



Sepsis Care in 2025: From Early Recognition to Long-Term Recovery

**Kyle R. Stinehart, MD, MPH**September 2025

# **Objectives**

- 1. Review sepsis by the numbers, including evolving definitions.
- 2. Discuss early recognition of sepsis and review the one-hour bundle.
- 3. Review what we know, and what we don't, about:
  - Antibiotics and source control
  - Fluid resuscitation
  - Vasopressors and hemodynamic support
- 4. Discuss sepsis survivorship, including evolving care models to improve post-hospitalization care.

# **Surviving Sepsis Campaign**

# Surviving Sepsis · · · Campaign · ·





# **Sepsis – Fast Facts**

1.7 million adults in the US/year

At least 350,000 adults with sepsis die during hospitalization

1 in 3 hospital deaths occur in patients who had sepsis

Most cases start before hospitalization

Disproportionally affects those with underlying chronic disease

~1/4 to 1/3 of people with sepsis had a healthcare visit the week before they were hospitalized

**Source:** CDC.gov

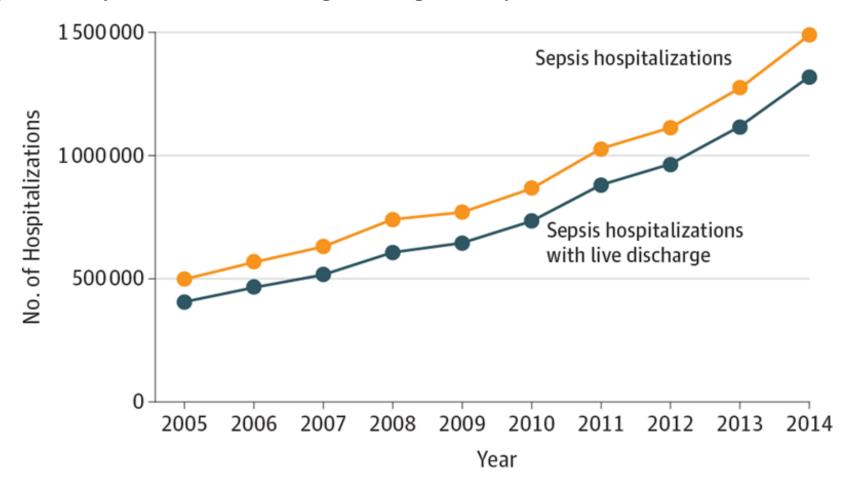
# **Sepsis – Fast Facts**

- Cost \$23.7 billion in 2013
  - 6% of cost for all hospitalizations
  - Acute MI: \$12.1 billion
  - CHF: \$10.2 billion
  - COPD: \$5 billion

Sources: CDC.gov, AHRQ.gov

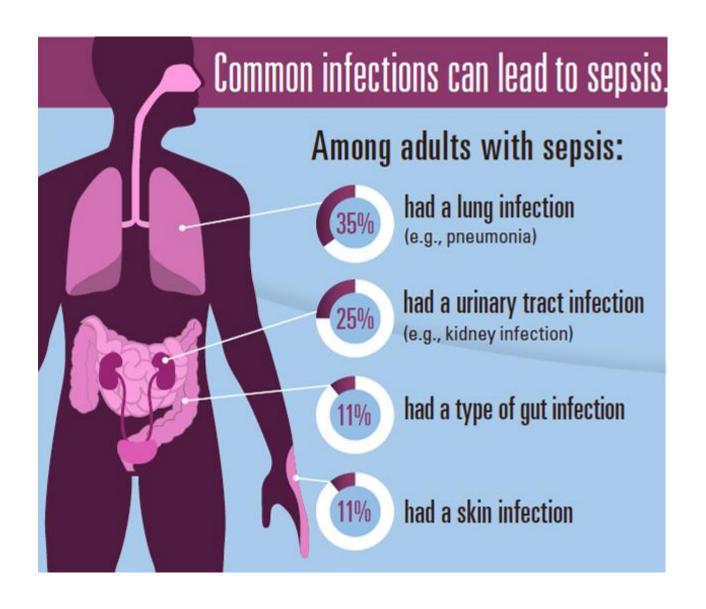
# Sepsis Hospitalizations are Increasing

Figure 1. US Hospitalizations and Live Discharges for a Diagnosis of Sepsis, 2005-2014

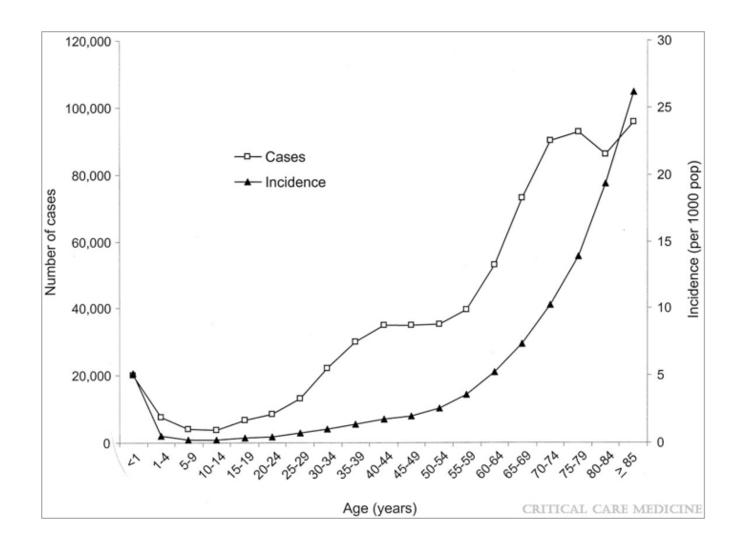


Source: Prescott JAMA 2018

#### Who is at risk?



# Who is at risk?



Source: Angus et al. Critical Care Medicine. 2001.

