Electronic Supplementary Material

Blot S, et al. Epidemiology of Intra-Abdominal Infection and Sepsis in Critically Ill Patients: "AbSeS", a Multinational Observational Cohort Study and ESICM Trials Group Project.

Supplement–1

Methods – full version

AbSeS was an international, multicenter, prospective observational cohort study conducted between January and December 2016. Consecutive, adult ICU patients diagnosed with intra-abdominal infection, either as primary diagnosis leading to ICU admission or as a complication occurring during the ICU course, were eligible for inclusion. To limit a center effect, a maximum of 15 cases per ICU could be included. ICUs voluntarily participated following an invitational mail within the European Society of Intensive Care Medicine (ESICM) network. Overall, approval by established national, regional or local institutional review boards was expedited and granted. The study is registered at ClinicalTrials.gov (number NCT03270345).

Procedures

Local investigators were supported by national representatives and through the study webpage (https://www.esicm.org/research/trials/trials-group-2/abses/) that provided key information, including the protocol. All data is collected by local site investigators and entered onto a secure internet-based electronic platform licensed from CLINFILE© [www.clinfile.com].

We obtained data describing the hospital and intensive care facility through a center report form. Anonymous patient data were collected through the case report form. Examples of the center and case report forms are in Supplement-2. During the study period participants were able to contact the principal investigator or the ESICM research office for any queries.

Data recorded and definitions

Demographics included age, sex, weight and length. Admission data included admission source, type of admission (medical, elective or emergency surgery, or trauma), primary and secondary diagnoses, underlying conditions and lifestyle risk factors. Severity of acute illness at ICU admission was assessed by the Simplified Acute Physiology Score (SAPS) II [1]. Type of intra-abdominal infection was defined according to the International Sepsis Forum Consensus Conference Definitions [2]. Intra-abdominal infections were classified according to setting of infection acquisition, anatomical barrier disruption, and severity of disease expression [3]. Setting is community-acquired, healthcare-associated and/or early-onset hospital-acquired (≤7 days of hospital admission), or late-onset hospital acquired (>7 days of hospital admission[4]). Healthcare-associated onset is defined by at least one of the following risk factors for multidrug

resistant pathogens: nursing home resident, out-of-hospital parenteral nutrition or vascular access, chronic dialysis, recent hospital admission (<6 months), or recent antimicrobial therapy (<6 months). Setting of infection acquisition is based on the assumed stepwise increased risk for the involvement of multidrug resistant pathogens. Compared to community-onset, patients with recent healthcare exposure (e.g., nursing home residents) are presumed to be at moderately increased risk for multidrug resistance, as do patients with early-onset hospital-acquired infection. Patients with late-onset hospital-acquired infection on the other hand, are considered at high risk for multidrug resistance. For convenience sake 'healthcare-associated and/or early-onset hospital-acquired' cases are designated 'early-onset hospital-acquired'. Intra-abdominal infections were classified as either without anatomical disruption, or with anatomical disruption resulting in localized or diffuse peritonitis (i.e. contamination spread to entire abdominal cavity). Severity of disease expression is defined as either infection, sepsis or septic shock, the latter two based on the sepsis-3 definitions [5]. The original study protocol was developed before the publication of the sepsis-3 definitions, but the CRF was detailed enough to allow transition to these recent definitions based on associated Sequential Organ Failure Assessment (SOFA) scores [6] and serum lactate values. Microbiological assessment was left at the discretion of the physician. Eligible cultures included intra-operative cultures, trans-abdominal fine-needle aspiration, blood cultures presumably related to the intra-abdominal infection, and cultures from abdominal drains sampled ≤24 hours post-surgery. A micro-organism-specific antibiogram could be completed through a dropdown menu. Thresholds for resistance were those as reported by The European Committee on Antimicrobial Susceptibility Testing (EUCAST)[7]. Antimicrobial resistance was defined as methicillin-resistance for *Staphylococcus aureus*, vancomycin-resistance for enterococci, and for Gram-negative bacteria either production of extended-spectrum beta-lactamase (ESBL), carbapenem-resistance, or fluoroquinolone-resistance (resistance against ciprofloxacin, levofloxacin, or moxifloxacin). To assess relationships between resistance and mortality we also used the definition of "difficult-to-treat" resistance for Gram-negative bacteria. This combines resistance to all tested carbapenem, beta-lactam, and fluoroquinolone agents [8]. We deviated from this definition however, by using ESBL-production as a proxy for resistance against penicillins, cephalosporins and monobactams. For reporting microbiological results, the number of patients with cultures sampled is used as denominator. Data on anti-infective management included antimicrobial therapy and source control. Antimicrobial coverage of empiric therapy was evaluated for basic coverage (i.e. coverage of Gram-positive, Gram-negative, and anaerobic bacteria), and the association of an antimicrobial agent or initial choice with potential clinical activity against *Pseudomonas aeruginosa*, methicillin-resistant *S. aureus* (MRSA), enterococci,

vancomycin-resistant enterococci (VRE), and *Candida*. In this regard, coverage of enterococci targets *Enterococcus faecalis* [9]. Outcome data included source control assessment 7 days post-diagnosis or earlier if the patient died within that time window. Source control was judged as either successful or having failed. Failure represented either persistent inflammation (clinical evidence of a remaining source of infection) or the necessity of re-intervention following the initial approach (conservative management or source control intervention). Main outcome is ICU mortality with a minimum of 28 days of observation.

Data management, study power & statistical analyses

Investigators were contacted when essential data was missing or in case of conflicting data input. Missing, extreme or implausible values were sent back to the study-ICU investigators for review. Where data remained questionable, the primary author (S.B.) made a final adjudication about study inclusion in agreement with the senior author (D.V.). Essential data needed to keep cases in the database included type of intra-abdominal infection, onset of infection, data on anatomical disruption, severity of disease expression, and microbiology or mortality.

For a risk factor with 15% prevalence in the study cohort (for example Pseudomonas involvement), a sample size of 1500 patients is required (alpha=0.05; Beta>0.80) for an outcome difference of 10% (45% vs. 35% mortality) to be statistically significant.

According to EPIC2 study 10.1% of critically patients experience an abdominal infection during their ICU stay. Assuming that an average of 200 patients are admitted to an ICU during the 6 month study period, 20 patients are likely to present with abdominal sepsis. Therefore, the maximum number of inclusions (n=15) must be achievable in the majority of centres and the collaboration of 100 ICUs might, mathematically, be appropriate. Notwithstanding, we aim to include 150 ICUs as we anticipate that patient inclusion will be suboptimal in half of the participating centres (75 ICUs including 15 cases + 75 ICUs including 8 cases = 1725 cases), and that approximately a 10% proportion of cases (n=175) will be excluded because of missing data in the e-CRFs. This adds to the following estimate:

- 75 ICUs including the maximum number of cases (n=15):		1125 cases
- 75 ICUs including suboptimal (8 cases/unit):		600 cases
	Subtotal:	**1725 cases**
- Minus 10% excluded for incomplete data:		-175 cases
	Total:	**1550 cases**

Simple descriptive statistics were used to characterize the study population, continuous data was summarized by median and interquartile range, categorical data as n (%). To assess relationships with mortality we used a logistic regression analysis with the logit link function. The performance of the models are assessed by plotting the receiver-operator characteristic (ROC) curve [10], computing the sensitivity and specificity, and calculating the area under the curve. A ROC curve is a performance measure for classification problems at various thresholds settings; as it is a probability curve, the area under the curve (AUC) represents the degree or measure of separability, which indicates the extent to which the model is capable of distinguishing classes. Therefore we split the cohort in a 4:1 random training and test data set. The model is fit (trained) using the training data set and then assessed by applying the model to the test data set. Feature selection and final fit is done through a stepwise forward and backward approach, depending on the Akaike Information Criterion (AIC) value (dropping and adding variables that lead to the smallest AIC) [11]. Results of the logistic regression analyses are reported as odds ratio (OR) and 95% confidence intervals (CI). Variables considered for the logistic regression model included origin of infection acquisition, anatomical disruption, severity of disease expression, type of intra-abdominal infection, time till intervention, source control achievement at day 7, multidrug resistance, *Candida* involvement, enterococcal involvement, aspects of antimicrobial coverage, age, sex, underlying conditions, length of ICU stay, and geographic region. These variables were included irrespective of their relationship with mortality in univariate analysis. It can be considered inappropriate to include 'source control achievement at day 7' in the model as this covariate is instrumental to the biological pathway between infection onset and mortality. Therefore we report a logistic regression model with and without source control achievement.

