# Sepsis: What Is It Really?

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# Goals

- Brief review on the background/epidemiology of sepsis
- Review the CMS Sepsis Metric SEP-1
  - All 141 points (does not include ~14 addendum's)
- Provide an update on the data surrounding the sepsis diagnosis used in those metrics
- Briefly provide an ID opinion on the treatment of sepsis in an era of antibiotic resistance

# Quote

- Quote from JAMA
- “Advances in the treatment of fever … have not kept pace with the rapid progress in our knowledge of the etiology. In the present condition of bacteriology we may expect great things in the near future, but meanwhile we jog along without any fixed aim, too often carried away by winds of doctrines and wild theories”.

# Quote

- — William Osler, from Osler W. The study of the Fevers of the South. JAMA 21, 999–1004 (1896)

# Epidemiology of Sepsis

- 1999-2014 CDC found that a total of 2,470,666 decedents (6% of all deaths) had sepsis listed among the causes of death
  - for 22% of these decedents, sepsis was listed as the underlying cause of death. *
- 750,000 annual cases
  - 2% of all hospital admissions are due to “severe sepsis”
- $23 billion in health care expenditures in 2013
- Most commonly occurs among patients with 1 or more risk factors
- Majority of patients have health care exposure or a chronic comorbidity
- **In many cases, a specific pathogen is not identified**

*https://www.cdc.gov/sepsis/datareports/index.html

# SEPSIS STEPS

## SIRS

T: >100.4 F
< 96.8 F
RR: >20
HR: >90
WBC: >12,000
<4,000
>10% bands
PCO2 < 32 mmHg

## SEPSIS

2 SIRS

+

Confirmed **or** suspected infection

## SEVERE SEPSIS

Sepsis +

Signs of End Organ Damage

Hypotension (SBP <90)

Lactate >4 mmol

## SEPTIC SHOCK

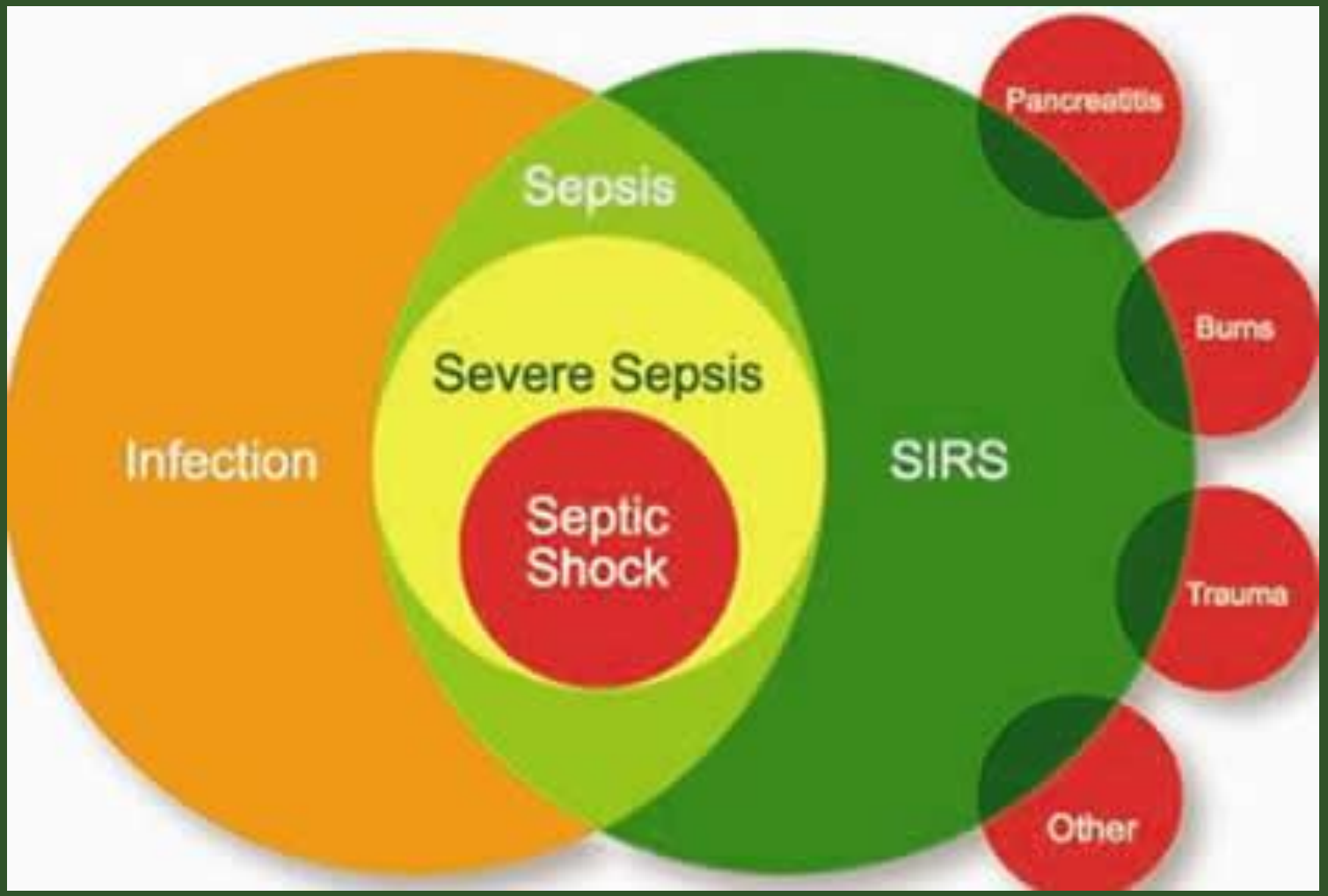
Severe Sepsis with persistent:

Signs of End Organ Damage

Hypotension (SBP <90)

Lactate >4 mmol

Slides Courtesy of Curtis Merritt, D.O.

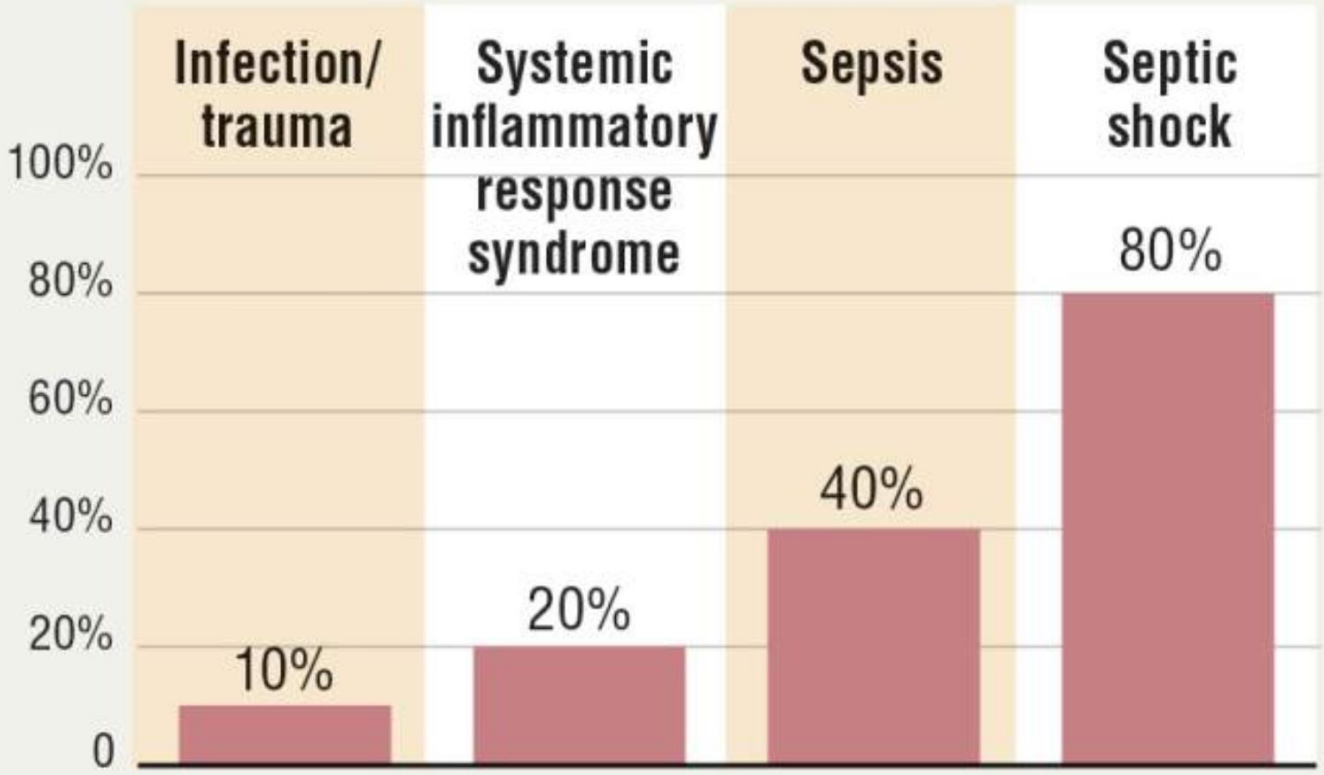



http://www.differencebetween.info/difference-between-sepsis-and-infection

# The sepsis continuum

Sepsis starts with an infection with a low risk of death, but as the condition progresses, the mortality rate climbs significantly.

