INFECTION 2018
FORUM INTERNAZIONALE DI TERAPIA ANTINFETTIVA

Sepsi: nuove definizioni, approccio diagnostico e terapia

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Sepsis: a never-ending story

- **Although common and associated with high morbidity and mortality, sepsis and related terms remain difficult to define.**

- **Two international consensus conferences in 1991 and 2001 used expert opinion to generate sepsis definitions.**

- **However, advances in the understanding of the pathobiology and appreciation that elements of the definitions may be outdated, inaccurate, or confusing prompted the European Society of Intensive Care Medicine and the Society of Critical Care Medicine to convene a Third International Consensus Task Force to reexamine the definitions.**

- **This is sepsis-3**

Bone RC et al. Chest 1992; 101:1644–1655
Levy MM et al. Crit Care Med 2003; 31: 1250-56
Singer M et al. JAMA 2016; 315: 801–8

- **SEPSIS-3 has solved a major problem of SEPSIS-2, which required the presence of systemic inflammatory response syndrome (SIRS) + suspected infection to define sepsis.**

- **For most physicians, the term “sepsis” is usually reserved for patients with a severe infection deserving critical care.**

- **Using the SEPSIS-2 criteria would “overestimate” the number of cases of this disease by considering uncomplicated infection as sepsis.**

- **Conversely, the SEPSIS-2 definition excludes a number of patients with potentially deleterious infection because SIRS is absent in one of eight patients with infection and organ dysfunction.**

The old definitions

Defining criteria of ACCP/SCCM named conditions.

ACCP/SCCM named condition	Defining criteria
SIRS	Core body temperature >38°C or <36°C HR ≥90 bpm Respirations ≥20/min (or $PaCO_2$ <32 mmHg) WBC ≥12,000/μl or ≤4000/μl or >10% immature forms
Sepsis	At least two SIRS criteria caused by known or suspected infection
Severe sepsis	Sepsis with acute organ dysfunction (including hypoperfusion and hypotension) caused by sepsis
Septic shock	Sepsis with persistent or refractory hypotension or tissue hypoperfusion despite adequate fluid resuscitation
MODS	The presence of organ dysfunction in an acutely ill patient such that homeostasis cannot be maintained without intervention

ACCP: American College of Chest Physicians; HR: Heart rate; MODS: Multiple organ dysfunction syndrome; $PaCO_2$: Partial pressure of carbon dioxide in the blood; SCCM: Society of Critical Care Medicine; SIRS: Systemic inflammatory response syndrome; WBC: White blood cell.

New definitions:

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection

NB:

- **The SIRS criteria have been removed**
- **It may be present in simple, non complicated infection, or in response to non infectious-triggers (i.e. trauma, pancreatitis, post-cardiac arrest synderome)**
- **Or may even be absent in critically ill patients with obvious evidence of a life-threatening infection.**

New definitions:

- **Organ dysfunction can be identified as an acute change in total SOFA score>2 points consequent to the infection**

- **A SOFA score>2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection.**

- **The baseline SOFA score can be assumed to be zero or in patients not known to have preexisting organ dysfunction**

New definitions

- **Septic shock** is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality

  Clinical criteria identifying such condition include the need for vasopressors to obtain a MAP≥ 65 mmHg and an increase in lactate concentration > 2 mmol/L, despite adequate fluid resuscitation.

Terms like severe sepsis/septicemia have been removed

New definitions (the screening tool)

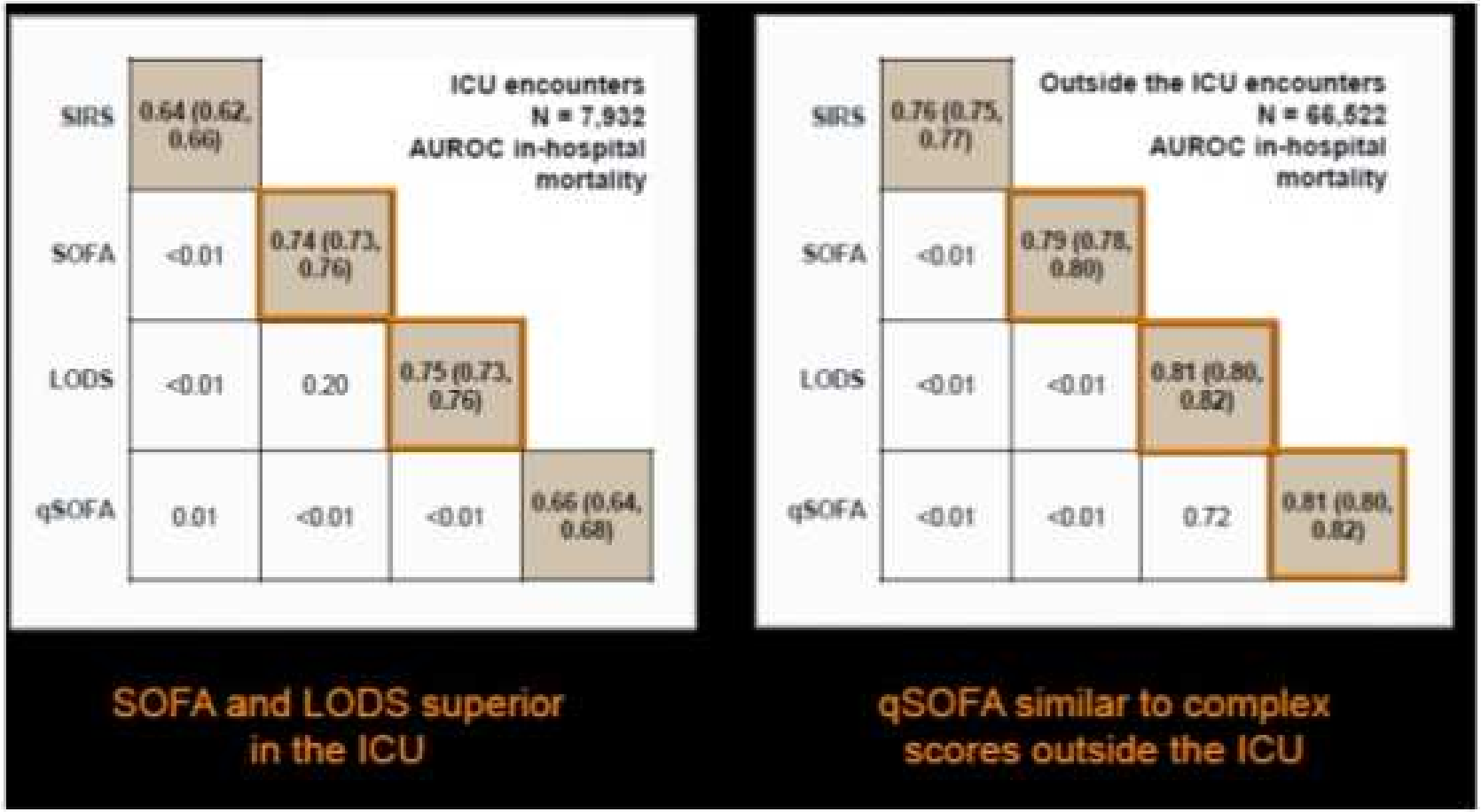
- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA,
  - Respiratory rate ≥22/min
  - Altered mentation
  - Systolic blood pressure ≤ 100mmHg
    - **The presence of at least two of these criteria strongly predicts the likelihood of poor outcome in out-of-ICU patients with clinical suspicion of sepsis.**

Analysis of electronic records

- The receiver operating characteristic curve (AUROC) has been assessed to predict the validity of the different scores.

