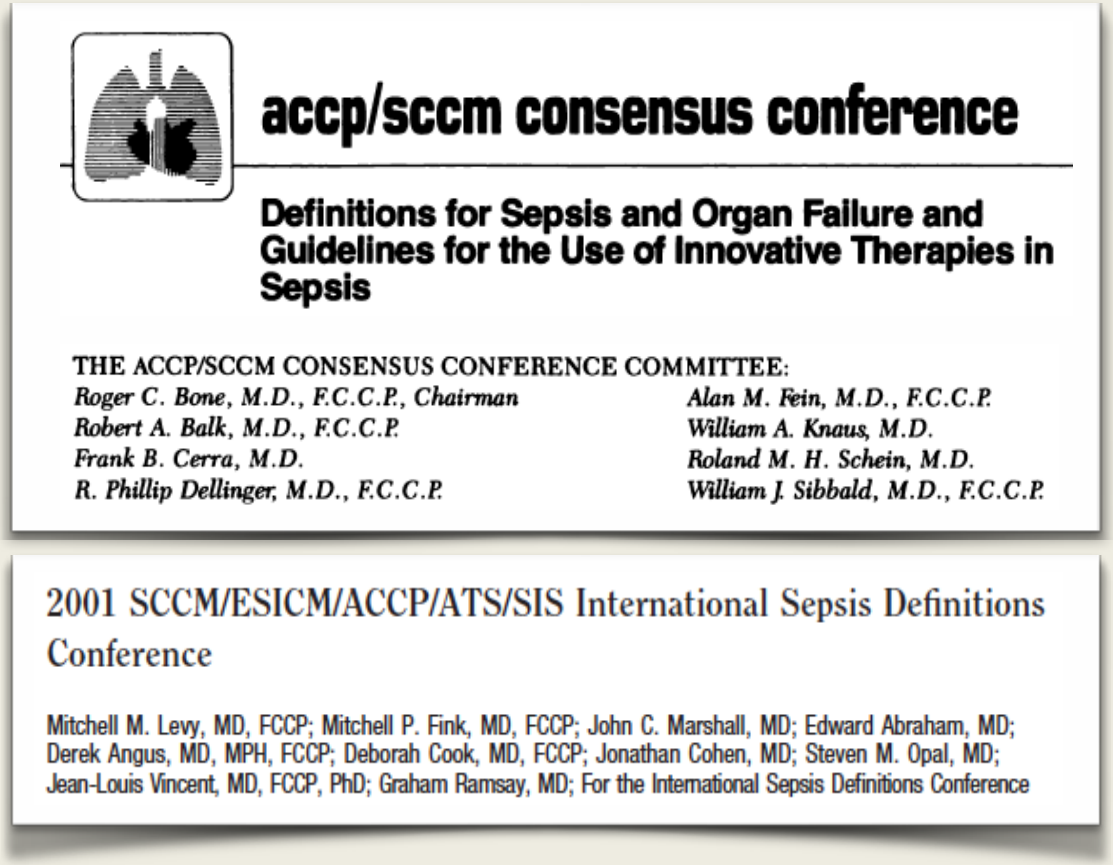
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Why the need a new definition ?

Issues with the 1991 and 2001 Definitions



accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:

Roger C. Bone, M.D., F.C.C.P., Chairman
Robert A. Balk, M.D., F.C.C.P.
Frank B. Cerra, M.D.
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Alan M. Fein, M.D., F.C.C.P.
William A. Knaus, M.D.
Roland M. H. Schein, M.D.
William J. Sibbald, M.D., F.C.C.P.

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

Mitchell M. Levy, MD, FCCP; Mitchell P. Fink, MD, FCCP; John C. Marshall, MD; Edward Abraham, MD; Derek Angus, MD, MPH, FCCP; Deborah Cook, MD, FCCP; Jonathan Cohen, MD; Steven M. Opal, MD; Jean-Louis Vincent, MD, FCCP, PhD; Graham Ramsay, MD; For the International Sepsis Definitions Conference

- SIRS – based
- "Severe Sepsis" is problematic
- Different assessment criteria yield different results

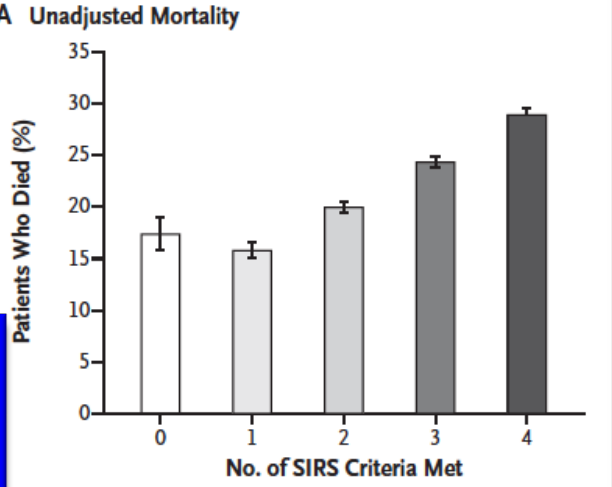
SIRS Sensitivity

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.

N Engl J Med 2015;372:1629-38.

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

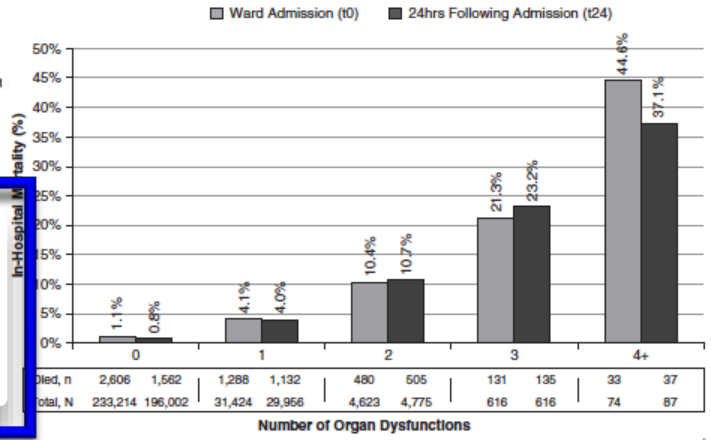


Incidence and Prognostic Value of the Systemic Inflammatory Response Syndrome and Organ Dysfunctions in Ward Patients

Matthew M. Churpek[1], Frank J. Zadravecz[1], Christopher Winslow[2], Michael D. Howell[1], and Dana P. Edelson[1]

Am J Respir Crit Care Med 2015; 192:958-964

Conclusions: Almost half of patients hospitalized on the wards developed SIRS at least once during their ward stay. Our findings suggest that screening ward patients using SIRS criteria for identifying those with sepsis would be impractical.



