Sepsis Grand Rounds

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J.K.'s Sepsis Story

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, and Derek C. Angus, MD, MPH

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

Source: Singer (1)

Key Concepts

- Sepsis is the primary cause of death from infection.

- Sepsis is a syndrome shaped by pathogen factors and host factors with characteristics that evolve over time.

- The clinical and biological phenotype of sepsis can be modified by preexisting acute illness, long-standing comorbidities, medication and interventions.

- Sepsis should be considered in any patient presenting with infection.

- Any unexplained organ dysfunction should raise the possibility of underlying infection.

Source: Singer (1)

Clinical Criteria to Identify Sepsis

- The task force evaluated which clinical criteria **easily** identified infected patients most likely to have sepsis.

- **Organ dysfunction** can be identified as an acute change in total SOFA (Sequential Organ Failure Assessment) score ≥ 2 points.

- A SOFA score ≥ 2 reflects an **overall mortality risk** of approximately 10%.

- 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 *q*SOFA or quick SOFA.

Source: Singer (1)

qSOFA

Quick Sequential Organ Failure Assessment

- Respiratory Rate ≥ 22

- Systolic Blood Pressure < 100 mmHg

- Altered Mental Status (GCS < 15)

The task force strongly encourages prospective validation in multiple health care settings.

Source: Singer (1)

Studies Challenging qSOFA

An Emergency Department Validation of the SEP-3 Sepsis and Septic Shock Definitions and Comparison With 1992 Consensus Definitions

Daniel J. Henning, MD; Michael A. Puskarich, MD; Wesley H. Self, MD; Michael D. Howell, MD, MPH; Michael W. Donnino, MD; Donald M. Yealy, MD; Alan E. Jones, MD; Nathan I. Shapiro, MD, MPH*
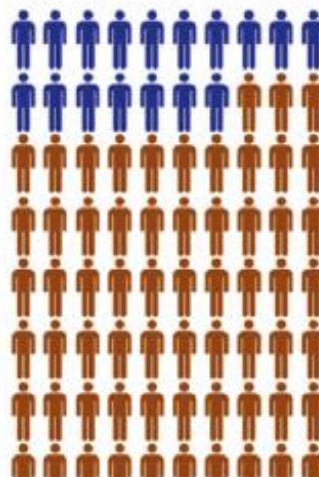
Source: Henning (2)

Sensitivity

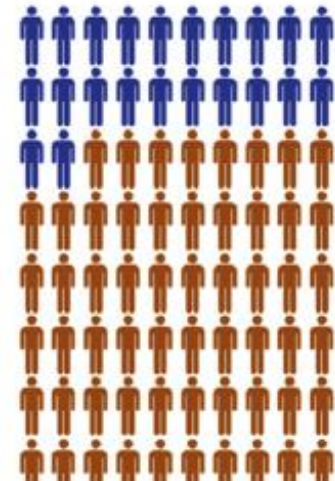**Among patients with infection who <u>died</u> during the hospitalization, how many were detected (Red)**
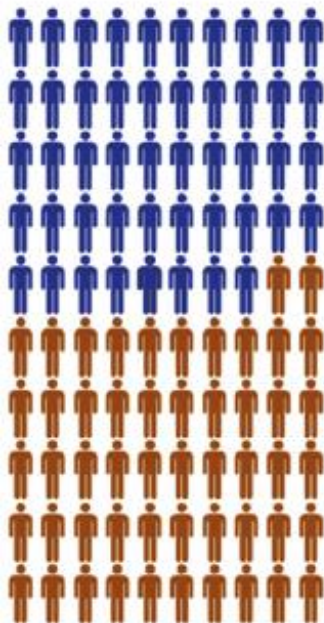
| qSOFA | OLD "SEPSIS" | SEVERE SEPSIS |

qSOFA detected 21% fewer patients with infection who died during hospitalization compared with SIRS.

Source: Henning (2)

Specificity

**Among patients who survived,
how many were marked as <u>high risk for dying</u> (Black)**

The SEP-3 definitions have improved specificity, but at the cost of sensitivity.

Source: Henning (2)
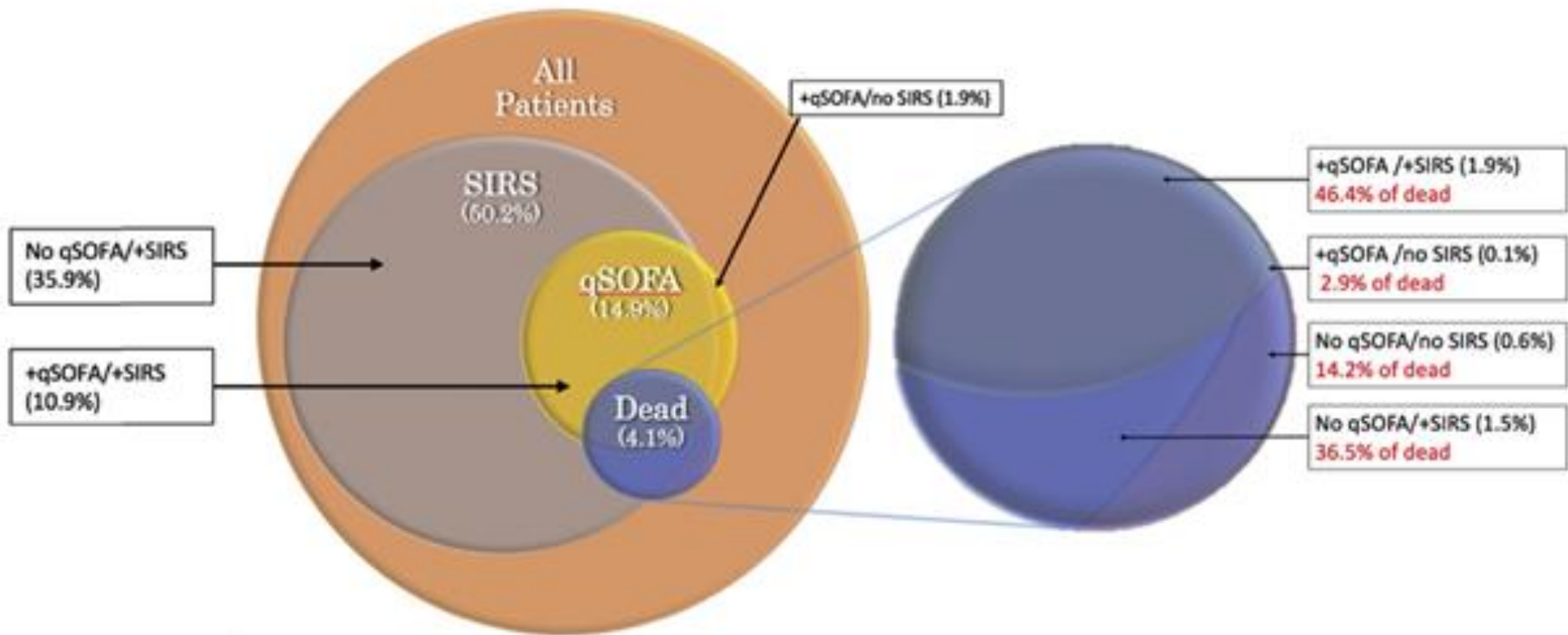
Of patients who <u>died:</u>