- The quick score was a better predictor of hospital mortality for patients with suspected infection who were not in the ICU than for those in the ICU.

Area Under the Receiver Operating Characteristic Curve and 95%Confidence Intervals for In-Hospital Mortality of Candidate Criteria (SIRS, SOFA, LODS, and qSOFA) Among Suspected Infection Encounters in the UPMC Validation Cohort (N = 74 454)



Which score to use !!

- "The SOFA score found patients more likely to be septic both in and out of the ICU. But it involves the use of many lab tests and is a bit complex.

- For patients not in the ICU, the performance of Quick SOFA score was similar to that of the sequential organ failure assessment score.

Sepsis

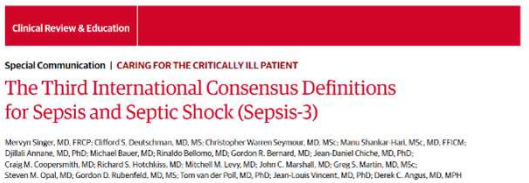
↓

Life-threatening organ dysfunction caused by a dysregulated host response to infection

↓

Organ dysfunction is represented by a SOFA score of 2 points or more (which is associated with an in-hospital mortality greater than 10%)

- **At present, sepsis can be identified by a constellation of clinical signs and symptoms in a patient with a suspected infection.**
- **For sepsis no golden standard diagnostic test exists**


Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MSc; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

- Sepsis : A life-threatening organ dysfunction caused by a dysregulated host response to infection.

- SOFA score ≥ 2 points = organ dysfunction

- SOFA score to evaluate sepsis in ICU settings
- qSOFA score to evaluate sepsis outside the ICU

Clinical case #1

- **A 82-year-old man presents to the hospital for an abdominal hernia intervention. He has a past medical history of hypertension, and diabetes mellitus.**

- **He is independently mobile, does his normal life activities, and has a 50-pack-a-year history of smoking. The operation was uncomplicated.**

- **On day 6 post-surgery, he becomes a bit confused, but on examination he has a Glasgow Coma Scale score of 14.**

- **He has a temperature of 38.7°C, a respiratory rate of 27 breaths/minute, and oxygen saturations of 91% on 2 L of oxygen.**

- **He is tachycardic at 120 bpm, and his blood pressure is 105/60 mmHg. On chest auscultation, he has coarse crackles in the left lower chest. His surgical wound appears to be healing well and his abdomen is soft and not tender.**

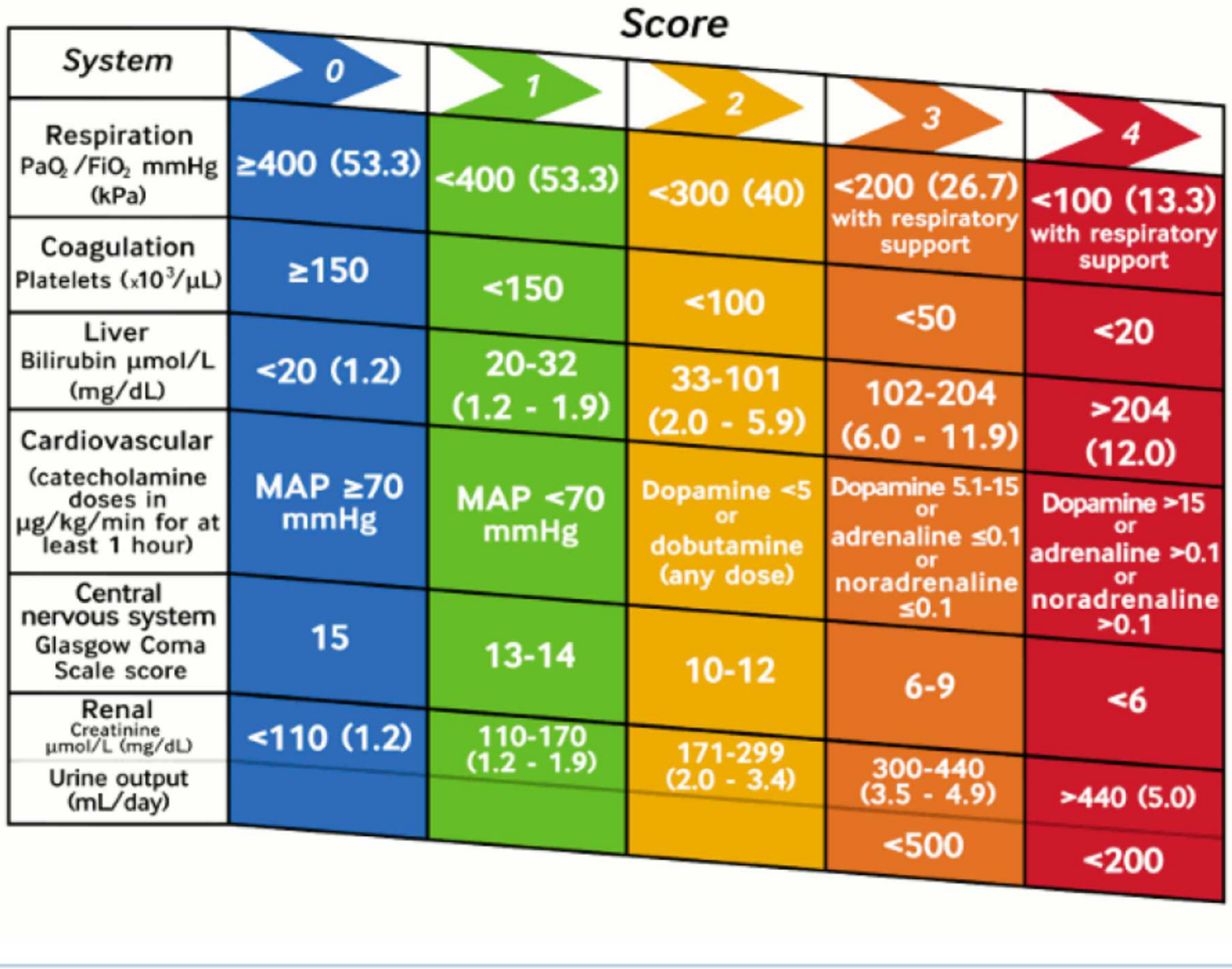
Diagnostic criteria

- **According to the international consensus definition published in 1991 (and reviewed in 2001), this person has a SIRS+ a lung infection→sepsis.**

- **Hyperglycemia and acutely altered mental status are not part of the original criteria for SIRS, but have since been included by the Surviving Sepsis Campaign in their screening tool.**

- **The Sepsis-3 advised that sepsis should be defined using the SOFA criteria.**

- **The SOFA score is calculated based on the assessment of the following systems (with a score of ≥2 in a patient with a suspected infection being suggestive of sepsis)**



Sequential (or Sepsis-related) Organ Failure Assessment (SOFA) criteria

Singer M et al. JAMA 2016; 315: 801–8

As the SOFA score has primarily been validated on patients in an ICU setting and requires multiple laboratory test results, the Third International Consensus Group suggested the use of the "quick SOFA" (qSOFA) as a bedside assessment to identify those at risk of deterioration due to sepsis.