# Pathophysiology (in 1 slide)

Anti-inflammatory mediators

Pro-inflammatory mediators

#### **Cellular injury caused by:**

- Tissue ischemia
- Direct injury from inflammatory mediators
- Endothelium damage and activation of coagulation cascade
- Changes in cell death pathways



**Organ Dysfunction** 

# **Sepsis – Current Definition**

#### Sepsis:

- Life-threatening organ dysfunction caused by a dysregulated host response to infection (Sepsis-3, 2016).
- Suspected or confirmed infection plus acute increase in SOFA score ≥ 2

#### Septic Shock

- Sepsis with circulatory and cellular/metabolic dysfunction
- Clinical criteria: vasopressor requirement to maintain MAP ≥ 65 mm Hg and lactate > 2 mmol/L despite appropriate fluids

# **Sepsis Defined**

Definitions	Sepsis-1 (1991)	Sepsis-2 (2001)
Sepsis	<ul> <li>Systemic response to infection</li> <li>2 or more SIRS criteria (fever, tachycardia, tachypnea, WBC abnormality)</li> </ul>	Similar to sepsis-1     with added     clinical details
Severe Sepsis	<ul> <li>Sepsis associated with organ dysfunction</li> </ul>	Similar to sepsis-1     with added     clinical details
Septic Shock	Severe sepsis +     persistent hypotension     despite fluids	Similar to sepsis-1     with added     clinical details

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Severe Sepsis	Sepsis associated with organ dysfunction	Similar to sepsis-1     with added     clinical details	No longer a diagnosis
Septic Shock	Severe sepsis +     persistent hypotension     despite fluids	Similar to sepsis-1     with added     clinical details	<ul> <li>Sepsis + vasopressor requirement to maintain MAP ≥ 65 mm Hg and lactate</li> <li>&gt; 2 mmol/L despite appropriate fluids</li> </ul>

# Systemic Inflammatory Response Syndrome (SIRS)

Two or more of the following:			
Temperature	>38°C or <36°C		
Heart Rate	>90 beats/min		
Respiratory Rate	>20 breaths/min or PaCO <sub>2</sub> <32 mm Hg on ABG		
WBC count	>12,000/mm³ or <4,000/mm³, or >10% bands		

Source: Meyer and Prescott, NEJM 2024

# Sequential Organ Failure Assessment (SOFA) Score

#### Sequential Organ Failure Assessment (SOFA) Score

System	Criteria	0		2	3	4
Respiratory	PaO <sub>2</sub> /FiO <sub>2</sub> (partial pressure	≥400 mmHg	<400 mmHg (53.3 kPa)	<300 mmHg (40 kPa)	<200 mmHg (26.7 kPa)	<100 mmHg (13.3 kPa)
	of oxygen over fraction of inspired oxygen)	(53.3 kPa)			with respiratory support	
Coagulation	Platelets	≥150 x10³/µL	<150 x10 <sup>3</sup> /µL	<100 x10 <sup>3</sup> /µL	<50 x10³/µL	<20 x10 <sup>3</sup> /µL
Liver	Bilirubin	<1.2 mg/dL (20 µmol/L)	1.2-1.9 mg/dL (20-32 µmol/L)	2.5-5.9 mg/dL (33-101 µmol/L)	6-11.9 mg/dL (102-204 µmol/L)	>12 mg/dL (204 µmol/L)
Cardiovascular	Mean aterial pressure (MAP) or vasopressors requirement	MAP ≥70mmHg	MAP <70mmHg	Dopamine <5 µg/kg/min or dobutamine (any dose)*	Dopamine 5.1-15 µg/kg/min* or epinephrine ≤0.1 µg/kg/min or norepinephrine ≤0.1 µg/kg/min*	Dopamine >15 µg/kg/min or epinephrine >0.1 µg/kg/min or norepinephrine >0.1 µg/kg/min'
Neurologic	Glasgow coma scale score	15	13-14	10-12	6-9	<6
Renal	Creatinine (Cr) or urine output (UOP)	Cr <1.2 mg/dL (110 µmol/L)	Cr 1.2-1.9 mg/dL (110-170 µmol/L)	Cr 2.0-3.4 mg/dL (171-299 µmol/L)	Cr 3.5-4.9 mg/dL (300-440 µmol/L) or UOP <500 cc/day	Cr >5 mg/dL (440 µmol/L) or UOP <200 cc/day

- Change in SOFA score of 2 or more points from baseline = how we define sepsis using the most updated definition (sepsis-3)
- Good sensitivity and specificity
- Not practical to use, especially outside of the ICU

<sup>\*</sup>Doses given for at least 1 hour

# Quick SOFA (qSOFA)

- At least two of the following:
  - Altered mental status (GCS ≤ 13)
  - RR ≥ 22/min
  - SBP ≤ 100 mm Hg

# SSC Recommendation: Don't Screen with qSOFA



We **recommend against** using qSOFA compared with SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock. Strong recommendation, moderatequality evidence.