## 28-day mortality rates




Source: sepsis.com

Greg Cross / The Bulletin

**Table 1. Characteristics of the Patients at Baseline.***

| Characteristic | Protocol-Based EGDT (N=439) | Protocol-Based Standard Therapy (N=446) | Usual Care (N=456) |
|---|---|---|---|
| Age — yr† | 60±16.4 | 61±16.1 | 62±16.0 |
| Male sex — no. (%) | 232 (52.8) | 252 (56.5) | 264 (57.9) |
| Residence before admission — no. (%)‡ | | | |
| Nursing home | 64 (14.6) | 72 (16.1) | 73 (16.0) |
| Other | 373 (85.0) | 373 (83.6) | 382 (83.8) |
| Charlson comorbidity score§ | 2.6±2.6 | 2.5±2.6 | 2.9±2.6 |
| Source of sepsis — no. (%) | | | |
| Pneumonia | 140 (31.9) | 152 (34.1) | 151 (33.1) |
| Urinary tract infection | 100 (22.8) | 90 (20.2) | 94 (20.6) |
| Intraabdominal infection | 69 (15.7) | 57 (12.8) | 51 (11.2) |
| Infection of unknown source | 57 (13.0) | 47 (10.5) | 66 (14.5) |
| Skin or soft-tissue infection | 25 (5.7) | 33 (7.4) | 38 (8.3) |
| Catheter-related infection | 11 (2.5) | 16 (3.6) | 11 (2.4) |
| Central nervous system infection | 3 (0.7) | 3 (0.7) | 4 (0.9) |
| Endocarditis | 1 (0.2) | 3 (0.7) | 3 (0.7) |
| Other | 28 (6.4) | 31 (7.0) | 26 (5.7) |
| Determined after review not to have infection | 5 (1.1) | 14 (3.1) | 12 (2.6) |
| Positive blood culture — no. (%) | 139 (31.7) | 126 (28.3) | 131 (28.7) |
| APACHE II score¶ | 20.8±8.1 | 20.6±7.4 | 20.7±7.5 |
| Entry criterion — no. (%) | | | |
| Refractory hypotension | 244 (55.6) | 240 (53.8) | 243 (53.3) |
| Hyperlactatemia‖ | 259 (59.0) | 264 (59.2) | 277 (60.7) |
| Physiological variables | | | |
| Systolic blood pressure — mm Hg | 100.2±28.1 | 102.1±28.7 | 99.9±29.5 |

ProCESS study NEJM 2016

Last Updated: Version 5.0a

**NQF-ENDORSED VOLUNTARY CONSENSUS STANDARDS FOR HOSPITAL CARE**

**Measure Information Form**
**Collected For: CMS Only**

**Measure Set:** Sepsis

**Set Measure ID #:** SEP-1

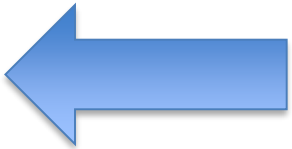
**Performance Measure Name:** Early Management Bundle, Severe Sepsis/Septic Shock

**Description:** This measure focuses on adults 18 years and older with a diagnosis of severe sepsis or septic shock. Consistent with Surviving Sepsis Campaign guidelines, it assesses measurement of lactate, obtaining blood cultures, administering broad spectrum antibiotics, fluid resuscitation, vasopressor administration, reassessment of volume status and tissue perfusion, and repeat lactate measurement. As reflected in the data elements and their definitions, the first three interventions should occur within 3 hours of presentation of severe sepsis, while the remaining interventions are expected to occur within 6 hours of presentation of septic shock.

# SEP-1

- Goal:  improve patient care and reduce variability in care
- SEP-1 is currently an IQR (inpatient quality reporting) clinical process measure-NOT an outcome claims-based measure.
  - In FY 2017, there is a **potential** HVBP cumulative penalty of 2%. In addition, process of care measures will be reassigned to a new domain-clinical care-and decrease to 5% of the HVBP composite.
  - Display of public outcomes data in media, non-compliant providers may face the repercussions of a tarnished reputation.

| Severe Sepsis | Septic Shock |
| --- | --- |
| All three must be met within 6 hours:<br>1. Documentation of a **suspected source** of infection<br>2. Two or more manifestations of **SIRS** criteria:<br>a. Temperature >38.3 C/101 F or <36 C/96.8 F<br>b. Heart rate >90<br>c. Respiratory rate >20<br>d. WBC >12 or <4 or >10% bands<br>3. **Organ Dysfunction**, evidenced by any one of the following:<br>a. SBP < 90 or MAP <65, or a SBP decrease of more than 40 pts<br>b. Cr >2.0 or urine output < 0.5 cc/kg/hour for 2 hours<br>c. Bilirubin >2 mg/dL (32.4 mol/L)<br>d. Platelet count < 100<br>e. INR >1.5 or PTT > 60<br>f. Lactate >2 mmol/L<br>4. Or if a provider documents severe sepsis, r/o sepsis, possible sepsis, or septic shock | 1. There must be documentation of septic shock present and<br>2. **Tissue hypoperfusion** persisting in the hour after crystalloid fluid administration, evidenced by:<br>a. SBP < 90<br>b. MAP < 65<br>c. Decrease in SBP by >40 points from the patient's baseline<br>d. Lactate ≥4<br>3. Or if the criteria are not met, but there is provider documentation of septic shock or suspected septic shock |



## SEP-1: Early Management Bundle, Severe Sepsis/Septic Shock

**Numerator:** Patients who received ALL of the following:

Received within three hours of presentation of severe sepsis:

- Initial lactate level measurement
- Broad spectrum or other antibiotics administered
- Blood cultures drawn prior to antibiotics

AND received within six hours of presentation of severe sepsis:

- Repeat lactate level measurement only if initial lactate level is elevated

AND ONLY if Septic Shock present:

Received within three hours of presentation of septic shock:

- Resuscitation with 30 ml/kg crystalloid fluids

AND ONLY if hypotension persists after fluid administration, received within six hours of presentation of septic shock:

- Vasopressors

AND ONLY if hypotension persists after fluid administration or initial lactate >= 4 mmol/L, received within six hours of presentation of septic shock:

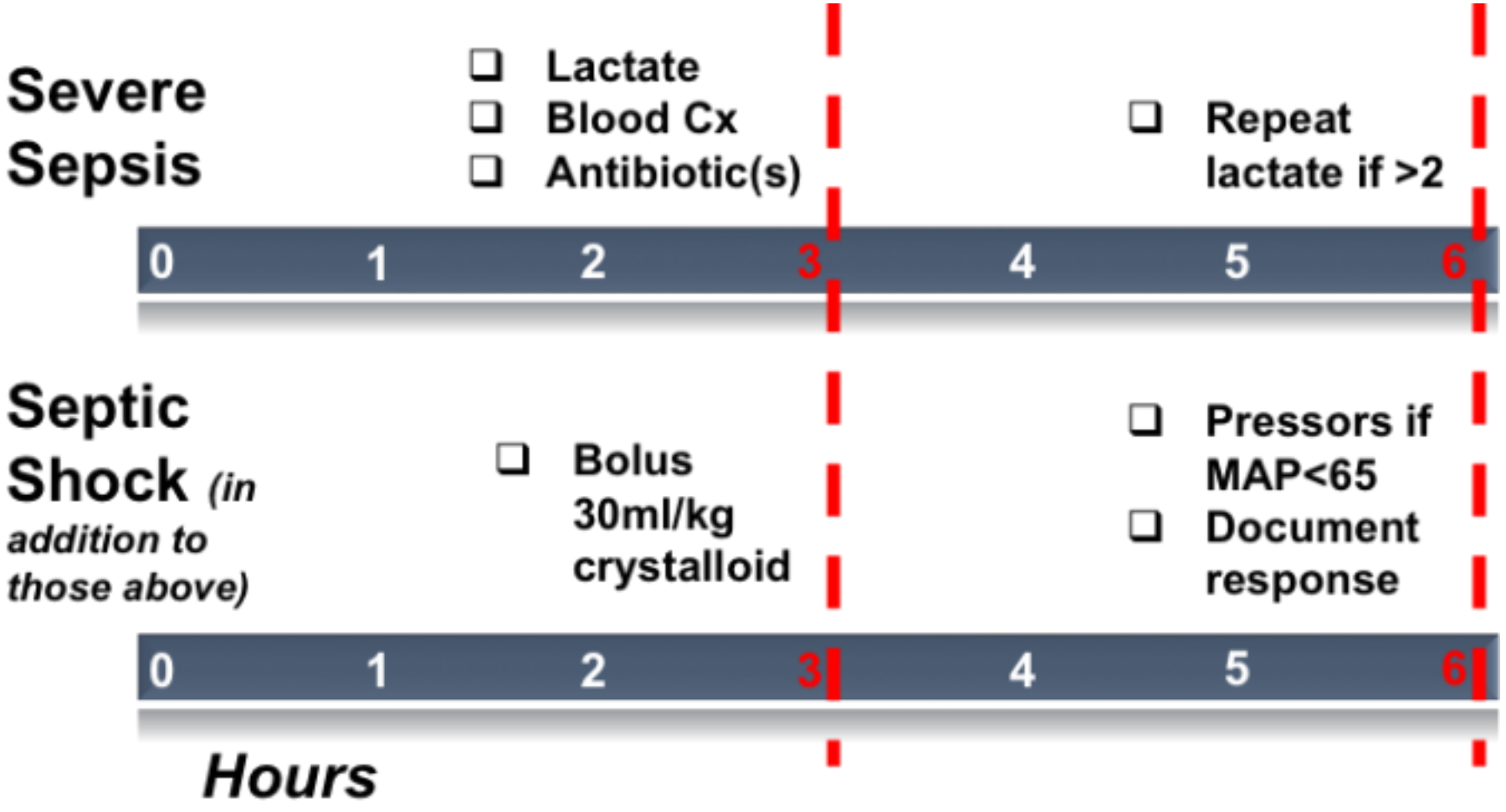
- Repeat volume status and tissue perfusion assessment consisting of either:
  - A focused exam including:
    - Vital signs, AND
    - Cardiopulmonary exam, AND
    - Capillary refill evaluation, AND
    - Peripheral pulse evaluation, AND
    - Skin examination

      OR
  - Any two of the following four:
    - Central venous pressure measurement
    - Central venous oxygen measurement
    - Bedside cardiovascular ultrasound
    - Passive leg raise or fluid challenge

**Denominator:** Inpatients age 18 and over with an ICD-10-CM Principal or Other Diagnosis Code of Sepsis, Severe Sepsis or Septic Shock as defined in Appendix A, Table 4.01

**Variable Ke**

Sepsis Discharge Tir
Shock Discharge Tir
Shock Three Hour Count
Shock Six Hour Count
Shock Physical Assessment Six Hour Count


