

Third International Consensus Definition for Sepsis and Septic Shock

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sepsis
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Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

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EDITORIAL

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New Definitions for Sepsis and Septic Shock Continuing Evolution but With Much Still to Be Done

Edward Abraham, MD

Old definitions

- Sepsis : infection + SIRS
- Severe sepsis : sepsis + sepsis -induced organ dysfunction or tissue hypoperfusion
- Septic shock : sepsis -induced hypotension persisting despite adequate fluid resuscitation

Sepsis

According to the new definitions, sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection clinically characterized by an acute change of 2 points or greater in the SOFA score



Elimination of mention of SIRS in the diagnosis of sepsis

Figure 1. The Systemic Inflammatory Response Syndrome (SIRS).⁸

Two or more of the following:

- Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$
 - Heart rate >90 beats/min
 - Respiratory rate >20 breaths/min or $\text{PaCO}_2 < 32$ torr
 - WBC $>12,000$ cell/mm³, $<4,000$ cells/mm³, or $>10\%$ immature (band) forms
-

Elimination of mention of SIRS in the diagnosis of sepsis

The presence of SIRS is nearly ubiquitous in hospitalized patients and occurs in many benign conditions, related or not to infection, thus **is not specific** for diagnosis of sepsis

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	

Abbreviation: FiO₂, fraction of inspired oxygen.

^a Measurement units for LODS variables per original description by Le Gall et al.⁹

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Assessment of the Validity of Clinical Criteria for Suspected Infection

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).

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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.

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Results

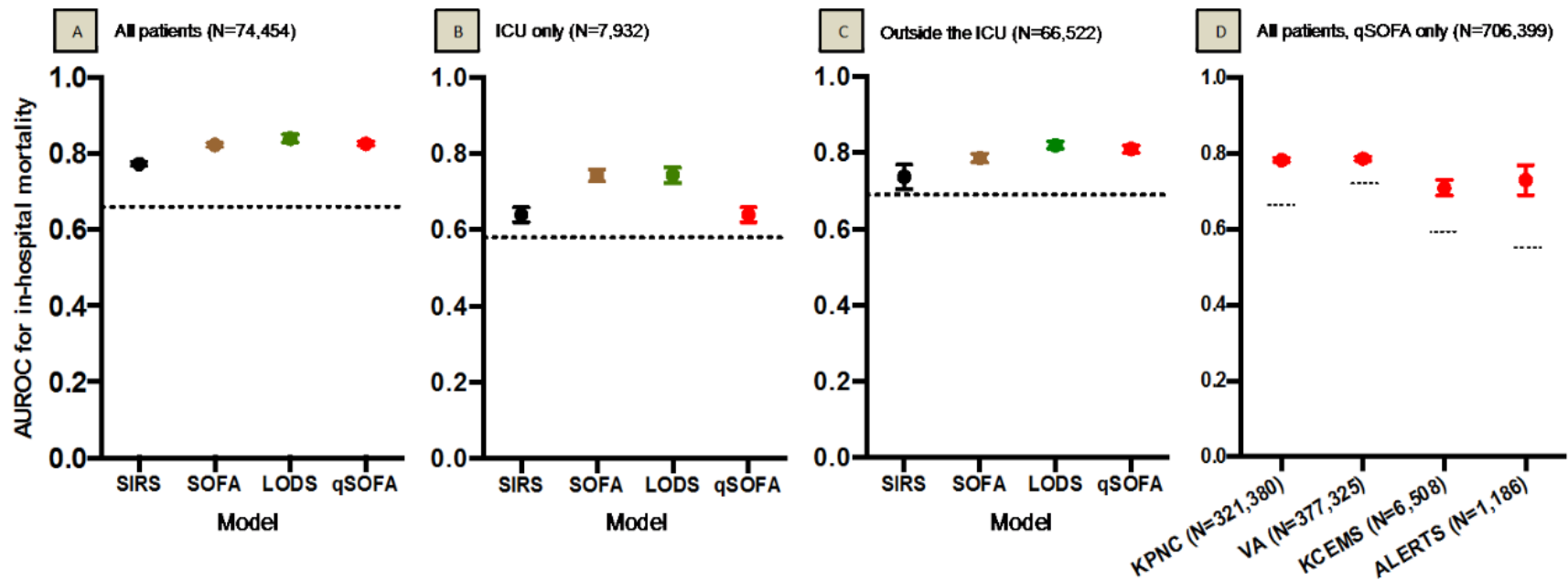
Among **ICU** encounters in the validation cohort (n= 7932 with suspected infection, of whom 16% died), the predictive validity for in-hospital mortality **was lower for SIRS** (AUROC 0,64) and **qSOFA** (AUROC 0,66) vs **SOFA** (AUROC 0,74) or **LODS** (AUROC 0,75)