References.

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Supplement–2
Center Report Form

To be filled out prior to patient inclusion

Institution (name): ……

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

Hospital capacity: __ __ __ __ beds

Type of ICU: ☐ Closed ☐ Open (non-ICU doctors may write orders)

ICU beds: __ __ __ beds

Number of patients admitted to the ICU in 2014 (approximately): __ __ __ __ __ patients

ICU speciality:

Surgical: ☐ cardiac ☐ non-cardiac ☐ transplantation
☐ mixed ☐ burns ☐ trauma

Medical ☐ coronary ☐ neurologic ☐ respiratory ☐ mixed

Mixed medical / surgical ☐

Other ☐

Availability of an infectious diseases specialist ☐ no
☐ consultant only
☐ an ICU clinician is qualified in ID

Availability of a general surgical team ☐ no
☐ only in hospital during day time
☐ in hospital day and night

Availability of an antibiotic policy committee ☐ yes ☐ no

Availability of written recommendations on peri-operative antimicrobial prophylaxis ☐ yes ☐ no

Case Report Form

Inclusion Criteria:

☐ **Adult** patient (≥18 years of age)

☐ **Hospitalized in an ICU**. The abdominal sepsis can be either the principal diagnosis leading to ICU admission or a complication during the ICU course. Abdominal sepsis may be either community- or healthcare-associated.

☐ **Infection of abdominal origin** (one of the following):

- ☐ Primary peritonitis
- ☐ Secondary peritonitis
- ☐ Tertiary peritonitis
- ☐ Peritoneal dialysis-related peritonitis
- ☐ Intra-abdominal abscess
- ☐ Biliary tract infection
- ☐ Pancreatic infection
- ☐ Typhlitis
- ☐ Toxic megacolon

Section 1 – Demographics
Date of birth (day/month/year): ___

Age (years): _____ (18 – 100 yrs)

Gender: ☐ Male ☐ Female

Weight (kg): _____ (30 – 180kg) measured ☐ estimated ☐
Height (m): _____ (1.30 – 2.20m) measured ☐ estimated ☐

Section 2 – Admission data

2.1. Date of hospital admission (day/month/year): __ ___ ____
2.2. Date of ICU admission (day/month/year): __ ___ ____
2.3. Admission source:
- ☐ other acute care hospital
  admission date referring centre (day/month/year): __ ___ ____
- ☐ emergency room
- ☐ operating room
- ☐ general ward
- ☐ other

2.4. Type of admission:
- ☐ medical
- ☐ surgical
  - ☐ elective
  - ☐ emergency
- ☐ burns
- ☐ trauma

2.5. Primary and secondary diagnoses
Principal diagnosis leading to ICU admission (only 1, see codes list):
__ __ __
Secondary diagnoses; present prior to or at the day of abdominal infection (max. 3, see codes list):
__ __ __

— — —
— — —

Description: The acute disease should be recorded for all patients, independent of the surgical status. It is the acute (or acute on chronic) disease that best explains the reason(s) for admission. It can be medical or surgical. Only one choice is possible for the primary diagnosis. Up to three secondary diagnoses can be reported on the case report form.

2.6. Underlying conditions (possible to calculate Charlson Comorbidity Index, J Chron Dis 1987)

- ☐ chronic pulmonary disease
  - ☐ COPD (GOLD stage III or IV)
  - ☐ other
- ☐ AIDS (not just HIV positive)
- ☐ malignancy
  - ☐ cancer (solid tumor)
  - ☐ metastatic cancer
  - ☐ hematologic cancer
- ☐ neurological disease
  - ☐ cerebrovascular disease
  - ☐ dementia
  - ☐ hemiplegia
- ☐ peptic ulcer disease
- ☐ liver disease
  - ☐ portal hypertension
  - ☐ hepatic cirrhosis

Modified Child-Pugh classification:

Ascites:	☐ none	☐ mild	☐ moderate/severe
Encephalopathy:	☐ none	☐ mild	☐ moderate/severe
Bilirubin (µmol/L):	☐ <34	☐ 35-50	☐ >50
or bilirubin (mg/dL):	☐ <2.0	☐ 2.0-2.9	☐ >2.9
Albumin (g/L):	☐ >35	☐ 28-35	☐ <28
Prothrombin time (seconds over normal)	☐ <4	☐ 4-6	☐ >6

- ☐ chronic renal failure
  - ☐ mild: GFR ≥60 mL/min.
  - ☐ moderate: GFR 30 – 59 mL/min.
  - ☐ severe: GFR 15 – 29 mL/min.
  - ☐ end-stage: GFR <15 mL/min. or requiring renal replacement therapy
- ☐ myocardial infarction (history, not ECG changes only)
- ☐ congestive heart failure
- ☐ chronic heart failure (NY Heart Association class IV)
- ☐ peripheral vascular disease
- ☐ diabetes mellitus
  - ☐ without end-organ damage (excludes diet controlled alone)
  - ☐ with end-organ damage (retinopathy, neuropathy, nephropathy, brittle diabetes)
- ☐ immunosuppressed status (check all that apply)
  - ☐ neutropenia (<1000 neutrophils/mm^3)
  - ☐ corticosteroid therapy (prednisolone or equivalent >0.5 mg/kg/day for >3 months)
  - ☐ chemotherapy within one year
  - ☐ radiotherapy within one year
  - ☐ bone marrow recipient
  - ☐ solid organ transplant recipient
  - ☐ immunosuppressive drug for auto-immune diseases
  - ☐ congenital immunodeficiency
- ☐ connective tissue disease
- ☐ life style risk factors
  - ☐ malnutrition (BMI<18)
  - ☐ obesity (BMI>30)
  - ☐ tobacco use (>20 pack years)
  - ☐ alcohol abuse (>1L of wine /day or equivalent = 10g alcohol day)
  - ☐ IV drug abuse

2.7. Severity of acute illness at ICU admission (SAPS II-score, JAMA 1993)

Heart rate (bpm)
☐ <40 (11 points) ☐ 40-69 (2 points) ☐ 70-119 (0 points) ☐ 120-159 (4 points) ☐ ≥160 (7 points)

Core body temperature (min.) __ __ . __ (max.) __ __ . __ °C
☐ <39°C (0 points) ☐ ≥39°C (3 points) or ☐ <102.2°F (0 points) ☐ ≥102.2°F (3 points)

Therapeutic hypothermia ☐ yes ☐ no

Systolic blood pressure (mmHg)
☐ <70 (13 points) ☐ 70-99 (5 points) ☐ 100-199 (0 points) ☐ ≥200 (2 points)

Mechanical ventilation ☐ yes ☐ no
Non-invasive ventilation ☐ yes ☐ no
PaO_2/FiO_2
☐ <100 (11 points) ☐ 100-199 (9 points) ☐ ≥200 (6 points)
Count points only IF on mechanical ventilation (invasive or non-invasive).

Blood urea (mg/dL) ☐ <0.6 (0 points) ☐ 6 – 1.79 (6 points) ☐ ≥1.80 (10 points)
or (mmol/L) ☐ <10 (0 points) ☐ 10 – 29.9 (6 points) ☐ ≥30 (10 points)
or BUN (mg/dL) ☐ <28 (0 points) ☐ 28 - 83 (6 points) ☐ ≥84 (10 points)

Leucocytes (cells/mcL) (min.) __ __ __ (range 300-40000) (max.) __ __ __ (range 300-40000)
☐ <1000 (12 points) ☐ 1000-19000 (0 points) ☐ ≥20000 (3 points)

Urine output (mL/24hours)
☐ <500 (11 points) ☐ 500 - 1000 (4 points) ☐ >1000 (0 points)

Serum potassium (mEq/L)
☐ <3 (3 points) ☐ 3 – 4.9 (0 points) ☐ ≥5 (3 points)

Serum sodium (mEq/L)
☐ >144 (1 points) ☐ 125 - 144 (0 points) ☐ <125 (5 points)

Total bilirubin (indicate max. value)
mg/dL ☐ <4 (0 points) ☐ 4 – 5.9 (4 points) ☐ ≥6 (9 points)
or µmol/L ☐ <68.4 (0 points) ☐ 68.4 – 102.5 (4 points) ☐ ≥102.6 (9 points)

Serum bicarbonate (mEq/L)(indicate min. value)
☐ <15 (6 points) ☐ 15 - 19 (3 points) ☐ ≥20 (0 points)