Severe Sepsis
❑ Lactate
❑ Blood Cx
❑ Antibiotic(s)
❑ Repeat lactate if >2
0 1 2 3 4 5 6
Septic Shock (in addition to those above)
❑ Bolus 30ml/kg crystalloid
❑ Pressors if MAP<65
❑ Document response
0 1 2 3 4 5 6
Hours

# My concerns

- 30 mg/kg crystalloids for EVERYONE
  - What about CHF/ESRD patients?
  - Pre-hospital fluids are not counted
- Cultures
  - Routine blood cultures for CAP are not recommended but are going to be mandated with this metric
  - You will be getting a lot of cultures on patients who have non-infectious diagnosis

**Table 5.0 Antibiotic Monotherapy, Sepsis**

| Antibiotic Selection Options (includes trade & generic name) | Generic Name Crosswalk |
|---|---|
| Doribax | Doripenem |
| Doripenem | Doripenem |
| Eratepenem | Eratepenem |
| Invanz | Eratepenem |
| Imipenem/Cilastatin | Imipenem/Cilastatin |
| Meropenem | Meropenem |
| Merrem | Meropenem |
| Primaxin | Imipenem/Cilastatin |
| Cefotaxime | Cefotaxime |
| Claforan | Cefotaxime |
| Ceftazidime | Ceftazidime |
| Ceftriaxone | Ceftriaxone |
| Fortaz | Ceftazidime |
| Rocephin | Ceftriaxone |
| Cefepime | Cefepime |
| Maxipime | Cefepime |
| Ceftaroline fosamil | Ceftaroline fosamil |

| Antibiotic Selection Options (includes trade & generic name) | Generic Name Crosswalk |
|---|---|
| Teflaro | Ceftaroline fosamil |
| Avelox | Moxifloxacin |
| Gatifloxacin | Gatifloxacin |
| Levaquin | Levofloxacin |
| Levofloxacin | Levofloxacin |
| Moxifloxacin | Moxifloxacin |
| Tequin | Gatifloxacin |
| Amoxicillin/clavulanate | Amoxicillin/clavulanate |
| Ampicillin/sulbactam | Ampicillin/sulbactam |
| Augmentin | Amoxicillin/clavulanate |
| Piperacillin/tazobactam | Piperacillin/tazobactam |
| Ticarcillin/clavulanate | Ticarcillin/clavulanate |
| Timentin | Ticarcillin/clavulanate |
| Unasyn | Ampicillin/sulbactam |
| Zosyn | Piperacillin/tazobactam |

## Combination Antibiotic Therapy Table

| Column A | | Column B |
|---|---|---|
| Aminoglycosides<br>OR<br>Aztreonam OR<br>Ciprofloxacin | + | Cephalosporins (1st and 2nd Generation) OR<br>Clindamycin IV OR<br>Daptomycin OR<br>Glycopeptides OR<br>Linezolid OR<br>Macrolides OR<br>Penicillins |

NOTE: Metronidazole (Flagyl) is not represented on any table because it is not approved for monotherapy and if given, must be given with 2 other combination antibiotic therapy drugs. Since giving those 2 antibiotic therapy drugs will allow Value "1" to be chosen, the metronidazole is not required to be administered or abstracted.

# My critiques of the antibiotics

- Does NOT allow for individualization of care
- Does NOT allow for optimal treatment of streptococcal toxic shock
- Encourages broad spectrum antibiotic use
- Augmentin for sepsis - Really?
- Ticarcillin-clavulonate has not been available for years!
- Gatifloxacin (Tequin) is LONG gone --> almost 10 years
- Ceftaroline monotherapy for sepsis?
  - Who here would use vanco and cefazolin for a early sepsis?
- Cannot even spell the antibiotics correctly
  - "Eratapenem"

# Sepsis Core Measure

IDSA Infectious Diseases Society of America

Society of Critical Care Medicine
The Intensive Care Professionals

American College of Emergency Physicians
ADVANCING EMERGENCY CARE

August 21, 2015

Andrew Slavitt
Acting Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-1461-P
P.O. Box 8013
Baltimore, MD 21244-8013

Re: *National Hospital Inpatient Quality Measures: Sepsis Bundle Project (SEP) Performance Measure*

Dear Mr. Slavitt:

As you know, the updated National Hospital Inpatient Quality Measures will be applied to discharges beginning October 1, 2015, and the undersigned organizations have major concerns with the clinical actions required to satisfactorily meet the Sepsis Bundle Project (SEP) performance measure and the potential unintended consequences that may result. We find the requirement for administration of specific broad-spectrum antibiotics as listed in the measure specifications in all patients to be problematic and potentially harmful.

So what the does literature have to say about foundation of SEP-1?

# Surviving Sepsis: early goal directed therapy

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

# A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

## ABSTRACT

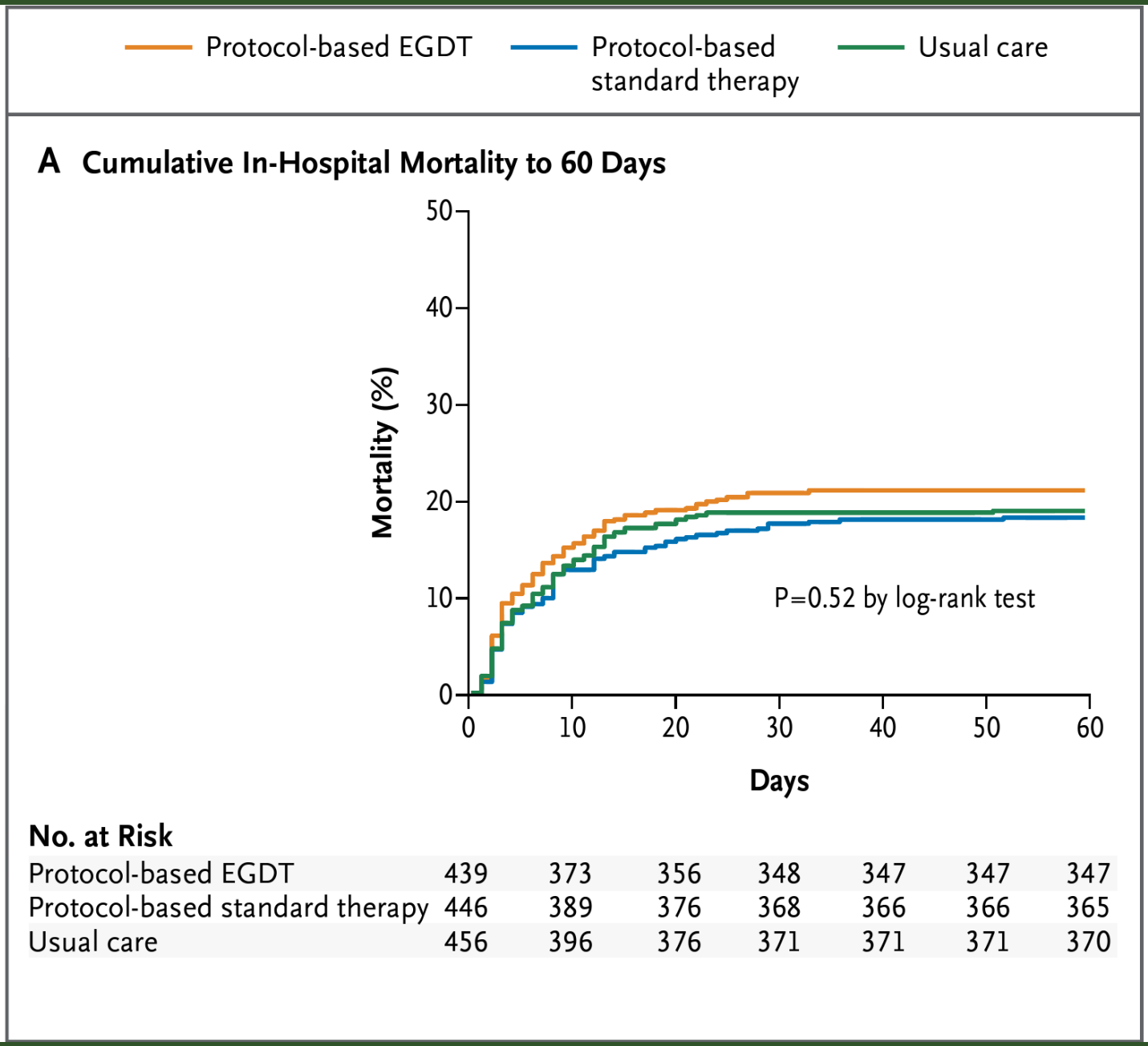
### BACKGROUND

In a single-center study published more than a decade ago involving patients presenting to the emergency department with severe sepsis and septic shock, mortality was markedly lower among those who were treated according to a 6-hour protocol of early goal-directed therapy (EGDT), in which intravenous fluids, vasopressors, inotropes, and blood transfusions were adjusted to reach central hemodynamic targets, than among those receiving usual care. We conducted a trial to determine whether these findings were generalizable and whether all aspects of the protocol

The members of the writing committee (Donald M. Yealy, M.D., John A. Kellum, M.D., David T. Huang, M.D., Amber E. Barnato, M.D., Lisa A. Weissfeld, Ph.D., and Francis Pike, Ph.D., University of Pittsburgh, Pittsburgh; Thomas Terndrup, M.D., Ohio State University, Columbus; Henry E. Wang, M.D., University of Alabama at

# ProCESS Study

- 31 EDs in the United States
- 1341 patients
  - 439 patients to EGDT
  - 446 to protocol –based standard therapy
  - 456 to usual care
- Day 60
  - 92 deaths in EGDT (21%)
  - 81 deaths in protocol based group (18.2%)
  - 86 deaths in the usual care group (18.9%)
- No differences in mortality at 90 days or 1 year or need for ongoing organ support




**No. at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Protocol-based EGDT | 439 | 373 | 356 | 348 | 347 | 347 | 347 |
| Protocol-based standard therapy | 446 | 389 | 376 | 368 | 366 | 366 | 365 |
| Usual care | 456 | 396 | 376 | 371 | 371 | 371 | 370 |

# ProCESS Study

- Sickest sub-group of patients (those with a baseline lactate >5.3 mmol/L) the mortality was significantly higher in the EGDT group as compared to usual care
  - 38.2 vs. 26.4; p = 0.05

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*


## ABSTRACT

### BACKGROUND

Early goal-directed therapy (EGDT) has been endorsed in the guidelines of the Surviving Sepsis Campaign as a key strategy to decrease mortality among patients presenting to the emergency department with septic shock. However, its effectiveness is uncertain.