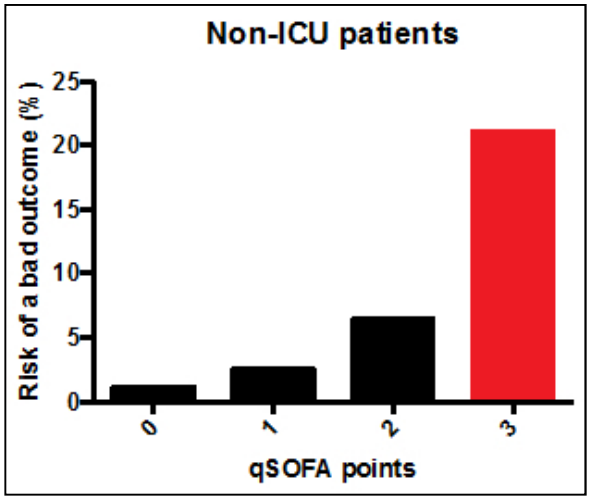
This is a simple clinical assessment that assesses for the presence of at least two of the following:

- **Altered mental state**
- **Systolic blood pressure ≤100 mmHg**
- **Respiratory rate≥ 22 breaths/minute.**

This patient has an infection with a low risk of deterioration in the out-ICU setting

Caveat: a large study in the US found qSOFA had poor sensitivity (particularly when compared with other bedside early warning scores and the SIRS criteria) and was a late indicator of deterioration. Churpek MM et al. Am J Respir Crit Care Med 2017;195:906-911

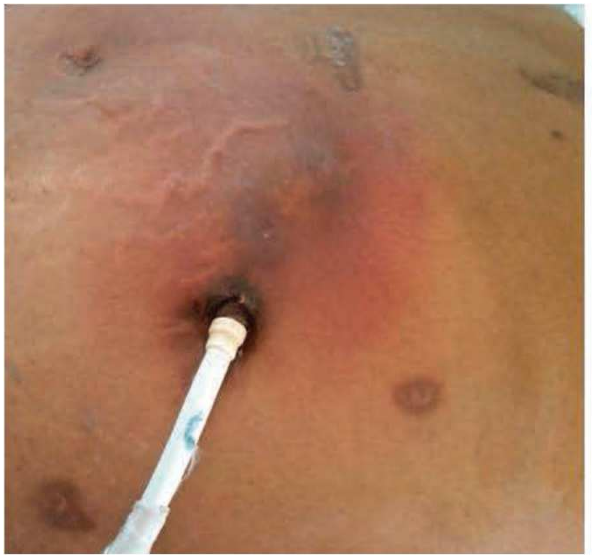
Is the patient in the ICU?	No
Altered Mentation	No
Respiratory rate (breaths per minute)	27
Systolic blood pressure (mmHg)	105
Total Score	1



Your patient with suspected infection not in the intensive care unit has a **2-3% risk** of a bad outcome.
This is a prompt to consider that sepsis is **very unlikely**

Clinical case #2

- PF: 64 y-o, idiopathic dilatative cardiomyopathy
- 2015 L-VAD destination therapy
- Poor compliance, admissions for heart failure
- Sept 2016: drive line infection→ MSSA
- Admission→ CRE gut colonization
- At 11 d from the beginning of treatment (Oxacillin)→ high fever, hypotensione, 13,000 WC, lactate: 3mmol/L, decreased urine output
- qSOFA:3
- Which diagnosis?
- Which treatment?



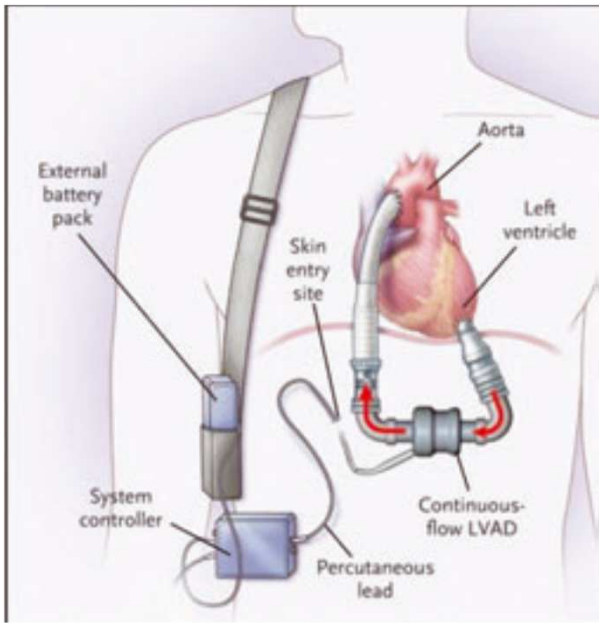


Table 1: VAD-Specific Infections (Refs. 6,11–14)

Site of infection	Distribution of organisms
Driveline	*Staphylococcus aureus* 30–44% *Pseudomonas aeruginosa* 10–28% Enteric gram-negative bacteria 13–30% Coagulase negative staphylococci 7–20% *Enterococcus* spp 5–15% *Corynebacterium* spp 2–15% *Candida* spp 0–8%

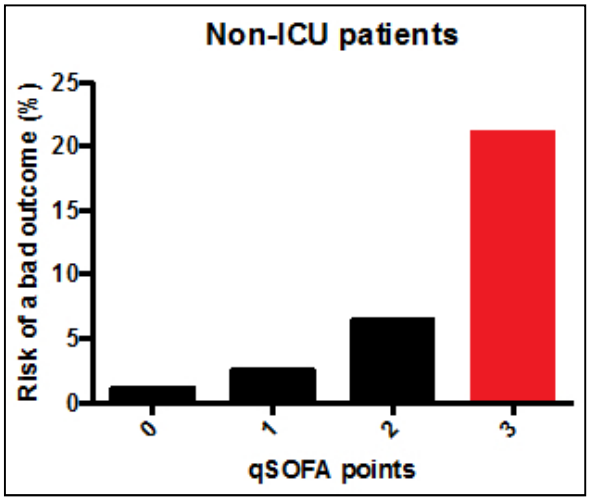
Clinical case #3

- **AS: 78 y-o man**
- **Diabetes (type II), arterial hypertension, ischemic cardiopathy, COPD, mild kidney insufficience.**
- **Admitted in CardioUnit and later in Internal Medicine (27 August 2016) for unstable angina.**
- **Diagnosis: critical common truncus stenosis. During the stay, diarrhea→ vanco 500 mg 4td**
- **After a 25d stay→ transferred in Cardiosurgery (other hospital)**
- **At admission→ rectal swab→ CRE**
- **Urinocolture→ KPC K pneumoniae**
- **Cdiff colitis→ transferred in Internal Medicine**
- **After 3 days→ fever (39°C), 15,000 WC, high CRP and PCT, altered mental status**
- **Blood culture, urine colture, Chest X rays: negatives**
- **Which diagnosis? Which treatment?**
- **qSOFA?**

- Case 2

Is the patient in the ICU?	No
Altered Mentation	Yes
Respiratory rate (breaths per minute)	23
Systolic blood pressure (mmHg)	90
Total Score	3

Your patient with suspected infection not in the intensive care unit has a **23% risk** of a bad outcome. This is a prompt to consider that sepsis is **very likely**



- Case 3

Is the patient in the ICU?	NO
Altered Mentation	Yes
Respiratory rate (breaths per minute)	28
Systolic blood pressure (mmHg)	80
Total Score	3

Your patient with suspected infection not in the intensive care unit has a **23% risk** of a bad outcome. This is a prompt to consider that sepsis is **very likely**