Glasgow Coma Score __ __ (range 3 – 15) (effective if not sedated, estimated if sedated)
☐ <6 (26 points) ☐ 6 - 8 (13 points) ☐ 9 - 10 (7 points) ☐ 11 - 13 (5 points) ☐ 14 - 15 (0 points)

2.8 Miscellaneous risk factors – information required to determine community or healthcare-associated onset of sepsis (check all that apply)

- ☐ Nursing home resident
- ☐ Out of hospital parenteral nutrition or vascular access
- ☐ Chronic dialysis
- ☐ Hospital admission in the past 6 months
- ☐ Antibiotic therapy in the past 6 months

Section 3 - Diagnosis of abdominal infection

Date of diagnosis (day/month/year): __ ___ ____
Time of diagnosis (hh:mn ; use 24 hrs clock): ___ : ___ (for the time of diagnosis, indicate the time of clinical suspicion of IAI.)
Time of puncture / surgical intervention (if any) (hh:mn ; use 24 hrs clock): ___ : ___

3.1. Diagnostic tools (check all that apply; specific microbiological investigation is mentioned later on, section…)

- ☐ Clinical investigation (palpation, auscultation)
- ☐ Abdominal ultrasound
- ☐ Abdominal CT-scan
- ☐ Diagnostic peritoneal lavage
- ☐ Puncture / trans-abdominal fine-needle aspiration
- ☐ Explorative laparoscopy
- ☐ Explorative laparotomy

3.2. Anatomical disruption (check only one)

- ☐ Without perforation
- ☐ Localized peritonitis
  - ☐ upper GI tract perforation (stomach & duodenum)
  - ☐ lower GI tract perforation (jejunum, ileum, colon, rectum)
- ☐ Diffuse peritonitis

3.3. Diagnosis – derived from the International Sepsis Forum Consensus Conference Definitions (Calandra T, et al. Crit Care Med 2005) (check all that apply)

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

☐ Peritoneal dialysis-related peritonitis is defined as microbial infection of the peritoneal fluid in patients treated with peritoneal dialysis, in the absence of indicators for gastrointestinal perforation (high peritoneal fluid leukocyte count, failure to clear with antimicrobials, …).

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

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

☐ Intra-abdominal abscess is a pocket of infected fluid and pus located within the peritoneal space or surrounding structures. There may be more than one abscess.

- ☐ single abscess
- ☐ multiple abscess formation

Location (free text): __ __ __

☐ Biliary tract infection is an acute inflammatory process of the biliary tract or surrounding structures as evidenced by either (i) the isolation of pathogenic microorganisms obtained via percutaneous or direct surgical collection of samples in the lumen of the gall bladder or the biliary tract or the blood, or (ii) surgical or radiographic evidence of suppurative complications.

☐ Pancreatic infection is defined as infection in the pancreas, following acute mostly necrotizing pancreatitis or infection of a structural abnormality such as a pseudocyst (as complication of chronic pancreatitis).

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

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

Section 4 – Microbiology

4.1. Microbiology at time of diagnosis/surgery

4.1.1. Perioperative cultures

- ☐ not applicable, no peri-operative cultures are sampled

☐ check box if patient already received empiric antimicrobial therapy prior to culture sampling

Type of sampling: ☐ histology
☐ swab
☐ peritoneal fluid
☐ peritoneal rinse fluid

Culture results:

…

4.1.2. Trans-abdominal fine-needle aspiration

☐ not applicable, no peri-operative cultures are sampled
☐ check box if patient already received empiric antimicrobial therapy prior to culture sampling

Culture results:

…

4.1.3. Blood cultures

☐ not applicable, no peri-operative cultures are sampled
☐ check box if patient already received empiric antimicrobial therapy prior to culture sampling

Culture results:

…

4.1.4. Cultures sampled from abdominal drains within 24 hrs. post surgery

☐ not applicable, no peri-operative cultures are sampled
☐ check box if patient already received empiric antimicrobial therapy prior to culture sampling

Culture results:

…

4.2. Additional microbiological results during the course of the abdominal infection – Cultures sampled from abdominal drains are not considered

☐ peri-operative (during surgical revision)
Date of culture sampling (day/month/year): __ ___ ____
Culture result: …

☐ trans-abdominal fine-needle aspiration
Date of culture sampling (day/month/year): __ ___ ____
Culture result: …

☐ blood culture
Date of culture sampling (day/month/year): __ ___ ____
Culture result: …

Section 5 – Anti-infective approach

5.1. Antimicrobial therapy

Drug name (generic)	Dose / day	Route (cf. menu)	Date and time of the first dose	Date of the last dose	Type of prescription (cf. menu)
Example 1: ceftazidime	Loading: 2g Maintenance: 6g Enter 8g	2	01/03/2009 13 :00	03/03/2009	2
Example 2: meropenem	Loading: - Maintenance: 4×1g Enter 4g	1	03/03/2009 14 :00	10/03/2009	3
1.			dd/mm/yyyy hh:mn	dd/mm/yyyy	
2.			dd/mm/yyyy	dd/mm/yyyy	

			hh:mn		
3.			dd/mm/yyyy hh:mn	dd/mm/yyyy	

Menu:

Route: (1) intravenous – intermittent;
(2) intravenous – continuous infusion or extended infusion;
(3) oral;
(4) intratracheal;
(5) intramuscular;

Type of prescription
(1) empirical therapy based on sepsis without knowledge of previous colonization;
(2) empirical therapy based on previous patient's colonization;
(3) targeted therapy based on the microbiological results

Infectious problems not related to the abdominal sepsis requiring antimicrobial therapy:

☐ community-acquired pneumonia
☐ healthcare-associated pneumonia
☐ ventilator-associated pneumonia
☐ bloodstream infection
☐ urinary tract infection / pyelonephritis
☐ central nervous system infection
☐ surgical site infections / soft tissue infections
☐ osteomyelitis
☐ other

5.2. Source control

☐ none
☐ drainage
  ☐ percutaneous drainage (without surgical intervention)
  ☐ surgical drainage
  ☐ high-volume peritoneal lavage during surgery
  ☐ placement of one or more percutaneous drains
☐ debridement of necrotic tissue
☐ decompression (to avoid abdominal compartment syndrome or to avoid obstruction of distended bowel)
☐ restoration of anatomy and function

5.3. Use of adjunctive therapy for sepsis

Did the patient receive any type of adjunctive therapy for sepsis?

☐ no
☐ yes, specify: ☐ immunoglobulins
☐ hydrocortisone (200-300 mg/day)
☐ other: _____

Section 6 – Severity of disease assessment: pre-diagnosis **(worst parameters observed at onset of abdominal sepsis within a 6 hrs. time frame before medical diagnosis, surgery or other invasive procedure to diagnose IAI, e.g. fine needle aspiration)**

6.1. Sepsis grading (tick and complete the severity of sepsis at day of diagnosis)

☐ Sepsis (≥2 systemic inflammatory response criteria):
  ☐ fever (body temperature >38°C) or hypothermia (<36°C)

☐ tachycardia (heart rate >90/min.)
☐ tachypnea (respiratory rate >20/min or PaCO2 <32 mmHg)
☐ leucocytosis (white blood cell count >12,000 cells/μL) or leucopenia (>4,000/μL)

☐ Severe sepsis – associated organ dysfunctions:
☐ non-invasive mechanical ventilation
☐ invasive mechanical ventilation with intubation or tracheotomy
☐ acute kidney injury (serum creatinin ≥1.2 mg/dL or 111 μmol/L)
☐ acute liver failure (serum bilirubin ≥1.2 mg/dL or 20 μmol/L)
☐ acute neurologic failure (Glasgow coma scale ≤14)
☐ coagulation disorder (platelet count <150,000 / L)

☐ Septic shock – associated hypotension (systolic blood pressure <90 mmHg unresponsive to fluid administration)

