Pro

The New Definition of Sepsis and Septic Shock

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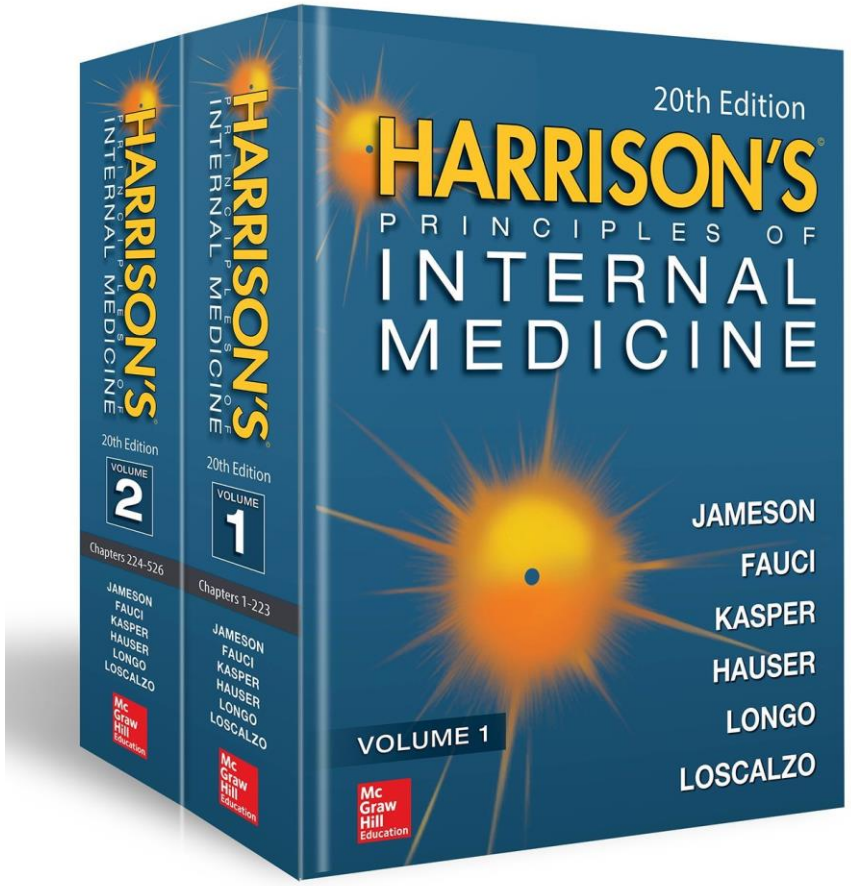
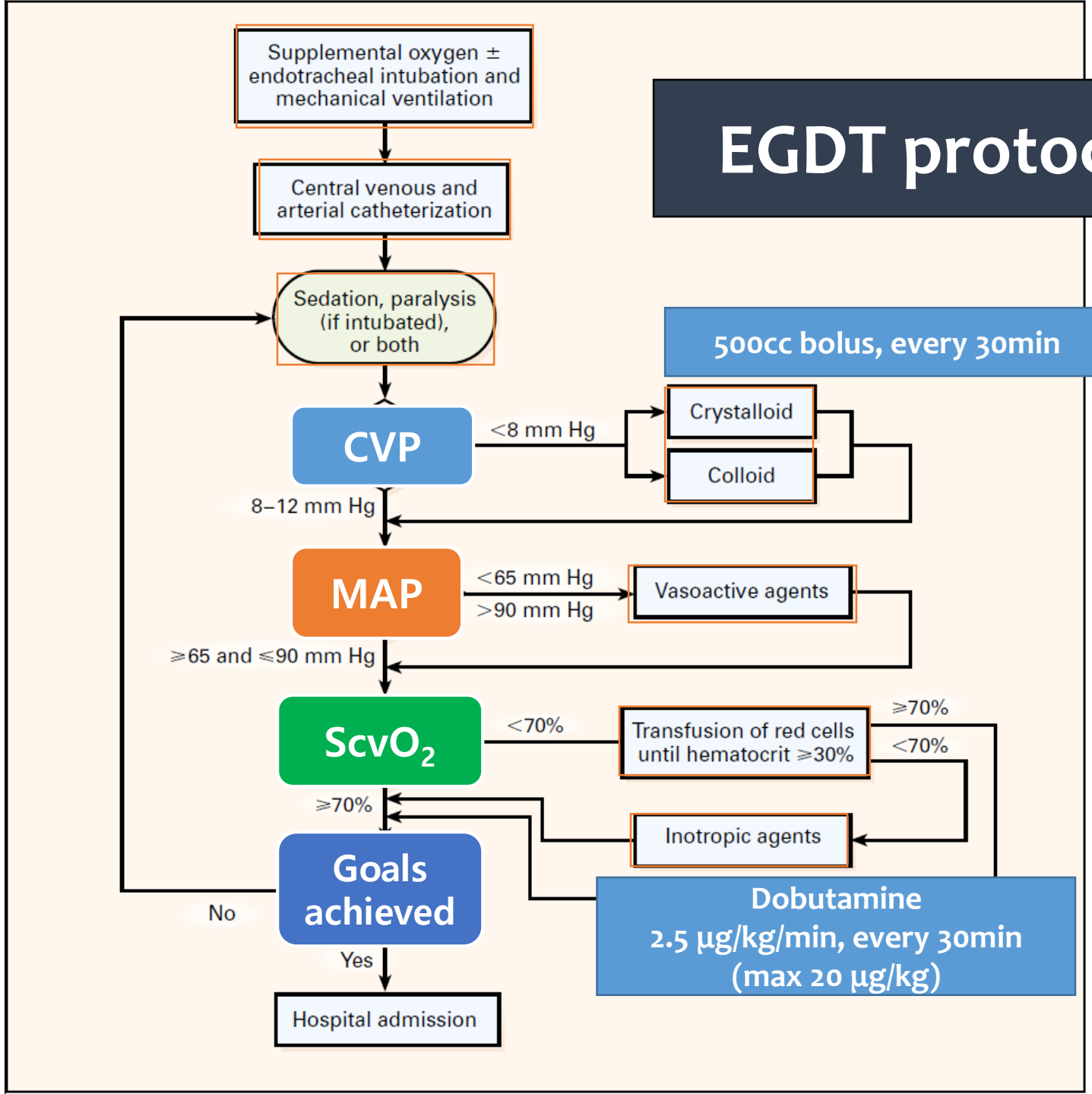
Medicine is an ever-changing science !!!



EGDT protocol



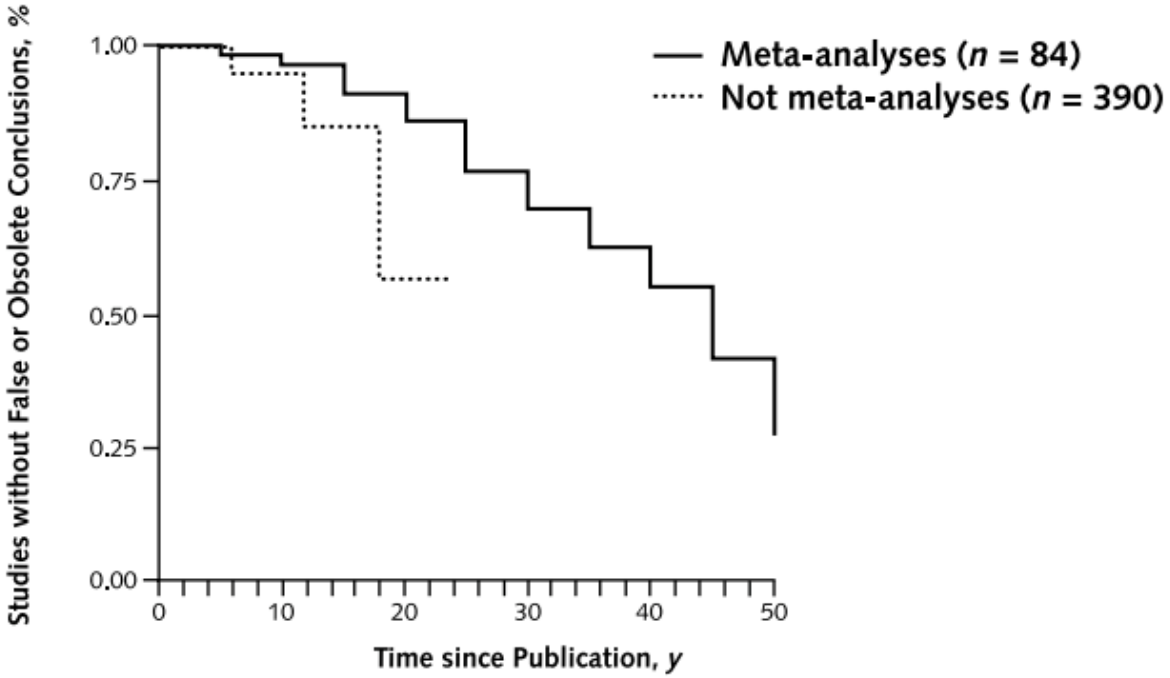
Recently, negative in RCTs…

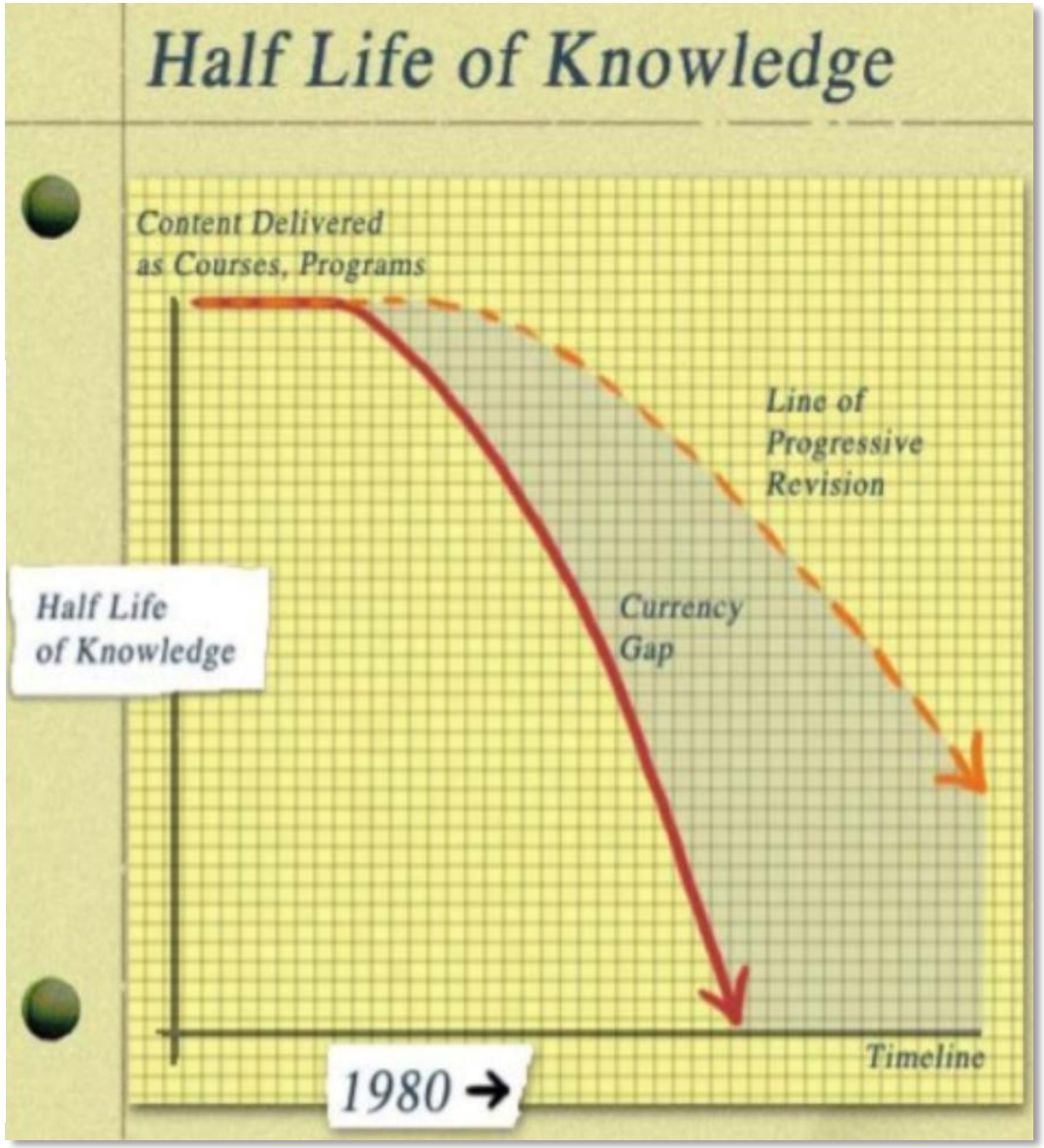
- **ProCESS trial**
  - **A Randomized Trial of Protocol-Based Care for Early Septic Shock**
  - **NEJM 2014;370:1683.**
- **ARISE trial**
  - **Goal-Directed Resuscitation for Patients with Early Septic Shock**
  - **NEJM 2014;371:1496**
- **ProMISe Trial**
  - **Trial of Early, Goal-Directed Resuscitation for Septic Shock**
  - **NEJM, 2015;372:1301**

Half-life of the medical facts

Truth Survival in Clinical Research: An Evidence-Based Requiem?

Thierry Poynard, MD, PhD; Mona Munteanu, MD; Vlad Ratziu, MD; Yves Benhamou, MD, PhD; Vincent Di Martino, MD; Julien Taieb, MD; and Pierre Opolon, MD





History of Sepsis

- 1st 1991 - SIRS, Sepsis, Severe sepsis, Septic shock
  An American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference

- 2nd 2001 – SIRS, Sepsis, Severe sepsis, Septic shock
  SCCM, ESICM, ACCP, American Thoracic Society (ATS), and the Surgical Infection Society (SIS)

- 3rd EHR based

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 *Alan M. Fein, M.D., F.C.C.P.*

Sepsis is the host's inflammatory response to infection.

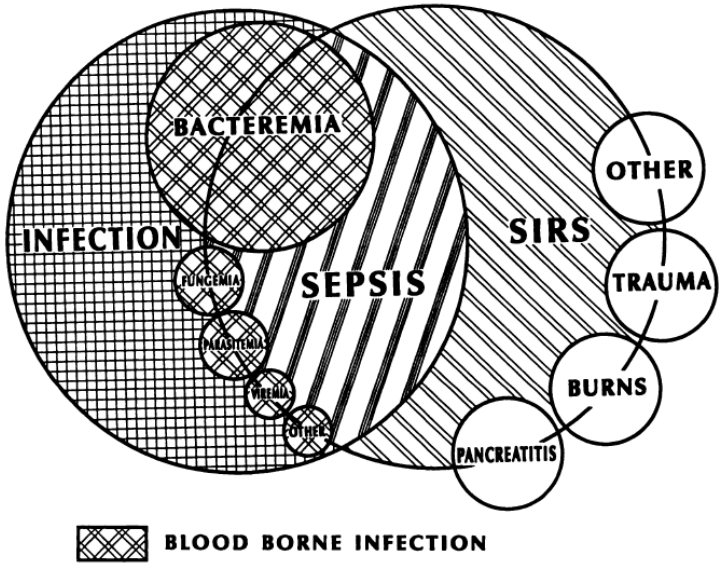


FIGURE 1. The interrelationship between systemic inflammatory response syndrome (SIRS), sepsis, and infection.

Table 1—*Definitions*

Infection = microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

Bacteremia = the presence of viable bacteria in the blood.

Systemic inflammatory response syndrome (SIRS) = the systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or $PaCO_2$ <32 mm Hg; and (4) white blood cell count >12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms

Sepsis = the systemic response to infection, manifested by two or more of the following conditions as a result of infection: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or $PaCO_2$ <32 mm Hg; and white blood cell count >12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms.

Severe sepsis = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.

Septic shock = sepsis-induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.

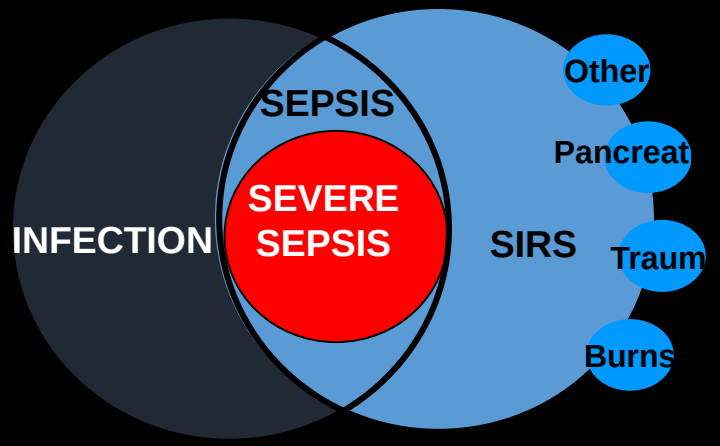
Sepsis-induced hypotension = a systolic blood pressure <90 mm Hg or a reduction of ≥40 mm Hg from baseline in the absence of other causes for hypotension.

Multiple organ dysfunction syndrome (MODS) = presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

ACCP/SCCM CONSENSUS DEFINITIONS

SIRS: Systemic Inflammatory Response Syndrome

- Systemic response to a variety of processes
- Manifested by ≥2 of the following
  - Temperature >38°C or <36°C
  - HR >90 bpm
  - RR >20/min
  - WBC >12,000/mL or <4,000/mL
    or >10% immature neutrophils
- Hemostatic changes are also involved



Bone RC, et al. Chest 1992;101:1644-55.

ACCP/SCCM CONSENSUS DEFINITIONS

- **Sepsis**
  - Infection + ≥2 SIRS criteria
- **Severe Sepsis**
  - Sepsis + Organ dysfunction
- **Septic shock**
  - Sepsis + hypotension despite fluid resuscitation
  - Sepsis-induced hypotension
    - SBP <90 mmHg or MAP< 70 mmHg
    - SBP decrease 40 mmHg or 2 SD below normal for age
    - Absence of other causes of hypotension

Bone RC, et al. Chest 1992;101:1644-55

Dear SIRS, I'm sorry to say that I don't like you

1. New terminology does not help us to understand the underlying problem
2. There are enough problems with the current terminology "sepsis," "infection," "septicemia"
3. SIRS is too sensitive, but is not specific (like, "critically ill")
4. SIRS does not reflect the severity of the disease process
5. SIRS may detract from the search for infection

Vincent, Jean-Louis MD, PhD, FCCM, Crit Care Med.1997;25(2):372

Table 1 Diagnostic criteria for sepsis

Infection[a]
Documented or suspected *and* some of the following[b]:
General parameters
Fever (core temperature >38.3°C)
Hypothermia (core temperature <36°C
Heart rate >90 bpm or >2 SD above the normal value for age
Tachypnea: >30 bpm
Altered mental status
Significant edema or positive fluid balance (>20 ml/kg over 24 h)
Hyperglycemia (plasma glucose >110 mg/dl or 7.7 mM/l) in the absence of diabetes
Inflammatory parameters
Leukocytosis (white blood cell count >12,000/µl)
Leukopenia (white blood cell count <4,000/µl)
Normal white blood cell count with >10% immature forms
Plasma C reactive protein >2 SD above the normal value
Plasma procalcitonin >2 SD above the normal value
Hemodynamic parameters
Arterial hypotension[b] (systolic blood pressure <90 mmHg, mean arterial pressure <70, or a systolic blood pressure decrease >40 mmHg in adults or <2 SD below normal for age)
Mixed venous oxygen saturation >70%[b]
Cardiac index >3.5 l min^{-1} m^{-2}[c,d]
Organ dysfunction parameters
Arterial hypoxemia (PaO_2/FIO2 <300)
Acute oliguria (urine output <0.5 ml kg^{-1} h^{-1} or 45 mM/l for at least 2 h)
Creatinine increase ≥0.5 mg/dl
Coagulation abnormalities (international normalized ratio >1.5 or activated partial thromboplastin time >60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count <100,000/µl)
Hyperbilirubinemia (plasma total bilirubin >4 mg/dl or 70 mmol/l)
Tissue perfusion parameters
Hyperlactatemia (>3 mmol/l)
Decreased capillary refill or mottling

[a] Defined as a pathological process induced by a micro-organism

[b] Values above 70% are normal in children (normally 75–80%) and should therefore not be used as a sign of sepsis in newborns or children

[c] Values of 3.5–5.5 are normal in children and should therefore not be used as a sign of sepsis in newborns or children

[d] Diagnostic criteria for sepsis in the pediatric population is signs and symptoms of inflammation plus infection with hyper- or hypothermia (rectal temperature >38.5°C or <35°C), tachycardia (may be absent in hypothermic patients) and at least one of the following indications of altered organ function: altered mental status, hypoxemia, elevated serum lactate level, and bounding pulses

Sepsis definitions: time for change

"Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs"

- First, the SIRS criteria are so sensitive that up to 90% of patients admitted to an intensive care unit (ICU) meet the criteria
- Second, some degree of host response is actually inherent to the infection
- Third, deciphering the role of infection in the pathogenesis of SIRS has been difficult

Jean-Louis Vincent et al. ***Lancet*** **2013; 381: 774–75**

Research

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

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

SingerM et al. **JAMA.2016;315[8]:801-810**

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- **Organ dysfunction**
  - Acute change in total SOFA score 2 points consequent to the infection.
    - Baseline SOFA = 0 if no hx of preexisting organ dysfuction
    - ΔSOFA ≥ 2 → mortality 10%
  - Bedside q SOFA ≥ 2
    - Alteration in mental status, systolic BP 100 mmHg, or respiratory rate 22/min
    - Identifies patients likely to have prolonged ICU stay or hospital mortality

Definitions of Organ Dysfunction

Acute change in total SOFA score ≥2 points consequent to the infection.

Sequential [Sepsis-Related] Organ Failure Assessment Score Vincent JL, et al. . Intensive Care Med. 1996;22(7):707-710.						
System		Score				
		0	1	2	3	4
Respiration (PaO_2/FIO_2, mmHg)		≥400	<400	<300	<200 with respiratory support	<100 with respiratory support
Coagulation (Platelets, $\times 10^3/\mu L$)		≥150	<150	<100	<50	<20
Liver (Bilirubin, mg/dL)		<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular		MAP ≥70 mm Hg	MAP <70 mm Hg	DP <5 or DB (any dose)	DP 5.1-15 or Epi ≤0.1 or NE ≤0.1	DP >15 or Epi >0.1 or NE >0.1
CNS (Glasgow Coma Scale)		15	13-14	10-12	6-9	<6
Renal	**Cr (mg/dL)**	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0
	UO, mL/d				<500	<200

- The baseline SOFA score: "o" in patients not known to have preexisting OD
- Presenting with modest dysfunction can deteriorate further
- **Overall mortality risk SOFA score ≥2 with suspected infection ≒10%**

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

Bedside Surrogate For Organ Dysfunction By Quick SOFA (qSOFA)

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"**.

Bedside clinical score, qSOFA

At least 2 of following	▪ Respiratory rate ≥22/min ▪ Altered mentation ▪ Systolic blood pressure ≤100 mmHg

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

1991 & 2001 Septic Shock definitions

- 1991
  - Sepsis-induced hypotension, persisting despite adequate fluid resuscitation, along with the presence of hypoperfusion abnormalities or organ dysfunction.

- 2001
  - State of acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes.

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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

"**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"

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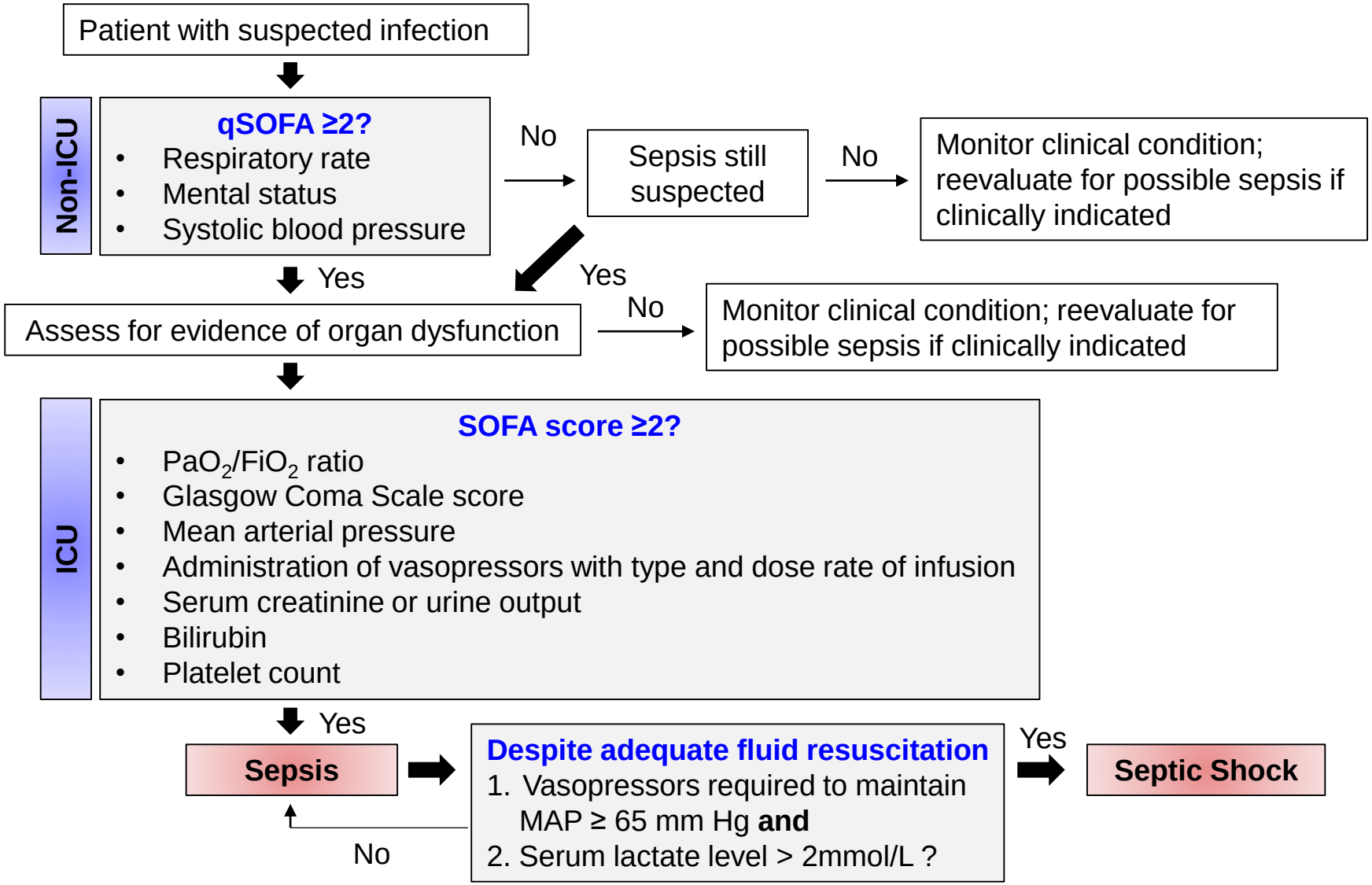
- Patients with sepsis with following features despite adequate volume resuscitation
  - Persisting hypotension requiring vasopressors to maintain MAP 65mmHg
  - Serum lactate level >2mmol/L(18mg/dL)

- **Hospital mortality is in excess 40%.**

Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



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Pro

Why to change ?

