ICUs were in public (83.8%), teaching (82.6%) hospitals, with a mixed medical-surgical (79.5%) and general case mix (91.7%). Median [IQR] ICU size was 14 [10; 21] ventilator-equivalent beds with wide variability in infrastructure and factors related to antimicrobial stewardship.

ICUs recruited a median [IQR] of 6 [3,10] patients. Most patients were male (63.7%), median [IQR] age was 64 [52;73] years, and 74.8% had at least one comorbidity (Table 1 and eTable 2). Most common ICU admission diagnoses were non-COVID-19-related respiratory failure (21.2%), sepsis or septic shock (20.4%), and COVID-19 (12.9%).

Median [IQR] time from hospital admission to HA-BSI was 13 [8;25] days. Most HA-BSI (78.5%) were ICU-acquired (median [IQR] time from ICU admission to diagnosis, 10 [5; 18] days). The median [IQR] SOFA score was 8 [5; 11] at HA-BSI diagnosis, with 4% of the patients not meeting the criteria for sepsis, while 64.2% and 31.7% met the criteria for sepsis and septic shock, respectively (Table 2).

Sources of infection were predominantly respiratory (pneumonia) (26.7%) and intravascular catheters (26.4%), followed by the abdomen (15.1%). While primary HA-BSI were common (16.3%), one third of the patients (32.8%) had more than one possible source of HA-BSI.

Pathogens

Most (88.8%) blood cultures were mono-microbial, with 10.0% containing two, and 1.2% more than two pathogens, resulting in a total of 2927 bacterial and fungal isolates. Pathogens were most commonly Gram-negative (1726/2927; 59.0%), with a predominance of *Klebsiella spp.* (482/1726; 27.9%), *Acinetobacter spp.* (350/1726; 20.3%), *Escherichia coli* (272/1726; 15.8%) and *Pseudomonas spp.* (247/1726; 14.3%) (Table 4 and ESM eFigure 3). Carbapenem resistance was encountered in 37.8% (182/482) *Klebsiella spp.*, 84.6% (296/350) *Acinetobacter spp.*, 7.4% (20/272) *Escherichia coli* and 33.2% (82/247) *Pseudomonas spp.* When analysing Enterobacterales, *Pseudomonas spp.* and *Acinetobacter spp.*, DTR was present in 23.5% (351/1492) and PDR in 1.5% (23/1492). Gram-positive pathogens (910/2972; 31.1%) were mainly *Enterococcus spp.* (314/910, 34.5%) and coagulase-negative *staphylococci* (273/910, 30%). Of the 27.6% (251/910) *Staphylococcus aureus*, 37.1% (93/251) were methicillin-resistant *Staphylococcus aureus* (MRSA). There were 2.1% (61/2927) strict anaerobe bacteria, and 7.9% (230/2927) fungi of which 39.6% (91/230) were C*andida albicans*, 57.8% (133/230) non-albicans *Candida spp.*, and 6 (2.6%) other fungi.

Antimicrobial therapy and source control

Adequate antimicrobial therapy was received by 51.5% within 24 hours of blood culture sampling. As shown in figure 1, time to adequate antimicrobial therapy increased with antimicrobial resistance ($p<0.0001$). The 3 antimicrobials most frequently administered in the 24 hours following HA-BSI diagnosis included meropenem 463/2600 (17.8%), piperacillin/tazobactam 380/2600 (14.6%), and vancomycin 266/2600 (10.2%). They were deemed adequate in 275/463 (59.4%), 244/380 (64.2%), and 132/266 (49.6%) prescriptions, respectively. Source control was deemed to be required for 52.5% of the patients and was effectively achieved in 81.8% of these, after a median of 24.5 [IQR 1;72] hours.

Mortality

By day-28, 966 (37.1%) patients had died, 91.0% in the ICU and 9.0% after ICU discharge. Death was preceded by a decision to withhold or withdraw life-sustaining treatment for 268 (27.7%). At that time point, 38.7% of the survivors were still in the ICU, 35.7% had been discharged from the ICU, and 25.6% had been discharged from the hospital, which represents 16.1% of the total cohort.

Multiple factors were associated with day-28 mortality in the univariable analysis (Tables 1 to 3). At center level these included medical ICUs, lower availability of clinical pharmacists and of TDM for aminoglycosides or vancomycin. Mortality was higher in patients with co-morbidities, medical and COVID-19 admissions, and those with higher severity of illness, including requirements for organ supportive therapy. Higher mortality was found in early ICU-acquired HA-BSI, respiratory sources, DTR Gram-negative bacteria or fungus, and patients who did not receive adequate antimicrobials or for whom source control was required but not achieved. There was no statistically significant association between time to adequate antimicrobial therapy and day-28 mortality.

Factors associated with death in the multivariable hierarchical logistic model and with an increased subdistribution hazard ratio (sHR) of death at day-28 in a competitive risk model are shown in eTable 5. In summary, factors that were statistically significant in both models included infrequent clinical

pharmacist consultation, older age, severity of illness at HA-BSI, DTR Gram negative bacteria, and not achieving source control for patients who required an intervention. Conversely, achieving source control was protective in both analyses.

Discussion

EUROBACT-2 provides an update on the epidemiology and prognostic factors of HA-BSI in the ICU by including 2600 patients from 333 ICUs in 5 continents. We report substantial day-28 mortality, especially in HA-BSI caused by DTR pathogens, patients with septic shock, and those who never received adequate antibiotics or source control. There was a broad range of sources of infection and pathogens. Gram-negative bacteria were frequently carbapenem resistant or DTR. Antibiotic resistance was associated with longer delays to adequate antibiotics. Center data showed important variability of service availability including for the variables related to antimicrobial stewardship.

To our knowledge, the Eurobact 2 study represents the largest international study of HA-BSI s in ICU patients. Few large international studies have investigated this population, which limits possibilities for direct comparisons with our data. We conducted the EUROBACT-1 study in 2010, with a similar methodology but a smaller group of ICUs [2]. The EPIC III point prevalence study investigated the prevalence and outcomes of ICU patients with infections in 2017 and was not limited to hospital-acquired or bloodstream infections [3]. As shown in table 4, the two Eurobact studies showed a predominance of Gram-negative bacteria. In comparison, bloodstream pathogens from the EPIC III cohort showed a higher proportion of Gram-positive bacteria, with more *Staphylococcus spp.* but less *Enterococcus spp*. The European Centre for Disease Prevention and Control (ECDC) epidemiological report of hospital-acquired infections in the ICU, computed from 2017 data, showed a predominance of Gram-positive pathogens in HA-BSI. There were 23.6% coagulase-negative *staphylococci* and 14.9% *Enterococcus spp*., followed by 12.4% *Klebsiella spp*. [20].While some of these differences may be explained by the inclusion of community-acquired infections in EPIC III, the lower proportion coagulase-negative *staphylococci* in our study is probably secondary to the careful

review of each case and discussion with the investigators, leading to the exclusion of all potential blood culture contaminants that did not meet the inclusion criteria. Between EUROBACT-1 and 2, the proportion of MRSA has decreased by 10%, and the proportion of vancomycin-resistant Enterococcus (VRE) has remained stable. Interestingly, there has been an increase in the proportion of non-albicans *candida spp.,* which have now become dominant. Carbapenem resistance has substantially increased, especially for *Enterobacter spp.* and *Acinetobacter spp.*, leading to a substantial proportion of DTR in Gram-negative pathogens, and up to 1.6% PDR for *Pseudomonas spp.* and 2.3% for *Acinetobacter spp.* In keeping with previous reports, and as shown in eTables 5 and 7, carbapenem resistance and DTR in Gram-negative bacteremia were associated with mortality, highlighting the importance of strategies aimed at preventing and treating infections caused by multidrug resistant pathogens [2, 18, 21, 22]. A detailed description of the of the pathogens causing HA-BSI in the COVID-19 population is reported separately [12].

Ten years after the first Eurobact study, we observed comparable delays to adequate antimicrobial therapy as around half of the patients received such within 24h of blood culture sampling. Antimicrobial resistance was associated with delays. In the setting of widespread resistance to broad-spectrum antibiotics, molecular rapid diagnostic testing may be a key for earlier adequate antimicrobial treatment [23, 24]. That delays to adequate antimicrobial therapy were not associated with day-28 mortality may be subsequent to multiple confounders and should be interpreted with caution. Indeed, the relationship between time to antimicrobial therapy and mortality in observational research is complicated [25]. On one hand, the clinical impression of severity may be a driver for earlier administration of broader spectrum antimicrobials to patients with an increased risk of death. Moreover, a non-negligible proportion of patients with sepsis may inexorably die, regardless of the antibiotic treatment. Others may have died before antibiogram results could be acted upon, eliminating an opportunity for antimicrobial adequacy. On the other hand, patients identified at lower risk may have been treated later, when positive microbiology was reported [26]. Another source of immortal-time bias may be present as some patients with HA-BSI may have never

been diagnosed or included in the study. Some may have died before they could be transferred to the ICU, underestimating mortality, while others may have rapidly improved, before ICU admission, overestimating mortality of HA-BSI. These findings do not challenge the recommendation for early adequate antimicrobial therapy for patients with sepsis or septic shock [27]. Indeed, while we need to avoid antibiotic overuse and its associated harms [28], early adequate antimicrobial therapy is one of the most important interventions for HA-BSI [27].

How can these observations improve clinical practice? The exploratory analysis suggests a protective effect of source control and a possible detrimental effect of infrequent clinical pharmacist consultation. These highlight the importance of a multidisciplinary approach for managing critically ill patients with HA-BSI, and by extension, severe infections. Hospitals require integrated pathways, protocols, and educational programs targeting recognition, diagnosis, and treatment of sepsis, including prediction of antimicrobial resistance, antimicrobial prescription, and source control [27, 29, 30]. The optimisation of antimicrobial therapy in critically ill patients involves a multifaceted approach. Pharmacodynamic/pharmacokinetic optimisation and adequate exposure at the source of infection requires optimal dosing and delivery, considering potential interactions, modified volume of distribution, and decreased or augmented renal clearance [31]. Integrated antimicrobial stewardship programs may facilitate clinically relevant advice and recommendations on antibiotic choice, dosing, mode of delivery, indications for therapeutic drug monitoring, and a discussion on source control [6, 27, 32].

There are important limitations to this study. Firstly, ICUs were predominantly from the Europe and Central Asia and the East Asia and Pacific regions, and from high-income and upper-middle-income countries, thus limiting the generalizability of our results. Secondly, we started data collection before and continued during the first year of the COVID-19 pandemic. This likely influenced the patient population, microorganism distribution, antimicrobial resistance and mortality [33, 34]. Some ICUs were unable to start or complete the study, leading to multiple exclusions. However, we

report similar patient severity, pathogen distribution, and mortality to the Eurobact 1 study, validating the current report. Thirdly, pathogen identification and antimicrobial susceptibility testing relied on each laboratory, with possible differences in interpretation leading to inconsistencies. The patients at risk of late onset BSI had to stay in the ICU for more than 7 days to be exposed to this risk, leading to potential selection bias. The method used for the multivariable analysis led to poor calibration, which is now presented in the ESM. Moreover, data collection was performed by individual investigators in 330 ICUs, without on-site monitoring. We improved the risk of inconsistencies with online checks through the electronic case report file, and by closely monitoring data quality and coherence for each case-report.

Interpretation

HA-BSI in ICU patients was mainly caused by Gram-negative bacteria, with widespread carbapenem resistance and DTR. Antibiotic resistance was associated with longer delays to adequate antimicrobial therapy. HA-BSI was associated with 37.1% mortality, and by day-28 only 16.1% of the patients had been discharged alive from the hospital. Multifaceted programs to decrease multidrug resistance as well as prevent, recognize, and manage HA-BSI, with a focus on antimicrobial adequacy and source control are suggested to improve patient management and outcomes.

Article Information

Corresponding Author: Alexis Tabah: a.tabah@uq.edu.au

Intensive Care Unit, Redcliffe Hospital, Anzac Avenue, Redcliffe, 4020 Queensland, Australia.

Author contributions

Alexis Tabah, Niccolò Buetti, Jean-François Timsit, Quentin Staiquly, and Stéphane Ruckly had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

All the authors approved the manuscript in its final format.

Concept and design: Alexis Tabah, Jean-François Timsit, Jan De Waele, Jeffrey Lipman, and Jose Artur Paiva.

Coordination: Alexis Tabah, Caroline Dallongeville, Quentin Staiquly, Stéphane Ruckly, Jean-François Timsit, Guy Francois, Murat Akova, Abdullah Tarik Aslan, Marc Leone, Andrew Conway Morris, Matteo Bassetti, Kostoula Arvaniti, Ricard Ferrer, Haibo Qiu, Jose Artur Paiva, Liesbet De Bus, Guy Francois, Farid Zand, Mohan Gurjar, Adel Alsisi, Khalid Abidi, Hendrik Bracht, Yoshiro Hayashi, Adam Mikstacki, Alexey Gritsan, Kyeongman Jeon, Liana Valeanu, Helmi Sulaiman, Tony Yeh, Muhammed Elhadi, Mounir Bouaziz, Khalid Mahmood Khan Nafees, Gabriela Vidal, Qing Yuan Goh, Dmitriy Viderman, Silvio A. Namendys-Silva, Josef Prazak, Phunsup Wongsurakiat, Wendy Sligl, Pierre Singer, Ali Aithssain, Fredrik Sjovall, Pedja Kovacevic, Bashir Kamal Eldin Hamid el Sanousi, Mario Arias, Aaron Mark Hernandez, Ignacio Martin-Loeches, Ina Filipovic-Grcic, Fayez Abillama, Raihan Rabbani, Mervyn Mer, Lowell Ling, Oyebola Olubodun Adekola.

Communication, centre registration and coordination: Caroline Dallongeville

Data acquisition: The Eurobact 2 study group investigators as listed in the ESM.

Quality control, data curation, analysis, and interpretation: Alexis Tabah, Niccolò Buetti, François Barbier, Caroline Dallongeville, Quentin Staiquly, Stéphane Ruckly, and Jean-François Timsit.

Statistical analysis and methodology: Quentin Staiquly, Stéphane Ruckly, and Jean-François Timsit.

Drafting of the manuscript: Alexis Tabah.

Initial revision of the manuscript: Niccolò Buetti, François Barbier, Jean-François Timsit and Jeffrey Lipman.

Revision of the manuscript for important intellectual content: All authors.

Administrative, technical, or material support: Caroline Dallongeville, Quentin Staiquly, Stéphane Ruckly, and Guy Francois.

Group Information: The Eurobact 2 national coordinators, scientific committee and investigators are listed in the electronic supplement.

Additional Contributions: We thank Guy Francois, Division of Scientific Affairs and Research of the ESICM for his unvaluable assistance in recruiting participating ICUs. We thank the health care workers at each study site, laboratory, and beyond that contributed to the Eurobact-2 study and acknowledge their work during the initial waves of the COVID-19 pandemic. We thank the patients who participated in the Eurobact-2 study. We thank Professor Andrea Marshall, PhD, and Doctor Mahesh Ramanan, MBBS, FCICM for proofreading and editing the manuscript.

Availability of data and material. The datasets used and/or analysed during the current study are available from the OUTCOMEREA organisation on reasonable request.

Competing Interests

Conflict of Interest Disclosures: Associate professor Alexis Tabah has nothing to disclose, Doctor Niccolò Buetti has nothing to disclose, Quentin Staiquly has nothing to disclose, Stéphane Ruckly has nothing to disclose, Professor Murat Akova reports honoraria paid to his university for educational activities by Pfizer, Sanofi, MSD and Astra Zeneca, Doctor Abdullah Tarik Aslan has nothing to disclose, Professor Marc Leone reported consulting and lecture fees from Amomed Pharma, Aspen, LFB and Gilead, Doctor Andrew Conway Morris has received payment for speaking on behalf of Boston Scientific and sits on the Scientific Advisory Board of Cambridge Infection Diagnostics, a start-up seeking to develop novel diagnostics for infectious diseases, Professor Matteo Bassetti received advisory board, speaker activities from Angelini, Bayer, Biomerieux, Cidara, Gilead, Menarini, MSD, Pfizer, Roche, Shionogi, study grants from: Angelini, Shionogi, Cidara, Gilead, Pfizer, and MSD, Doctor Kostoula Arvaniti has nothing to disclose, Professor Jeffrey Lipman has received lecture fees and honoraria from MSD, Professor Ricard Ferrer reports Payment for lectures, speakers bureaus or advisory boards from Grifols, MSD, Pfizer, Gilead, Shionogi, Thermofisher, Hill Rom, AOP Health, BD, Doctor Haibo Qiu has nothing to disclose, Professor José Artur Paiva reports consulting, advisory boards or lectures fees and honoraria for MSD, Pfizer, Astra-Zeneca, Gilead, Jansen, Cepheid, AOP Orphan Pharmaceuticals, Professor Pedro Póvoa reported advisory boards participation for Gilead, Technophage and Sanofi, lectures fees from MSD, Gilead and Pfizer, and research grant from Abionic, Doctor Liesbet De Bus has nothing to disclose, Professor Jan de Waele has consulted for Pfizer, MSD (honoraria paid to institution), Professor Farid Zand has nothing to disclose, Professor

Mohan Gurjar has nothing to disclose, Doctor Adel Alsisi has nothing to disclose, Professor Khalid Abidi has nothing to disclose, Professor Hendrik Bracht has nothing to disclose, Doctor Yoshiro Hayashi has nothing to disclose, Professor Kyeongman Jeon has nothing to disclose, Doctor Muhammed Elhadi has nothing to disclose, Doctor François Barbier reported consulting and lecture fees, conference invitation from MSD and lecture fees from BioMérieux, Professor Jean-François Timsit reported advisory boards participation for Merck, Gilead, Beckton-Dickinson, Pfizer, Shinogi, Medimune, Paratek, research grants from Merck, Pfizer, Thermofischer.

Other acknowledgements: Professor Jan de Waele is a senior clinical investigator funded by the Research Foundation Flanders (FWO, Ref. 1881020N). Doctor Andrew Conway Morris is supported by a Medical Research Council Clinician Scientist Fellowship (MR/V006118/1). Doctor Niccolò Buetti received a fellowship grant (Grant number: P4P4PM_194449) from the Swiss National Science Foundation

The Eurobact 2 study was endorsed by the European Society of Intensive Care Medicine (ESICM), the infection section of the ESCIM and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) study Group for Infections in Critically Ill Patients (ESGCIP), with scientific input of the OUTCOMEREA network.

Funding

Research grants were obtained from the European Society of Intensive Care Medicine (ESICM), the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) study Group for Infections in Critically Ill Patients (ESGCIP), the Norva Dahlia foundation and the Redcliffe Hospital Private Practice Trust Fund.