- 2.9% were identified by qSOFA alone
- 36.5% were identified by SIRS alone
- 46.4% were identified by both
- **14.2% did not meet either criterion**
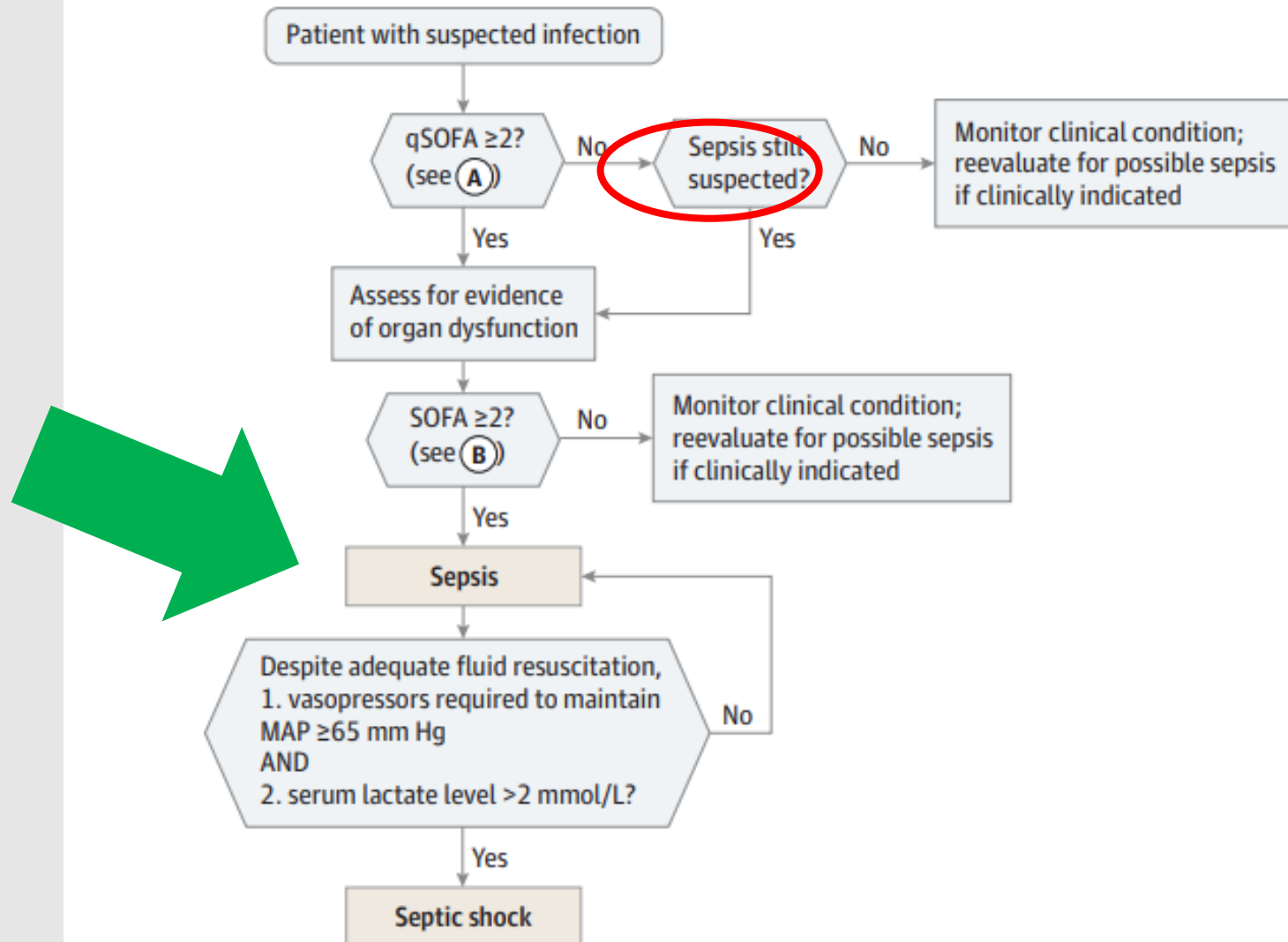
Source: Henning (2)

Low Accuracy of Positive qSOFA Criteria for Predicting 28-Day Mortality in Critically Ill Septic Patients During the Early Period After Emergency Department Presentation.