### METHODS

In this trial conducted at 51 centers (mostly in Australia or New Zealand), we randomly assigned patients presenting to the emergency department with early septic shock to receive either EGDT or usual care. The primary outcome was all-cause mortality within 90 days after randomization.

### RESULTS


The members of the writing committee (Sandra L. Peake, M.D., Ph.D., Anthony Delaney, M.D., Ph.D., Michael Bailey, Ph.D., Rinaldo Bellomo, M.D., Peter A. Cameron, M.D., D. James Cooper, M.D., Alisa M. Higgins, M.P.H., Anna Holdgate, M.D., Belinda D. Howe, M.P.H., Steven A.R. Webb, M.D., Ph.D., and Patricia Williams, B.N.) assume responsibility for the overall content and integrity of the article. Address reprint requests to Ms. Belinda Howe at the Australian and New Zealand Intensive Care Research Centre, Alfred Centre, Level 6 (Lobby B), 99 Commercial Rd., Melbourne, VIC 3004, Australia, or at anzicrc@monash.edu.

# ARISE Study

- 51 centers in Australia and New Zealand
- 1600 patients
- EGDT group received more fluids, vasopressors, transfusions and dobutamine
- At day 90, 147 (18.6%) deaths in the EGDT group and 150 (18.8% death in the “usual-care group)

ORIGINAL ARTICLE

# Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D., for the ProMISe Trial Investigators*

## ABSTRACT

### BACKGROUND

Early, goal-directed therapy (EGDT) is recommended in international guidelines for the resuscitation of patients presenting with early septic shock. However, adoption has been limited, and uncertainty about its effectiveness remains.

### METHODS

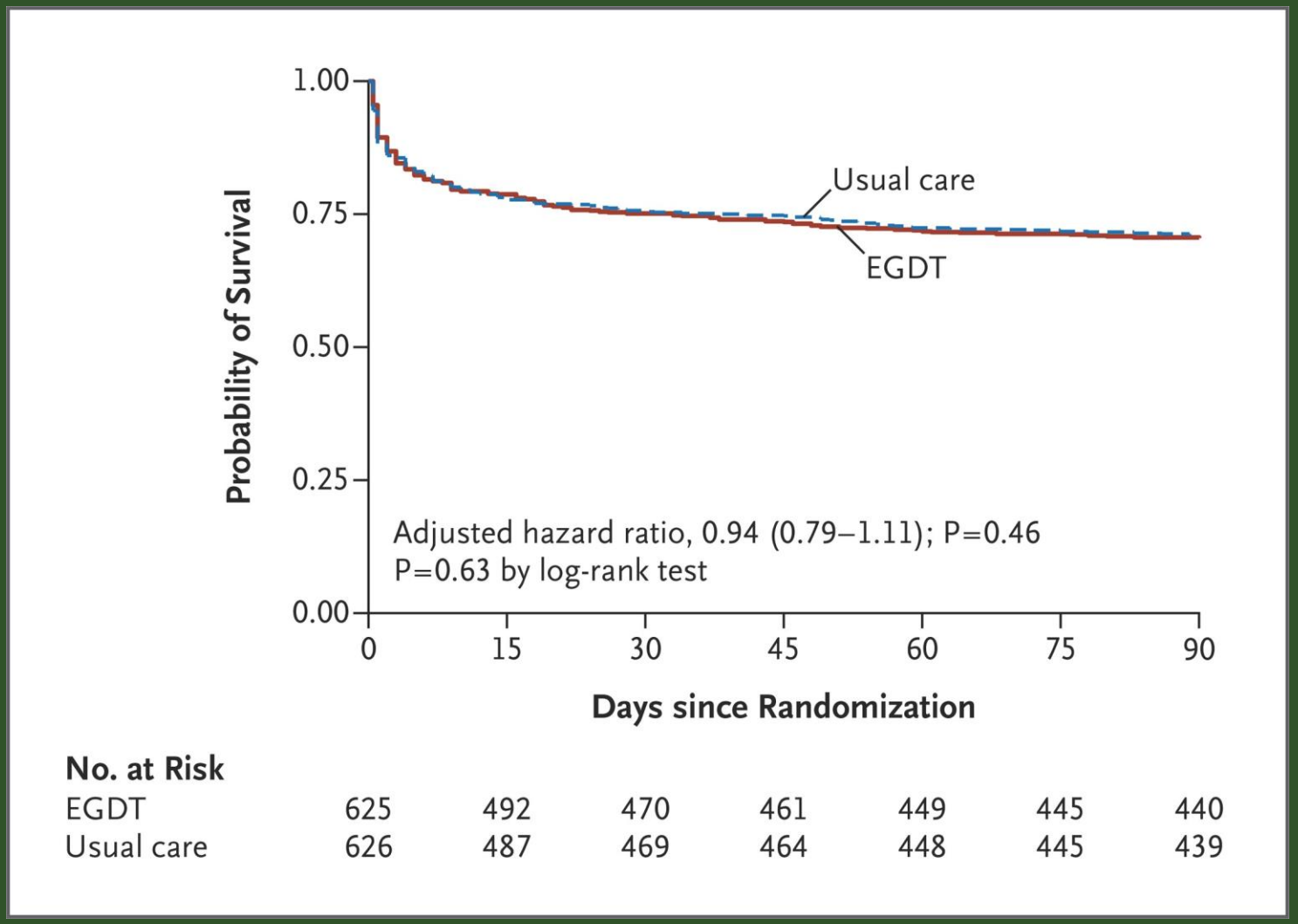
We conducted a pragmatic randomized trial with an integrated cost-effectiveness analysis in 56 hospitals in England. Patients were randomly assigned to receive either EGDT (a 6-hour resuscitation protocol) or usual care. The primary clinical outcome was all-cause mortality at 90 days.

From the Clinical Trials Unit, Intensive Care National Audit and Research Centre (P.R.M., G.S.P., D.A.H., R.J., S.E.H., K.M.R.), Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine (M.Z.S., R.D.G.), and Faculty of Medicine, Imperial College London (D.B.), Department of Acute Medicine, Chelsea and Westminster Hospital NHS Foundation Trust (D.B.), and Bloomsbury Institute of Intensive Care Medicine, University College London (M.S.), London, the Department of Inten-

# ProMISe Trial

- 56 hospitals in England, 1260 patients
- EGDT had increased IV fluids, vasoactive drugs and blood transfusions
- EGDT had worse organ dysfunction, longer stays in ICU and more need for cardiovascular support
- Mortality in EGDT was 29.5% and 29.2% in usual care group

## Kaplan–Meier Survival Estimates.




**No. at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| EGDT | 625 | 492 | 470 | 461 | 449 | 445 | 440 |
| Usual care | 626 | 487 | 469 | 464 | 448 | 445 | 439 |

Mouncey PR et al. N Engl J Med 2015;372:1301-1311

## Conclusions

- In patients with septic shock who were identified early and received intravenous antibiotics and adequate fluid resuscitation, hemodynamic management according to a strict EGDT protocol did not lead to an improvement in outcome.

# Management of Sepsis and Septic Shock

Michael D. Howell, MD, MPH; Andrew M. Davis, MD, MPH

**GUIDELINE TITLE** Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

**DEVELOPERS** Surviving Sepsis Campaign (SSC), Society of Critical Care Medicine (SCCM), and European Society of Intensive Care Medicine (ESICM)

**RELEASE DATE** January 18, 2017

**PRIOR VERSIONS** 2012, 2008, 2004

**TARGET POPULATION** Adults with sepsis or septic shock

**SELECTED MAJOR RECOMMENDATIONS**

Managing infection:

- Antibiotics: Administer broad-spectrum intravenous antimicrobials for all likely pathogens within 1 hour after sepsis recognition (strong recommendation; moderate quality of evidence [QOE]).
- Source control: Obtain anatomic source control as rapidly as is practical (best practice statement [BPS]).
- Antibiotic stewardship: Assess patients daily for deescalation of antimicrobials; narrow therapy based on cultures and/or clinical improvement (BPS).

Managing resuscitation:

- Fluids: For patients with sepsis-induced hypoperfusion, provide 30 mL/kg of intravenous crystalloid within 3 hours (strong recommendation; low QOE) with additional fluid based on frequent reassessment (BPS), preferentially using dynamic variables to assess fluid responsiveness (weak recommendation; low QOE).
- Resuscitation targets: For patients with septic shock requiring vasopressors, target a mean arterial pressure (MAP) of 65 mm Hg (strong recommendation; moderate QOE).
- Vasopressors: Use norepinephrine as a first-choice vasopressor (strong recommendation; moderate QOE).

Mechanical ventilation in patients with sepsis-related ARDS:

- Target a tidal volume of 6 mL/kg of predicted body weight (strong recommendation; high QOE) and a plateau pressure of $\leq$30 cm $H_2O$ (strong recommendation; moderate QOE).

Formal improvement programs:

- Hospitals and health systems should implement programs to improve sepsis care that include sepsis screening (BPS).