References

1. Cassini A, Plachouras D, Eckmanns T, Abu Sin M, Blank H-P, Ducomble T, et al., (2016) Burden of six healthcare-associated infections on European population health: estimating incidence-based disability-adjusted life years through a population prevalence-based modelling study. PLoS Med 13(10): e1002150
2. Tabah A, Koulenti D, Laupland K, Misset B, Valles J, Bruzzi de Carvalho F, et al., (2012) Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study. Intensive Care Med 38(12): 1930-1945
3. Vincent JL, Sakr Y, Singer M, Martin-Loeches I, Machado FR, Marshall JC, et al., (2020) Prevalence and Outcomes of Infection Among Patients in Intensive Care Units in 2017. JAMA 323(15): 1478-1487
4. Adrie C, Garrouste-Orgeas M, Ibn Essaied W, Schwebel C, Darmon M, Mourvillier B, et al., (2017) Attributable mortality of ICU-acquired bloodstream infections: Impact of the source, causative micro-organism, resistance profile and antimicrobial therapy. J Infect 74(2): 131-141

5. Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al., (2011) Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. Crit Care 15(2): R100
6. De Waele JJ, Akova M, Antonelli M, Canton R, Carlet J, De Backer D, et al., (2018) Antimicrobial resistance and antibiotic stewardship programs in the ICU: insistence and persistence in the fight against resistance. A position statement from ESICM/ESCMID/WAAAR round table on multi-drug resistance. Intensive Care Med 44(2): 189-196
7. Bezabih YM, Bezabih A, Dion M, Batard E, Teka S, Obole A, et al., (2022) Comparison of the global prevalence and trend of human intestinal carriage of ESBL-producing Escherichia coli between healthcare and community settings: a systematic review and meta-analysis. JAC Antimicrob Resist 76(1): 22-29
8. World Health Organization, (2021) Global antimicrobial resistance and use surveillance system (GLASS) report: 2021
9. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al., (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet 399(10325): 629-655
10. Cosgrove SE, (2006) The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. Clin Infect Dis 42(Suppl 2): S82-89
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S, (2008) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 61(4): 344-349
12. Buetti N, Tabah A, Loiodice A, Ruckly S, Aslan AT, Montrucchio G, et al., (2022) Different epidemiology of bloodstream infections in COVID-19 compared to non-COVID-19 critically ill patients: a descriptive analysis of the Eurobact II study. Critical Care 26(1): 319
13. UN Statistics Division. Standard Country and Area Codes for Statistical Use. Retrieved from https://unstats.un.org/unsd/methodology/m49/
14. Le Gall JR, Lemeshow S, Saulnier F, (1993) A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 270(24): 2957-2963
15. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, et al., (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 22(7): 707-710
16. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al., (2016) The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 315(8): 801-810
17. Center for disease control and prevention C. (2019). Carbapenem-resistant Enterobacterales (CRE): CRE Technical Information. Retrieved from https://www.cdc.gov/hai/organisms/cre/technical-info.html#Definition
18. Kadri SS, Adjemian J, Lai YL, Spaulding AB, Ricotta E, Prevots DR, et al., (2018) Difficult-to-Treat Resistance in Gram-negative Bacteremia at 173 US Hospitals: Retrospective Cohort Analysis of Prevalence, Predictors, and Outcome of Resistance to All First-line Agents. Clin Infect Dis 67(12): 1803-1814
19. Fine JP, Gray RJ, (1999) A proportional hazards model for the subdistribution of a competing risk. Journal of the American statistical association 94(446): 496-509
20. European Centre for Disease Prevention and Control. (2019). Healthcare-associated infections acquired in intensive care units. In: ECDC. Annual epidemiological report for 2017. Retrieved from https://www.ecdc.europa.eu/en/publications-data/healthcare-associated-infections-intensive-care-units-annual-epidemiological-1
21. Bonnet V, Dupont H, Glorion S, Aupee M, Kipnis E, Gerard JL, et al., (2019) Influence of bacterial resistance on mortality in intensive care units: a registry study from 2000 to 2013 (IICU Study). J Hosp Infect 102(3): 317-324

22. Huh K, Chung DR, Ha YE, Ko JH, Kim SH, Kim MJ, et al., (2020) Impact of Difficult-to-Treat Resistance in Gram-negative Bacteremia on Mortality: Retrospective Analysis of Nationwide Surveillance Data. Clin Infect Dis 71(9): e487-e496
23. Giacobbe DR, Giani T, Bassetti M, Marchese A, Viscoli C, Rossolini GM, (2020) Rapid microbiological tests for bloodstream infections due to multidrug resistant Gram-negative bacteria: therapeutic implications. Clin Microbiol Infect 26(6): 713-722
24. Banerjee R, Teng CB, Cunningham SA, Ihde SM, Steckelberg JM, Moriarty JP, et al., (2015) Randomized Trial of Rapid Multiplex Polymerase Chain Reaction-Based Blood Culture Identification and Susceptibility Testing. Clin Infect Dis 61(7): 1071-1080
25. Weinberger J, Rhee C, Klompas M, (2020) A Critical Analysis of the Literature on Time-to-Antibiotics in Suspected Sepsis. The Journal of infectious diseases 222(Suppl 2): S110-S118
26. Hranjec T, Rosenberger LH, Swenson B, Metzger R, Flohr TR, Politano AD, et al., (2012) Aggressive versus conservative initiation of antimicrobial treatment in critically ill surgical patients with suspected intensive-care-unit-acquired infection: a quasi-experimental, before and after observational cohort study. The Lancet Infectious Diseases 12(10): 774-780
27. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al., (2021) Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 47(11): 1181-1247
28. Curran J, Lo J, Leung V, Brown K, Schwartz KL, Daneman N, et al., (2022) Estimating daily antibiotic harms: an umbrella review with individual study meta-analysis. Clin Microbiol Infect 28(4): 479-490
29. Goodman KE, Lessler J, Cosgrove SE, Harris AD, Lautenbach E, Han JH, et al., (2016) A Clinical Decision Tree to Predict Whether a Bacteremic Patient Is Infected With an Extended-Spectrum beta-Lactamase-Producing Organism. Clin Infect Dis 63(7): 896-903
30. Dellit TH, Owens RC, McGowan Jr JE, Gerding DN, Weinstein RA, Burke JP, et al., (2007) Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clinical Infectious Diseases 44(2): 159-177
31. Heffernan AJ, Mohd Sazlly Lim S, Lipman J, Roberts JA, (2021) A personalised approach to antibiotic pharmacokinetics and pharmacodynamics in critically ill patients. Anaesth Crit Care Pain Med 40(6): 100970
32. Tabah A, Lipman J, Barbier F, Buetti N, Timsit J-F, (2022) Use of Antimicrobials for Bloodstream Infections in the Intensive Care Unit, a Clinically Oriented Review. Antibiotics 11(3): 362
33. Grasselli G, Scaravilli V, Mangioni D, Scudeller L, Alagna L, Bartoletti M, et al., (2021) Hospital-Acquired Infections in Critically Ill Patients With COVID-19. Chest 160(2): 454-465
34. Buetti N, Ruckly S, de Montmollin E, Reignier J, Terzi N, Cohen Y, et al., (2021) COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network. Intensive Care Med 47(2): 180-187

Eurobact 2, tables and figures

Contents

Table 1 Characteristics of participating ICUs and association with day-28 patient mortality.

Characteristics *	All ICUs (n=333)*	All patients (N= 2600)	Dead on D28 (n= 966)	Alive on D28 (n= 1634)	OR [95% CI]	P value
Geographic region						0.824
Europe and Central Asia	184 (55.3)	1775 (68.3)	689 (71.3)	1086 (66.5)	1	
East Asia and Pacific	69 (20.7)	412 (15.8)	127 (13.1)	285 (17.4)	0.83 [0.54; 1.27]	
Middle East and North Africa	48 (14.4)	268 (10.3)	91 (9.4)	177 (10.8)	0.96 [0.61; 1.54]	
South Asia	14 (4.2)	54 (2.1)	24 (2.5)	30 (1.8)	1.29 [0.52; 3.2]	
Latin America and the Caribbean	11 (3.3)	52 (2)	17 (1.8)	35 (2.1)	0.78 [0.33; 1.85]	
Sub-Saharan Africa	5 (1.5)	20 (0.8)	6 (0.6)	8 (0.5)	1.7 [0.55; 5.21]	
North America	2 (0.6)	19 (0.7)	8 (0.8)	11 (0.7)	1.34 [0.34; 5.31]	
National Income						0.145
High-income	202 (60.7)	1479 (56.9)	485 (50.2)	994 (60.8)	1	
Upper-middle-income	80 (24)	870 (33.5)	393 (40.7)	477 (29.2)	1.42 [0.99; 2.04]	
Low & Lower-middle-income **	51 (14.1)	251 (9.2)	88 (9.1)	163 (10)	1.11 [0.72; 1.72]	
Academic status of the hospital						
Teaching Hospital	270 (82.6)	2207 (85.4)	823 (85.4)	1384 (85.4)	1	0.122
Non-teaching Hospital	57 (17.4)	378 (14.6)	141 (14.6)	237 (14.6)	1.28 [0.94; 1.76]	
Type of ICU						
Mixed (medical-surgical)	260 (79.5)	2040 (78.9)	732 (75.9)	1308 (80.7)	1	0.048
Medical	41 (12.5)	383 (14.8)	180 (18.7)	203 (12.5)	1.49[1.07; 2.09]	
Surgical	26 (8)	162 (6.3)	52 (5.4)	110 (6.8)	0.9[0.57; 1.43]	
Number of ventilator equivalent beds in the ICU >=15	176 (53.82)	1464 (56.63)	499 (51.8)	965 (59.5)	0.81[0.65; 1.03]	0.081
Nurse to ventilator-bed ratio	2 [1.3; 2.9]	2.2 [1.6; 2.8]	2.2 [1.6; 2.8]	2.2 [1.5; 2.9]	0.99[0.97; 1]	0.106
Senior doctor to ventilator-bed ratio	6.7 [4.3; 10]	6 [4; 9.5]	6 [4; 9]	6.3 [4.3; 9.5]	0.99[0.97; 1.01]	0.213
Senior medical cover is available 24/7	304 (93.3)	2355 (91.5)	869 (90.3)	1486 (92.1)	0.81[0.53; 1.23]	0.319
General surgery is available 24/7	321(98.2)	2556 (98.9)	951 (98.7)	1605 (99)	0.8[0.31; 2.05]	0.637
Infectious diseases specialist or clinical microbiologist are consulted						
24/7	170 (54.8)	1479 (60)	566 (60.9)	913 (59.4)	1	0.57
During business hours	114 (36.8)	855 (34.7)	313 (33.7)	542 (35.3)	1.06 [0.82; 1.38]	
Never or sporadically	26 (8.4)	131 (5.3)	50 (5.4)	81 (5.3)	1.29 [0.8; 2.09]	
Clinical pharmacists are consulted						
24/7	82 (25.5)	636 (25.1)	188 (19.9)	448 (28.2)	1	0.007
During business hours	129 (40.1)	811 (32)	284 (30.1)	527 (33.2)	1.32 [0.99; 1.78]	
Never or sporadically	111 (34.5)	1084 (42.8)	471 (49.9)	613 (38.6)	1.64[1.21; 2.24]	
TDM of aminoglycosides is available						
Everyday	171 (52.5)	1249 (48.5)	383 (39.8)	866 (53.7)	1	0.002
At least once a week	30 (9.2)	213 (8.3)	81 (8.4)	132 (8.2)	1.32[0.88; 1.98]	
Not available	125 (38.3)	1113 (43.2)	498 (51.8)	615 (38.1)	1.6[1.23; 2.09]	
TDM of vancomycin is available						
Everyday	200 (61.3)	1419 (55.1)	462 (48)	957 (59.3)	1	0.012
At least once a week	43 (13.2)	319 (12.4)	120 (12.5)	199 (12.3)	1.07[0.74; 1.53]	
Not available	83 (25.5)	837 (32.5)	380 (39.5)	457 (28.3)	1.55[1.15; 2.07]	
TDM of β-lactams is available						
Everyday	35 (10.7)	256 (9.9)	87 (9)	169 (10.5)	1	0.255
At least once a week	51 (15.6)	408 (15.8)	117 (12.2)	291 (18)	0.81[0.52; 1.27]	
Not available	240 (73.6)	1911 (74.2)	758 (78.8)	1153 (71.5)	1.1[0.75; 1.62]	

Legend: Full report of center characteristics is available in ESM eTable 3. results reported as n (%) for categorical variables and median [IQR] for continuous variables; * All Center data was missing for 6 ICUs and 7 to 12 did not provide staffing or stewardship data. ** There were 4 ICUs and 11 patients in the Low-income category. 24/7: 24 hours a day, 7 days a week. ICU: intensive care unit. TDM: therapeutic drug monitoring. Ventilator equivalent beds refers to the maximum number of ventilated patients the ICU can accommodate at one time.

Table 2 Baseline (admission to the ICU) patient characteristics and day-28 mortality

Variable	All patients (n= 2600)	Dead on D28 (n= 966)	Alive on D28 (n= 1634)	OR [95% CI]	P value
Age (years)					<.001
<52	649 (25.0)	175 (18.1)	474 (29)	Ref.	
[52-64]	691 (26.6)	256 (26.5)	435 (26.6)	1.59 [1.25; 2.04]	
[65-73]	618 (23.8)	223 (23.1)	395 (24.2)	1.53 [1.19; 1.97]	
>=74	642 (24.7)	312 (32.3)	330 (20.2)	2.46 [1.91; 3.16]	
SAPS II score on ICU admission (age excluded) [+]					<.001
<26	585 (22.5)	186 (19.3)	399 (24.4)	Ref.	
[26-35]	708 (27.2)	227 (23.5)	481 (29.4)	1.09 [0.84; 1.39]	
[36-47]	618 (23.8)	223 (23.1)	395 (24.2)	1.37 [1.06; 1.77]	
≥48	689 (26.5)	330 (34.2	359 (22)	2.28 [1.78; 2.93]	
Male gender	1657 (63.7)	596 (61.7)	1061 (64.9)	0.89 [0.75; 1.06]	0.192
Body Mass Index (kg per m^2)					
<18.5	98 (3.8)	32 (3.3)	66 (4)	1	0.771
[18.5; 30[	1845 (71.1)	687 (71.3)	1158 (71)	1.13 [0.71; 1.78]	
≥30	652 (25.1)	245 (25.4)	407 (25)	1.18 [0.73; 1.9]	
Charlson comorbidity index					
0	792 (30.5)	223 (23.1)	569 (34.8)	1	<.001
1-2	935 (36)	371 (38.4)	564 (34.5)	1.59 [1.28; 1.97]	
>2	873 (33.6)	372 (38.5)	501 (30.7)	1.83 [1.47; 2.28]	
Solid Tumor, no metastasis	242 (9.3)	88 (9.1)	154 (9.4)	0.99 [0.74; 1.32]	0.931
Solid Tumor, with metastasis	159 (6.1)	76 (7.9)	83 (5.1)	1.54 [1.09; 2.17]	0.013
Haematological malignancy	159 (6.1)	71 (7.3)	88 (5.4)	1.55 [1.1; 2.2]	0.013
Type of ICU Admission					
Medical	1922 (73.9)	777 (80.4)	1145 (70.1)	1	<.001
Surgical elective	186 (7.2)	56 (5.8)	130 (8)	0.69 [0.49; 0.97]	
Surgical emergency	492 (18.9)	133 (13.8)	359 (22)	0.6 [0.47; 0.76]	
Primary ICU admission diagnosis*					
Sepsis or septic shock	530 (20.4)	189 (19.6)	341 (20.9)	1	<.001
Respiratory admission *	550 (21.2)	232 (24)	318 (19.5)	1.14 [0.88; 1.48]	
COVID-19 *	336 (12.9)	195 (20.2)	141 (8.6)	2.07 [1.5; 2.85]	
Post-operative admission	258 (9.9)	83 (8.6)	175 (10.7)	0.84 [0.6; 1.17]	
Other admission diagnoses	926 (35.6)	267 (27.6)	659 (40.3)	0.68 [0.53; 0.87]	

Legend: Continuous variables are presented as median [IQR]. Categorical variables are presented as n (%). CI: confidence interval. Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range. ICU: Intensive care unit, SAPS II: Simplified Acute Physiology Score II, [+] The SAPS II score was calculated excluding age-related points to avoid collinearity. *Respiratory admission refers to admission for respiratory failure other than COVID-19 that has been categorized separately. A full list of co-morbidities as defined in Charlson score and admission diagnosis can be found in the electronic supplement eTable 3.

Table 3 Patient characteristics at diagnosis of hospital-acquired bloodstream infection and day-28 mortality.

Characteristics	All patients (N= 2600)	Dead on D28 (n= 966)	Alive on D28 (n= 1634)	OR [95% CI]	p-Value
Time from ICU admission to HA-BSI					
Acquired prior to ICU admission	558 (21.5)	188 (19.5)	370 (22.6)	1.03 [0.82; 1.29]	0.017
Early ICU-acquired (≤7 days)	810 (31.2)	327 (33.9)	483 (29.6)	1.32 [1.08; 1.6]	
Late ICU-acquired (>7 days)	1232 (47.4)	451 (46.7)	781 (47.8)	1	
Maximum Temperature					
<38.2°C	1412 (54.5)	588 (61.2)	824 (50.6)	1	<.001
≥38.2°C	1179 (45.5)	373 (38.8)	806 (49.4)	0.72 [0.6; 0.86]	
Sepsis or septic shock					
No sepsis or Sepsis without shock	1776 (68.5)	538 (55.9)	1238 (76)	1	<.001
Septic shock - No steroids	446 (17.2)	213 (22.1)	233 (14.3)	2.38 [1.89; 2.99]	
Septic shock – Steroids administered	370 (14.3)	211 (21.9)	159 (9.8)	3.85 [2.98; 4.97]	
SOFA score	8 [5; 11]	10 [7; 13]	7 [5; 10]	1.21 [1.19; 1.24]	<.001
Ventilation status					
Low flow oxygen or no oxygen	493 (19)	104 (10.8)	389 (23.8)	1	<.001
High Flow Oxygen Nasal Canula	163 (6.3)	50 (5.2)	113 (6.9)	1.69 [1.11; 2.57]	
Non-Invasive Mechanical Ventilation or CPAP	153 (5.9)	50 (5.2)	103 (6.3)	1.84 [1.2; 2.81]	
Invasive Mechanical Ventilation	1791 (68.9)	762 (78.9)	1029 (63)	2.81 [2.18; 3.61]	
ECMO (VA or VV)	41 (1.6)	21 (2.2)	20 (1.2)	1.92 [0.99; 3.72]	0.053
Vasopressors (adrenaline or noradrenaline)	1376 (52.9)	614 (63.6)	762 (46.6)	2.44 [2.04; 2.93]	<.001
Vasopressin	113 (4.3)	61 (6.3)	52 (3.2)	2.89 [1.89; 4.4]	<.001
Gram-negative bacteria*	1623 (62.4)	608 (62.9)	1015 (62.1)	0.98 [0.82; 1.17]	0.823
DTR Gram-negative	350 (13.5)	185 (19.2)	165 (10.1)	1.71 [1.33; 2.21]	<.001
Gram-positive bacteria*	859 (33)	312 (32.3)	547 (33.5)	0.98 [0.82; 1.17]	0.821
Resistant Gram-positive (MRSA, MRSE or VRE)	323 (12.4)	112 (11.6)	211 (12.9)	0.86 [0.66; 1.11]	0.248
Fungus*	227 (8.7)	102 (10.6)	125 (7.6)	1.39 [1.04; 1.86]	0.026
Strict anaerobe bacteria*	57 (2.2)	15 (1.6)	42 (2.6)	0.76 [0.41; 1.41]	0.382
Polymicrobial blood culture	290 (11.2)	106 (11)	184 (11.3)	1 [0.77; 1.32]	0.973
Source of HA-BSI					
Intravascular catheter	686 (26.4)	239 (24.7)	447 (27.4)	1	0.027
Intra-abdominal	392 (15.1)	145 (15)	247 (15.1)	1.33 [1; 1.76]	
Other	217 (8.3)	69 (7.1)	148 (9.1)	1.01 [0.71; 1.44]	
Primary	425 (16.3)	169 (17.5)	256 (15.7)	1.26 [0.96; 1.65]	
Respiratory	694 (26.7)	288 (29.8)	406 (24.8)	1.39 [1.09; 1.77]	
Urinary	186 (7.2)	56 (5.8)	130 (8)	0.9 [0.62; 1.3]	
More than 1 possible source of infection	853 (32.8)	322 (33.3)	531 (32.5)	1.14 [0.94; 1.37]	0.191
Time to adequate antimicrobial therapy					
≤24 hours, n (%)	1339 (51.5)	463 (47.9)	876 (53.6)	1	<.001
]24;48] hours, n (%)	336 (12.9)	117 (12.1)	219 (13.4)	1.03 [0.79; 1.34]	
]48;120] hours, n (%)	396 (15.2)	134 (13.9)	262 (16)	0.96 [0.74; 1.23]	
> 120 hours, n (%)	125 (4.8)	38 (3.9)	87 (5.3)	0.72 [0.47; 1.09]	
Never, n (%)	403 (15.5)	214 (22.2)	189 (11.6)	1.98 [1.55; 2.53]	
Source control					
Not required	1235 (47.5)	488 (50.5)	747 (45.7)	1	<.001
Required, achieved	1117 (43)	321 (33.2)	796 (48.7)	0.63 [0.52; 0.76]	
Required, but NOT achieved	248 (9.5)	157 (16.3)	91 (5.6)	2.6 [1.92; 3.51]	

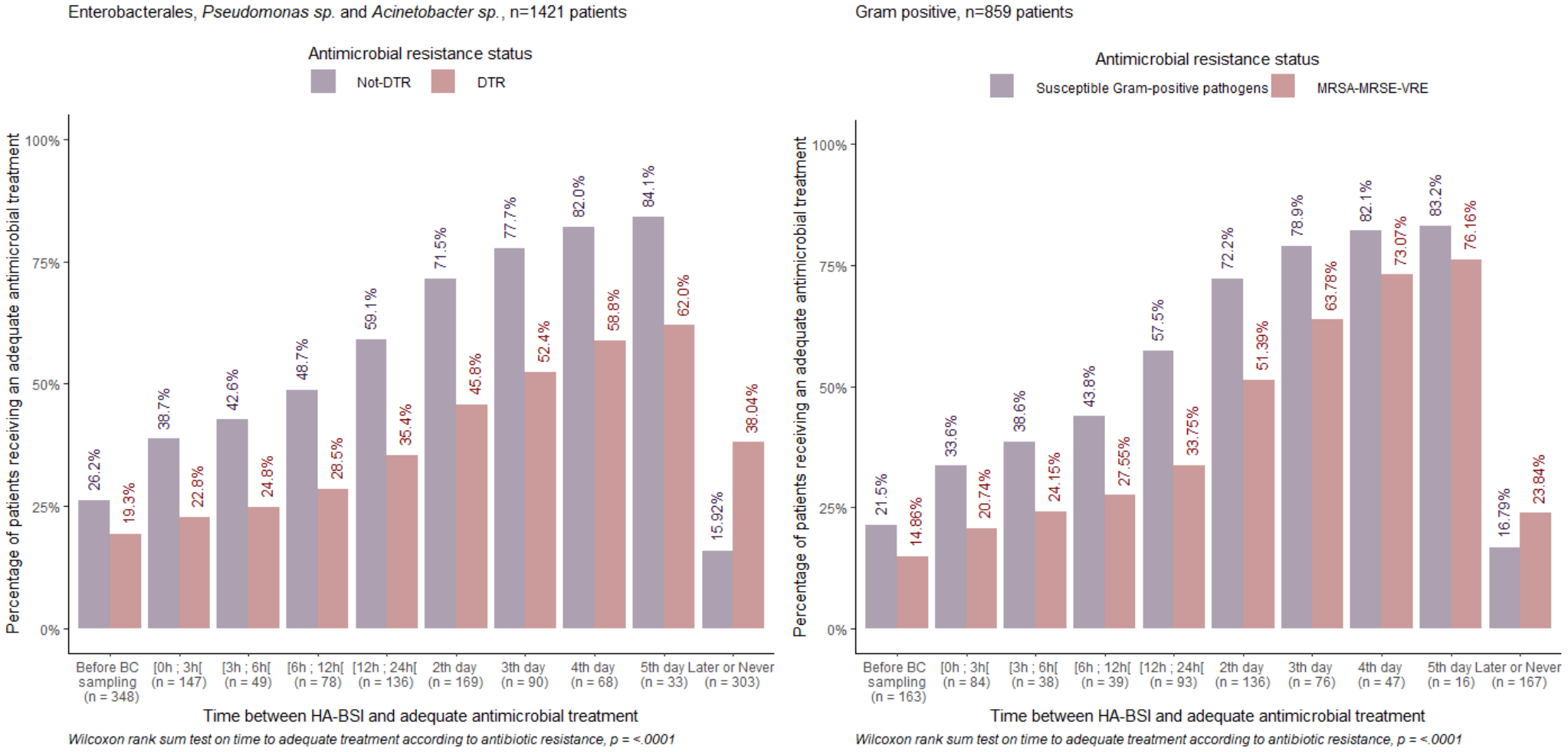
Legend: Continuous variables are presented as median [IQR] and categorical variables as n(%).Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range. HA-BSI: hospital-acquired blood stream infection, CPAP: continuous positive airway pressure ECMO: extra-corporeal membrane oxygenation, VA: venoarterial, VV: venovenous. DTR: Difficult to treat resistance MRSA: Methicillin-resistant *Staphylococcus aureus,* MRSE: Methicillin-resistant *Staphylococcus epidermidis* and includes all coagulase negative staphylococcus reported as non-susceptible to methicillin, VRE: Vancomycin-resistant Enterococcus. * Sum of percentages exceed 100 because a patient may have had several pathogens in the blood culture, referring to the 11.2% polymicrobial blood cultures

Table 4 Characteristics of the pathogens in the initial blood culture in Eurobact 2 and comparison with Eurobact 1 and EPIC III studies.