Only 60% of patients had + qSOFA in the first 5 hours in the ED.
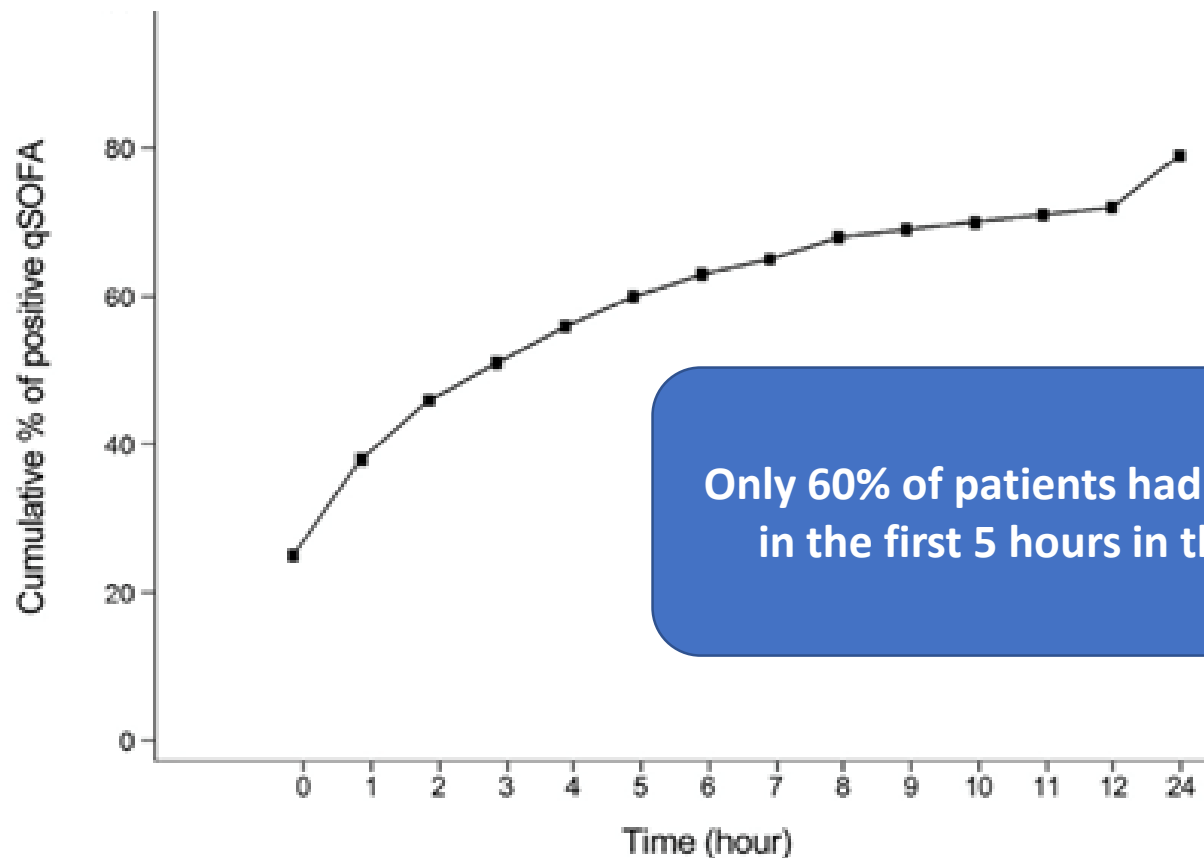
Time (hr)		0	1	2	3	4	5	6	7	8	9	10	11	12	24
Positive qSOFA (Total 1,396)	n	350	528	644	717	783	830	875	911	941	966	975	995	1,007	1,104
	%	25	38	46	51	56	60	63	65	67	69	70	71	72	79

Figure 2. Cumulative proportion of patients with positive qSOFA score.

Source: Hwang (3)

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

Patient with suspected infection

qSOFA ≥2? (see Ⓐ) — No → Sepsis still suspected? — No → Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Yes ↓ (qSOFA)
Yes ↑ (Sepsis still suspected)

Assess for evidence of organ dysfunction

SOFA ≥2? (see Ⓑ) — No → Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Yes ↓

Sepsis

Despite adequate fluid resuscitation,
1. vasopressors required to maintain MAP ≥65 mm Hg
AND
2. serum lactate level >2 mmol/L? — No → Sepsis

Yes ↓

Septic shock

Source: Singer (1)

Sepsis is ▮▮▮▮▮▮ life-threatening ▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮ ▮▮▮▮▮▮▮▮▮▮▮▮▮ infection.

YKHC's Adult Sepsis Clinical Guidelines

B

Yukon-Kuskokwim
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Sepsis – Adult

MSEC approved 7/12/17

qSOFA – 2 or more of the following:
RR > 22
altered mental status (GCS<15)
SBP < 100

Consider sepsis EARLY in *any* pt with suspected infection

Does pt meet criteria for sepsis or septic shock? —NO→

Reassess after initial evaluation -- consider
fever, leukocytosis, hypotension?
unexplained altered mental status?
tachypnea? especially if lungs CTA and SaO_2 WNL?
unexplained organ dysfunction?
clinical concern during ongoing care?

YES

Airway stable? —NO→

ET intubation
target tidal volume 6 mL/kg
for pts without ARDS

YES

Large bore IV x 2
LABS INCLUDING LACTATE, PCT & BLOOD CULTURES
START FLUID RESUSCITATION immediately: Give 1 L NS or LR bolus with target at least 30 ml/kg within 1-3 hr

START EMPIRIC ABX (see guidelines) within 1 hr of recognition of sepsis/septic shock

REASSESS FREQUENTLY
Assess for adequacy of fluid resuscitation or complications from fluid therapy

Monitor vital signs, UOP, shock index (HR/SBP > 0.7), mental status and clinical exam

SEPSIS 3 & ACEP NOTES

4-6L of total IVF is often needed during the first 6 hrs, after 2L of NS consider switch to LR, remember that if the patient fails to respond after the first 2-3 L, pressors should be considered.

