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Navigating Best Practices to Optimize Sepsis Care

January 23, 2019
Colorado Hospital Association HIIN
Steven Tremain, MD, Cynosure Health

Disclosures

- None relevant to today's discussion

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Severe Sepsis:
A Significant Healthcare Challenge

- Hospitalizations have doubled 2000-2008
- Most costly reason for hospitalization in 2011
  - $20 billion in aggregate hospital cost
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  - Leading cause of death in non-coronary ICU
  - 10th leading cause of death overall
- In the U.S., **more than 700 patients die of severe sepsis daily**
  - (1.6 million new cases per year)

1 Patient dies every 2 minutes

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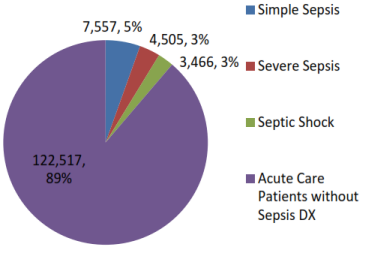
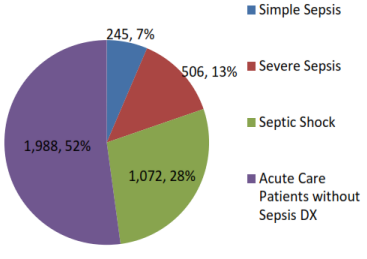
The # 1 Cause of Inpatient Death

2014 Acute Care Discharges
11% of Patients Have Sepsis DX



2014 Acute Care Deaths
48% of Patients Have Sepsis DX



The same pattern in every hospital

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Severe Sepsis vs Other Disease Priorities

Care Priorities	U.S. Incidence	# of Deaths	Mortality Rate
AMI	900,000	225,000	25%
Stroke	700,000	163,500	23%
Trauma (Motor Vehicle)	2.9 million (injuries)	42,643	1.5%
Severe Sepsis	751,000	215,000	29%

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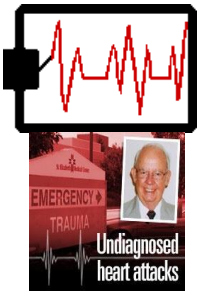
Time Sensitive Diagnoses: Changing the Paradigm of Practice

AMI



Stroke

Trauma

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Critical Actions

The Keys to achieving a reduction in mortality from severe sepsis are **Early Recognition** & **Evidence Based Treatment**. BOTH MUST occur.

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Sepsis Diagnosis Is Difficult

- No single criteria makes the diagnosis
  - Unlike New ST Elevation on ECG, or New Onset Focal Neuro Exam
- Patient status changes during encounter
- Diagnosis not black and white but gray
- Patient may look good, yet crash two hours later
- *Many physicians like an observation period before reacting, and they lose the critical window of opportunity*
- **HUMAN FACTORS**
  - Competing priorities, lack of awareness, patient looking good leads physicians down another path

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Screening tools

- **SIRS: Systemic Inflammatory Response Syndrome**
  - Temp < 36°C or > 38°C
  - Heart Rate > 90/min
  - Respiratory Rate > 20/min or PaCO2 32mmHg
  - WBC < 4,000 or > 12,000 or 10% bands
  - *With signs or symptoms suspicious for an infection*

2 or more of either

- **qSOFA**
  - Decreased blood pressure < 110mmHg (SBP)
  - Increased respiratory rate > 22/min
  - Change in LOC GCS < 15

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Positive Sepsis Screen: 3-hr Bundle

To be completed within 3 hours of presentation

- Measure lactate level
- Obtain blood cultures prior to administration of antibiotics
- Administer broad spectrum antibiotics
- *Administer 30ml/kg crystalloid **for** hypotension or lactate ≥ 4mmol/L*

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Positive Sepsis Screen: 6-hr Bundle

Persistent Hypotension or Lactate >4mmol/L

- Apply vasopressors
  - For hypotension that does not respond to initial fluid resuscitation - to maintain a mean arterial pressure (MAP) ≥65mmHg - Norepinephrine
- Re-assess volume status and tissue perfusion and document findings
  - In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L
- Re-measure lactate if initial lactate elevated
  - Guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion

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Updates For 6-Hour Bundle

- Requiring measurement of CVP and ScvO2 in all patients with lactate >4 mmol/L and/or persistent hypotension after initial fluid challenge and timely antibiotics is NOT supported by available evidence
- *Dynamic measures vs. static measures are now recommended to predict fluid responsiveness where available*
- Frequent assessment of the patients' volume status is crucial throughout the resuscitation period

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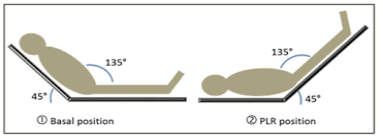
Re-assess Volume Status and Tissue Perfusion and Document Findings By….