Pathogens	Eurobact-2 n= 2927 (%)	Eurobact-1 (n=1317)*	EPIC III BSI (n=1239)**
Gram-negative bacteria	1726 (59.0)	759 (57.6)	515 (44.6)
Klebsiella spp.	482 (27.9)	156 (20.1)	144 (28.0)
Carbapenem Resistant	182 (37.8)	59 (37.8)	86 (59.7)
DTR*	133 (27.6)	.	.
PDR*	11 (2.3)	3 (1.9)	.
Escherichia coli	272 (15.8)	98(12.9)	116 (22.5)
Carbapenem Resistant	20 (7.4)	1(1)	32 (27.6)
DTR*	9 (3.3)	.	.
PDR*	0 (0.0)	0(0)	.
Enterobacter spp.	141 (8.2)	88 (11.6)	.
Carbapenem Resistant	31 (22.0)	5 (5.7)	.
DTR*	8 (5.7)	.	.
PDR*	0 (0.0)	0(0)	.
Pseudomonas spp.	247 (14.3)	150 (19.7)	67 (13.0)
Carbapenem Resistant	82 (33.2)	56 (37.3)	10 (14.9)
DTR*	25 (10.1)	.	.
PDR*	4 (1.6)	0(0)	.
Acinetobacter spp.	350 (20.3)	160 (21.1)	68 (13.2)
Carbapenem Resistant	296 (84.6)	110 (68.7)	53 (77.9)
DTR*	176 (50.3)	.	.
PDR*	8 (2.3)	1 (0.6)	.
Other Gram-negative bacteria	234 (13.6)	107 (14.1)	177 (34.4)
Carbapenem Resistant	24 (12.5)	.	.
Gram-positive bacteria	910 (31.1)	440 (33.4)	494 (42.7)
Enterococcus spp.	314 (34.5)	144 (32.7)	58 (11.7)
Enterococcus faecium	156 (49.7)	70 (48.6)	.
VRE	37 (23.7)	16 (22.9)	.
Coagulase-negative *Staphylococcus*	273 (30.0)	141(32.0)	182 (36.8)
MRSE	200 (73.3)	.	73 (40.1)
Staphylococcus aureus	251 (27.6)	119 (27.0)	180 (36.4)
MRSA	93 (37.1)	57 (47.9)	54 (30.0)
Other Gram-positive bacteria	72 (7.9)	36 (8.2)	40 (8.1)
Strict anaerobe bacteria	61 (2.1)	20 (1.5)	19 (1.6)
Bacteroides	29 (47.5)	.	.
Other anaerobes	32 (52.5)	.	.
Fungi	230 (7.9)	98 (7.4)	126 (10.9)
Candida albicans	91 (39.6)	56 (57.1)	71 (56.3)
Candida non-albicans spp.	133 (57.8)	39 (39.8)	53 (42.1)
Other fungi	6 (2.6)		4 (3.2)

Legend: Percentages shown for the relevant pathogen or category. A "." denotes unavailable or not comparable data. MRSA and MRSE denotes the % of *Staphylococcus aureus* and C*oagulase negative Staphylococcus* resistant to methicillin, VRE the % of enterococcus faecium resistant to vancomycin. Carbapenem resistant is defined as at least one carbapenem has been tested and the isolate is resistant to all the carbapenems that have been tested. DTR: Difficult to treat resistance. PDR: Pan-drug resistant (resistant to all tested antibiotics). DTR status is determined on Enterobacteriaceae, *Pseudomonas* and A*cinetobacter species* and requires require antibiogram results for ≥1 carbapenem, ≥1 extended-spectrum cephalosporin, and ≥1 fluoroquinolone. Candida unknown species have been classified in non-albicans. All PDR pathogens are DTR, and all DTR are carbapenem-R, thus the count and proportion of DTR and carbapenem-R micro-organisms includes that of the more resistant categories. EUROBACT 1 reported susceptibilities on monomicrobial infections. EPIC III reported the pathogens from 1154 bacterial or fungal bloodstream infections, not restricted to hospital-acquired infections. Sum of percentages exceeds 100 because patients may have had more than 1 infection.

Figure 1 Relationship between resistance and timing of adequate antimicrobial therapy.



Legend: Cumulative percentage of patients receiving at least one adequate antimicrobial, on each time-period before and after the date of collection of the first positive blood culture, shown by antimicrobial resistance status. MRSA: Methicillin-resistant *Staphylococcus aureus,* MRSE: Methicillin-resistant *Staphylococcus epidermidis* includes all Methicillin resistant Coagulase-negative Staphylococcus*,* VRE: vancomycin-resistant *Enterococcus.* Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range.

Epidemiology and outcomes of hospital-acquired bloodstream infections in intensive care units: the EUROBACT II International Cohort Study

Electronic Supplemental Material (ESM)

Contents

Protocol and definitions

Timeline

The study start date was the 1st of August 2019. It was planned to continue for 1 year. Two pilot centers started recruitment on 1/06/2019. Delays caused by the COVID-19 pandemic led to extending the recruitment period up to the 30st of January 2021 for the date of HA-BSI. Centers could choose the study start date for their intensive care unit (ICU) between the date of obtention of all required ethical and regulatory approvals and the 31st of October 2020. The minimal study recruitment period was 3 months or 10 consecutive cases (whichever came first) and could be extended on request from the local investigator for up to the whole duration of the study. The database was closed on the 12th of August 2021.

Data quality processes

A dual verification and query process was used, including electronic verification of all collected data through a set of coherence routines, and reviewing of each case report form (CRF) by a group of experts (AT, NB, FB) assessing data quality and completeness. Complex cases were reviewed at regular meetings to resolve any disagreement. We excluded patients that did not meet the inclusion criteria and those missing core outcome data (i.e., dates of hospital-acquired bloodstream infection (HA-BSI) and hospital/ICU admission, discharge and/or death as applicable, pathogen and treatment inclusive of antimicrobials and source control as applicable). We ensured correlation between the recorded source, source control and microbiology results. Inserted intravascular catheters are often removed as a possible source of infection in patients who develop sepsis, septic shock, or HA-BSI, we reviewed each case with the investigators in light of clinical progress and microbiology data. We ensured that intravascular catheters that had been removed but ended up not being the source of HA-BSI were not recorded as catheter-related bloodstream infection. Particular attention was given to only include true infections with possible skin contaminants. Any question or incoherence was fed back to the investigator through eCRF-embedded queries and checked until satisfactory resolution. In the absence of a response, we attempted to contact the center, with assistance from the NC, for a minimum of three times. In extreme cases where no response was obtained, or the investigator became unavailable to respond, the patients and/or the center were excluded from the study.

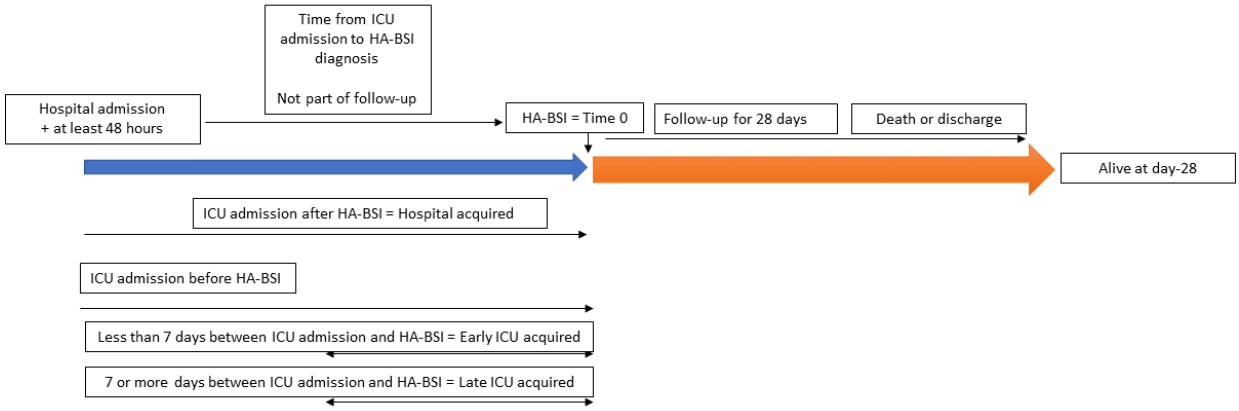
Definitions

- Intensive care unit: ICUs eligible to participate were defined as managing patients with organ failures within a health-care facility and able to provide invasive mechanical ventilation for a duration of at least 24 hours.
- Ventilator equivalent beds refers to the maximum number of ventilated patients the ICU can accommodate at one time.
- Admission source: refers to where was the patient prior to admission to the ICU.
- Primary diagnosis: The main reason for admission to the ICU. Only one primary diagnosis should be entered (see codes). If surgical admission the site of surgery should be entered as primary diagnosis.
- Type of admission: Surgical - defined as having surgery within 7 days of ICU admission. Elective surgery was defined as surgery scheduled > 24 hours in advance and emergency surgery as that scheduled within 24 hours of operation. All other admissions were considered medical.

- HA-BSIs were defined as isolation of a pathogenic organism from at least one blood culture 48 hours or more after hospital admission; the same 48-hour criterion was used to define ICU-acquired cases among HA-BSIs. For common skin contaminants (coagulase-negative staphylococci, *Corynebacterium* species, *Bacillus* species, *Propionibacterium* species, *Aerococcus* species, *Micrococcus* species), two blood cultures with the same antimicrobial susceptibility profile were mandatory or strong clinical grounds that it is not a contaminant. One example was infected material proven as a source for the HA-BSI. Where strong evidence supported HA-BSI but only one culture was positive (*e.g.,* positive catheter tip following line removal for suspected infection with prescription of additional treatment), all clinical and microbiological data were reviewed to decide whether the case should be included. Patients with BSIs acquired outside the ICU were eligible for inclusion if less than 2 days elapsed between collection of the first positive blood sample and ICU admission and/or if ICU admission was directly related to the consequences of HA-BSI. The inclusion date was the time of collection of the first positive blood culture.
- Comorbidities: Chronic diseases present prior to ICU admission. More than one can be chosen according to the following definitions:
- Metastatic cancer: Metastases proven by surgery, computed tomography or magnetic resonance scan, or any other method.
- Hematologic cancer: Lymphoma, Leukaemia.
- AIDS: HIV positive patients with clinical complications such as Pneumocystis carinii pneumonia, Kaposi's sarcoma, lymphoma, tuberculosis, or toxoplasma infection.
- Chronic renal failure: Defined as either chronic dialysis dependent renal failure or history of chronic renal insufficiency with a serum creatinine > 3.6 g/dL (300 µmol/L).
- Immunosuppression: Administration within the 6 months prior to ICU admission of corticosteroid treatment (at least 0.3 mg/kg/day prednisolone for at least one month) or other immunosuppressant drugs, severe malnutrition, congenital immune-humoral or cellular immune deficiency state.
- Chemotherapy/radiotherapy: If within 6 months prior to ICU admission.
- COPD / Chronic Pulmonary Disease Severe: Chronic restrictive, obstructive or vascular disease resulting in severe exercise limitation (*e.g.*, unable to climb stairs or perform household duties) or documented chronic hypoxia, hypercapnia, secondary polycythaemia, severe pulmonary hypertension (>40 mmHg) or home oxygen or non-invasive ventilation (NIV).
- Liver disease, severe: Biopsy-proven cirrhosis with portal hypertension; episodes of past upper gastro-intestinal bleeding attributed to portal hypertension; or prior episodes of hepatic failure, encephalopathy, or coma.
- For scoring purposes, we recorded minimal and maximal or worse biological and physiological values of the first 24 hours following ICU admission.
- For the Glasgow coma scale (GCS) we defined the following: For non-sedated patients, enter the lowest GCS during the 24 hours. For patients sedated, enter the GCS at the time of/just prior to sedation. If not available, please enter an estimated GCS score as it would be if the patient was not receiving sedation.

- Delirium: Delirium is defined as an acute or fluctuating mental state (which represents a change from the patient's normal baseline) and is characterized by inattention with altered level of consciousness, agitation or disorganized thought processes. It can be diagnosed by standardized assessment tools such as (but not limited to) the Confusion Assessment Method for ICU (CAM-ICU)
  Hyperactive delirium is characterized by agitation, restlessness, and attempts to remove tubes and lines. Hypoactive delirium is characterized by withdrawal, flat affect, apathy, lethargy, and decreased responsiveness. Mixed delirium is when patients fluctuate between the two.
- Decision to withhold or withdraw life-sustaining treatment was defined as the ethical decision to change goal of treatment from life-prolonging to palliative. It should only be entered if organ supportive therapy was stopped or not started when it would otherwise have been indicated
- Blood cultures, antimicrobial susceptibility testing, and interpretation were processed locally and following usual practice for each participating centre as detailed in eTable 3.
- Selective reporting of the antibiogram is a laboratory based antimicrobial stewardship process where the laboratory only reports a selection of the antimicrobials that were tested as susceptible for the pathogen. Selective reporting can be used to encourage the use of drugs that are appropriate for the site of infection, discourage the use of drugs for which susceptibility results may be misleading or drugs that may have negative consequences for a patient group or to avoid the overuse of broad-spectrum antibiotics. (see Pulcini et al. 2016 https://doi.org/10.1016/j.ijantimicag.2016.11.014).
- Methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant (coagulase-negative) *Staphylococcus epidermidis* (MRSE) were defined as resistance to methicillin/oxacillin.
- Vancomycin-resistant enterococci (VRE) were reported as the percentage of *Enterococcus faecium* resistant to vancomycin.
- Carbapenem resistance for Enterobacterales was defined as resistance to at least one carbapenem as recommended by the United States of America Center For Disease Control And Prevention [1].
- Adequate antimicrobial therapy was defined as receiving at least 1 antimicrobial with in-vitro activity for the pathogen at the considered timepoint, with adequacy of antimicrobial selection, dosing and administration manually reviewed for all infections and sources of HA-BSI. Time to antimicrobial therapy for antimicrobials that were ongoing at time of HA-BSI was labelled as "Before BC sampling" and patients were categorized as having received adequate antimicrobial therapy ≤ 24 hours after HA-BSI. For the patients without susceptibility data or with incomplete antibiograms, antimicrobial therapy was considered adequate if the intrinsic organism characteristics and usual susceptibilities indicated a high likelihood of drug susceptibility. Antimicrobials administered at ineffective or very low dose and/or route of administration, relative to the source of infection, were considered as not adequate.
- Times are calculated from the time of blood culture sampling, which represents the time 0 of the study as shown in the diagram below.

- Time to adequate antimicrobial therapy was defined as the time between sampling of the study blood culture and receipt of one adequate antimicrobial for each pathogen in the blood culture.



Sources of Hospital acquired blood stream-infection and source control

The presumed source of the BSI was determined by the treating clinician from the following pre-defined list of categories and subcategories, and if multiple possible sources we requested ordering/numbering in order of likelihood.

- Primary: defined as no clear focus or portal of entry identified
- Catheter-related (Intra-vascular catheter only)
- Respiratory tract
    - Pneumonia
    - Pleural, empyema
    - Tracheobronchitis
- Intra-abdominal
    - Peritonitis
    - Biliary source
    - Other intra-abdominal
- Urinary tract
- Bone or soft tissues
    - Necrotizing fasciitis
    - Other soft tissue
    - Joint or bone
    - Spine
- Endocarditis
- Mediastinitis
- Central Nervous System

Source control was recorded according to the clinician's report as

- Not required
- Required, completed
- Source control required but not achieved

When it was required, we recorded the time, date and effectiveness of the intervention according to pre-defined categories, and if a specimen was sent for microbiology and if it was positive. When patients had multiple interventions we recorded the number of interventions, date of the last intervention and if it was deemed effective after the last intervention.

Source control interventions were recorded according to the following categories

Intravascular catheter Related
- Catheter removal
- Surgical vascular procedure (ligature)

Respiratory tract (pulmonary, pleural, empyema)
- Surgical thoracic
- Percutaneous thoracic (including chest drain)
- Percutaneous mediastinal

Vascular
- Surgical vascular
- Percutaneous vascular
- Other vascular

Cardiac and mediastinal
- Surgical cardiac
- Surgical mediastinal
- Percutaneous mediastinal
- other cardiac or mediastinal

Intra-abdominal
- Surgical abdominal
- Percutaneous abdominal
- Surgical other (mediastinal, pleural, …)
- Percutaneous other (mediastinal, pleural, …)

Urinary tract
- Surgical urinary (JJ stent)
- Surgical urinary (nephrectomy or other)
- Percutaneous urinary (nephrostomy)
- Other urinary

Bone or soft tissues
- Surgical skin
- Surgical bone
- Other bone or soft tissue

Other
- Percutaneous other
- Surgical other
- Other

eTable 1 Imputation of missing data.

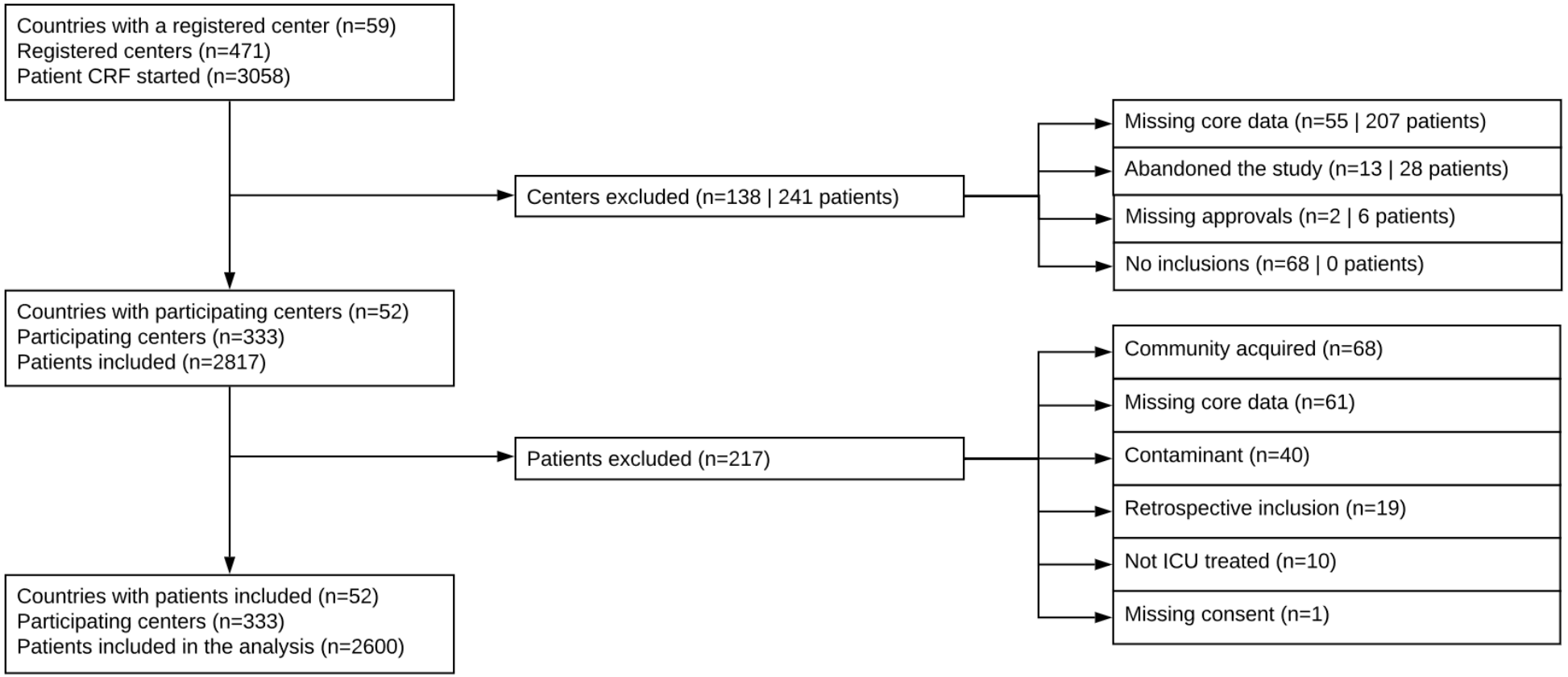
Variable	**Number of missing values**		**Imputed value**
	Center level	Patient level	
Type of ICU	6	15	Mixed (medical-surgical)
Clinical pharmacists are consulted	11	69	Available only during business hours
Aminoglycosides	7	25	TDM is available everyday
Vancomycin	7	25	TDM is available everyday
Number of ventilator-equivalent beds in the ICU ≥15	6	15	<15
Septic shock in class	n/a	8	No sepsis or sepsis without septic shock
Time before adequate treatment	n/a	2	24-48 hours

We used simple imputation of missing data to the median for continuous variables and to the mode for categorical variables.