SIRS is an *appropriate* response to infection – or any other stimulus that activates inflammation

Sepsis/Severe Sepsis

Confusing

- Most people say “sepsis” when they mean “severe sepsis”

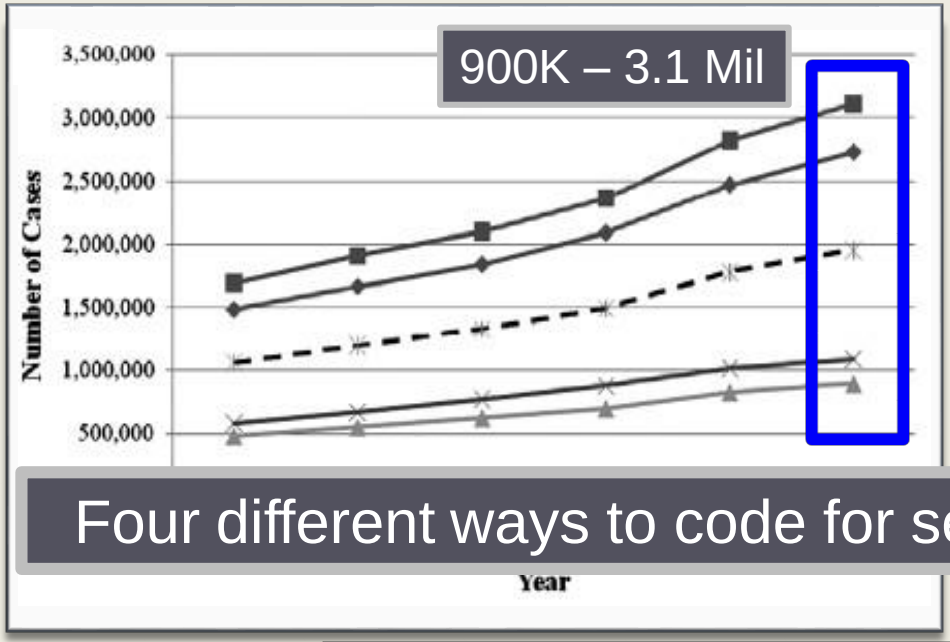
- What the initial two task forces called “sepsis” is what most people call “infection”

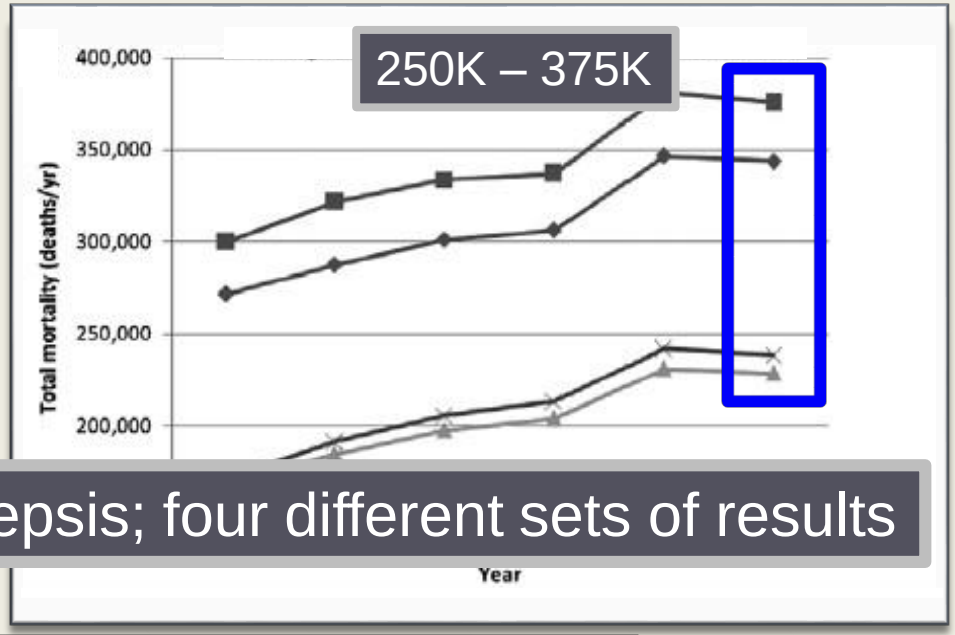
Different Criteria, Different Results

Benchmarking the Incidence and Mortality of Severe Sepsis in the United States*

David F. Gaieski MD[1]; J. Matthew Edwards, MD[1]; Michael J. Kallan, MS[2]; Brendan G. Carr, MD, MA, MS[1]

Crit Care Med 2013; 41: 1167-1174





Four different ways to code for sepsis; four different sets of results

Different Criteria, Different Results

Mortality from septic shock

- Australia – 22%
  - Kaukonen et al, 2014
- Germany – 60.5%
  - Heublein et al, In press
- The Netherlands – 60%
  - Klein-Klouwenberg et al, 2012

Increased Understanding of Sepsis Pathobiology

- More than just unimpeded inflammation
- Key role of immunosuppression
- Contribution of non-immune mechanisms
- Possible adaptive nature of organ dysfunction – hibernation
- Re-appraisal of the nature of septic shock

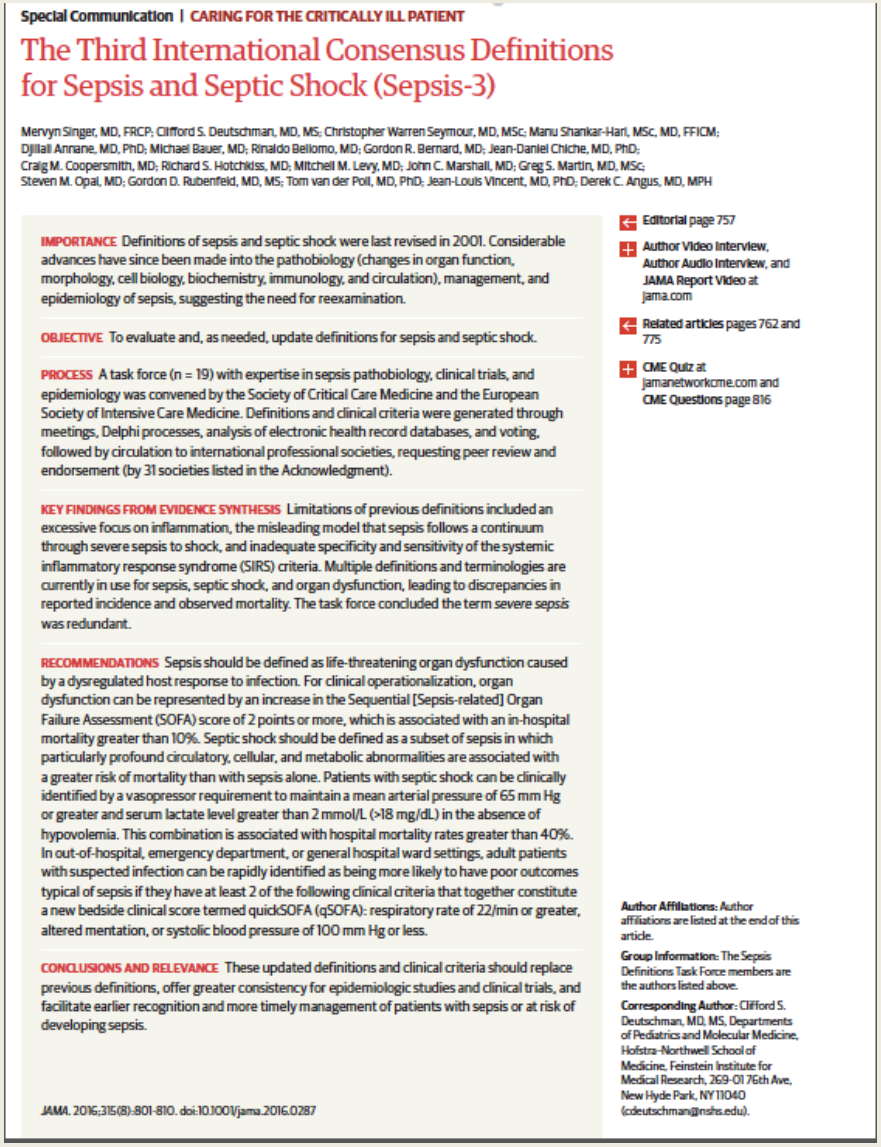
SCCM/ESICM Task Force to Re-Define Sepsis

- Co-Chairs – Mervyn Singer, Cliff Deutschman

Derek Angus
Djilalli Annane
Michael Bauer
Rinaldo Bellomo
Gordon Bernard
Jean-Daniel Chiche
Craig Coopersmith

Richard Hotchkiss
Mitchell Levy
John Marshall
Steve Opal
Gordon Rubenfeld
Tom van der Poll
Jean-Louis Vincent

Greg Martin
Manu Shankar-Hari
Chris Seymour



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).