Results

Among **non-ICU** encounters in the validation cohort (n=66.522 with suspected infection, of whom 3% died), **qSOFA** had predictive validity (AUROC 0,81) that **was greater than** SOFA (AUROC 0,79) and SIRS (AUROC 0,76)

Results

eFigure 4. Area under the receiver operating characteristic (AUROC) curves for SIRS, SOFA, LODS, and qSOFA overall (*panel A*), in the ICU (*panel B*) or non-ICU patients (*panel C*) in the UPMC validation cohort (N=74,454). Performance of qSOFA across four external datasets shown in *panel D*. Dotted line corresponds to AUROC of baseline risk. Error bars represent 95% confidence intervals.



SOFA score

Because SOFA is better known and simpler than LODS, the task force recommends using a change in baseline of SOFA > 2 .

The baseline SOFA score should be assumed to be zero unless the patient is known to have preexisting organ dysfunction

SOFA score

Patients with SOFA score >2 had an overall mortality risk of 10% in a general hospital population with presumed infection.

This is greater than the overall mortality rate of 8% for ST-segment elevation myocardial infarction

qSOFA (Quick SOFA Score) for Sepsis Identification

Predicts poor outcome in infection patients; initial screen for sepsis (2016).

Note: The qSOFA was introduced in February 2016 as a way to screen for sepsis by the Sepsis-3 group as an evolving definition and understanding of sepsis, moving away from the previous SIRS criteria-based definitions.

New/Worsened Altered Mentation

YES

RR \geq 22

YES

Systolic BP \leq 100

YES

Patient high risk by qSOFA. Assess for evidence of organ dysfunction with blood testing including serum lactate and calculation of the full SOFA Score.

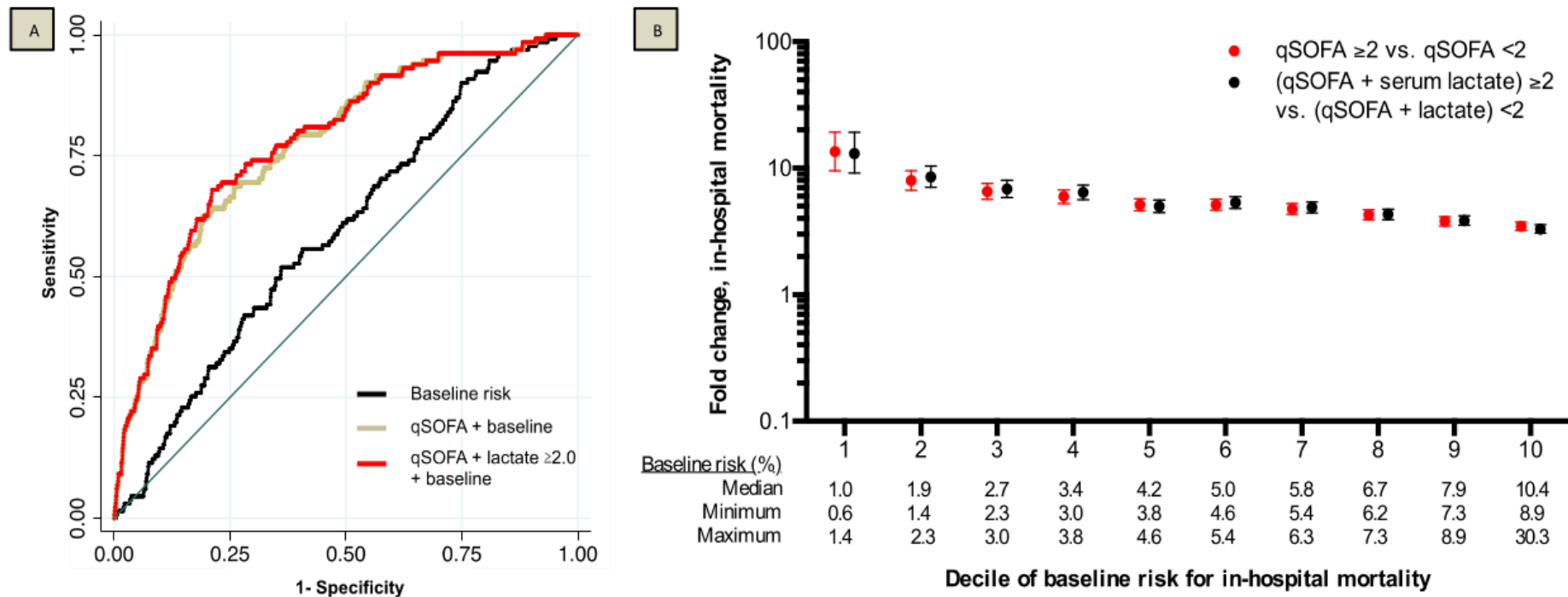
Patients meeting these qSOFA criteria should have infection considered even if it was previously not.