6.2. Organ failure assessment (SOFA-score)

- **Respiratory failure (PaO2/FiO2)**
  - ☐ <400
  - ☐ <300
  - ☐ <200 (with respiratory support)
  - ☐ <100 (with respiratory support)
- **Coagulation disorder (platelet count x 10^9/L.)**
  - ☐ <150
  - ☐ <100
  - ☐ <50
  - ☐ <20
- **Liver failure (bilirubin, mg/dL)**
  - ☐ 1.2 – 1.9 (or 20 – 33 μmol/L)
  - ☐ 2.0 – 5.9 (or 34 – 101 μmol/L)
  - ☐ 6.0 – 11.9 (or 102 – 204 μmol/L)
  - ☐ ≥12.0 (or ≥204 μmol/L)
- **Renal failure (creatinine, mg/dL or urine output)**
  - ☐ 1.2 – 1.9 (or 110 – 170 μmol/L)
  - ☐ 2.0 – 3.4 (or 171 – 299 μmol/L)
  - ☐ 3.5 – 4.9 (or 300 – 440 μmol/L) or <500 mL/day
  - ☐ ≥5.0 (or ≥440 μmol/L) or <200mL/day
- **Hypotension**
  - ☐ mean art. pressure <70 mmHg or systolic art. pressure <90 mmHg
  - ☐ dopamine ≤5 mcg/kg/min or dobutamine (any dose)
  - ☐ dopamine >5 mcg/kg/min or (nor)adrenaline at ≤1 mcg/kg/min
  - ☐ dopamine >15 mcg/kg/min or (nor)adrenaline at >0.1 mcg/kg/min
- **Glasgow coma scale (effective if not sedated, estimated if sedated)**
  - ☐ 13-14
  - ☐ 10-12
  - ☐ 6-9
  - ☐ <6

6.3. Organ support
☐ mechanical ventilation (invasive or non-invasive)
☐ inotropic/vasopressor support
☐ renal replacement therapy
  ☐ for acute kidney injury
  ☐ for removal of inflammatory cytokines/endotoxins

6.4. Miscellaneous

Lactate	(max.) __ __ . __ mmol/L
pH	(min.) __ . __ __ (range 6.8 – 7.8)
c-reactive protein	__ __ . __ __ mg/L (range 0.02 – 250)
procalcitonin	__ __ . __ __ mcg/L (range 0.05 – 100)
white blood cell count	__ __ __ __ __ cells/mcL (range 300 – 40,000)

Intra-abdominal pressure: __ __ __ mm Hg

Indicate method used to measure IAP

☐ inferior vena cave ☐ intra-gastric ☐ transgastral
☐ urinary bladder ☐ transvesical technique (?)

Section 7 – Severity of disease assessment: early post-diagnosis
(worst parameters observed within a 24 hrs. time frame after medical diagnosis, surgery or other invasive procedure to diagnose IAI, e.g. fine needle aspiration)

7.1. Sepsis grading (tick and complete the severity of sepsis 72 hrs after diagnosis)

☐ Sepsis (≥2 systemic inflammatory response criteria):
- ☐ fever (body temperature >38°C) or hypothermia (<36°C)
- ☐ tachycardia (heart rate >90/min.)
- ☐ tachypnea (respiratory rate >20/min or PaCO2 <32 mmHg)
- ☐ leucocytosis (white blood cell count >12,000 cells/mcL) or leucopenia (>4,000/mcL)

☐ Severe sepsis – associated organ dysfunctions:
- ☐ non invasive mechanical ventilation
- ☐ invasive mechanical ventilation with intubation or tracheotomy
- ☐ acute kidney injury (serum creatinin ≥1.2 mg/dL or 111 µmol/L)
- ☐ acute liver failure (serum bilirubin ≥1.2 mg/dL or 20 µmol/L)
- ☐ acute neurologic failure (Glasgow coma scale ≤14)
- ☐ coagulation disorder (platelet count <150,000 / L)

☐ Septic shock – associated hypotension (systolic blood pressure <90 mmHg unresponsive to fluid administration)

7.2. Organ failure assessment (SOFA-score)

- **Respiratory failure (PaO2/FiO2)**
  - ☐ <400
  - ☐ <300
  - ☐ <200 (with respiratory support)
  - ☐ <100 (with respiratory support)
- **Coagulation disorder (platelet count x 10^9/L.)**
  - ☐ <150
  - ☐ <100
  - ☐ <50
  - ☐ <20
- **Liver failure (bilirubin, mg/dL)**
  - ☐ 1.2 – 1.9 (or 20 – 33 µmol/L)
  - ☐ 2.0 – 5.9 (or 34 – 101 µmol/L)
  - ☐ 6.0 – 11.9 (or 102 – 204 µmol/L)
  - ☐ ≥12.0 (or ≥204 µmol/L)
- **Renal failure (creatinine, mg/dL or urine output)**
  - ☐ 1.2 – 1.9 (or 110 – 170 µmol/L)
  - ☐ 2.0 – 3.4 (or 171 – 299 µmol/L)
  - ☐ 3.5 – 4.9 (or 300 – 440 µmol/L) or <500 mL/day
  - ☐ ≥5.0 (or ≥440 µmol/L) or <200mL/day
- **Hypotension**
  - ☐ mean arterial pressure <70 mmHg or systolic arterial pressure <90 mmHg
  - ☐ dopamine ≤5 mcg/kg/min or dobutamine (any dose)
  - ☐ dopamine >5 mcg/kg/min or (nor)adrenaline at ≤1 mcg/kg/min
  - ☐ dopamine >15 mcg/kg/min or (nor)adrenaline at >0.1 mcg/kg/min
- **Glasgow coma scale (effective if not sedated, estimated if sedated)**
  - ☐ 13-14
  - ☐ 10-12

☐ 6-9
☐ <6

7.3. Organ support
- ☐ mechanical ventilation (invasive or non-invasive)
- ☐ inotropic/vasopressor support
- ☐ renal replacement therapy
  - ☐ for acute kidney injury
  - ☐ for removal of inflammatory cytokines/endotoxins

7.4. Miscellaneous

Lactate (max.) __ __ . __ mmol/L
pH __ . __ __
c-reactive protein__ __ . __ __ mg/L
procalcitonin __ __ . __ __ mcg/L
white blood cell count __ __ __ __ __ cells/mL
Intra-abdominal pressure: __ __ __ mm Hg

Indicate method used to measure IAP

☐ inferior vena cave ☐ intra-gastric ☐ transgastral
☐ urinary bladder ☐ transvesical technique

Section 8 – Severity of disease assessment: 72 hrs. post-diagnosis **(worst parameters observed 72 hrs. after medical diagnosis, surgery or other invasive procedure to diagnose IAI, e.g. fine needle aspiration)**

8.1. Sepsis grading (tick and complete the severity of sepsis 72 hrs after diagnosis)

☐ Sepsis (≥2 systemic inflammatory response criteria):
- ☐ fever (body temperature >38°C) or hypothermia (<36°C)
- ☐ tachycardia (heart rate >90/min.)
- ☐ tachypnea (respiratory rate >20/min or PaCO2 <32 mmHg)
- ☐ leucocytosis (white blood cell count >12,000 cells/μL) or leucopenia (>4,000/μL)

☐ Severe sepsis – associated organ dysfunctions:
- ☐ non-invasive mechanical ventilation
- ☐ invasive mechanical ventilation with intubation or tracheotomy
- ☐ acute kidney injury (serum creatinin ≥1.2 mg/dL or 111 μmol/L)
- ☐ acute liver failure (serum bilirubin ≥1.2 mg/dL or 20 μmol/L)
- ☐ acute neurologic failure (Glasgow coma scale ≤14)
- ☐ coagulation disorder (platelet count <150,000 / L)

☐ Septic shock – associated hypotension (systolic blood pressure <90 mmHg unresponsive to fluid administration)

8.2. Organ failure assessment (SOFA-score)
- **Respiratory failure (PaO2/FiO2)**
  - ☐ <400
  - ☐ <300
  - ☐ <200 (with respiratory support)
  - ☐ <100 (with respiratory support)
- **Coagulation disorder (platelet count x 10^9/L.)**
  - ☐ <150
  - ☐ <100
  - ☐ <50
  - ☐ <20
- **Liver failure (bilirubin, mg/dL)**
  - ☐ 1.2 – 1.9 (or 20 – 33 μmol/L)
  - ☐ 2.0 – 5.9 (or 34 – 101 μmol/L)
  - ☐ 6.0 – 11.9 (or 102 – 204 μmol/L)

☐ ≥12.0 (or ≥204 µmol/L)

- **Renal failure (creatinine, mg/dL or urine output)**
  - ☐ 1.2 – 1.9 (or 110 – 170 µmol/L)
  - ☐ 2.0 – 3.4 (or 171 – 299 µmol/L)
  - ☐ 3.5 – 4.9 (or 300 – 440 µmol/L) or <500 mL/day
  - ☐ ≥5.0 (or ≥440 µmol/L) or <200mL/day