KEY FINDINGS FROM EVIDENCE SYNTHESIS Limitations of previous definitions included an excessive focus on inflammation, the misleading model that sepsis follows a continuum through severe sepsis to shock, and inadequate specificity and sensitivity of the systemic inflammatory response syndrome (SIRS) criteria. Multiple definitions and terminologies are currently in use for sepsis, septic shock, and organ dysfunction, leading to discrepancies in reported incidence and observed mortality. The task force concluded the term *severe sepsis* was redundant.

RECOMMENDATIONS Sepsis should be defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more, which is associated with an in-hospital mortality greater than 10%. Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia. This combination is associated with hospital mortality rates greater than 40%. In out-of-hospital, emergency department, or general hospital ward settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least 2 of the following clinical criteria that together constitute a new bedside clinical score termed quickSOFA (qSOFA): respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100 mm Hg or less.

CONCLUSIONS AND RELEVANCE These updated definitions and clinical criteria should replace previous definitions, offer greater consistency for epidemiologic studies and clinical trials, and facilitate earlier recognition and more timely management of patients with sepsis or at risk of developing sepsis.

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

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The Sepsis Definitions Task Force members are the authors listed above.

Corresponding Author: Clifford S. Deutschman, MD, MS, Departments of Pediatrics and Molecular Medicine, Hofstra-Northwell School of Medicine, Feinstein Institute for Medical Research, 269-01 76th Ave, New Hyde Park, NY 11040 (cdeutschman@nshs.edu).

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

The Document

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M et al.

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

JAMA 2016; 315: 801-10

What are the new definitions ?

Definitions

Per the Merriam – Webster English Dictionary:

- Definition
  - “a statement expressing the essential nature of something”

    or, more generically,
  - “a statement that describes what something is”

A definition therefore requires an understanding of the pathobiology of the disorder ..

.. which, for sepsis, is at best incomplete

The Definition of Sepsis

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

The Definition of Septic Shock

More problematic

- Is septic shock sepsis where the dysfunctional organ is the cardiovascular system ?
  - Task force opinion - NO
    - Also involves cellular/metabolic abnormalities
- What distinguishes septic shock from sepsis ?
  - Treatment ?
    - NO. Management is the same
  - Pathobiology ?
    - Maybe … but at this time not known

The Definition of Septic Shock

- What tangibly differentiates septic shock from sepsis ?

  MORTALITY

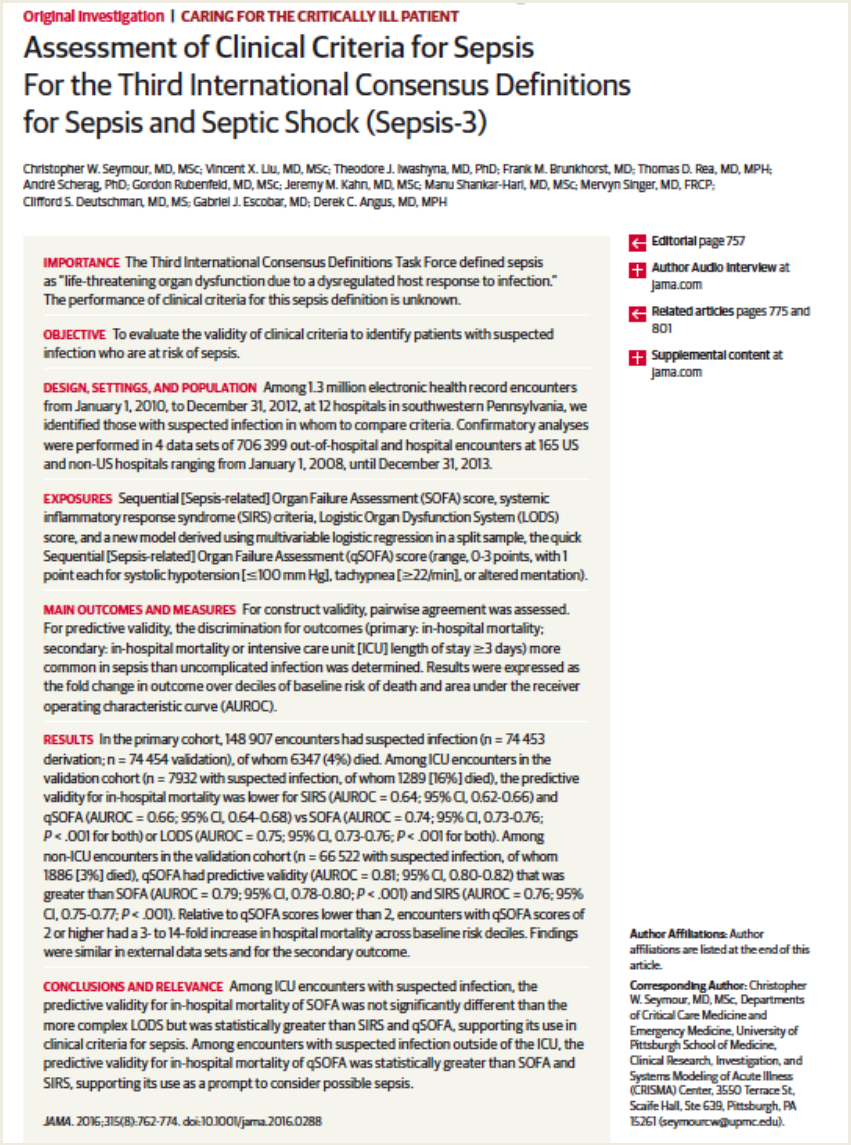
  - Septic shock is “really, really, really bad” sepsis

Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

Sepsis Definitions

- Advantages
  - Incorporates most up-to-date thinking on sepsis pathobiology
  - Provides closest approximation possible to describing “what sepsis is”
- Concerns
  - Of limited practical utility as they contain elements that cannot be clinically identified
    - “organ dysfunction”
    - “dysregulated host response”

What is qSOFA ?



Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Assessment of Clinical Criteria for Sepsis For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Theodore J. Iwashyna, MD, PhD; Frank M. Brunkhorst, MD; Thomas D. Rea, MD, MPH; André Scherag, PhD; Gordon Rubenfeld, MD, MSc; Jeremy M. Kahn, MD, MSc; Manu Shankar-Hari, MD, MSc; Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Gabriel J. Escobar, MD; Derek C. Angus, MD, MPH

IMPORTANCE The Third International Consensus Definitions Task Force defined sepsis as "life-threatening organ dysfunction due to a dysregulated host response to infection." The performance of clinical criteria for this sepsis definition is unknown.

OBJECTIVE To evaluate the validity of clinical criteria to identify patients with suspected infection who are at risk of sepsis.

DESIGN, SETTINGS, AND POPULATION Among 1.3 million electronic health record encounters from January 1, 2010, to December 31, 2012, at 12 hospitals in southwestern Pennsylvania, we identified those with suspected infection in whom to compare criteria. Confirmatory analyses were performed in 4 data sets of 706 399 out-of-hospital and hospital encounters at 165 US and non-US hospitals ranging from January 1, 2008, until December 31, 2013.

EXPOSURES Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score, systemic inflammatory response syndrome (SIRS) criteria, Logistic Organ Dysfunction System (LODS) score, and a new model derived using multivariable logistic regression in a split sample, the quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) score (range, 0-3 points, with 1 point each for systolic hypotension [≤100 mm Hg], tachypnea [≥22/min], or altered mentation).