In pts with concern for fluid overload (hx CHF, renal or liver failure) or complications from fluid resuscitation, use less total fluid or smaller boluses with more frequent reassessment of volume status, but **DO NOT DELAY FLUID AND VASOPRESSOR TREATMENT**

Persistence of elevated lactate, even in the absence of hypotension, is associated with poor outcomes

Village Management
- Aggressive hydration, PO if you can't get an IV and the patient is alert enough to drink
- Spplemental oxygen via nasal cannula
- Consider Ceftriaxone 2 grams IM
- Activate medevac
- Consider VTC

Early Recognition

gSOFA – 2 or more of the following:
RR > 22
altered mental status (GCS<15)
SBP < 100

Consider sepsis EARLY in *any* pt with suspected infection

Does pt meet criteria for sepsis or septic shock?

NO →

YES

Early Recognition

Suspected infection is difficult to identify

Consider screening for illness severity

Lower the threshold for treating infection

Yukon-Kuskokwim
HEALTH CORPORATION

Village Management

- Aggressive hydration, PO if you can't get an IV and the patient is alert enough to drink
- Spplemental oxygen via nasal cannula
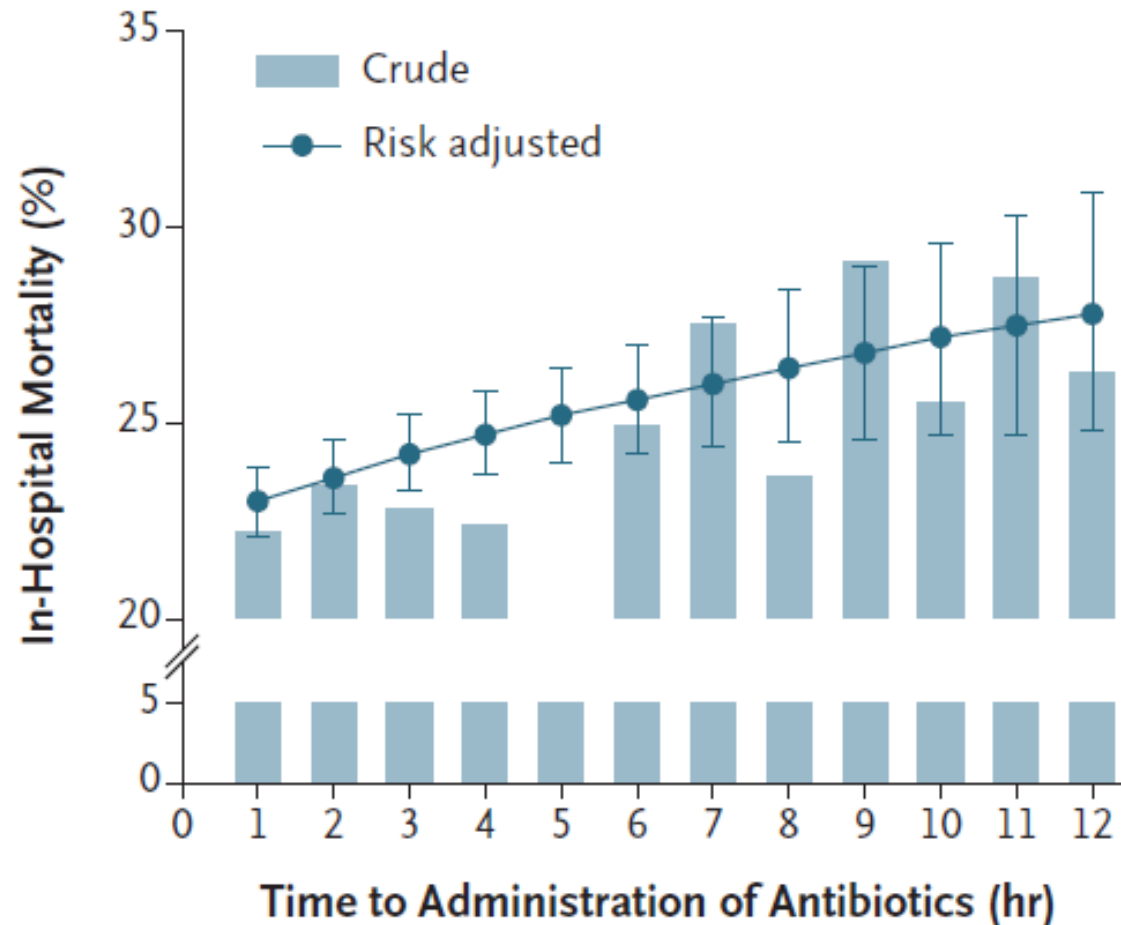- Consider Ceftriaxone 2 grams IM
- Activate medevac
- Consider VTC