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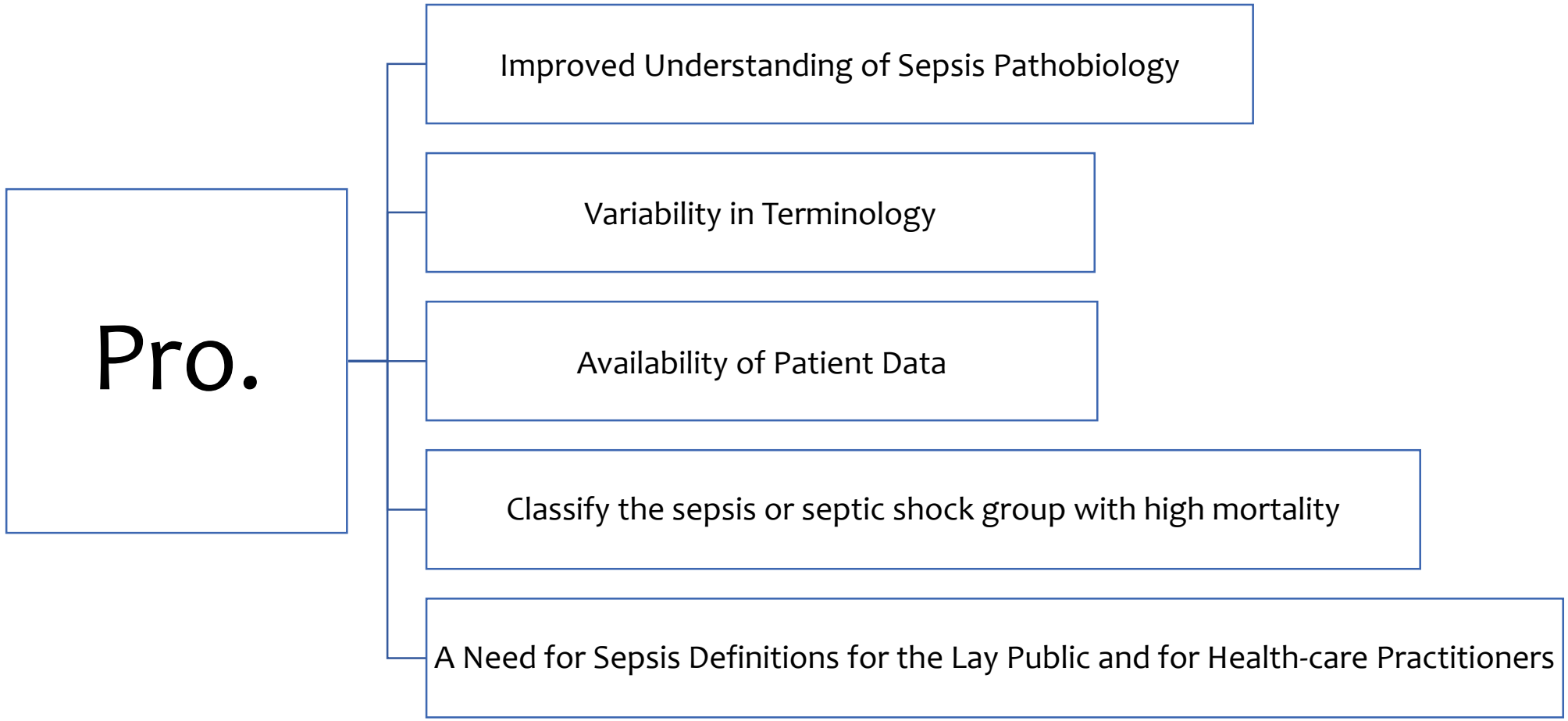

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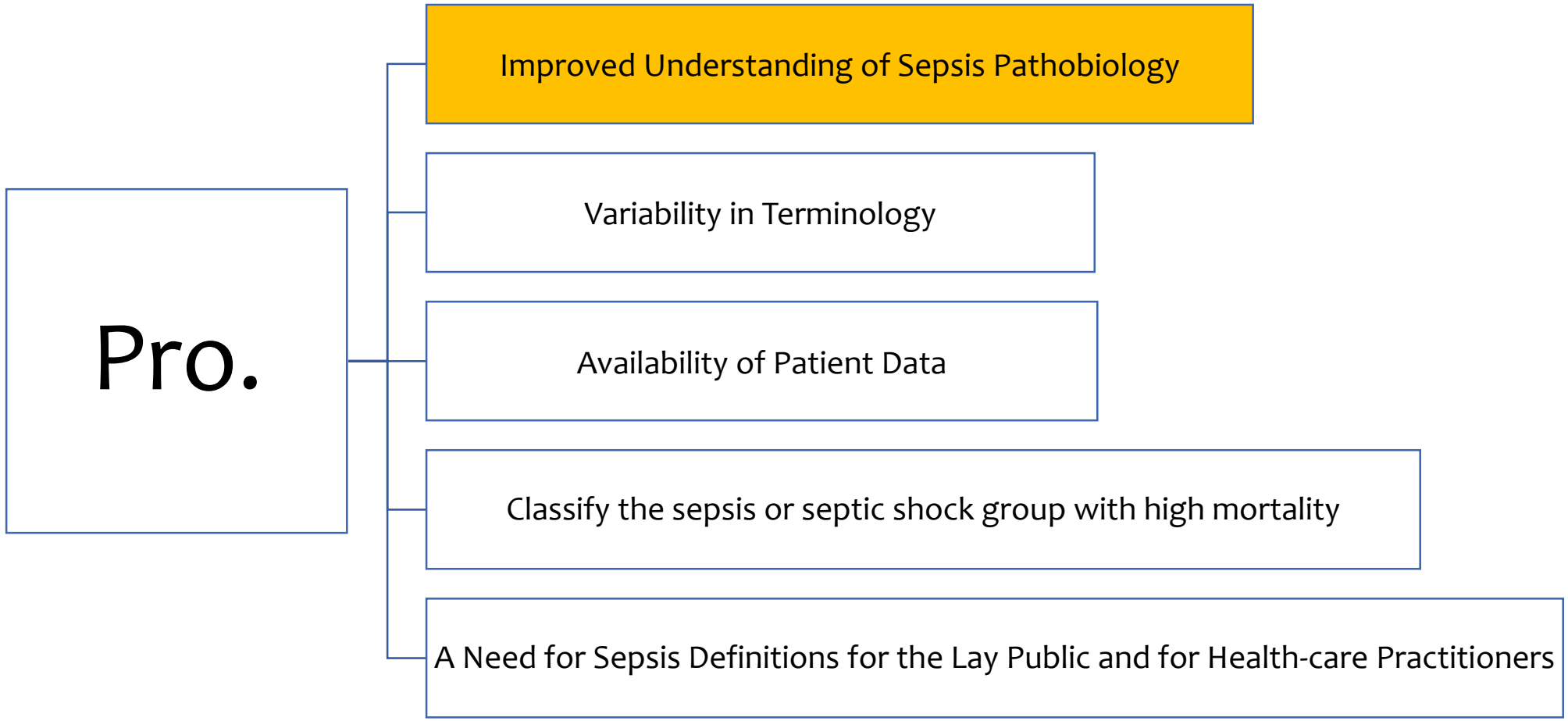
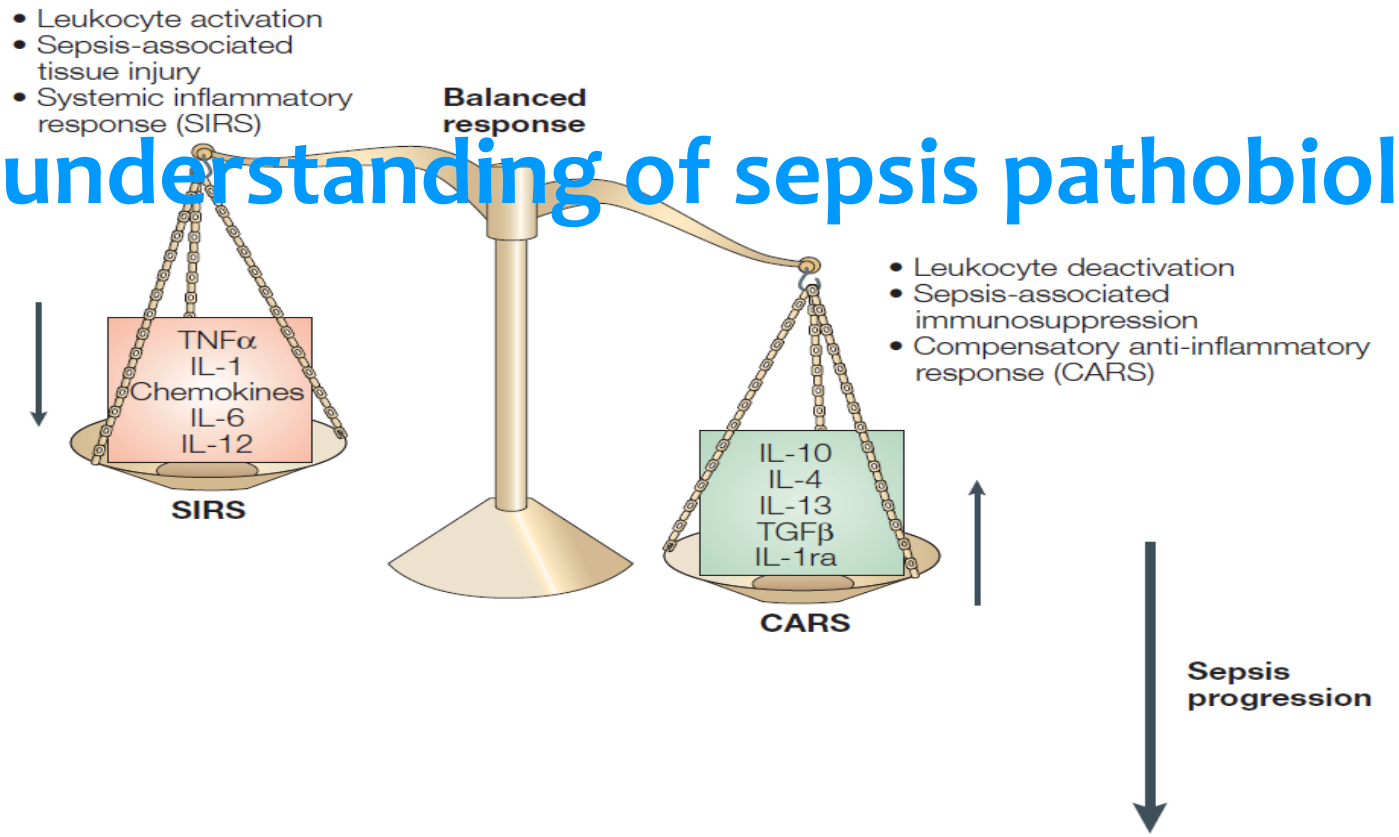


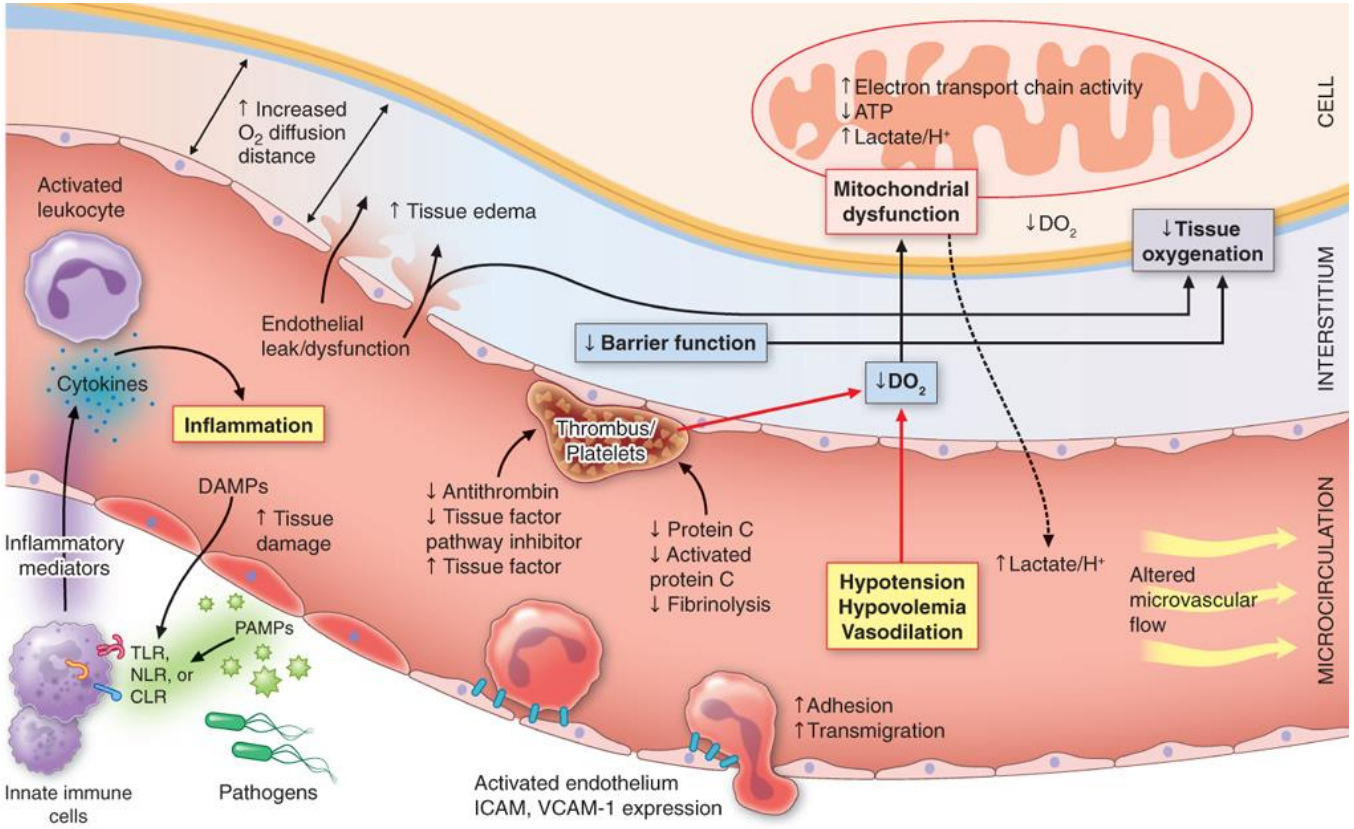
Improved understanding of sepsis pathobiology

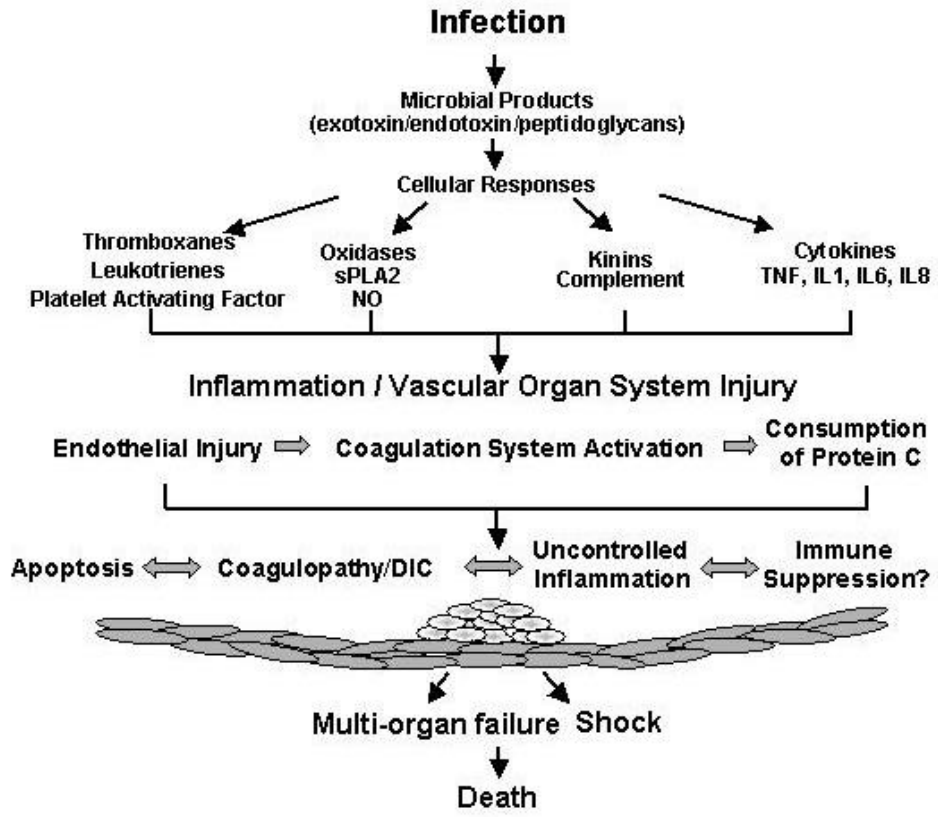


focused solely on inflammatory excess.

Nature Reviews Drug Discovery **4,** 854-865 (October 2005)

Improved understanding of sepsis pathobiology





Early activation of [both pro- and anti-inflammatory responses](), → [major modifications in nonimmunologic pathways]() such as cardiovascular, neuronal, autonomic, hormonal, bioenergetic, metabolic, and coagulation

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.
R. Phillip Dellinger, M.D., F.C.C.P.
Alan M. Fein, M.D., F.C.C.P.
William A. Knaus, M.D.
Roland M. H. Schein, M.D.
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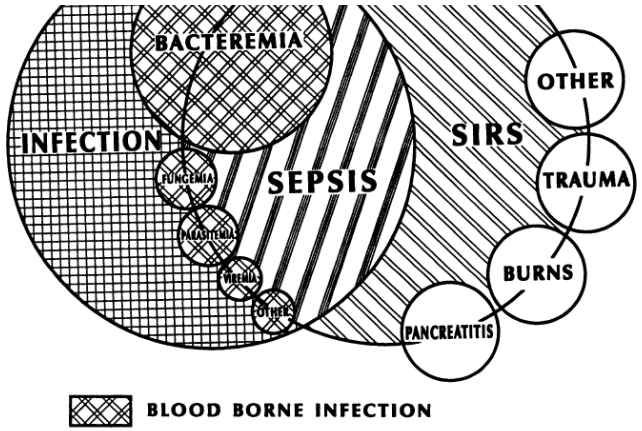

FIGURE 1. The interrelationship between systemic inflammatory response syndrome (SIRS), sepsis, and infection.

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

SingerM et al. **JAMA.2016;315[8]:801-810**

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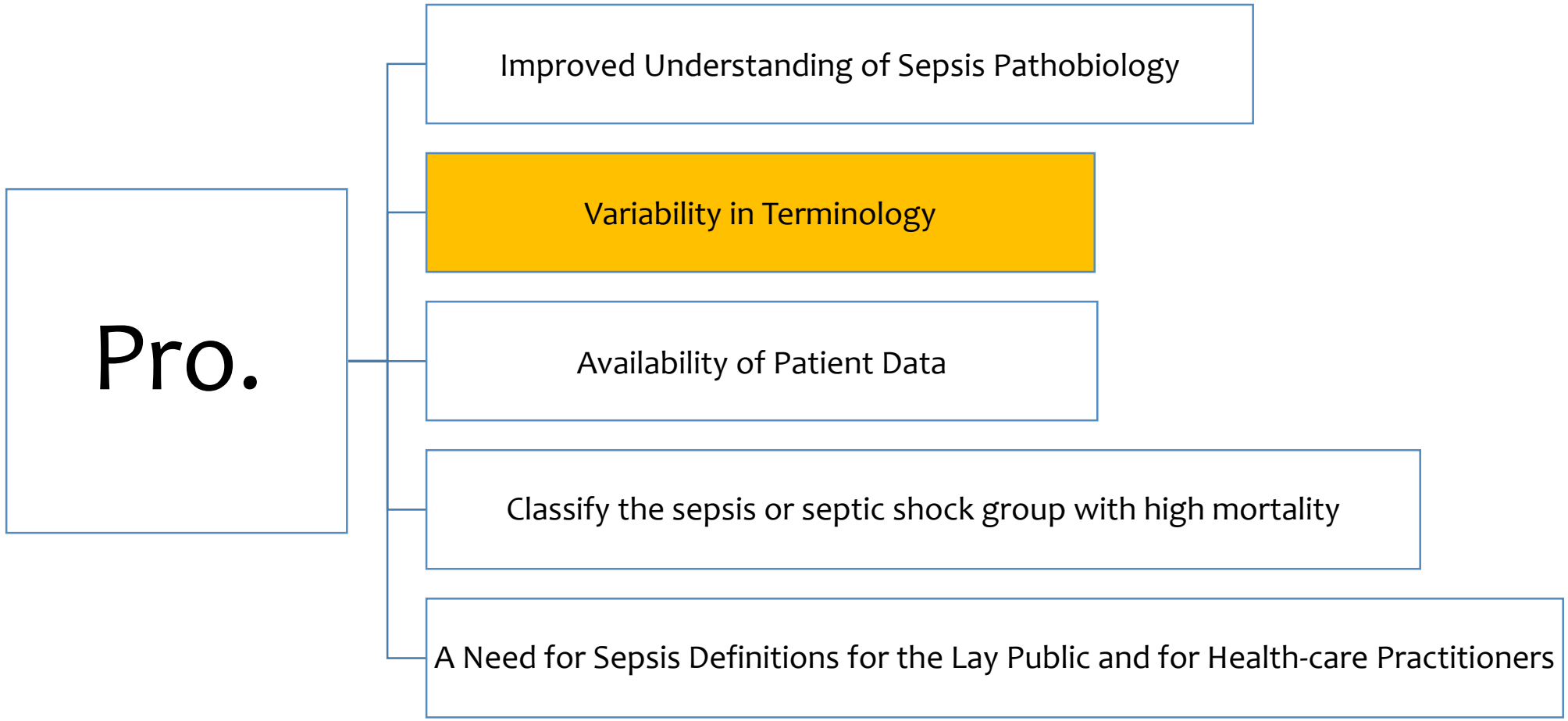


Variability in Terminology

- Definition… simple and definitively

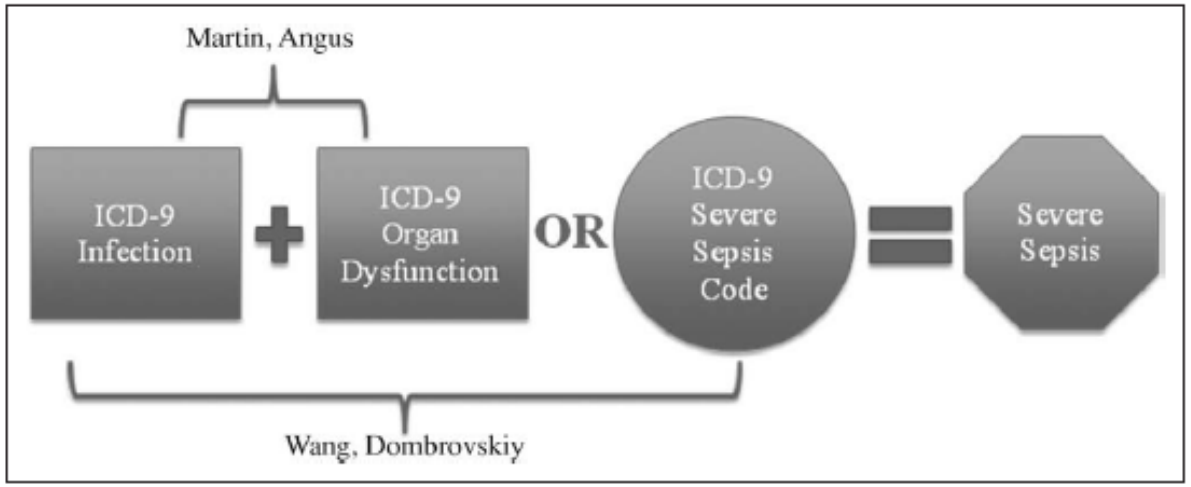
- **Severe sepsis(organ dysfunction)**
  - **Degree and Cut-off of organ dysfunction**
  - **Validated tool(score)**