MAIN OUTCOMES AND MEASURES For construct validity, pairwise agreement was assessed. For predictive validity, the discrimination for outcomes (primary: in-hospital mortality; secondary: in-hospital mortality or intensive care unit [ICU] length of stay ≥3 days) more common in sepsis than uncomplicated infection was determined. Results were expressed as the fold change in outcome over deciles of baseline risk of death and area under the receiver operating characteristic curve (AUROC).

RESULTS In the primary cohort, 148 907 encounters had suspected infection (n = 74 453 derivation; n = 74 454 validation), of whom 6347 (4%) died. Among ICU encounters in the validation cohort (n = 7932 with suspected infection, of whom 1289 [16%] died), the predictive validity for in-hospital mortality was lower for SIRS (AUROC = 0.64; 95% CI, 0.62-0.66) and qSOFA (AUROC = 0.66; 95% CI, 0.64-0.68) vs SOFA (AUROC = 0.74; 95% CI, 0.73-0.76; $P < .001$ for both) or LODS (AUROC = 0.75; 95% CI, 0.73-0.76; $P < .001$ for both). Among non-ICU encounters in the validation cohort (n = 66 522 with suspected infection, of whom 1886 [3%] died), qSOFA had predictive validity (AUROC = 0.81; 95% CI, 0.80-0.82) that was greater than SOFA (AUROC = 0.79; 95% CI, 0.78-0.80; $P < .001$) and SIRS (AUROC = 0.76; 95% CI, 0.75-0.77; $P < .001$). Relative to qSOFA scores lower than 2, encounters with qSOFA scores of 2 or higher had a 3- to 14-fold increase in hospital mortality across baseline risk deciles. Findings were similar in external data sets and for the secondary outcome.

CONCLUSIONS AND RELEVANCE Among ICU encounters with suspected infection, the predictive validity for in-hospital mortality of SOFA was not significantly different than the more complex LODS but was statistically greater than SIRS and qSOFA, supporting its use in clinical criteria for sepsis. Among encounters with suspected infection outside of the ICU, the predictive validity for in-hospital mortality of qSOFA was statistically greater than SOFA and SIRS, supporting its use as a prompt to consider possible sepsis.

JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Christopher W. Seymour, MD, MSc, Departments of Critical Care Medicine and Emergency Medicine, University of Pittsburgh School of Medicine, Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center, 3550 Terrace St, Scaife Hall, Ste 639, Pittsburgh, PA 15261 (seymourcw@upmc.edu).

Christopher W. Seymour, MD MSc

The CRISMA Center
University of Pittsburgh
Departments of Critical Care and Emergency Medicine

Seymour CW, Liu VX, Iwashyna TJ et al.

Assessment of Clinical Criteria for Sepsis

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

JAMA 2016; 315: 762-774

What is sepsis ?

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

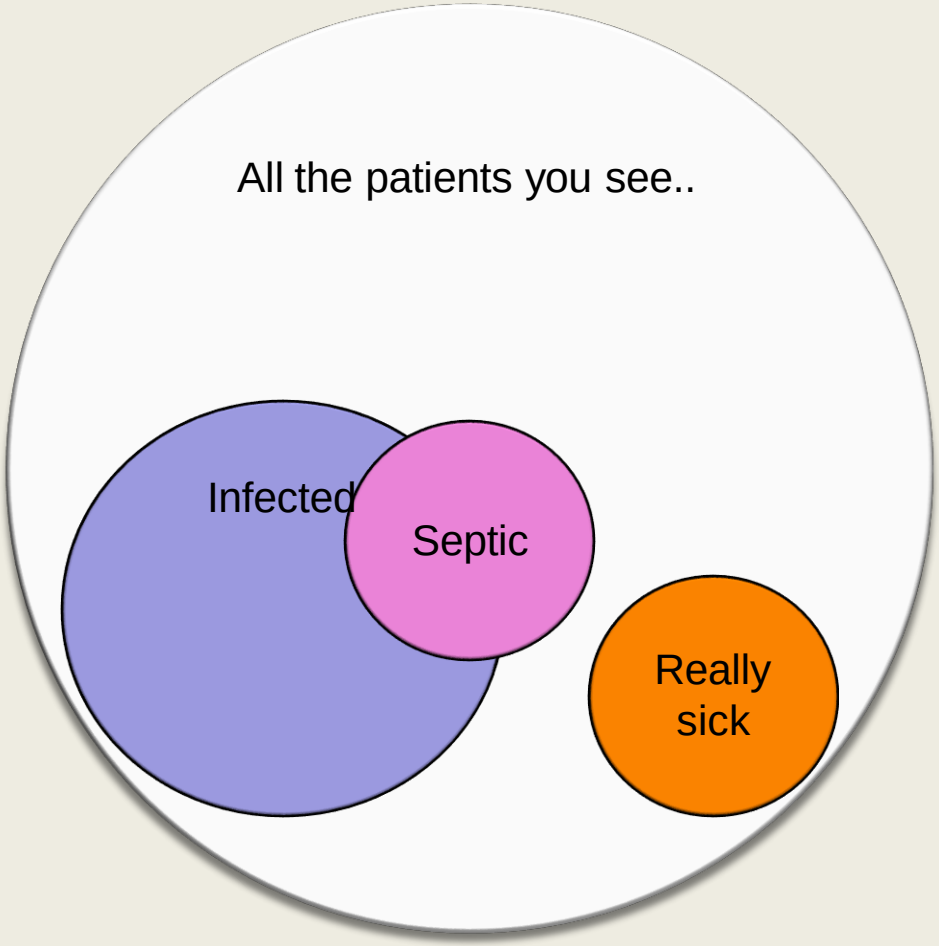
What is sepsis ?

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

Among patients with suspected infection,

who is really sick?

What is sepsis ?

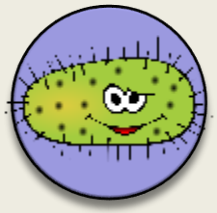


Challenges

- How to identify infection ?
- What clinical criteria to study ?
- How to identify who is “really sick” ?

What data sources to use ?

- Derivation - 1.3 million EHR records from UPMC
- Validation – almost 6 million records
  - KPNC
  - VA
  - “ALERTS” database from Germany
  - Kings County (Seattle) EMS



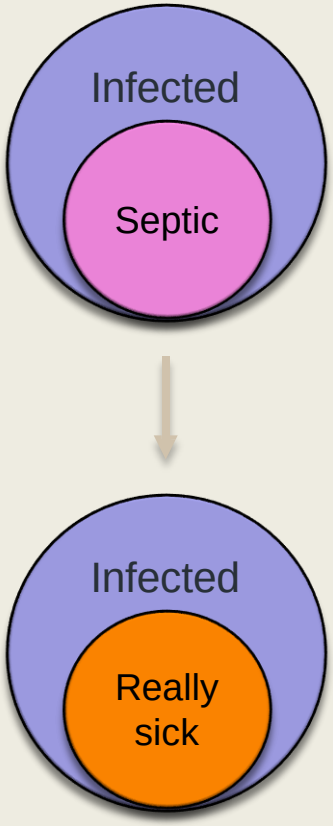
How to identify infection ?

- First episode of cultures, antibiotics
- Derivation - 1.3 million EHR records from UPMC
  - 148,000 with suspected infection
- Validation – almost 6 million records
  - KPNC
  - VA
  - “ALERTS” database from Germany
  - Kings County (Seattle) EMS
  - > 700,000 with suspected infection

What clinical criteria to study ?

- SIRS
  - 0-4 points
    - Temp, HR, RR, WBC count
- SOFA
  - 0-24 points
    - 13 variables, clinical labs, therapeutic data
- LODS
  - 0-22 points
    - Similar to SOFA

How to identify who is “really sick” ?