EITHER:

Repeat focused exam (after initial fluid resuscitation) a by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse and skin findings



OR TWO OF THE FOLLOWING:

- Measure CVP - static
- Measure ScVO2 - static
- Bedside cardiovascular ultrasound-dynamic IVC
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge - dynamic

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The Controversies

- SIRS or qSOFA or clinical judgement…or what?
- Timing of antibiotics
- Fluids? When? How Much?
- The Hour 1 Bundle

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qSOFA Good to Find "Sick"; Not So Good for Sepsis

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Prognostic Accuracy of Sepsis-3 Criteria for In-Hospital Mortality Among Patients With Suspected Infection Presenting to the Emergency Department

Yonathan Freund, MD, PhD; Najla Lemachatti, MD; Evguenia Krastinova, MD, PhD; Marie Van Laer, MD; Yann-Erick Claessens, MD, PhD; Aurélie Avondo, MD; Céline Occelli, MD; Anne-Laure Feral-Pierssens, MD; Jennifer Truchot, MD; Mar Ortega, MD; Bruno Carneiro, MD; Julie Pernet, MD; Pierre-Géraud Claret, MD, PhD; Fabrice Dami, MD; Ben Bloom, MD; Bruno Riou, MD, PhD; Sébastien Beaune, MD, PhD; for the French Society of Emergency Medicine Collaborators Group

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Findings

- qSOFA better at predicting in-hospital mortality
  - Predictor of need for ICU bed
  - Easy to score in field
  - Can aid hospitals to prepare for prompt receipt/transfer when alerted from field
- Worse than SIRS for finding sepsis

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SIRS Better Than qSOFA for Sepsis Screening and Initiation of Intervention

Annals of Internal Medicine REVIEW

Prognostic Accuracy of the Quick Sequential Organ Failure Assessment for Mortality in Patients With Suspected Infection

A Systematic Review and Meta-analysis

Shannon M. Fernando, MD, MSc; Alexandre Tran, MD; Monica Taljaard, PhD; Wei Cheng, PhD; Bram Rochwerg, MD, MSc; Andrew J.E. Seely, MD, PhD; and Jeffrey J. Perry, MD, MSc

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Findings

Conclusion: qSOFA had poor sensitivity and moderate specificity for short-term mortality. The SIRS criteria had sensitivity superior to that of qSOFA, supporting their use for screening of patients and as a prompt for treatment initiation.

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But Don't These Cry "Wolf?"

- Yes
- There are no alerts that have optimal sensitivity and specificity
- But often there is a…

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Time to Revisit Biostatistics

- Sensitivity
- Specificity

- No perfect test
- Any choice to make a test/screening tool more specific will decrease its sensitivity
  - More cases missed or delayed diagnosis

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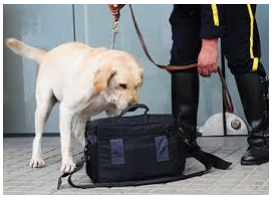
How Good is Your Sepsis Sniffer?

- Measure it. Track it…
- Are you better than SIRS?
  - Probably not!



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Wise Advice or Contrarian?

JAMA September 14, 2018

Antibiotics for Sepsis – Finding the Equilibrium

Michael Klompas, MD, MPH[1,2]; Thierry Calandra, MD, PhD[3]; Mervyn Singer, MD, FRCP[4]

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Klompas argues…

- Current sepsis identification and treatment guidelines
  - Oversimplify the sepsis diagnostic process
  - Are based on flawed studies
  - Are not consistent with antibiotic stewardship principles

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What about EGDT?

ORIGINAL ARTICLE

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D., Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D., Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H., Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

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What about EGDT?

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Findings

- EGDT vs "usual care" does not reduce mortality
- Timely antibiotics improve mortality, but not fluids

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Confounders

- Since the early SSC studies (Rivers et al.), ”usual care” has migrated to early fluids, so there may be little difference between usual care and protocolized EGDT
- In fact, in both of these studies, patients on average received 2+ liters (30 mg/kg)

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What about those CHF and CRF patients?