The consensus document also introduces a **bedside index**, called **qSOFA**, which is proposed to help identify patients with **suspected infection** who are being treated **outside of critical care units** and likely to develop complications of sepsis.

The qSOFA requires at least **2 of the 2 risk variables**

qSOFA and lactate

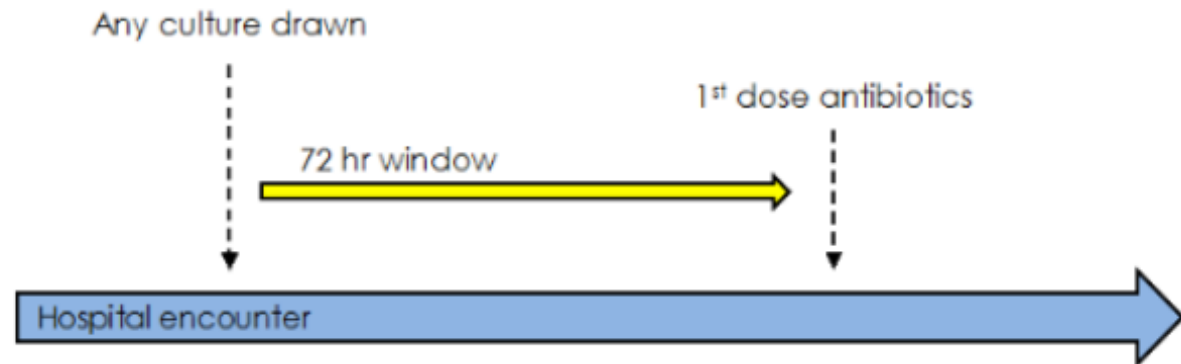
eFigure 10. (A) Receiver operating characteristic curve for qSOFA with and without serum lactate ≥ 2.0 mmol/L compared to baseline risk of in-hospital mortality. (B) Fold change in rate of in-hospital mortality within decile of baseline risk comparing qSOFA with and without serum lactate. All data from KPNC (N=321,380).



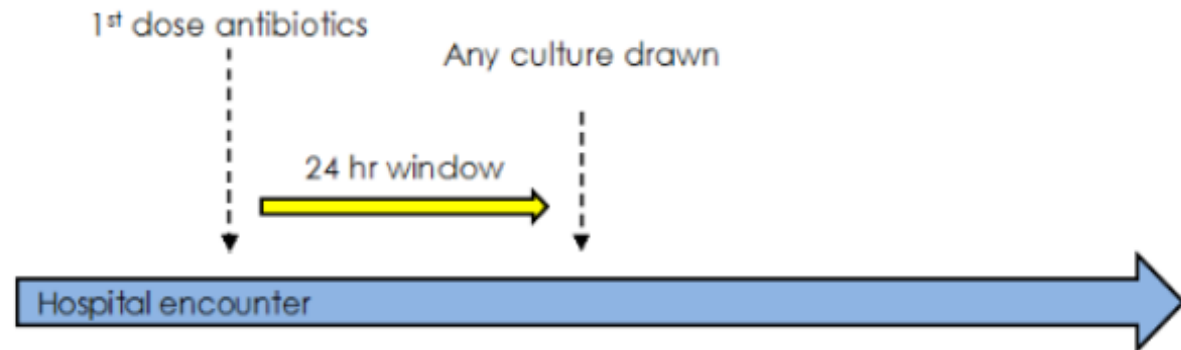
Identification of infection

- Order of administration
- Order of body fluid
- “Time zero” of infection occurred
- Exclusion: antibiotic operating room and

Option 1: Antibiotics must be within 72 hrs of first culture



Option 2: Culture must be within 24 hrs of first antibiotic dose



Septic shock

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

Septic shock – clinical criteria

- Sepsis with fluid-unresponsive hypotension
- Need for vasopressors to maintain mean arterial pressure > 65 mmHg
- Serum lactate level > 2 mmol/L

Septic shock – clinical criteria

Three sets of studies were conducted to determine clinical criteria currently reported to identify septic shock