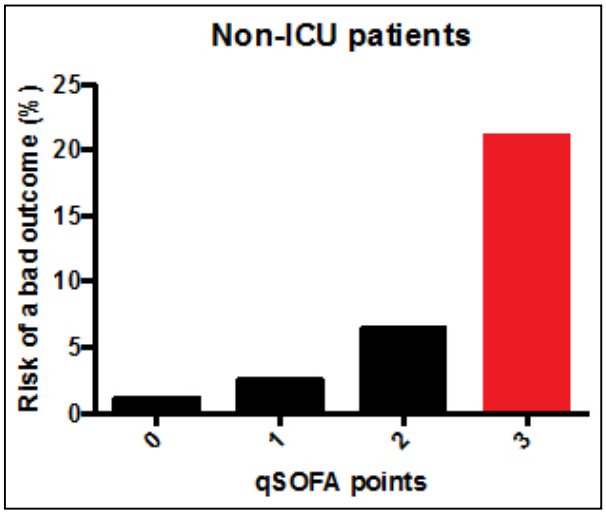
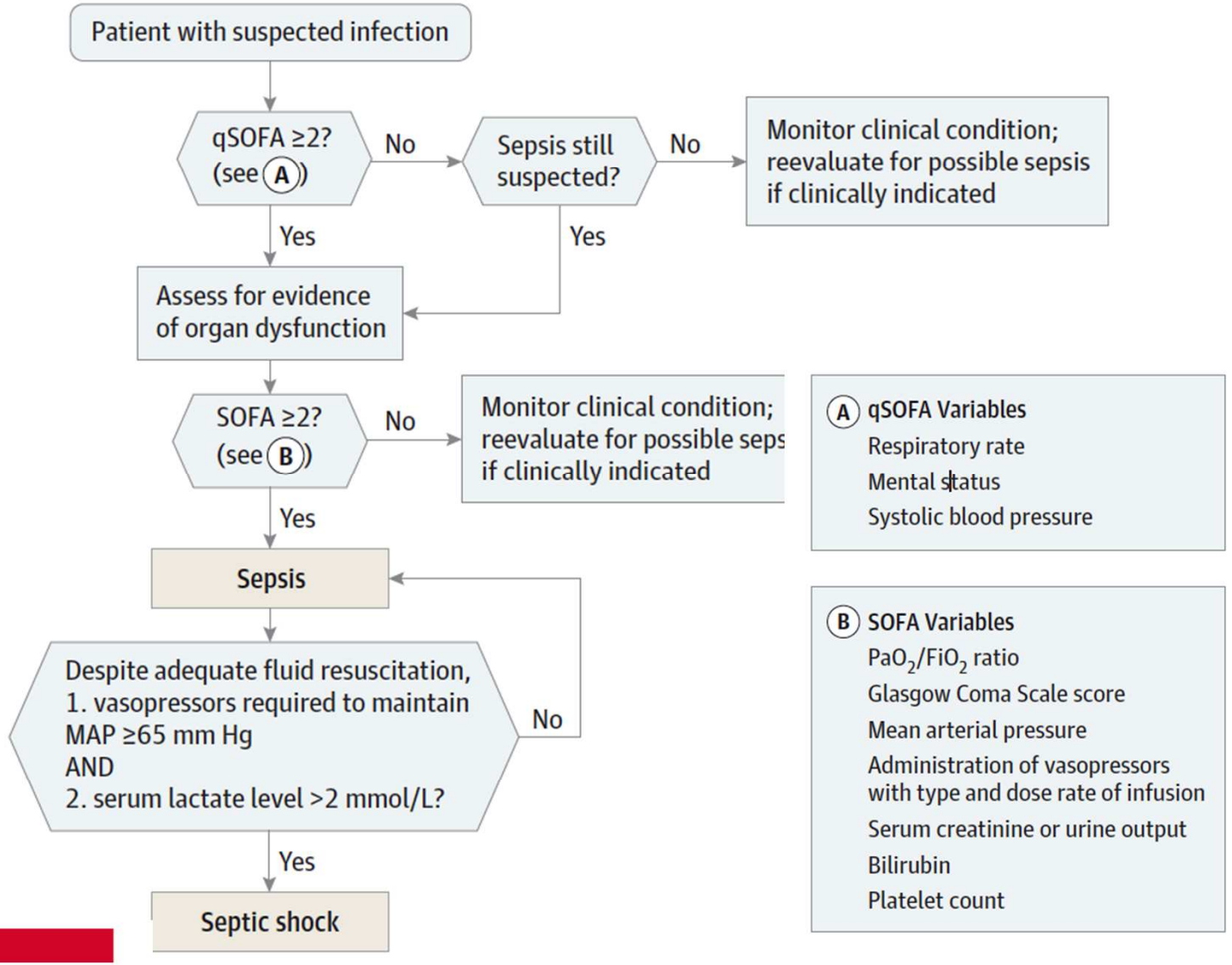


Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



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OUTLINE (1)

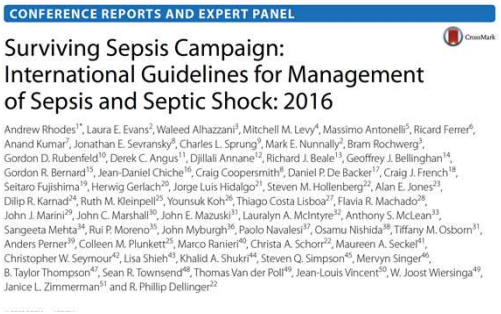
- A: INITIAL RESUSCITATION
- B: SCREENING FOR SEPSIS AND PERFORMANCE IMPROVEMENT
- C: DIAGNOSIS
- D: ANTIMICROBIAL CHEMOTHERAPY
- E: SOURCE CONTROL
- F: FLUID THERAPY
- G: VASOACTIVE MEDICATIONS
- H: CORTICOSTEROIDS
- BLOOD PRODUCTS

OUTLINE (2)

- J: IMMUNOGLOBULINS
- K: BLOOD PURIFICATION
- L: ANTICOAGULANTS
- M. MECHANICAL VENTILATION
- N: SEDATION AND ANALGESIA
- O: GLUCOSE CONTROL
- P: RENAL REPLACEMENT THERAPY
- Q. BICARBONATE THERAPY
- R. VENOUS THROMBOEMBOLISM PROHYLAXIS
- S: STRESS ULCER PROPHYLAXIS
- T: NUTRITION
- U: SETTING GOALS OF CARE

C: Diagnosis (1)

1. **We recommend that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis and septic shock if doing so results in no substantial delay in the start of antimicrobials (BPS*).**
   - **Remarks: Appropriate routine microbiologic cultures always include at least two sets of blood cultures (aerobic and anaerobic).**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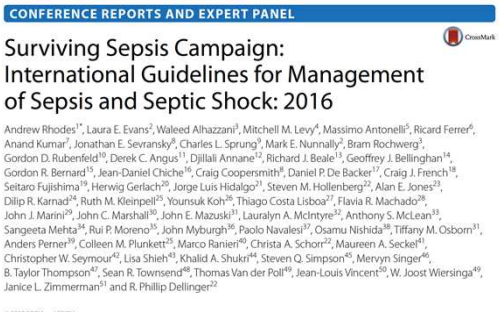
*Best Practice Statement

C: Diagnosis (2)

- All necessary blood cultures may be drawn together on the same occasion. Blood culture yield has not been shown to be improved with sequential draws or timing to temperature spikes

- In patients with suspected sepsis or septic shock, appropriate routine microbiologic cultures should be obtained before initiation of antimicrobial therapy from all sites considered to be potential sources of infection if it results in no substantial delay in the start of antimicrobials. This may include blood, cerebrospinal fluid, urine, wounds, respiratory secretions, and other body fluids, but does not normally include samples that require an invasive procedure such as bronchoscopy or open surgery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C: Diagnosis (3)