Multicenter Implementation of a Treatment Bundle for Patients with Sepsis and Intermediate Lactate Values

Vincent X. Liu[1,2], John W. Morehouse[2], Gregory P. Marelich[2], Jay Soule[2], Thomas Russell[2], Melinda Skeath[3], Carmen Adams[3], Gabriel J. Escobar[1,2], and Alan Whippy[2]

[1]Kaiser Permanente Division of Research, Oakland, California; [2]The Permanente Medical Group, Oakland, California; and [3]Kaiser Foundation Hospitals and Health Plan, Oakland, California

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Whoa…Wait a Minute….

- That's a lot of fluid for some *folks*
  - *physicians or patients*!
- Common point of physician resistance

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0.81 (95% confidence interval, 0.66–0.99; $P = 0.04$). Decreased hospital mortality was observed primarily in patients with a heart failure and/or kidney disease history ($P < 0.01$) compared with patients without this history ($P > 0.40$). This corresponded to notable changes in the volume of fluid resuscitation in patients with heart failure and/or kidney disease after implementation.

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Delays Increase Mortality

Crit Care Med. 2018 Jan 2. doi: 10.1097/CCM.0000000000002949. [Epub ahead of print]

Wolters Kluwer

Delay Within the 3-Hour Surviving Sepsis Campaign Guideline on Mortality for Patients With Severe Sepsis and Septic Shock.

Pruinelli L[1], Westra BL[1,2], Yadav P[3], Hoff A[3], Steinbach M[3], Kumar V[3], Delaney CW[1,2], Simon G[2,4].

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Study Design

- Looked at timing of 4 SSC recommendations and link to mortality
  - BC before Abx
  - Obtain lactate level
  - Administer broad spectrum antibiotics
  - Administer 30 cc/kg IBW for MAP < 65 or lactate > 4

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Findings

- Shorter delays improve outcomes
- No evidence that 3 hours was safe
- Any delay adversely affected outcomes

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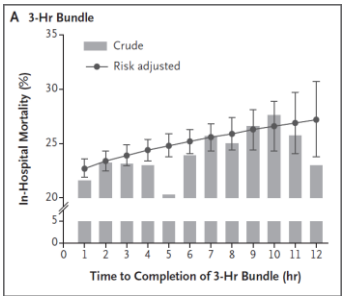
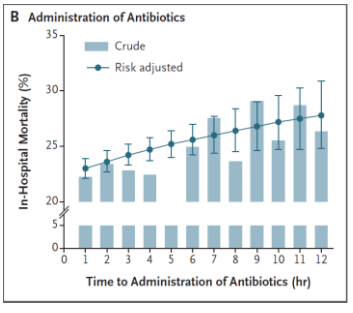
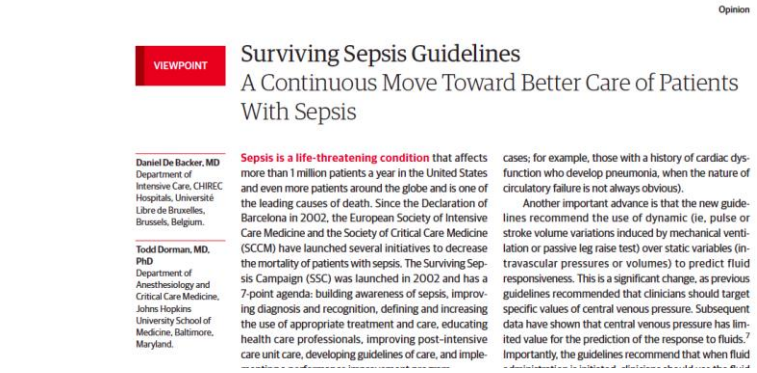




Seymour CW, Gesten F, Prescott H et al. Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. N Engl J Med 2017; 376:2235-2244.

The preponderance of the evidence remains that SSC guidelines reduce sepsis mortality



Opinion

VIEWPOINT

Surviving Sepsis Guidelines
A Continuous Move Toward Better Care of Patients With Sepsis

Daniel De Backer, MD
Department of Intensive Care, CHIREC Hospitals, Université Libre de Bruxelles, Brussels, Belgium.

Todd Dorman, MD, PhD
Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Sepsis is a life-threatening condition that affects more than 1 million patients a year in the United States and even more patients around the globe and is one of the leading causes of death. Since the Declaration of Barcelona in 2002, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine (SCCM) have launched several initiatives to decrease the mortality of patients with sepsis. The Surviving Sepsis Campaign (SSC) was launched in 2002 and has a 7-point agenda: building awareness of sepsis, improving diagnosis and recognition, defining and increasing the use of appropriate treatment and care, educating health care professionals, improving post-intensive care unit care, developing guidelines of care, and imple-

cases; for example, those with a history of cardiac dysfunction who develop pneumonia, when the nature of circulatory failure is not always obvious).