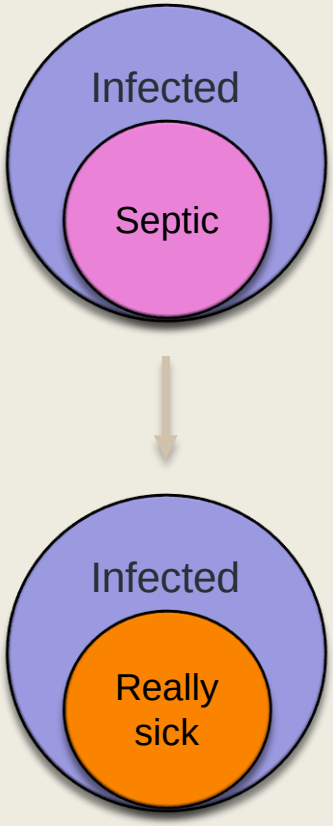


- Sepsis is “life threatening organ dysfunction caused by a dysregulated host response to infection”

  But that can’t be measured clinically

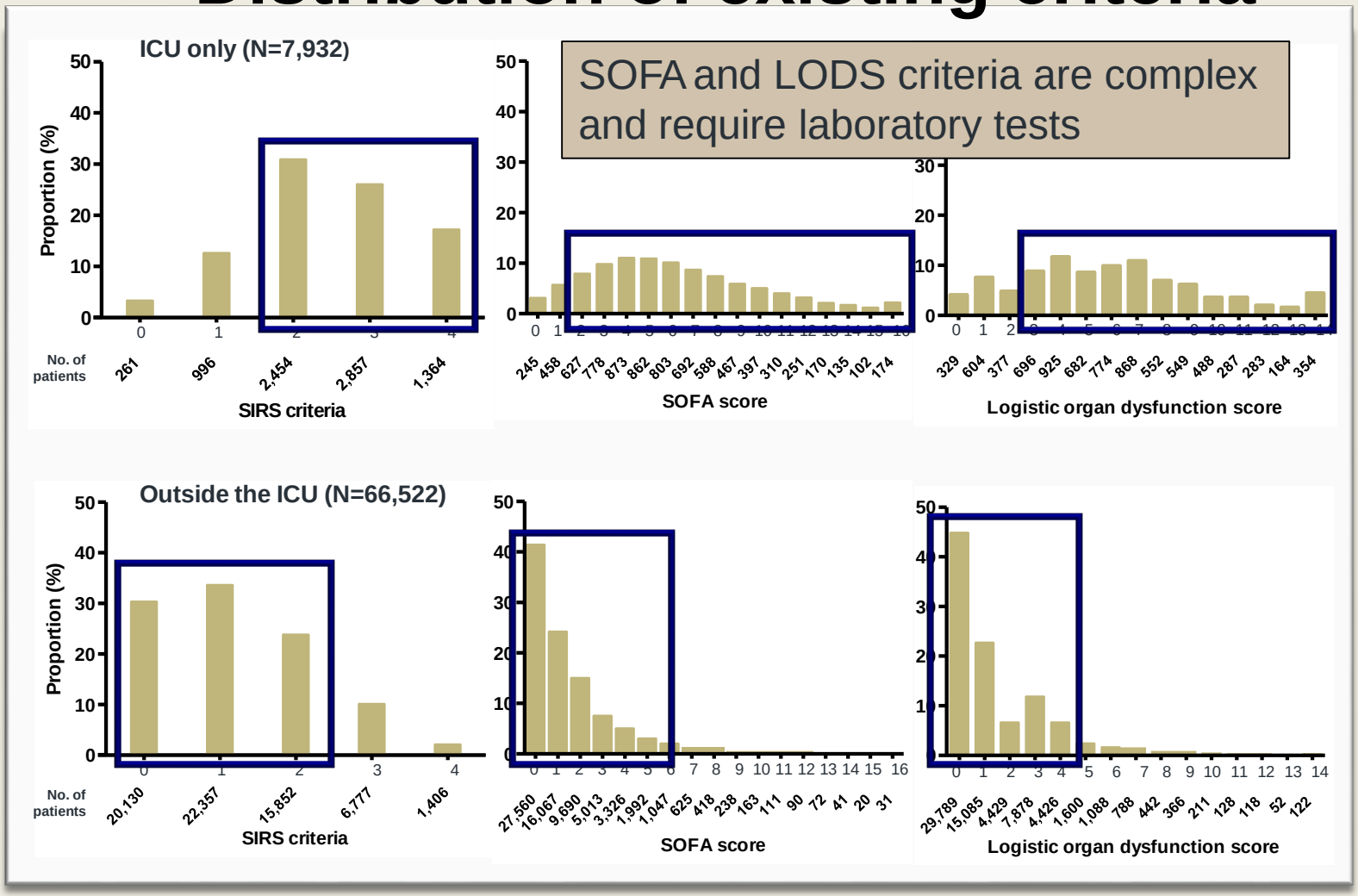
- “Really sick” is a proxy
- More common among infected patients who are septic than those who are not

How to identify who is “really sick” ?



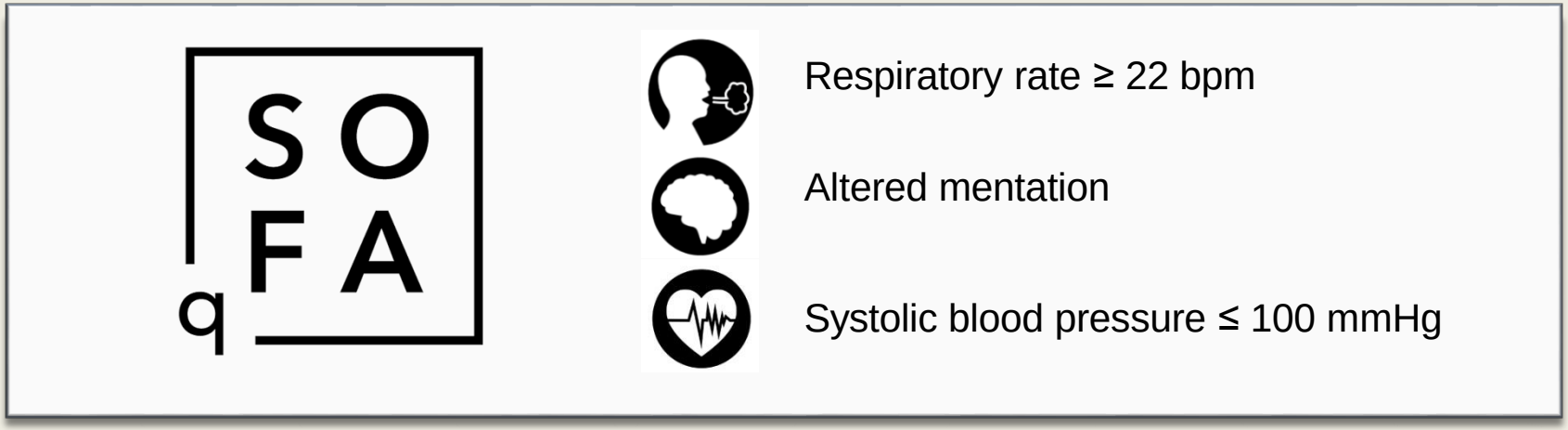
- Possible Proxies
  - Clinical review committees
  - Death in the hospital
  - Prolonged stay in the ICU
  - Discharge diagnosis of sepsis
  - Positive microbiologic cultures