- **Hypotension**
  - ☐ mean arterial pressure <70 mmHg or systolic arterial pressure <90 mmHg
  - ☐ dopamine ≤5 mcg/kg/min or dobutamine (any dose)
  - ☐ dopamine >5 mcg/kg/min or (nor)adrenaline at ≤1 mcg/kg/min
  - ☐ dopamine >15 mcg/kg/min or (nor)adrenaline at >0.1 mcg/kg/min

- **Glasgow coma scale (effective if not sedated, estimated if sedated)**
  - ☐ 13-14
  - ☐ 10-12
  - ☐ 6-9
  - ☐ <6

8.3. Organ support

- ☐ mechanical ventilation (invasive or non-invasive)
- ☐ inotropic/vasopressor support
- ☐ renal replacement therapy
  - ☐ for acute kidney injury
  - ☐ for removal of inflammatory cytokines/endotoxins

8.4. Miscellaneous

Lactate (max.) __ __ . __ mmol/L
pH __ . __ __
c-reactive protein__ __ . __ __ mg/L
procalcitonin __ __ . __ __ mcg/L
white blood cell count __ __ __ __ __ cells/mL
Intra-abdominal pressure (if the patient was operated for abdominal source control, report the post-surgical procedure value) __ __ __ mm Hg

Indicate method used to measure IAP

☐ inferior vena cave ☐ intra-gastric ☐ transgastral
☐ urinary bladder ☐ transvesical technique

Section 9 – Source control assessment: 7 days after intervention
(day of surgical intervention = day zero)

☐ not applicable (no source control performed/required)

Is adequate source control achieved?

- ☐ Yes, no signs of perforation or persistent inflammation are present
- ☐ No, signs of persistent inflammation are present but no surgical revision has been executed
- ☐ No, the patient required additional surgical intervention because of:
  - ☐ anastomotic leakages, perforation
  - ☐ intestinal obstruction
  - ☐ abdominal compartment syndrome (decompressive laparotomy)
  - ☐ haemorrhage
  - ☐ other

Date of 1st surgical revision: (day/month/year): __ ___ ____

Number of surgical interventions during the first week: __ __

Section 10 – Outcome (28-day follow up)

☐ Additional surgical intervention for abdominal sepsis (later than those mentioned within the first 7 days following initial source control procedure; section 9)

Number of surgical interventions during the first week: __ __

Stop antimicrobial therapy (for abdominal sepsis): (day/month/year): __ ___ ____
☐ not applicable (ongoing)

ICU discharge: (day/month/year): __ ___ ____
☐ not applicable (ongoing)

Organ support during ICU stay
- ☐ mechanical ventilation (invasive or non-invasive)
- ☐ inotropic/vasopressor support
- ☐ renal replacement therapy
  - ☐ for acute kidney injury
  - ☐ for removal of inflammatory cytokines/endotoxins

Survival status
- ☐ alive
- ☐ death

  Death related to abdominal sepsis (clinical judgement)
  - ☐ yes
  - ☐ uncertain
  - ☐ no (other complication likely to cause death)

Supplement–3

Number of intensive care units and patients included according to geographic region

Region, country (n ICUs)	Patients
Western Europe	**858**
Belgium (12)	107
France (16)	194
Netherlands (8)	90
UK (42)	467
Central Europe	**134**
Czech Republic (7)	29
Denmark (1)	15
Germany (3)	14
Poland (11)	61
Switzerland (1)	15
Eastern & South-East Europe	**170**
Croatia (5)	55
Romania (2)	39
Russia (5)	46
Serbia (4)	30
Southern Europe	**668**
Greece (31)	211
Italy (13)	129
Portugal (13)	101
Spain (28)	227
North-Africa & Middle-East	**214**
Algeria (1)	6
Egypt (1)	15
Iran (5)	47
Israel (1)	15
Saudi Arabia (3)	28
Oman (1)	1
Qatar (1)	10
Turkey (10)	84
United Arab Emirates (1)	8
Asia-Pacific	**174**
Australia (8)	72
China (4)	23
India (5)	34
Japan (3)	30
Thailand (1)	15
North-America	**29**
Canada (1)	9
USA (3)	20
Middle & South-America, & Caribbean	**366**
Argentina (37)	220
Chile (1)	4
Colombia (4)	31
Ecuador (6)	32
Jamaica (1)	15
Mexico (5)	39
Paraguay (1)	4
Peru (2)	21
Sub-Saharan Africa	**8**
South-Africa (1)	8

Supplement–4

Patient characteristics of intensive care unit patients with intra-abdominal infection/sepsis according to setting of infection acquisition (Table 1 – full version)

Characteristic	Total cohort (n=2621)	Community-acquired (n=828)	Early-onset hospital-acquired (n=656)	Late-onset hospital-acquired (n= 1137)	P*
Demographics					
Age, years	66 (54-75)	67 (52-77)	66 (54-77)	66 (55-74)	0.213
Sex, male	1488/2615 (56.9)	452 (54.6)	364 (55.5)	672 (59.1)	0.133
Type of ICU admission	2592**	799**	656	1137	
Medical	472 (18.2)	109 (13.7)	131 (20.0)	232 (20.4)	<0.001
Surgical, non-emergency	233 (9.0)	19 (2.4)	39 (5.9)	175 (15.4)	<0.001
Surgical, emergency	1847 (71.3)	660 (82.6)	478 (72.9)	709 (62.4)	<0.001
Trauma	40 (1.5)	11 (1.4)	8 (1.2)	21 (1.8)	0.496
ICU stay, days	9 (4-18)	9 (4 – 18)	9 (4 – 17)	10 (5 – 19)	0.183
Underlying conditions					
Chronic pulmonary disease	342 (13.0)	96 (11.6)	90 (13.7)	156 (13.7)	0.324
Chronic obstructive pulmonary disease (GOLD stage III or IV)	180 (6.9)	48 (5.8)	46 (7.0)	86 (7.6)	0.306
Chronic pulmonary disease, other	162 (6.2)	48 (5.8)	44 (6.7)	70 (6.2)	0.769
AIDS	14 (0.5)	6 (0.7)	3 (0.5)	5 (0.4)	0.661
Malignancy	699 (26.7)	116 (14.0)	170 (25.9)	413 (36.3)	<0.001
Cancer, solid tumor	539 (20.6)	87 (10.5)	119 (21.1)	334 (29.4)	<0.001
Metastatic cancer	114 (4.3)	22 (2.7)	35 (5.3)	57 (5.0)	0.015
Hematologic cancer	45 (1.7)	7 (0.8)	16 (2.4)	22 (1.9)	0.102
Neurologic disease	165 (6.3)	42 (5.1)	60 (9.1)	75 (6.6)	0.008
Cerebrovascular disease	95 (3.6)	25 (3.0)	30 (4.6)	40 (3.5)	0.237
Dementia	57 (2.2)	12 (1.5)	22 (3.4)	23 (2.0)	0.040
Hemiplegia	13 (0.5)	0	4 (0.6)	9 (0.8)	-
Peptic ulcer disease	176 (6.7)	57 (6.9)	52 (7.9)	67 (5.9)	0.246