- **Septic shock ; Particularly evident.**

Variability in Terminology

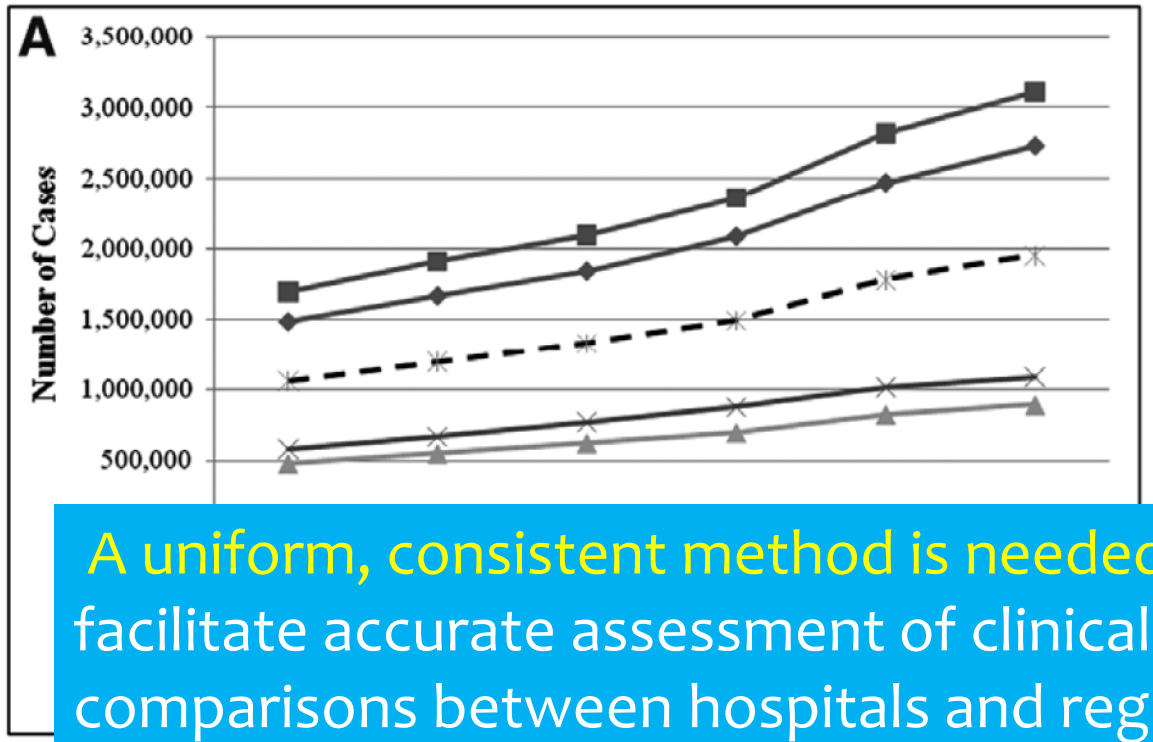
Benchmarking the Incidence and Mortality of Severe Sepsis in the United States*

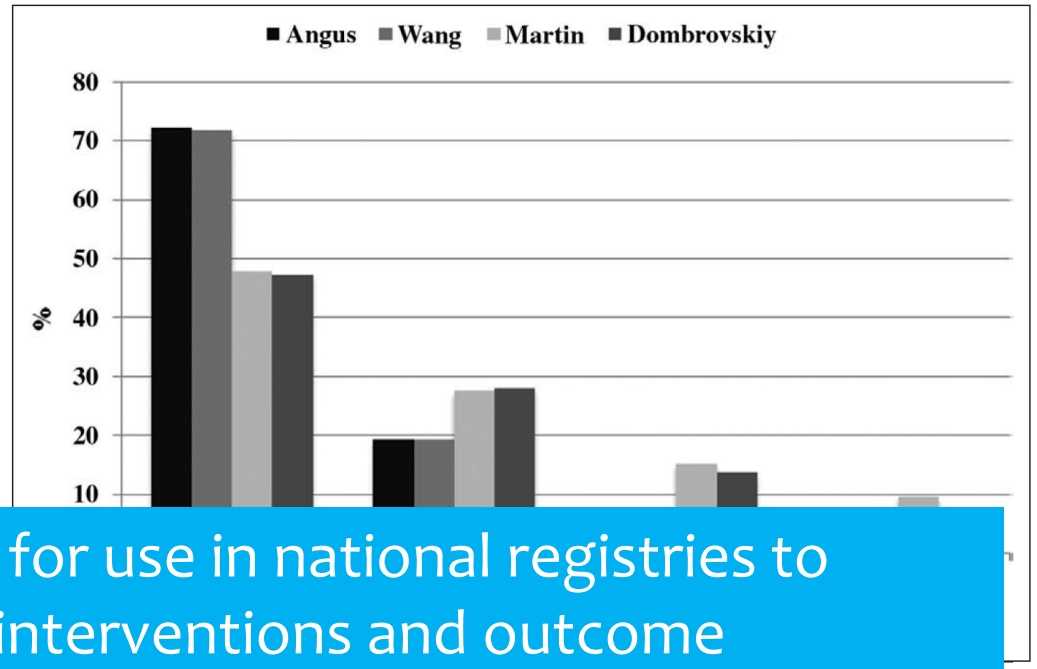
David F. Gaieski MD[1]; J. Matthew Edwards, MD[1]; Michael J. Kallan, MS[2]; Brendan G. Carr, MD, MA, MS[1–3]



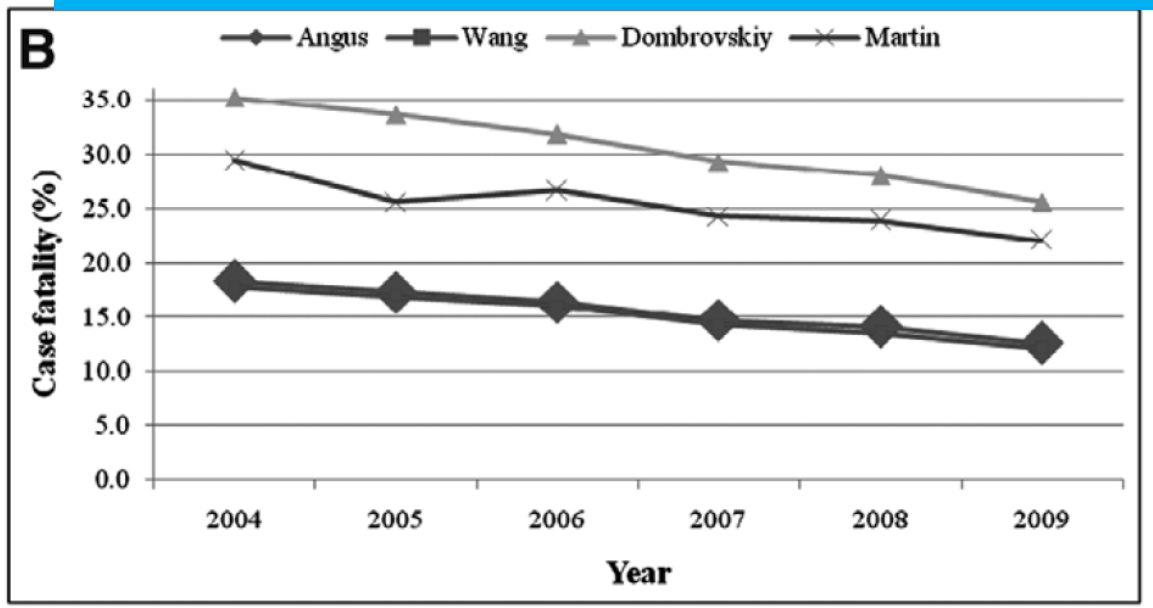
A nationally representative sample, cases of severe sepsis over a 6-year period (2004–2009).

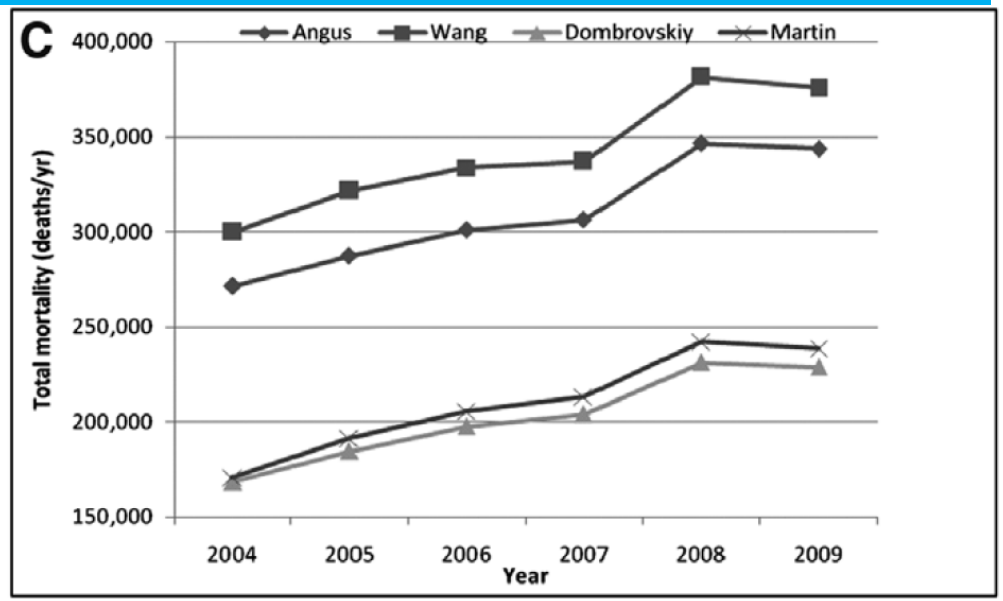
Gaieski, DF et al. Crit Care Med 2013; 41:1167–1174)





A uniform, consistent method is needed for use in national registries to facilitate accurate assessment of clinical interventions and outcome comparisons between hospitals and regions.





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Vincent and Moreno *Critical Care* 2010, 14:207
http://ccforum.com/content/14/2/207

CRITICAL CARE

REVIEW

Clinical review: Scoring systems in the critically ill

Jean-Louis Vincent*[1] and Rui Moreno[2]

Table 2. Comparison of three organ dysfunction scores

Characteristics	LODS [29]	MODS [30]	SOFA [31]
Year of publication	1996	1995	1996
Selection of variables and their weights	Multiple logistic regression	Literature review and logistic regression	Panel of experts
Variables used to assess organ dysfunction			
Neurologic	Glasgow Coma Scale	Glasgow Coma Scale	Glasgow Coma Scale
Cardiovascular	Heart rate, systolic blood pressure	Pressure-adjusted heart rate	Mean arterial blood pressure, vasopressor use
Renal	Serum urea or urea nitrogen, creatinine, urine output	Serum creatinine	Serum creatinine, urine output
Respiratory	PaO_2/FiO_2 ratio, mechanical ventilation	PaO_2/FiO_2 ratio	PaO_2/FiO_2 ratio, mechanical ventilation
Hematologic	White blood cell count, platelet count	Platelet count	Platelet count
Hepatic	Serum bilirubin, prothrombin time	Serum bilirubin	Serum bilirubin

LODS, Logistic Organ Dysfunction Score; MODS, Multiple Organ Dysfunction Score; SOFA, Sequential Organ Dysfunction Score.

LODS(Logistic Organ Dysfuction Score)

Measurements of organic systems	5	3	1	0	1	3	5
Neurological (GCS)	3-5	6-8	9-13	14-15			
Cardiovascular							
HR (beats/min)	<30	40-69	70-89	30-139	≥140		
SBP (mmHg)	<40			0-239	240-269	≥270	
Renal							
Ureic nitrogen (mmol/L)	-	-	-	<6	6-9.98	9.99-19.98	≥19.99
Serum creatinine (μmol/L)	-	-	-	<106.08	106.08-140.55	≥141.44	-
Urine output (L/24 h)	<0.5	0.5-0.74	-	0.75-0.99	-	≥10	-
Respiratory							
PaO_2 (Torr)/FiO_2 (%) in MV or CPAP	-	<150	≥150	With no ventilation, CPAP or IPAP	-	-	-
Hematologic							
TLC (mm^3)×10^3	-	<1.0	1.0-2.4	2.5-49.9	≥50	-	-
Platelets (mm^3)×10^3	-	-	<50	≥50	-	-	-
Hepatic							
Serum bilirubin (μmol/L)				<34.2	≥34.2		
PT (seconds and %)			<25	<3 s, >25	≥3 s		

LOD: Logistic organ dysfunction; GCS: Glasgow coma score; HR: Heart rate; SBP: Systolic blood pressure; PaO_2: (Torr) arterial oxygen tension; FiO_2: Fractional concentration of inspired oxygen; MV: Mechanical ventilation, CPAP: Continued positive airways pressure; IPAP: Intermittent positive airways pressure; TLC: Total leucocyte count; PT: Prothrombin time. The probability of death is then calculated using the formula: Probability of death=$e^{logit}/(1+e^{logit})$. Logit=−3.4043+0.4173 (LOD score)

MODS(Multiple Organ Dysfunction Score)

Multiple organ dysfunction score

Organ system and their variables	Score						
	0	1	2	3	4		
Hematologic: Platelet count ($\times 10^3/mm^3$ or $10^9/L$)	>120	81-120	51-80	21-50	≤20		
Hepatic: Serum bilirubin (μmol/L)	≤20	21-60	61-120	121-240	>240		
Renal: Serum creatinine (μmol/L)	≤100	101-200	201-350	351-500	>500		
Cardiovascular: PAR*	≤10	10.1-15	15.1-20	21-30	>30		
Glasgow coma score	15	13-14	10-12	7-9	≤6		
Respiratory: PO_2/FiO_2	>300	226-300	151-225	76-150	≤75		
Score	0	1-4	5-8	9-12	13-16	17-20	21-24
ICU mortality %	0	1-2	3-5	25	50	75	100

ICU: Intensive care unit; CVP: Central venous pressure (mmHg); GCS: Glasgow coma score; HR: Heart rate (beats/min); MAP: Mean arterial pressure (mmHg); PAR: Pressure adjusted heat rate (which is calculated as the product of the HR and the ratio of CVP to MAP); PaO_2 (Torr) arterial oxygen tension; FiO_2: Fractional concentration of inspired oxygen. If the result for a specific test is not available, then a score of 0 is used for that test. The serum creatinine concentration is measured without the use of dialysis and the PO_2/FiO_2 ratio (PO_2 in mmHg and FiO_2 in %) is calculated without the use of mechanical ventilation or positive end-expiratory pressure

SOFA (Sequential[sepsis-related] Organ Failure Assessment Score)

Organ system	Variable	Score 0	1	2	3	4
Pulmonary	Lowest PaO_2 (Torr)/FiO_2 (%)	>400	≤400	≤300	≤200+respiratory support	≤100+respiratory support
Coagulation	Lowest platelet (10^3/mm^3)	>150	≤150	≤100	≤50	≤20
Hepatic	Highest bilirubin (μmol/L)	<20	20-32	33-101	102-204	>204
Circulatory	Blood pressure status	Mean arterial pressure (mmHg) >70	Mean arterial pressure (mmHg) <70	Dopamine* dose≤5 or dobutamine any dose	Dopamine dose>5 or epinephrine≤0.1 or norepinephrine≤0.1	Dopamine dose>15 or epinephrine>0.1 or norepinephrine>0.1
Neurologic	GCS	15	13–14	10-12	6–9	<6
Renal	Highest creatinine level (μmol/L)	<110	110-170	171-299	300-440	>440
	Total urine output (mL/24 h)				<500	<200
Score	0-6	7-9	10-12	13-14	15	15-24
Score %	<10	15-20	15-20	50-60	>80	>90

PaO_2: (Torr) arterial oxygen tension; FiO_2: Fractional concentration of inspired oxygen; GCS: Glasgow coma score

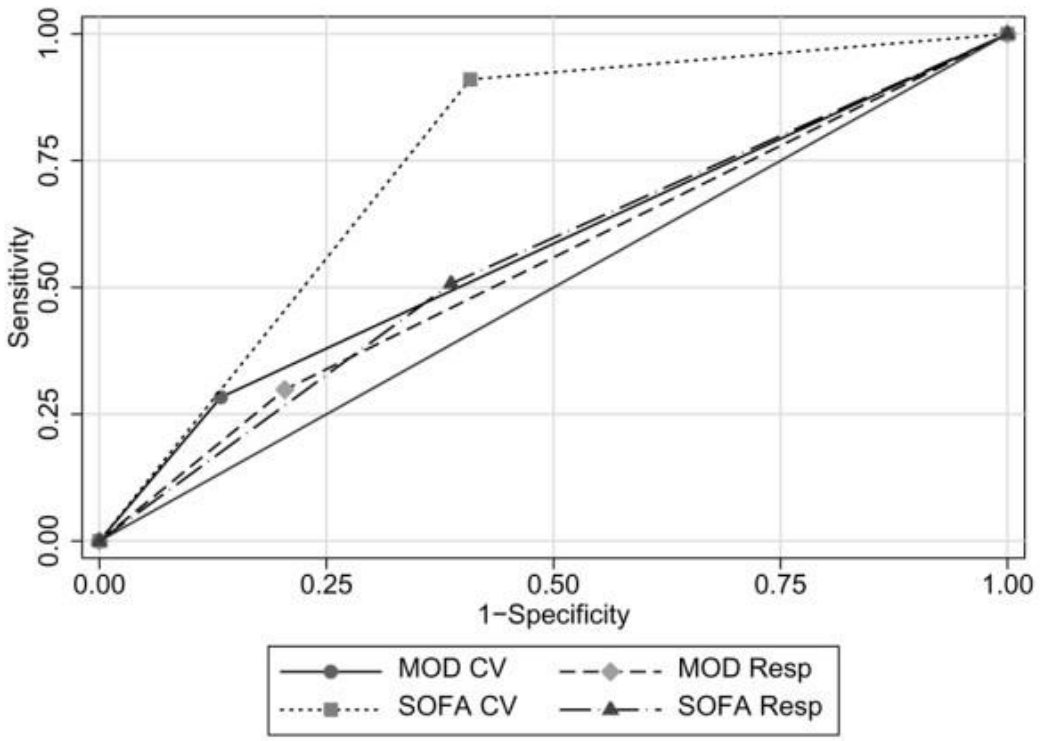
Research

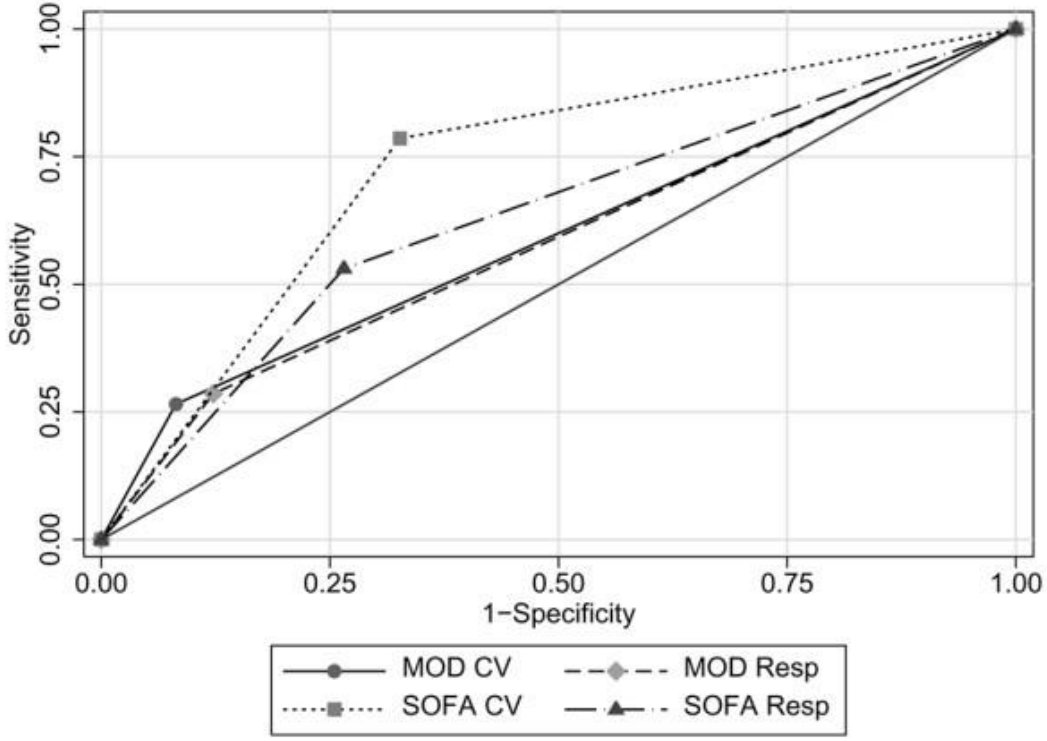
Open Access

SOFA is superior to MOD score for the determination of non-neurologic organ dysfunction in patients with severe traumatic brain injury: a cohort study

David Zygun[1,2,3], Luc Berthiaume[1,4], Kevin Laupland[1,3,4], John Kortbeek[1,5] and Christopher Doig[1,3,4]

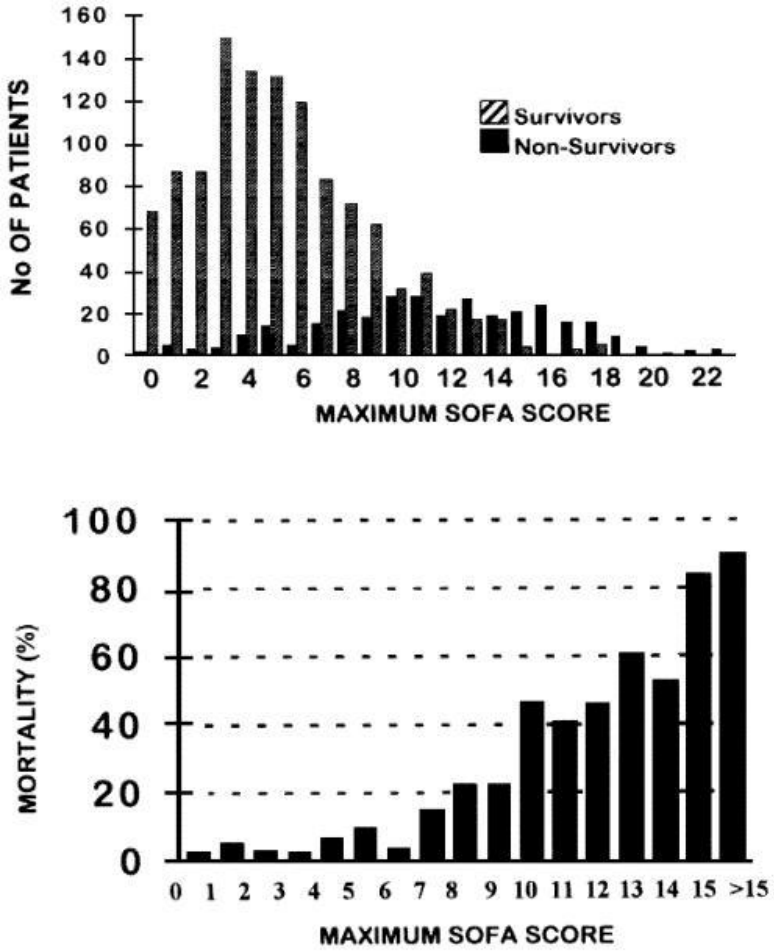
And… Better known and simpler





Crit Care. 2006; 10(4): R115.

Use of the SOFA can predict Mortality



Vincent Jean-Louis, et al. Crit Care Med.1998;26(11):1793

Research

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

- **Organ dysfunction**
  - Acute change in total SOFA score 2 points consequent to the infection.
    - Baseline SOFA = 0 if no hx of preexisting organ dysfuction
    - ΔSOFA ≥ 2 → mortality 10%
  - Bedside q SOFA ≥ 2
    - Alteration in mental status, systolic BP 100 mmHg, or respiratory rate 22/min
    - Identifies patients likely to have prolonged ICU stay or hospital mortality

Variability in Terminology

- **Particularly evident when septic shock is examined.**
  - Hypotension
    - (SBP [systolic blood pressure] <90 mm Hg *or* MAP [mean arterial pressure] <60 or < 70 mm Hg *or* fall in SAP pressure >40 mm Hg from baseline or >2 standard deviations from the norm for age despite "adequate fluid resuscitation")
  - The presence of abnormal biochemical variable
    - (e. g., lactate >2 or >4 mmol/L or base deficit >5 mmol/L)
  - The use of inotropes or vasopressors
    - (not necessarily above a prespecified dose)
  - New onset organ dysfunction
    - (defined variably with various scoring systems such as APACHE [A cute Physiology and Chronic Health Evaluation] Ⅱ, APACHE Ⅲ, or the cardiovascular component of the SOFA score)
  - Further complicating matters are the following:
    - Variable endpoints of adequacy of fluid resuscitation(rarely defined or reported)
    - Variable durations of hypotension or vasopressor therapy
    - Failure to account for the underlying blood pressure of the patient or other comorbidities
    - Failure to account for the hypotensive effect of cointerventions such as vasodilating and / or cardiodepressant sedative agents.