Distribution of existing criteria



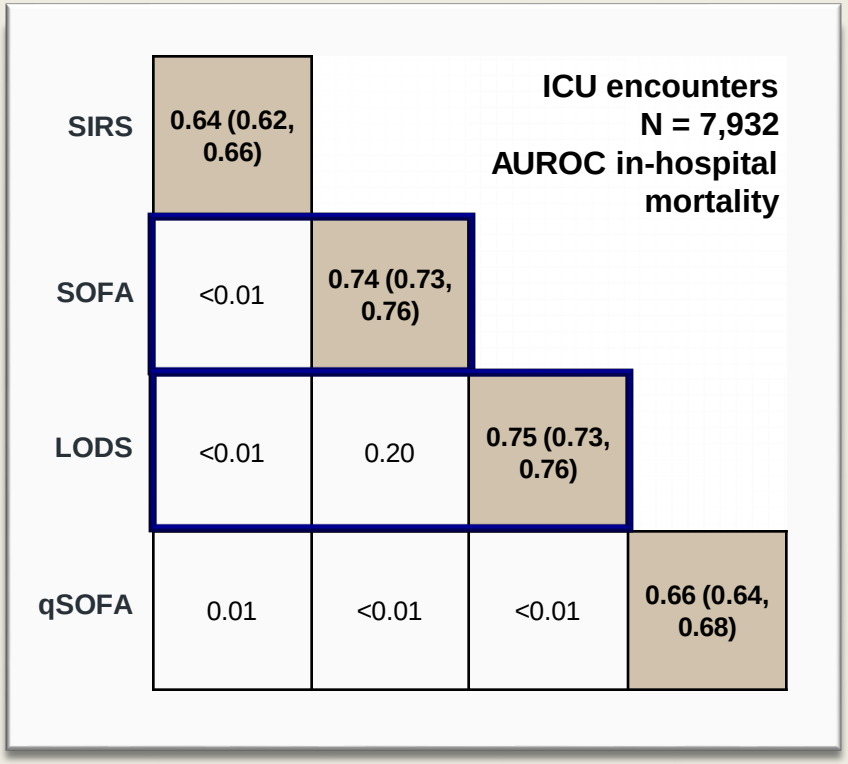
Developing new criteria

- Focus on timeliness, ease of use
- Studied 21 variables from Sepsis-2
- Multivariable logistic regression for in-hospital mortality
  - UPMC EHR as derivation dataset

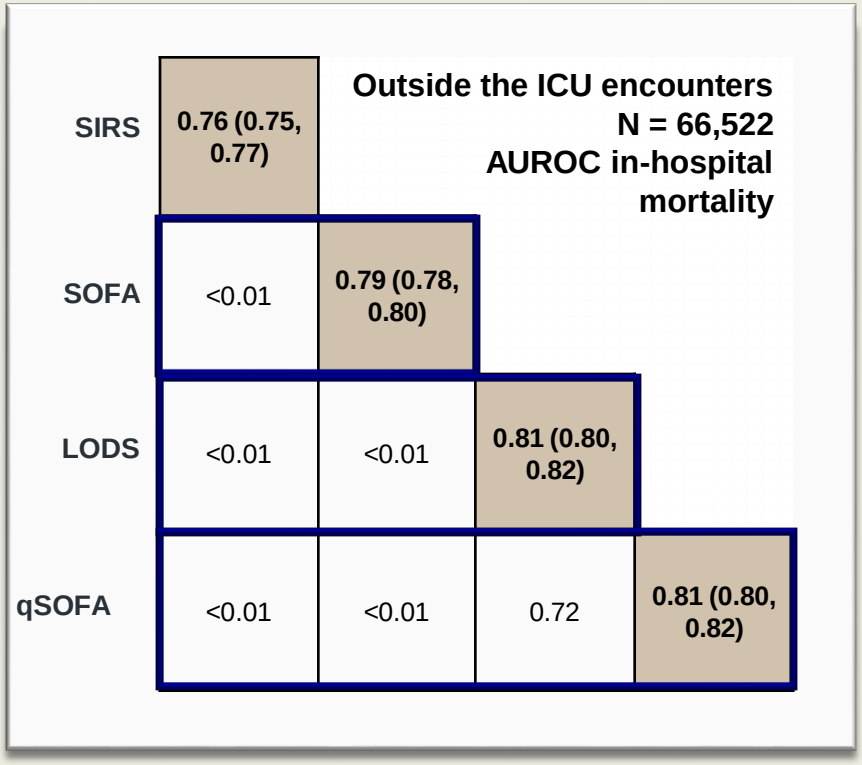


  - Validated with EHR data - KPNC, VA, KC (Seattle) EMS, “ALERTS” (Germany)

Assessment of criteria



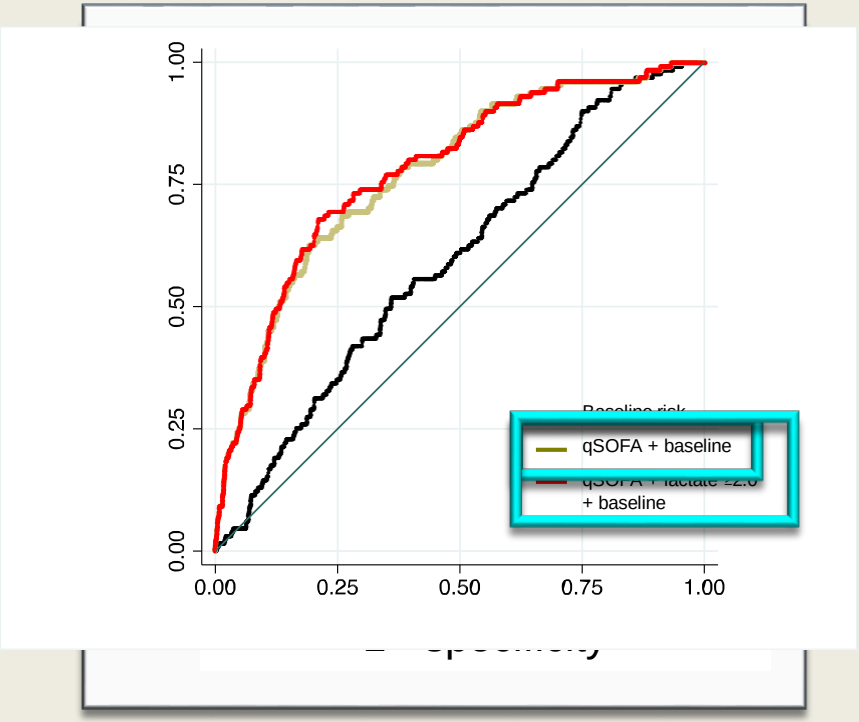
SOFA and LODS superior in the ICU



qSOFA similar to complex scores outside the ICU

Serum lactate

- Not retained during qSOFA model building
- Serum lactate at various thresholds added to qSOFA



New Definition of Sepsis

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

New Clinical Criteria for Sepsis

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

Among patients with suspected infection

- SOFA ≥ 2 (or a change ≥ 2, ΔSOFA)

  or

- in ED/on wards, qSOFA

What clinical criteria identify patients with septic shock ?

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Developing a New Definition and Assessing New Clinical Criteria for Septic Shock

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

Manu Shankar-Hari, MD, MSc; Gary S. Phillips, MAS; Mitchell L. Levy, MD; Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Clifford S. Deutschman, MD; Derek C. Angus, MD, MPh; Gordon D. Rubenfeld, MD, MSc; Mervyn Singer, MD, FRCP; for the Sepsis Definitions Task Force

IMPORTANCE Septic shock currently refers to a state of acute circulatory failure associated with infection. Emerging biological insights and reported variation in epidemiology challenge the validity of this definition.

OBJECTIVE To develop a new definition and clinical criteria for identifying septic shock in adults.

