Sepsis

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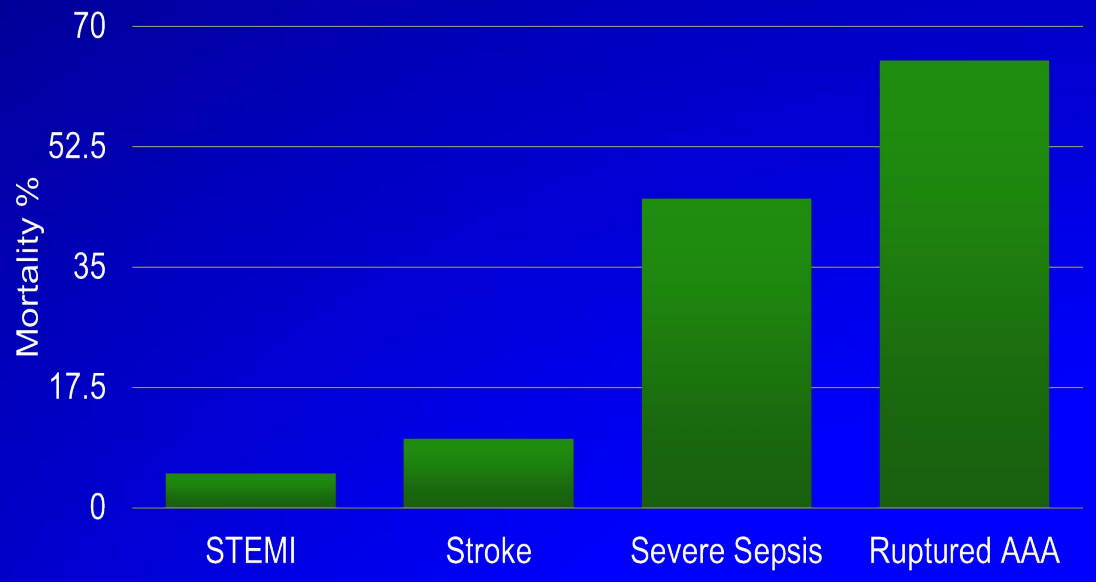
No fifancial disclosures to report

Objectives

- Define sepsis and recognize signs / symptoms of sepsis
- Discuss and review sepsis bundles and Evidence-Based sepsis care
- Describe limitations of current definitions of sepsis

Why is sepsis so important?

- Over 30 million cases per year in the world, estimated 6 million deaths
- Over 750000 cases of severe sepsis per year in the US
- Leading cause of US hospital readmissions
- Increasing incidence



Groups at higher risk for sepsis

- Host factors
  - Age, gender, genetics, comorbidities
- Immunosuppression
  - Underlying disease, medications
- Exposure risk
  - Community acquired: pneumonia, urinary, wounds, trauma
  - Health care acquired: invasive devices, secondary infections and skin breakdown

Causes of sepsis

- Bacterial infections are the most common
  - Pneumonia, UTI, surgery, skin, C. difficile, bacteremia
- Fungal, parasitic or viral infections can also cause sepsis
- Unknown (1/3 of all sepsis cases)

Snigdha J. Am J Med Sci 2018; 356:277. Howell MD, et al. JAMA 2017; 317:847

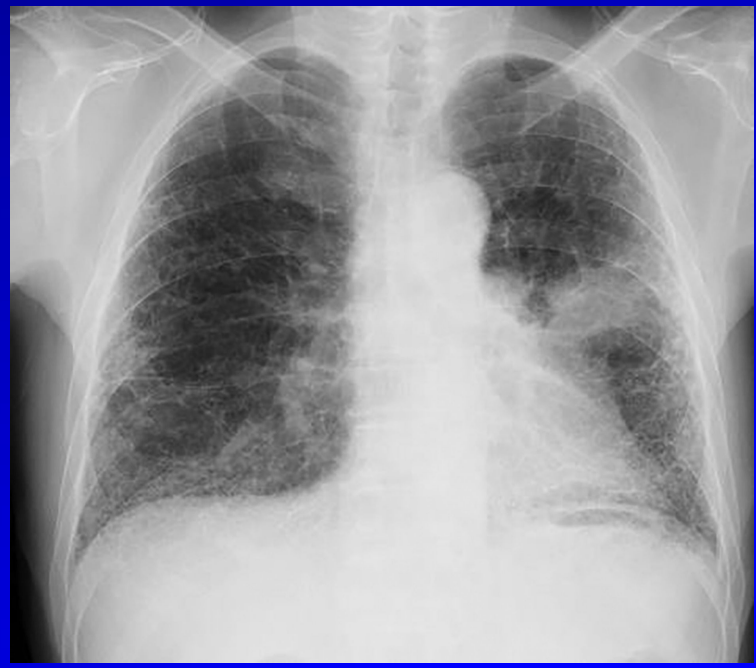
Pathophysiology of sepsis

- Uncontrolled immune response
  - Widespread neutrophil and endothelial cellular activation
  - Microcirculatory injury, increased permeability and interstitial edema
- Widespread coagulation activation
- Circulatory changes
  - Changes in cardiac output and circulation distribution
  - Increase production of NO, prostaglandins
- Hypotension, microcirculatory dysfunction, tissue hypoxia, lactic acidosis, multiorgan failure

34 yo woman with 2 days of fever, cough, dyspnea. No significant medical history

On exam VS BP 104/54, HR 120, RR 22, sats 90% RA crackles in left lung

Admitted to the floor and started on ceftriaxone and azithromycin



Is this sepsis?