#### **MEWS** and **NEWS**

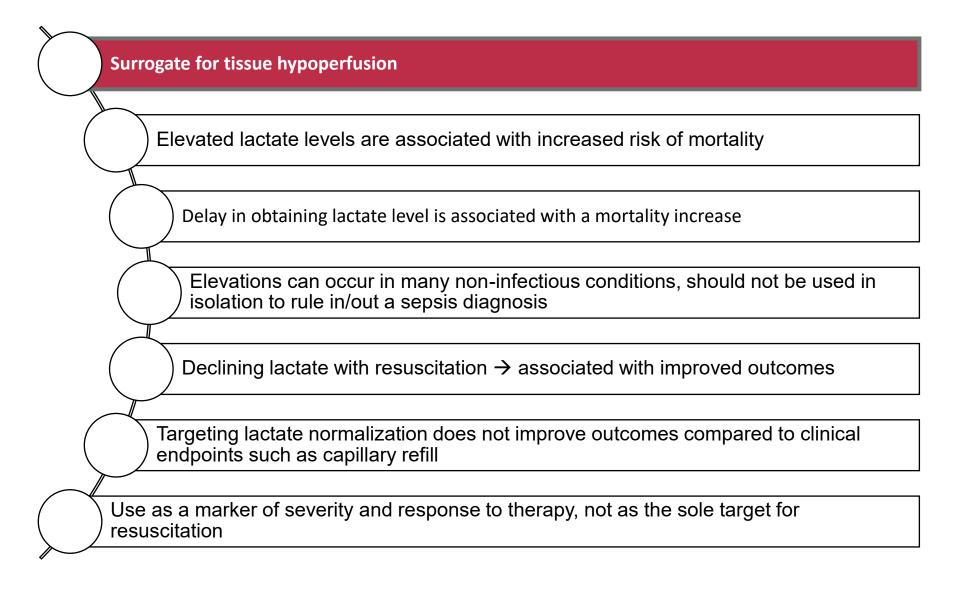
Score	Components	Positive Threshold	Sensitivity (Sepsis)	Specificity (Sepsis)	AUROC (Sepsis)	References
Modified Early Warning Score (MEWS)	RR, HR, SBP, Temp, AVPU*	≥5	59–87%	69–70%	0.70-0.84	[1-4]
National Early Warning Scale (NEWS)	RR, O2 sat, O2 use, Temp, SBP, HR, AVPU*	≥7	71–84%	66–85%	0.80-0.91	[2-3, 5-9]

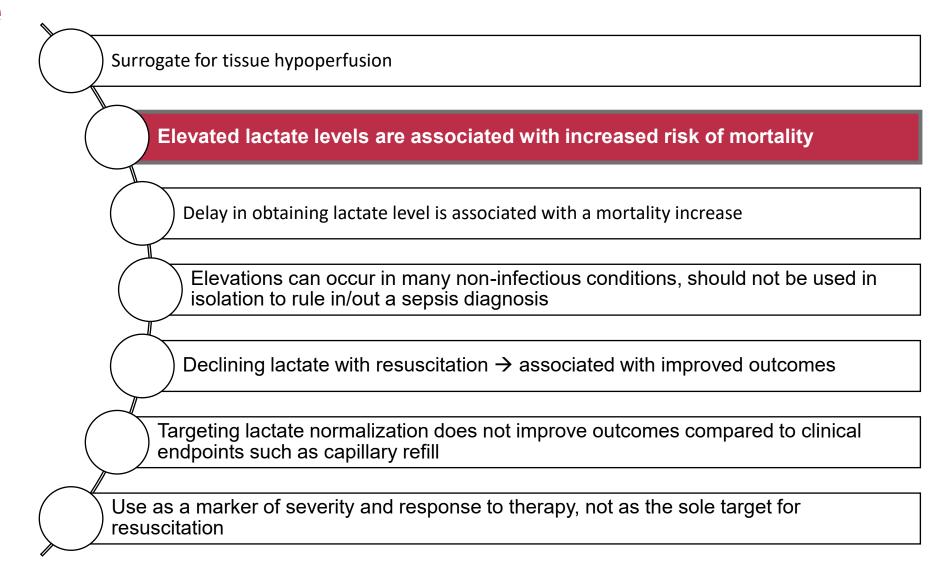
<sup>\*</sup>AVPU = mental status evaluation (Alert, Verbal, Pain, Unresponsive)

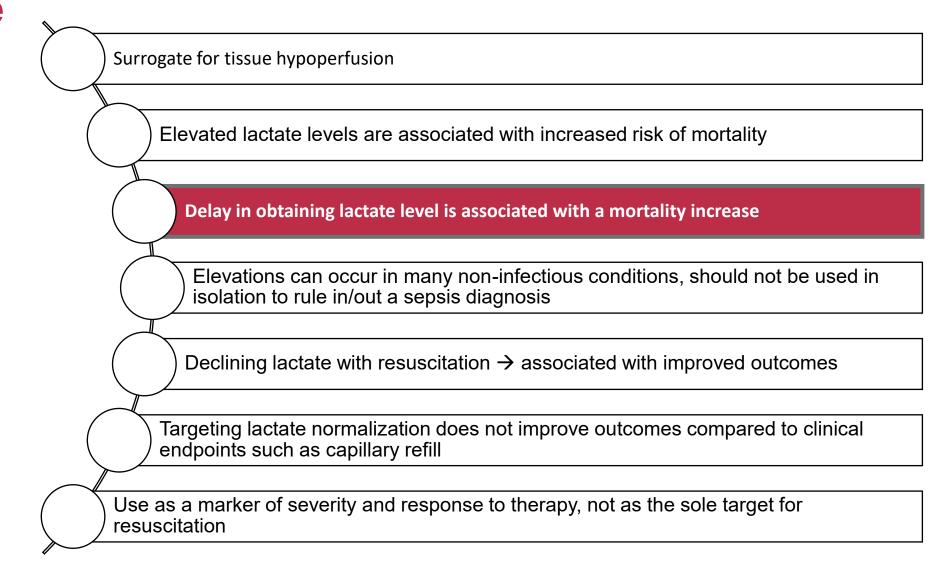
**Sources:** 1. Wattanasit and Khwannimit, AJEM 2021. 2. Guan et al, PloS One 2022. 3. Churpek et al, AJRCCM 2017. 4. Lin et al, Clinical Chemistry and Laboratory Medicine 2023. 5. Usman OA et al AJEM 2019. 6. Qiu et al, Expert Review of Anti-Infective Therapy 2023. 7. Brink et al, PloS One 2019. 8.Oduncu et al, AJEM 2021. 9. Lie VX et al, JAMA Network Open 2020.