DESIGN, SETTING, AND PARTICIPANTS The Society of Critical Care Medicine and the European Society of Intensive Care Medicine convened a task force (19 participants) to revise current sepsis/septic shock definitions. Three sets of studies were conducted: (1) a systematic review and meta-analysis of observational studies in adults published between January 1, 1992, and December 25, 2015, to determine clinical criteria currently reported to identify septic shock and inform the Delphi process; (2) a Delphi study among the task force comprising 3 surveys and discussions of results from the systematic review, surveys, and cohort studies to achieve consensus on a new septic shock definition and clinical criteria; and (3) cohort studies to test variables identified by the Delphi process using Surviving Sepsis Campaign (SSC) (2005-2010; n = 28 150), University of Pittsburgh Medical Center (UPMC) (2010-2012; n = 1309 025), and Kaiser Permanente Northern California (KPNC) (2009-2013; n = 1 847 165) electronic health record (EHR) data sets.

MAIN OUTCOMES AND MEASURES Evidence for and agreement on septic shock definitions and criteria.

RESULTS The systematic review identified 44 studies reporting septic shock outcomes (total of 166 479 patients) from a total of 92 sepsis epidemiology studies reporting different cutoffs and combinations for blood pressure (BP), fluid resuscitation, vasopressors, serum lactate level, and base deficit to identify septic shock. The septic shock–associated crude mortality was 46.5% (95% CI, 42.7%-50.3%), with significant between-study statistical heterogeneity (I^2 = 99.5%; τ^2 = 182.5; P < .001). The Delphi process identified hypotension, serum lactate level, and vasopressor therapy as variables to test using cohort studies. Based on these 3 variables alone or in combination, 6 patient groups were generated. Examination of the SSC database demonstrated that the patient group requiring vasopressors to maintain mean BP 65 mm Hg or greater and having a serum lactate level greater than 2 mmol/L (18 mg/dL) after fluid resuscitation had a significantly higher mortality (42.3% [95% CI, 41.2%-43.3%]) in risk-adjusted comparisons with the other 5 groups derived using either serum lactate level greater than 2 mmol/L alone or combinations of hypotension, vasopressors, and serum lactate level 2 mmol/L or lower. These findings were validated in the UPMC and KPNC data sets.

CONCLUSIONS AND RELEVANCE Based on a consensus process using results from a systematic review, surveys, and cohort studies, septic shock is defined as a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone. Adult patients with septic shock can be identified using the clinical criteria of hypotension requiring vasopressor therapy to maintain mean BP 65 mm Hg or greater and having a serum lactate level greater than 2 mmol/L after adequate fluid resuscitation.

JAMA. 2016;315(8):775-787. doi:10.1001/jama.2016.0289

Editorial page 757

Author Audio Interview at jama.com

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Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: Members of the Sepsis Definitions Task Force are listed at the end of this article.

Corresponding Author: Manu Shankar-Hari, MD, MSc, Department of Critical Care Medicine, Guy's and St Thomas' NHS Foundation Trust, London SE1 7EH, United Kingdom (manu.shankar-hari@kcl.ac.uk).

Manu Shankar-Hari, MD MSc, FFICM
Guy's and St Thomas' Hospitals NHS Trust, London, UK
King's College London, London, UK

Shankar-Hari M, Phillips GS, Levy ML et al.

Developing a New Definition and Assessing New Clinical Criteria for Septic Shock

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

JAMA 2016; 315: 775-787

New Septic Shock Definition

Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

- Arrived at via by use of Delphi method among members of task force
- As with sepsis, elements are difficult to identify clinically

What is septic shock ?

A subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater **risk** of mortality than with sepsis alone

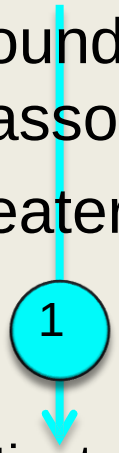
So these are patients with sepsis who are *especially* sick

What is septic shock ?

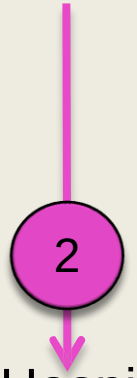
A subset of sepsis in which

profound circulatory, cellular and metabolic abnormalities are associated with

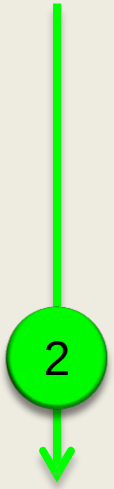
a greater **risk** of mortality than with sepsis alone



Among patients with sepsis (that is, who have suspected infection and are *really sick*)

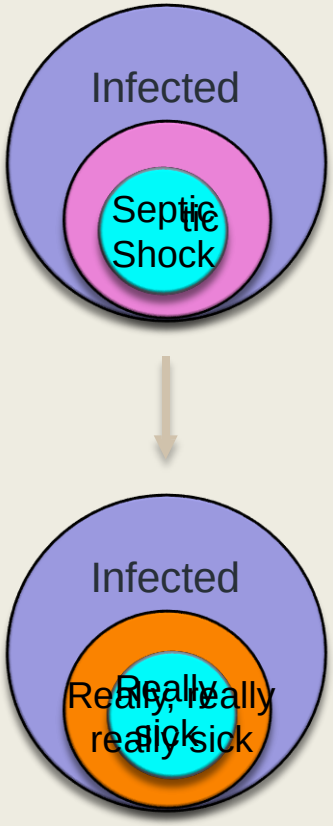


Hospital mortality



Who is *really, really, really* sick ?
(eg, has a 50:50 chance of dying)

How to identify who is sick?



- Septic shock is a subset of sepsis
- It is characterized by “profound circulatory, cellular and metabolic abnormalities”
- Once again, these elements cannot really be measured clinically

- This time, need a proxy for “really, really, really sick”
- What proxies can be used ?

Data analysis

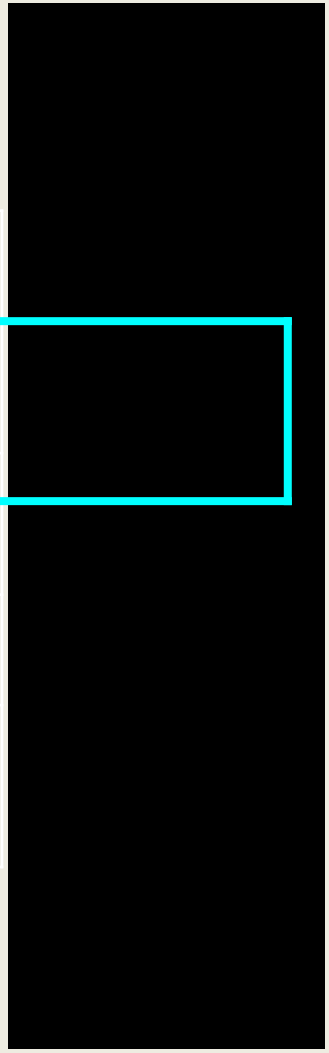
- Derivation cohort
  - Surviving Sepsis Campaign Database (SSC)
    - 28,150 patients with severe sepsis or septic shock
- Validation cohort
  - UPMC
  - KPNC
- Criteria – identified by modified Delphi process – task force
  - After fluids
    - Hypotension, vasopressor dependence, elevated lactate

6 patient groups based on 3 variables

	hypotension after fluids	vasopressors	lactate >2	Prevalence (SSC)	Mortality
Group 1	Yes	Yes	Yes	45.2%	42.3 (41.2-43.3)
Group 2	Yes	Yes	No	21.2%	30.1 (28.6-31.5)
Group 3	Yes	No	Yes	1.2%	
Group 4	No	No	Yes	17.6%	25.7 (24.2-27.2)
Group 5	No hypotension pre-fluid	No	Yes	14.3%	29.7 (28.0-31.5)
Group 6	Yes	No	No	0.8%	