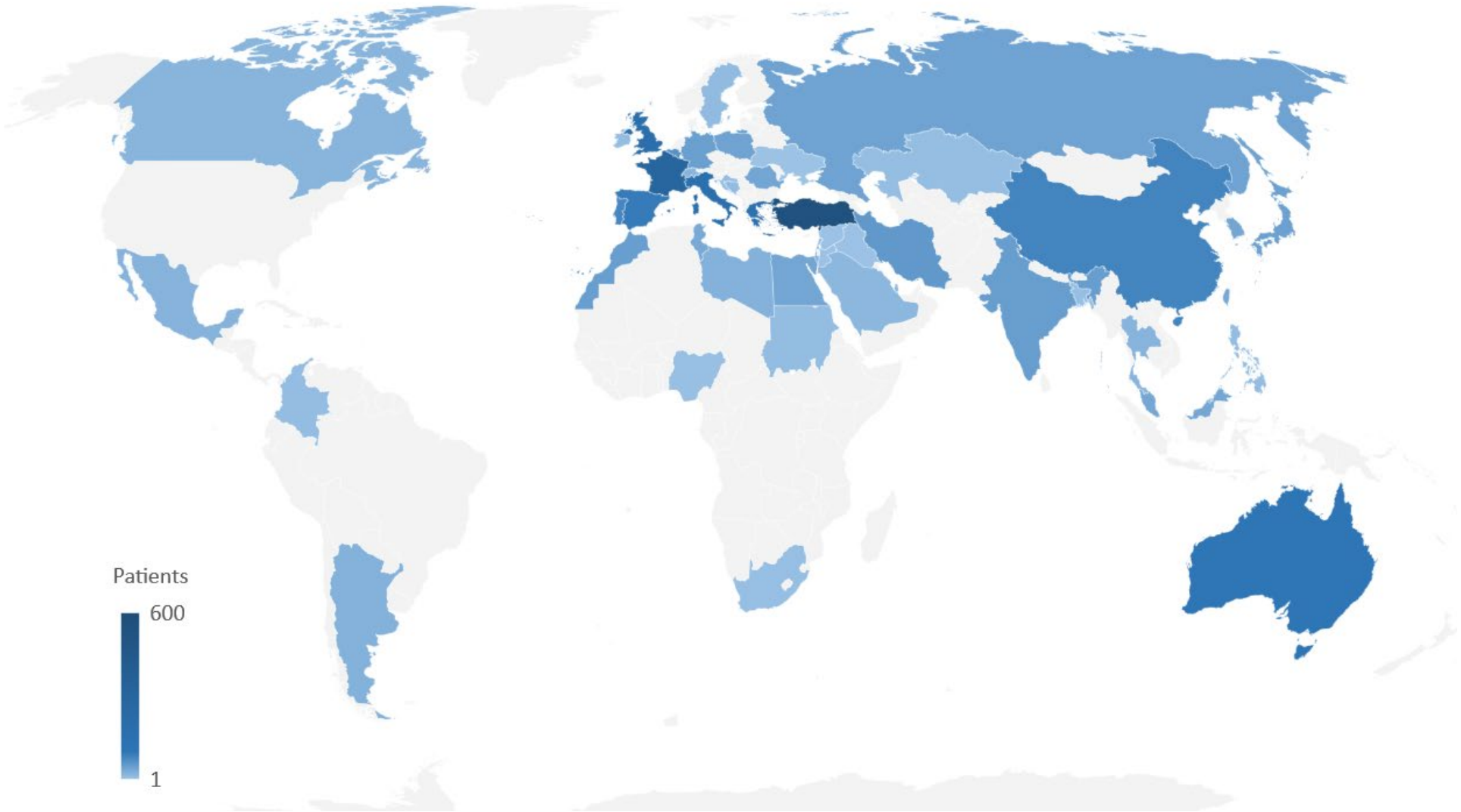
Missing times of blood culture sampling (n=26) and antibiotic start time (n=160) were imputed at 12:00 p.m.

TDM: therapeutic drug monitoring.

eFigure 1 Flowchart of the Eurobact II study



eFigure 2 Geographic distribution of participating ICUs and included patients



Legend: World-map participating countries and territories. Colour gradient denotes the number of included patients in each country.

eTable 2 Geographic distribution of participating ICUs

	ICUs	Patients		ICUs	Patients
East Asia and Pacific	**69**	**412**	**Europe and Central Asia**	**184**	**1775**
Australia	14	99	Belgium	12	64
Brunei	4	29	Bosnia and Herzegovina	1	10
China	15	80	Croatia	2	7
Hong Kong	1	5	France	35	288
Japan	11	44	Germany	6	46
Malaysia	6	36	Greece	19	144
Philippines	1	8	Italy	10	160
Republic of Korea	5	38	Kazakhstan	2	7
Singapore	6	18	Poland	6	41
Taiwan	4	35	Portugal	13	78
Thailand	2	20	Republic of Ireland	1	8
Middle East and North Africa	**48**	**268**	Romania	5	38
Dubai	1	10	Russian Federation	5	41
Egypt	7	38	Spain	13	92
Iran	13	54	Sweden	3	11
Iraq	1	2	Switzerland	2	20
Israel	2	19	Turkey	24	547
Lebanon	1	7	UK	24	172
Libya	5	22	Ukraine	1	1
Morocco	7	47	**North America**	**2**	**19**
Qatar	3	17	Canada	2	19
Saudi Arabia	3	15	**South Asia**	**14**	**54**
Syria	2	2	Bangladesh	2	6
Tunisia	2	33	India	12	48
Jordan	1	2	**Sub-Saharan Africa**	**5**	**20**
Latin America and the Caribbean	**11**	**52**	Nigeria	2	5
Argentina	4	23	South Africa	1	6
Colombia	1	8	Sudan	2	9
Mexico	6	21			

Legend: Number of participating ICUs and included patients in the Eurobact-2 database.

eTable 3 Characteristics of participating ICUs and patient outcomes

Characteristics *	All ICUs (n=333)*	All patients (N= 2600)	Dead on D28 (n= 966)	Alive on D28 (n= 1634)	OR [95% CI]	P value
Funding of the hospital						
Public	274 (83.8)	2198 (85)	808 (83.8)	1390 (85.7)	1	0.844
Private	35 (10.7)	263 (10.2)	108 (11.2)	155 (9.6)	1.06[0.73; 1.55]	.
Mixed	18 (5.5)	124 (4.8)	48 (5)	76 (4.7)	1.14[0.69; 1.88]	.
Structure of the ICU						
Closed-ICU	246 (75.2)	2039 (78.9)	739 (76.7)	1300 (80.2)	1	0.2
Open-ICU	81 (24.8)	546 (21.1)	225 (23.3)	321 (19.8)	1.19[0.91; 1.56]	.
Specific Recruitment **						
General ICU	300 (91.7)	2440 (94.4)	924 (95.9)	1516 (93.5)	1.46[0.9; 2.36]	0.124
Paediatric $	20 (6.1)	124 (4.8)	32 (3.3)	92 (5.7)	0.55[0.32; 0.93]	0.025
Cardiac-surgical	86 (26.3)	638 (24.7)	221 (22.9)	417 (25.7)	0.92[0.71; 1.2]	0.534
Coronary-care	89 (27.2)	559 (21.6)	194 (20.1)	365 (22.5)	0.99[0.76; 1.3]	0.955
Post-operative	235 (71.9)	1895 (73.3)	681 (70.6)	1214 (74.9)	0.76[0.59; 0.97]	0.031
Neuro-surgical	158 (48.3)	1373 (53.1)	503 (52.2)	870 (53.7)	0.77[0.61; 0.96]	0.024
Trauma	197 (60.2)	1574 (60.9)	584 (60.6)	990 (61.1)	0.9[0.71; 1.14]	0.389
Burns	65 (19.9)	446 (17.3)	161 (16.7)	285 (17.6)	1.07[0.8; 1.43]	0.629
Number of ventilator equivalent beds in the ICU	14 [10; 21]	15 [11; 22]	14 [11; 22]	15 [11; 23]	1 [0.99; 1]	0.415
Number high-dependency unit (HDU) beds in the ICU	0 [0; 6]	0 [0; 6]	0 [0; 5]	0 [0; 6]	0.99[0.98; 1.01]	0.227
Antibiotic choice is guided by **						
Local guidelines	194 (59.3)	1417 (54.8)	472 (49)	945 (58.3)	0.87[0.69; 1.11]	0.265
National/international guidelines	195 (59.6)	1570 (60.7)	551 (57.2)	1019 (62.9)	0.89[0.7; 1.12]	0.311
Surveillance cultures	157 (48)	1318 (51)	487 (50.5)	831 (51.3)	0.93[0.75; 1.17]	0.556
Consultation with ID, clinical microbiologists or pharmacists	135 (41.3)	1230 (47.6)	485 (50.3)	745 (46)	0.98[0.76; 1.25]	0.844
The treating physician	222 (67.9)	1648 (63.8)	572 (59.3)	1076 (66.4)	0.94[0.73; 1.22]	0.658
SOD or SDD						
In All ICU patients	58 (17.8)	296 (11.6)	180 (19)	342 (21.3)	1	0.211
In a selected group of patients	38 (11.7)	1735 (68)	95 (10)	201 (12.5)	0.97[0.63; 1.51]	.
Never			672 (71)	1063 (66.2)	1.23[0.92; 1.65]	
Inside the hospital or same campus	296 (90.5)	2378 (92)	897 (93)	1481 (91.4)	1	0.229
At another hospital with a partnership or agreement	25 (7.6)	178 (6.9)	52 (5.4)	126 (7.8)	0.79[0.5; 1.25]	
Off-site at an independent microbiology laboratory	6 (1.8)	29 (1.1)	15 (1.6)	14 (0.9)	1.93[0.74; 5.06]	
Selective reporting of antibiogram						
Not selective	155 (48)	1304 (50.9)	471 (49.1)	788 (49.2)	1	0.679
Selective	168 (52)	1259 (49.1)	489 (50.9)	815 (50.8)	0.95[0.75; 1.21]	
Recommendations used for the interpretation of antibiotic susceptibility testing						
EUCAST	194 (60.06)	1827 (71.56)	1121 (70.2)	706 (73.8)	1	0.802
CLSI	116 (35.91)	671 (26.28)	436 (27.3)	235 (24.6)	0.92 [0.69; 1.21]	
Other	13 (4.02)	55 (2.15)	39 (2.4)	16 (1.7)	0.89 [0.43; 1.85]	

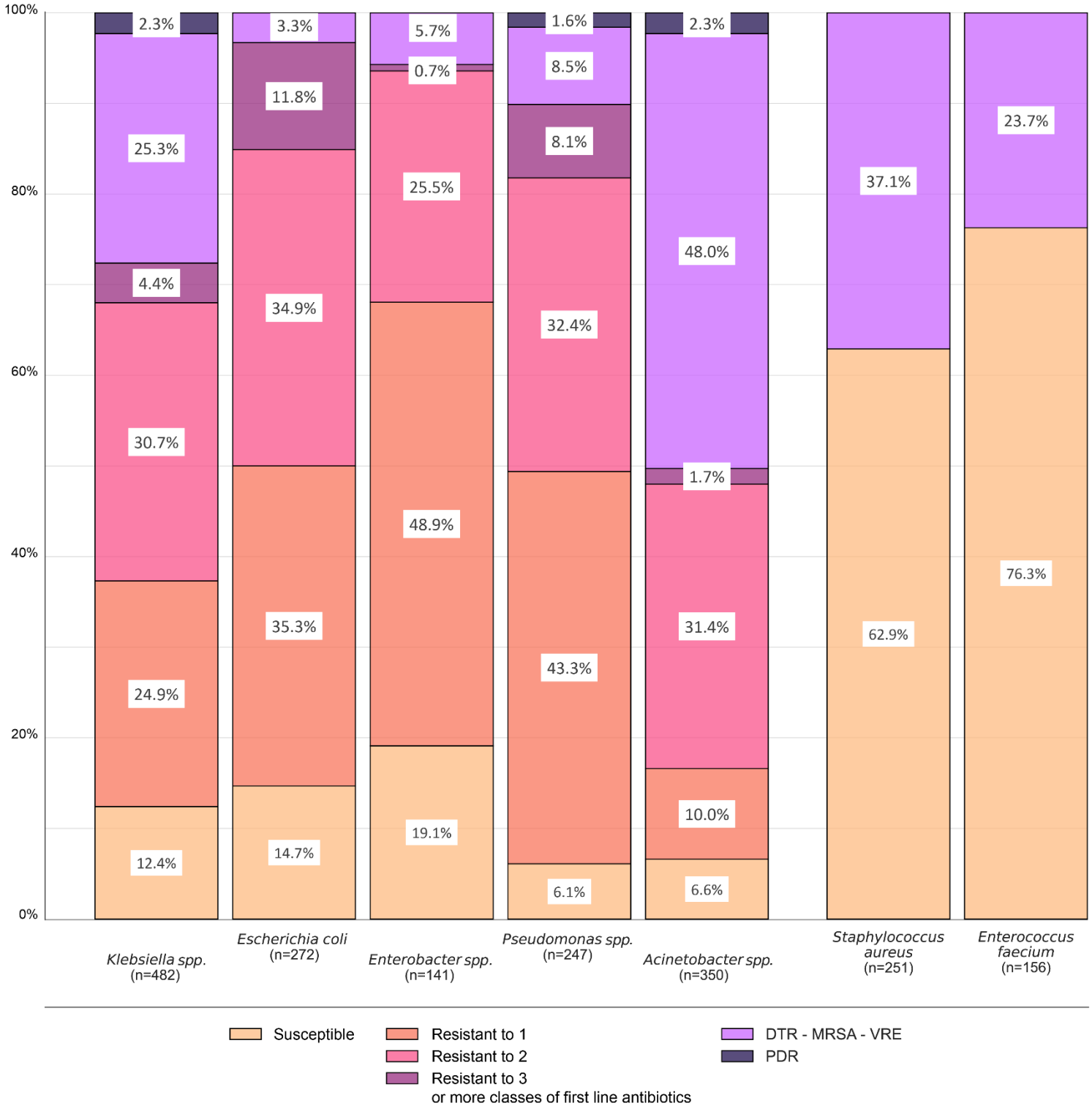
Legend: results reported as n (%) for categorical variables and median [IQR] for continuous variables; * All Center data was missing for 6 ICUs and 7 to 12 did not provide staffing or stewardship data. ** Percentage does not equate to 100% because multiple categories could be selected. $: Refers to ICUs with paediatric admission capacity – Only adult patients could be included in the study. *** There were 4 ICUs and 11 patients in the Low-income category Selective reporting of antibiogram results refers to the reporting to the clinician of a selection only of the tested antibiotics. 24/7: 24 hours a day, 7 days a week. ICU: intensive care unit, SOD: selective oral decontamination, SDD: selective digestive decontamination. TDM: therapeutic drug monitoring. Ventilator equivalent beds refers to the maximum number of ventilated patients the ICU can accommodate at one time.

eTable 4 Additional baseline (admission to the ICU) patient characteristics and day-28 mortality

Variable	All patients (N= 2600)	Dead on D28 (n= 966)	Alive on D28 (n= 1634)	OR [95% CI]	p-Value
Chronic illnesses*					
Moderate COPD	304 (11.7)	111 (11.5)	193 (11.8)	0.98 [0.76; 1.28]	0.905
Severe COPD	112 (4.3)	43 (4.5)	69 (4.2)	1.09 [0.72; 1.64]	0.685
Heart Failure (NYHA 3)	217 (8.3)	112 (11.6)	105 (6.4)	1.83 [1.35; 2.47]	<.001
Heart Failure (NYHA 4)	60 (2.3)	27 (2.8)	33 (2)	1.37 [0.79; 2.36]	0.26
Previous myocardial infarction	239 (9.2)	100 (10.4)	139 (8.5)	1.27 [0.95; 1.69]	0.102
Peripheral vascular disease	176 (6.8)	84 (8.7)	92 (5.6)	1.74 [1.25; 2.42]	0.001
Cerebrovascular disease	277 (10.7)	103 (10.7)	174 (10.6)	0.94 [0.71; 1.23]	0.631
Dementia	109 (4.2)	46 (4.8)	63 (3.9)	0.98 [0.64; 1.49]	0.919
Hemiplegia	70 (2.7)	20 (2.1)	50 (3.1)	0.64 [0.37; 1.11]	0.112
Diabetes without end organ damage	476 (18.3)	188 (19.5)	288 (17.6)	1.16 [0.94; 1.44]	0.174
Diabetes with end organ damage	272 (10.5)	118 (12.2)	154 (9.4)	1.15 [0.87; 1.51]	0.316
Renal disease, moderate	256 (9.8)	103 (10.7)	153 (9.4)	1.17 [0.88; 1.55]	0.282
Renal disease, severe (chronic dialysis)	129 (5)	51 (5.3)	78 (4.8)	1.09 [0.74; 1.59]	0.671
Connective tissue disease	67 (2.6)	31 (3.2)	36 (2.2)	1.54 [0.92; 2.59]	0.1
Ulcer disease (gastro-duodenal)	87 (3.3)	32 (3.3)	55 (3.4)	1.02 [0.63; 1.64]	0.949
Liver disease, mild to moderate	93 (3.6)	39 (4)	54 (3.3)	1.42 [0.91; 2.2]	0.119
Liver disease, severe	67 (2.6)	33 (3.4)	34 (2.1)	1.76 [1.06; 2.94]	0.03
Immunosuppression					
Steroids	134 (5.2)	60 (6.2)	74 (4.5)	1.49 [1.03; 2.16]	0.034
Chemotherapy/Radiotherapy within 6 months	220 (8.5)	93 (9.6)	127 (7.8)	1.37 [1.01; 1.85]	0.044
Targeted therapy for cancer	57 (2.2)	28 (2.9)	29 (1.8)	1.8 [1.03; 3.14]	0.039
Organ Transplant	73 (2.8)	26 (2.7)	47 (2.9)	0.93 [0.55; 1.56]	0.78
AIDS	16 (0.6)	7 (0.7)	9 (0.6)	1.73 [0.6; 5.01]	0.312
Other immunosuppression	95 (3.7)	39 (4)	56 (3.4)	1.21 [0.78; 1.88]	0.401
Source of ICU admission					
Hospital ward/floor, n (%)	1101 (42.3)	436 (45.1)	665 (40.7)	1	0.078
Emergency department	764 (29.4)	275 (28.5)	489 (29.9)	0.76 [0.61; 0.93]	
Other hospital, n (%)	352 (13.5)	136 (14.1)	216 (13.2)	0.92 [0.71; 1.2]	
Operating Room/recovery	286 (11)	89 (9.2)	197 (12.1)	0.75 [0.56; 1.01]	
Other intermediate care unit, n (%)	69 (2.7)	21 (2.2)	48 (2.9)	0.66 [0.37; 1.17]	
Other, n (%)	28 (1.1)	9 (0.9)	19 (1.2)	0.71 [0.3; 1.67]	
Primary diagnosis at ICU admission					
Sepsis or septic shock	530 (20.4)	189 (19.6)	341 (20.9)	1	<.001
Cardiac arrest	91 (3.5)	39 (4)	52 (3.2)	1.2 [0.75; 1.94]	
Cardio-vascular causes	137 (5.3)	45 (4.7)	92 (5.6)	0.86 [0.56; 1.31]	
Gastro-intestinal causes	85 (3.3)	36 (3.7)	49 (3)	1.27 [0.78; 2.07]	
Hypovolemic or Haemorrhagic shock	46 (1.8)	16 (1.7)	30 (1.8)	1.02 [0.53; 1.97]	
Metabolic causes	44 (1.7)	11 (1.1)	33 (2)	0.57 [0.27; 1.18]	
Multiple trauma (no TBI)	93 (3.6)	19 (2)	74 (4.5)	0.42 [0.24; 0.74]	
Neurologic causes	286 (11)	74 (7.7)	212 (13)	0.55 [0.39; 0.78]	
COVID-19**	336 (12.9)	195 (20.2)	141 (8.6)	2.04 [1.48; 2.83]	
Post-Operative admission	258 (9.9)	83 (8.6)	175 (10.7)	0.83 [0.6; 1.16]	
Renal failure	46 (1.8)	14 (1.4)	32 (2)	0.75 [0.38; 1.49]	
Respiratory admission	550 (21.2)	232 (24)	318 (19.5)	1.13 [0.87; 1.47]	
Traumatic brain injury	93 (3.6)	11 (1.1)	82 (5)	0.2 [0.1; 0.4]	
Other	5 (0.2)	2 (0.2)	3 (0.2)	1.14 [0.18; 7.35]	