	Liver disease	127 (4.8)	24 (1.5)	44 (6.7)	59 (5.2)	0.002
	Portal hypertension	18 (0.7)	3 (0.4)	8 (1.2)	7 (0.6)	-
	Hepatic cirrhosis	109 (4.2)	21 (2.5)	36 (5.5)	52 (4.6)	0.012
	Chronic renal failure	282 (10.8)	57 (6.9)	100 (15.2)	125 (11.0)	<0.001
	Mild, GFR ≥60 mL/min.	52 (2.0)	11 (1.3)	19 (2.9)	22 (1.9)	0.098
	Moderate, GFR 30-59 mL/min.	98 (3.7)	28 (3.4)	32 (4.9)	38 (3.3)	0.206
	Severe, GFR 15-29 mL/min.	57 (2.2)	12 (1.4)	24 (3.7)	21 (1.8)	0.009
	End-stage, GFR <15 mL/min. or requiring RRT	75 (2.9)	6 (0.7)	25 (3.8)	44 (3.9)	<0.001
	Myocardial infarction	188 (7.2)	48 (5.8)	57 (8.7)	83 (7.3)	0.098
	Chronic heart failure (NY Heart Association class IV)	184 (7.0)	36 (4.3)	64 (9.8)	84 (7.4)	<0.001
	Peripheral vascular disease	169 (6.4)	34 (4.1)	48 (7.3)	87 (7.7)	0.004
	Diabetes mellitus	488 (18.6)	116 (14.0)	141 (21.5)	231 (20.3)	<0.001
	Without end-stage organ failure	339 (12.9)	79 (9.5)	97 (14.8)	163 (14.3)	0.002
	With end-stage organ failure	149 (5.7)	37 (4.5)	44 (6.7)	68 (6.0)	0.153
	Immunosuppression	253 (9.7)	47 (5.7)	83 (12.7)	123 (10.8)	<0.001
	Neutropenia (<1000 neutrophils/mm^3)	23 (0.9)	2 (0.2)	10 (1.5)	11 (1.0)	0.029
	Corticosteroid treatment (prednisolone or equivalent >0.5 mg/kg/day for >3 months)	71 (2.7)	19 (2.3)	25 (3.8)	27 (2.4)	0.133
	Chemotherapy	107 (4.1)	8 (1.0)	42 (6.4)	57 (5.0)	<0.001
	Radiotherapy	38 (1.4)	2 (0.2)	17 (2.6)	19 (1.7)	0.001
	Bone marrow transplant	2 (0.1)	0	1 (0.2)	1 (0.1)	0.562
	Solid organ transplant	30 (1.1)	5 (0.6)	7 (1.1)	18 (1.6)	0.128
	Immunosuppressive drug	47 (1.8)	14 (1.7)	11 (1.7)	22 (1.9)	0.892
	Congenital immunodeficiency	3 (0.1)	1 (0.1)	1 (0.2)	1 (0.1)	-
	Connective tissue disease	68 (2.6)	20 (2.4)	16 (2.4)	32 (2.8)	0.952
Lifestyle risk factors		**1363 (52.0)**	**413 (49.9)**	**355 (54.1)**	**595 (52.3)**	**0.257**
	Malnutrition (body mass index <20)	177 (6.8)	46 (5.6)	53 (8.1)	78 (6.9)	0.154
	Obesity (body mass index ≥30)	735 (28.0)	236 (28.5)	197 (30.0)	302 (26.6)	0.271
	Tobacco use (>20 pack years)	446 (17.0)	127 (7.1)	106 (16.2)	213 (18.7)	0.113
	Alcohol abuse (>10g alcohol /day)	196 (7.5)	59 (7.1)	49 (7.5)	88 (7.7)	0.261

	IV drug abuse	17 (0.6)	8 (1.0)	3 (0.5)	6 (0.5)	-
Severity of acute illness						
	SAPS II score at time of ICU admission	49 (39-60)	48 (38-59)	49 (39-61)	49 (38-60)	0.183
	SOFA score at diagnosis	6 (3-10)	5 (3-9)	7 (3-10)	6 (3-10)	<0.001
	Severity of disease expression					
		Infection without sepsis	164 (6.3)	51 (6.2)	42 (6.4)	71 (6.2)	0.981
		Sepsis	1590 (60.7)	528 (63.8)	399 (60.8)	663 (58.3)	0.050
		Septic shock	867 (33.1)	249 (30.1)	215 (32.8)	403 (35.4)	0.043
Anatomical disruption						
	Not present	615 (23.5)	186 (22.5)	166 (25.3)	263 (23.1)	0.413
	Yes, with localized peritonitis	981 (37.4)	342 (41.3)	256 (39.0)	383 (33.7)	0.002
	Yes, with diffuse peritonitis	1025 (39.1)	300 (36.2)	234 (35.7)	491 (43.2)	0.001

Data are reported as n (%) or median (1^{st} – 3^{rd} quartile).

* p-value indicates differences between patients with community-acquired infection, healthcare-associated infection or early-onset hospital-acquired infection, and late-onset hospital-acquired infection

** data missing from 29 patients

GRF, glomerular filtration rate; RRT, renal replacement therapy; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment

Supplement–5

Multidrug resistance rates in intra-abdominal infections according geographic region and setting of infection acquisition

Community-acquired infection

MDR pathogen	Total cohort (n=664)	Geographic region							
		Western Europe (n=179)	Southern Europe (n=230)	Eastern & South-East Europe (n=48)	Central Europe (n=42)	North-Africa & Middle-East (n=79)	Latin-America (n=41)	North-America (n=3)	Asia-Pacific (n=40)
Difficult-to-treat Gram-negative bacteria	24 (3.6)	0	10 (4.3)	4 (8.3)	0	7 (8.9)	0	0	3 (7.5)
Any resistant Gram-negative bacteria*	165 (24.8)	14 (7.8)	55 (23.9)	24 (50.0)	8 (19.0)	38 (48.1)	15 (36.6)	0	10 (25.0)
ESBL-producing Gram-negative bacteria	114 (17.2)	10 (5.6)	28 (12.2)	17 (35.4)	3 (7.1)	34 (43.0)	12 (29.3)	0	9 (22.5)
Carbapenem-resistant Gram-negative bacteria	49 (7.4)	1 (0.6)	21 (9.1)	11 (22.9)	0	9 (11.4)	3 (7.3)	0	4 (10.0)
Fluoroquinolone-resistant Gram-negative bacteria	106 (16.0)	6 (3.4)	38 (16.5)	14 (29.2)	8 (19.0)	23 (29.1)	8 (19.5)	0	9 (22.5)
MRSA	7 (1.1)	0	3 (1.3)	1 (2.1)	0	1 (1.3)	1 (2.4)	0	1 (2.5)
VRE	15 (2.3)	2 (1.1)	7 (3.0)	0	1 (2.4)	4 (5.1)	1 (52.4)	0	0
Antibiotic resistance** (total)	45 (6.8)	2 (1.1)	20 (8.7)	5 (10.4)	1 (2.4)	12 (15.2)	2 (4.9)	0	3 (7.5)
Antibiotic resistance*** (total)	176 (26.5)	14 (7.8	61 (26.5)	25 (52.1)	9 (21.4)	39 (49.4)	17 (41.5)	0	10 (25.0)

% represent proportion per column; Resistance rates reflect proportion of patients in which resistant strains are isolated (eg, n MRSA / total n patients) and do not represent proportion of resistance within particular pathogens (eg, n MRSA / total *S. aureus* isolates).
Denominator for microbiological data includes only patients in which cultures were sampled (data from South-Africa are excluded as they included only 7 patients).
MDR, multidrug resistant; ESBL, extended-spectrum beta-lactamase-producing; MRSA, methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant enterococci;
*Gram-negative bacteria that are either ESBL-producing, or carbapenem-resistant, or fluoroquinolone-resistant
**Total rates of multidrug resistance considering difficult-to-treat resistant Gram-negative bacteria, MRSA, and VRE
***Total rates of multidrug resistance considering any type of Gram-negative resistance (either ESBL-producing, or carbapenem-resistant, or fluoroquinolone-resistant bacteria), MRSA, and VRE

Healthcare-associated/early-onset hospital-acquired infection

MDR pathogen		Total cohort (n=482)	Geographic region							
			Western Europe (n=136)	Southern Europe (n=123)	Eastern & South-East Europe (n=47)	Central Europe (n=22)	North-Africa & Middle-East (n=54)	Latin-America (n=66)	North-America (n=6)	Asia-Pacific (n=26)
Difficult-to-treat Gram-negative bacteria		28 (5.8)	1 (0.7)	9 (7.3)	5 (10.6)	0	6 (11.1)	7 (10.6)	0	0
Any resistant Gram-negative bacteria*		127 (26.3)	17 (12.5)	32 (26.0)	21 (44.7)	4 (18.2)	27 (50.0)	20 (30.3)	2 (33.3)	4 (15.4)
	ESBL-producing Gram-negative bacteria	87 (18.0)	12 (8.8)	20 (16.3)	12 (25.5)	1 (4.5)	21 (38.9)	17 (25.8)	2 (33.3)	2 (7.7)
	Carbapenem-resistant Gram-negative bacteria	47 (9.8)	1 (0.7)	13 (10.6)	11 (23.4)	1 (4.5)	11 (20.4)	9 (13.6)	0	1 (3.8)
	Fluoroquinolone-resistant Gram-negative bacteria	93 (19.3)	9 (6.6)	26 (21.1)	15 (31.9)	2 (9.1)	20 (37.0)	17 (25.8)	1 (16.7)	3 (11.5)
MRSA		7 (1.5)	0	1 (0.8)	3 (6.4)	0	1 (1.9)	2 (3.0)	0	0
VRE		18 (3.7)	4 (2.9)	4 (3.3)	2 (4.3)	0	4 (7.4)	3 (3.5)	0	1 (3.8)
Antibiotic resistance** (total)		47 (9.8)	5 (3.7)	13 (10.6)	7 (14.9)	0	11 (20.4)	10 (15.2)	0	1 (3.8)
Antibiotic resistance*** (total)		140 (29.0)	21 (15.4)	35 (28.5)	22 (46.8)	4 (18.2)	28 (51.9)	23 (34.8)	2 (33.3)	5 (19.2)

% represent proportion per column; Resistance rates reflect proportion of patients in which resistant strains are isolated (eg, n MRSA / total n patients) and do not represent proportion of resistance within particular pathogens (eg, n MRSA / total *S. aureus* isolates).