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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

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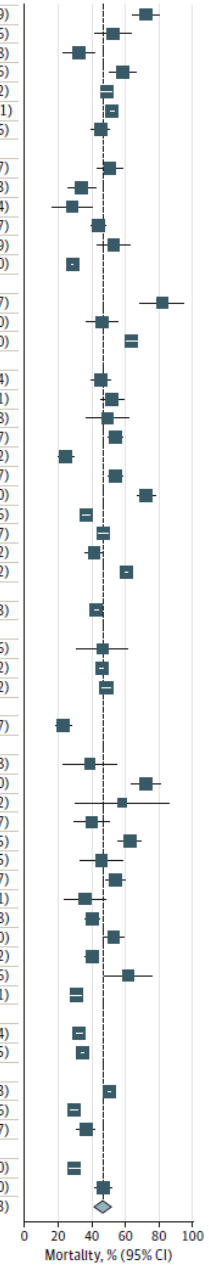
Manu Shankar-Hari, MD, MSc; Gary S. Phillips, MAS; Mitchell L. Levy, MD; Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Clifford S. Deutschman, MD; Derek C. Angus, MD, MPh; Gordon D. Rubenfeld, MD, MSc; Mervyn Singer, MD, FRCP; for the Sepsis Definitions Task Force

Table 1. Summary of Septic Shock Definitions and Criteria Reported in the Studies Identified by the Syster

	Septic Shock Case Definitions and Corresponding Variables Reported in Literature			
	Consensus Definitions		Other Definitions	
Criteria	Bone et al[1]	Levy et al[2]	SSC[111]	Trial
Infection	Suspected or proven	Suspected or proven	Suspected or proven	Susp
SIRS criteria, No.	2	One or more of 24 variables[b]	2	3
Septic shock description	Sepsis-induced hypotension despite adequate resuscitation OR receiving vasopressors/Inotropes plus presence of perfusion abnormalities	State of acute circulatory failure characterized by persistent arterial hypotension after adequate resuscitation unexplained by other causes	Sepsis-induced hypotension persisting despite adequate fluid resuscitation	Card dysf hypo adeq or ne
Hypotension, mm Hg				
Systolic BP	<90	<90	<90	<90
Decrease in systolic BP	Decrease >40	Decrease >40	Decrease >40	NA<
MAP	No	<60	<70	Hypo >1 h
Adequate resuscitation definition	Not defined	Not defined	Goals set as CVP 8-12 mm Hg; urine output ≥0.5 mL/kg/h; $ScvO_2$ >70%	Not
Vasopressor use	Yes (not absolute requirement)	Yes (CVS SOFA score)	Yes (not absolute requirement)	Yes (requ
Hypoperfusion abnormalities	Hypoperfusion abnormality defined as lactic acidosis; oliguria; low Glasgow Coma Score	Tissue hypoperfusion defined as serum lactate >1 mmol/L or delayed capillary refill	Tissue hypoperfusion defined as infection-induced hypotension, elevated serum lactate (>4 mmol/L), or oliguria	No d

Figure 2. Random-Effects Meta-analysis of Studies Identified in the Systematic Review, Reporting Septic Shock Mortality

Source	Septic Shock Deaths, No.	Patients With Septic Shock, No.	Mortality, % (95% CI)
Consensus Definition			
Degoricija et al,[46] 2006	90	125	72.0 (64.1-79.9)
Angkasekwinai et al,[38] 2007	41	78	52.6 (41.5-63.6)
Nesseler et al,[27] 2013	30	93	32.3 (22.8-41.8)
Sakr et al,[25] 2013	85	145	58.6 (50.6-66.6)
Goncalves-Pereira et al,[23] 2014	418	856	48.8 (45.5-52.2)
Leligdowicz et al,[5] 2014	4146	7974	52.0 (50.9 -53.1)
Ortiz et al,[19] 2014	144	319	45.1 (39.7-50.6)
Hypotension			
Laupland et al,[47] 2004	81	159	50.9 (43.2-58.7)
Gaspraovic et al,[45] 2006	44	129	34.1 (25.9-42.3)
Shapiro et al,[44] 2006	15	53	28.3 (16.2-40.4)
Povoa et al,[35] 2009	202	458	44.1 (39.6-48.7)
Klein Klowenberg et al,[7] 2012	52	98	53.1 (43.2-62.9)
Kaukonen et al,[22] 2014	14609	51079	28.6 (28.2-29.0)
Hypotension + Perfusion Abnormalities and/or Vasopressor Therapy			
Rangel-Frausto et al,[56] 1995	51	110	46.4 (37.0-55.7)
Salvo et al,[55] 1995	27	33	81.8 (68.7-95.0)
Alberti et al,[52] 2002	752	1180	63.8 (60.7-67.0)
Hypotension + Vasopressor Therapy			
Rodriguez et al,[31] 2001	129	283	45.6 (39.8-51.4)
Silva et al,[48] 2004	106	203	52.2 (45.3-59.1)
Laupland et al,[49] 2005	28	57	49.1 (36.5-61.8)
Vincent et al,[43] 2006	250	462	54.1 (49.6-58.7)
Karlsson et al,[40] 2007	90	363	24.8 (20.4-29.2)
Sakr et al,[39] 2007	250	462	54.1 (49.6-58.7)
Kauss et al,[34] 2010	185	255	72.5 (67.1-78.0)
Levy et al,[6] 2010	915	2494	36.7 (34.8-38.6)
Phua et al,[32] 2011	441	939	47.0 (44.3-49.7)
Ogura et al,[20] 2014	117	282	41.5 (35.7-47.2)
GIVITI database, 2015[a]	15935	26295	60.6 (60.0-61.2)
Hypotension + Vasopressor Therapy + Serum Lactate Level >2 mmol/L			
Group 1[b]	3602	8520	42.3 (41.2-43.3)
Hypotension + Perfusion Abnormalities + Vasopressor Therapy			
Lundberg et al,[54] 1998	19	41	46.3 (31.1-61.6)
Levy et al,[6] 2010	3428	7436	46.1 (45.0-47.2)
Quenot et al,[26] 2013	728	1495	48.7 (46.2-51.2)
Hypotension ± Vasopressor Therapy or Metabolic Abnormalities			
Peake et al,[36] 2009	75	324	23.1 (18.6-27.7)
Hypotension or Vasopressor Therapy			
Dahmash et al,[59] 1993	14	36	38.9 (23.0-54.8)
McLauchlan et al,[58] 1995	73	101	72.3 (63.5-81.0)
Pittet et al,[57] 1995	7	12	58.3 (30.4-86.2)
Schoenberg et al,[53] 1998	32	80	40.0 (29.3-50.7)
Engel et al,[42] 2007	119	190	62.6 (55.8-69.5)
Esteban et al,[41] 2007	27	59	45.8 (33.1-58.5)
Khwannimit and Bhuayanontachai,[37] 2009	164	303	54.1 (48.5-59.7)
Moore et al,[33] 2011	22	61	36.1 (24.0-48.1)
Zahar et al,[30] 2011 (community)	215	530	40.6 (36.3-44.8)
Zahar et al,[30] 2011 (ICU)	123	232	53.0 (47.1-59.0)
Zahar et al,[30] 2011 (nosocomial)	233	580	40.2 (36.1-44.2)
Klein Klowenberg et al,[7] 2012	29	47	61.7 (47.8-75.6)
Park et al,[28] 2012	228	740	30.8 (27.5-34.1)
Hypotension or Serum Lactate Any Value or Vasopressor Therapy			
Liu et al,[21] 2014	827	2536	32.6 (30.8-34.4)
SSC database,[16] 2016[b]	6556	18840	34.8 (34.1-35.5)
***International Classification of Diseases* Codes**			
Annane et al,[51] 2003	13269	26172	50.7 (50.1-51.3)
Flaatten,[50] 2004	457	1562	29.3 (27.1-31.6)
Whittaker et al,[24] 2013	117	321	36.4 (31.2-41.7)
Serum Lactate Level >4 mmol/L			
Levy et al,[6] 2010	242	811	29.8 (26.7-33.0)
Phua et al,[32] 2011	219	466	47.0 (42.0-52.0)
Overall (I^2 = 99.5%; P = .000)			46.5 (42.7-50.3)



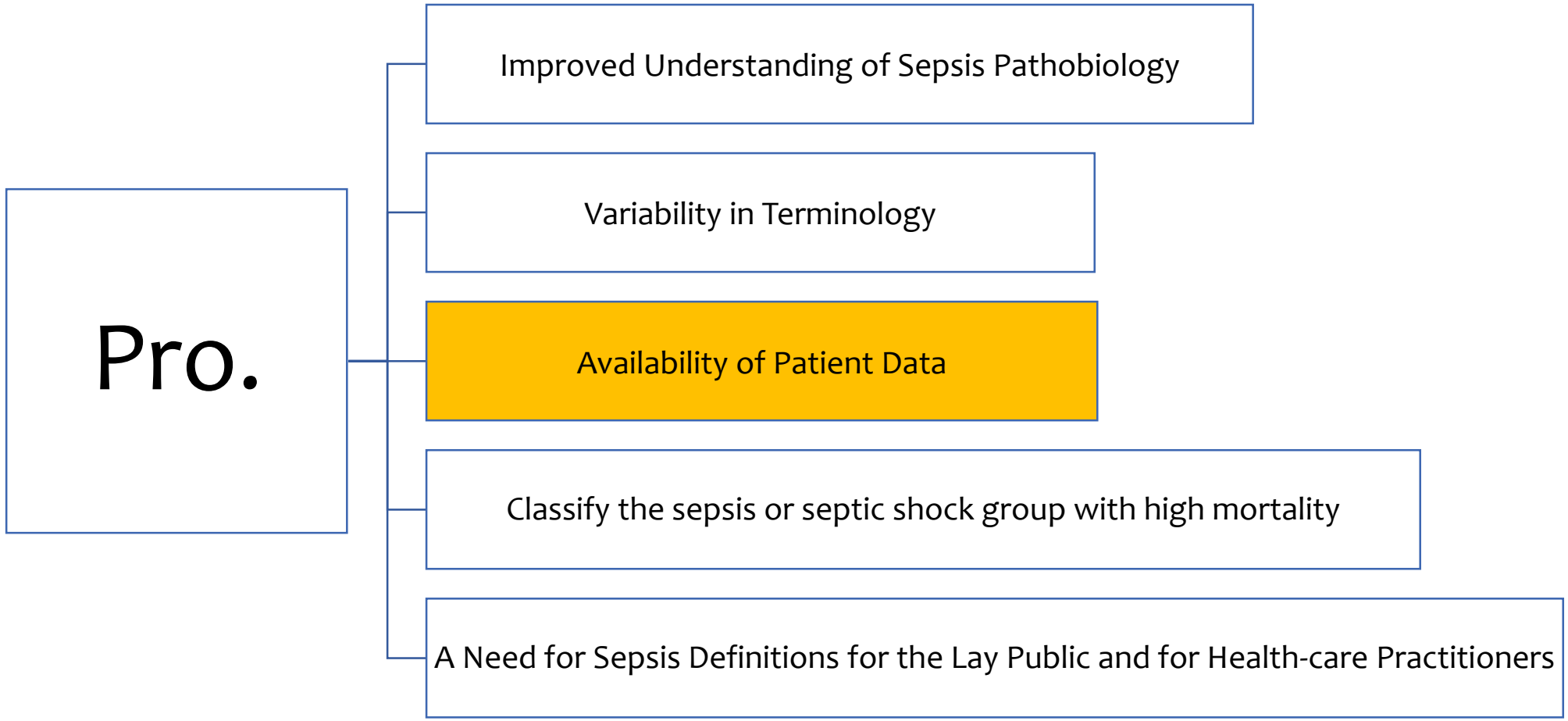
New definition of septic shock

"**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"

- Patients with sepsis with following features despite adequate volume resuscitation
  - Persisting hypotension requiring vasopressors to maintain MAP 65mmHg
  - Serum lactate level >2mmol/L(18mg/dL)

- Hospital mortality is in excess 40%.

Why to change ?



Availability of Patient Data

… Validation and Evidence-based

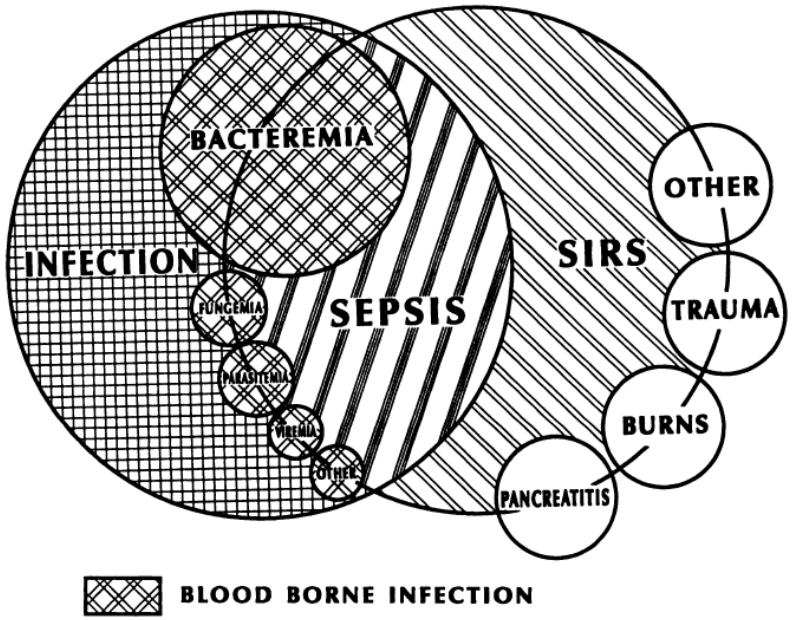
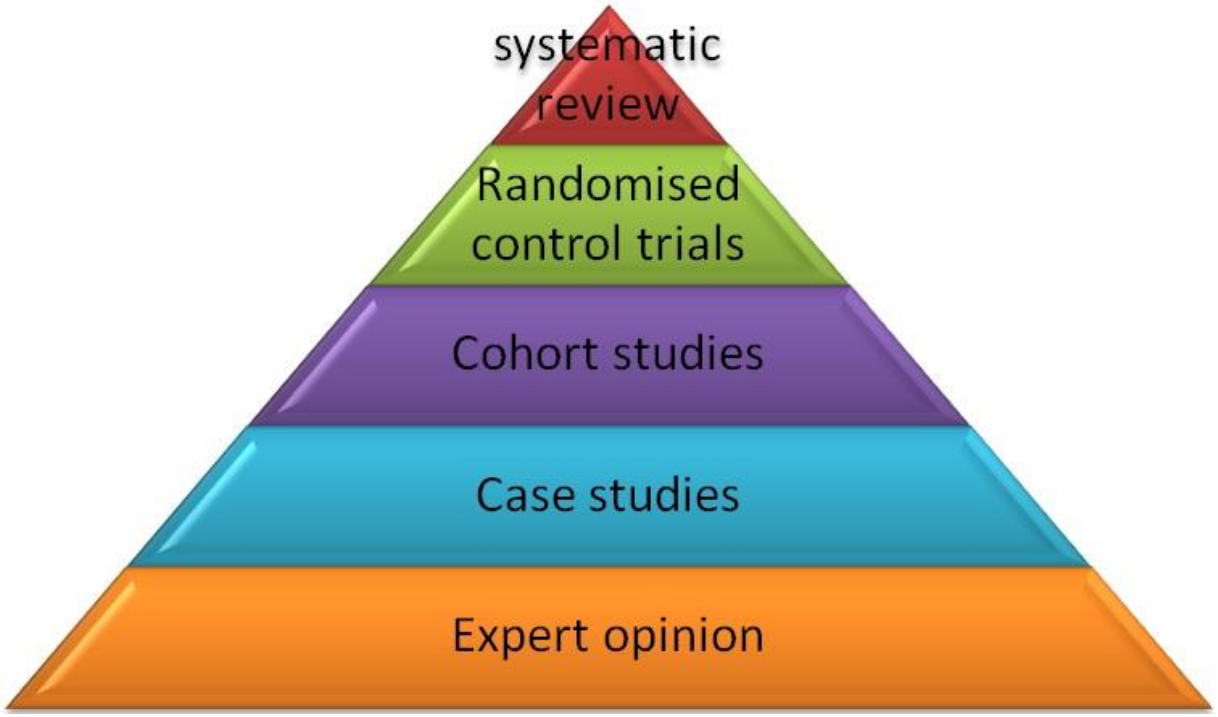


FIGURE 1. The interrelationship between systemic inflammatory response syndrome (SIRS), sepsis, and infection.



Based reflects findings from small studies or <u>expert opinions</u>

Research

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- Focus on timeless, ease of use.
- Studied 21 variables from Sepsis-2
- Multi-variable logistic regression for in-hospital mortality
- Primary cohort; UPMC healthcare system in southwestern Pennsylvania
  - Random split sample (50/50); derivation and validation cohort
- 4 external data sets;

Figure 1. Accrual of Encounters for Primary Cohort

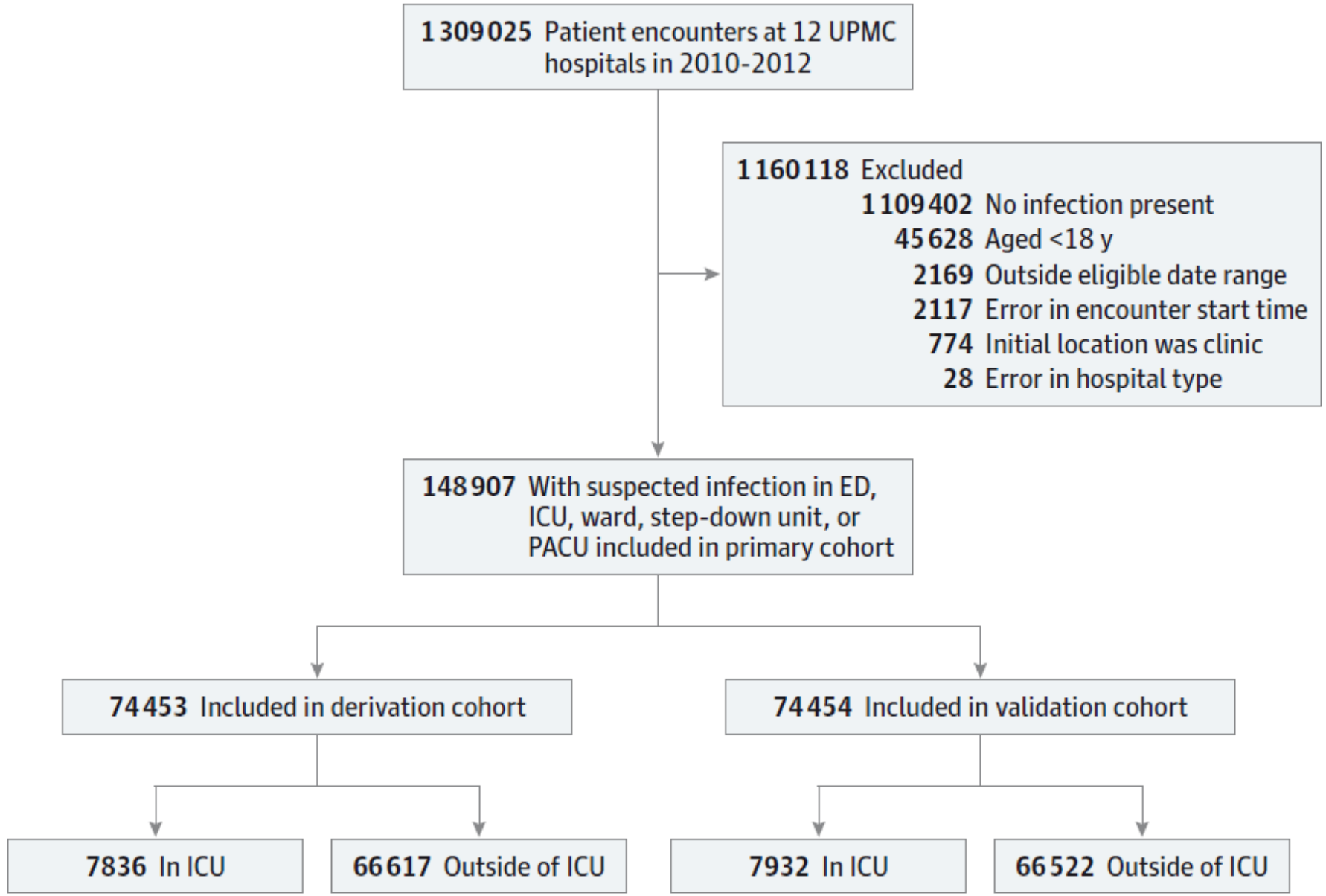


Table 2. Summary of Data Sets

Characteristics	UPMC[a]	KPNC	VA	ALERTS	KCEMS
Years of cohort	2010-2012	2009-2013	2008-2010	2011-2012	2009-2010
No. of hospitals	12	20	130	1	14
Total No. of encounters	1 309 025	1 847 165	1 640 543	38 098	50 727
Data source and study design	Retrospective study of EHRs	Retrospective study of EHRs	Retrospective study of EHRs	Prospective cohort study	Retrospective study of administrative records
Setting	Integrated health system in southwestern Pennsylvania	Integrated health system in northern California	All hospitals in the US VA system	Single university hospital, Jena, Germany	Out-of-hospital records from integrated emergency medical services system in King County, Washington
Definition of suspected infection	Combination of body fluid culture and nonprophylactic antibiotic administration in the EHR[b]	Combination of body fluid culture and nonprophylactic antibiotic administration in the EHR[b]	Combination of body fluid culture and nonprophylactic antibiotic administration in the EHR[b]	CDC criteria for hospital-acquired infections[c]	*ICD-9-CM* codes for infection, with present-on-admission indicators[d]
No. with suspected infection (% of total)	148 907 (11)	321 380 (17)	377 325 (23)	1186 (3)	6508 (13)
Location at onset of infection, No. (%) infected					
Intensive care unit	15 768 (11)	7031 (2)	73 264 (19)	300 (25)	0
Outside of intensive care unit	133 139 (89)	314 349 (98)	304 061 (81)	886 (75)	6508 (100)
In-hospital mortality, No. (%) infected[e]	6347 (4)	16 092 (5)	22 593 (6)	210 (18)	700 (11)

KCEMS, King County Emergency Medical Services; KPNC, Kaiser Permanente Northern California; EHR, electronic health record; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; VA, Veterans Administration

Bedside Surrogate For Organ Dysfunction By Quick SOFA (qSOFA)

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"**.

Bedside clinical score, qSOFA

At least 2 of following	▪ Respiratory rate ≥22/min ▪ Altered mentation ▪ Systolic blood pressure ≤100 mmHg

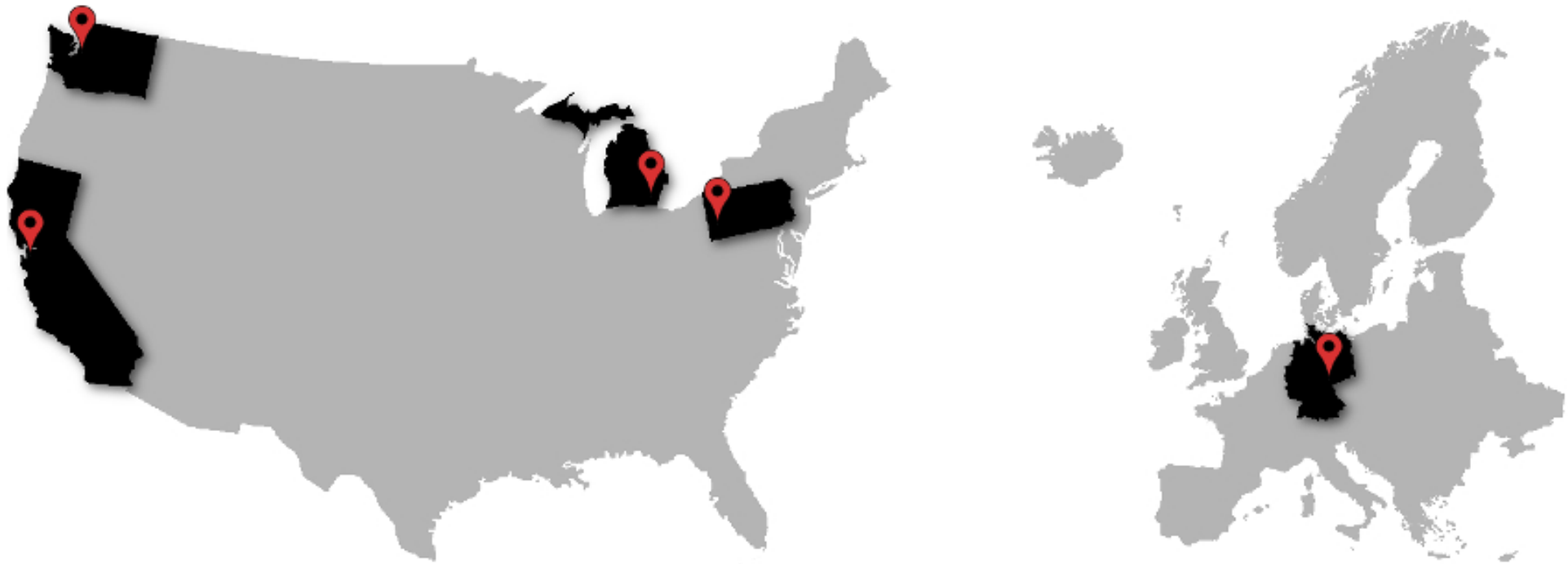
JAMA. 2016; 315(8):801-810. doi:10.1001/jama.2016.0287

Table 1. Variables for Candidate Sepsis Criteria Among Encounters With Suspected Infection

Systemic Inflammatory Response Syndrome (SIRS) Criteria (Range, 0-4 Criteria)	Sequential [Sepsis-related] Organ Failure Assessment (SOFA) (Range, 0-24 Points)	Logistic Organ Dysfunction System (LODS) (Range, 0-22 Points)[a]	Quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) (Range, 0-3 Points)
Respiratory rate, breaths per minute	Pao_2/Fio_2 ratio	Pao_2/Fio_2 ratio	Respiratory rate, breaths per minute
White blood cell count, 10^9/L	Glasgow Coma Scale score	Glasgow Coma Scale score	Glasgow Coma Scale score
Bands, %	Mean arterial pressure, mm Hg	Systolic blood pressure, mm Hg	Systolic blood pressure, mm Hg
Heart rate, beats per minute	Administration of vasopressors with type/dose/rate of infusion	Heart rate, beats per minute	
Temperature, °C	Serum creatinine, mg/dL, or urine output, mL/d	Serum creatinine, mg/dL	
Arterial carbon dioxide tension, mm Hg	Bilirubin, mg/dL	Bilirubin, mg/dL	
	Platelet count, 10^9/L	Platelet count, 10^9/L	
		White blood cell count, 10^9/L	
		Urine output, L/d	
		Serum urea, mmol/L	
		Prothrombin time, % of standard	

Multivariable logistic regression

Data Sources



qSOFA was studied among more than 800,000 electronic health record encounters at 177 hospitals worldwide, including community and academic, rural, suburban, and urban, public, private, and federal hospitals.

http://qsofa.org/data.php

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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Methods