Another important advance is that the new guidelines recommend the use of dynamic (ie, pulse or stroke volume variations induced by mechanical ventilation or passive leg raise test) over static variables (intravascular pressures or volumes) to predict fluid responsiveness. This is a significant change, as previous guidelines recommended that clinicians should target specific values of central venous pressure. Subsequent data have shown that central venous pressure has limited value for the prediction of the response to fluids.[7] Importantly, the guidelines recommend that when fluid

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Finally, the SSC guidelines will be translated into bundles that are key elements in sepsis improvement efforts. In a 1-day observational study conducted in 62 countries worldwide, adherence to the bundles, even though not present in the majority of patients, was associated with a marked reduction in the odds of death.[9] In response to the changes in the SSC guidelines, these bundles will be updated later this year and will be available online.[10]

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Barriers to Change

- Culture
  - Resistance to nurse driven protocols
- Tradition
  - I am the doctor
  - I don't do cookbook medicine
  - Residents need to learn to think for themselves

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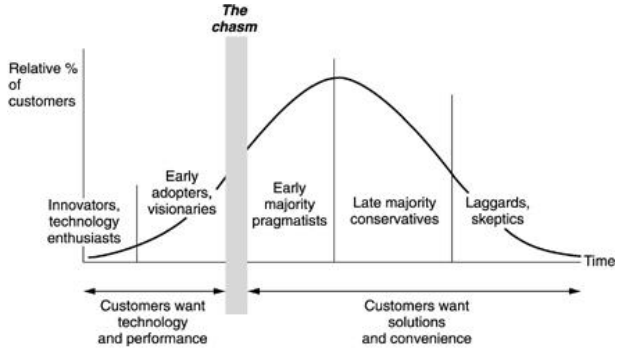
Adoption of Innovation



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The 2018 SSC Guideline

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GUIDELINE TITLE Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

DEVELOPERS Surviving Sepsis Campaign (SSC), Society of Critical Care Medicine (SCCM), and European Society of Intensive Care Medicine (ESICM)

RELEASE DATE January 18, 2017

PRIOR VERSIONS 2012, 2008, 2004

TARGET POPULATION Adults with sepsis or septic shock

SELECTED MAJOR RECOMMENDATIONS

Managing infection:

- Antibiotics: Administer broad-spectrum intravenous antimicrobials for all likely pathogens within 1 hour after sepsis recognition (strong recommendation; moderate quality of evidence [QOE]).
- Source control: Obtain anatomic source control as rapidly as is practical (best practice statement [BPS]).
- Antibiotic stewardship: Assess patients daily for deescalation of antimicrobials; narrow therapy based on cultures and/or clinical improvement (BPS).

Managing resuscitation:

- Fluids: For patients with sepsis-induced hypoperfusion, provide 30 mL/kg of intravenous crystalloid within 3 hours (strong recommendation; low QOE) with additional fluid based on frequent reassessment (BPS), preferentially using dynamic variables to assess fluid responsiveness (weak recommendation; low QOE).
- Resuscitation targets: For patients with septic shock requiring vasopressors, target a mean arterial pressure (MAP) of 65 mm Hg (strong recommendation; moderate QOE).
- Vasopressors: Use norepinephrine as a first-choice vasopressor (strong recommendation; moderate QOE).

Mechanical ventilation in patients with sepsis-related ARDS:

- Target a tidal volume of 6 mL/kg of predicted body weight (strong recommendation; high QOE) and a plateau pressure of ≤30 cm H_2O (strong recommendation; moderate QOE).

Formal improvement programs:

- Hospitals and health systems should implement programs to improve sepsis care that include sepsis screening (BPS).

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The Hour 1 Bundle

Intensive Care Med
https://doi.org/10.1007/s00134-018-5085-0

SPECIAL EDITORIAL

The Surviving Sepsis Campaign Bundle: 2018 update

Mitchell M. Levy[1*], Laura E. Evans[2] and Andrew Rhodes[3]

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Surviving Sepsis Campaign Hour 1 Bundle

- Measure lactate level. Remeasure if initial lactate level > 2 mmol/L
- Obtain blood cultures before administering antibiotics
- Administer broad-spectrum antibiotics
- Begin rapid administration of 30mL/kg crystalloid for hypotension or lactate level ≥ 4 mmol/L
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mm Hg