# Is SIRS the answer?

# SIRS and Sepsis --> Related?

- Sepsis involves organ dysfunction
  - Complex pathobiology involving more than just the inflammatory response to infection
- Changes in WBC, temperature and heart rate reflect inflammation which is a normal host response to "danger" such as infection, trauma, surgery
  - Criteria are reasonable to identify infection though
- SIRS does NOT equate to a dysregulated, life-threatening response
- Does NOT identify adequately infection in all organs
- SIRS has a poor discriminant validity and is not overly sensitive

Intensive Care Med (2006) 32:421–427
DOI 10.1007/s00134-005-0039-8

ORIGINAL

**Charles L. Sprung**
**Yasser Sakr**
**Jean-Louis Vincent**
**Jean-Roger Le Gall**
**Konrad Reinhart**
**V. Marco Ranieri**
**Herwig Gerlach**
**Jonathan Fielden**
**C. B. Groba**
**Didier Payen**

# An evaluation of systemic inflammatory response syndrome signs in the Sepsis Occurrence in Acutely ill Patients (SOAP) study

Received: 13 December 2005
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Published online: 15 February 2006


**Electronic Supplementary Material**
The electronic reference of this article is http://dx.doi.org/10.1007/s00134-0039-8. The online full-text version of this article includes electronic supplementary material

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University of Turin, S. Giovanni Battista Hospital, Department of Anaesthesiology and Intensive Care,

ICUs *Design and setting:* Cohort, multicentre, observational study of 198 ICUs in 24 European countries. *Patients and interventions:* All 3,147 new adult admissions to participating ICUs between 1 and 15 May 2002 were included. Data were collected prospectively, with common SIRS criteria. *Results:* During the ICU

**Table 5** ICU outcome according to maximum number of SIRS criteria stratified by presence or absence of infection and by presence of severe sepsis and septic shock on admission[a]

| | No infection ($n = 2{,}370$) | | | | | | Infection ($n = 777$) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Frequency | | ICU mortality | | Hospital mortality | | Frequency | | ICU mortality | | Hospital mortality | |
| | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % |
| No SIRS | 119 | 5.0 | 5 | 4.2 | 9 | 7.6 | 0 | – | 0 | – | 0 | – |
| One SIRS | 303 | 12.8 | 26 | 8.6 | 38 | 12.9 | 0 | – | 0 | – | 0 | – |
| Two SIRS | 677 | 28.6 | 68 | 10.0 | 88 | 13.2 | 135 | 17.4 | 21 | 15.6 | 34 | 25.6 |
| Three SIRS | 776 | 32.7 | 147 | 19.0 | 180 | 23.6 | 377 | 48.5 | 104 | 27.6 | 139 | 37.1 |
| Four SIRS | 495 | 20.9 | 126 | 25.5 | 149 | 30.5 | 265 | 34.1 | 86 | 32.5 | 110 | 42.0 |

| | Severe sepsis ($n = 552$) | | | | | | Septic shock ($n = 243$) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Frequency | | ICU mortality | | Hospital mortality | | Frequency | | ICU mortality | | Hospital mortality | |
| | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % |
| No SIRS | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| One SIRS | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| Two SIRS | 77 | 13.9 | 17 | 22.1 | 25 | 33.3 | 11 | 4.5 | 4 | 36.4 | 5 | 45.5 |
| Three SIRS | 271 | 49.1 | 92 | 33.9 | 120 | 44.6 | 111 | 45.7 | 50 | 45.0 | 59 | 53.2 |
| Four SIRS | 204 | 37.0 | 76 | 37.3 | 95 | 47.3 | 121 | 49.8 | 57 | 47.1 | 69 | 57.0 |

[a] $p < 0.001$ for both ICU and hospital mortality according to the number of SIRS criteria

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

Kirsi-Maija Kaukonen, M.D., Ph.D., Michael Bailey, Ph.D., David Pilcher, F.C.I.C.M., D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.

## ABSTRACT

### BACKGROUND

The consensus definition of severe sepsis requires suspected or proven infection, organ failure, and signs that meet two or more criteria for the systemic inflammatory response syndrome (SIRS). We aimed to test the sensitivity, face validity, and construct validity of this approach.

### METHODS

We studied data from patients from 172 intensive care units in Australia and New Zealand from 2000 through 2013. We identified patients with infection and organ failure and categorized them according to whether they had signs meeting two or more SIRS criteria (SIRS-positive severe sepsis) or less than two SIRS criteria (SIRS-negative severe sepsis). We compared their characteristics and outcomes and assessed them for the presence of a step increase in the risk of death at a threshold

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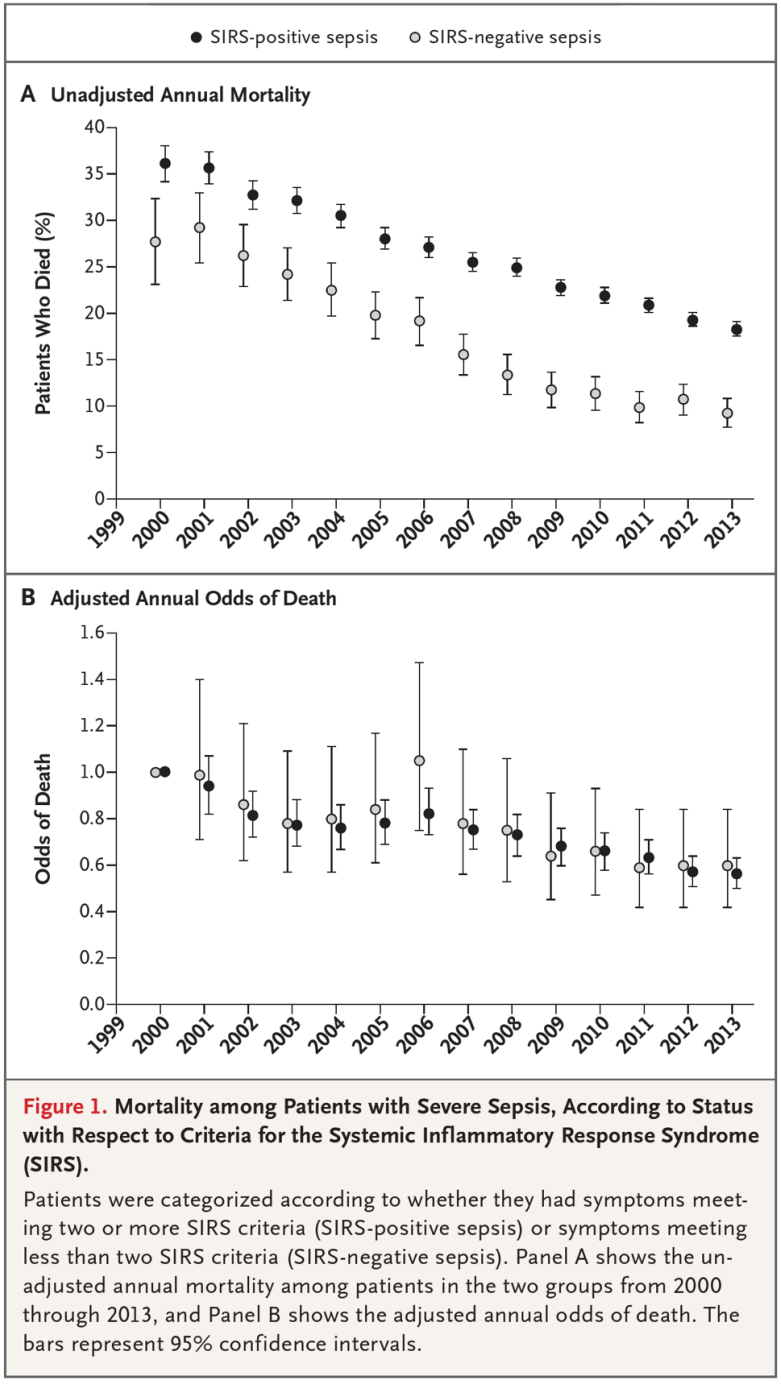



**Figure 1. Mortality among Patients with Severe Sepsis, According to Status with Respect to Criteria for the Systemic Inflammatory Response Syndrome (SIRS).**

Patients were categorized according to whether they had symptoms meeting two or more SIRS criteria (SIRS-positive sepsis) or symptoms meeting less than two SIRS criteria (SIRS-negative sepsis). Panel A shows the unadjusted annual mortality among patients in the two groups from 2000 through 2013, and Panel B shows the adjusted annual odds of death. The bars represent 95% confidence intervals.

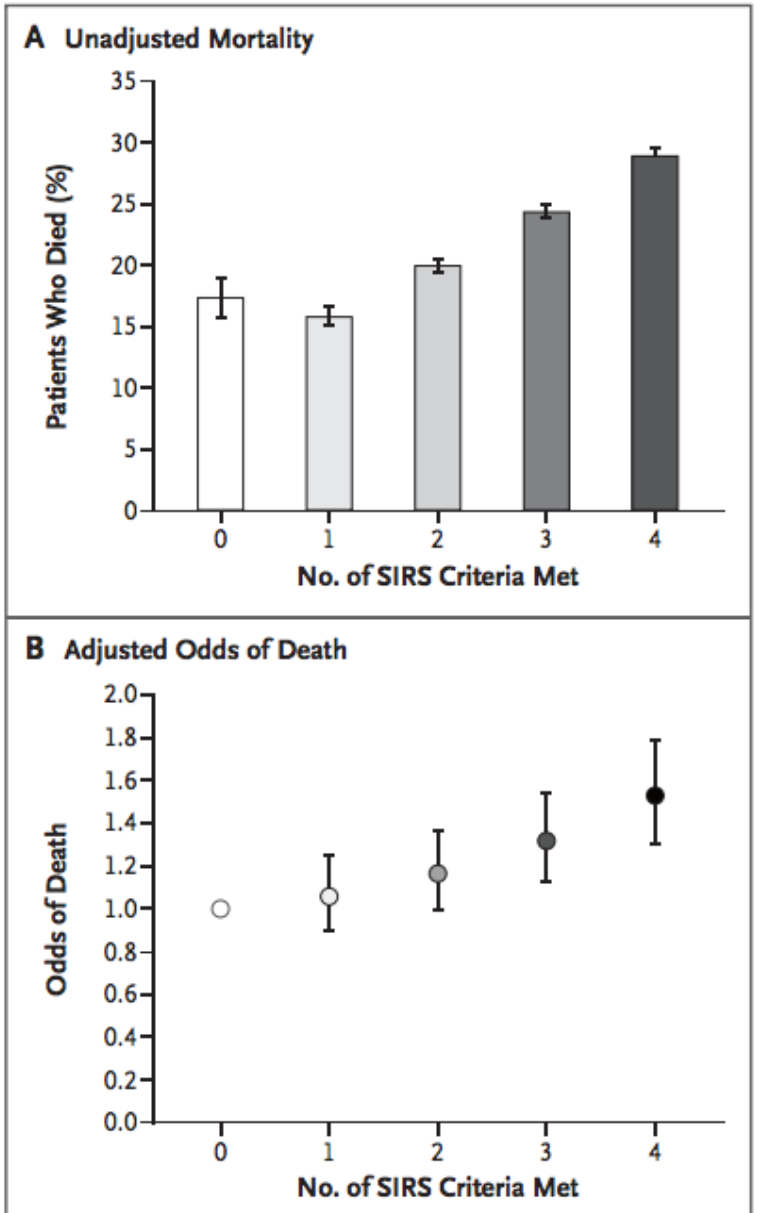



**Figure 2. Mortality among Patients with Severe Sepsis, According to Number of SIRS Criteria Met.**

The bars represent 95% confidence intervals.