Research

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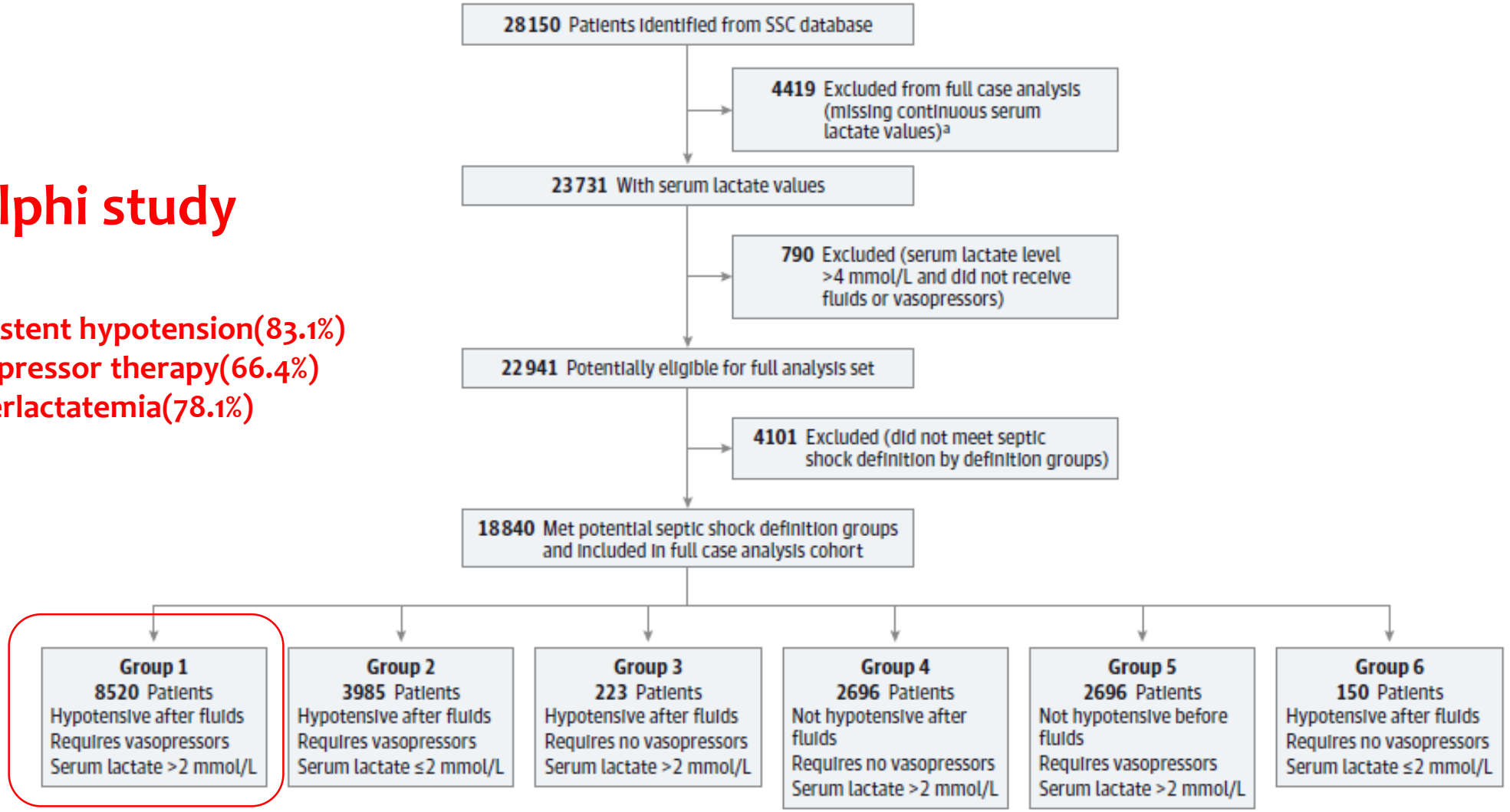
- Task Force – SCCM, ESICM
  - 2 cochairs, 17 participants
- Systematic Review and Meta-analysis – 44 studies(166,479pts)
  - 1992-2015 (≥19years)
- Delphi study – meetings, questionnaires, email discussions
  - 3 surveys and discussions of results from the systematic review, surveys, and cohort studies.
  - Hypotension, serum lactate level, vasopressor therapy as variables
- Cohort study –
  - SSC registry; 218 hospitals in 18 countries
  - External validation;
    UPMC(12 hospitals, 2010-2012, n=1,309,025),
    KPNC(20 hospitals. 2009-2013, n=1,847,165)
  - 6 patients group

Table 2. Random Effects Meta-Analysis by Septic Shock Criteria Groups

Septic Shock Case Definition Criteria[a]	No.[b]	Mortality, No. of Events/ No. of Patients (%) [95% CI][c]	Heterogeneity Statistic[d]	df	*P* Value	I^2, %[e]	τ^{2f}

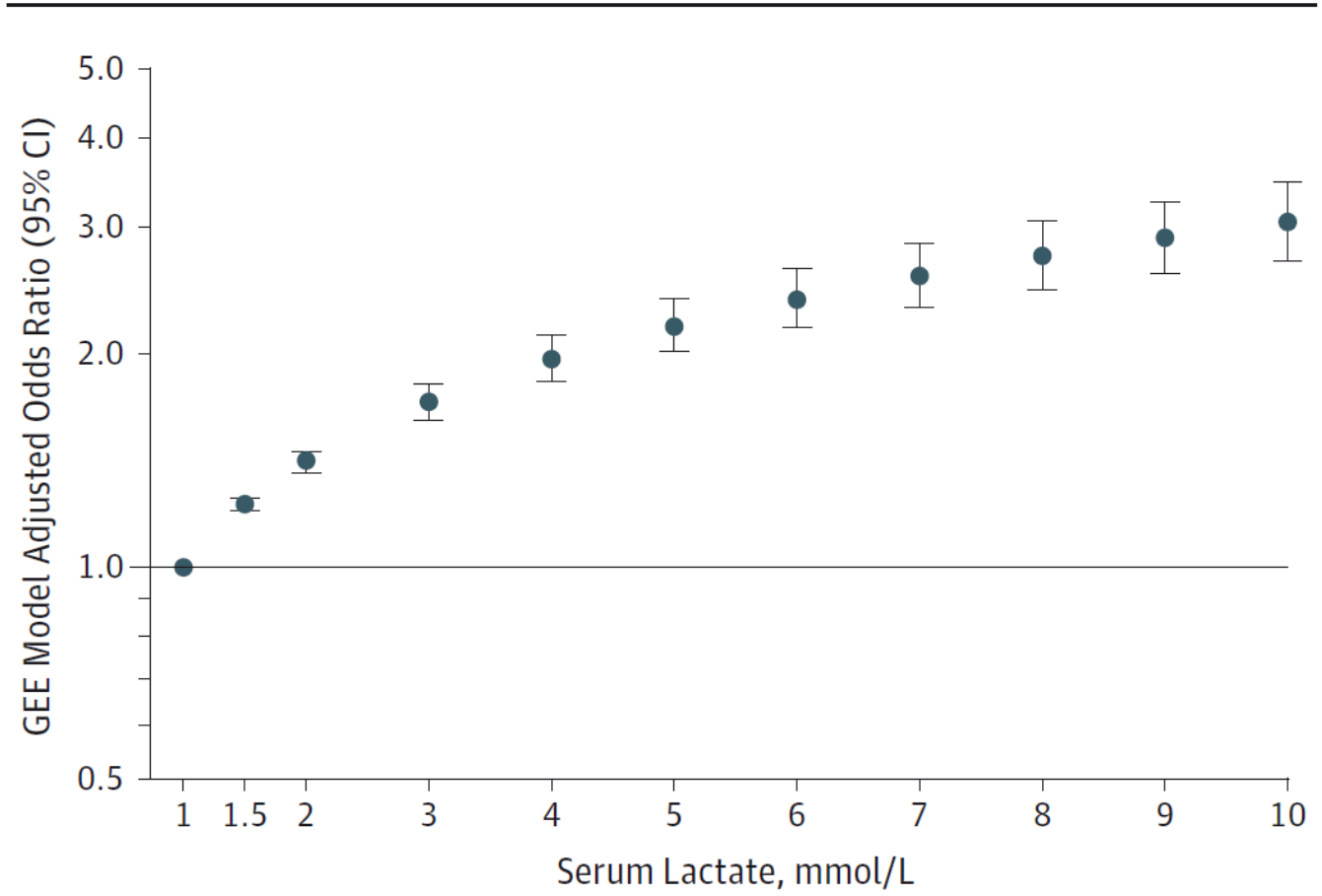
Figure 3. Selection of Surviving Sepsis Campaign Database Cohort



Delphi study

Persistent hypotension(83.1%)
Vasopressor therapy(66.4%)
Hyperlactatemia(78.1%)

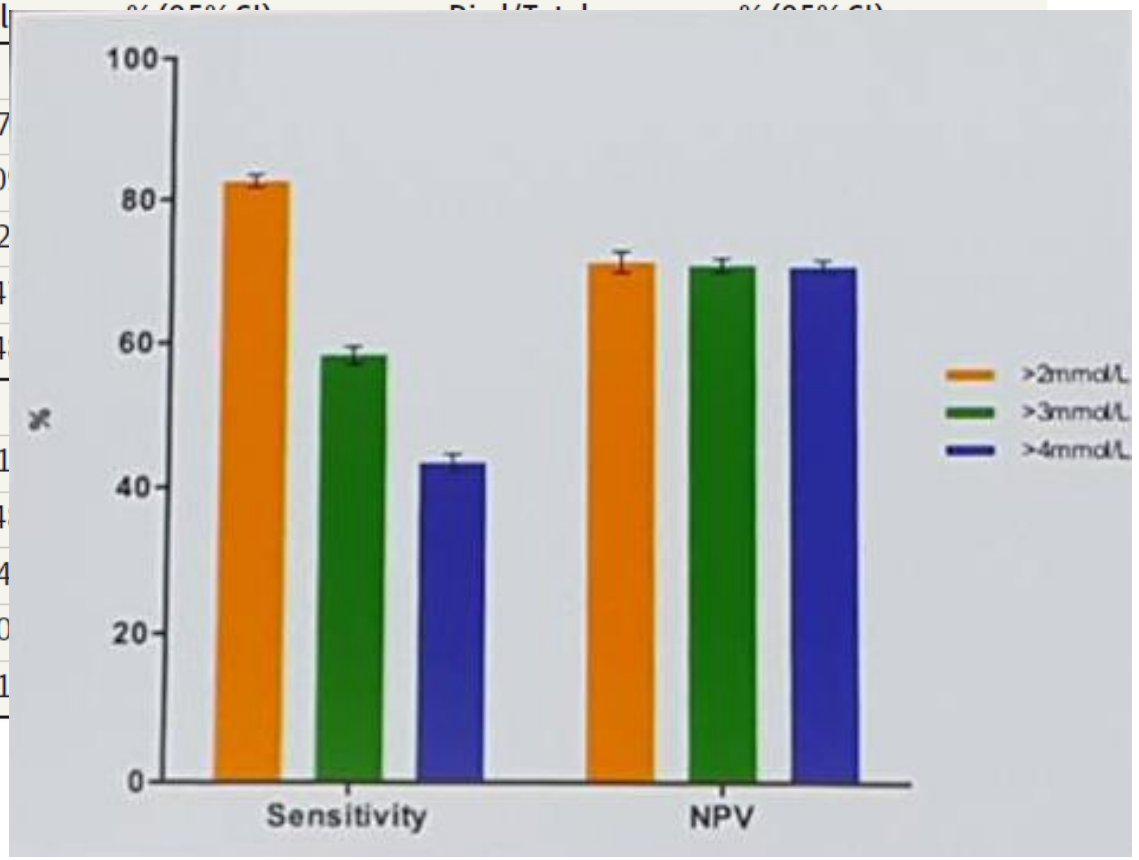
Serum Lactate Level Analysis



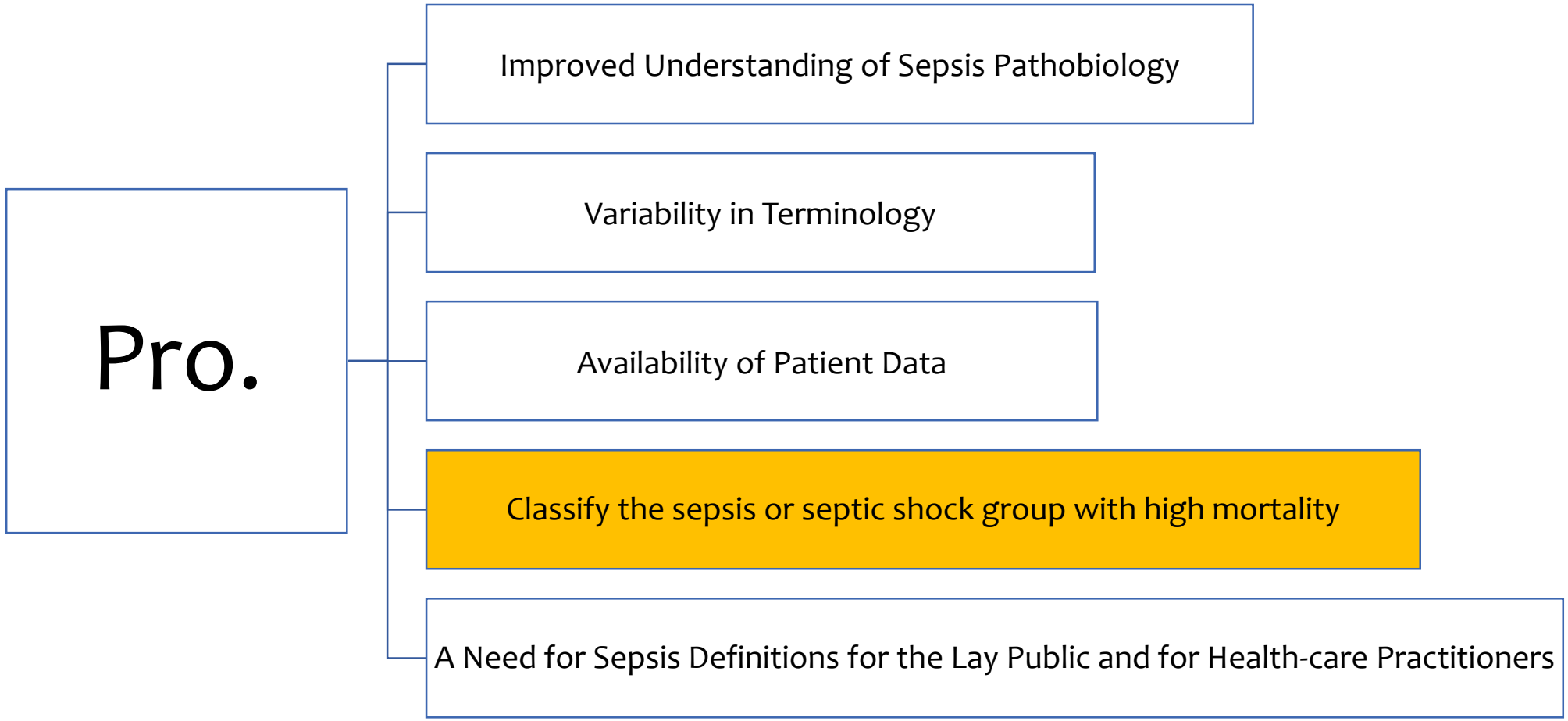
Serum lactate level from 2 to 10 mmol/L increased the adjusted OR for hospital mortality from 1.4 (95%CI, 1.35-1.45) to 3.03 (95%CI, 2.68-3.45)

Characteristics of Serum Lactate Level Cut-off Values (SSC database)

Characteristic	Serum Lactate Level, mmol/L			
	>2		>3	>4
	Died/Total	% (95% CI)	Died/Total	
Complete Case Analysis (n = 18 795)				
Hospital mortality, %	5757/18 795	30.6 (29.9-31.4)	6101/18 7	
Sensitivity, %	5372/6509	82.5 (81.6-83.4)	3779/650	
Specificity, %	2748/12 286	22.4 (21.6-23.1)	6418/12 2	
PPV, %	5372/14 910	36.0 (35.3-36.8)	3779/964	
NPV, %	2748/3885	70.7 (69.3-72.2)	6418/914	
Imputed Missing Serum Lactate Level (n = 22 182)				
Hospital mortality, %	6965/22 182	31.4 (30.8-32.0)	7363/22 1	
Sensitivity, %	6457/7748	83.3 (82.5-84.2)	4461/774	
Specificity, %	3341/14 434	23.1 (22.5-23.8)	7833/14 4	
PPV, %	6457/17 550	36.8 (36.1-37.5)	4461/11 0	
NPV, %	3341/4634	72.1 (70.8-73.4)	7833/11 1	

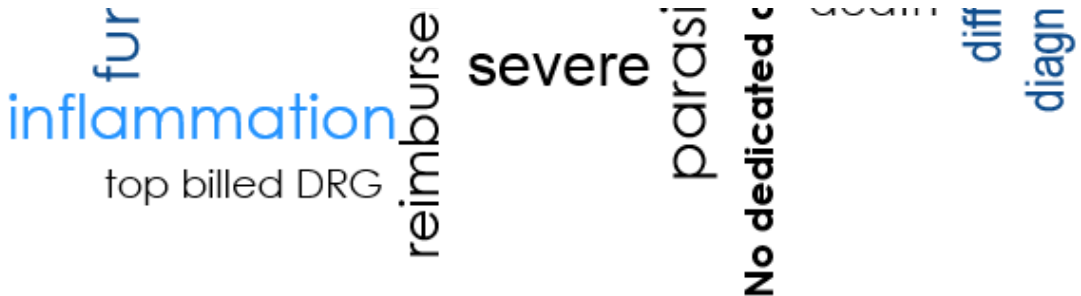


Why to change ?



Sepsis하면 뭐가 떠오르시나요?

- 안좋은 예후(Poor prognosis)
- 조기 진단 및 치료(Early detection and management)
- 중환자실로 조기전동(Early transfer to critical care unit)
- 전과협진(Refer to …)



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

Table 4 ICU outcome according to the maximum number of SIRS criteria at admission

	Frequency	SAPS II score[a]	Length of stay[a]	ICU mortality[b]
No SIRS	119 (3.8%)	24.4 ± 11.0	1.6 (0.8–3.3)	5 (4.2%)
One SIRS	303 (9.6%)	28.5 ± 14.6	2.1 (1.0–4.4)	26 (8.6%)
Two SIRS	812 (25.8%)	31.7 ± 15.1	2.7 (1.6–5.5)	89 (11.0%)
Three SIRS	1153 (36.6%)	38.7 ± 16.5	3.7 (1.9–8.9)	251 (21.8%)
Four SIRS	760 (24.1%)	43.3 ± 18.1	3.9 (1.9–8.9)	212 (27.9)

[a] $p < 0.001$,
[b] $p < 0.001$

High sensitivity, but low specificity

Intensive Care Med. 2006; 32:421–427

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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

Intensive Care Med. 2006; 32:421–427

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.

- 109,6634 patients with infection and organ dysfunction.
- 172 ICUs – Austrailia and New Zealand(ANZICS) 2000 to 2013.

ORIGINAL ARTICLE

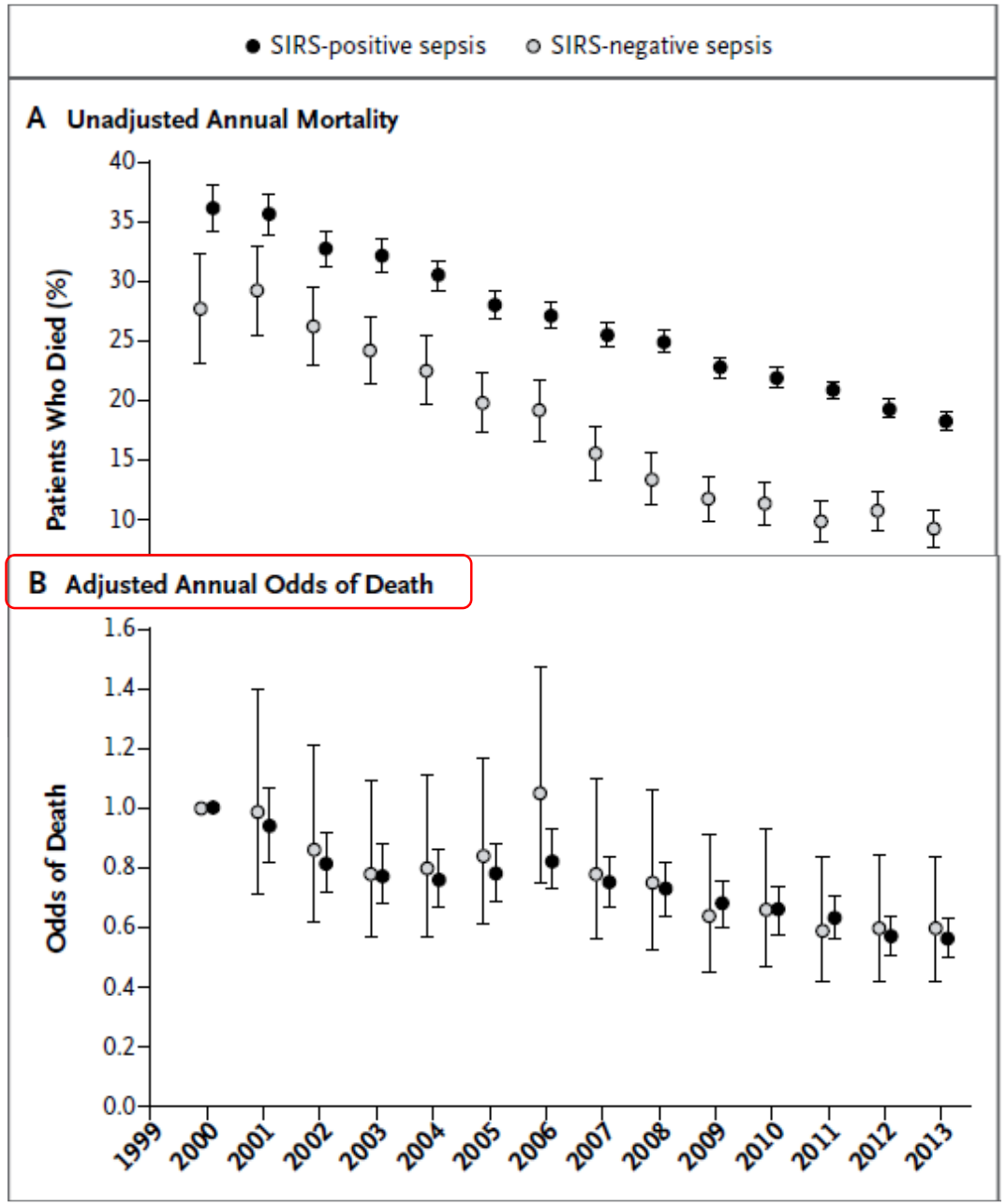
Table 2. Distribution of Signs Meeting SIRS Criteria in Patients with Severe Sepsis, According to SIRS-Positive and SIRS-Negative Status.*

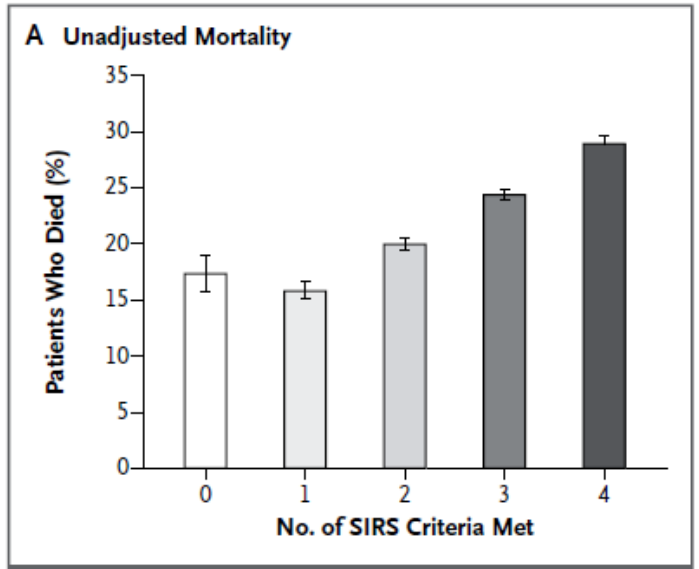
Variable	All Patients (N=109,663)	Patients with SIRS-Positive Severe Sepsis (N=96,385)	Patients with SIRS-Negative Severe Sepsis (N=13,278)
SIRS criterion met — no. (%)†			
Abnormal temperature	64,365 (58.7)	62,430 (64.8)	1,935 (14.6)
High	33,059 (30.1)	32,605 (33.8)	454 (3.4)
Low	36,130 (32.9)	34,599 (35.9)	1,531 (11.5)
Increased heart			2,746 (20.7)
Increased respi decrease			2,515 (18.9)
Abnormal white			3,458 (26.0)
High			3,118 (23.5)
Low			351 (2.6)
No. of SIRS criteria			
Median			1
Interquartile rar			1–1
Distribution			
>1	96,385 (87.9)	96,385 (100)	0
0	2,624 (2.4)	0	2,624 (19.8)
1	10,654 (9.7)	0	10,654 (80.2)
2	26,820 (24.5)	26,820 (27.8)	0
3	41,315 (37.7)	41,315 (42.9)	0
4	28,250 (25.7)	28,250 (29.3)	0

SIRS + (≥2 SIRS) | **SIRS - (<2 SIRS)**

88% | **12%**

Will miss 1 in 8 !!!





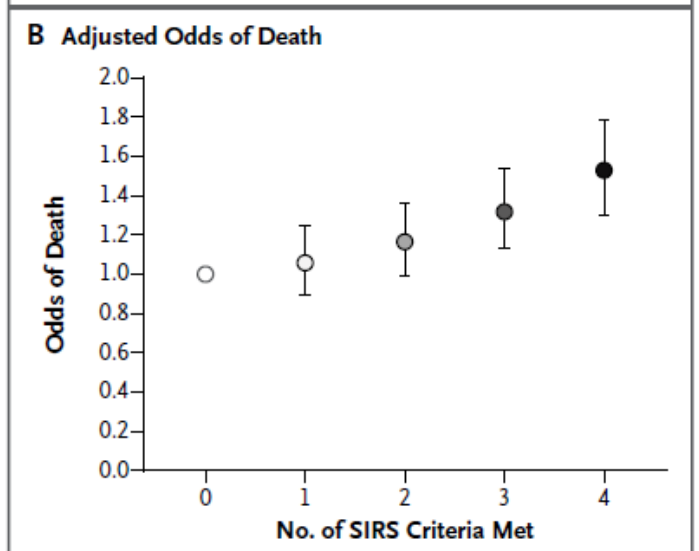


Figure 2. Mortality among Patients with Severe Sepsis, According to Number of SIRS Criteria Met.

The bars represent 95% confidence intervals.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

- 109,6634 patients with infection and organ dysfunction.
- 172 ICUs – Austrailia and New Zealand(ANZICS) 2000 to 2013.

- Mortality increases with increasing SIRS, but requiring ≥2 SIRS has no meaningful mortality risk transition.
- Improved approaches to define sepsis severity are needed.