Is this sepsis?

- Do we have enough data to make a diagnosis of sepsis?
- Do we need additional info? (lactate, creatinine, other labs)
- Do we have general agreement among providers when we make a diagnosis of sepsis?

- Sorry… what sepsis definition are you talking about?

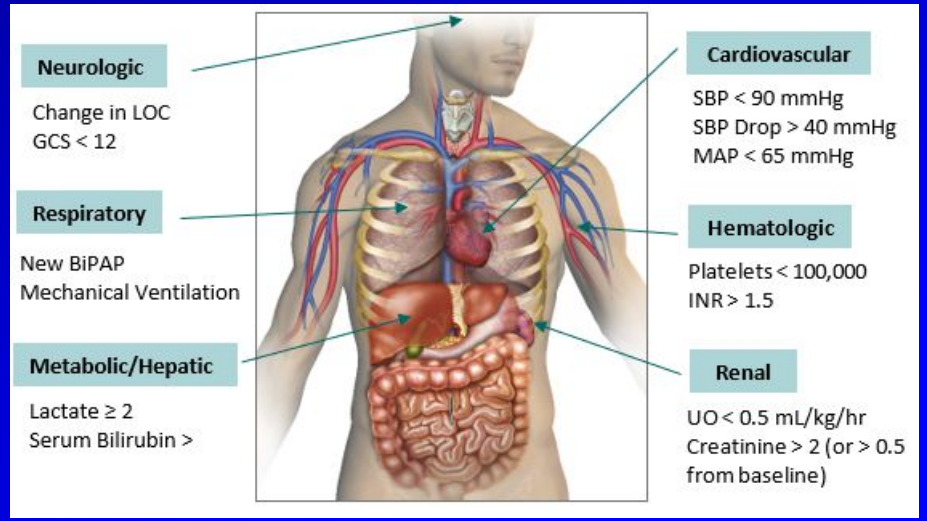
Is this sepsis? Consensus definitions

- Sepsis-1, 1991
  - SIRS: 2 or more of temp (<36 or >38), HR (>90), RR (>20), WBC (>12 or <4)
  - Sepsis: SIRS as systemic response to infection
  - Severe sepsis: sepsis plus hypoperfusion or hypotension
  - Septic shock: sepsis and hypotension, no response to fluids
- Sepsis-2, 2001
  - Infection, documented or suspected
  - Long list of parameters and definitions

Snigdha J. Am J Med Sci 2018; 356:277. Howell MD, et al. JAMA 2017; 317:847

Is this sepsis? Consensus definitions

- Sepsis-3, 2014
  - Life-threatening organ dysfunction caused by dysregulated host response to infection
  - Severe sepsis: new organ dysfunction
  - Septic shock: subset with circulatory and cellular/metabolic dysfunction, higher risk of mortality
    - ✔ Refractory hypotension or lactate >4 mmol/L