## Conclusions

- The need for two or more SIRS criteria to define severe sepsis excluded one in eight otherwise similar patients with infection, organ failure, and substantial mortality and failed to define a transition point in the risk of death.
- Most commonly positive criteria: Increased heart rate and respiratory rate
- Use of 2 as the cut off for sepsis does NOT adequately identify a cut off point for increased mortality

The NEW ENGLAND JOURNAL of MEDICINE

# SIRS and Infection

- Liao et al Em J Emerg Med 2014
  - 1152 Emergency Department Patients
  - Of those patients with SIRS criteria, only 38% had a presumed infection
  - Of those with 0 or 1 SIRS criteria, 21% had an infection

| | Sn (%) | 95% CI (%) | Sp (%) | 95% CI (%) | LR+ | 95% CI | LR− | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **All patients (n = 1152)** | | | | | | | | |
| ≥1 SIRS criteria | 85 | 80, 89 | 29 | 26, 32 | 1.2 | 1.1, 1.3 | 0.5 | 0.4, 0.7 |
| **≥ 2 SIRS criteria**[d] | **52** | **46, 58** | **65** | **62, 68** | **1.5** | **1.3, 1.7** | **0.7** | **0.6, 0.8** |
| ≥3 SIRS criteria | 22 | 17, 27 | 89 | 87, 91 | 2.0 | 1.5, 2.7 | 0.9 | 0.8, 0.9 |
| 4 SIRS criteria | 5 | 3, 9 | 98 | 96, 99 | 2.2 | 1.1, 4.3 | 1.0 | 0.9, 1.0 |
| **Patients with presumed infection (n = 313)**[e] | | | | | | | | |
| ≥1 SIRS criteria | 90 | 83, 95 | 19 | 14, 25 | 1.1 | 1.0, 1.2 | 0.5 | 0.3, 1.0 |
| **≥2 SIRS criteria**[d] | **66** | **56, 75** | **52** | **45, 59** | **1.4** | **1.1, 1.7** | **0.6** | **0.5, 0.9** |
| ≥3 SIRS criteria | 27 | 19, 37 | 77 | 71, 83 | 1.2 | 0.8, 1.8 | 0.9 | 0.8, 1.1 |
| 4 SIRS criteria | 7 | 3, 14 | 94 | 90, 97 | 1.2 | 0.5, 2.9 | 1.0 | 0.9, 1.1 |
| **Patients without presumed infection (n = 839)**[e] | | | | | | | | |
| ≥1 SIRS criteria | 81 | 74, 87 | 32 | 29, 36 | 1.2 | 1.1, 1.3 | 0.6 | 0.4, 0.8 |
| **≥2 SIRS criteria**[d] | **43** | **36, 51** | **69** | **66, 73** | **1.4** | **1.2, 1.7** | **0.8** | **0.7, 0.9** |
| ≥3 SIRS criteria | 18 | 13, 25 | 93 | 91, 95 | 2.5 | 1.7, 3.8 | 0.9 | 0.8, 1.0 |
| 4 SIRS criteria | 4 | 2, 9 | 99 | 98, 99 | 3.2 | 1.2, 8.5 | 1.0 | 0.9, 1.0 |

Abbreviations: SIRS, systemic inflammatory response syndrome; ED, emergency department; Sn, sensitivity; Sp, specificity

[a] SIRS was defined as 2 or more of the following: temperature >38° C or <36° C; heart rate >90 per minute; respiratory rate

[b] 53 patients were missing 1 of the 4 SIRS criteria variables. All instances of missing criteria variables were assumed to not h

[c] Critical illness defined as ≥24 hours in the intensive care unit or in hospital death.

[d] The results are bolded for the original SIRS criteria cutoff defined as 2 or more SIRS criteria.

[e] Presumed infection defined as having received antibiotics within 48 hours of admission.

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, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

**IMPORTANCE** Definitions of sepsis and septic shock were last revised in 2001. Considerable advances have since been made into the pathobiology (changes in organ function, morphology, cell biology, biochemistry, immunology, and circulation), management, and epidemiology of sepsis, suggesting the need for reexamination.

**OBJECTIVE** To evaluate and, as needed, update definitions for sepsis and septic shock.

**PROCESS** A task force (n = 19) with expertise in sepsis pathobiology, clinical trials, and epidemiology was convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. Definitions and clinical criteria were generated through meetings, Delphi processes, analysis of electronic health record databases, and voting, followed by circulation to international professional societies, requesting peer review and endorsement (by 31 societies listed in the Acknowledgment).

Editorial page 757

Author Video Interview, Author Audio Interview, and JAMA Report Video at jama.com

Related articles pages 762 and 775

CME Quiz at jamanetworkcme.com and CME Questions page 816

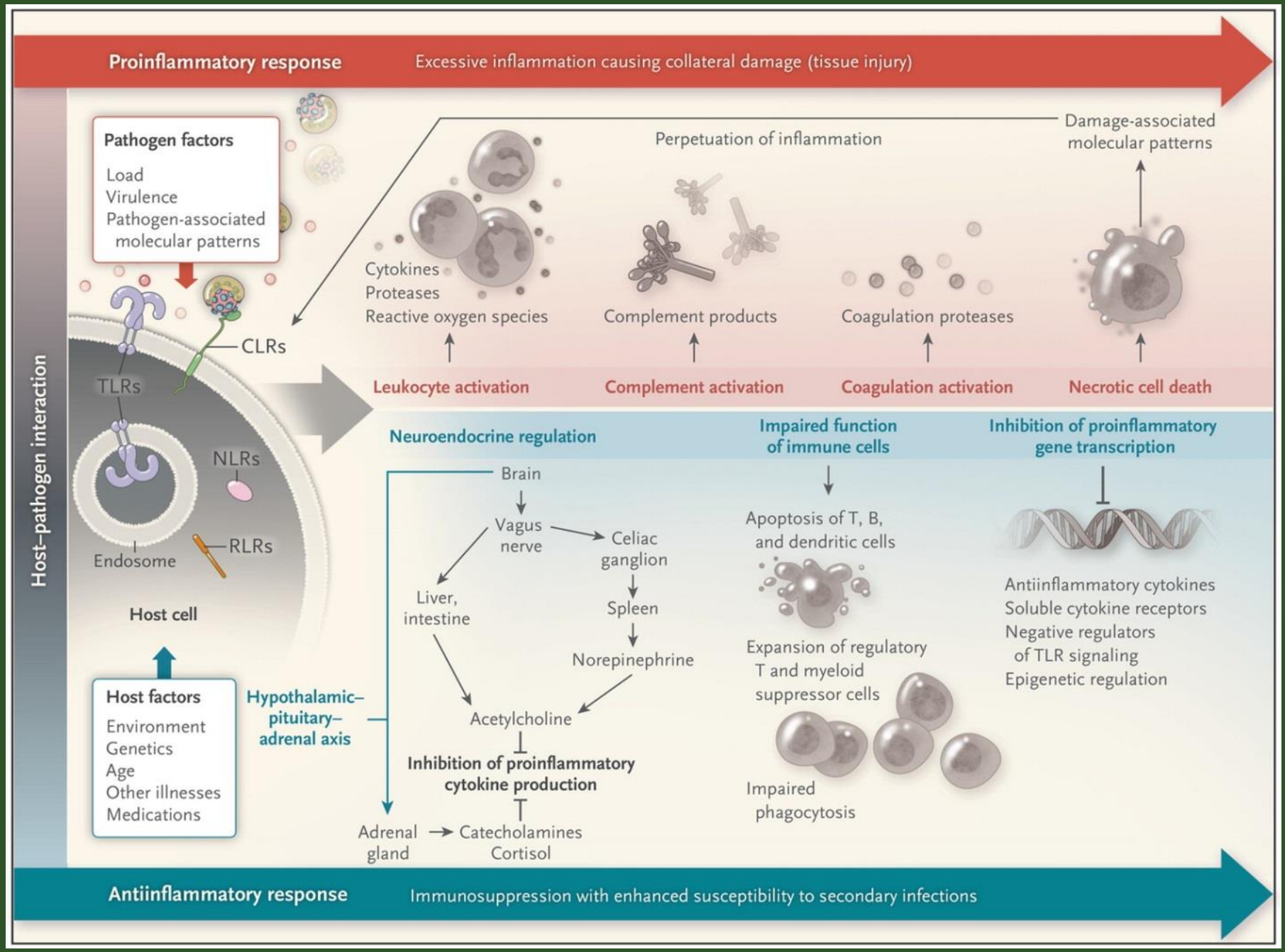
*JAMA*. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

# New definitions

- Sepsis = **life threatening organ dysfunction** caused by a dysregulated host response to infection
- Term “severe sepsis” is gone
- Organ dysfunction represented by an increase the SOFA score of 2 or more (associated with an in-hospital mortality of >10%)
  - or a qSOFA >2
  - Tool to clinically characterize a septic patient

# New definitions

- **qSOFA can be used to  to prompt clinicians to further evaluate for organ dysfunction, initiate or escalate therapy as appropriate and consider appropriate referral**
- Septic shock = subset of sepsis with profound circulatory, cellular or metabolic abnormalities associated with a greater risk of mortality
  - Vasopressors required to maintain a MAP>65 and serum lactate level >2 mmol/L in the absence of hypovolemia