Denominator for microbiological data includes only patients in which cultures were sampled (data from South-Africa are excluded as they included only 7 patients).

MDR, multidrug resistant; ESBL, extended-spectrum beta-lactamase-producing; MRSA, methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant enterococci;

*Gram-negative bacteria that are either ESBL-producing, or carbapenem-resistant, or fluoroquinolone-resistant

**Total rates of multidrug resistance considering difficult-to-treat resistant Gram-negative bacteria, MRSA, and VRE

***Total rates of multidrug resistance considering any type of Gram-negative resistance (either ESBL-producing, or carbapenem-resistant, or fluoroquinolone-resistant bacteria), MRSA, and VRE

Late-onset hospital-acquired infection

MDR pathogen	Total cohort (n=836)	Geographic region							
		Western Europe (n=286)	Southern Europe (n=205)	Eastern & South-East Europe (n=56)	Central Europe (n=35)	North-Africa & Middle-East (n=39)	Latin-America (n=142)	North-America (n=13)	Asia-Pacific (n=57)
Difficult-to-treat Gram-negative bacteria	33 (3.9)	1 (0.3)	19 (9.3)	0	0	2 (5.1)	9 (6.3)	0	2 (3.5)
Any resistant Gram-negative bacteria*	18 (22.5)	23 (8.0)	53 (25.9)	14 (25.0)	8 (22.9)	17 (43.6)	55 (38.7)	5 (38.5)	12 (21.1)
ESBL-producing Gram-negative bacteria	125 (15.0)	15 (5.2)	33 (16.1)	8 (14.3)	5 (14.3)	10 (25.6)	40 (28.2)	5 (38.5)	9 (15.8)
Carbapenem-resistant Gram-negative bacteria	49 (5.9)	1 (0.3)	27 (13.2)	1 (1.8)	0	4 (7.0)	13 (9.2)	0	0
Fluoroquinolone-resistant Gram-negative bacteria	140 (16.7)	14 (4.9)	44 (31.0)	8 (14.3)	8 (22.9)	5 (8.8)	14 (35.9)	2 (15.4)	5 (8.8)
MRSA	6 (0.7)	1 (0.3)	1 (0.5)	1 (1.8)	0	3 (7.7)	0	0	0
VRE	23 (2.8)	5 (1.7)	4 (2.0)	3 (5.4)	1 (2.9)	1 (2.6)	7 (4.9)	1 (7.7)	1 (1.8)
Antibiotic resistance** (total)	61 (7.3)	7 (2.4)	24 (11.7)	4 (7.1)	1 (2.9)	6 (15.4)	15 (10.6)	1 (7.7)	3 (5.3)
Antibiotic resistance*** (total)	206 (24.6)	28 (9.8)	56 (27.3)	18 (32.1)	8 (22.9)	20 (51.3)	56 (39.4)	6 (46.2)	13 (22.8)

% represent proportion per column; Resistance rates reflect proportion of patients in which resistant strains are isolated (eg, n MRSA / total n patients) and do not represent proportion of resistance within particular pathogens (eg, n MRSA / total *S. aureus* isolates).

Denominator for microbiological data includes only patients in which cultures were sampled (data from South-Africa are excluded as they included only 7 patients).

MDR, multidrug resistant; ESBL, extended-spectrum beta-lactamase-producing; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci;

*Gram-negative bacteria that are either ESBL-producing, or carbapenem-resistant, or fluoroquinolone-resistant

**Total rates of multidrug resistance considering difficult-to-treat resistant Gram-negative bacteria, MRSA, and VRE

***Total rates of multidrug resistance considering any type of Gram-negative resistance (either ESBL-producing, or carbapenem-resistant, or fluoroquinolone-resistant bacteria), MRSA, and VRE

Supplement–6

Empiric antimicrobial coverage according to origin of intra-abdominal infection acquisition

	Community-acquired infection (n=779)	Early-onset hospital acquired infection (n=608)	Late-onset hospital-acquired infection (n=1040)	p
Basic coverage*	737 (94.6)	575 (94.6)	979 (94.1)	0.888
Pseudomonas sp.	650 (83.7)	494 (81.5)	834 (80.5)	0.224
MRSA	212 (27.2)	175 (28.8)	260 (25.0)	0.224
Enterococci (i.e. *E. faecalis*)	550 (71.9)	457 (75.3)	773 (74.3)	0.314
VRE	50 (6.4)	32 (5.3)	58 (5.6)	0.871
Candida spp.	155 (19.9)	108 (17.8)	173 (16.6)	0.198
Double anaerobic coverage**	111 (14.2)	117 (19.2)	137 (13.2)	0.003

*Coverage of Gram-positive, Gram-negative, and anaerobic bacteria; MRSA, methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant enterococci

**Combination of two antimicrobial agents with activity against anaerobe bacteria (e.g., piperacillin/tazobactam + metronidazole).

Supplement–7

Univariate relationships with 28-day mortality

		Survivors	Non-survivors	p
Sex, male		1041 (56.8)	431 (57.5)	0.753
Infection type				0.020
	Primary peritonitis	69 (3.8)	30 (4.0)	
	Secondary peritonitis	1239 (67.5)	531 (70.6)	
	Peritoneal dialysis related peritonitis	7 (0.4)	2 (0.3)	
	Intra-abdominal abscess	142 (7.7)	37 (4.9)	
	Biliary tract infection	241 (13.1)	75 (10)	
	Pancreatic infection	106 (5.8)	58 (7.7)	
	Typhlitis	5 (0.3)	4 (0.5)	
	Toxic megacolon	27 (1.5)	15 (2.0)	
Underlying conditions				
	Chronic pulmonary disease	217 (11.8)	119 (15.8)	0.006
	AIDS	7 (0.4)	7 (0.9)	0.084
	Malignancy	457 (24.9)	233 (31.0)	0.001
	Neurologic disease	99 (5.4)	75 (10.0)	<0.001
	Peptic disease	111 (6.0)	65 (8.6)	0.017
	Liver disease	70 (3.8)	57 (7.6)	<0.001
	Chronic renal failure	173 (9.4)	107 (14.2)	<0.001
	Myocardial infarction	113 (6.2)	72 (9.6)	0.002