- **"Pan culture" of all sites that could potentially be cultured should be discouraged (unless the source of sepsis is not clinically apparent), because this practice can lead to inappropriate antimicrobial use**

- **In potentially septic patients with an intravascular catheter (in place > 48 hours) in whom a site of infection is not clinically apparent or a suspicion of intravascular catheter-associated infection exists, at least one blood culture set should be obtained from the catheter (along with simultaneous peripheral blood cultures)**

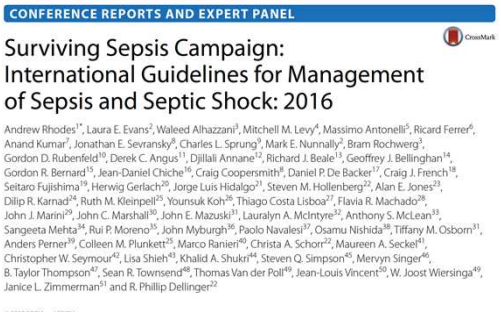

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TABLE 6. SURVIVING SEPSIS CAMPAIGN BUNDLE 2016

To be completed within 3 hours

1. Measure lactate level.
2. Obtain blood cultures prior to administration of antibiotics.
3. Administer broad spectrum antibiotics.
4. Administer 30 ml/kg crystalloid for hypotension or lactate ≥4 mmol/L.

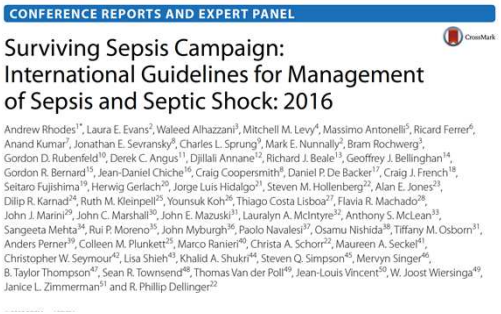
''Time of presentation'' is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review.

To be completed within 6 hours

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65 mm Hg.
6. In the event of persistent hypotension after initial fluid administration (MAP <65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings according to Table 1.
7. Re-measure lactate if initial lactate elevated.

D: ANTIMICROBIAL THERAPY (1)

- **1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within one hour for both sepsis and septic shock (strong recommendation, moderate quality of evidence; grade applies to both conditions).**



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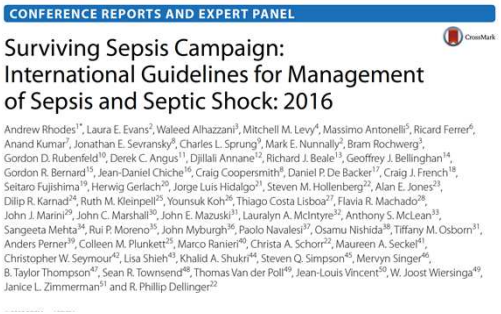
Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[18], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[23], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

D: ANTIMICROBIAL THERAPY (2)

- **2. We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage) (strong recommendation, moderate quality of evidence).**
- **3. We recommend that empiric antimicrobial therapy be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted (BPS).**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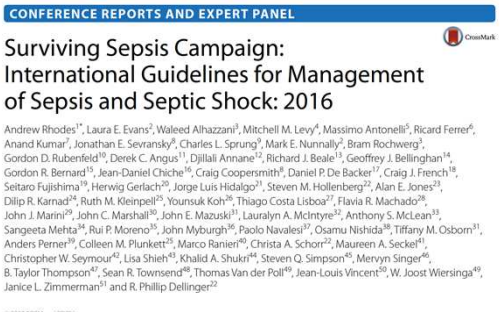
Several factors must be assessed and used in determining the appropriate antimicrobial regimen at eachmedical center and for each patient. These include:

a) **The anatomic site of infection with respect to the typical pathogen profile and to the properties of individual antimicrobials to penetrate that site**

b) **Prevalent pathogens within the community, hospital, and even hospital ward**

c) **The resistance patterns of those prevalent pathogens**

d) **The presence of specific immune defects such as neutropenia, splenectomy, poorly controlled HIV infection and acquired or congenital defects of immunoglobulin, complement or leukocyte function or production**



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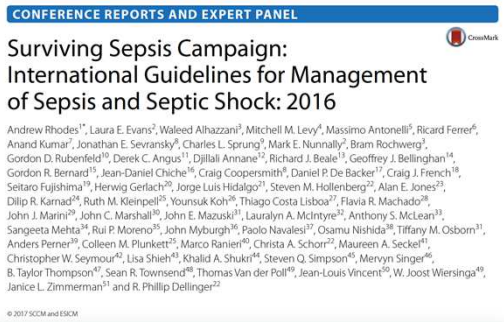
e) Age and patient **comorbidities** including chronic illness (e.g., diabetes) and **chronic organ dysfunction** (e.g., liver or renal failure), the presence of **invasive devices** (e.g., central venous lines or urinary catheter) that compromise the defense to infection.

f) **Risk factors for infection with multidrug-resistant** pathogens including prolonged hospital/chronic facility stay, recent antimicrobial use, prior hospitalization, and prior colonization or infection with multidrug- resistant organisms.



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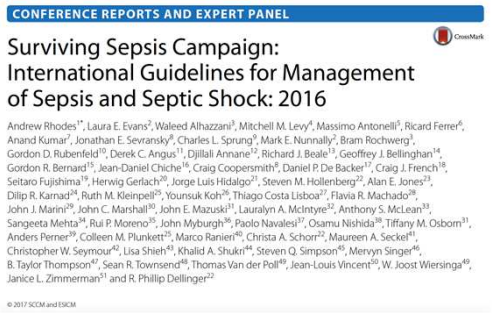
g) Consider risk factors for: carbapenem resistant Gram negative rods (add a second agent….), MRSA, and legionella

l) Consider risk factors for Candida spp (echinocandins in critically ill pts): β-D-glucan?

m) Superior empiric coverage can be obtained using local and unit-specific antibiograms or an infectious diseases consultation. Where uncertainty regarding appropriate patient-specific antimicrobial therapy exists, infectious diseases consultation is warranted. Early involvement of infectious diseases specialists can improve outcome in some circumstances (e.g., *S aureus* bacteremia)

n) The decisions to continue, narrow, or stop antimicrobial therapy must be made on the basis of clinician judgment and clinical information.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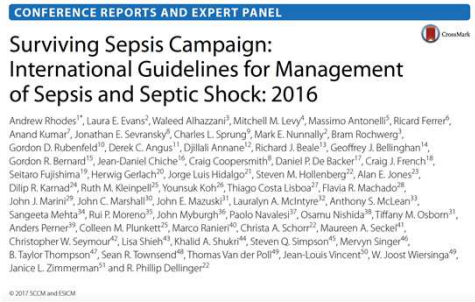
D: ANTIMICROBIAL THERAPY (3)

- **4. We recommend against sustained systemic antimicrobial prophylaxis in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury) (BPS).**
  - Although the prophylactic use of systemic antimicrobials for severe necrotizing pancreatitis has been recommended in the past, recent guidelines have favored avoidance of this approach
  - Current guidelines for burn management do not support sustained antimicrobial prophylaxis

- **5. We recommend that dosing strategies of antimicrobials be optimized based on accepted pharmacokinetic/pharmacodynamic principles and specific drug properties in patients with sepsis or septic shock (BPS).**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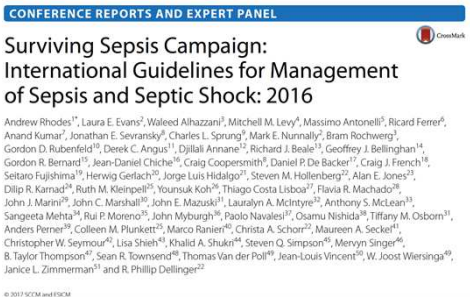
D: ANTIMICROBIAL THERAPY (4)

6. We suggest empiric combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of septic shock (weak recommendation, low quality of evidence).