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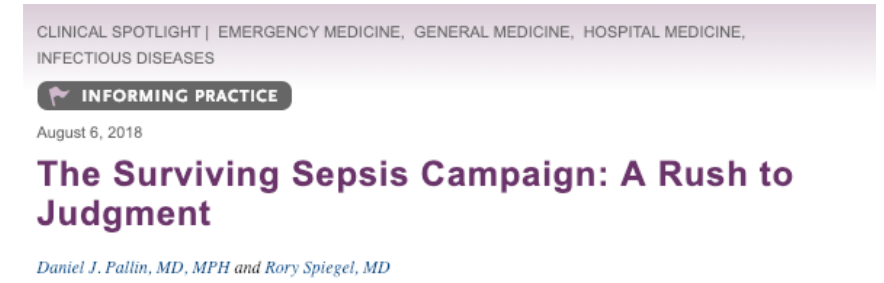
Not So Fast?



CLINICAL SPOTLIGHT | EMERGENCY MEDICINE, GENERAL MEDICINE, HOSPITAL MEDICINE, INFECTIOUS DISEASES

INFORMING PRACTICE

August 6, 2018

The Surviving Sepsis Campaign: A Rush to Judgment

Daniel J. Pallin, MD, MPH and Rory Spiegel, MD

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Concerns

- Quality of evidence is low to moderate
- Compliance would be measured retrospectively
- Might harm some patients with overdiagnosis, overtreatment
- Unjustly divert attention from other patients, particularly in busy emergency departments

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What About Inpatients?

- Highest Mortality
  - Sepsis diagnosed on the floors
  - Lactate >2 mmol/l but < 4 mmol/l
- Bundle Compliance
  - Worst on the floor
- Hospitals with RRT/Sepsis Alert as resource saves most lives

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What About Morbidity?


Clinical Review & Education

JAMA | Review

Enhancing Recovery From Sepsis
A Review

Hallie C. Prescott, MD, MSc; Derek C. Angus, MD, MPH

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The Morbidity in Sepsis Survivors is Severe

- Each year 14 million of the 19 million sepsis patients survive
- One half recover
- One third die within 12 months
- Impairments

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Impairments

- 1-2 new functional disabilities (e.g. ADLs)
- 3x increase in cognitive disability (6% on admit, 17% on discharge)
- Mental health impairments
  - Anxiety 32%
  - Depression 29%
  - PTSD 44%
- 40% readmitted within 90 days
- 50% increase in risk of subsequent infection as compared to patients discharged with other diagnoses
- 3x increase in renal failure
- 10-40% increase in CV events

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Discharge From Hospital is Only First Step

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What is Agreed Upon?

- Look for sepsis
- If suspicious don't delay starting treatment
- Start targeted antibiotics promptly
  - Use algorithms supported by your antibiogram based on systems
- Give fluids
  - Everyone gets 30 ml/kg IBW
  - Don't fear CFH and CRF patients, they need the fluid the most!

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What is Not Agreed Upon?

- The Hour 1 Bundle
- Rapidity of fluid administration

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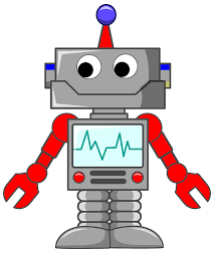
What No One is Suggesting…

- Robotic care without thought (but don't overthink!)



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So Where Does This All Leave Us?

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Groundhog Day

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Create a Learning Environment

- Measure and Track adherence to bundle
- Segment morbidity and mortality results based on bundle adherence
- Segment by physician/resident
- Learn and Improve…
- You don't get a Groundhog Day 'do-over' but you do get to apply learnings to subsequent patients

YOU CAN'T IMPROVE WHAT YOU DON'T MEASURE

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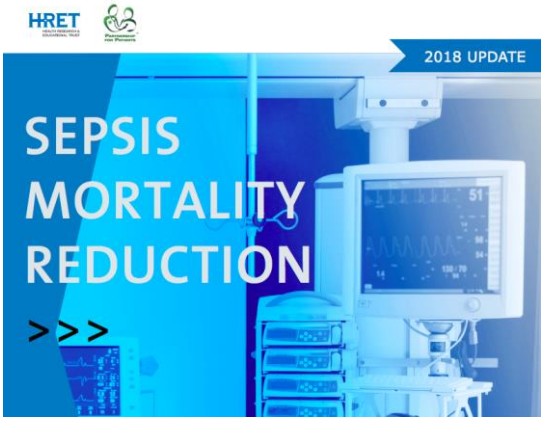
A Key Resource



http://www.hret-hiin.org/Resources/sepsis/18/sepsis-and-septic-shock-change-package.pdf

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