VASOPRESSOR + LAC >2 mmol/L



**HIGHER MORTALITY
(42,3%)**

vs

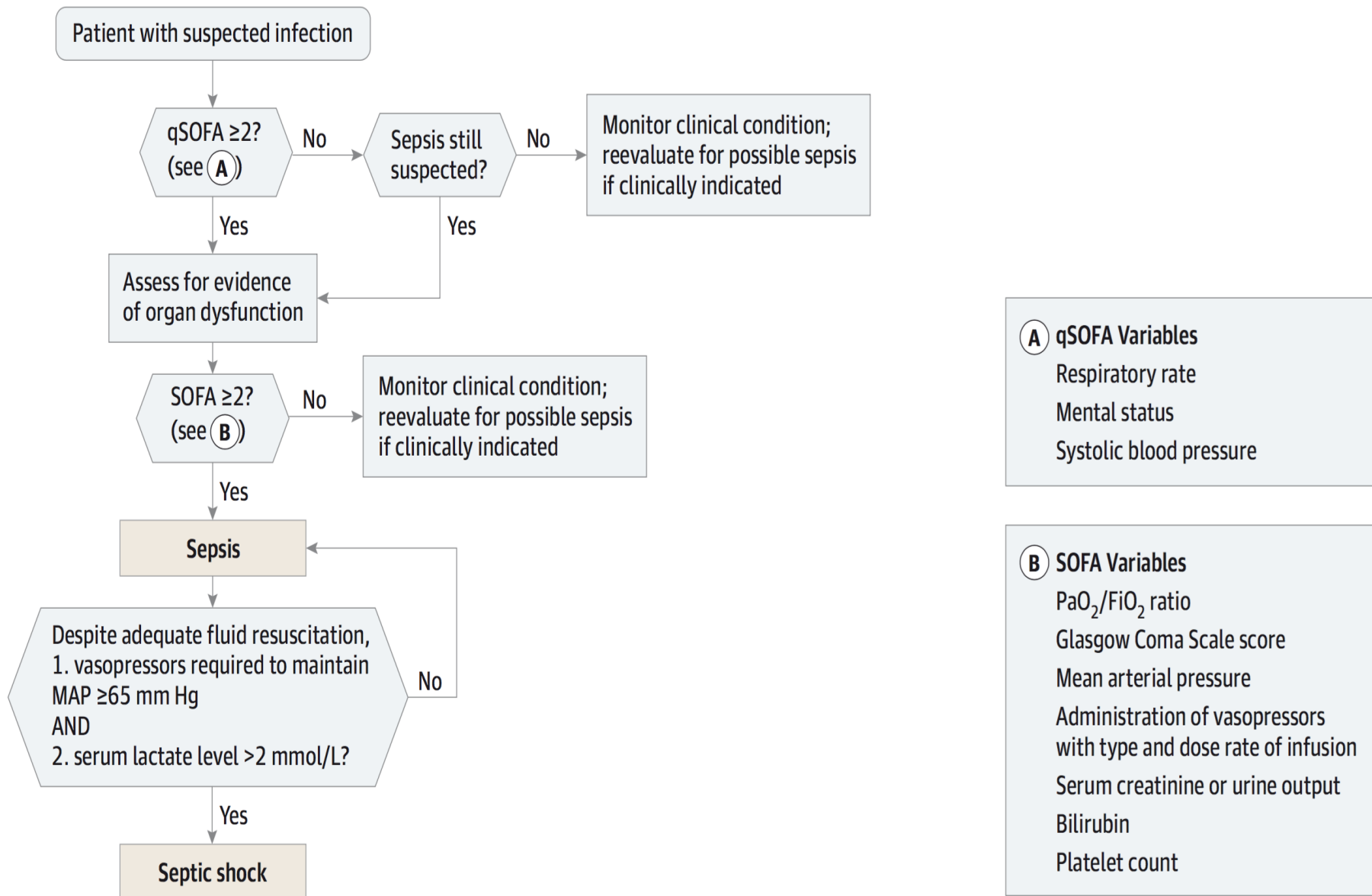
LAC > 2 mmol/L alone or + hypotention, vasopressor and LAC < 2 mmol/L

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.

Septic shock and lactate

A serum lactate level greater than 2 mmol/L was chosen as the preferred cutoff value for the new septic shock criteria, the rationale being the trade-off between highest sensitivity (82.5% when using the n = 18 840 subset, and 74.9% when using patients in groups 1 and 2 combined [n = 12 475]), and the decision from the Delphi process to identify the lowest serum lactate level independently associated with a greater risk of death

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



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



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Grazie per l'attenzione