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Colistin alone versus colistin plus meropenem for treatment of severe infections caused by carbapenem-resistant Gram-negative bacteria: an open-label, randomised controlled trial

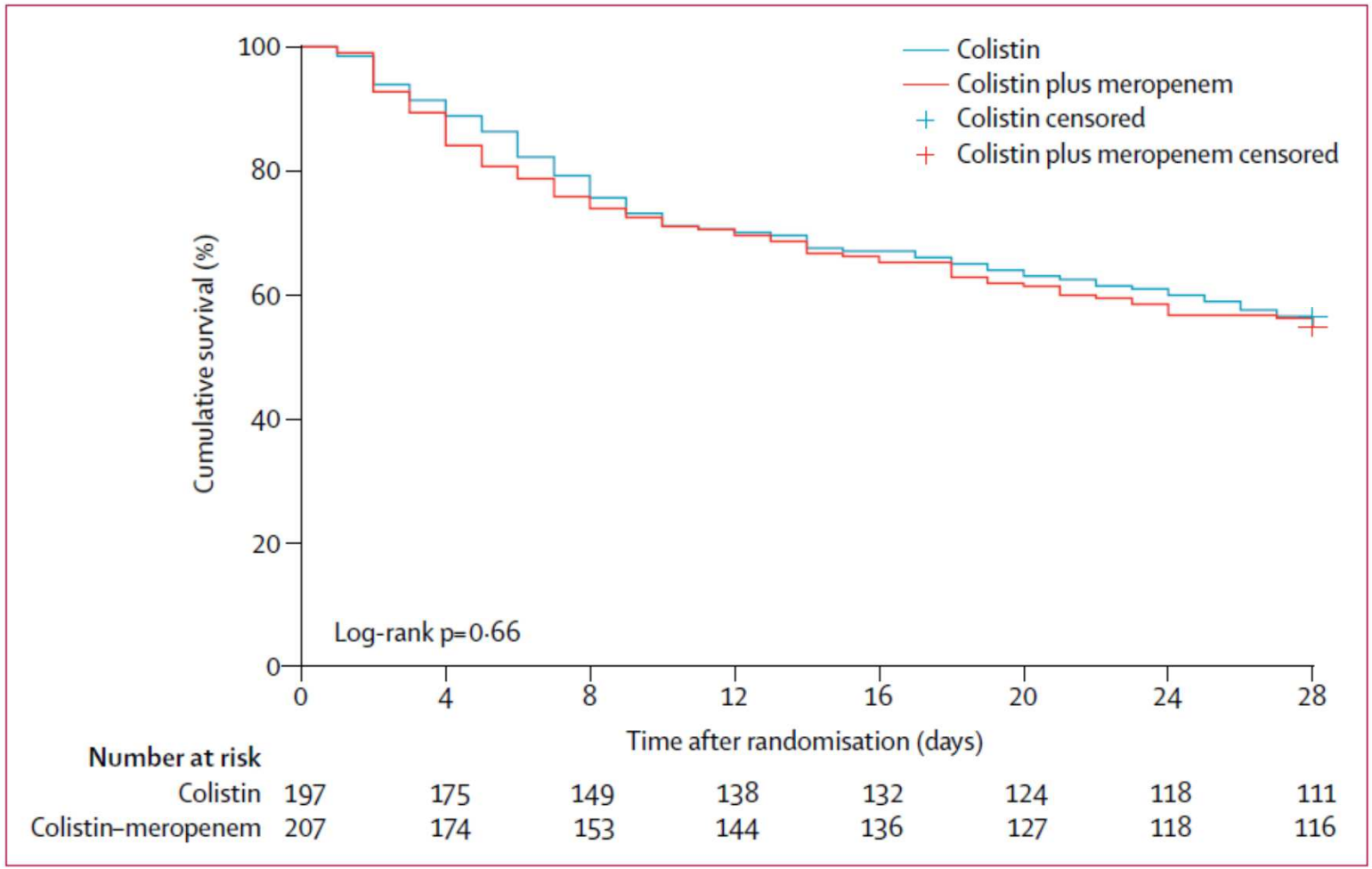

Figure 2: Survival analysis to day 28 after randomisation

Paul M et al. Lancet Infect Dis 2018

Application of the Third International Consensus Definitions for Sepsis (Sepsis-3) Classification: a retrospective population-based cohort study

Donnelly JP et al *Lancet Infect Dis* 2017; 17: 661–70

- **Retrospective analysis using data from 30 239 participants from the USA who were aged at least 45 years and enrolled in the Stroke (REGARDS) cohort.**

- **Patients were enrolled between Jan 25, 2003, and Oct 30, 2007.**

They applied three classifications:

- **SIRS+infection criteria**
- **SOFA score from Sepsis-3, and**
- **qSOFA score from Sepsis-3.**

- **They estimated incidence during the study period, in-hospital mortality, and 1-year mortality.**

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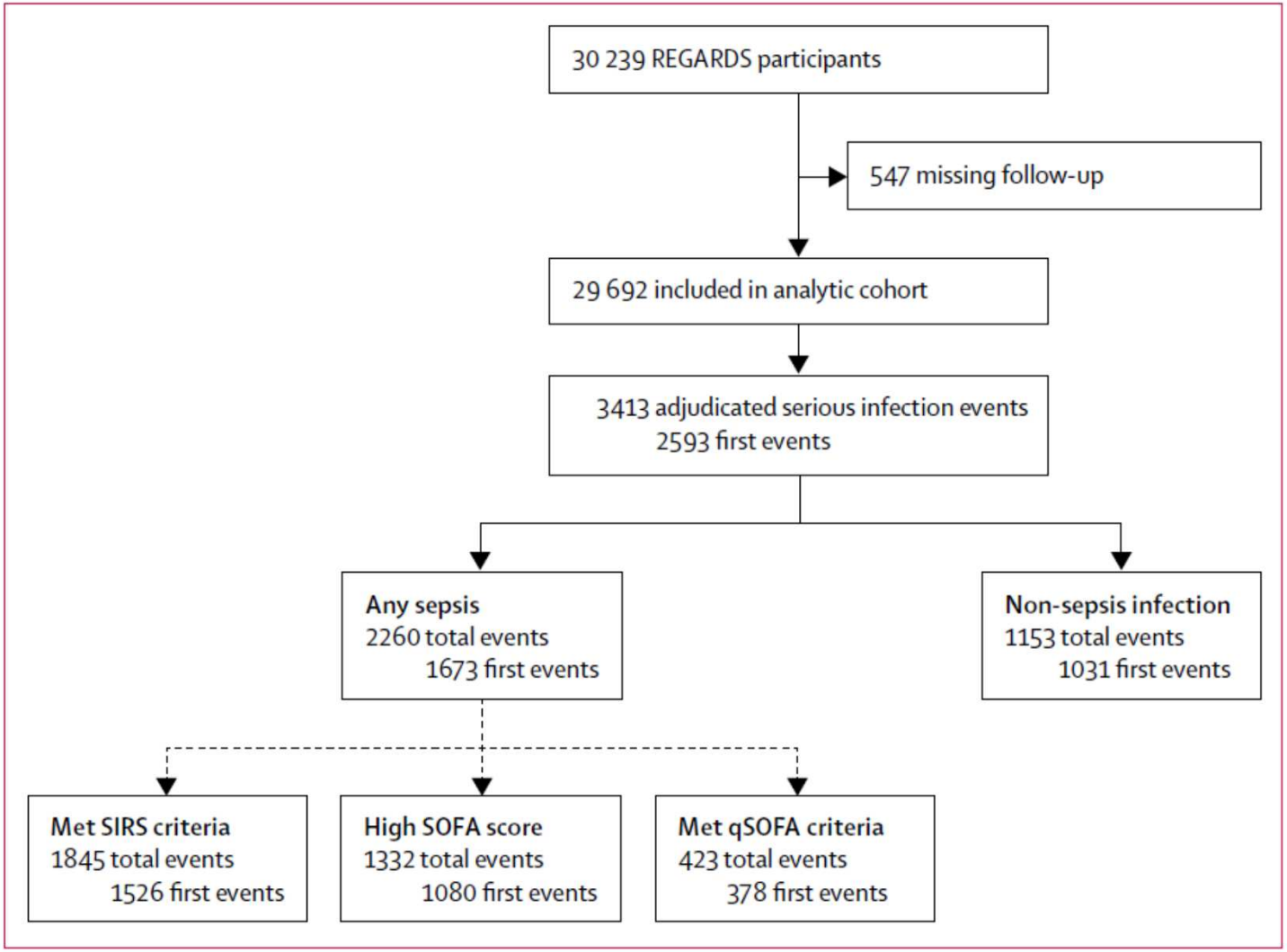