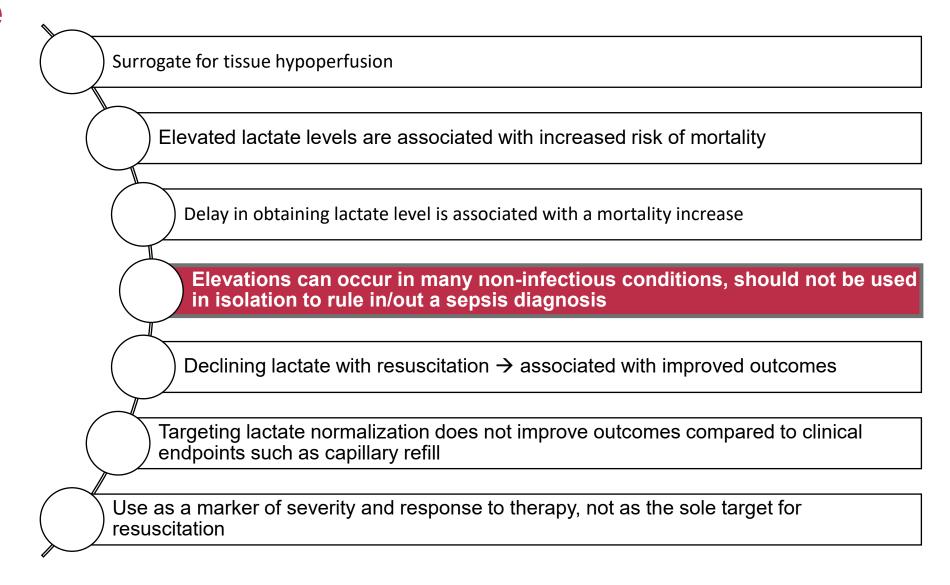
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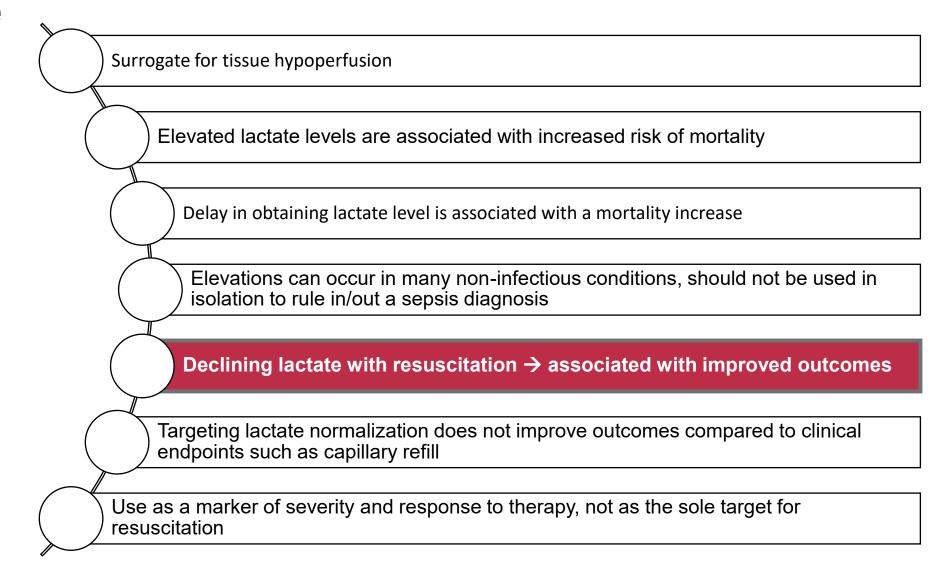
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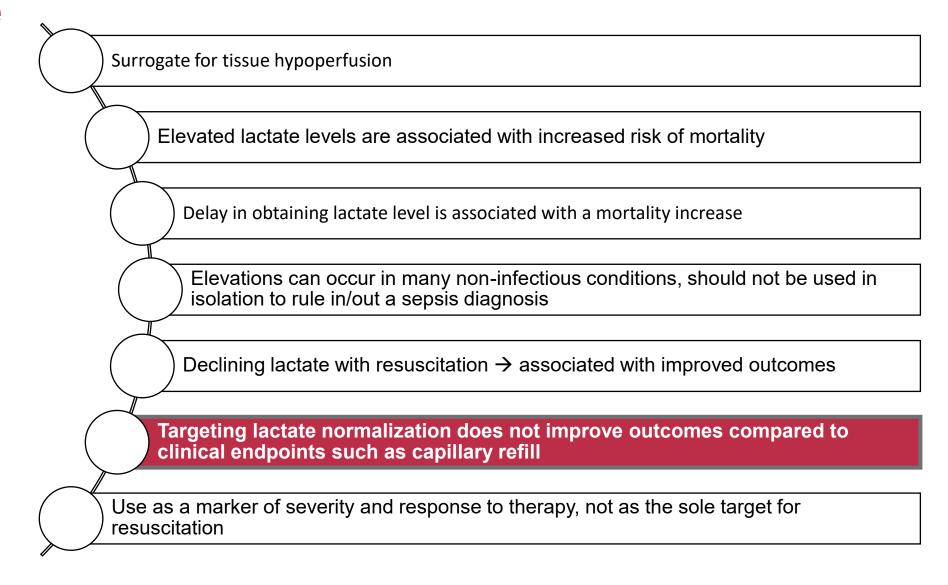