Start Empiric Antibiotics

START EMPIRIC ABX (see guidelines) within 1 hr of recognition of sepsis/septic shock
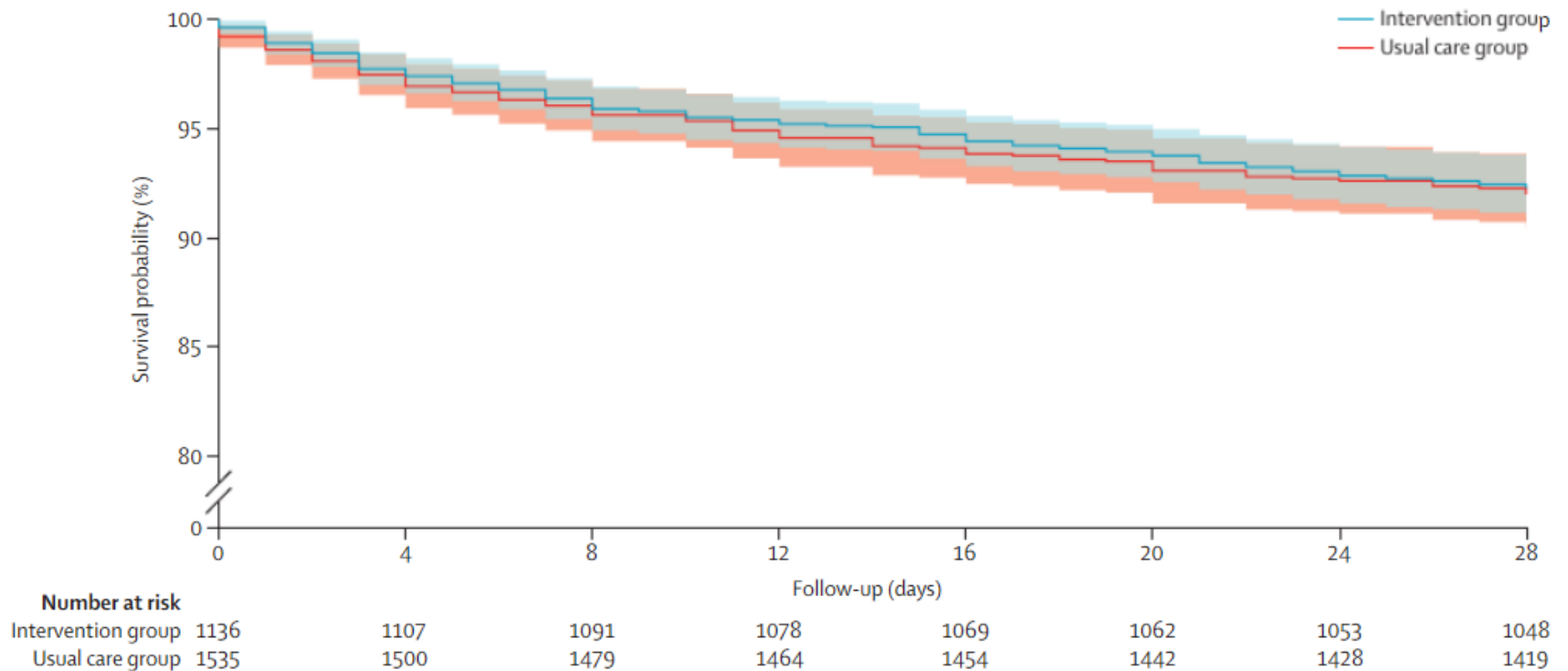
Antibiotic Administration

Source: Liu (4)

Antibiotic Administration

Source: Seymour (5)
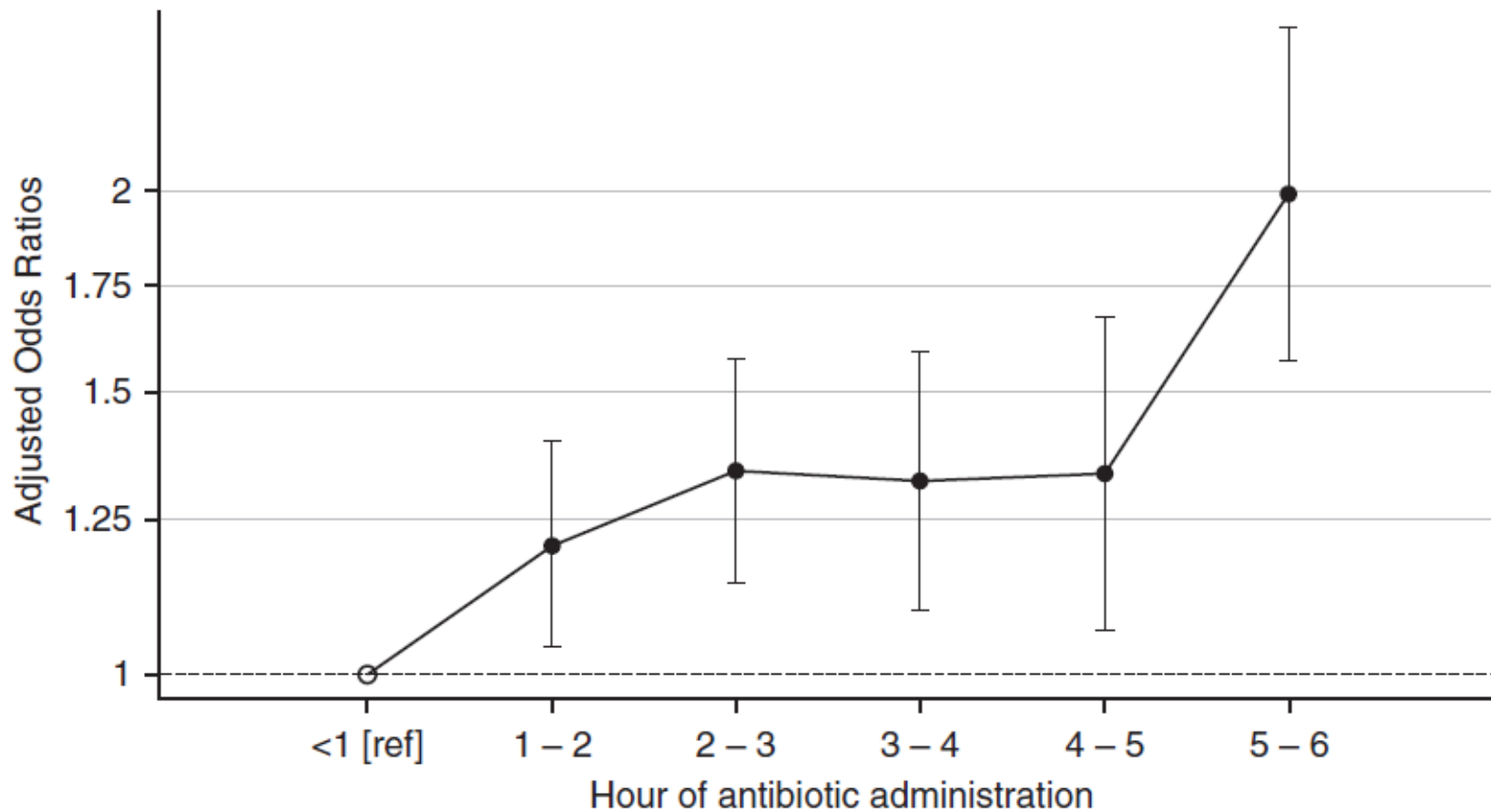
Antibiotic Administration