Classify the sepsis or septic shock group with high mortality

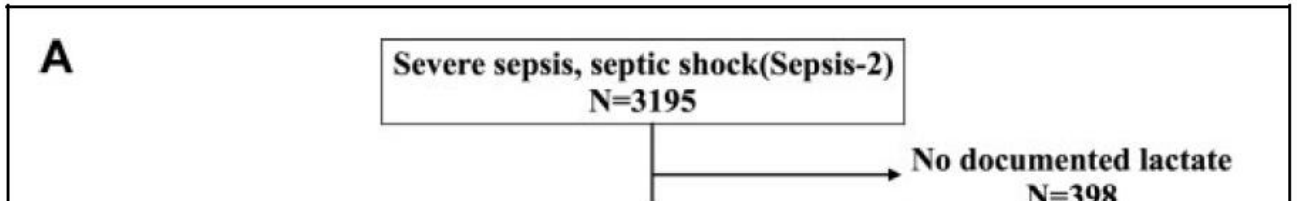
Original Research

A Nationwide Comparison Between Sepsis-2 and Sepsis-3 Definition in Japan

Shuhei Takauji, MD[1], Mineji Hayakawa, MD, PhD[2], and and Satoshi Fujita, MD, PhD[1]

- A multicenter registry conducted at 42 ICUs throughout Japan
- Patients received treatment for severe sepsis or septic shock between January 2011 and December 2013

Takauji et al. J Intensive Care Med. 2019



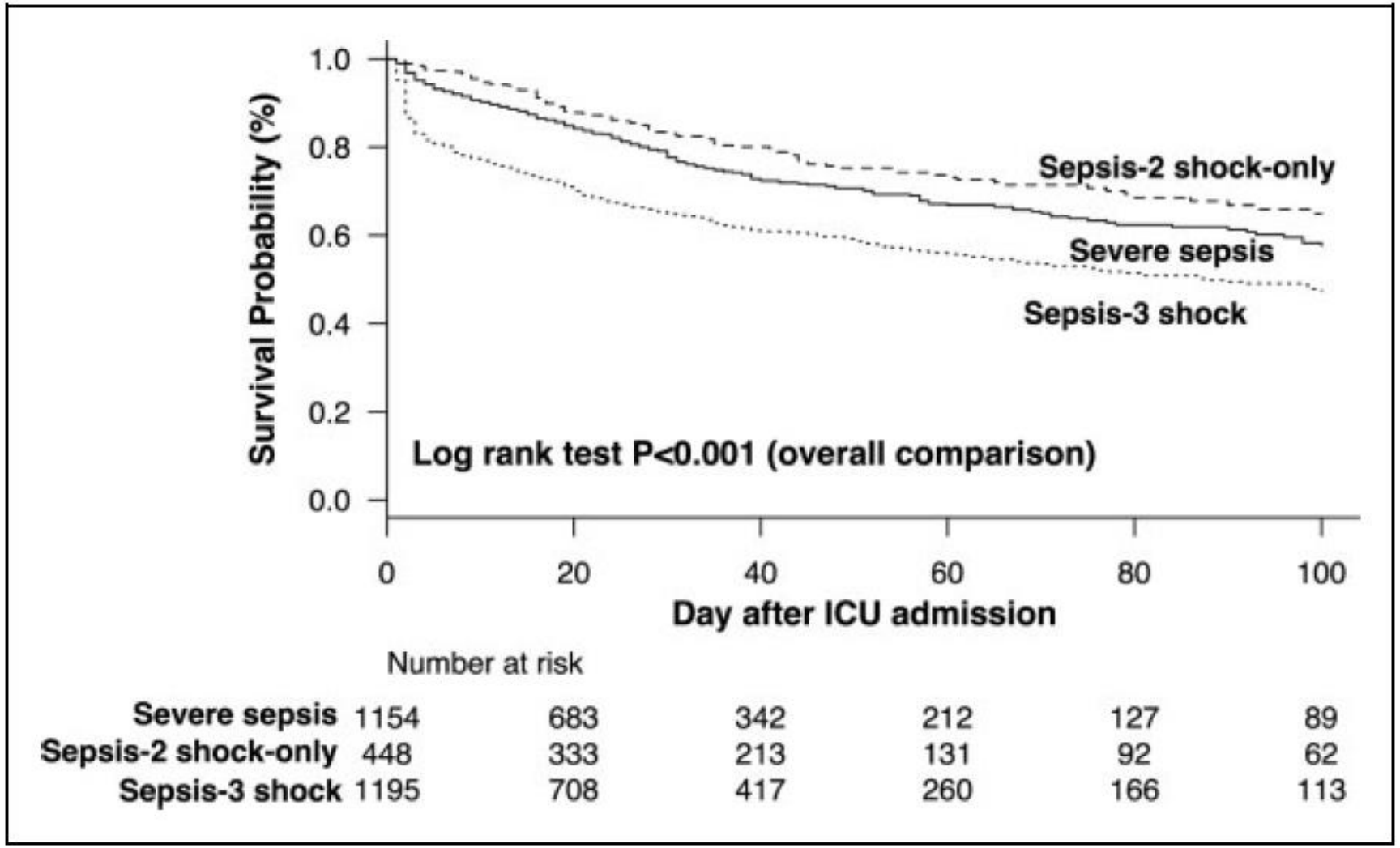


Table 2. C

Outcomes							Value	P^c Value
ICU mortali							300	<.001
In-hospital m							000	<.001
ICU-free da							000	<.001
Vasopressor							001	<.001
Ventilator-fr							310	<.001
Renal replac							001	<.001
The number							001	<.001
Maximum S							001	<.001

Abbreviations
[a]Bonferroni c
[b]Comparison between "severe sepsis" group and "Sepsis-2 shock-only" group.
[c]Comparison between "Sepsis-2 shock-only" group and "Sepsis-3 shock" group.

Takauji et al. J Intensive Care Med. 2019

Zhang *et al. BMC Infectious Diseases* (2019) 19:139
https://doi.org/10.1186/s12879-019-3790-0

BMC Infectious Diseases

Classify the sepsis or septic shock group with high mortality

RESEARCH

Systemic
in Sepsis

Wei Zhang[1,2*], Ya

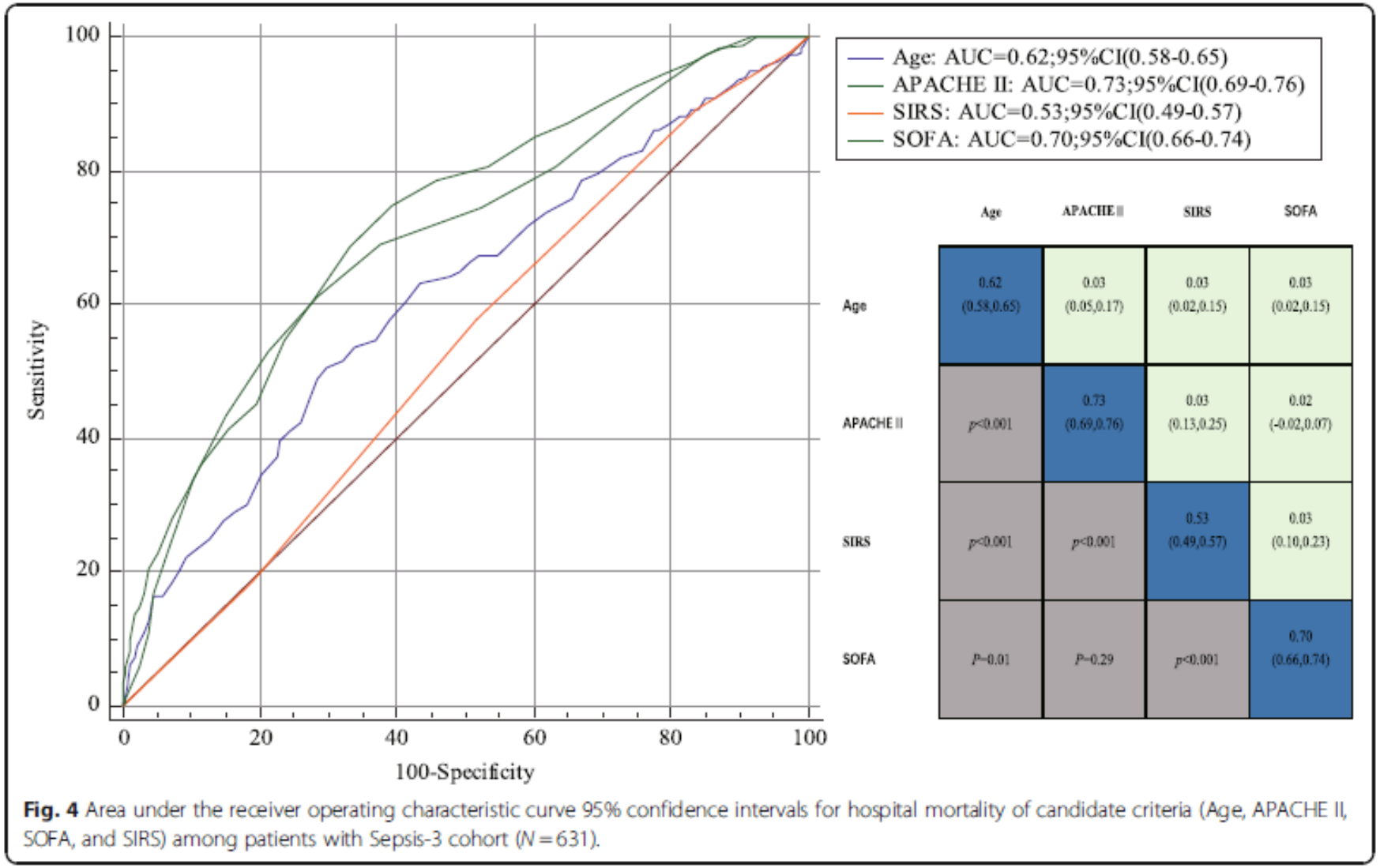
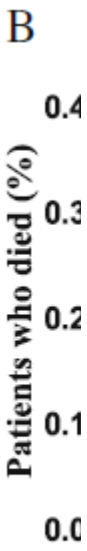
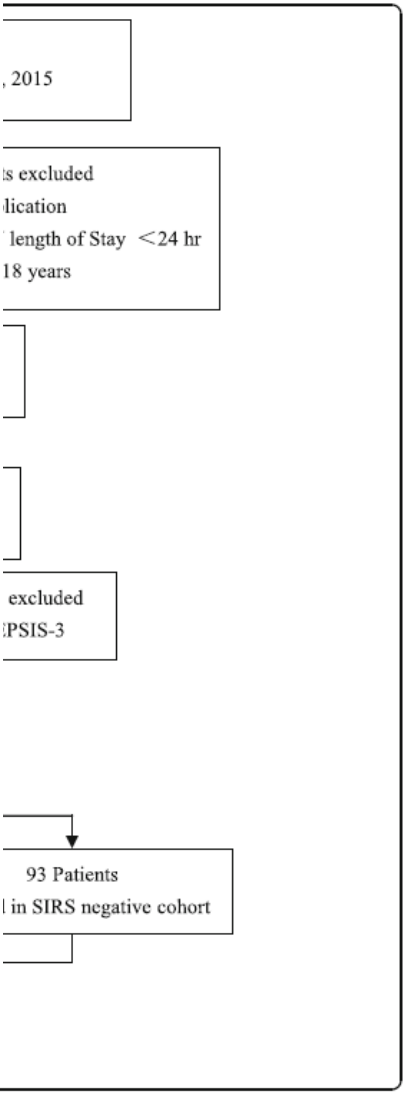
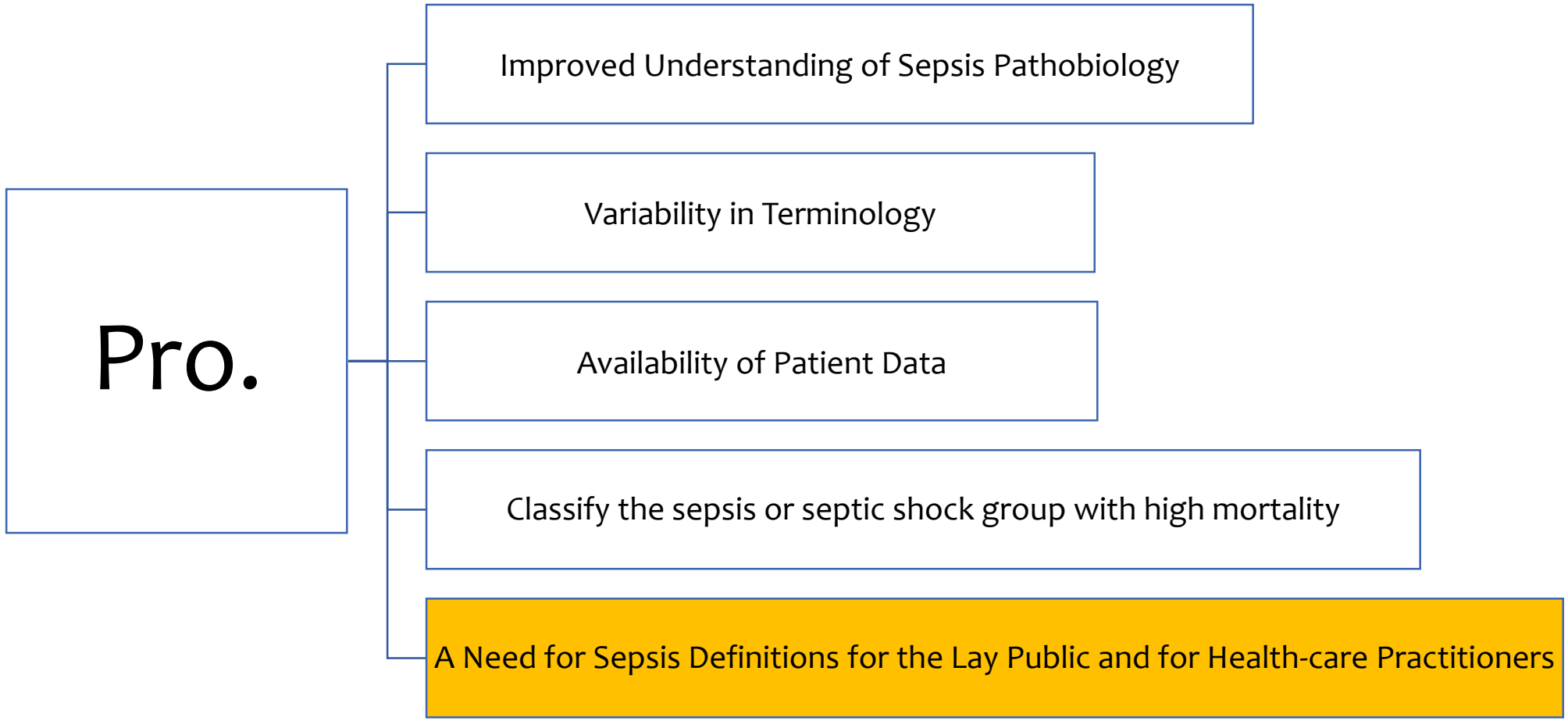


Fig. 4 Area under the receiver operating characteristic curve 95% confidence intervals for hospital mortality of candidate criteria (Age, APACHE II, SOFA, and SIRS) among patients with Sepsis-3 cohort ($N = 631$).





Why to change ?



An Infection, Unnoticed, Turns Unstoppable

About New York

By JIM DWYER JULY 11, 2012

Rory Staunton taking his first flying lesson in 2011.

RELATED COVERAGE

Medical Documents in Sepsis Death JULY 11, 2012

TIMES TOPIC
Jim Dwyer

The New York Times

STOP Sepsis Collaborative

A GNYHA / UHF Partnership in Quality

SEVERE SEPSIS TRIAGE SCREENING TOOL

Does the patient have any three of the following?

- ☐ Suspected Infection
- ☐ Temp > 100.4 or < 96.5 or rigors
- ☐ HR > 90
- ☐ RR > 20
- ☐ Any alteration of mental status
- ☐ O2 Sat < 90%
- ☐ SBP < 90
- ☐ Suspected/Known Immunocompromise (AIDS/Active Cancer/Organ T… Patient)

☐Yes ☐No

If Yes clicked:
Go to Nursing Sepsis Panel Orders.

Triage Sepsis Panel Orders
(all boxes should be checked by default)

- ☐ Notify clinician to initiate verbal order for sepsis panel
- ☐ CBC
- ☐ Metabolic Panel
- ☐ Lactate (venous or arterial)
- ☐ Draw and Hold PT/PTT
- ☐ Draw and Hold Blood Cultures
- ☐ Record Vital Signs Q1 hour plus temperature

Is the patient's SBP < 90 or MAP < 65

☐Yes ☐No

If Yes clicked:
Present case to physician.

If patient meets criteria, but you feel the patient doesn't need lab testing, please speak to attending.

NYU Medical Center

NYU …
Patie…
NYU…

This report contai…

Vital Signs & Measu…
03/29/2012 21:26

BLOOD PR…
Blood Press…
Blood Press…
Blood Press…
TEMPERA…
Temperatur…
Temperatur…
PULSE
Pulse Pulse…
RESPIRAT…
Respirations…
PULSE OXI…
Pulse Oxim…
29-Mar-201…
Norma (Nu…

NYU Medical Center

NYU Hospitals Center
Test Result Summary
NYUMC

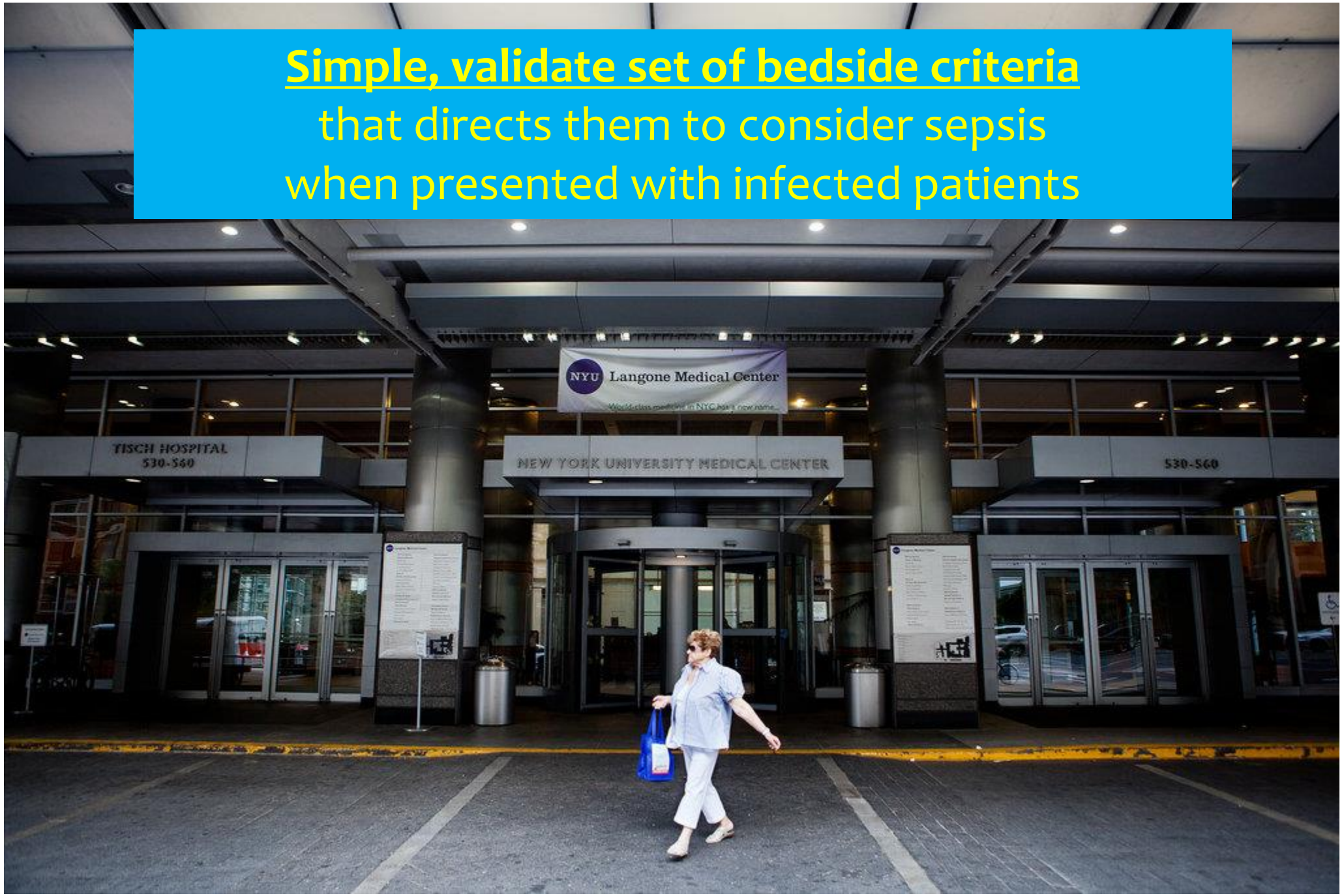
Patient:	STAUNTON, RORY	MR #:	8979937
DOB:	05/13/1999 Age: 12y	Gender:	M
Attending:	[redacted]		
Admit Date:	03/29/2012	Visit #:	489040745
Location:	EMERG-TH		

This report contains documentation entered between 03/29/2012 and 03/29/2012

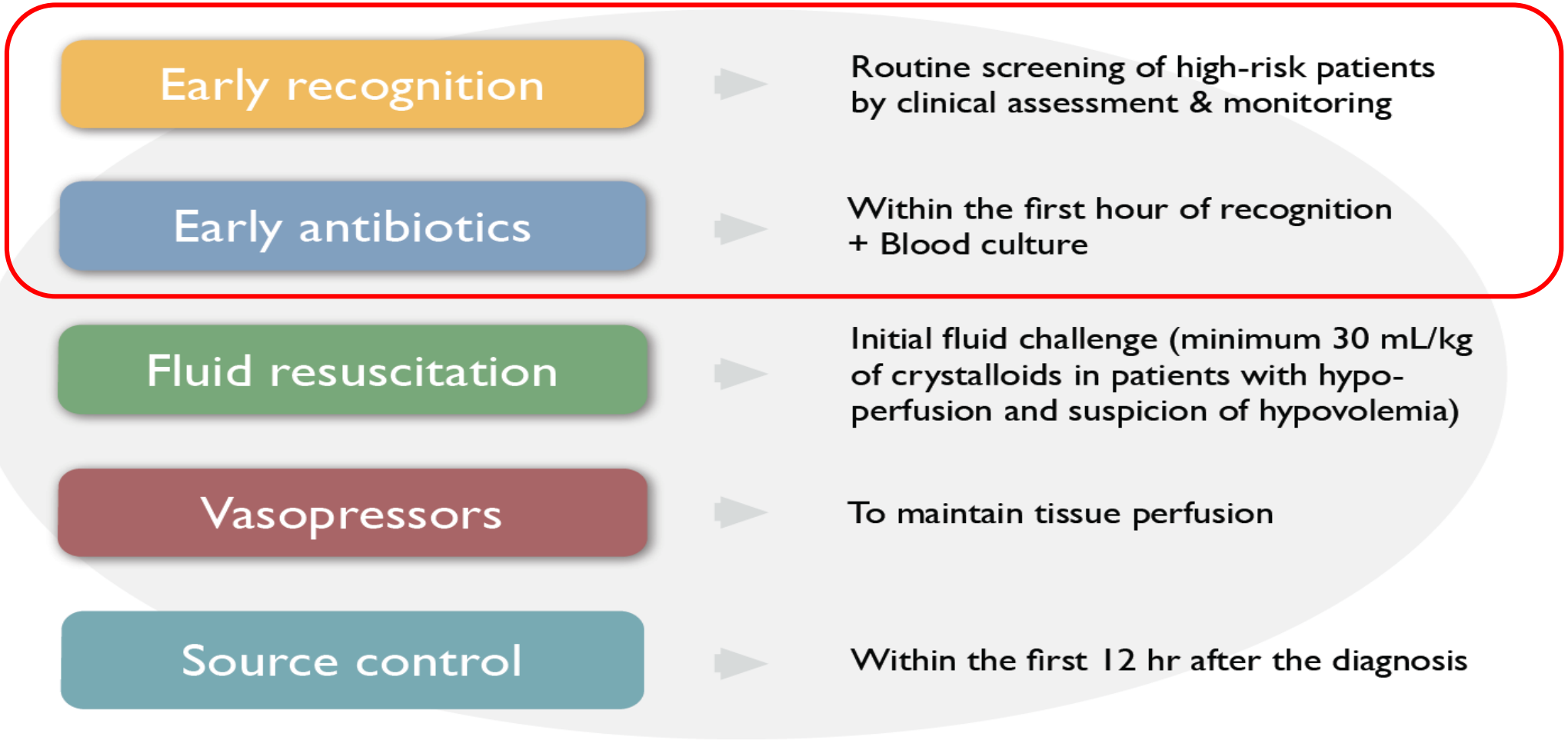
03/29/2012 20:00 CBC				
White Blood Cells	14.7	H	[3.7-11.4 K/uL]	Final
Nucleated RBCs	0		[0 /100WBC]	Final
Red Blood Cells	4.94		[4.20-5.60 M/uL]	Final
Hemoglobin	14.3		[12.5-16.1 g/dL]	Final
Hematocrit	42.4		[36.0-47.0 %]	Final
MCV	85.7		[78-95 FL]	Final
MCH	28.9		[26-32 pg]	Final
MCHC	33.7		[32-36 g/dL]	Final
RDW	13.1		[11.5-14.5 %]	Final
Platelet Count	117	L	[150-400 K/uL]	Final
MPV	9.03		[6.0-11.0 FL]	Final

03/29/2012 20:00 Differential Count				
Segs	39		[33-63 %]	Final
Bands	53	H	[5-15 %]	Final
Lymphocytes	3	L	[28-48 %]	Final
Monocytes	5		[3-12 %]	Final
Absolute Neutrophils	13.5	H	[1.5-8.2 K/uL]	Final
Absolute Segs	5.7		[1.3-6.6 K/uL]	Final
Absolute Bands	7.8	H	[0.2-1.7 K/uL]	Final
Absolute Lymphs	0.4	L	[0.8-4.2 K/uL]	Final
Absolute Monocytes	0.7		[0.1-1.1 K/uL]	Final