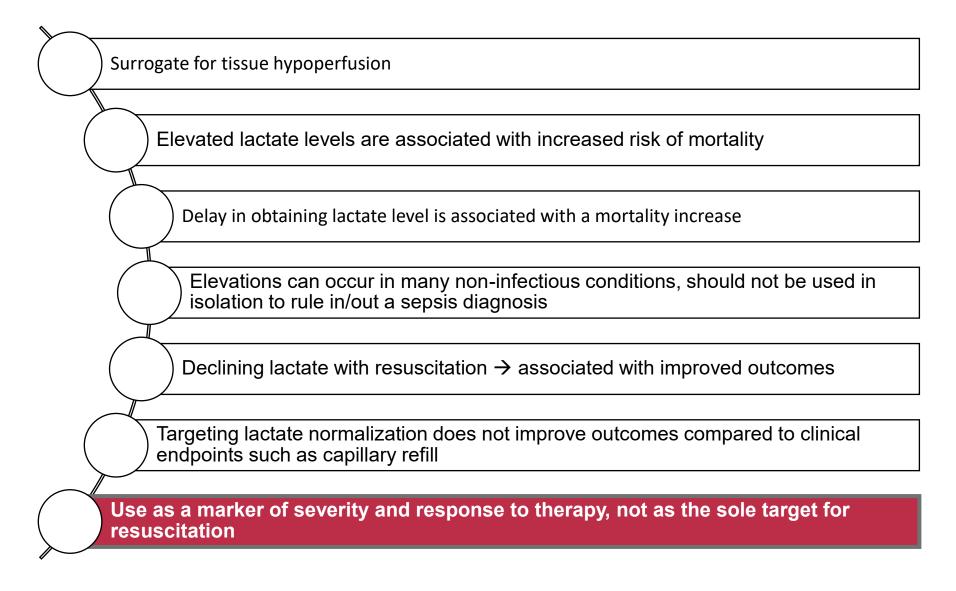












#### **SSC Recommendation: Lactate**



For adults suspected of having sepsis, we **suggest** measuring blood lactate.

#### SSC Recommendation: The Hour-1 Bundle





**BUNDLE** 

# HOUR-1 BUNDLE: INITIAL RESUSCITATION FOR SEPSIS AND SEPTIC SHOCK:

- Measure lactate level.\*
- 2) Obtain blood cultures before administering antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30mL/kg crystalloid for hypotension or lactate ≥4 mmol/L.
- Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure ≥ 65 mm Hg.

\*Remeasure lactate if initial lactate elevated (> 2 mmol/L).

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survivingsepsis.org

#### Recognize sepsis/septic shock. Within one hour, begin the following:

- 1. Measure lactate level. Remeasure lactate if initial lactate is > 2 mmol/L.
- 2. Obtain blood cultures before administering antibiotics (but don't delay antibiotics).

- 3. Administer broad spectrum antibiotics.
- 4. Begin rapid administration of 30 mL/kg of crystalloid for hypotension or lactate ≥ 4 mmol/L.
- 5. Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure of ≥ 65 mm Hg.

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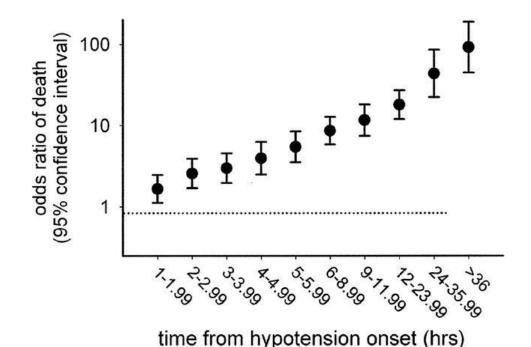
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# Antibiotic Delay in Septic Shock → Higher Mortality

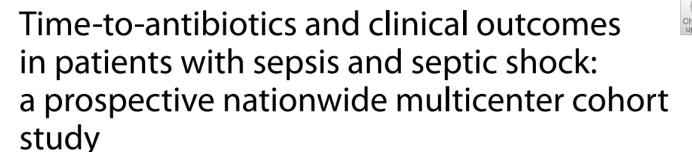
# Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock

Kumar, Anand MD; Roberts, Daniel MD; Wood, Kenneth E. DO; Light, Bruce MD; Parrillo, Joseph E. MD; Sharma, Satendra MD; Suppes, Robert BSc; Feinstein, Daniel MD; Zanotti, Sergio MD; Taiberg, Leo MD; Gurka, David MD; Kumar, Aseem PhD; Cheang, Mary MSc **Author Information** ⊗

Critical Care Medicine: June 2006 - Volume 34 - Issue 6 - p 1589-1596



RESEARCH Open Access



Yunjoo Im<sup>1†</sup>, Danbee Kang<sup>2†</sup>, Ryoung-Eun Ko<sup>3</sup>, Yeon Joo Lee<sup>4</sup>, Sung Yoon Lim<sup>4</sup>, Sunghoon Park<sup>5</sup>, Soo Jin Na<sup>3</sup>, Chi Ryang Chung<sup>3</sup>, Mi Hyeon Park<sup>6</sup>, Dong Kyu Oh<sup>6</sup>, Chae-Man Lim<sup>6</sup> and Gee Young Suh<sup>1,3,7\*</sup> on behalf of the Korean Sepsis Alliance (KSA) investigators

- In patients with sepsis and shock who received antibiotics within 3 hours, every 1-hour delay in antibiotics showed a 35% increased risk of mortality
- In patients with sepsis but without shock timing less clear

**Source:** Im et al. Critical Care Medicine, 2022.

RESEARCH Open Access



# Mortality and antibiotic timing in deep learning-derived surviving sepsis campaign risk groups: a multicenter study

Ben J. Gross<sup>3</sup>, Allison Donahue<sup>1</sup>, James S. Ford<sup>1</sup>, Xiaolei Lu<sup>3</sup>, Aaron Boussina<sup>3</sup>, Atul Malhotra<sup>4</sup>, Kai Zheng<sup>5</sup>, Shamim Nemati<sup>3</sup> and Gabriel Wardi<sup>1,2,4\*</sup>

	Likelihood of Sepsis		
	Shock unlikely to develop, sepsis possible	Shock unlikely to develop, sepsis probable	
Likelihood of shock	Shock likely to develop, sepsis possible	Shock likely to develop, sepsis probable	

- Patients with possible sepsis and low risk of shock had similar rates of mortality when given antibiotics within 1 hour of triage, between 1-3 hours of triage, and >3 hours after triage
- Patients with probable sepsis had lower mortality if antibiotics were administered within 1 hour from triage, regardless of the risk of shock