Legend: Continuous variables are presented as median [IQR] and categorical variables as n(%). COPD: chronic obstructive pulmonary disease, ICU: intensive care unit, NYHA: New York heart association, AIDS: acquired immunodeficiency syndrome, TBI: Traumatic brain injury ** Respiratory admission refers to admission for respiratory failure other than COVID-19 that has been categorized separately.

eFigure 3 Proportion of drug resistant pathogens



Legend: Resistant to 1, 2 or 3 or more first line antibiotics was assessed among carbapenem, β-lactam, and fluoroquinolone categories and if tested piperacillin-tazobactam and ampicillin-sulbactam (*Acinetobacter spp.* ly) and aztreonam (not applicable for *Acinetobacter spp.*). DTR = difficult to treat resistance, PDR = Pandrug resistant (resistant to all tested antibiotics). DTR assessment requires antibiogram results for ≥1 carbapenem, ≥1 extended-spectrum cephalosporin, and ≥1 fluoroquinolone. PDR status only assessed for DTR pathogens. All PDR micro-organisms are DTR. MRSA= methicillin resistant *Staphylococcus aureus*

Multivariable models

Statistical methods for the multivariable models

To identify factors associated with day-28 death, we built a three-tiered hierarchical logistic mixed model using the GLIMMIX procedure of the SAS software. The variables were organized into 3 tiers: country, ICU, and patient. The effects of country-based and center-based variables on the day28 survival were included as random intercepts. Multilevel modelling takes into account the hierarchical structure of the data, which may manifest as intraclass correlations [2]. To obtain a conservative estimate of the standard error, a separate random-error term was specified for each level of the analysis. Therefore, to avoid overestimating the significance of risk factors of day-28 mortality, we took intraclass correlations into account, and we specified a separate random-error term for each tier. Variables potentially associated with death were introduced into the multivariable model. The hierarchical model comprised three levels: country (level 3), center (level 2), and patient (level 1). All variables not obviously correlated (e.g., SOFA score and vasopressor use, age or temperature and SAPS II excluding age related points) with P-values less than 0.10 by univariate analysis were introduced into the multivariable model. We did not correct for multiplicity of statistical tests. Owing to the low number of missing values, simple imputation to the median for continuous variables and to the mode for categorical variables was used (ESM eTable 1). The COVID-19 status was not included in the multivariable analysis because of co-linearity of the admission diagnosis with sepsis or septic shock. To mitigate the bias (*i.e.*, high mortality and different epidemiology of HA-BSI) introduced by patients infected with SARS-CoV-2 [3], we performed a sensitivity analysis excluding the 276 COVID-19 patients. Following the peer review process, and to mitigate the risk of bias introduced by logistic regression with day-28 mortality as an outcome variable (*i.e.,* a substantial part of the cohort was still in the ICU), we computed a competing-risk, subdistribution hazard frailty model as suggested by Fine and Gray [4]. We introduced ICU discharge as a competing risk and a random centre effect to model cluster dependence on the cumulative incidence function of the event of interest in the presence of competing events using the finalfit() package of the R software

Variable selection for the multivariable models.

Variable selection for the multivariable models used full pre-specification and was performed as follows:

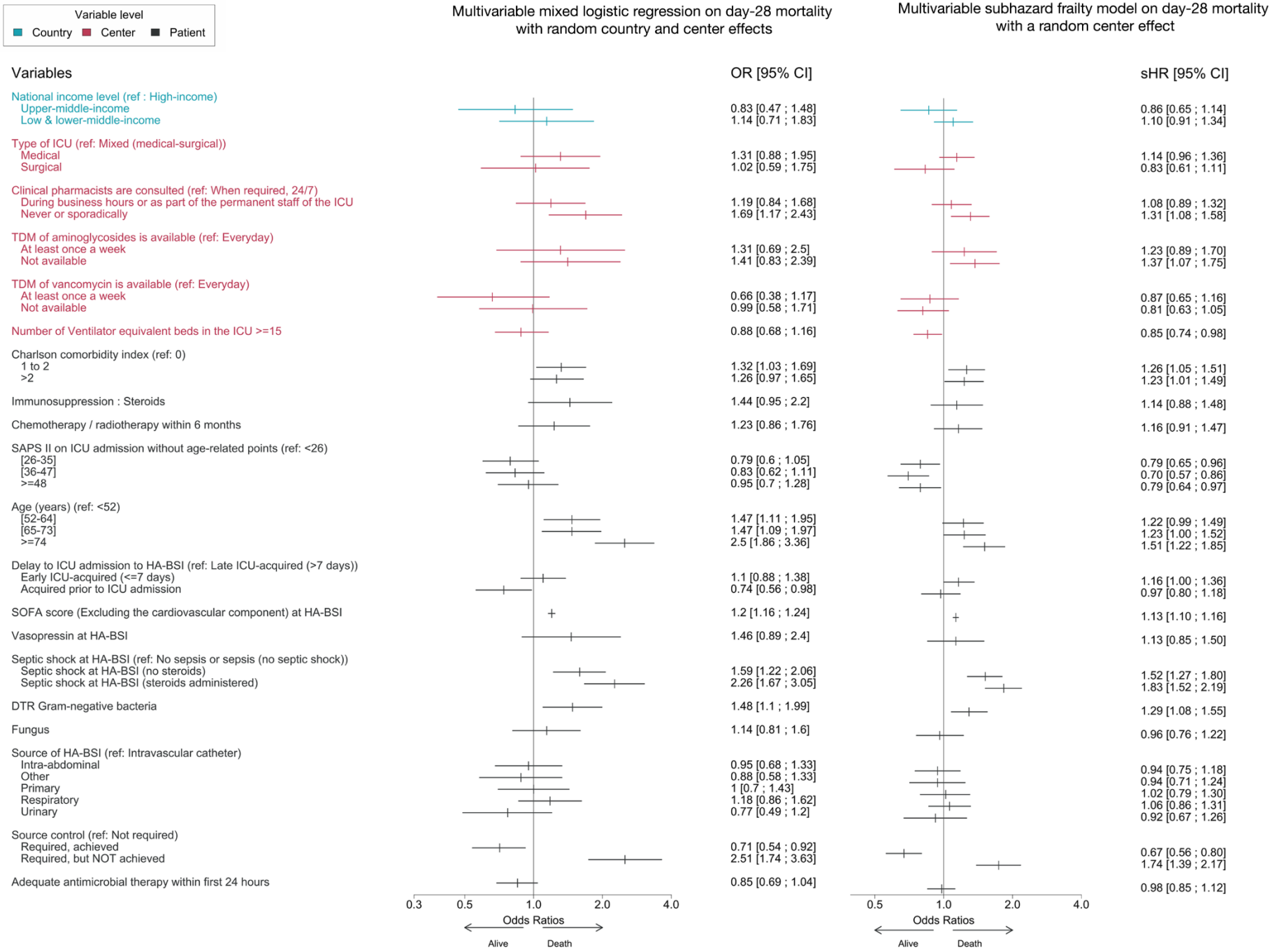
At database close a selection of clinically relevant variables was made to be presented in the manuscript and in the multivariable model. All candidate variables that were statistically significant with a threshold of 10% were included in the multivariable model. There was no stepwise process. We excluded variables that involved less than 5% of the cohort and those that were deemed collinear because of overlapping or used in the calculation of scores as shown in the table below.

Level	Variable	Selected for multivariable analysis	reason
Country	National income	Yes	
Center	Type of ICU	Yes	
Center	Paediatric	No	Collinear with type of ICU
Center	Post-operative	No	
Center	Neuro-surgical	No	
Center	Number of Ventilator equivalent beds in the ICU >=15	Yes	
Center	Clinical pharmacists are consulted	Yes	
Center	TDM of aminoglycosides is available	Yes	
Center	TDM of vancomycin is available	Yes	
Patient	Age	Yes	
Patient	SAPS-II on admission, excluding Age related points	Yes	SAPS-II score was computed excluding age related points to avoid collinearity with the variable Age.
Patient	Charlson co-morbidity index in class	Yes	
Patient	Solid-tumours – Proven metastasis	No	Already included as part of the computation of the SAPS-II score.
Patient	Haematological malignancy (Leukaemia or lymphoma)	No	
Patient	Immunosuppression: Steroids	Yes	
Patient	Chemotherapy / radiotherapy within 6 months	Yes	
Patient	Targeted Cancer Therapy (ongoing)	No	Size < 5%
Patient	Type of ICU admission	No	Already included as part of the computation of the SAPS-II score.
Patient	Primary ICU admission diagnosis	No	Collinear with sepsis / septic shock as 20.4% patients were admitted for sepsis or septic shock
Patient	Time from ICU admission to HA-BSI	Yes	
Patient	Temperature at HA-BSI (max) in class	No	Already included as part of the computation of the SAPS-II score.
Patient	SOFA score without the cardiovascular component at HA-BSI	Yes	The SOFA score cardiovascular component includes the use of dopamine, epi. or norepi. and as such is collinear with septic shock. We have included in the multivariable analysis a SOFA score excluding the cardiovascular component to avoid this issue.
Patient	SOFA score at HA-BSI	No	
Patient	Ventilation status	No	Collinear with the SOFA score
Patient	Vasopressors (adrenaline or noradrenaline)	No	Collinear with sepsis / septic shock
Patient	ECMO (VA OR VV)	No	Size < 5%
Patient	Vasopressin	Yes	This variable is not included in the SOFA score or in sepsis / septic shock.
Patient	Septic shock in class	Yes	
Patient	DTR Gram-negative pathogen	Yes	
Patient	Fungus	Yes	
Patient	Source of HA-BSI	Yes	
Patient	Source control	Yes	
Patient	Time to adequate antimicrobial therapy	Yes	

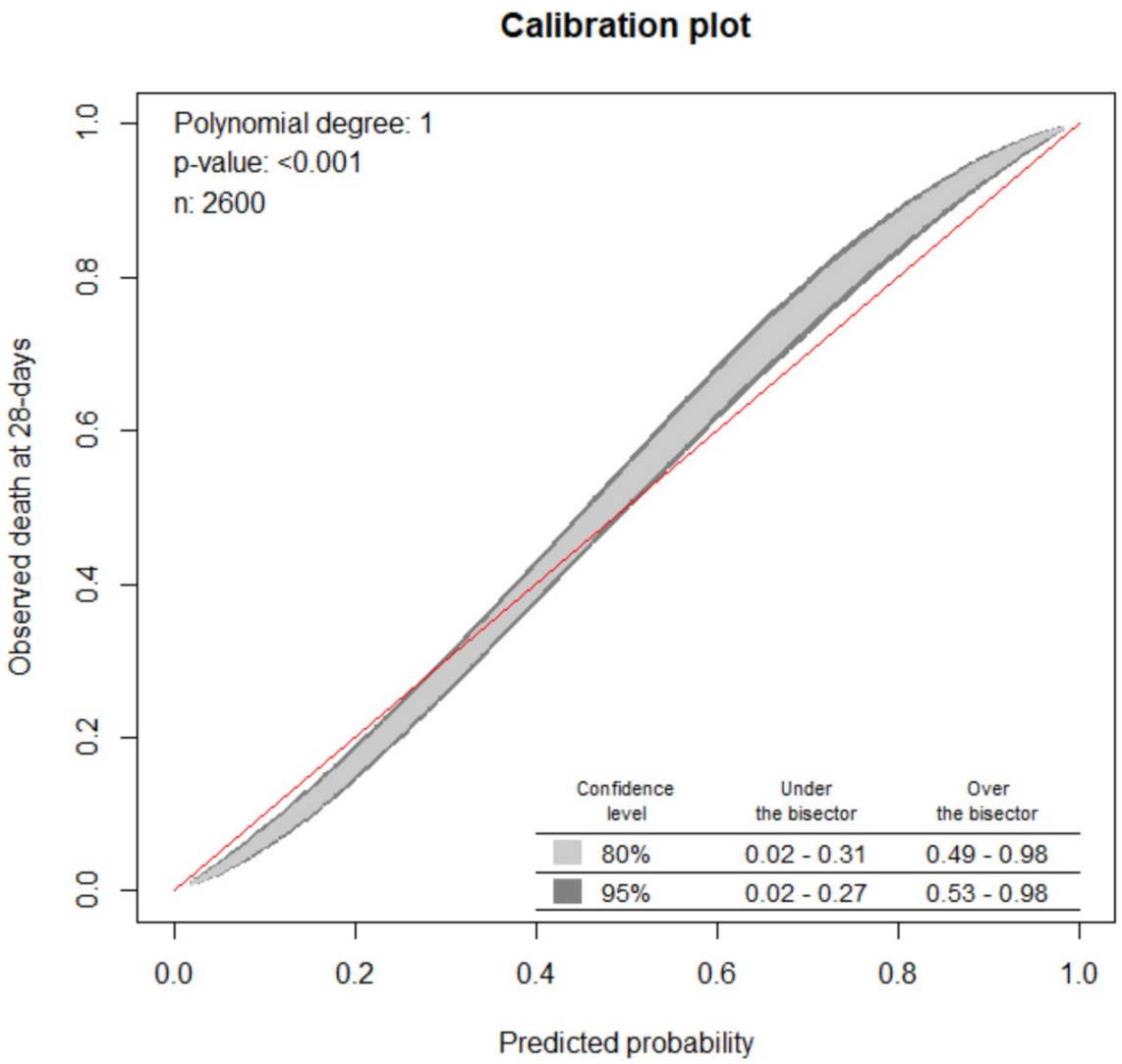
eTable 5 Competing-risks frailty model and comparison with hierarchical logistic model

		Hierarchical logistic mixed model	Competing-risks frailty model (Fine & Gray)
Variable	**items**	OR [CI 95%]	sHR [CI 95%]
National income level	High-Income	1	1
	Upper-middle-income	0.83 [0.47;1.48]	0.86 [0.65;1.14]
	Low & Lower-middle-income	1.14 [0.71;1.83]	1.10 [0.91;1.34]
Type of ICU	Mixed (medical-surgical)	1	1
	Medical	1.31 [0.88;1.95]	1.14 [0.96;1.36]
	Surgical	1.02 [0.59;1.75]	0.83 [0.61;1.11]
Clinical pharmacists are consulted	When required, 24/7	1	1
	During business hours or part of the ICU staff	1.19 [0.84;1.68]	1.08 [0.89;1.32]
	Never or sporadically	1.69 [1.17;2.43]	1.31 [1.08;1.58]
TDM of aminoglycosides is available	Everyday	1	1
	At least once a week	1.31 [0.69;2.5]	1.23 [0.89;1.70]
	Not available	1.41 [0.83;2.39]	1.37 [1.07;1.75]
TDM of vancomycin is available	Everyday	1	1
	At least once a week	0.66 [0.38;1.17]	0.87 [0.65;1.16]
	Not available	0.99 [0.58;1.71]	0.81 [0.63;1.05]
Number of Ventilator equivalent beds in the ICU ≥15		0.88 [0.68;1.16]	0.85 [0.74;0.98]
Charlson comorbidity index	0	1	1
	1 to 2	1.32 [1.03;1.69]	1.26 [1.05;1.51]
	>2	1.26 [0.97;1.65]	1.23 [1.01;1.49]
Immunosuppression: Steroids		1.44 [0.95;2.2]	1.14 [0.88;1.48]
Chemotherapy / radiotherapy within 6 months		1.23 [0.86;1.76]	1.16 [0.91;1.47]
SAPS II on ICU admission without age-related points	< 26	1	1
	[26-35]	0.79 [0.6;1.05]	0.79 [0.65;0.96]
	[36-47]	0.83 [0.62;1.11]	0.70 [0.57;0.86]
	>=48	0.95 [0.7;1.28]	0.79 [0.64;0.97]
Age (years)	<52	1	1
	[52-64]	1.47 [1.11;1.95]	1.22 [0.99;1.49]
	[65-73]	1.47 [1.09;1.97]	1.23 [1.00;1.52]
	>=74	2.5 [1.86;3.36]	1.51 [1.22;1.85]
Time from ICU admission to HA-BSI	Late ICU-acquired (>7 days)	1	1
	Early ICU-acquired (≤7 days)	1.1 [0.88;1.38]	1.16 [1.00;1.36]
	Acquired prior to ICU admission	0.74 [0.56;0.98]	0.97 [0.80;1.18]
SOFA score (Excluding the cardiovascular component) at HA-BSI		1.2 [1.16;1.24]	1.13 [1.10;1.16]
Vasopressin at HA-BSI		1.46 [0.89;2.4]	1.13 [0.85;1.50]
Septic shock at HA-BSI	No sepsis or sepsis (no septic shock)	1	1
	Septic shock at HA-BSI (no steroids)	1.59 [1.22;2.06]	1.52 [1.27;1.80]
	Septic shock at HA-BSI (received steroids)	2.26 [1.67;3.05]	1.83 [1.52;2.19]
DTR Gram-negative bacteria		1.48 [1.1;1.99]	1.29 [1.08;1.55]
Fungus		1.14 [0.81;1.6]	0.96 [0.76;1.22]
Most likely source of infection	Intravascular catheter	1	1
	Intra-abdominal	0.95 [0.68;1.33]	0.94 [0.75;1.18]
	Other	0.88 [0.58;1.33]	0.94 [0.71;1.24]
	Primary	1 [0.7;1.43]	1.02 [0.79;1.30]
	Respiratory	1.18 [0.86;1.62]	1.06 [0.86;1.31]
	Urinary	0.77 [0.49;1.2]	0.92 [0.67;1.26]
Source control	Not required	1	1
	Required, achieved	0.71 [0.54;0.92]	0.67 [0.56;0.80]
	Required, but NOT achieved	2.51 [1.74;3.63]	1.74 [1.39;2.17]
Adequate antimicrobial therapy within 24h of HA-BSI		0.85 [0.69;1.04]	0.98 [0.85;1.12]

Legend: Initially planned the hierarchical logistic mixed model and comparison with a competing risk frailty model. The covariance parameters for the logistic model (3-level hierarchical logistic regression) are as follows: Country-Level 3 (estimate: 0.08314, Standard error (SE) 0.09173), Center-Level 2 (estimate 0.4104, SE 0.1037). The c-statistic for the primary model was 0.8279 (95% CI 0.8119; 0.8439), indicating good discrimination. Calibration was tested using a calibration belt as shown below. Income level categories were defined using the United Nations M49 standard. HA-BSI: Hospital-acquired bloodstream infection, SAPS II: Simplified Acute Physiology Score II, TDM: Therapeutic drug monitoring, SOFA: Sequential Organ Failure Assessment. Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range.


Variable level
Country
Center
Patient
Multivariable mixed logistic regression on day-28 mortality with random country and center effects
Multivariable subhazard frailty model on day-28 mortality with a random center effect
Variables
OR [95% CI]
sHR [95% CI]
National income level (ref : High-income)
Upper-middle-income
0.83 [0.47 ; 1.48]
0.86 [0.65 ; 1.14]
Low & lower-middle-income
1.14 [0.71 ; 1.83]
1.10 [0.91 ; 1.34]
Type of ICU (ref: Mixed (medical-surgical))
Medical
1.31 [0.88 ; 1.95]
1.14 [0.96 ; 1.36]
Surgical
1.02 [0.59 ; 1.75]
0.83 [0.61 ; 1.11]
Clinical pharmacists are consulted (ref: When required, 24/7)
During business hours or as part of the permanent staff of the ICU
1.19 [0.84 ; 1.68]
1.08 [0.89 ; 1.32]
Never or sporadically
1.69 [1.17 ; 2.43]
1.31 [1.08 ; 1.58]
TDM of aminoglycosides is available (ref: Everyday)
At least once a week
1.31 [0.69 ; 2.5]
1.23 [0.89 ; 1.70]
Not available
1.41 [0.83 ; 2.39]
1.37 [1.07 ; 1.75]
TDM of vancomycin is available (ref: Everyday)
At least once a week
0.66 [0.38 ; 1.17]
0.87 [0.65 ; 1.16]
Not available
0.99 [0.58 ; 1.71]
0.81 [0.63 ; 1.05]
Number of Ventilator equivalent beds in the ICU >=15
0.88 [0.68 ; 1.16]
0.85 [0.74 ; 0.98]
Charlson comorbidity index (ref: 0)
1 to 2
1.32 [1.03 ; 1.69]
1.26 [1.05 ; 1.51]
>2
1.26 [0.97 ; 1.65]
1.23 [1.01 ; 1.49]
Immunosuppression : Steroids
1.44 [0.95 ; 2.2]
1.14 [0.88 ; 1.48]
Chemotherapy / radiotherapy within 6 months
1.23 [0.86 ; 1.76]
1.16 [0.91 ; 1.47]
SAPS II on ICU admission without age-related points (ref: <26)
[26-35]
0.79 [0.6 ; 1.05]
0.79 [0.65 ; 0.96]
[36-47]
0.83 [0.62 ; 1.11]
0.70 [0.57 ; 0.86]
>=48
0.95 [0.7 ; 1.28]
0.79 [0.64 ; 0.97]
Age (years) (ref: <52)
[52-64]
1.47 [1.11 ; 1.95]
1.22 [0.99 ; 1.49]
[65-73]
1.47 [1.09 ; 1.97]
1.23 [1.00 ; 1.52]
>=74
2.5 [1.86 ; 3.36]
1.51 [1.22 ; 1.85]
Delay to ICU admission to HA-BSI (ref: Late ICU-acquired (>7 days))
Early ICU-acquired (<=7 days)
1.1 [0.88 ; 1.38]
1.16 [1.00 ; 1.36]
Acquired prior to ICU admission
0.74 [0.56 ; 0.98]
0.97 [0.80 ; 1.18]
SOFA score (Excluding the cardiovascular component) at HA-BSI
1.2 [1.16 ; 1.24]
1.13 [1.10 ; 1.16]
Vasopressin at HA-BSI
1.46 [0.89 ; 2.4]
1.13 [0.85 ; 1.50]
Septic shock at HA-BSI (ref: No sepsis or sepsis (no septic shock))
Septic shock at HA-BSI (no steroids)
1.59 [1.22 ; 2.06]
1.52 [1.27 ; 1.80]
Septic shock at HA-BSI (steroids administered)
2.26 [1.67 ; 3.05]
1.83 [1.52 ; 2.19]
DTR Gram-negative bacteria
1.48 [1.1 ; 1.99]
1.29 [1.08 ; 1.55]
Fungus
1.14 [0.81 ; 1.6]
0.96 [0.76 ; 1.22]
Source of HA-BSI (ref: Intravascular catheter)
Intra-abdominal
0.95 [0.68 ; 1.33]
0.94 [0.75 ; 1.18]
Other
0.88 [0.58 ; 1.33]
0.94 [0.71 ; 1.24]
Primary
1 [0.7 ; 1.43]
1.02 [0.79 ; 1.30]
Respiratory
1.18 [0.86 ; 1.62]
1.06 [0.86 ; 1.31]
Urinary
0.77 [0.49 ; 1.2]
0.92 [0.67 ; 1.26]
Source control (ref: Not required)
Required, achieved
0.71 [0.54 ; 0.92]
0.67 [0.56 ; 0.80]
Required, but NOT achieved
2.51 [1.74 ; 3.63]
1.74 [1.39 ; 2.17]
Adequate antimicrobial therapy within first 24 hours
0.85 [0.69 ; 1.04]
0.98 [0.85 ; 1.12]
0.3
0.5
1.0
2.0
4.0
Odds Ratios
Alive
Death
0.5
1.0
2.0
4.0
Odds Ratios
Alive
Death

eFigure 4: Calibration belt for the hierarchical logistic model.