Angus DC NEJM 2013

**Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]**

| | Score | | | | |
|---|---|---|---|---|---|
| System | 0 | 1 | 2 | 3 | 4 |
| Respiration | | | | | |
| $Pao_2/Fio_2$, mm Hg (kPa) | ≥400 (53.3) | <400 (53.3) | <300 (40) | <200 (26.7) with respiratory support | <100 (13.3) with respiratory support |
| Coagulation | | | | | |
| Platelets, $\times 10^3/\mu L$ | ≥150 | <150 | <100 | <50 | <20 |
| Liver | | | | | |
| Bilirubin, mg/dL (μmol/L) | <1.2 (20) | 1.2-1.9 (20-32) | 2.0-5.9 (33-101) | 6.0-11.9 (102-204) | >12.0 (204) |
| Cardiovascular | MAP ≥70 mm Hg | MAP <70 mm Hg | Dopamine <5 or dobutamine (any dose)[b] | Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b] | Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b] |
| Central nervous system | | | | | |
| Glasgow Coma Scale score[c] | 15 | 13-14 | 10-12 | 6-9 | <6 |
| Renal | | | | | |
| Creatinine, mg/dL (μmol/L) | <1.2 (110) | 1.2-1.9 (110-170) | 2.0-3.4 (171-299) | 3.5-4.9 (300-440) | >5.0 (440) |
| Urine output, mL/d | | | | <500 | <200 |

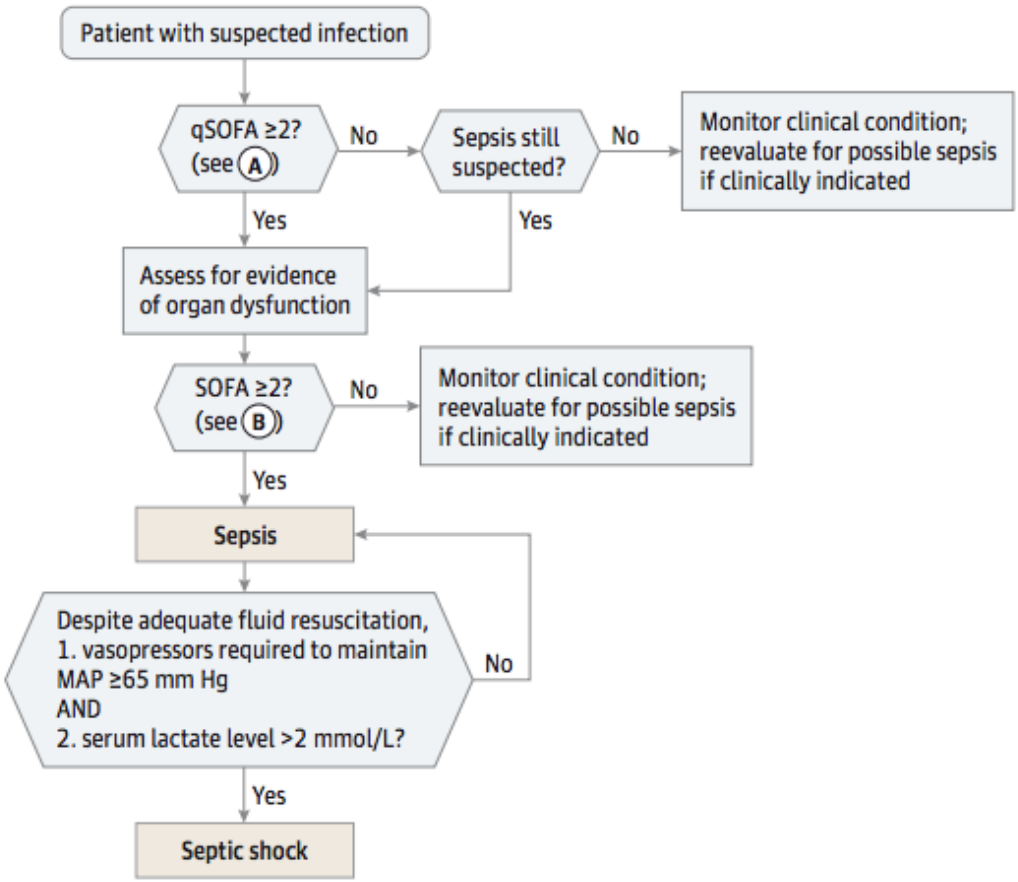
Abbreviations: $Fio_2$, fraction of inspired oxygen; MAP, mean arterial pressure; $Pao_2$, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

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




**A qSOFA Variables**

- Respiratory rate
- Mental status
- Systolic blood pressure

**B SOFA Variables**

- $PaO_2/FiO_2$ ratio
- Glasgow Coma Scale score
- Mean arterial pressure
- Administration of vasopressors with type and dose rate of infusion
- Serum creatinine or urine output
- Bilirubin
- Platelet count

The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.

Original Paper

# Prediction of Sepsis in the Intensive Care Unit With Minimal Electronic Health Record Data: A Machine Learning Approach

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## Abstract

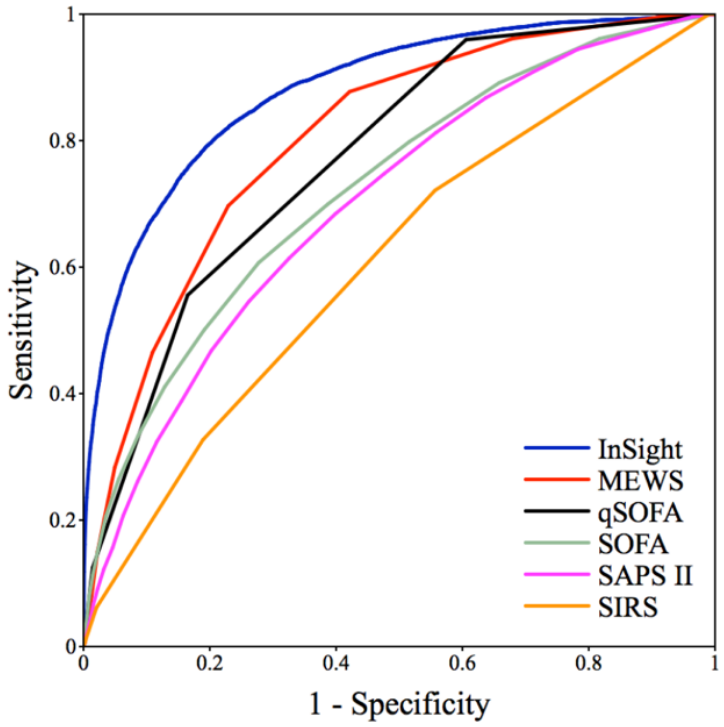
**Background:** Sepsis is one of the leading causes of mortality in hospitalized patients. Despite this fact, a reliable means of predicting sepsis onset remains elusive. Early and accurate sepsis onset predictions could allow more aggressive and targeted therapy while maintaining antimicrobial stewardship. Existing detection methods suffer from low performance and often require time-consuming laboratory test results.

**Objective:** To study and validate a sepsis prediction method, *InSight*, for the new Sepsis-3 definitions in retrospective data, make predictions using a minimal set of variables from within the electronic health record data, compare the performance of this approach with existing scoring systems, and investigate the effects of data sparsity on *InSight* performance.

**Methods:** We apply *InSight*, a machine learning classification system that uses multivariable combinations of easily obtained patient data (vitals, peripheral capillary oxygen saturation, Glasgow Coma Score, and age), to predict sepsis using the retrospective Multiparameter Intelligent Monitoring in Intensive Care (MIMIC)-III dataset, restricted to intensive care unit (ICU) patients aged 15 years or more. Following the Sepsis-3 definitions of the sepsis syndrome, we compare the classification performance of *InSight* versus quick sequential organ failure assessment (qSOFA), modified early warning score (MEWS), systemic inflammatory response syndrome (SIRS), simplified acute physiology score (SAPS) II, and sequential organ failure assessment (SOFA) to determine whether or not patients will become septic at a fixed period of time before onset. We also test the robustness of the *InSight* system to random deletion of individual input observations.

**Results:** In a test dataset with 11.3% sepsis prevalence, *InSight* produced superior classification performance compared with the alternative scores as measured by area under the receiver operating characteristic curves (AUROC) and area under precision-recall curves (APR). In detection of sepsis onset, *InSight* attains AUROC = 0.880 (SD 0.006) at onset time and APR = 0.595 (SD 0.016), both of which are superior to the performance attained by SIRS (AUROC: 0.609; APR: 0.160), qSOFA (AUROC: 0.772; APR: 0.277), and MEWS (AUROC: 0.803; APR: 0.327) computed concurrently, as well as SAPS II (AUROC: 0.700; APR: 0.225) and SOFA (AUROC: 0.725; APR: 0.284) computed at admission ($P<.001$ for all comparisons). Similar

**Figure 3.** Receiver operating characteristic curves for *InSight* versus competing methods at time of onset. MEWS: Modified Early Warning Score; SOFA: Sequential (Sepsis-Related) Organ Failure Assessment; qSOFA: quick SOFA; SAPS II: Simplified Acute Physiology Score II; SIRS: systemic inflammatory response syndrome.



| | *InSight*: 0 hours | *InSight*: 4 hours | SIRS[a] | quick SOFA | MEWS[b] | SAPS II[c] | SOFA[d] |
|---|---|---|---|---|---|---|---|
| AUROC[e] | 0.88 (SD 0.006) | 0.74 (SD 0.010) | 0.61 | 0.77 | 0.80 | 0.70 | 0.73 |
| APR[f] | 0.60 (SD 0.016) | 0.28 (SD 0.013) | 0.16 | 0.28 | 0.33 | 0.23 | 0.28 |
| Sensitivity | 0.80 | 0.80 | 0.72 | 0.56 | 0.70 | 0.75 | 0.80 |
| Specificity | 0.80 | 0.54 | 0.44 | 0.84 | 0.77 | 0.52 | 0.48 |
| F1[g] | 0.47 | 0.30 | 0.24 | 0.39 | 0.40 | 0.27 | 0.27 |
| DOR[h] | 15.51 | 4.75 | 2.06 | 6.33 | 7.85 | 3.26 | 3.71 |
| LR+[i] | 3.90 | 1.75 | 1.30 | 3.37 | 3.05 | 1.57 | 1.55 |
| LR-[j] | 0.25 | 0.37 | 0.63 | 0.53 | 0.39 | 0.48 | 0.42 |
| Accuracy | 0.80 | 0.57 | 0.47 | 0.80 | 0.76 | 0.55 | 0.52 |

[a]SIRS: systemic inflammatory response syndrome

[b]MEWS: Modified Early Warning Score.