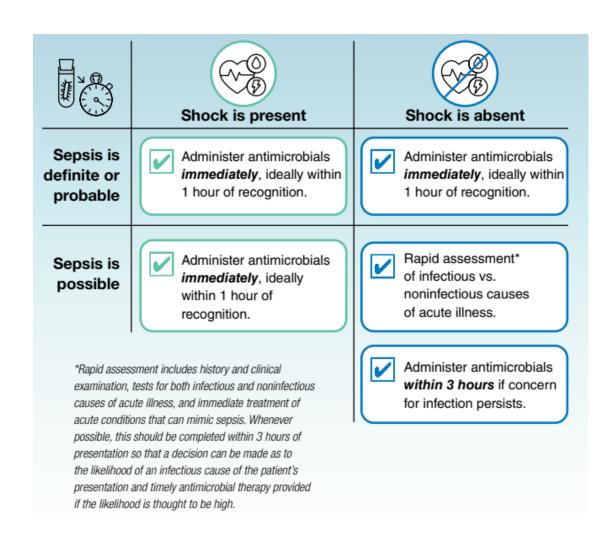
**Source:** Gross et al. Critical Care, 2025.

# **Antibiotic Timing – Summary of Data**

- Earlier administration in patients with septic shock or high likelihood of sepsis is associated with a lower mortality
  - 35% increase in mortality risk for every hour delay in patients with septic shock
- Patients with lower likelihood of shock or less certain sepsis, more lenient timing (up to three hours) does not appear to adversely affect outcomes and may allow for more diagnostic clarity, reducing unnecessary antibiotic exposure

# **SSC Recommendations: Antibiotic Timing**





#### **Antibiotic Choice**

- Appropriate initial antibiotics improve survival
- What are appropriate antibiotics?
  - Broad, dependent on source and local antibiograms
  - Consider MRSA, MDR Gram negative coverage
- Early de-escalation based on microbiologic data and clinical response reduces adverse effects and resistance
- Don't forget about source control

#### **The Hour-1 Bundle**

Recognize sepsis/septic shock. Within one hour, begin the following:		Questions:
1.	Measure lactate level. Remeasure lactate if initial lactate is > 2 mmol/L.	
2.	Obtain blood cultures before administering antibiotics (but don't delay antibiotics).	Antibiotic timing? Antibiotic choice?
3.	Administer broad spectrum antibiotics.	
4.	Begin rapid administration of 30 mL/kg of crystalloid for hypotension or lactate ≥ 4 mmol/L.	How much fluid? Which type of fluid is best?
5.	Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure of ≥ 65 mm Hg.	

**Source:** Surviving Sepsis Campaign, 2021.

#### SSC Recommendation: Initial Resuscitation

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For patients with sepsis induced hypoperfusion or septic shock, we suggest that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hours of resuscitation.

Weak, low quality of evidence

#### How Much Fluid: Initial Resuscitation

- Observational/retrospective data:
  - Under-resuscitation (<20 mL/kg) → increased mortality
  - Over-resuscitation (>45 mL/kg) → possible harm
  - Survival benefit is observed when 30 mL/kg is completed within 3 hours

Source: Ward, Kuttab, and Badgett. Critical Care Medicine, September 2025.

## How Much Fluid: Subsequent Resuscitation

#### Trial:

- CLASSIC (Conservative vs. Liberal Approach to Fluid Therapy of Septic Shock in Intensive Care)
- All patients received initial IV fluids for resuscitation, then:
  - Restrictive group (only given for signs of severe hypoperfusion)
  - Liberal group/standard of care

#### **Outcome:**

- No difference in 90-day mortality, AKI, days alive out of the hospital
- Restrictive group received about 1.6 fewer liters of fluid over five days, but no difference in survival or organ function

**Source:** Meyhoff TS et al. NEJM, 2022.

## How Much Fluid: Subsequent Resuscitation

#### Trial:

- CLOVERS (Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis)
- All patients received initial IV fluids for resuscitation (30 mL/kg), then:
  - Restrictive group (vasopressor-predominant)
  - Liberal (fluid-predominant)

#### **Outcome:**

No difference in 90-day mortality, organ failure, hospital free days

**Source:** Shapiro et al. NEJM, 2023.

#### How Much Fluid: Subsequent Resuscitation

#### Assessment for further fluids should be guided by dynamic measures:

- Passive leg raise test
- Stroke volume
- Pulse pressure
- Echocardiogram
- Capillary refill time

Source: Surviving Sepsis Campaign, 2021.

#### **SSC Recommendations: Fluid Choice**



For adults with sepsis or septic shock, we **recommend** using crystalloids as first-line fluid for resuscitation.

Strong recommendation, moderate quality of evidence.

For adults with sepsis or septic shock, we **suggest** using balanced crystalloids instead of normal saline for resuscitation.

Weak recommendation, low quality of evidence.

#### **Fluid Choice**

## Balanced crystalloids (lactated Ringers, Plasma-Lyte) preferred over normal saline

 Rationale: balanced crystalloids have a lower chloride content, which reduces the risk of hyperchloremic metabolic acidosis and AKI

#### SMART trial

- 1,641 patients with sepsis
- Balanced fluids resulted in a **lower rate of major adverse kidney events** and a **significant reduction in 30-day in-hospital mortality** (26.3% with balanced fluids versus 31.2% with normal saline)

Source: Semler et al. NEJM, 2018.

#### **The Hour-1 Bundle**

Recognize sepsis/septic shock. Within one hour, begin the following:		Questions:
1.	Measure lactate level. Remeasure lactate if initial lactate is > 2 mmol/L.	
2.	Obtain blood cultures before administering antibiotics (but don't delay antibiotics).	Antibiotic timing? Antibiotic choice?
3.	Administer broad spectrum antibiotics.	
4.	Begin rapid administration of 30 mL/kg of crystalloid for hypotension or lactate ≥ 4 mmol/L.	How much fluid? Which type of fluid is best?
5.	Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure of ≥ 65 mm Hg.	Vasopressor choice? When to start?

**Source:** Surviving Sepsis Campaign, 2021.

#### SSC Recommendations: Vasopressor Choice



For adults with septic shock, we **recommend** using norepinephrine as the first-line agent over other vasopressors.