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Donnelly JP et al *Lancet Infect Dis 2017; 17: 661–70*

	In-hospital mortality		28-day mortality (time from hospital admission or emergency department visit)*			1-year mortality (time from discharge)†		
	Total infection events	Deaths	Deaths	Total exposure (person-years)	Mortality per 100 person-years (95% CI)	Deaths	Total exposure (person-years)	Mortality per 100 person-years (95% CI)
All Infections	2593	163 (6%)	167 (7%)	184	90·7 (77·9–105·6)	238 (10%)	2058	11·6 (10·2–13·1)
Non-sepsis infection	916	19 (2%)	21 (2%)	68	31·0 (20·2–47·6)	38 (4%)	796	4·8 (3·5–6·6)
Met SIRS criteria	1392	128 (9%)	128 (10%)	96	133·2 (112·0–158·4)	154 (13%)	1050	14·7 (12·5–17·2)
High SOFA score	960	125 (13%)	122 (13%)	64	191·0 (160·0–228·1)	147 (18%)	650	22·6 (19·2–26·6)
Met qSOFA criteria	295	67 (23%)	62 (23%)	17	350·4 (273·2–449·5)	51 (23%)	173	29·4 (22·3–38·7)

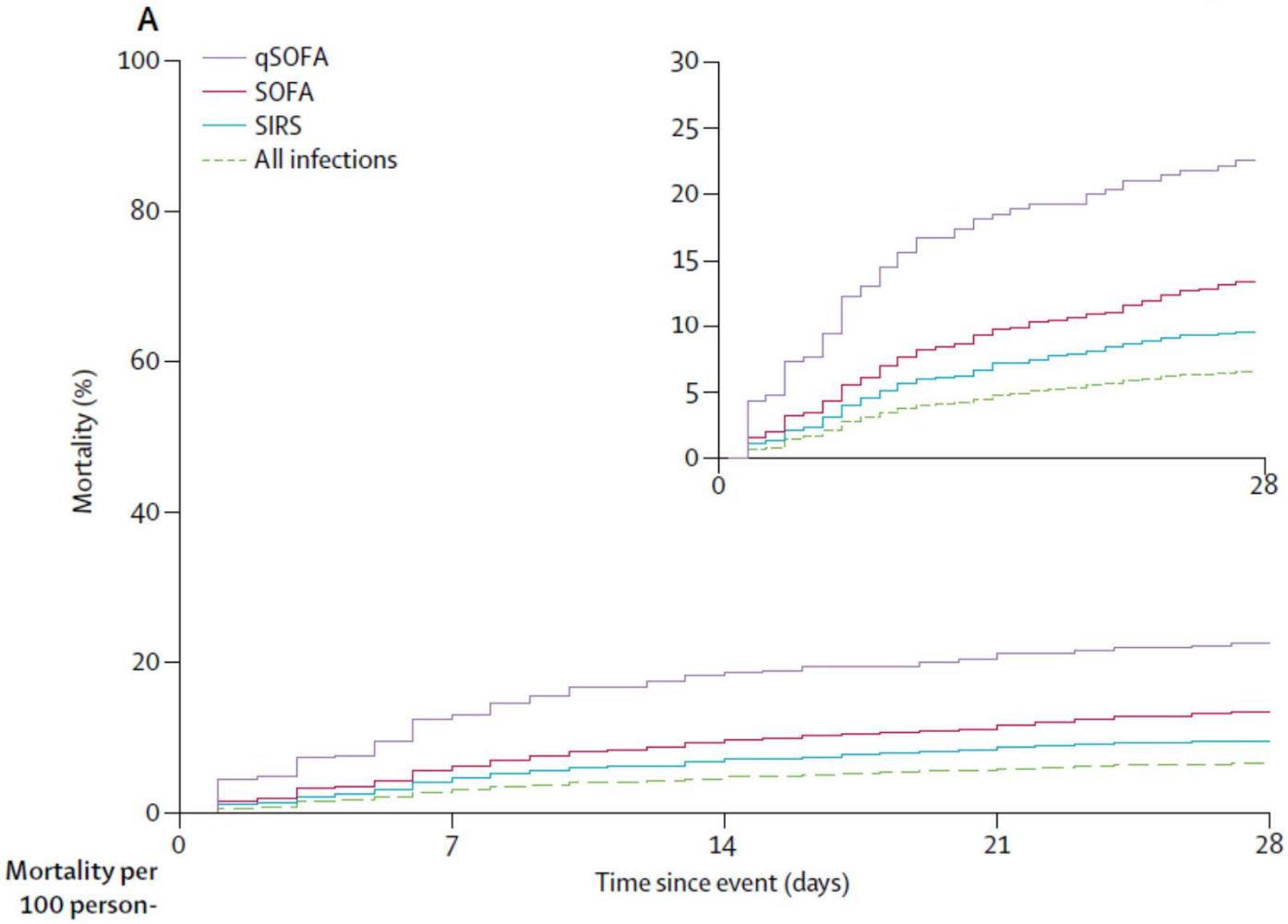
Only first events were included. All infections included those defined as sepsis events as well as non-sepsis infection. Non-sepsis infections were defined as infections not meeting any criteria for sepsis and were mutually exclusive from any sepsis events. Sepsis classifications were not mutually exclusive and events could belong to multiple groups. Mortality per 100 person years of follow-up is relative to the date of encounter or discharge. SIRS=systemic inflammatory response syndrome. SOFA=sepsis-related organ failure assessment. qSOFA=quick sepsis-related organ failure assessment. *Excludes patients with no follow-up after the date of encounter and patients who died on the day of the encounter, leaving 2519 events. †Excludes patients who died in hospital or on the day of discharge and those with no follow-up after discharge, leaving 2386 events.

Table 2: Mortality by classification

However, SOFA and qSOFA do not define sepsis, but instead might serve as indicators of an increased risk of death among patients with infection.