6 patient groups based on 3 variables

	hypotension after fluids	vasopressors	lactate >2	Prevalence (SSC)
Group 1	Yes	Yes	Yes	45.2%
Group 2	Yes	Yes	No	21.2%
Group 4	No	No	Yes	17.3%
Group 5	No hypotension pre-fluid	No	Yes	14.3%



New Septic Shock Definition

Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

New Clinical Criteria for Septic Shock

Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

Despite adequate fluid resuscitation

- vasopressors needed to maintain MAP ≥65 mmHg AND
- lactate >2 mmol/l

Summary (I)

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

- Septic shock is defined as a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

Summary (II)

- Outside the ICU, patients with suspected or presumed infection who are highly likely to have poor outcomes can be clinically identified using qSOFA
  - SBP < 100mm Hg
  - RR > 22 breath/min
  - Altered mental status
- In the ICU, patients with suspected or presumed infection who are highly likely to have poor outcomes can be clinically identified by the presence of 2 or more SOFA points

Summary (III)

- Patients with septic shock can be clinically identified if, despite adequate resuscitation,
- They require vasopressors to maintain MAP ≥65 mmHg

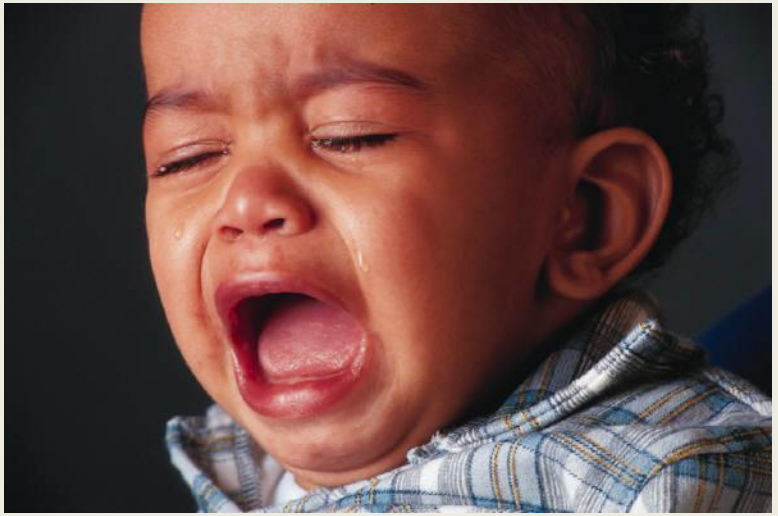
- AND

- Their serum lactate level is > 2 mmol/l

Application of a Framework to Assess the Usefulness of Alternative Sepsis Criteria

Christopher W. Seymour, MD[1]; Craig M. Coopersmith, MD[2]; Clifford S. Deutschman, MD[3]; Foster Gesten, MD[4]; Michael Klompas, MD[5]; Mitchell Levy, MD[6]; Gregory S. Martin, MD[7]; Tiffany M. Osborn, MD[8]; Chanu Rhee, MD[5]; David k. Warren, MD[9]; R. Scott Watson, MD[10]; Derek C. Angus, MD[1]

- Definitions of sepsis
  - 3rd International consensus definitions
  - CDC
  - CMS



Crit Care Med 2016; 44:e122–e130

What's the Problem?

- There is no perfect method to unambiguously categorize patients as having sepsis or not
- Multiple initiatives for sepsis with different goals
- ***Four*** broad purposes for sepsis criteria:
  - Clinical Care
  - Research
  - Surveillance
  - QI and audit

Clinical Care

Objective	Example	Criteria	Caveats
To inform the direct clinical care of sepsis at the bedside	ESICM/ SCCM 3rd International Consensus Definitions for Sepsis and Septic Shock Task Force	Among patients in whom the clinician suspects infection: •Acute change in SOFA score ≥ 2 points For clinical prompt in infected patients: •≥ 2 qSOFA points outside the ICU	• Sepsis not restricted to confirmed infection • No criteria proposed for infection; left to clinician • SOFA baseline may not be always available

Research: Clinical

Objective	Example	Criteria	Caveats
Guide the conduct of clinical research in sepsis	Enrollment criteria for ACCESS trial	Among patients with evidence of infection, all of: • 3 or more SIRS criteria • 1 major organ dysfunction • High risk of death (APACHE II)	• Sepsis not restricted to confirmed infection • No criteria proposed for infection; left to clinician • SOFA baseline may not be always available

Research: Basic

Objective	Example	Criteria	Caveats
Guide the study of fundamental principles of sepsis, often animal models	Murine sepsis score after fecal-induced peritonitis	Score ranging from 0-28, 4 points for: • Appearance • LOC • Activity • Response to stimulus • Eyes • Respiratory rate • Respiration quality	• Reported with high inter-rater and test-retest reliability • May be species specific • Alternative models under study

Surveillance and Epidemiology

Objective	Example	Criteria	Caveats
To track local and national burden, incidence and outcomes of sepsis across hospitals over time • Not dependent on coding	Center for Disease Control (CDC) and Prevention Epicenters *Preliminary Criteria*	Among patients with infection, ≥ 1 of: •Vasopressor use •≥ 2 days of mechanical ventilation •Rise in serum creatinine by ≥ 0.5	• Avoids data elements not readily available in the EHR (vital signs) • Feasibility • For similar patients, clinicians may provide organ support differently

QI and Audit

Objective	Example	Criteria	Caveats
To inform quality improvement initiatives and audit performance across hospitals	Centers for Medicare and Medicaid Services (SEP-1)	• ICD-10 claims based identification to find denominator of sepsis patients • Manual chart review for SIRS criteria and organ dysfunction criteria	• Restricts to cohort of patients identified with administrative data • Some hospitals using EHR algorithm • *May result in smaller, sicker subset of patients*

Case Identification by Different Criteria

Variable	Clinical Criteria in 2016 Consensus Definitions: Acute Change in ≥ 2 SOFA Points	Clinical Criteria in 2016 Consensus Definitions: Bedside Prompt of ≥ 2 qSOFA Points	Prevention Epicenters Criteria for Surveillance: Simple	Prevention Epicenters Criteria for Surveillance: Complete	CMS Criteria for QI and Audit
Total no.	11,011	9,823	9,176	12,041	2,709
Positive blood cultures, no. (%)	854 (8)	786 (8)	824 (9)	1,034 (9)	N/A
Maximum day 1 SOFA score, mean (SD)	2.9 (3.0)	2.9 (3.5)	3.1 (3.6)	2.6 (3.4)	4.2 (4.2)
≥ 2 SIRS criteria, no. (%)	7,003 (64)	7,487 (76)	5,903 (64)	7,166 (60)	2,709 (100)
ICU admission, no. (%)	5,402 (49)	6,808 (69)	6,658 (73)	7,288 (61)	2,239 (83)
ICU length of stay, median days (IQR)	5 (3–10)	5 (3–10)	6 (4–12)	6 (4–11)	7 (3–13)
Hospital length of stay, median days (IQR)	8 (5–13)	9 (6–16)	12 (7–19)	11 (7–18)	12 (7–20)
In-hospital mortality, no. (%)	977 (8.9)	1,072 (11)	1,256 (14)	1,319 (11)	663 (24)

Conclusions

- Unrealistic goal to have a single gold-standard definition of sepsis
  - Different populations, goals, purpose
- Possible to develop methodologic framework to develop and assess different definitions and criteria
- Each set of criteria valuable for different purpose
- Harmonization and standardization may be possible over time as new technologies and markers develop


thank you
danke
謝謝
ngiyabonga
teşekkür ederim
спасибо
dank je
gracias
tapadh leat
bedankt
hvala
mauruuru
mochchakkeram
dziękuję
go raibh maith agat
obrigado
sukriya
kop khun krap
taiku
arigatō
takk
dakujem
grazie
merci
terima kasih
감사합니다
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