[c]SAPS II: Simplified Acute Physiology Score II.

[d]SOFA: Sequential (Sepsis-Related) Organ Failure Assessment.

[e]AURUC: area under the receiver operating characteristic curve.

[f]APR: area under the precision-recall curve.

[g]F1: harmonic mean of precision and recall.

[h]DOR: diagnostic odds ratio.

[i]LR+: positive likelihood ratio.

[j]LR-: negative likelihood ratio.

# JAMA January 18th, 2017

- 30 European EDs between May and June 2016.
- The prospective cohort analysis included 879 patients with suspected infection
  - Overall in-hospital mortality rate of 8%.
- The mortality rate was 3% in patients with a qSOFA <2 compared to 24% in those with a score ≥2.
- The qSOFA score was better at predicting in-hospital mortality than SIRS or severe sepsis
- The results support the Sepsis-3 recommendations,
- Low mortality rate observed in patients with qSOFA <2 supports the safety of replacing SIRS with qSOFA.
- Adding blood lactate to qSOFA did not improve prognostication.
- Study was limited by use of the worst qSOFA score during ED stay

# JAMA February 2017

- Retrospective cohort analysis of 184,875 patients admitted to ICUs in Australia or New Zealand with an infection-related primary diagnosis.
- In-hospital mortality was 18.7%, and 55.7% of patients died or had an ICU length of stay of three days or more.
- During the first 24 hours in the ICU, the SOFA score increased by two or more points in 90.1% of patients, while 86.7% met two or more SIRS criteria, and 54.4% had a qSOFA ≥2.
- The researchers found that SOFA demonstrated significantly greater discrimination for in-hospital mortality than SIRS or qSOFA, also supporting the Sepsis-3 recommendations.

# Core concepts in Antibiotic Selection

- Cook book medicine has to end!!!
- Key concepts when selecting antibiotics:
  - What antibiotics have they been exposed to (90 days)
  - Prior health-care exposure
  - Comorbidities
  - Prior culture results / colonization
  - Patient allergies

# Treatment: The balancing act

- Weighing the risks/benefits of antibiotics
  - Risks of overuse:
    - Antimicrobial resistance
    - C difficile infection
    - Renal failure
    - Systemic toxicities
  - Benefits of correct and appropriate antibiotics:
    - Improved outcomes
      - Chest 2000: 118:146
      - Mortality rate was associated with inadequate initial antimicrobial therapy
      - Prior antibiotics, Candida, low albumin, central lines days all associated with inadequate therapy
    - Reduced deaths

# Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

**Andre C. Kalil,[1,a] Mark L. Metersky,[2,a] Michael Klompas,[3,4] John Muscedere,[5] Daniel A. Sweeney,[6] Lucy B. Palmer,[7] Lena M. Napolitano,[8] Naomi P. O'Grady,[9] John G. Bartlett,[10] Jordi Carratalà,[11] Ali A. El Solh,[12] Santiago Ewig,[13] Paul D. Fey,[14] Thomas M. File Jr,[15] Marcos I. Restrepo,[16] Jason A. Roberts,[17,18] Grant W. Waterer,[19] Peggy Cruse,[20] Shandra L. Knight,[20] and Jan L. Brozek[21]**

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It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

These guidelines are intended for use by healthcare professionals who care for patients at risk for hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), including specialists in infectious diseases, pulmonary diseases, critical care, and surgeons, anesthesiologists, hospitalists, and any clinicians and healthcare providers caring for hospitalized patients with nosocomial pneumonia. The panel's recommendations for the diagnosis and treatment of HAP and VAP are based upon evidence derived from topic-specific systematic literature reviews.

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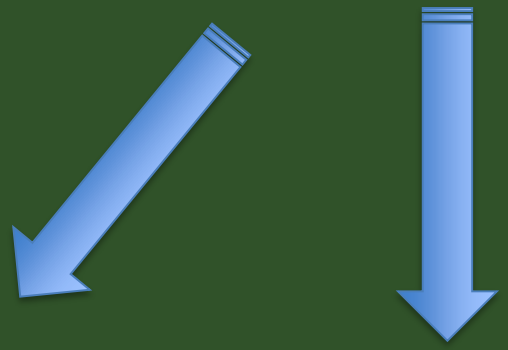
# Pneumonia

Hospital-Acquired Pneumonia

Ventilator Associated Pneumonia

Community-acquired Pneumonia



MDR Risk Factors Present

No MDR Risk Factors Present

**Table 4. Recommended Initial Empiric Antibiotic Therapy for Hospital-Acquired Pneumonia (Non-Ventilator-Associated Pneumonia)**

| Not at High Risk of Mortality[a] and no Factors Increasing the Likelihood of MRSA[b,c] | Not at High Risk of Mortality[a] but With Factors Increasing the Likelihood of MRSA[b,c] | High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d[a,c] |
|---|---|---|
| One of the following: | One of the following: | Two of the following, avoid 2 β-lactams: |
| Piperacillin-tazobactam[d] 4.5 g IV q6h | Piperacillin-tazobactam[d] 4.5 g IV q6h | Piperacillin-tazobactam[d] 4.5 g IV q6h |
| OR | OR | OR |
| Cefepime[d] 2 g IV q8h | Cefepime[d] or ceftazidime[d] 2 g IV q8h | Cefepime[d] or ceftazidime[d] 2 g IV q8h |
| OR | OR | OR |
| Levofloxacin 750 mg IV daily | Levofloxacin 750 mg IV daily | Levofloxacin 750 mg IV daily |
| | Ciprofloxacin 400 mg IV q8h | Ciprofloxacin 400 mg IV q8h |
| | OR | OR |
| Imipenem[d] 500 mg IV q6h | Imipenem[d] 500 mg IV q6h | Imipenem[d] 500 mg IV q6h |
| Meropenem[d] 1 g IV q8h | Meropenem[d] 1 g IV q8h | Meropenem[d] 1 g IV q8h |
| | OR | OR |
| | Aztreonam 2 g IV q8h | Amikacin 15–20 mg/kg IV daily |
| | | Gentamicin 5–7 mg/kg IV daily |
| | | Tobramycin 5–7 mg/kg IV daily |
| | | OR |
| | | Aztreonam[e] 2 g IV q8h |
| | Plus:<br>Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness) | Plus:<br>Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg IV × 1 for severe illness) |
| | OR | OR |
| | Linezolid 600 mg IV q12h | Linezolid 600 mg IV q12h |
| | | If MRSA coverage is not going to be used, include coverage for MSSA.<br>Options include:<br>Piperacillin-tazobactam, cefepime, levofloxacin, imipenem, meropenem. Oxacillin, nafcillin, and cefazolin are preferred for the treatment of proven MSSA, but would ordinarily not be used in an empiric regimen for HAP. |
| If patient has severe penicillin allergy and aztreonam is going to be used instead of any β-lactam–based antibiotic, include coverage for MSSA. | | |

Abbreviations: HAP, hospital-acquired pneumonia; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

[a] Risk factors for mortality include need for ventilatory support due to pneumonia and septic shock.

[b] Indications for MRSA coverage include intravenous antibiotic treatment during the prior 90 days, and treatment in a unit where the prevalence of MRSA among *S. aureus* isolates is not known or is >20%. Prior detection of MRSA by culture or non-culture screening may also increase the risk of MRSA. The 20% threshold was chosen to balance the need for effective initial antibiotic therapy against the risks of excessive antibiotic use; hence, individual units can elect to adjust the threshold in accordance with local values and preferences. If MRSA coverage is omitted, the antibiotic regimen should include coverage for MSSA.

[c] If patient has factors increasing the likelihood of gram-negative infection, 2 antipseudomonal agents are recommended. If patient has structural lung disease increasing the risk of gram-negative infection (ie, bronchiectasis or cystic fibrosis), 2 antipseudomonal agents are recommended. A high-quality Gram stain from a respiratory specimen with numerous and predominant gram-negative bacilli provides further support for the diagnosis of a gram-negative pneumonia, including fermenting and non-glucose-fermenting microorganisms.

[d] Extended infusions may be appropriate.

[e] In the absence of other options, it is acceptable to use aztreonam as an adjunctive agent with another β-lactam–based agent because it has different targets within the bacterial cell wall [137].

# Who gets triple antibiotics with HAP/VAP in 2016?

- High risk for mortality (septic shock)

AND

- Patient exposed to IV antibiotics in the last 90 days*

# Duration of antibiotic therapy: shorter = better

| Diagnosis | Short (d) | Long (d) | Result |
|---|---|---|---|
| CAP | 3 or 5 | 7,8 or 10 | Equal |
| HAP | 7 | 10-15 | Equal |
| VAP | 8 | 15 | Equal |
| Pyelonephritis | 5 or 7 | 10 or 14 | Equal |
| Intra-abd | 4 | 10 | Equal |
| AECB | <5 | >7 | Equal |
| Cellulitis | 5 or 6 | 10 | Equal |
| Osteomyelitis | 42 | 84 | Equal |

Spellberg JAMA 2016

# Summary

- SIRS is a marker of infection not necessarily a marker of sepsis
  - Not all patients that meet SIRS criteria are infected!
- Sepsis is a disease continuum, not a snapshot of vital signs taken at a single point in time
- Sepsis involves organ dysfunction and is associated with the dysregulation of the inflammatory response, not the normal regulated inflammatory response
- Aggressively evaluate and treat our patients, keeping in mind the core measures and the available literature
- We need better, rapid diagnostic assays to help evaluate for infectious pathogens
- More antibiotic is not always better

When taking care of an ill patient……be an INTERNIST! Treat the patient, not the numbers!!!

Thank you!