Strong recommendation.

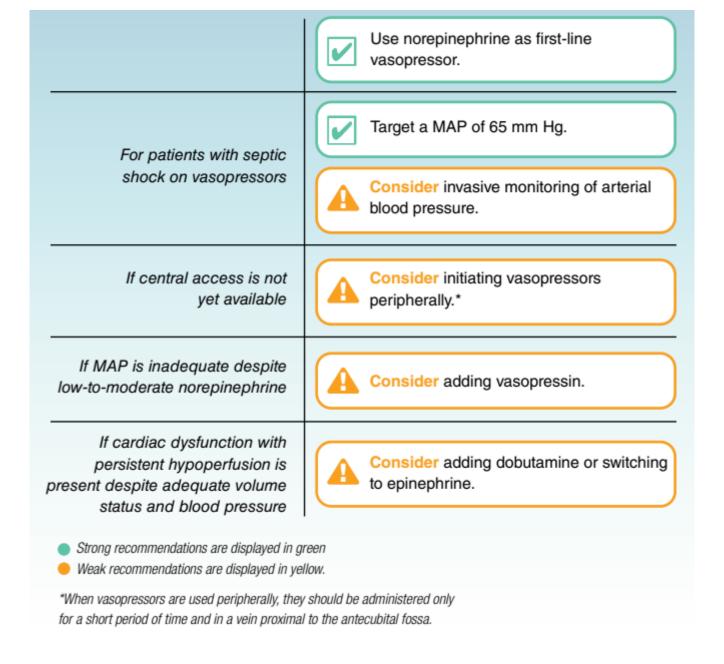
## **Vasopressor Choice**



- Norepinephrine recommended as first-line
- Add vasopressin if MAP is still inadequate

## **Vasopressor Timing**

- Newer data suggests earlier initiation of norepinephrine, within the first
   1 to 3 hours of septic shock onset and often in parallel with initial fluid resuscitation, is associated with:
  - Reduced short-term mortality
  - Less fluid overload
  - Improved organ function
- Don't delay vasopressors for central line consider starting peripherally



**Source:** Surviving Sepsis Campaign, 2021.

## **Sepsis Survivorship**

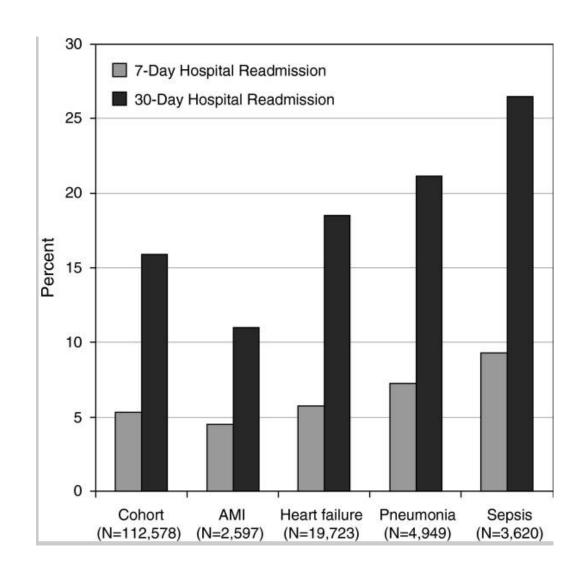
Mean 1-year mortality for patients with sepsis: 16.1%

More severe, ICU-level cases: ~1/3

Sources: Goodwin. Crit Care Med, 2015. Shankar-Hari et al. JAMA Network Open, 2020.

#### Sepsis Survivorship

**40%** will be readmitted within 90 days



Sources: Goodwin. Crit Care Med, 2015. Jones. Ann Am Thorac Soc, 2015.

## Sepsis Survivorship

- Over 30% are discharged to SNF, LTACH, or acute rehab
- An additional 30% require home healthcare services, more likely than non-sepsis patients
- Majority of costs related to sepsis occur after the initial hospitalization



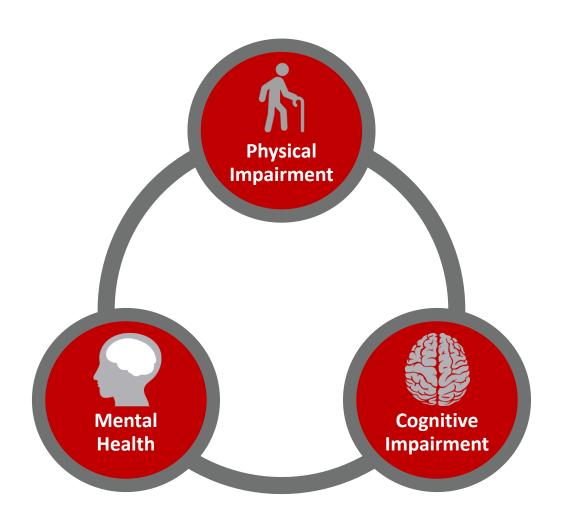
Sources: Tiru. Pharmaco Economics, 2015. Jones. Ann Am Thorac Soc, 2015. Prescott et al. AJRCCM, 2014.