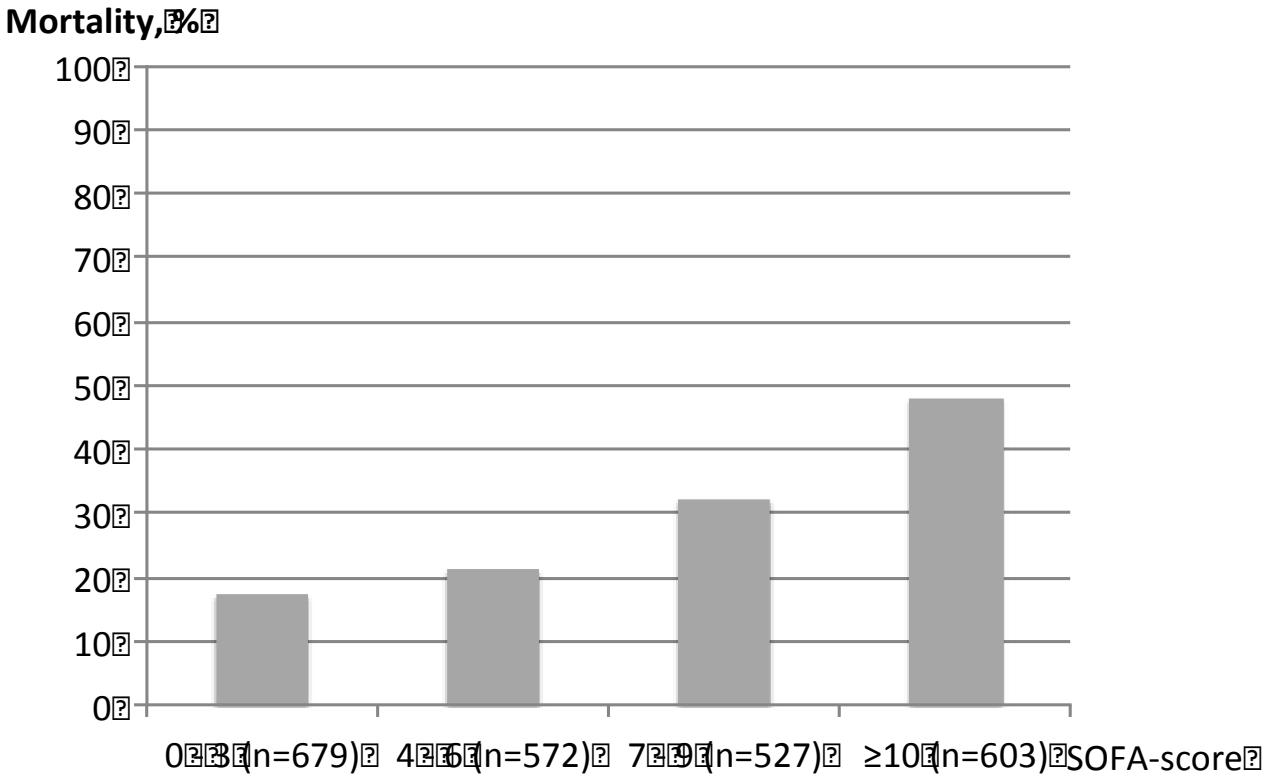
	Congestive heart failure	85 (4.6)	95 (12.6)	<0.001
	Acute heart failure	32 (1.7)	46 (6.1)	<0.001
	Peripheral vascular disease	98 (5.3)	71 (9.4)	<0.001
	Diabetes mellitus	299 (16.3)	185 (24.6)	<0.001
	Immunosuppressive status	174 (9.5)	78 (10.4)	0.486
	Malnutrition (BMI<20)	102 (5.6)	72 (9.6)	<0.001
	Obesity (BMI>30)	536 (29.2)	188 (25.0)	0.031
	Tobacco use	310 (16.9)	132 (13.3)	0.168
	Alcohol abuse	134 (7.3)	61 (8.1)	0.506
	IV drug use	11 (0.6)	6 (0.8)	0.323
Phenotypic characteristics intra-abdominal infection/sepsis				
	Origin of infection onset			<0.001
	Community-acquired	619 (33.7)	192 (25.5)	
	Early-onset hospital-acquired	469 (25.5)	176 (23.4)	
	Late-onset hospital-acquired	748 (40.0)	384 (51.1)	
	Anatomical disruption			<0.001
	No anatomical disruption	455 (24.8)	152 (20.2)	
	Anatomical disruption with localized peritonitis	729 (39.7)	233 (31.0)	
	Anatomical disruption with diffuse peritonitis	652 (35.5)	367 (48.8)	
	Severity of disease expression			<0.001
	Infection	143 (7.8)	21 (2.8)	
	Sepsis	1176 (64.1)	382 (50.8)	
	Septic shock	517 (28.2)	349 (46.4)	
Time till intervention (source control procedure, if any)				0.015

	Diagnosis by intervention or <2 hrs. of clinical signs of abdominal infection	656 (40.2)	313 (45.6)	
	2 – 12 hrs.	697 (42.7)	244 (35.6)	
	12 – 24 hrs.	129 (7.9)	69 (10.1)	
	24 – 48 hrs.	56 (3.4)	21 (3.1)	
	>48 hrs.	93 (5.7)	39 (5.7)	
Antibiotic resistance patterns (only patients with cultures sampled considered)				
	ESBL	225 (16.2)	98 (17.2)	0.579
	Carbapenem-resistance	97 (7.0)	44 (7.7)	0.560
	Fluoroquinolone-resistance	237 (17.1)	99 (17.4)	0.858
	Difficult-to-treat resistant Gram-negative bacteria	61 (3.3)	23 (3.1)	0.731
	MRSA	12 (0.9)	8 (1.4)	0.279
	VRE	37 (2.7)	18 (3.2)	0.543
	Antibiotic resistance (total – either MRSA, VRE, or difficult-to-treat resistant Gram-negative bacteria)	105 (5.7)	46 (6.1)	0.695
	Candida sp.	183 (10.0)	69 (9.2)	0.381
Antimicrobial coverage				
	Basic coverage (Gram-positive, Gram-negative, and anaerobe coverage)	1609 (94.6)	650 (93.8)	0.444
	Pseudomonas sp.	1407 (83.0)	541 (78.3)	0.007
	MRSA	476 (28.0)	160 (23.1)	0.014
	Enterococci (i.e. *E. faecalis*)	1264 (74.4)	500 (72.2)	0.267
	VRE	100 (5.9)	38 (5.5)	0.707
	Candida coverage	315 (18.5)	115 (16.6)	0.266
	Double anaerobic coverage	244 (14.3)	114 (16.5)	0.190

AIDS, acquired immune deficiency syndrome; BMI, body mass index; ESBL, production of extended spectrum beta-lactamase; MRSA, methicillin-resistant Staphylococcus aureus, VRE, vancomycin-resistant enterococci

Supplement–8

Mortality according to SOFA-score at the time of diagnosis



SOFA-scores are divided in quartiles

Supplement–9

Definitions of antibiotic resistance are often a matter of controversy. We hereby report the logistic regression models with an alternative definition of resistance in Gram-negative bacteria. Drug resistance for Gram-negative bacteria in these models is based on production of ESBL and/or carbapenem-resistance instead of the "difficult-to-treat resistant Gram-negative" definition by Kadri SS, et al. (Clin Infect Dis 2018) that combines resistance to all reported agents in carbapenem, beta-lactam, and fluoroquinolone.

Independent relationships with mortality in critically ill patients with intra-abdominal infection with use of an alternative definition for multidrug resistance in Gram-negative bacteria

		Model with source control achievement*	Model without source control achievement**
Variable		**OR[#] (95% CI)[##]**	**OR[#] (95% CI)[##]**
Setting of infection acquisition			
	Community-acquired infection	Reference	Reference
	Early-onset hospital-acquired infection (≤7 days)	1.16 (0.85 – 1.59)	1.19 (0.88 – 1.60)
	Late-onset hospital-acquired infection (>7 days)	1.80 (1.37 – 2.37)	1.79 (1.38 – 2.32)
Anatomical disruption			
	No anatomical barrier disruption	Reference	Reference
	Anatomical disruption with localized peritonitis	1.27 (0.94 – 1.73)	1.25 (0.94 – 1.68)
	Anatomical disruption with diffuse peritonitis	1.97 (1.48 – 2.65)	2.02 (1.53 – 2.67)
Severity of disease expression			
	Infection	Reference	Reference
	Sepsis	2.45 (1.38 – 4.68)	2.29 (1.31 – 4.30)
	Septic shock	5.25 (2.92 – 10.1)	4.95 (2.82 – 9.35)
Age (per year increase)		1.03 (1.02 – 1.04)	1.03 (1.03 – 1.04)
Underlying conditions			
	Malnutrition (body mass index <20)	2.05 (1.33 – 3.15)	2.13 (1.41 – 3.18)
	Diabetes mellitus	1.31 (0.99 – 1.73)	1.32 (1.01 – 1.72)
	Liver failure	2.02 (1.23 – 3.32)	2.49 (1.54 – 4.00)
	Congestive heart failure	1.86 (1.24 – 2.80)	1.92 (1.31 – 2.81)
Empiric antimicrobial coverage			
	Anti-MRSA[###] agent	0.76 (0.58 – 0.99)	0.75 (0.59 – 0.97)
	Double anaerobe coverage	-	1.29 (0.97 – 1.71)
Antibiotic resistance involvement		1.49 (1.07 – 2.05)	1.36 (1.00 – 1.85)
Source control achievement at day 7			
	Success	Reference	-
	Failure, persistent signs of inflammation	4.92 (3.84 – 6.31)	-
	Failure, additional intervention required following initial approach	1.94 (1.41 – 2.66)	-

*Area under the receiver operating curve characteristic: 0.776; **Area under the receiver operating curve characteristic: 0.686; [#]OR, odds ratio; [##]CI, confidence interval; [###]MRSA, methicillin-resistant *Staphylococcus aureus*