Recommendations

Caution a strong push for antibiotics within 1 hour if not in septic shock

Start antibiotics as early as possible

Intravenous Fluids

SEPSIS 3 & ACEP NOTES

4-6L of total IVF is often needed during the first 6 hrs, after 2L of NS consider switch to LR, remember that if the patient fails to respond after the first 2-3 L, pressors should be considered.

Intravenous Fluids in first 6 hours

	ProCESS		ARISE		ProMISe	
	EGDT	Usual Care	EGDT	Usual Care	EGDT	Usual Care
Pre-hospital to presentation	*	*	*	*	607	599
Presentation to randomization	2254	2083	2515	2591	1600	1790
Randomization to 6 hours	2805	2279	1964	1713	2000	1784
Total	**5059**	**4362**	**4479**	**4304**	**4207**	**4173**

Article titles above columns:
- ProCESS: A Randomized Trial of Protocol-Based Care for Early Septic Shock
- ARISE: Goal-Directed Resuscitation for Patients with Early Septic Shock
- ProMISe: Trial of Early, Goal-Directed Resuscitation for Septic Shock

Initial Bolus of Intravenous Fluids

Source: Seymour (5)
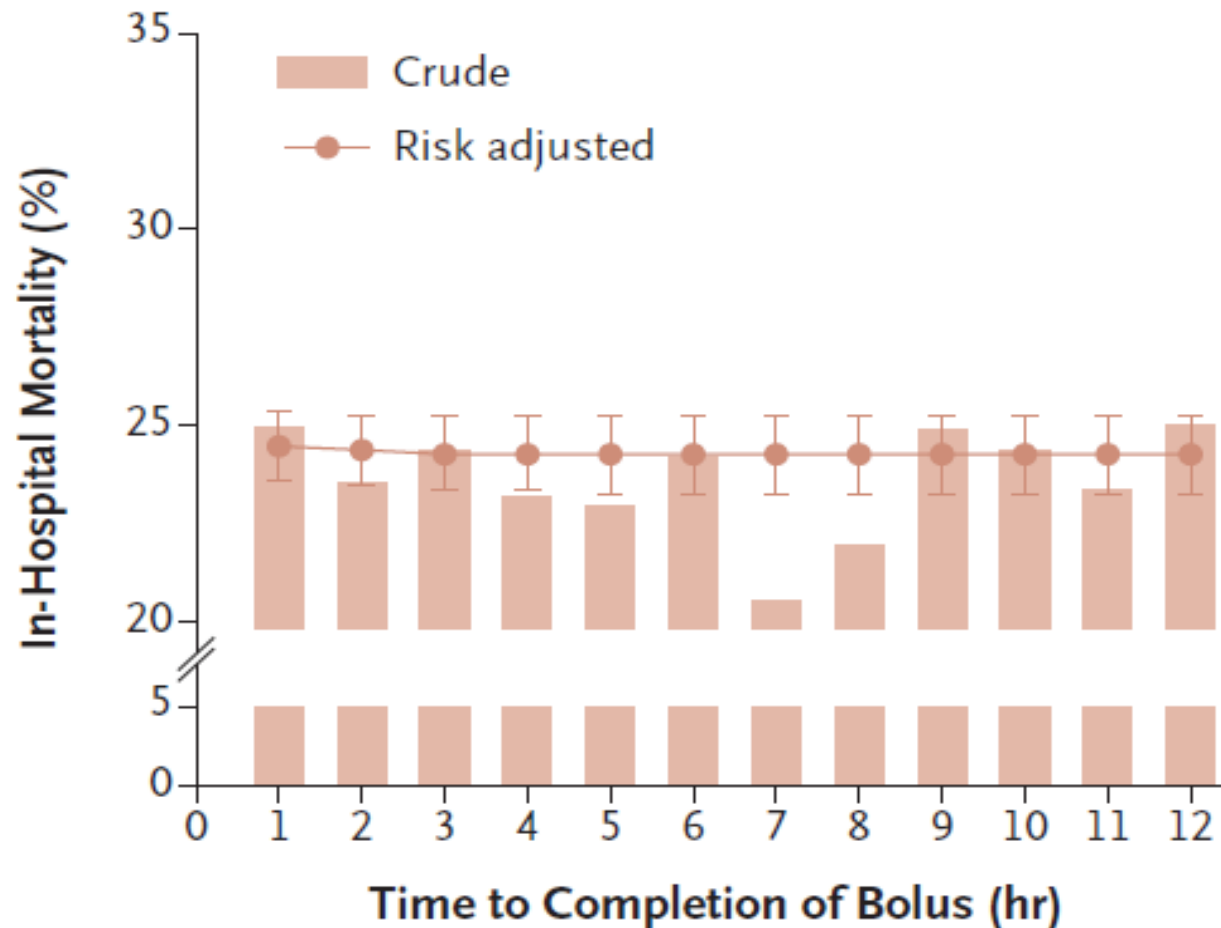
Recommendations

Fluid resuscitate to vital signs

Use Lactate Ringers as the primary if available

Lactate-Guided Resuscitation

No

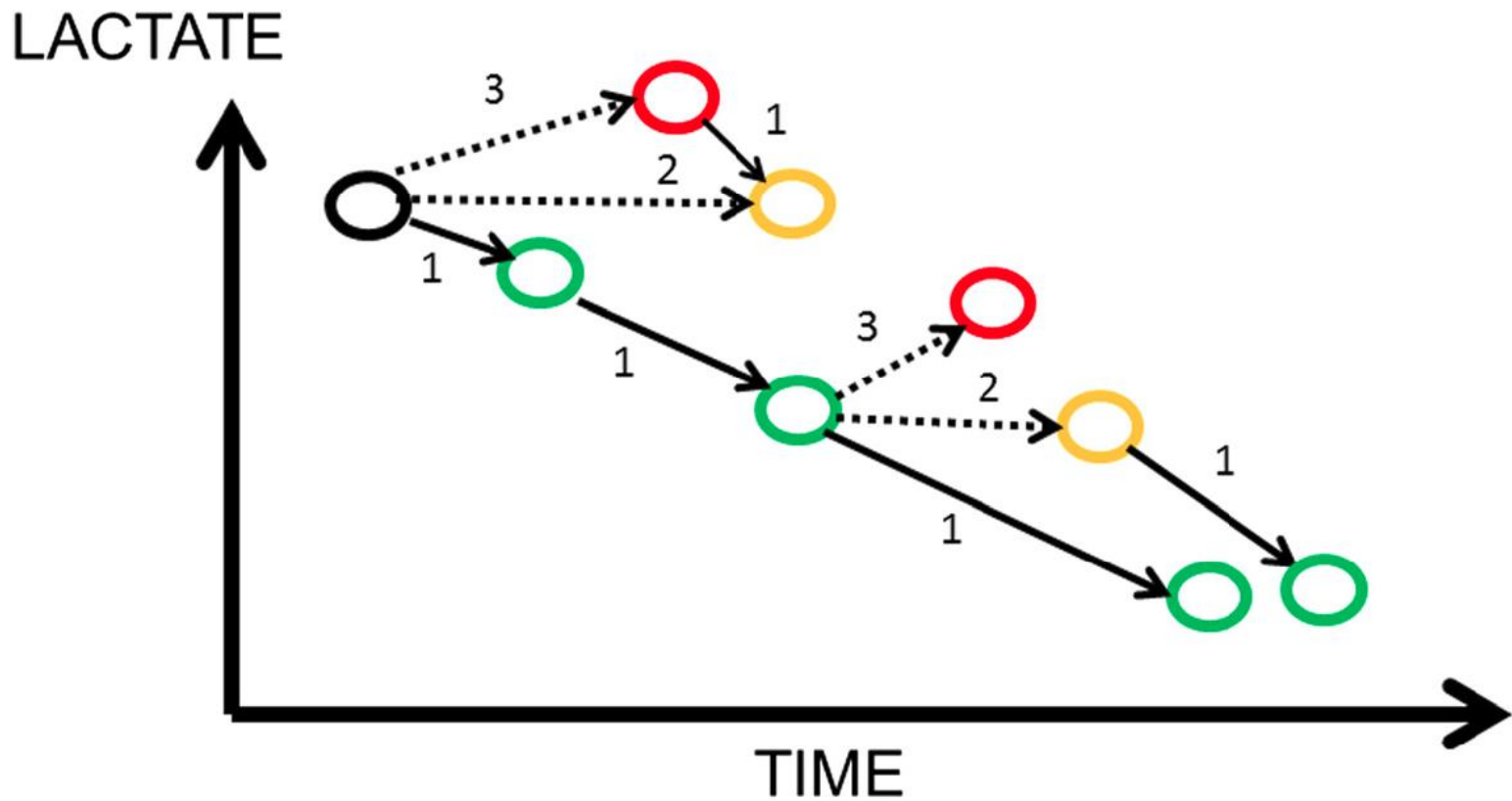If initial lactate is > 2:

RECHECK LACTATE 1-2 hrs after starting resuscitation

GUIDE RESUSCITATION TO NORMALIZE LACTATE
Primary goal should be to achieve a relative lactate
clearance of at least 10% in 1-2 hours

Lactate > 4 may indicate hypoperfusion and the need for
aggressive/continued fluid resuscitation

Blood Lactate Levels Over Time

Recommendations

Do not guide resuscitation to normalize lactate

Use vital signs, cap refill and urine output to guide resuscitation

Reassessments

REASSESS FREQUENTLY

Assess for adequacy of fluid resuscitation or complications from fluid therapy

Monitor vital signs, UOP, shock index (HR/SBP > 0.7), mental status and clinical exam

Use more than one method to assess resuscitation adequacy and use dynamic variables if possible