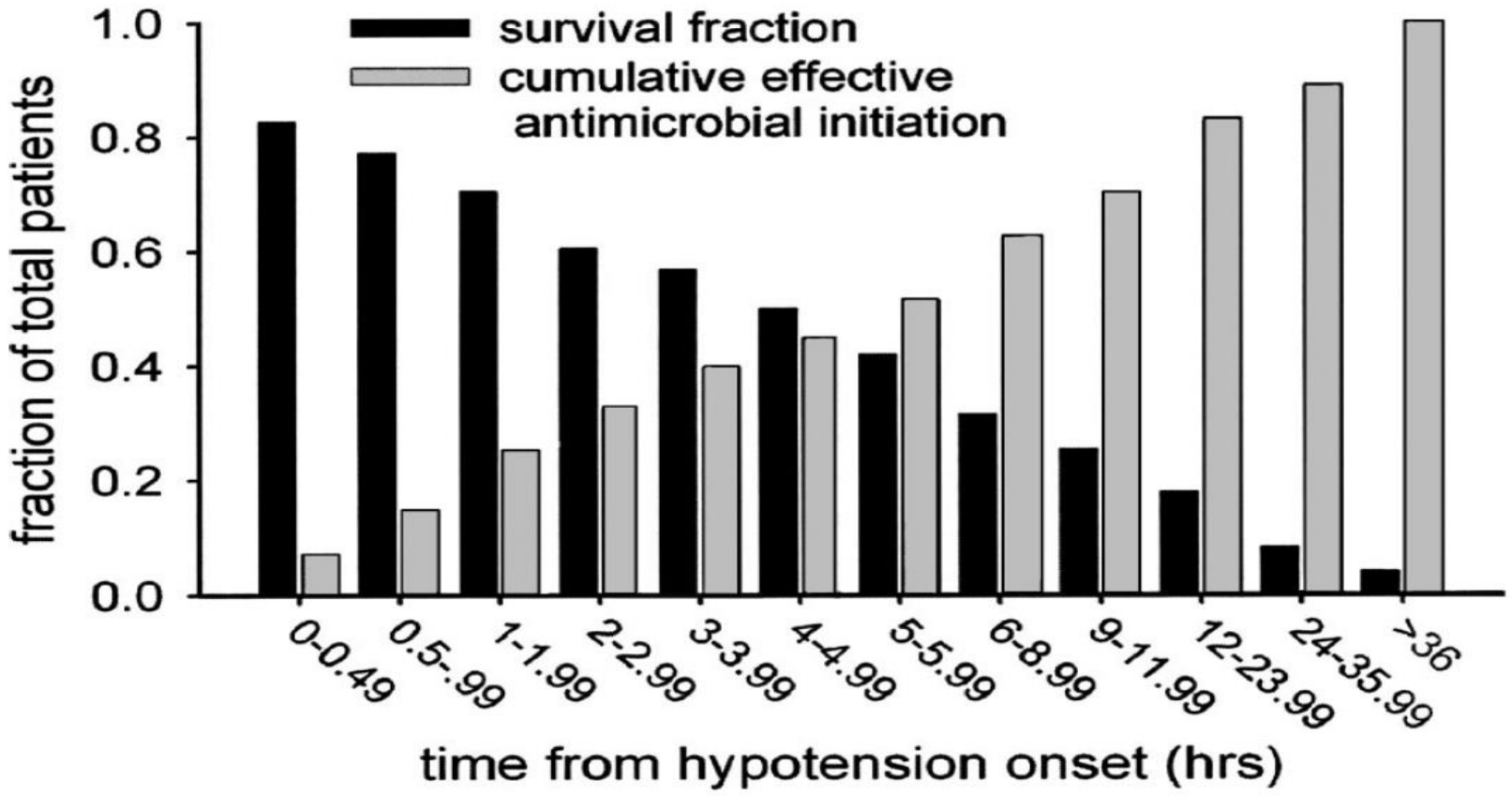
03/29/2012 20:00 Basic Metabolic				
Sodium	131	L	[134-146 mmol/L]	Final
Potassium	3.9		[3.6-5.2 mmol/L]	Final
Chloride	96	L	[98-108 mmol/L]	Final
CO2	24		[22-31 mmol/L]	Final
Urea Nitrogen	13		[10-26 mg/dL]	Final
Creatinine	0.7		[0.7-1.3 mg/dL]	Final
Glucose, Random	118	H	[70-100 mg/dL]	Final
Calcium	8.6		[8.3-10.3 mg/dL]	Final
GFR Estimate (MDRD)Non-African			[>60 mL/min/1.73m^2]	Final


Simple, validate set of bedside criteria
that directs them to consider sepsis
when presented with infected patients
NYU Langone Medical Center
TISCH HOSPITAL
530-560
NEW YORK UNIVERSITY MEDICAL CENTER
530-560

Sepsis management



Early Appropriate Antibiotics



Critical Care Med (2006) 34:1589–96

The SSC guidelines and bundles can be used as the basis of a sepsis performance improvement program.

SURVIVING SEPSIS CAMPAIGN BUNDLES

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 ≥4mmol/L

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 arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation ($Scvo_2$)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, $Scvo_2$ of ≥70%, and normalization of lactate.

Figure 1. Surviving Sepsis Campaign Care Bundles.

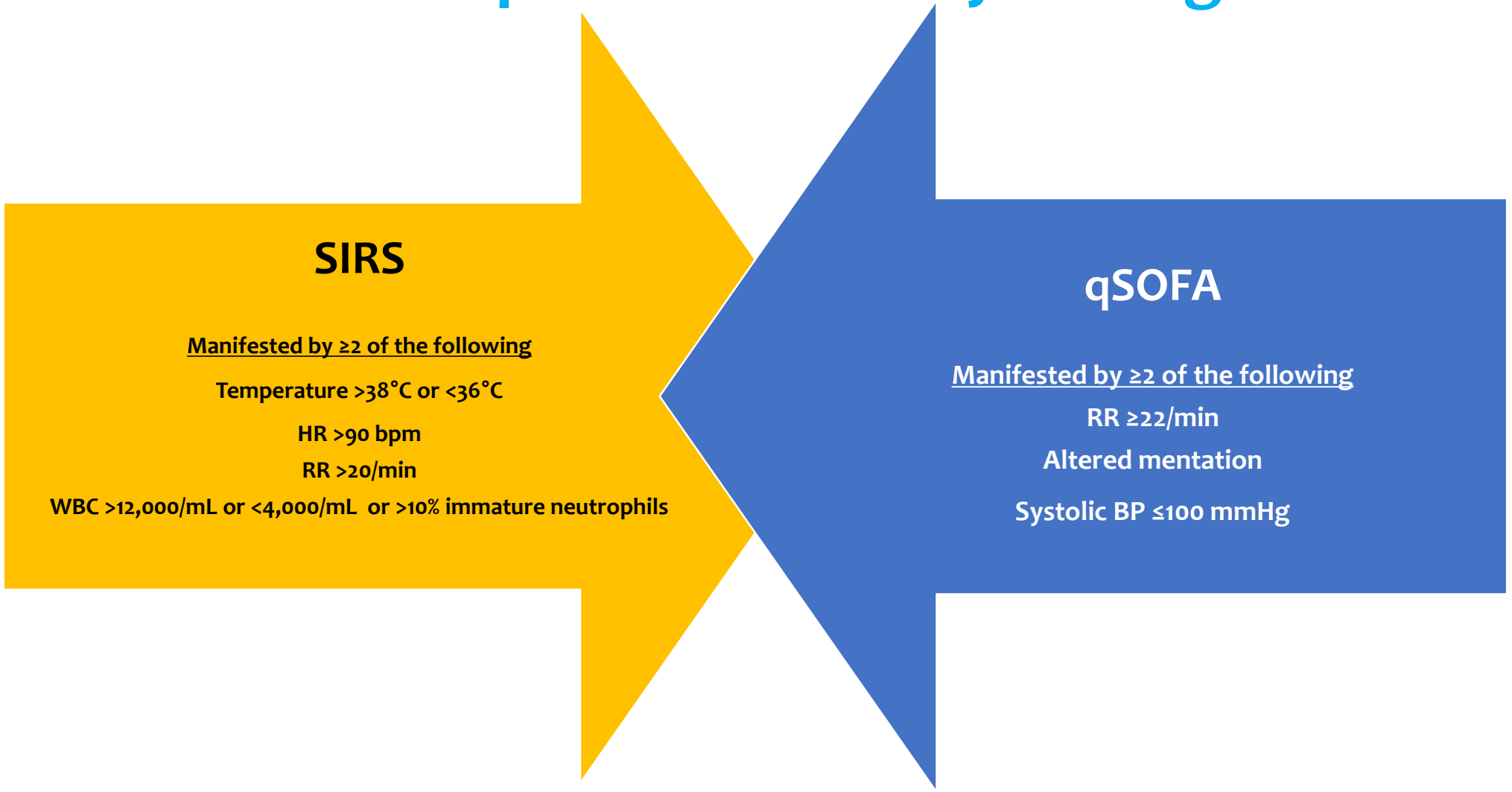
The Surviving Sepsis Campaign Bundle: 2018 Update

Mitchell M. Levy, MD, MCCM[1]; Laura E. Evans, MD, MSc, FCCM[2]; Andrew Rhodes, MBBS, FRCA, FRCP, FFICM, MD (res)[3]

TABLE 1. Bundle Elements With Strength of Recommendations and Under-Pinning Quality of Evidence (12, 13)

Bundle Element	Grade of Recommendation and Level of Evidence
Measure lactate level. Re-measure if initial lactate is > 2 mmol/L	Weak recommendation, low quality of evidence
Obtain blood cultures prior to administration of antibiotics	Best practice statement
Administer broad-spectrum antibiotics	Strong recommendation, moderate quality of evidence
Rapidly administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L	Strong recommendation, low quality of evidence
Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure ≥ 65 mm Hg	Strong recommendation, moderate quality of evidence

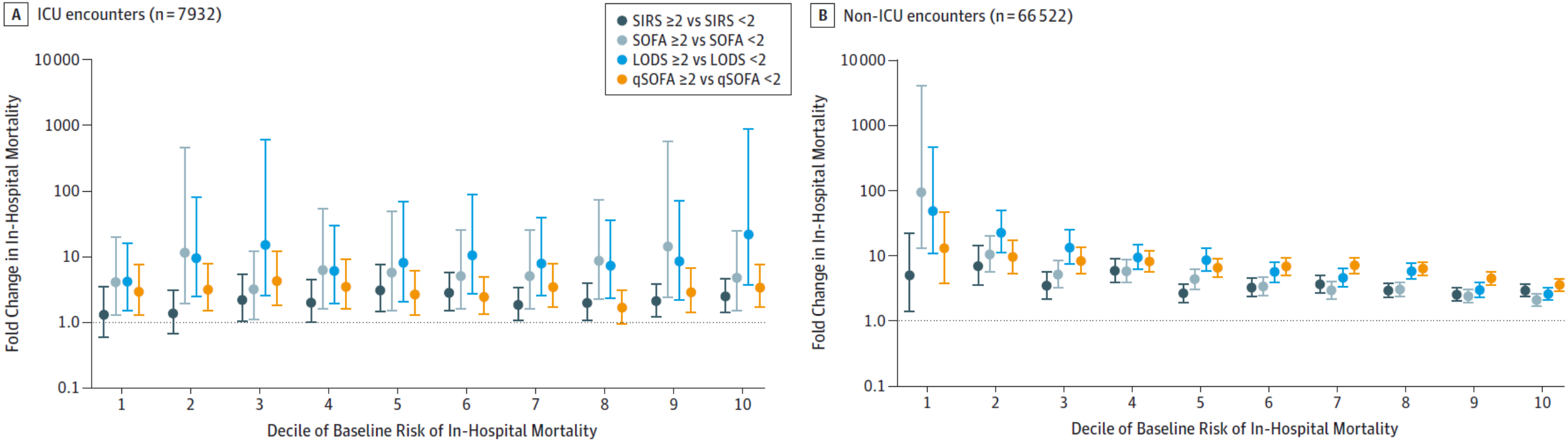
Which is simple ? And early management



Bedside clinical score, qSOFA

At least 2 of following

- Respiratory rate ≥22/min
- Altered mentation
- Systolic blood pressure ≤100 mmHg



[Original Research **Critical Care**]

CHEST

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

A Systematic Review and Meta-Analysis

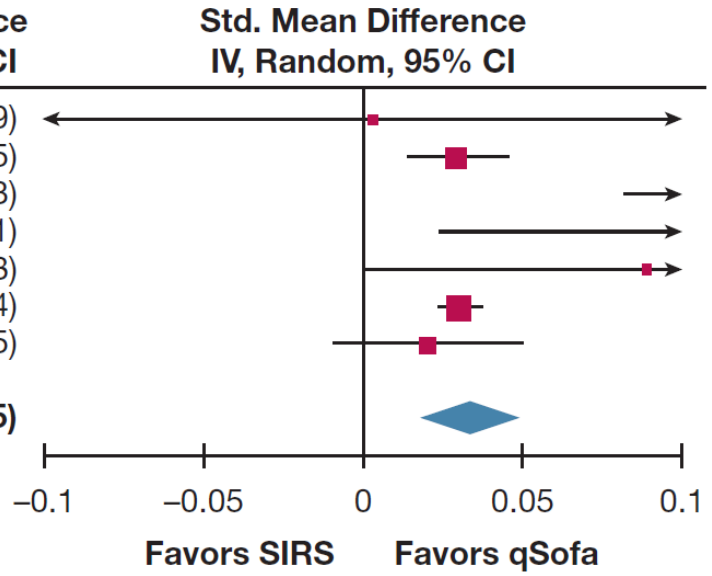
Rodrigo Serafim, MD; José Andrade Gomes, MD; Jorge Salluh, MD, PhD; and Pedro Póvoa, MD, PhD

Validation

Mortality of sepsis.

Study or Subgroup	qSOFA Mean	qSOFA SD	qSOFA Total	SIRS Mean	SIRS SD	SIRS Total	Weight	Std. Mean Difference IV, Random, 95% CI
April, 2017	0.66	2.61	214	0.65	2.61	214	0.7%	0.00 (–0.19 to 0.19)
Churpek, 2017	0.69	1.34	30,677	0.65	1.34	30,677	31.9%	0.03 (0.01 to 0.05)
Finkelsztein, 2017	0.74	0.47	152	0.59	0.5	152	0.5%	0.31 (0.08 to 0.53)
Freund, 2017	0.8	1.59	879	0.65	0.83	879	2.8%	0.12 (0.02 to 0.21)
Park, 2017	0.733	1.54	1,009	0.599	1.46	1,009	3.2%	0.09 (0.00 to 0.18)
Raith, 2017	0.607	0.88	184,875	0.58	0.88	184,875	42.6%	0.03 (0.02 to 0.04)
Williams, 2017	0.73	0.48	8,871	0.72	0.48	8,871	18.3%	0.02 (–0.01 to 0.05)
Total (95% CI)			**226,677**			**226,677**	**100.0%**	**0.03 (0.02 to 0.05)**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 11.39$, df = 6 ($P = .08$); $I^2 = 47\%$
Test for overall effect: $Z = 4.12$ ($P < .0001$)



Rodrigo serafim, et al. CHEST 2018; 153(3):646-655

[Original Research **Critical Care**]

CHEST

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

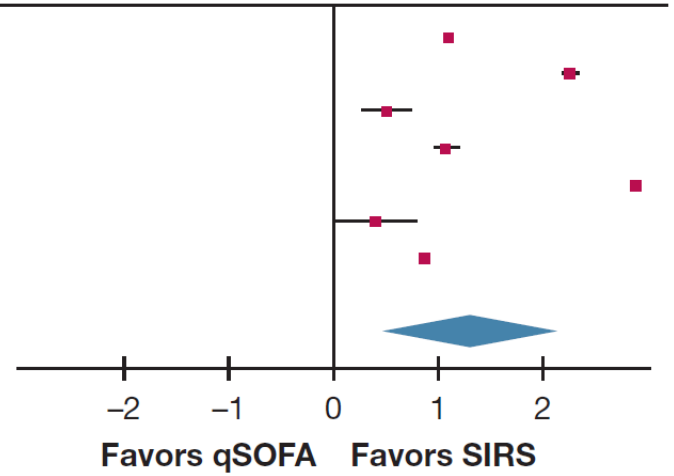
A Systematic Review and Meta-Analysis

Rodrigo Serafim, MD; José Andrade Gomes, MD; Jorge Salluh, MD, PhD; and Pedro Póvoa, MD, PhD

Sensitivity for diagnosis of sepsis.

Study or Subgroup	SIRS Mean	SIRS SD	SIRS Total	qSOFA Mean	qSOFA SD	qSOFA Total	Weight	Std. Mean Difference IV, Random, 95% CI
Churpek, 2017	0.88	0.45	30,677	0.38	0.45	30,677	14.4%	1.11 (1.09 to 1.13)
Donnelly, 2017	0.54	0.02	2,593	0.12	0.26	2,593	14.3%	2.28 (2.21 to 2.35)
Dorsett, 2017	0.39	0.5	152	0.16	0.38	152	14.2%	0.52 (0.29 to 0.75)
Freund, 2017	0.74	0.45	879	0.25	0.45	879	14.3%	1.09 (0.99 to 1.19)
Raith, 2017	0.86	0.11	184,875	0.54	0.11	184,875	14.4%	2.91 (2.90 to 2.92)
Siddiqui, 2017	0.62	0.47	58	0.42	0.51	58	14.0%	0.41 (0.04 to 0.77)
Williams, 2017	0.47	0.48	8,871	0.1	0.34	8,871	14.4%	0.89 (0.86 to 0.92)
Total (95% CI)			**228,105**			**228,105**	**100.0%**	**1.32 (0.40 to 2.24)**

Heterogeneity: $Tau^2 = 1.53$; $Chi^2 = 43948.08$, df = 6 ($P < .00001$); $I^2 = 100\%$
Test for overall effect: Z = 2.81 ($P = .005$)



Rodrigo serafim, et al. CHEST 2018; 153(3):646-655

Acute and Critical Care

Acute and Critical Care 2019 February 34(1):30-37
https://doi.org/10.4266/acc.2018.00318

Application of Sepsis-3 Criteria to Korean Patients with Critical Illnesses

Jae Yeol Kim[1]*, Hwan Il Kim[2]*, Gee Young Suh[3], Sang Won Yoon[1], Tae-Yop Kim[4], Sang Haak Lee[5], Jae Young Moon[6], Jae-Young Kwon[7], Sungwon Na[8], Ho Geol Ryu[9], Jisook Park[10], Younsuck Koh[11]

- Korean participants from the fever and antipyretics in critically ill patients evaluation (FACE) study, a joint study between Korea and Japan.
- Concordance rates for sepsis diagnosis between Sepsis-2 and Sepsis-3 criteria
- Mortality rates of sepsis, sepsis with organ dysfunction, and septic shock by Sepsis-3 criteria

Acute and Critical Care

Acute and Critical Care 2019 February 34(1):30-37
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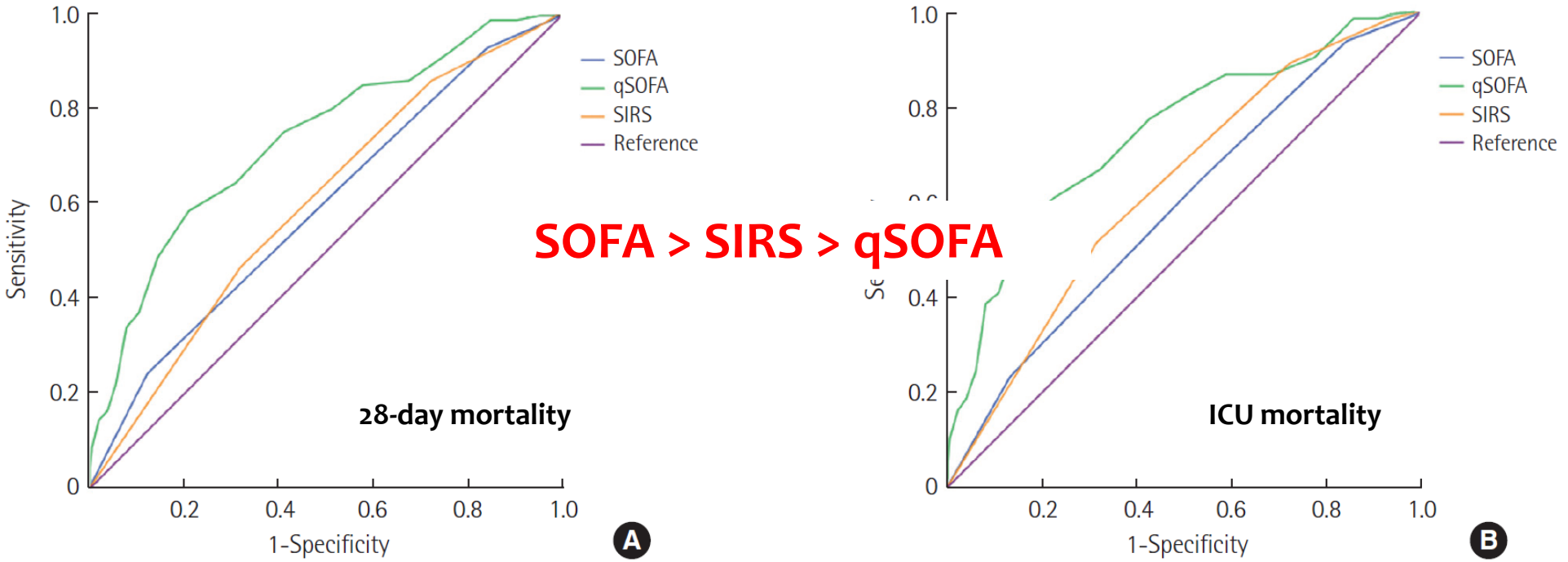
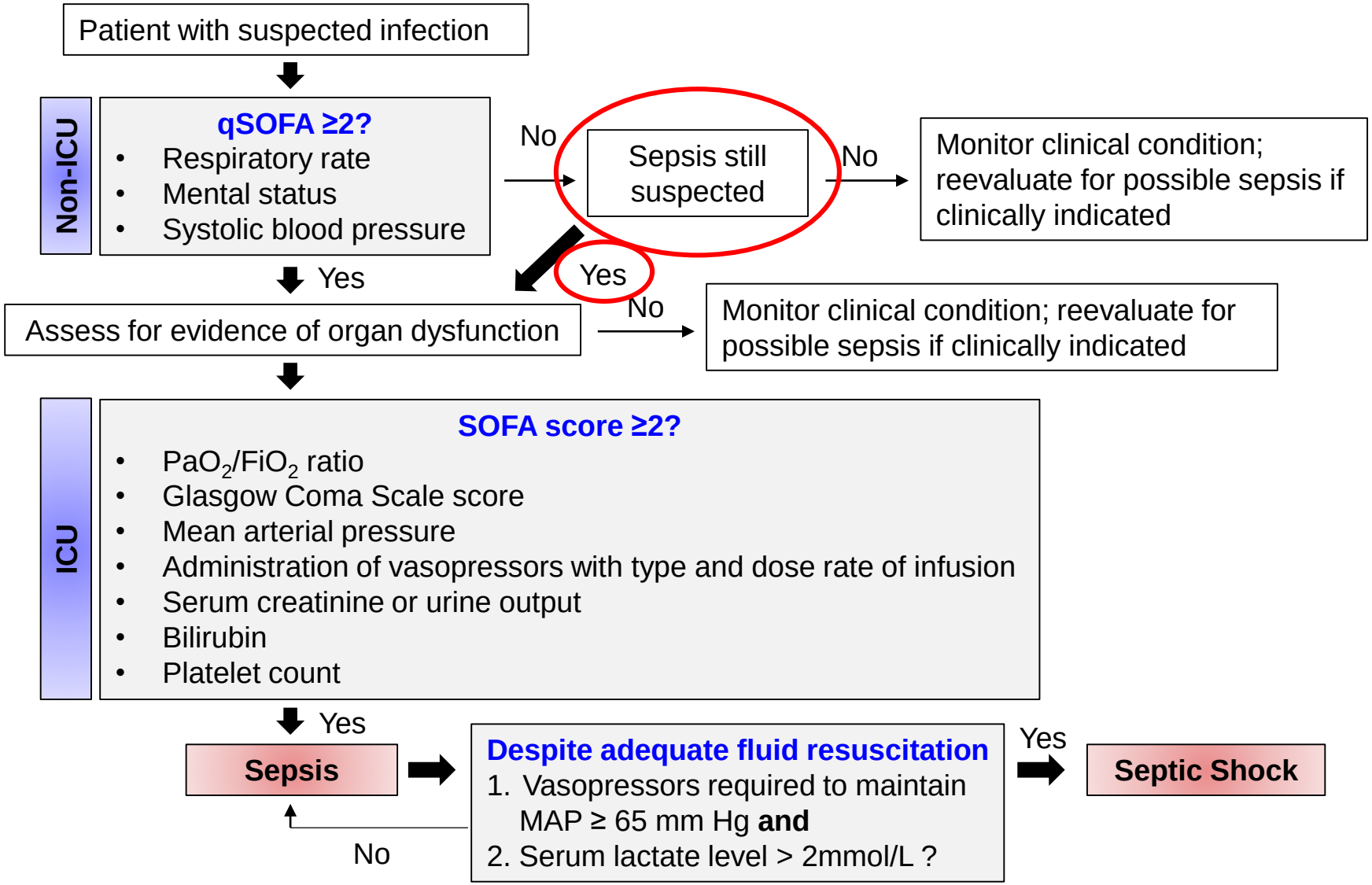


Figure 2. Area under the receiver operating characteristic curves (AUROCs) for discriminatory capacity for 28-day mortality and ICU mortality. (A) Twenty-eight-day mortality. AUROC: SOFA, 0.74 (95% CI, 0.68 to 0.79); qSOFA, 0.59 (95% CI, 0.53 to 0.66); SIRS, 0.60 (95% CI, 0.54 to 0.66). (B) ICU mortality. AUROC: SOFA, 0.74 (95% CI, 0.68 to 081); qSOFA, 0.59 (95% CI, 0.52 to 0.66); SIRS, 0.63 (95% CI, 0.57 to 0.70). SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA; SIRS: systemic inflammatory response syndrome; CI: confidence interval; ICU: intensive care unit.

Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



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

Validation

DO SEPSIS-3 CRITERIA FACILITATE EARLIER RECOGNITION OF SEPSIS AND SEPTIC SHOCK? A RETROSPECTIVE COHORT STUDY

Christian S. Scheer,[*] Sven-Olaf Kuhn,[*] Christian Fuchs,[*] Marcus Vollmer,[†] Arnd Modler,[‡] Frank Brunkhorst,[§||¶] Manu Shankar-Hari,[**] Klaus Hahnenkamp,[*] Matthias Gründling,[*] and Sebastian Rehberg[*]

[*]Department of Anesthesiology, University Hospital of Greifswald, Greifswald, Germany; [†]Institute of Bioinformatics, University Hospital of Greifswald, Greifswald, Germany; [‡]Arnd Modler, University of Greifswald, Greifswald, Germany; [§]Center for Clinical Studies, Jena University Hospital, Jena, Germany; [||]Department of Anesthesiology and Intensive Care, Jena, Germany; [¶]Center for Sepsis Control and Care (CSCC), Jena University Hospital, Jena, Germany; and [**]Department of Critical Care Medicine, ICU Offices, Guy's and St Thomas' Hospital, London, United Kingdom

- between 01/2010 and 12/2015
- In a cohort of ICU patients diagnosed with severe sepsis or septic shock according to Sepsis-1 criteria prospectively
- The time differences between meeting Sepsis-1 vs. Sepsis-3 criteria
  - time of sepsis onset and the corresponding differences in illness severity were tested

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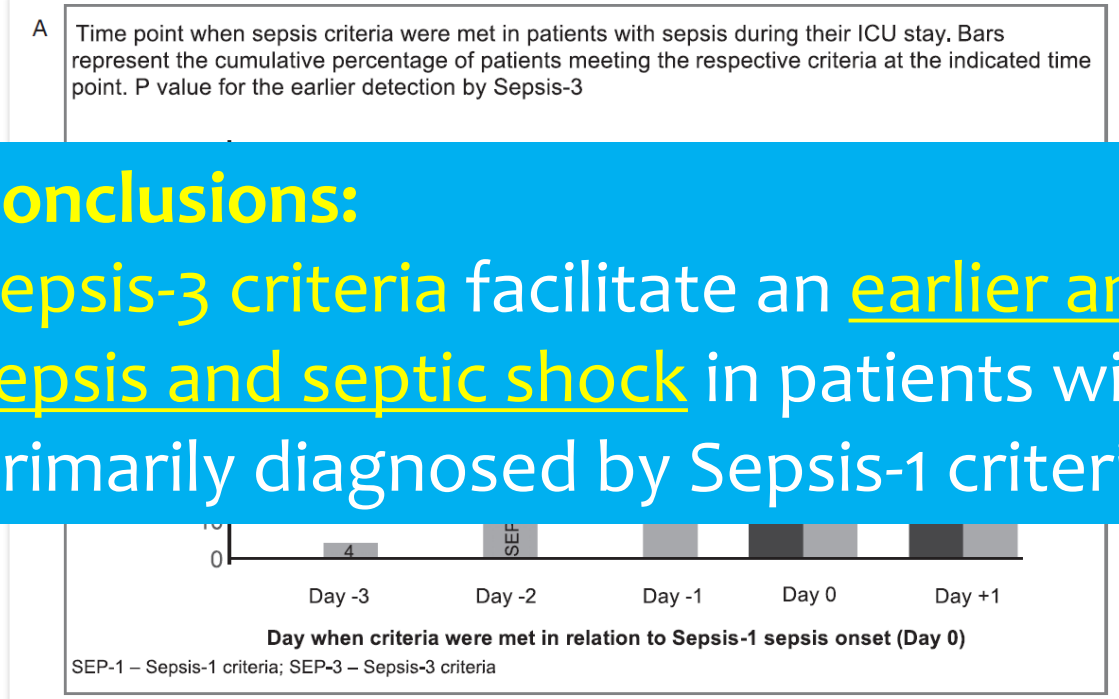
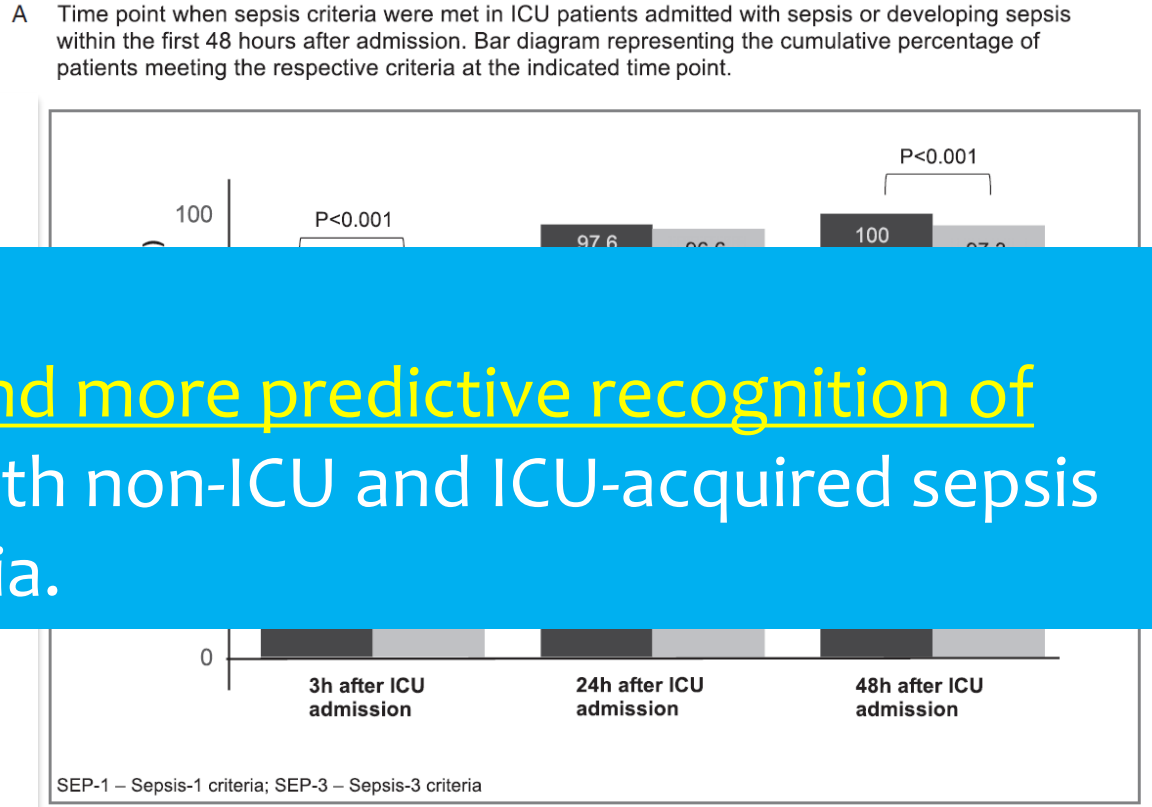
883 patients
with **severe sepsis or septic shock**[1]
and admission to the intensive care unit (1.1.2010 – 31.12.2015) were eligible



Time point of sepsis onset and corresponding severity among patients with ICU-acquired sepsis.



Time point of sepsis onset and corresponding severity among patients with non-ICU-acquired sepsis.

Conclusions:

Sepsis-3 criteria facilitate an earlier and more predictive recognition of sepsis and septic shock in patients with non-ICU and ICU-acquired sepsis primarily diagnosed by Sepsis-1 criteria.

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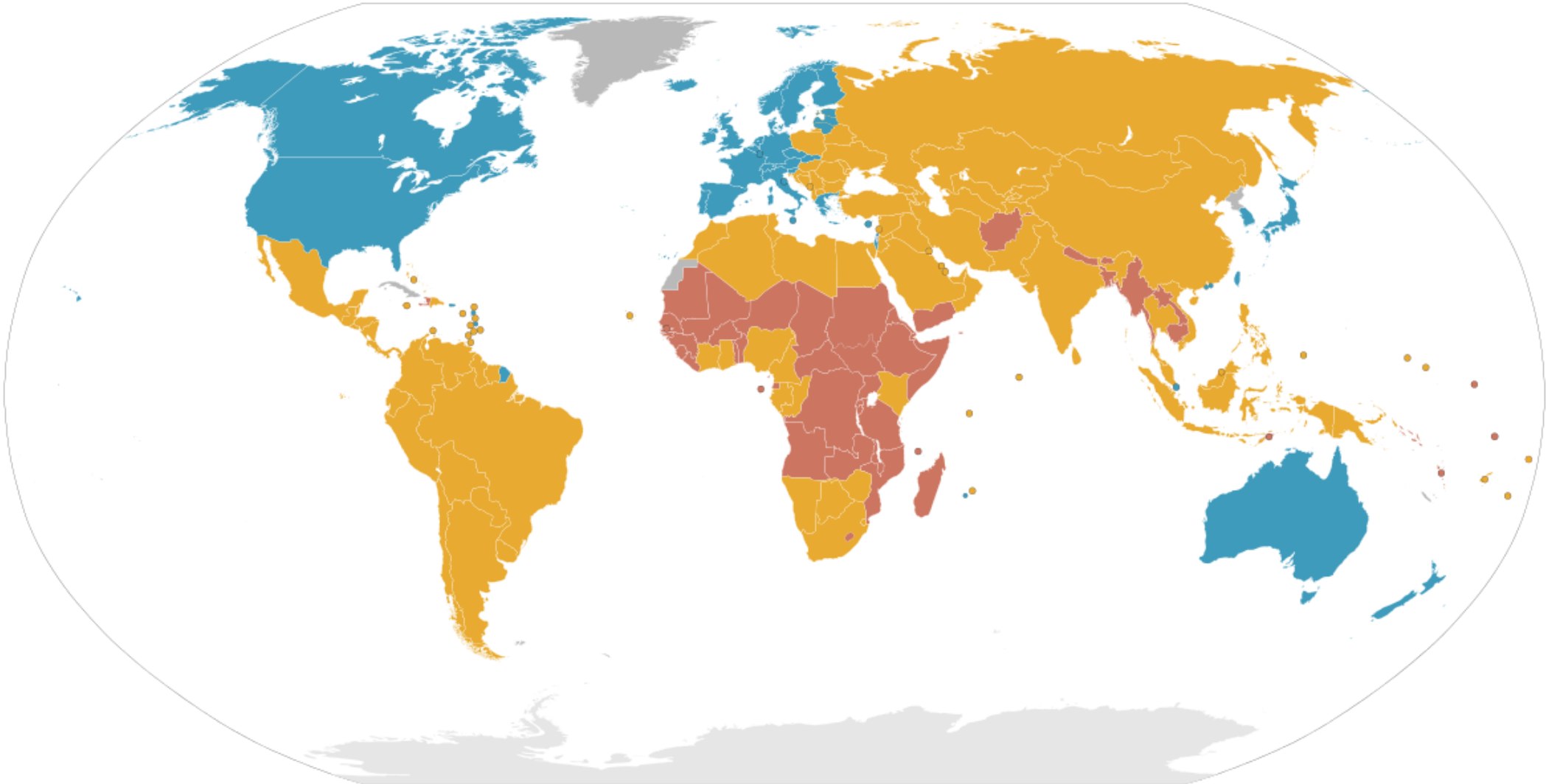
For patients with sepsis in Low-and Middle-Income Countries.



JAMA | Original Investigation

Association of the Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries

Kristina E. Rudd, MD, MPH; Christopher W. Seymour, MD, MSc; Adam R. Aluisio, MD, MSc; Marc E. Augustin, MD; Danstan S. Bagenda, PhD; Abi Beane, MSc; Jean Claude Byiringiro, MD; Chung-Chou H. Chang, PhD; L. Nathalie Colas, MD; Nicholas P. J. Day, MD, PhD; A. Pubudu De Silva, MD; Arjen M. Dondorp, MD, PhD; Martin W. Dünser, MD; M. Abul Faiz, MBBS, PhD; Donald S. Grant, MBChB, MPH; Rashan Haniffa, MD; Nguyen Van Hao, PhD; Jason N. Kennedy, MS; Adam C. Levine, MD, MPH; Direk Limmathurotsakul, MD, PhD; Sanjib Mohanty, MD; François Nosten, MD, PhD; Alfred Papali, MD; Andrew J. Patterson, MD, PhD; John S. Schieffelin, MD, MSPH; Jeffrey G. Shaffer, PhD; Duong Bich Thuy, MD; C. Louise Thwaites, PhD; Olivier Urayeneza, MD; Nicholas J. White, MD, DSc; T. Eoin West, MD, MPH; Derek C. Angus, MD, MPH; for the Sepsis Assessment and Identification in Low Resource Settings (SAILORS) Collaboration

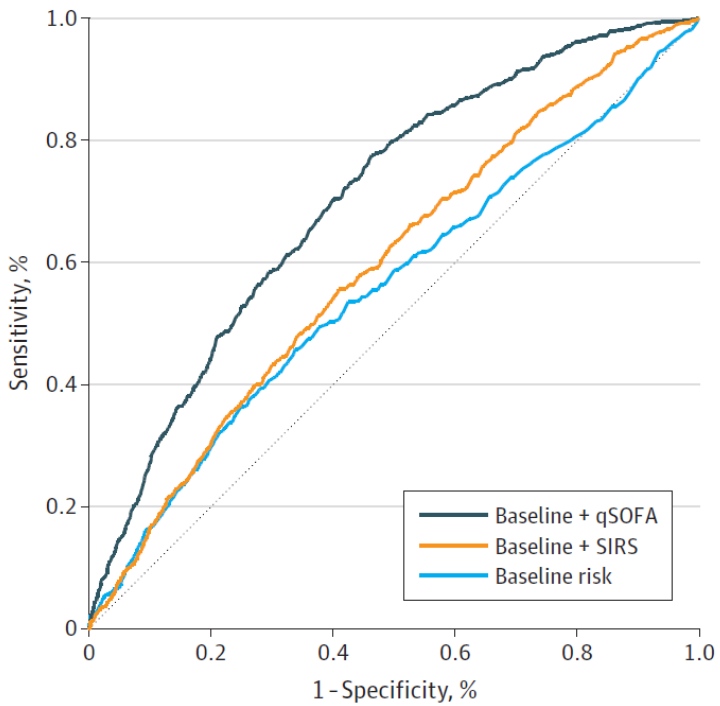
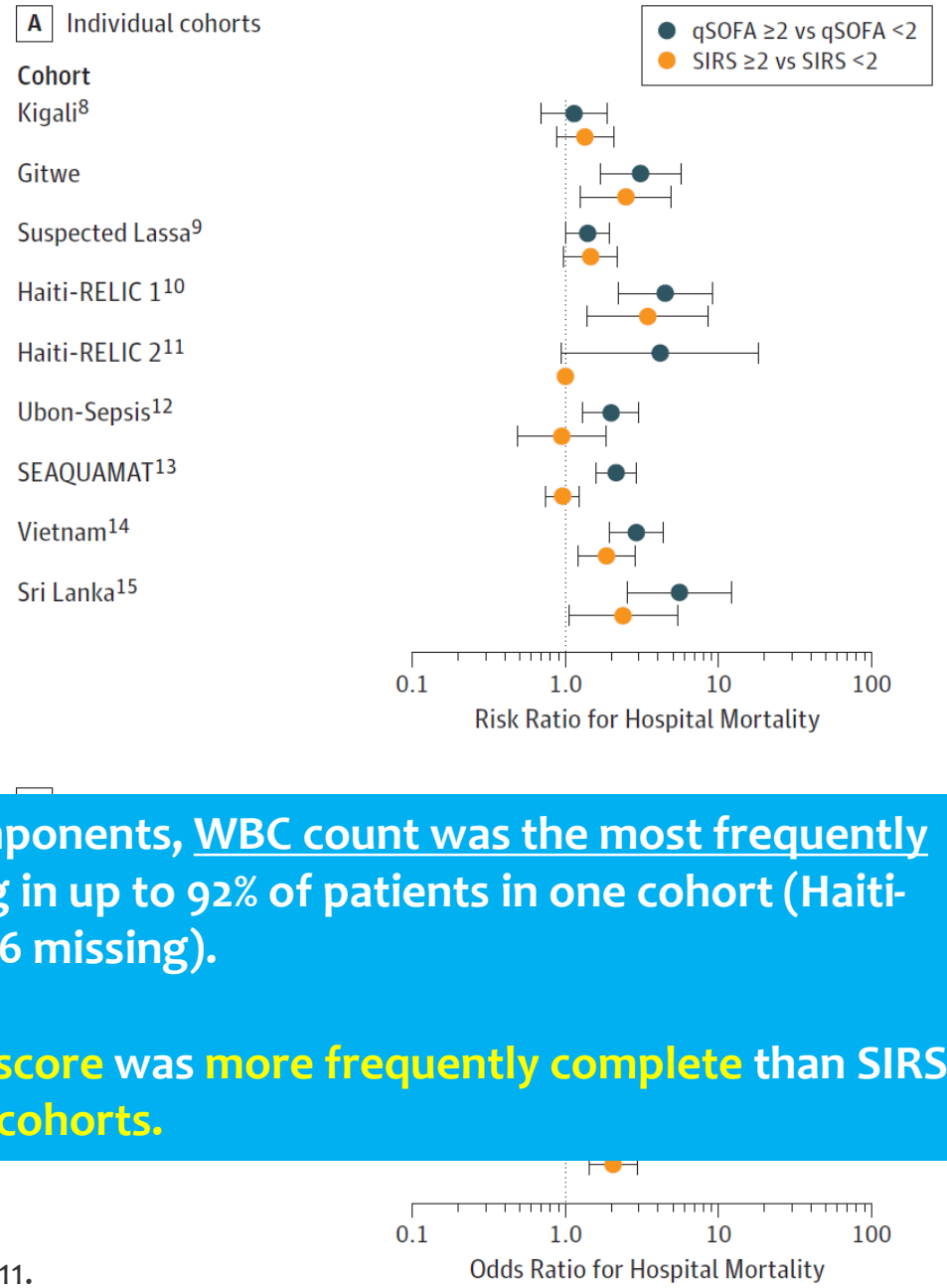


Figure 2. Risk Ratios and Odds Ratios for Hospital Mortality



Of the SIRS components, WBC count was the most frequently missing, missing in up to 92% of patients in one cohort (Haiti-RELIC1, 143 of 156 missing).

Overall, qSOFA score was more frequently complete than SIRS criteria in most cohorts.

JAMA. 2018;319(21):2202-2211.

The predictive ability of a weighted systemic inflammatory response syndrome score for microbiologically confirmed infection in hospitalised patients with suspected sepsis

Nai An Lai and Peter Kruger

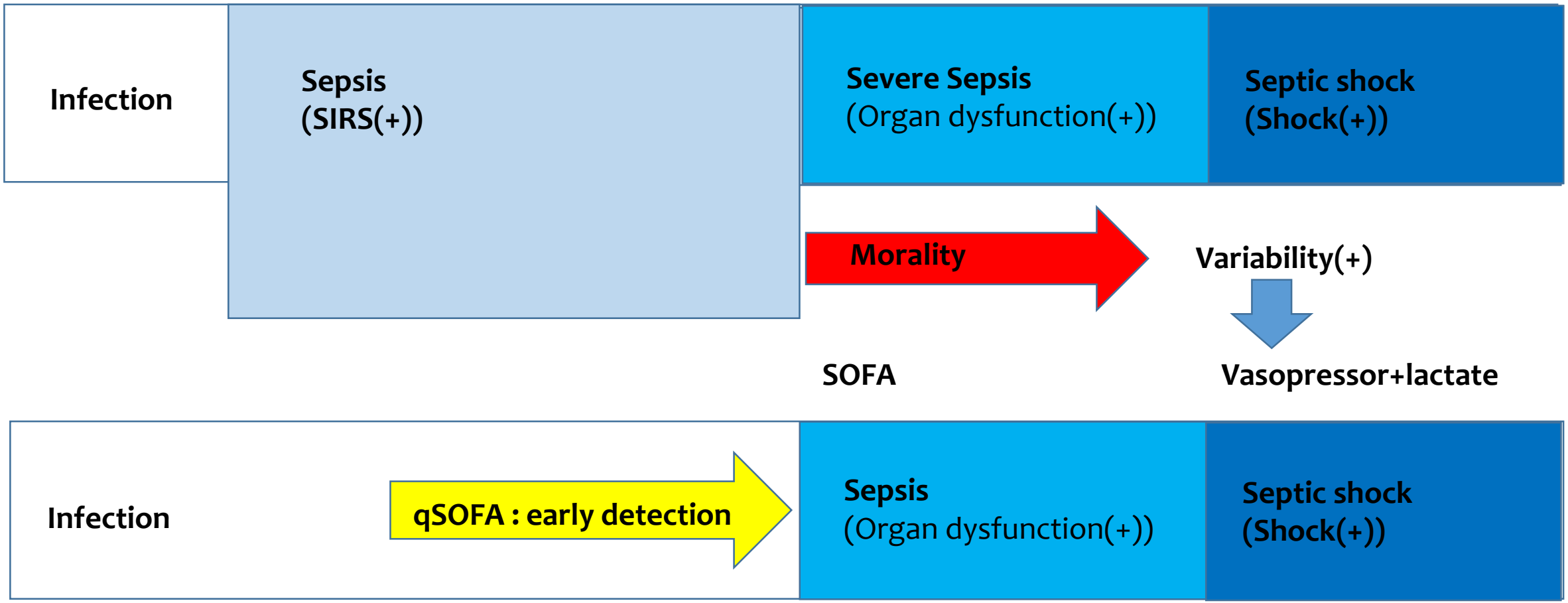
Crit Care Resusc 2011; 13: 146–150

Table 1. SIRS criteria and weighted SIRS scores in predicting microbiologically confirmed infection

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
WCC	52.5%	52.8%	63.3%	41.7%	1.11	0.90
Temperature	46.6%	59.0%	63.8%	41.6%	1.13	0.90
Tachycardia	65.2%	41.0%	63.2%	43.2%	1.11	0.85
Tachypnoea	49.4%	51.9%	61.5%	39.8%	1.03	0.97
Traditional (⩾ 2) SIRS	70.6%	37.5%	63.7%	45.1%	1.13	0.79
Weighted SIRS ⩾ 3	63.5%	45.7%	64.5%	44.6%	1.17	0.80
Both temp and WCC present	27.3%	77.5%	65.3%	40.7%	1.21	0.94

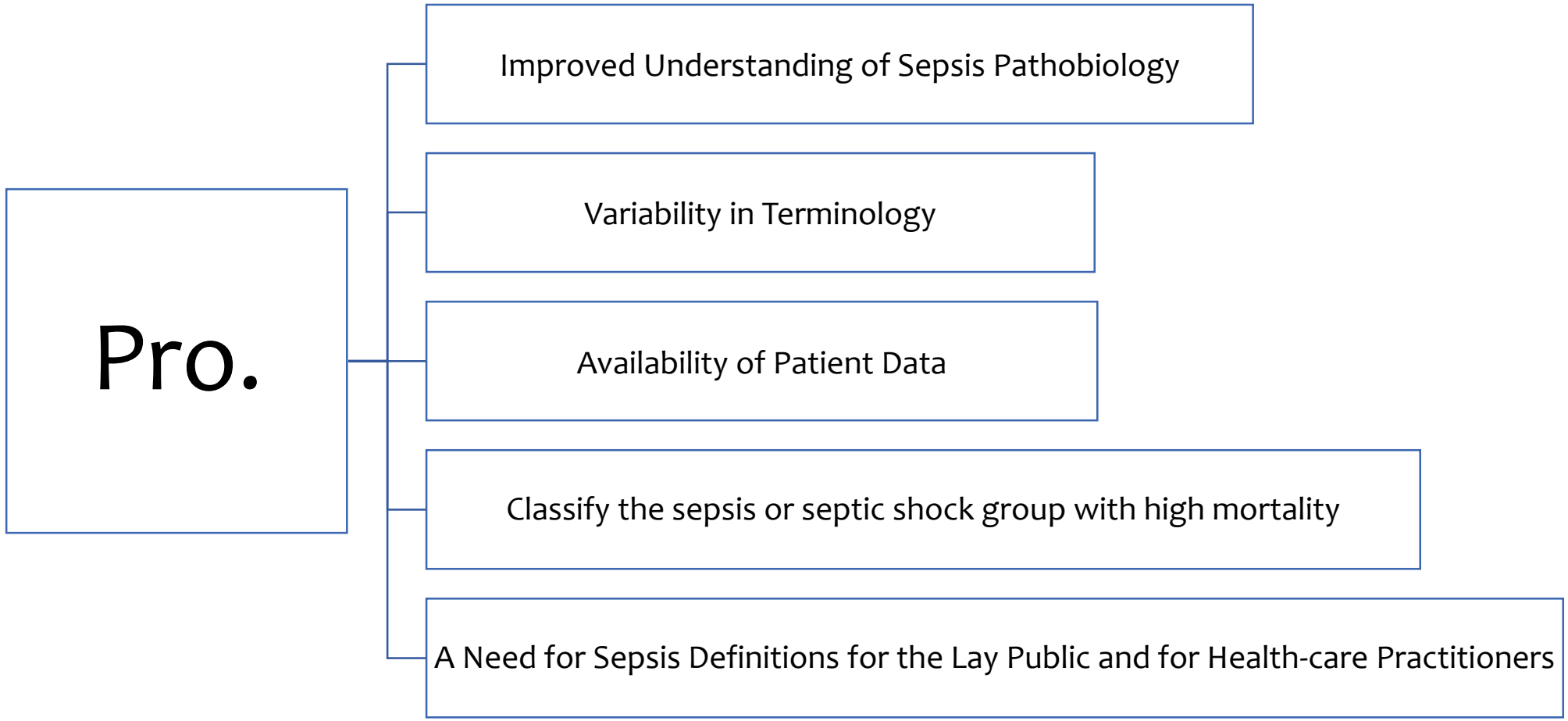
SIRS = systemic inflammatory response syndrome. WCC = white cell count.

Summary



Low sensitivity of qSOFA and lactate evaluation

Summary; Why to change ?



Thank you for your attention.