#### **Sepsis and Patient Experience**

- Survey from US, UK, Canada
- Survivors were "somewhat dissatisfied" to "somewhat satisfied" with the support services provided:
  - Counseling
  - PT
  - Knowledge about sepsis
  - Expectations after discharge

**Source:** Huang, Critical Care Medicine, 2016.

## Post-Sepsis (Post Intensive-Care) Syndrome



- One or more new or worsening impairments that occur after sepsis and persist beyond the hospital stay
- Common (>50%) and underrecognized

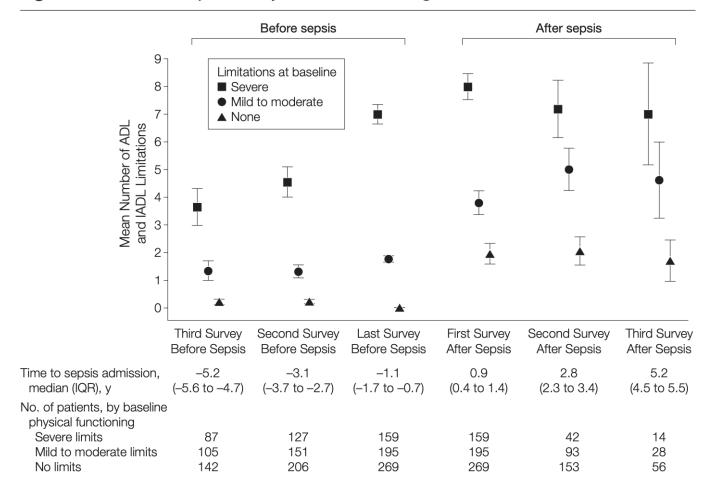
## **Physical Function After Sepsis**

- Fatigue, insomnia
- Weakness
- Dyspnea
- Muscle, joint pain
- Swelling
- Poor appetite
- Difficulty swallowing
- Hair loss



## **Physical Function After Sepsis**

Figure 3. Functional Trajectories by Baseline Functioning



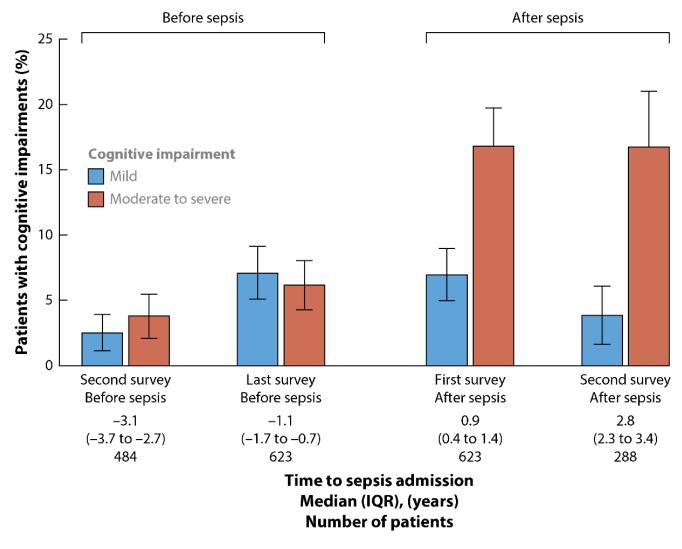
Those that went into a sepsis hospitalization with no physical impairments or a mild/moderate number of impairments left with **1-2** *new* impairments

#### **Cognitive Function After Sepsis**



- Attention
- Memory
- Verbal fluency and word-finding
- Executive functioning

## **Cognitive Function After Sepsis**



## **Mental Health After Sepsis**

- Anxiety
- Depression
- PTSD





#### **Prevention of Post-Sepsis Impairments**

- Early recognition and evidence-based treatment of sepsis to avoid prolonged hospitalizations
- Implementation of the ICU Liberation Bundle for critically-ill patients
- Early mobility to decrease physical deficits and delirium

**Source:** Prescott. JAMA, 2018.

#### **ICU Liberation Bundle**



## **SSC:** Post-Hospital Recommendations



Screening for economic and social support

Referral to peer support groups

Shared decision-making regarding disposition plans and follow-up

Written and verbal sepsis education prior to discharge

Use of a critical care transition program upon transfer to the floor

Medication reconciliation prior to ICU to floor transition

Schedule follow-up with provider able to identify, support, and manage long-term sequelae

**Source:** Surviving Sepsis Campaign, 2021.

## **Post-Hospital Sepsis Care**

## Multicomponent Sepsis Transition and Recovery Program (STAR)

#### In-Hospital

- Assess health literacy
- Mental health screen
- Verify PT/OT consult

## Near Hospital D/C

- Provide infectionspecific education to patient and caregivers
- Confirm med rec with inpatient pharmacist

#### Post-Hospital

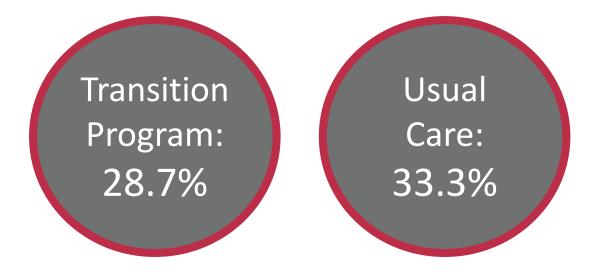
- Medication review and confirm fills
- Appointment reminder and confirm transportation
- Ongoing symptom screenings

**Source:** Taylor, SP et al. Crit Care Med 2021.

## **Post-Hospital Sepsis Care**

Multicomponent Sepsis Transition and Recovery Program (STAR)

Composite mortality or hospital readmission at 30 days:



**Source:** Taylor, SP et al. Crit Care Med 2021.

# The Critical Illness Transition and Recovery Program (CI-TRP) at OSU

#### Increases access through various visit modalities:

In-Person Clinic

Telehealth (Video and Phone)

#### Uses a multidisciplinary team:

RN Coordinator MICU Pharmacists Critical Care Provider

Social Work

PT/OT

Cognitive and Behavioral Health

#### Addresses two distinct clinical needs:

1. Immediate post-hospitalization transition of care

2. Post-ICU Impairment Screening



#### **Summary**

- 1. Sepsis is common, and early recognition is key to improve survival.
- 2. The SSC 1-Hour Bundle focuses on early identification, early cultures/lactate assessment, early antibiotics (1 hour for those with shock or higher probability of sepsis), and timely/appropriate volume resuscitation.
- Treatment guidelines continue to evolve with new data, and some remain controversial.
- 4. Mortality is improving, so survivorship needs are evolving.
- 5. Post-hospital care for sepsis survivors has shown promise, and care models for post-sepsis and post-ICU care are growing.

Always excited for opportunities to collaborate – please reach out!

## **Thank You**