Application of the Third International Consensus Definitions for Sepsis (Sepsis-3) Classification: a retrospective population-based cohort study

Donnelly JP et al *Lancet Infect Dis* 2017; 17: 661–70



Clinical Evaluation of Sepsis-1 and Sepsis-3 in the ICU

21,291 infected ICU pts, of these

- 18.4% with sepsis-1 criteria did not meet sepsis-3 criteria→ their 21-d mortality was 6%
- 6% with sepsis-3 did not meet sepsi-1 criteria→ 21-d mortality rate was 9.11%

Sensitivity for 21-d mortality

- sepsis-1: 96%
- Sepsis-3 (SOFA) 91%

Sepsis-3 diagnostic criteria narrow the sepsis population at the expense of sensitivity (false negatives may have delayed diagnosis)

Fang X et al. Chest 2017

The Impact of the Sepsis-3 Septic Shock Definition on Previously Defined Septic Shock Patients*

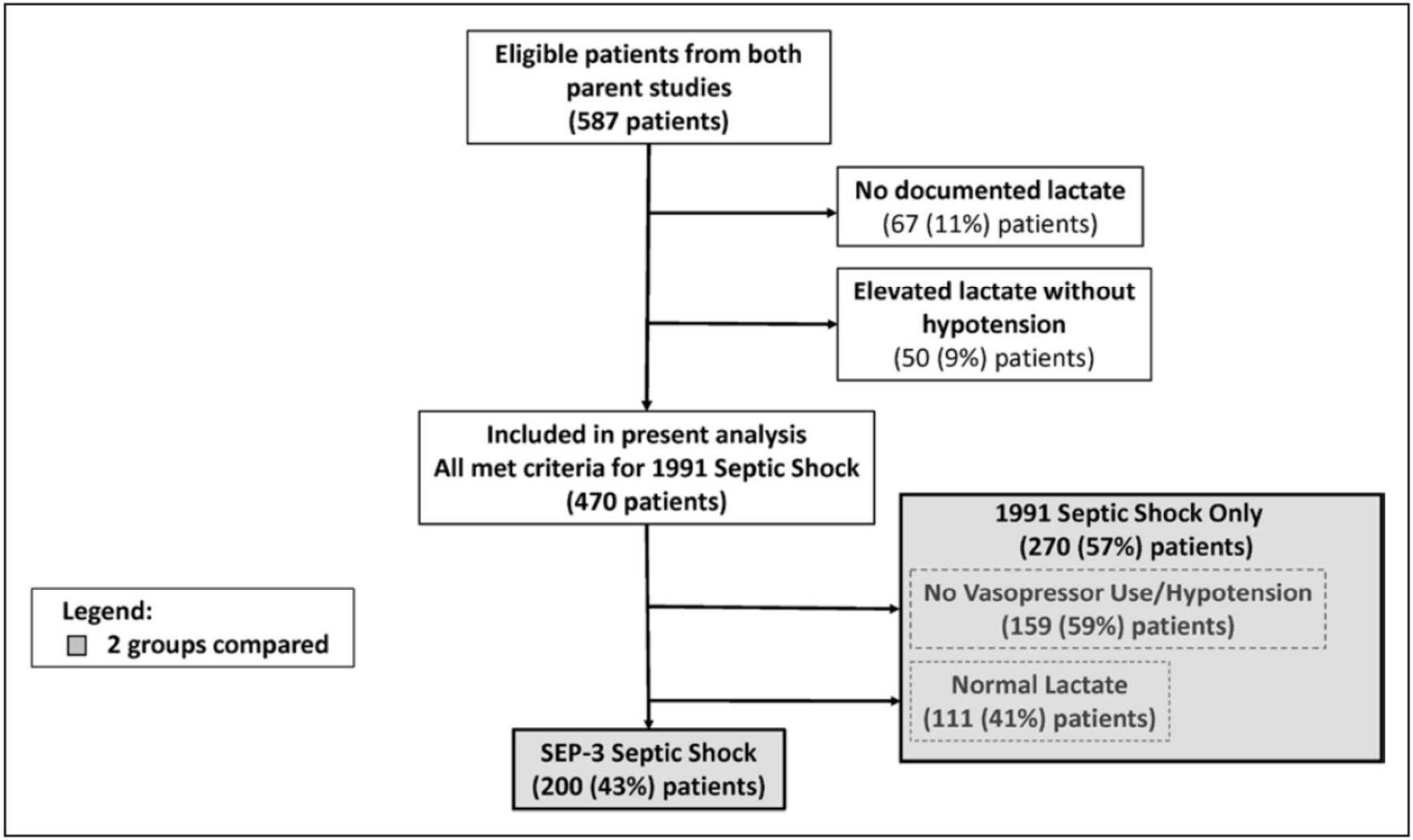


Figure 1. Flowchart of included patients.

Sterling SA et al. Crit Care Med 2017; 45: 1436-42

The Impact of the Sepsis-3 Septic Shock Definition on Previously Defined Septic Shock Patients*

TABLE 2 . Results of In-Hospital Patient Outcomes

Variable	"New" Septic Shock Criteria (Sepsis-3) (*n* = 200)	"Old" Septic Shock Criteria (1991 Only) (*n* = 270)	*p*
Mortality, *n* (%)[a]	57 (28.5); 95% CI, 22–35	39 (14.4); 95% CI, 10–19	< 0.001
Length of stay (IQR)			
Vasopressors days	1.3 (0.9–4); 95% CI, 2.3–4.2	1 (0–2); 95% CI, 0.9–1.4	< 0.001
Total hospital days	8 (5–16); 95% CI, 9.8–12.7	8 (4.5–12); 95% CI, 9.6–12.2	0.466
Total ICU days	3.2 (1.8–7); 95% CI, 4.9–7.1	2.5 (1–5); 95% CI, 3.6–5.1	0.006

TABLE 3. Quick Sequential Organ Failure Assessment Scores and Mortality

qSOFA Score and Mortality Rate	Septic Shock Criteria		
	"New" Septic Shock Criteria (Sepsis-3) (*n* = 200)	"Old" Septic Shock Criteria (1991 Only) (*n* = 270)	*p*
qSOFA < 2; mortality, *n* (%)	73; 11 (15)	133; 18 (14)	0.926
qSOFA ≥ 2; mortality, *n* (%)	127; 46 (36)	137; 21 (15)	< 0.001

Sterling SA et al. Crit Care Med 2017; 45: 1436-42

The Impact of the Sepsis-3 Septic Shock Definition on Previously Defined Septic Shock Patients*

Subgroup analysis of 127 patients meeting only the old definition demonstrated significant mortality benefit following implementation of a early quantitative resuscitation protocol (35% vs 10%; p=0.006)

Puskarich MA, Marchick MR, Kline JA, et al: One year mortality of patients treated with an emergency department based early goal directed therapy protocol for severe sepsis and septic shock: A before and after study. *Crit Care* 2009; 13:R167

Resuscitation interventions utilized in the initial six hours
Intervention
Endotracheal intubation n, (%)
Crystalloid volume (median, (IQR) liters)
Vasopressor administration n, (%)
Dobutamine administration n, (%)
PRBC transfusion n, (%)

Sterling SA et al. Crit Care Med 2017; 45: 1436-42

Take home messages

- **Sepsis-3 is a helpful tool for identifying severe organ dysfunction and rapid progression to septic shock and ICU admission**

- **However, Sepsis-3 diagnostic criteria narrow the sepsis population at the expense of sensitivity (false negatives may have delayed diagnosis)**

- **Diagnostic management includes SOFA and qSOFA, but clinicians should be aware that both SOFA and qSOFA do not define sepsis, but instead might serve as indicators of an increased risk of death among patients with infection**