Legend: Calibration belt, following the recommendations by Nattino et al. (2017), showing poor calibration. Given that our primary goal was to describe clinical features of HA-BSI patients and associations with mortality, we chose to fully pre-specify clinically relevant variables to be introduced in the model and have not attempted to improve model calibration through addition or deletion of variables, techniques of handling variables or other model specifications. Our preference was to present clinically relevant variables and their associations with mortality that physicians may use at the bedside.

eTable 6 Sensitivity analysis: Hierarchical logistic mixed model with random effects for country and ICU, excluding the 276 patients with a COVID-19 diagnosis.

Legend:

		Hierarchical logistic mixed model
Variable	**items**	OR [CI 95%]
National income level	High-Income	1
	Upper-middle-income	0.9 [0.5;1.61]
	Low & Lower-middle-income	1.18 [0.73;1.91]
Type of ICU	Mixed (medical-surgical)	1
	Medical	1.38 [0.92;2.07]
	Surgical	1.12 [0.65;1.91]
Clinical pharmacists are consulted	When required, 24/7	1
	During business hours or part of the ICU staff	1.14 [0.81;1.62]
	Never or sporadically	1.64 [1.13;2.38]
TDM of aminoglycosides is available	Everyday	1
	At least once a week	1.41 [0.75;2.69]
	Not available	1.52 [0.89;2.59]
TDM of vancomycin is available	Everyday	1
	At least once a week	0.67 [0.38;1.17]
	Not available	0.89 [0.52;1.52]
Number of Ventilator equivalent beds in the ICU ≥15		0.86 [0.65;1.14]
Charlson comorbidity index	0	1
	1 to 2	1.29 [0.99;1.68]
	>2	1.19 [0.9;1.58]
Immunosuppression: Steroids		1.52 [0.98;2.35]
Chemotherapy / radiotherapy within 6 months		1.29 [0.9;1.84]
SAPS II on ICU admission without age-related points	< 26	1
	[26-35]	0.71 [0.52;0.98]
	[36-47]	0.84 [0.61;1.16]
	>=48	0.96 [0.69;1.34]
Age (years)	<52	1
	[52-64]	1.54 [1.14;2.08]
	[65-73]	1.43 [1.04;1.95]
	>=74	2.6 [1.91;3.55]
Time from ICU admission to HA-BSI	Late ICU-acquired (>7 days)	1
	Early ICU-acquired (≤7 days)	1.13 [0.89;1.45]
	Acquired prior to ICU admission	0.81 [0.6;1.08]
SOFA score (Excluding the cardiovascular component) at HA-BSI		1.23 [1.19;1.28]
Vasopressin at HA-BSI		1.56 [0.95;2.58]
Septic shock at HA-BSI	No sepsis or sepsis (no septic shock)	1
	Septic shock at HA-BSI (no steroids)	1.52 [1.15;2]
	Septic shock at HA-BSI (received steroids)	2.08 [1.51;2.87]
DTR Gram-negative bacteria		1.38 [1.01;1.89]
Fungus		1.4 [1.01;1.92]
Most likely source of infection	Intravascular catheter	1
	Intra-abdominal	1.06 [0.75;1.5]
	Other	0.99 [0.65;1.52]
	Primary	1 [0.68;1.48]
	Respiratory	1.18 [0.83;1.66]
	Urinary	0.87 [0.55;1.39]
Source control	Not required	1
	Required, achieved	0.75 [0.57;0.99]
	Required, but NOT achieved	2.59 [1.77;3.8]
Adequate antimicrobial therapy within 24h of HA-BSI		0.84 [0.68;1.04]

Sensitivity analysis conducted on 2324 patients after exclusion of the 276 patients with a COVID-19 diagnosis, Income level categories were defined using the United Nations M49 standard. DTR: difficult-to-treat resistance, HA-BSI: Hospital-acquired Bloodstream Infection, ICU: intensive care unit, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential Organ Failure Assessment, TDM: Therapeutic drug monitoring. Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range.

eTable 7 Sensitivity analysis: Hierarchical logistic mixed model with random effects for country and ICU, investigating carbapenem resistance instead of difficult to treat resistance.

		Hierarchical logistic mixed model
Variable	**items**	OR [CI 95%]
National income level	High-Income	1
	Upper-middle-income	0.83 [0.46;1.48]
	Low & Lower-middle-income	1.14 [0.71;1.84]
Type of ICU	Mixed (medical-surgical)	1
	Medical	1.3 [0.87;1.94]
	Surgical	1.02 [0.59;1.75]
Clinical pharmacists are consulted	When required, 24/7	1
	During business hours or part of the ICU staff	1.19 [0.84;1.68]
	Never or sporadically	1.68 [1.16;2.42]
TDM of aminoglycosides is available	Everyday	1
	At least once a week	1.31 [0.69;2.49]
	Not available	1.39 [0.82;2.38]
TDM of vancomycin is available	Everyday	1
	At least once a week	0.67 [0.38;1.18]
	Not available	1 [0.58;1.72]
Number of Ventilator equivalent beds in the ICU ≥15		0.88 [0.67;1.16]
Charlson comorbidity index	0	1
	1 to 2	1.32 [1.03;1.69]
	>2	1.27 [0.97;1.65]
Immunosuppression: Steroids		1.41 [0.93;2.16]
Chemotherapy / radiotherapy within 6 months		1.24 [0.86;1.77]
SAPS II on ICU admission without age-related points	< 26	1
	[26-35]	0.79 [0.6;1.05]
	[36-47]	0.84 [0.62;1.12]
	>=48	0.95 [0.7;1.29]
Age (years)	<52	1
	[52-64]	1.48 [1.11;1.96]
	[65-73]	1.47 [1.1;1.98]
	>=74	2.52 [1.88;3.38]
Time from ICU admission to HA-BSI	Late ICU-acquired (>7 days)	1
	Early ICU-acquired (≤7 days)	1.1 [0.88;1.38]
	Acquired prior to ICU admission	0.74 [0.56;0.98]
SOFA score (Excluding the cardiovascular component) at HA-BSI		1.23 [1.18;1.27]
Vasopressin at HA-BSI		1.49 [0.91;2.43]
Septic shock at HA-BSI	No sepsis or sepsis (no septic shock)	1
	Septic shock at HA-BSI (no steroids)	1.58 [1.22;2.05]
	Septic shock at HA-BSI (received steroids)	2.26 [1.67;3.06]
Carbapenem resistant enterobacterales		1.31 [1.02;1.68]
Fungus		1.15 [0.81;1.62]
Most likely source of infection	Intravascular catheter	1
	Intra-abdominal	0.95 [0.68;1.33]
	Other	0.88 [0.58;1.33]
	Primary	1 [0.7;1.43]
	Respiratory	1.18 [0.86;1.62]
	Urinary	0.77 [0.49;1.2]
Source control	Not required	1
	Required, achieved	0.71 [0.55;0.92]
	Required, but NOT achieved	2.48 [1.72;3.59]
Adequate antimicrobial therapy within 24h of HA-BSI		0.85 [0.7;1.04]

Legend: Sensitivity analysis computed by imputing carbapenem resistance in Gram-negative pathogens in place of DTR. Income level categories were defined using the United Nations M49 standard. DTR: difficult-to-treat resistance, HA-BSI: Hospital-acquired Bloodstream Infection, ICU: intensive care unit, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential Organ Failure Assessment, TDM: Therapeutic drug monitoring. Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range.

The Eurobact 2 study group: National coordinators, scientific committee, and participating intensive care units.

East Asia and Pacific

Australia

National Coordinator: A/Prof. Alexis Tabah

Scientific Committee: Prof. Jeffrey Lipman

Participating ICUs: Redcliffe Hospital, ICU: A/Prof. Alexis Tabah, Dr Hamish Pollock, Dr Ben Margetts. Alfred Hospital, Department of Intensive Care and Hyperbaric Medicine: Prof Andrew Udy, Ms Meredith Young. Ipswich Hospital, Intensive Care Unit: Dr Neeraj Bhadange, Mr Steven Tyler. Mater Hospital, And Mater Research Institute – The University of Queensland, Mater Misericordiae Limited, The Department of Intensive Care: Dr Anne Ledtischke, Miss Mackenzie Finnis. Mater Private Hospital, And Mater Research Institute – The University of Queensland, Mater Misericordiae, The Department of Intensive Care: Dr Anne Ledtischke, Miss Mackenzie Finnis. Bankstown-Lidcombe Hospital, Intensive Care Unit: Dr Jyotsna Dwivedi, Dr Manoj Saxena. Lyell Mcewin Hospital, Lyell Mcewin Hospital Intensive Care Unit: Dr Vishwanath Biradar, Mrs Natalie Soar. Cabrini Hospital, Intensive Care: A/Prof Vineet Sarode, A/Prof David Brewster. St John Of God Murdoch Hospital, Intensive Care Unit: A/Prof Adrian Regli, Dr Elizabeth Weeda. Royal Brisbane and Women S Hospital, Intensive Care Services: Dr Samiul Ahmed, Ms Cheryl Fourie, Prof. Kevin Laupland. The Prince Charles Hospital, Adult Intensive Care Services: Dr Mahesh Ramanan. Princess Alexandra Hospital, Intensive Care: Dr James Walsham, Mr Jason Meyer. Fiona Stanley Hospital, Intensive Care Unit: Dr Edward Litton, Ms Anna Maria Palermo, Mr Timothy Yap, Mr Ege Eroglu. Rockhampton Hospital, Intensive Care Unit: Dr Antony George Attokaran, Dr C'havala Jaramillo.

Brunei

National Coordinator: Dr. Khalid Mk Nafees

Participating ICUs: Ripas Hospital, Icu 3: Dr Khalid Mahmood Khan Nafees. Raja Isteri Pengiran Anak Saleha Hospital, Icu1: Dr Nurhikmahtul Aqilah Haji Abd Rashid, Dr Haji Adi Muhamad Ibnu Walid. Gleneagles Jpmc, Icu: Dr Tomas Mon, Dr P. Dhakshina Moorthi. Suri Seri Begawan Hospital, Intensive Care Unit: Dr Shah Sudhirchandra, Dr Dhadappa Damodar Sridharan.

China

National Coordinator: Dr. Qiu Haibo and Dr. Jianfeng Xie

Participating ICUs: Zhongda Hospital, Southeast University, Department of Critical Care Medicine: Dr Qiu Haibo, Dr Xie Jianfeng. Yijishan Hospital, First Affiliated Hospital of Wannan Medical College, Department of Critical Care Medicine: Dr Lu Wei-Hua, Dr Wang Zhen. First Affiliate Hospital of Kunming Medical University, Micu/Eicu: Prof Chuanyun Qian, Dr Jili Luo. Qilu Hospital of Shandong University, Department of Critical Care Medicine: Dr Xiaomei Chen, Dr Hao Wang. Hebei Petrochina Central Hospital, Intensive Care Unit: Dr Peng Zhao, Dr Juan Zhao. Hangzhou Second Hospital, Affiliated Hospital of Hangzhou Normal University: Prof Qiu Wusi, Miss Chen Mingmin. Tianjin Third Central Hospital, Department of Critical Care Medicine: Dr Lei Xu, Dr Chengfen Yin. Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Department Of Critical Care Medicine: Dr Ruilan Wang, Dr Jinfeng Wang. The Second Hospital of Jilin University, Department Of Critical Care: Dr Yongjie Yin, Dr Min Zhang. Taizhou People S Hospital, Intensive Care Unit: Dr Jilu Ye, Dr Chungfang Hu. The First Affiliated Hospital of Nanjing Medical University, Department Of Geriatrics Intensive Care Unit: Dr Suming Zhou, Dr Min Huang. Zhejiang Hospital, Intensive Care Unit: Prof Jing Yan, Dr Yan Wang. Henan Provincial People S Hospital, Department of Critical Care Medicine: Dr Bingyu Qin, Dr Ling Ye. Qingdao Municipal Hospital, Intensive Care Unit: Dr Xie Weifeng. The Second Hospital of Lanzhou University, Department Of Critical Care Medicine: Dr Li Peije, Dr Nan Geng.

Hong Kong

National Coordinator: Dr. Lowell Ling

Participating ICUs: The Chinese University of Hong Kong, Prince of Wales Hospital, Department Of Anaesthesia And Intensive Care: Dr Lowell Ling.

Japan

National Coordinator: Dr. Yoshiro Hayashi

Participating ICUs: Kameda Medical Center, Department of Intensive Care Medicine: Dr Yoshiro Hayashi, Dr Toshiyuki Karumai. University Hospital Kyoto Prefectural University of Medicine, Intensive Care Unit: Dr Masaki Yamasaki, Dr Satoru Hashimoto. Hiroshima University Hospital, ICU: Dr Koji Hosokawa. Yokosuka General Hospital Uwamachi, Critical Care Medicine: Dr Jun Makino. Tokyo Metropolitan Tama Medical Center, Emergency and Critical Care Center: Dr Takeo Matsuyoshi. Kurashiki Central Hospital, Emergency Intensive Care Unit: Dr Akira Kuriyama. Tokyo Medical and Dental University, Department of Intensive Care Medicine: Dr Hidenobu Shigemitsu, Dr Yuka Mishima, Dr Michio Nagashima. St. Marianna University School of Medicine Hospital, Mixed ICU: Dr Hideki Yoshida, Prof. Shigeki Fujitani. Osaka City General Hospital, Emergency and Critical Care Medical Hospital: Dr Koichiro Omori, Dr Hiroshi Rinka. St. Marianna University School of Medicine, Yokohama City Seibu Hospital, Mixed ICU: Dr Hiroki Saito, Dr Kaori Atobe. Yokohama City University Hospital, Infection Prevention and Control Department: Dr Hideaki Kato. Yokohama City University Hospital, Intensive Care Department: Dr Shunsuke Takaki.

Malaysia

National Coordinator: Dr. Helmi Sulaiman

Participating ICUs: University Malaya Medical Centre, Department of Anaesthesiology and Intensive Care: Dr M. Shahnaz Hasan, Dr Muhamad Fadhil Hadi Jamaluddin. Hospital Tengku Ampuan Rahimah, Anaesthesia and Intensive Care: Dr Lee See Pheng, Dr Sheshendrasurian Visvalingam. Hospital Sarikei, Anaesthesiology & Intensive Care Unit: Dr Mun Thing Liew, Dr Siong Ling Danny Wong. Queen Elizabeth 1 Hospital, Department of Anaesthesiology and Intensive Care: Dr Kean Khang Fong, Dr Hamizah Bt Abdul Rahman. Hospital Serdang, Cardiothoracic and Perfusion Unit: Dr Zuraini Md Noor, Dr Lee Kok Tong. Hospital Tuanku Fauziah, Intensive Care Unit: Dr Abd. Hamid Azman. School Of Medical Sciences Universiti Sains Malaysia, Department of Anaesthesiology and Intensive Care: Dr Mohd Zulfakar Mazlan. Hospital Universiti Sains Malaysia, Department of Anaesthesiology and Intensive Care: Dr Saedah Ali.

Philippines

National Coordinator: Dr. Aaron Mark Hernandez

Participating ICUs: The Medical City Ortigas, Intensive Care Unit: Dr Anton Abello.

Republic Of Korea

National Coordinator: Dr Kyeongman Jeon

Participating ICUs: Samsung Medical Center, Medical Icu: Dr Kyeongman Jeon. Seoul National University Hospital, Medical Icu: Dr Sang-Min Lee. Hallym University Sacred Heart Hospital, Micu: Dr Sunghoon Park. Micu, Chonbuk National University Hospital: Prof Dr Seung Yong Park. Seoul National University Bundang Hospital, Medical Icu: Dr Sung Yoon Lim.

Singapore

National Coordinator: A/Prof Andrea Lay Hoon Kwa, Dr Qing Yuan Goh

Participating ICUs: Singapore General Hospital, Surgical Intensive Care Unit: Dr Qing Yuan Goh, A/Prof Shin Yi Ng. Singapore General Hospital, Neurosurgical Intensive Care Unit: Dr Sui An Lie, A/Prof Andrea Lay Hoon Kwa. Singapore General Hospital, Medical Intensive Care Unit: Dr Ken Junyang Goh. National University Hospital System Medical Intensive Care Unit: Dr Andrew Yunkai Li. Tan Tock Seng Hospital, Surgical Intensive Care Unit, Neurological Intensive Care Unit: Adj Asst Prof Caroline Yu Ming Ong, Dr Jia Yan Lim. Changi General Hospital, Medical Intensive Care Unit: Dr Jessica Lishan Quah, Dr Kangqi Ng. Changi General Hospital, Surgical Intensive Care Unit: Dr Louis Xiang Long Ng.

Taiwan

National Coordinator: Dr. Tony Yu-Chang Yeh

Participating ICUs: National Taiwan University Hospital, Sicu: Dr Yu Chang Yeh, Dr Nai-Kuan Chou. National Cheng Kung University Hospital, Division of Critical Care Medicine, Department of Internal Medicine: Dr Cong-Tat Cia. Mackay Memorial Hospital, Department of Critical Care Medicine: Dr Ting-Yu Hu, Dr Li-Kuo Kuo. National Taiwan University Hospital, Department of Internal Medicine, Micu: Dr Shih-Chi Ku.

Thailand

National Coordinator: Prof (Associate) Phunsup Wongsurakiat

Participating ICUs: Siriraj Hospital, Mahidol University, Critical Respitarory Care Unit, Department of Medicine: Prof (Associate) Phunsup Wongsurakiat. Vajira Hospital, Department of Internal Medicine: Dr Yutthana Apichatbutr, Dr Supattra Chiewroongroj.

Middle East and North Africa

Dubai

National Coordinator: Dr. Adel Alsisi

Participating ICUs: Dubai Hospital, Icu Department: Dr Rashid Nadeem, Dr Ashraf El Houfi.

Egypt

National Coordinator: Dr. Adel Alsisi

Participating ICUs: Cairo University Hospital (Qasr Al Ainy), Critical Care Department: Dr Adel Alsisi, Dr Amr Elhadidy, Dr Mina Barsoum.Medical Research Institute, Alexandria University, Biomedical Informatics and Medical Statistics (Icu): Dr Nermin Osman. Tanta University Hospital, Anaesthesia and Critical Care Department: Dr Tarek Mostafa. Tanta University Faculty of Medicine, Emergency Medicine and Traumatology Department: Dr Mohamed Elbahnasawy. Tanta University Emergency Hospital, Emergency, And Traumatology Department Critical Care Unit: Dr Ahmed Saber. Nasr City Health Insurance Hospital, Medical Icu: Dr Amer Aldhalia. Wingat Royal Hospital, Wingat Icu: Dr Omar Elmandouh. Elsahel Teaching Hospital, Icu: Dr Ahmed Elsayed. Ain Shams University Hospitals, Department of General Surgery: Dr Merihan A. Elbadawy, Dr Ahmed K. Awad. Alexandria Faculty of Medicine, Dialysis Intensive Care Unit: Miss Hanan M. Hemead.