**CONSIDER CONSULT/TRANSFER** if unstable or not improving and **ACTIVATE MEDEVAC EARLY** if needed

Hydrocortisone

Consider hydrocortisone (see guidelines) *only* for septic shock not responsive to adequate fluid resuscitation and vasopressors
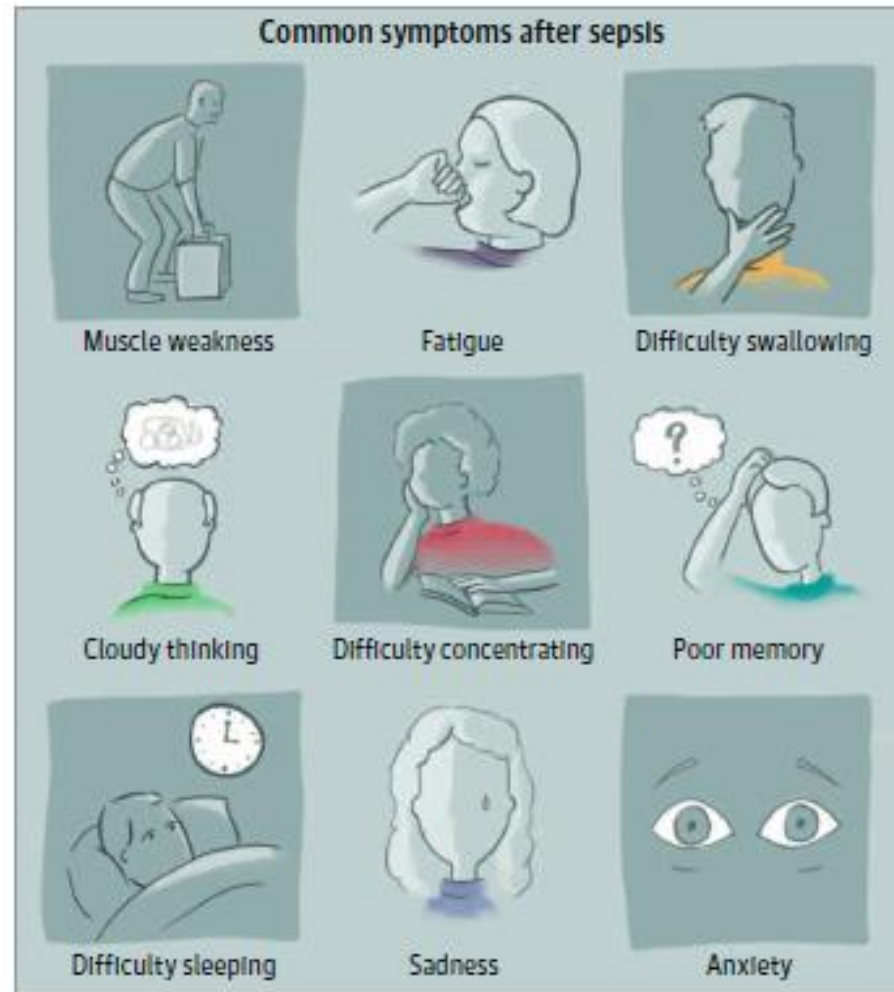
Recovery from Sepsis

Long-term Outcome After Sepsis

Figure 2. A Conceptual Model of the Potential Network of Factors and Interactions Important to Determining a Patient's Clinical Course and Long-term Outcome After Sepsis

Source: Prescott (11)
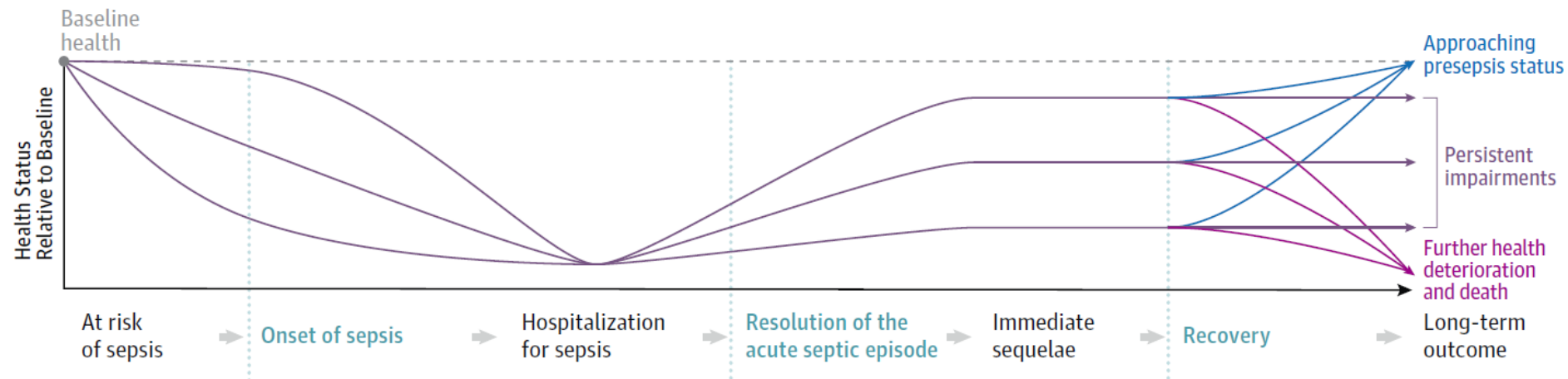
Common Symptoms After Sepsis

Source: Prescott (11)

J.K.'s Sepsis Story Continued

Questions

References

1. Singer, M.D., et al. *The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3*). JAMA, 2016.

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3. Hwang, S.Y., et al. *Low Accuracy of Positive qSOFA Criteria for Predicting 28-Day Mortality in Critically Ill Septic Patients During the Early Period After Emergency Department Presentatio*n. Annals of Emergency Medicine. 2018.

4. Liu, V.X., et al., *The Timing of Early Antibiotics and Hospital Mortality in Sepsis.* American Journal of Respiratory and Critical Care Medicine, 2017.

5. Seymour, C.W., et al., *Time to Treatment and Mortality during Mandated Emergency Care for Sepsis.* The New England Journal of Medicine, 2017.

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6. Alam, N., et al., *Prehospital antibiotics in the ambulance for sepsis: a multicentre, open label, randomised trial.* The Lancet Respiratory Medicine, 2018.

7. The ProCESS Investigators, *A randomized trial of protocol-based care for early septic shock.* The New England Journal of Medicine, 2014.

8. The ARISE Investigators and the ANZICS Clinical Trials Group. *Goal-directed resuscitation for patients with early septic shock.* The New England Journal of Medicine, 2014.

9. Mouncey, P.R., et al. *Trial of early, goal-directed resuscitation for septic shock*. The New England Journal of Medicine, 2015.

10. Vincent, J.L., et al., *The Value of Blood Lactate Kinentics in Critically Ill Patients: A Systematic Review,* Critical Care, 2016.

11. Prescott, H.C., Angus, D.C., *Enhancing Recovery from Sepsis: A Review.* JAMA, 2018.