Iran

National Coordinator: Prof. Farid Zand

Participating ICUs: Shiraz University of Medical Sciences, Anesthesiology and Critical Care Research Center: Prof Farid Zand, Dr Maryam Ouhadian. Ahvaz Jundishapur University of Medical Sciences, Air Pollution and Respiratory Diseases Research Center: Dr Seyed Hamid Borsi,, Dr Zahra Mehraban. Ahvaz Jundishapur University of Medical Sciences, Neurology Department: Dr Davood Kashipazha. Ahvaz Jundishapur University of Medical Sciences, Infectious and Tropical Diseases Research Center, Health Research Institute: Dr Fatemeh Ahmadi. Ahvaz Jundishapur University of Medical, Pain Research Center: Dr Mohsen Savaie, Dr Farhad Soltani, Dr Mahboobeh Rashidi, Dr Reza Baghbanian, Dr Fatemeh Javaherforoosh, Dr Fereshteh Amiri. Ahvaz Jundishapur University of Medical Sciences, Neurosurgery Department, Dr Arash Kiani. Ahvaz Jundishapur University of Medical Sciences, General Surgery Department, Dr Mohammad Amin Zargar. Tabriz University of Medical Sciences, Research Center for Integrative Medicine in Aging, Aging Research Institute: Prof Ata Mahmoodpoor. Jahrom University of Medical Sciences, Peimanieh Hospital : Dr Fatemeh Aalinezhad. Shiraz University of Medical Sciences, Shahid Rajaee Trauma Hospital : Dr Gholamreza Dabiri. Shiraz University of Medical Sciences, Trauma Research Center, Shahid Rajaee Hospital : Dr Golnar Sabetian, Dr Hakimeh Sarshad. Shiraz University of Medical Sciences, Anesthesiology and Critical Care Research Center: Dr Mansoor Masjedi, Dr Ramin Tajvidi. Zahedan University of Medical Sciences, Anesthesiology and Critical Care Department: Dr Seyed Mohammad Nasirodin (S.M.N.) Tabatabaei.

Iraq

Participating ICUs: Ibn Zuhur Hospital, Icu: Dr Abdullah Khudhur Ahmed.

Israel

National Coordinator: Prof. Pierre Singer

Participating ICUs: Rabin Medical Center Beilinson Hospital, General Intensive Care: Prof Pierre Singer, Dr Ilya Kagan, Dr Merav Rigler. Shaare Zedek Medical Center, Intensive Care Unit: Dr Daniel Belman, Dr Phillip Levin.

Jordan

Participating ICUs: Abdali Hospital, Icu: Dr Belal Harara, Dr Adei Diab.

Lebanon

National Coordinator: Dr Fayez Abillama

Participating ICUs: Lebanese American University Medical Center Rizk Hospital, Intensive Care: Dr Fayez Abilama, Dr Rebecca Ibrahim, Dr Aya Fares.

Libya

National Coordinator: Dr. Muhammed Elhadi

Participating ICUs: Aljalla Benghazi Center, Micu: Dr Ahmad Buimsaedah. Almokhtar Clinic, Intensive Care Unit: Dr Marwa Gamra. Althawra Central Hospital, Intensive Care Unit: Dr Ahmed Aqeelah. Brega General Hospital Bgh Libya, Icu: Dr Almajdoub Ali Mohammed Ali, Dr Ahmed Gaber Sadik Homaidan. National Heart Institute, Micu: Dr Bushray Almiqlash, Dr Hala Bilkhayr. Tobruk Medical Centre, Medical Icu: Dr Ahmad Bouhuwaish, Dr Ahmed Sa Taher. Tripoli Central Hospital, Icu: Dr Eman Abdulwahed, Dr Fathi A Abousnina, Dr Aisha Khaled Hdada. Tripoli Central Hospital, Unit C: Dr Rania Jobran. Zliten Medical Center, Icu of Zliten Medical Center: Dr Hayat Ben Hasan, Dr Rabab Shaban Ben Hasan.

Morocco

National Coordinator: Prof. Khalid Abidi

Participating ICUs: Avicenne Military Hospital, Icu: Dr Issam Serghini, Pr Rachid Seddiki. CHU Hassan II Fès, Intensive Care Unit A4: Dr Brahim Boukatta, Dr Nabil Kanjaa. Hospital Of Specialties, Critical Care Unit of Neurology and Neurosurgery: Prof Doumiri Mouhssine, Prof Maazouzi Ahmed Wajdi. Ibn Sina University Hospital, faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Medical Icu: Pr Tarek Dendane, Pr Amine Ali Zeggwagh. Mohammed VI University Hospital of Oujda, Faculty Of Medicine and Pharmacy Oujda, Mohammed Premier University, Anesthesia and Resuscitation Department: Prof Brahim Housni, Dr Oujidi Younes. Mohammed VI University Hospital, Medical Icu, Marrakech: Prof Abdelhamid Hachimi. National Institute of Oncology of Rabat, Intensive Care Unit: Prof A Ghannam, Prof Z Belkhadir.

Palestine

Participating ICUs: ICU, Alia governmental hospital, Hebron / West Bank, Palestine: Dr. Sarah Amro. Gaza city, Alshifaa hospital, Gaza, Palestine: DR. Mustafa Abu Jayyab.

Qatar

National Coordinator: Dr Ali Aithssain

Participating ICUs: Hamad General Hospital, Medical Icu: Dr Ali Ait Hssain, Dr Abdurahaman Elbuzidi. Al Wakrah Hospital, Critical Care: Dr Edin Karic. Hamad General Hospital, Sicu: Dr Marcus Lance, Dr Shaikh Nissar.

Saudi Arabia

Participating ICUs: King Faisal Specialist Hospital &Research Center, Adult Critical Care Medicine: Dr Hend Sallam. Prince Sultan Medical Military Center, Intensive Care Unit: Dr Omar Elrabi, Dr Ghaleb A Almekhlafi. Security Force Hospital - Riyadh, Critical Care Unit: Dr Maher Awad, Dr Ahmed Aljabbary.

Syria

Participating ICUs: Al Mouwasat University Hospital, Icu: Dr Mohammad Karam Chaaban. Assad University Hospital, Neurological Intensive Care Unit: Dr Natalia Abu-Sayf. Damascus University Cardiac Surgery Hospital Near Al-Mouwasat University Hospital, Mazzeh Kiwan, Cardiac Surgery Icu: Dr Mohammad Al-Jadaan, Miss Lubna Bakr.

Tunisia

National Coordinator: Dr Mounir Bouaziz

Participating ICUs: Habib Bourguiba University Hospital, Department of Intensive Care: Dr Mounir Bouaziz, Dr Olfa Turki. Military Hospital of Tunis, Department of Anesthesiology And Intensive Care Unit, Lr12dn01: Pr Walid Sellami.

Latin America and The Caribbean

Argentina

National Coordinator: Dr. Gabriela Vidal

Participating ICUs: Hcas Cuenca Alta, Terapia Intensiva: Dr Pablo Centeno, Lic Natalia Morvillo. Hospital Central De Formosa, Servicio De Terapia Intensiva: Dr José Oscar Acevedo, Dr Patricia Mabel Lopez. Hospital Español De Mendoza, Terapia Intensiva De Adultos: Dr Rubén Fernández, Dr Matías Segura. Hospital Zatti, Ucia: Dra Marta Aparicio, Microbiologa Irene Alonzo. Instituto De Diagnostico De La Plata, Unidad De Terapia Intensiva: Dr Yanina Nuccetelli, Dr Pablo Montefiore.

Colombia

National Coordinator: Mario Arias

Participating ICUs: Clinica Universidad De La Sabana, Critical Care Unit : Dr Luis Felipe Reyes. Universidad De La Sabana, Infectious Diseases Department: Dr Luis Felipe Reyes.

Mexico

National Coordinator: Dr Silvio A. Ñamendys-Silva

Participating ICUs: Hospital Medica Sur, Department of Critical Care Medicine: Dr Silvio A. Ñamendys-Silva, Dr Juan P. Romero-Gonzalez. Centenario Hospital Miguel Hidalgo, Centenario Hospital Miguel Hidalgo: Dr Mariana Hermosillo, Dr Roberto Alejandro Castillo. Hospital General De Zona 14, Intensive Care Unit: Dr Jesús Nicolás Pantoja Leal, Dr Candy Garcia Aguilar. Hospital General Regional No.1, IMSS Tlaxcala: Dr Mara Ocotlan Gonzalez Herrera, Dr Missael Vladimir Espinoza Villafuerte. Hospital H+ Queretaro, Unidad De Terapia Intensiva Adultos: Dr Manuel Lomeli-Teran. Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Division of Pulmonary, Anesthesia and Critical Care Medicine: Dr Jose G. Dominguez-Cherit, Dr Adrian Davalos-Alvarez, Dr Silvio A. Ñamendys-Silva. UMAE Hospital de Especialidades Antonio Fraga Mouret, Centro Médico Nacional La RazaIMSS, Terapia Intensiva Hospital de Especialidades CMN La Raza: Dr Luis Sánchez-Hurtado, Dr Brigitte Tejeda-Huezo. Hospital General San Juan del Rio, Querétaro, , Unidad de Terapia Intensiva de Adultos: Dr Orlando R Perez-Nieto, Dr Ernesto Deloya Tomas.

Europe And Central Asia

Belgium

National Coordinator: Dr. Liesbet De Bus

Scientific Committee: Prof. Jan De Waele

Recruitment of participating ICUs worldwide: Mr. Guy Francois

Participating ICUs: Ghent University Hospital, Intensive Care Unit: Dr Liesbet De Bus, Dr Jan De Waele. A.S.Z., Iz: Dr Isabelle Hollevoet. Az Nikolaas, Icu: Dr Wouter Denys. Az Sint-Jan Av Brugge - Oostende Campus Brugge, Icu: Dr Marc Bourgeois. Az Sint-Lucas, Department of Intensive Care: Dr Sofie F.M. Vanderhaeghen. Centre Hospitalier De Jolimont, Soins Intensifs : Dr Jean-Baptiste Mesland, Dr Pierre Henin. Chu Ambroise Paré, Unité Des Soins Intensifs : Dr Lionel Haentjens. Chu Charleroi, Medico-Surgical Icu: Dr Patrick Biston, Mrs Cindérella Noel. Chu Liège, Soins Intensifs : Dr Nathalie Layos, Dr Benoît Misset. Clinique Saint-Pierre, Intensive Care Unit : Dr Nicolas De Schryver, Dr Nicolas Serck. Cliniques Universitaires Saint-Luc, UCLouvain, Soins Intensifs : Dr Xavier Wittebole. Uzbrussel, Intensieve Zorgen: Prof Elisabeth De Waele, Mrs Godelive Opdenacker.

Bosnia And Herzegovina

National Coordinator: Dr Pedja Kovacevic

Participating ICUs: University Clinical Centre of The Republic Of Srpska, Medical Intensive Care Unit: Dr Pedja Kovacevic, Dr Biljana Zlojutro.

Croatia

National Coordinator: Dr Ina Filipovic-Grcic

Participating ICUs: General Hospital Dubrovnik, Anesthesiology, And Intensive Care: Dr Aida Custovic, Dr Ina Filipovic-Grcic. University Hospital Centre Zagreb, Medical Intensive Care Unit: Prof Radovan Radonic, Dr Ana Vujaklija Brajkovic. University

Hospital Dubrava, Clinical Department of Anesthesiology, Reanimatology and Intensive Care: Prof Jasminka Persec, Dr Sanja Sakan, Dr Mario Nikolic, Dr Hrvoje Lasic.

France

National Coordinator: Prof. Marc Leone

Scientific Committee: Prof. Jean-François Timsit, Prof. Etienne Ruppe, Mr. Stephane Ruckly, Prof. Philippe Montravers

Participating ICUs: Hôpital Nord, Réanimation Polyvalente et Traumatologique : Pr Marc Leone, Dr Charlotte Arbelot. Bichat Claude Bernard, Réanimation Médicale et Infectieuse : Prof Jean-François Timsit, Mme Juliette Patrier. Bichat-Claude Bernard Hospital, Ap-Hp, Anesthesiology And Critical Care Medicine Department, Dmu Parabol: Dr N.Zappela, Pr P. Montravers. Centre Hospitalier De Bigorre, Service De Réanimation Polyvalente : Dr Thierry Dulac, Dr Jérémy Castanera. Centre Hospitalier De Cholet, Réanimation Polyvalente : Dr Johann Auchabie, Dr Anthony Le Meur. Centre Hospitalier De Dieppe, Médecine Intensive Réanimation : Dr A. Marchalot, Dr M. Beuzelin. Centre Hospitalier De Pau, Réanimation Polyvalente : Dr Alexandre Massri, Dr Charlotte Guesdon. Ch Annecy Genevois, Réanimation Polyvalente : Dr Etienne Escudier. Ch De Charleville-Mézières, Médecine Intensive Réanimation : Dr Philippe Mateu, Dr Jérémy Rosman. Ch Tourcoing, Service De Reanimation: Dr Olivier Leroy, Dr Serge Alfandari. Chu Compiegne Noyon, Réanimation : Dr Alexandru Nica. Chu Gabriel Montpied, Médecine Intensive Et Réanimation : Dr Bertrand Souweine, Dr Elisabeth Coupez. Chu Lille, Hôpital Roger Salengro, Pôle De Réanimation : Dr Thibault Duburcq. Chu Lille, Surgical Critical Care, Department of Anesthesiology and Critical Care: Prof Eric Kipnis, Dr Perrine Bortolotti. Chu Rennes, Service De Maladies Infectieuses Et Réanimation Médicale : Dr Mathieu Le Souhaitier. Cochin, Medecine Intensive Reanimation: Dr Jean-Paul Mira. Ghef Site De Marne-La-Vallée, Réanimation Polyvalente : Dr Pierre Garcon, Dr Matthieu Duprey. Groupe Hospitalier Nord Essonne - Site Longjumeau, Réanimation Polyvalente : Dr Martial Thyrault, Dr Rémi Paulet. Groupe Hospitalier Paris Saint Joseph, Médecine Intensive et Réanimation : Dr François Philippart, Dr Marc Tran, Dr Cédric Bruel. Hôpital Beaujon, Department of Anesthesiology and Critical Care: Dr Emmanuel Weiss, Dr Sylvie Janny, Dr Arnaud Foucrier. Hopital De Gui De Chauliac, Departement Anesthesie Reanimation Gui De Chauliac : Dr Pierre-François Perrigault, Dr Flora Djanikian. Hôpital De La Source, Centre Hospitalier Régional D'orléans, Médecine Intensive & Réanimation (Medical Icu): Dr François Barbier. Hôpital De La Timone, Médecine Intensive Réanimation : Dr Marc Gainnier, Dr Jérémy Bourenne. Hopital De Mercy, Chr Metz-Thionville, Service De Réanimation Polyvalente Et Usc: Dr Guillaume Louis. Hopital Du Scorff, Service De Réanimation : Dr Roland Smonig. Hôpital Edouard Herriot, Médecine Intensive-Réanimation : Dr Laurent Argaud, Dr Thomas Baudry. Hôpital Henri Mondor, Service De Réanimation Médicale : Pr Armand Mekonted Dessap, Dr Keyvan Razazi. Hôpital Louis Pasteur, Réanimation : Dr Pierre Kalfon, Mr Gaëtan Badre. Montpellier University Hospital, Intensive Care Medicine Lapeyronie Hospital: Dr Romaric Larcher. Nimes University Hospital, Service Des Réanimations : Prof Jean-Yves Lefrant, Dr Claire Roger. Purpan, Réanimation Polyvalente : Dr Benjamine Sarton, Dr Stein Silva. Sorbonne Universite Pitie Salpetriere, Médecine Intensive Et Réanimation Neurologique : Dr Sophie Demeret, Dr Loïc Le Guennec. Sud Essonne Hospital, Department of Intensive Care Medicine: Dr Shidasp Siami, Mrs Christelle Aparicio. Tenon Hospital, Service De Médecine Intensive Réanimation : Dr Guillaume Voiriot, Dr Muriel Fartoukh. University Hospital Of Poitiers, Surgical And Neuro Intensive Care Units: Dr Claire Dahyot-Fizelier, Dr Nadia Imzi. University Of Montpellier, Phymedexp Inserm Cnrs: Dr Kada Klouche.

Germany

National Coordinator: Prof. Hendrik Bracht

Participating ICUs: University Hospital Ulm, Icu G1: Dr Hendrik Bracht, Dr Sandra Hoheisen. Jena University Hospital, Dept. Of Anesthesiology and Intensive Care Medicine: Dr Frank Bloos, Dr Daniel Thomas-Rueddel. Universitätsklinikum Leipzig, Medical Icu: Dr Sirak Petros, Dr Bastian Pasieka. University Hospital Heidelberg, Station 13 Iopsis: Dr Simon Dubler, Dr Karsten Schmidt. University Hospital Muenster, Department of Anesthesiology, Intensive Care Medicine and Pain Therapy: Dr Antje Gottschalk, Dr Carola Wempe. University Hospital of Saarland, Dept. Of Internal Medicine V - Pneumology, Allergology and Critical Care Medicine: Prof Philippe Lepper, Dr Carlos Metz.

Kazakhstan

National Coordinator: Dr. Dmitriy Viderman

Participating ICUs: University Medical Center, National Research Oncology Center, Intensive Care Unit: Dr Dmitriy Viderman, Dr Yerlan Ymbetzhanov. Karaganda Medical University, Department of Emergency Medicine, Anesthesiology and Resuscitation Non-Commercial Joint-Stock Company: Associate Prof., Dr Miras Mugazov, Dr Yelena Bazhykayeva. Medical Center Hospital of The President's Affairs Administration of The Republic of Kazakhstan, Intensive Care Unit: Dr Zhannur Kaligozhin, Dr Baurzhan Babashev. National Research Oncology Center, Department of Oncohematological Resuscitation, Resuscitation, Intensive Care: Dr Yevgeniy Merenkov, Dr Talgat Temirov.

Greece

National Coordinator: Dr. Kostoula Arvaniti

Participating ICUs: Papageorgiou Hospital, Intensive Care Unit: Dr Kostoula Arvaniti, Dr Dimitrios Smyrniotis. Agioi Anargiroi Hospital, Agioi Anargiroi Icu: Dr Vasiliki Psallida, Dr Georgios Fildisis. G Papanikolaou General Hospital, 1st Icu: Dr Vasiliki Soulountsi, Dr Evangelos Kaimakamis. G Papanikolaou General Hospital, B Icu: Dr Cristina Iasonidou, Dr Sofia Papoti. General Hospital G. Gennhmatas, Gnth "G Gennhmatas": Dr Foteini Renta, Dr Maria Vasileiou. General Hospital of Athens G. Gennimatas, Icu: Dr Vasiliki Romanou, Dr Vasiliki Koutsoukou. Gh Imathia Veria, Icu: Dr Mariana Kristina Matei, Dr Leora Moldovan. Icu, Hygeia General Hospital: Dr Ilias Karaiskos, Dr Harry Paskalis. Intensive Care Unit, General Hospital of Giannitsa: Dr Kyriaki Marmanidou. Intensive Care Unit, Hippocration General Hospital Of Athens: Dr M. Papanikolaou, Dr C.Kampolis. Katerini General Hospital, Gnk Icu: Dr Marina Oikonomou, Dr Evangelos Kogkopoulos. Konstantopoulion-Patision Hospital, Icu: Dr Charikleia Nikolaou, Dr Anastasios Sakkalis. Mediterraneo Hospital, Icu/Hdu : Dr Marinos Chatzis, Dr Maria Georgopoulou. Saint Savvas Hospital, Icu: Dr Anna Efthymiou, Dr Vasiliki Chantziara. Sismanogleio Hospital, Sismanogleion Icu: Dr Aikaterini Sakagianni, Dr Zoi (Zoe) Athanasa (Athanassa). Theageneio Anticancer Hospital, Icu: Dr Eirini Papageorgiou, Dr Fadi Ali. University Hospital Attikon, National And Kapodistrian University Of Athens, Department Of Critical Care: Pr Georges Dimopoulos, Dr Mariota Panagiota Almiroudi. University Hospital Heraklion, Department of Intensive Care: Dr Polychronis Malliotakis, Dr Diamantina Marouli. University Hospital of Alexandroupolis, Department Of Intensive Care: Dr Vasiliki Theodorou, Dr Ioannis Retselas. University Hospital of Ioannina, Intensive Care Unit: Pr Vasilios Kouroulas, A/Pr Georgios Papathanakos.

Italy

National Coordinator: Prof. Matteo Bassetti and Dr. Daniele Giacobbe

Participating ICUs: Città Della Salute E Della Scienza - Molinette, Anestesia E Rianimazione Universitaria: Dr Giorgia Montrucchio, Dr Gabriele Sales. Fondazione Policlinico Universitario A. Gemelli Irccs. Universita Cattolica Del Sacro Cuore. Italy, Uoc Di Anestesia, Rianimazione, Terpia Intensiva E Tossicologia Clinica: Dr Gennaro De Pascale, Dr Luca Maria Montini, Dr Simone Carelli, Dr Joel Vargas, Ms Valentina Di Gravio. Irccs Ospedale Policlinico San Martino, U.O. Anestesia E Rianimazione: Prof Daniele Roberto Giacobbe, Dr Angelo Gratarola, Dr Elisa Porcile, Dr Michele Mirabella. Irccs Sacro Cuore Don Calabria, Terapia Intensiva: Dr Ivan Daroui, Dr Giovanni Lodi. Madonna Delle Grazie, U.O.C. Anestesia E Rianimazione: Dr Francesco Zuccaro, Dr Maria Grazia Schlevenin. Ospedale Policlinico San Martino, Irccs Per L'oncologia E Le Neuroscienze, Uo Clinica Anestesiologica E Terapia Intensiva: Prof Paolo Pelosi, Dr Denise Battaglini. Policlino Paolo Giaccone, Università Degli Studi Di Palermo, Terapia Intensiva Polivalente: Dr Andrea Cortegiani, Dr Mariachiara Ippolito, Dr Davide Bellina, Dr Andrea Di Guardo. Regina Elena National Cancer Institute of Rome, Anesthesia and Intensive Care Department: Dr Lorella Pelagalli, Dr Marco Covotta. Sant'andrea Hospital Sapienza University of Rome, Department of Medical And Surgical Science And Translational Medicine Intensive Care Unit: Dr Monica Rocco, Dr Silvia Fiorelli. University Hospital O.O.R.R., Department of Anesthesia And Intensive Care: Prof Antonella Cotoia, Dr Anna Chiara Rizzo.

Poland

National Coordinator: Dr Adam Mikstacki

Participating ICUs: Hospital In Puszczykowo, Poznan University of Medical Sciences, Department of Anaesthesiology and Intensive Therapy: Dr Adam Mikstacki, Dr Barbara Tamowicz. 10 Wojskowy Szpital Kliniczny, Oddzial Kliniczny Anestezjologii I Intensywnej Terapii: Dr Irmina Kaptur Komorowska, Dr Anna Szczesniak. Szpital Wojewodzki W Opolu, Oddzial Anestezjologii I Intensywnej Terapii: Dr Jozef Bojko, Dr Anna Kotkowska. Uck Wum, Oddzial Intensywnej Terapii (Icu): Dr Paulina Walczak-Wieteska, Dr Dominika Wasowska. Wojewodzki Szpital Zespolony, Oddzial Anestezjologii I Intensywnej Terapii: Dr Tomasz Nowakowski, Dr Hanna Broda. Wss Im. Wl. Bieganskiego, Oddzial Anestezjologii I Intensywnej Terapii - Osrodek Pozaustrojowych Technik Wspomagania Czynnosci Nerek I Wątroby: Prof Assoc Mariusz Peichota, Dr Iwona Pietraszek-Grzywaczewska.

Republic Of Ireland

National Coordinator: Prof Ignacio Martin-Loeches

Participating ICUs: St Jame's Hospital, Intensive Care Unit: Prof Ignacio Martin-Loeches, Dr Alessandra Bisanti.

Portugal

National Coordinator: Prof. José Artur Paiva

Scientific Committee: Prof. Pedro Póvoa

Participating Icus: Centro Hospitalar Medio Tejo - Unidade Abrantes, Ucip: Dr Nuno Cartoze, Dr Tiago Pereira. Centro Hospitalar Universitário do Porto, Sci 1: Dr Nádia Guimarães, Dr Madalena Alves. Centro Hospitalar Vila Nova De Gaia/Espinho, Unidade De Cuidados Intensivos Polivalente: Dr Ana Josefina Pinheiro Marques, Dr Ana Rios Pinto. CHUA Faro, Smi-1 : Dr Andriy Krystopchuk, Dr Ana Teresa. Hospital De Cascais Dr Jose De Almeida, Unidade de Cuidados Intensivos: Dr António Manuel Pereira de Figueiredo, Dr Isabel Botelho. Hospital Curry Cabral, Intensive Care Medicine Department: Dr Tiago Duarte. Hospital Sao Francisco Xavier, CHLO, Unidade De Cuidados Intensivos Polivalente: Dr Vasco Costa, Dr Rui Pedro Cunha. Hospital Pedro Hispano, Serviço De Medicina Intensiva: Dr Elena Molinos, Dr Tito da Costa. CHULC, Hospital Sao José, Unidade de Urgência Médica: Dr Sara Ledo, Dr Joana Queiró. ULS Litoral Alentejano, Serviço de Medicina Intensiva: Dr Dulce Pascoalinho. ULS Nordeste, Unidade de Cuidados Intensivost: Dr Cristina Nunes. ULSAM, UCI: Dr José Pedro Moura, Dr Énio Pereira. ULS Baixo Alentejo, Unidade Cuidados Intensivos Polivalente: Dr António Carvalho Mendes.

Romania

National Coordinator: Dr Liana Valeanu

Participating ICUs: Emergency Institute for Cardiovascular Diseases Prof. Dr. C. C. Iliescu, 1st Anesthesia and Intensive Care Department: Dr Liana Valeanu, Prof Serban Bubenek-Turconi. Clinical Emergency Hospital Bucharest, Anesthesia and Intensive Care Department: Prof Ioana Marina Grintescu, Dr Cristian Cobilinschi. Emergency Institute for Cardiovascular Diseases Prof. Dr. C. C. Iliescu, 2nd Anesthesia and Intensive Care Department: Prof Daniela Carmen Filipescu, Dr Cornelia Elena Predoi. Fundeni Clinical Institute, 3rd Department of Anesthesia and Intensive Care: Prof Dana Tomescu, Dr Mihai Popescu, Dr Alexandra Marcu. University Of Medicine and Pharmacy "Grigore T Popa", Anesthesia and Intensive Care Department: Prof Ioana Grigoras, Dr Olguta Lungu.

Russian Federation

National Coordinator: Prof. Alexey Gritsan

Participating ICUs: V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk Regional Clinical Hospital, Dep. Anaesthesiology and Intensive Care #3: Prof Alexey Gritsan. City Clinical N.I.Pirogov Hospital, Clinical Pharmacology: Dr Anastasia Anderzhanova, Dr Yulia Meleshkina. City Clinical N.I.Pirogov Hospital, Icu: Dr Marat Magomedov. E.A. Vagner Perm State Medical University, Intensive Care Unit: Prof Nadezhda Zubareva, Dr Maksim Tribulev. Krasnoyarsk Regional Clinical Hospital, Dep. Anaesthesiology and Intensive Care #3: Dr Denis Gaigolnik. Petrovsky National Research Centre of Surgery, Intensive Care: Dr Aleksandr Eremenko, Dr Natala Vistovskaya, Dr Maria Chukina. Privolzhskiy District Medical Center, Department Anesthesiology and Intensive Care: Dr Vladislav Belskiy, Dr Mikhail Furman.

Spain

National Coordinator: Dr. Ricard Ferrer Rocca

Participating ICUs: Vall D'herbon, Intensive Care Medicine: Dr Ricard Ferrer Rocca, Dr Maria Martinez, Dr Vanessa Casares. Hospital Clinic De Barcelona, Surgical Icu: Dr Ricard Mellado Artigas. Hospital De La Santa Creu I Sant Pau, Intensive Care Unit : Dr Paula Vera, Dr Matias Flores. Hospital De Terrassa, Medicina Intensiva: Dr Joaquin Amador Amerigo. Hospital Del Mar, Critical Care Unit: Dr Maria Pilar Gracia Arnillas, Dr Rosana Munoz Bermudez. Hospital Germans Trias I Pujol, Critical Care Unit: Prof, Dr Fernando Armestar, Dr Beatriz Catalan, Dr Regina Roig, Dr Laura Raguer, Dr María Dolores Quesada. Hospital Parc Tauli, Icu: Dr Emilio Diaz Santos, Dr Gemma Gomà. Hospital Punta De Europa, Intensive Care Unit : Dr Alejandro Ubeda, Dra Maria Salgado. Hospital Universitario Central De Asturia, Uci-Huca: Dr Lorena Forcelledo Espina, Dr Emilio Garcia Prieto. Hospital Universitario La Paz, Intensive Care Unit, Servicio De Medicina Intensiva: Dra Mj Asensio, Dra M. Rodriguez. Hospital Universitario La Paz, Surgical Critical Care Unit : Dr Emilio Maseda, Dr Alejandro Suarez De La Rica. Hospital Universitarion Son Espases, Unidad De Cuidados Intensivos: Dr J Ignacio Ayestaran, Dr Mariana Novo. University Hospital Severo Ochoa, Intensive Care Unit: Dr Miguel Angel Blasco-Navalpotro, Dr Alberto Orejas Gallego.

Sweden

National Coordinator: Dr Fredrik Sjovall

Participating ICUs: Skane University Hospital, Intensive- And Perioperative Care: Dr Fredrik Sjövall, Dr Dzana Spahic. Ostra Sjukhuset Sahlgrenska University Hospital, Anopiva: Dr Carl Johan Svensson. Umeå University, Anesthesiology and Intensive Care Medicine, Surgical and Perioperative Sciences: Dr Michael Haney, Dr Alicia Edin. Universitetssjukhuset I Linkoping, Anopiva: Dr Joyce Åkerlund, Dr Lina De Geer.

Switzerland

National Coordinator: Dr. Josef Prazak

Scientific Committee: Dr. Niccolò Buetti

Participating ICUs: Inselspital, Bern University Hospital, Department of Intensive Care Medicine: Dr Josef Prazak, Dr Stephan Jakob. Chuv, Service De Médecine Intensive Adulte : Dr Jl Pagani, Mrs S Abed-Maillard.

Turkey

National Coordinator: Prof. Murat Akova, Dr. Abdullah Tarık Aslan

Participating ICUs: Hacettepe University of Faculty of Medicine, Intensive Care Unit(ICU): Dr Murat Akova, Dr Abdullah Tarik Aslan, Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Department of Anesthesiology: Dr Arif Timuroglu. Acibadem Fulya Hospital, Infectious Diseases: Dr Sesin Kocagoz, Dr Hulya Kusoglu. Acibadem Kadikoy Hospital, ICU: Dr Selcuk Mehtap, Dr Solakoğlu Ceyhun. Ankara University Faculty Medicine Ibni Sina Hospital, Medical ICU: Prof. Dr. Neriman Defne Altintas, Dr Leyla Talan. Ankara Yildirim Beyazit University, Ankara City Hospital, Infectious Diseases and Clinical Microbiology: Dr Bircan Kayaaslan, Dr Ayşe Kaya Kalem. Aydin Adnan Menderes University Research Hospital, Anesthesia and Reanimation ICU: Prof. Dr. Ibrahim Kurt, Dr (Professor) Murat Telli, Dr (Associate Professor) Barcin Ozturk. Baskent University Hospital, Infectious Diseases and Clinical Microbiology: Dr Çiğdem Erol. Bitlis Goverment Central Hospital, Bitlis Icu: Dr Emine Kubra Dindar Demiray, Dr Sait Çolak. Duzce University Hospital, Medical ICU: Dr Türkay Akbas. Erciyes University, ICU: Prof. Dr. Kursat Gundogan, Dr Ali Sari. Fatih Sultan Mehmet Research and Training Hospital, Infection Diseases: Dr Canan Agalar, Dr Onur Çolak. Hitit University Erol Olcok Education and Research Hospital, Infectious Diseases and Clinical Microbiology: Prof. Dr. Nurcan (N) Baykam, Assistant Prof. Dr Ozlem (O) Akdogan. Istanbul Medipol University, Kosuyolu Hospital, Infectious Diseases and Clinical Microbiology: Dr Mesut Yilmaz, Dr Burcu Tunay, Dr Rumeysa Cakmak. Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Sadi Sun ICU: Prof.Dr. Nese Saltoglu, Ass Prof.Dr. Ridvan Karaali. Karadeniz Technical University Faculty of Medicine, Infectious Disease and Clinical Microbiology: Prof Dr. Iftihar Koksal, Assist. Prof. Firdevs Aksoy. Karadeniz Technical University Farabi Hospital, Anesthesia ICU 1: Dr Ahmet Eroglu. Kartal Dr. Lutfi Kirdar Training and Research Hospital, ICU: Dr Kemal Tolga Saracoglu, Dr Yeliz Bilir. Kayseri City Hospital, ICU: Dr Seda Guzeldag. Mersin University Hospital, Department of Infectious Diseases and Clinical Microbiology: Dr Gulden Ersoz, Dr Guliz Evik. Pamukkale Univ, Anesthesiology and Reanimation: Prof Hulya Sungurtekin, Dr Cansu Ozgen. School Of Medicine, Medipol Mega University Hospitals Complex, Department of Anesthesiology and Reanimation: Dr Cem Erdoğan. University of Health Sciences Diskapi Yildirim Beyazit Training and Research Hospital, The Department of Infectious Diseases and Clinical Microbiology and ICU: Dr Yunus Gürbüz, Dr Nilgün Altin. Turgut Ozal Medical Center, Department of Infectious Diseases and Clinical Microbiology: Dr Yasar Bayindir, Dr Yasemin Ersoy. University of Health Sciences Istanbul Umraniye Training and Research Hospital, Anaestesia and Reanimation: Dr Senay Goksu, Dr Ahmet Akyol. University of Health Sciences, Kartal Dr. Lutfi Kirdar Training and Research Hospital, Infectious Diseases and Clinical Microbiology: Prof Ayse Batirel, Dr Sabahat Cagan Aktas.

The United Kingdom

National Coordinator: Dr. Andrew Conway Morris

Participating ICUs: Addenbrookes Hospital, John V Farman Intensive Care Unit: Dr Andrew Conway Morris, Dr Matthew Routledge. Addenbrookes Hospital, Neurocritical Care Unit (NCCU): Dr Andrew Conway Morris, Dr Ari Ercole. Charing Cross Hospital - Imperial College NHS Trust, Intensive Care Unit, Level 11: Dr David Antcliffe, Ms Roceld Rojo. Countess Of Chester Foundation Trust, Intensive Care Unit: Dr Kate Tizard, Dr Maria Faulkner. Darlington Memorial Hospital Intensive Care Unit, County Durham and Darlington NHS Foundation Trust: Dr Amanda Cowton, Dr Melanie Kent. Croydon University Hospital, Critical Care Unit: Dr Ashok Raj, Dr Artemis Zormpa, Dr George Tinaslanidis, Mrs Reena Khade. Department Of Anaesthetics and Intensive Care Medicine, Queen Elizabeth Hospital Birmingham: Dr Tomasz Torlinski, Dr Randeep Mulhi, Dr Shraddha Goyal, Dr Manan Bajaj, Dr Marina Soltan, Dr Aimee Yonan, Dr Rachael Dolan. Department Of Microbiology, Queen Elizabeth Hospital Birmingham: Dr Aimee Johnson. Freeman Hospital, ICCU 37: Dr Caroline Macfie, Dr James Lennard. Hammersmith Hospital - Imperial College NHS Trust, Intensive Care Unit, Level 11: Ms Maie Templeton, Ms Sonia Sousa Arias. James Cook University Hospital, Icu2/3: Dr Uwe Franke, Mr Keith Hugill. Medway Maritime Hospital, Intensive Care Unit: Mrs Hollie Angell. Ninewells Hospital and Medical School NHS Tayside, Intensive Care Unit: Dr Benjamin J Parcell, Dr Katherine Cobb, Dr Stephen Cole. North Cumbria University Hospitals NHS Trust, North Cumbria University Hospitals NHS Trust: Dr Tim Smith, Dr Clive Graham. North Manchester General Hospital, Critical Care Ward: Dr Jaroslav Cerman, Dr Allison Keegan. Queen Elizabeth Hospital, Gateshead Health NHS Foundation Trust, Critical Care Department: Mrs Jenny Ritzema, Mrs Amanda Sanderson. Queen Elizabeth Hospital, Lewisham and Greenwich NHS Trust, Critical Care Unit: Dr Ashraf Roshdy. Royal Gwent Hospital, Critical Care Unit: Dr Tamas Szakmany, Dr Tom Baumer. Royal London Hospital, Adult Critical Care Unit: Dr Rebecca Longbottom, Dr Daniel Hall. Royal Marsden NHS Foundation Trust, Critical Care Unit: Dr Kate Tatham, Dr S Loftus, Dr A Husain, Dr E Black, Dr S Jhanji, Dr R Rao Baikady. Royal Victoria Hospital, Belfast, Regional Intensive Care Unit: Dr Peter Mcguigan, Dr Rachel Mckee. Sandwell And West Birmingham Hospitals NHS Trust, Intensive Care Unit: Dr Santhana Kannan, Dr Supriya Antrolikar, Dr Nicholas Marsden. St Mary's Hospital - Imperial College NHS Trust, Intensive Care Unit, Level 11: Dr Valentina Della Torre, Ms Dorota Banach. Stepping Hill Hospital, Stepping Hill ICU: Dr Ahmed Zaki, Dr Matthew Jackson. University Hospitals of North Midlands, Critical Care Unit: Dr Moses Chikungwa. Warwick Hospital, Intensive Care Unit: Dr Ben Attwood, Dr Jamie Patel. West Suffolk NHS Foundation Trust, Critical Care: Dr Rebecca E Tilley, Miss Sally K Humphreys. Wirral University Teaching Hospital, Intensive Care Unit: Dr Paul Jean Renaud.

Ukraine

Participating ICUs: Kharkiv Clinical Infectious Diseases Hospital, Intensive Care: Prof Anton Sokhan, Dr Yaroslava Burma.

North America

Canada

National Coordinator: Prof. Wendy Sligl

Participating ICUs: University of Alberta Hospital, General Systems Intensive Care Unit (Gsicu): Dr Wendy Sligl, Nadia Baig, Lorena McCoshen. Royal Alexandra Hospital, General Systems Intensive Care Unit (Gsicu): Dr Demetrios J Kutsogiannis, Dr Wendy Sligl, Patricia Thompson, Tayne Hewer.

South Asia

Bangladesh

National Coordinator: Dr Raihan Rabbani

Participating ICUs: General Icu, Dhaka: Dr Raihan Rabbani, Dr Shihan Mahmud Redwanul Huq. Asgar Ali Hospital, Critical Care Medicine: Dr Rajib Hasan, Dr Mohammad Motiul Islam.

India

National Coordinator: Prof. Mohan Gurjar

Participating ICUs: Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, Department of Critical Care Medicine: Dr Mohan Gurjar, Dr Arvind Baronia. All India Institute of Medical Sciences (AIIMS) Jodhpur, Department of Anaesthesiology & Critical Care Medicine: Dr Nikhil Kothari, Dr Ankur Sharma. All India Institute of Medical Sciences (AIIMS), Pulmonary Medicine ICU, Department of Pulmonary Medicine: Dr Saurabh Karmakar, Dr Priya Sharma. Breach Candy Hospital Trust, SICU: Dr Janardan Nimbolkar, Dr Pratit Samdani. Cauvery Heart And Multi-Speciality Hospital, MICU: Dr Vaidyanathan R, Dr Noor Ahmedi Rubina. CHL Hospitals, Dept of Critical Care Services: Dr Nikhilesh Jain, Dr Madhumati Pahuja. Indira Gandhi Institute of Medical Sciences, Trauma & Emergency: Dr Ritu Singh, Dr Saurav Shekhar. King George's Medical University, Department of Critical Care Medicine: Dr Syed Nabeel Muzaffar, Dr Ahmad Ozair, Dr Suhail Sarwar Siddiqui. Medica Superspecialty Hospital, Medica Institute of Critical Care: Dr Payel Bose, Dr Avijatri Datta. Sir H N Reliance Foundation Hospital, Critical Care Unit: Dr Darshana Rathod, Dr Mayur Patel. Sri Ramachandra Institute of Higher Education and Research, Department of Critical Care Medicine: Prof MK Renuka, Dr Sailaja K Baby. St Johns Medical College Hospital, Department of Critical Care Medicine, MICU: Dr Carol Dsilva, Dr Jagadish Chandran. Tata Medical Center, Critical Care Medicine: Dr Pralay Ghosh, Dr Sudipta Mukherjee. Yashoda Hospital, Somajiguda, Hyderabad: Dr Kaladhar Sheshala, Dr Krushna Chandra Misra.

Sub-Saharan Africa

Nigeria

National Coordinator: Dr. Oyebola O. Adekola

Participating ICUs: Ahmadu Bello University Teaching Hospital Shika Zaria Abuth Zari, Icu Abuth Zaria: Dr Saidu Yusuf Yakubu, Dr Euphemia Mgbosoro Ugwu. Lagos University Teaching Hospital, Department of Anaesthesia And Intensive Care: Dr John (O) Olatosi, Dr Ibironke Desalu. One Life Hospital, One Life Intensive Care Unit: Dr Gabriel Asiyanbi, Dr Motunrayo Oladimeji. University College Hospital, Anaesthesia: Dr Olusola Idowu, Dr Fowotade Adeola.

South Africa

National Coordinator: Prof. Mervyn Mer

Participating ICUs: Charlotte Maxeke Johannesburg Academic Hospital, Ward 576: Prof Mervyn Mer, Mrs Melanie Mc Cree.

Sudan

National Coordinator: Dr. Bashir El Sanousi

*Participating ICUs:*Al-Rajhi Hospital, Medicine: Dr Ali Adil Ali Karar. East Nile Hospital, Intensive Care Unit: Dr Elfayadh Saidahmed, Dr Hytham K.S. Hamid.

References

[1] Center for disease control and prevention C. Carbapenem-resistant Enterobacterales (CRE): CRE Technical Information, https://www.cdc.gov/hai/organisms/cre/technical-info.html#Definition; 2019 [accessed 22/12/2021.

[2] Blakely TA, Woodward AJ. Ecological effects in multi-level studies. J Epidemiol Community Health 2000;54(5):367-74

[3] Massart N, Maxime V, Fillatre P, Razazi K, Ferre A, Moine P, et al. Characteristics and prognosis of bloodstream infection in patients with COVID-19 admitted in the ICU: an ancillary study of the COVID-ICU study. Ann Intensive Care 2021;11(1):183

[4] Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. Journal of the American statistical association 1999;94(446):496-509