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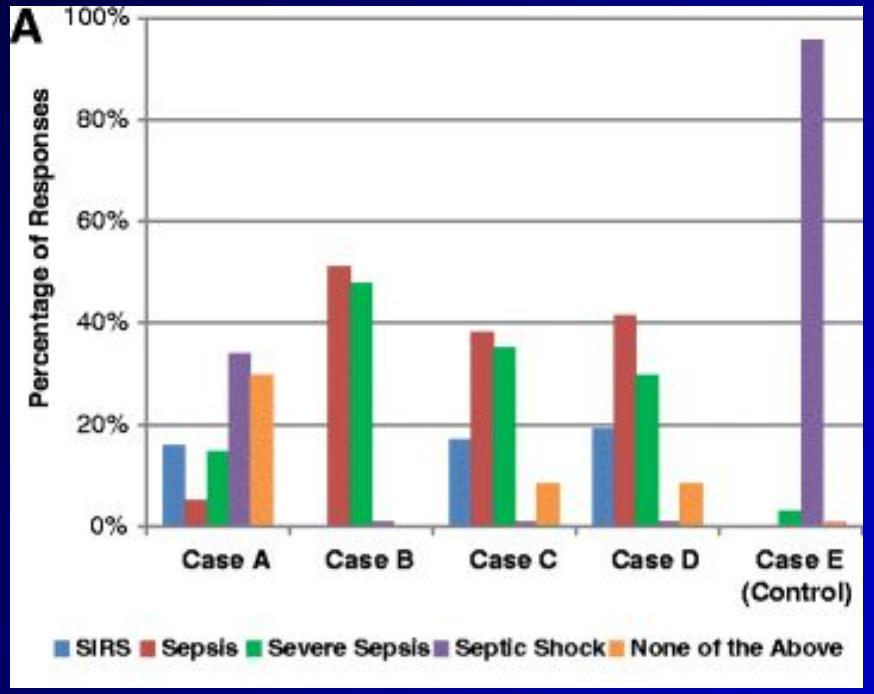
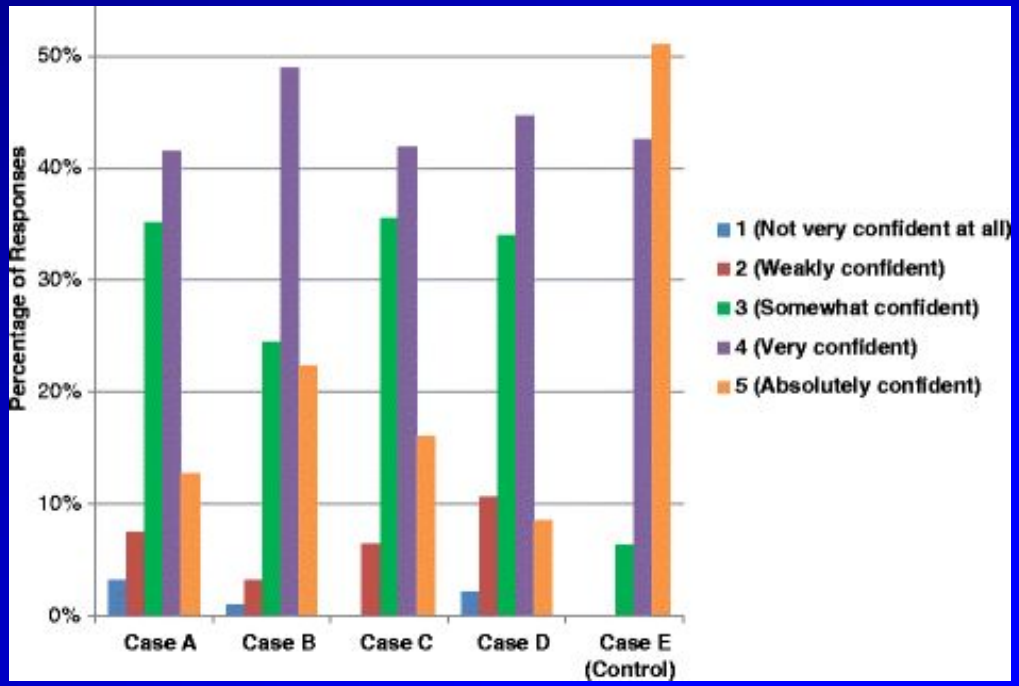
Is this sepsis?

- How certain are you?

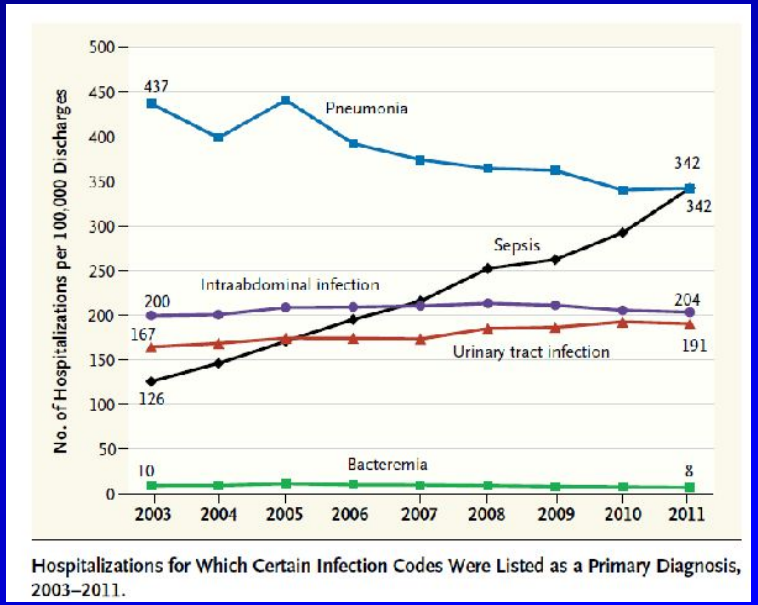




Rhee C, et al. Critical Care 2016; 20:89

Diagnosis of sepsis is subjective and highly variable

- Claims data show increased incidence in the last several years
- Different results if data from EHR are used, instead of coding data
- Studies have shown that >40% of patients who have working diagnosis of sepsis don't have it



Hospitalizations for Which Certain Infection Codes Were Listed as a Primary Diagnosis, 2003–2011.

Rhee C, et al. N Engl J Med 2014; 370:1673

Management of sepsis, SEP-1 (CMS bundle)

Sepsis Bundle Algorithms

07-01-2021 (3Q21) through 12-31-2021 (4Q21)

SEP-1: Early Management Bundle, Severe Sepsis/Septic Shock (Composite Measure)

Numerator:

(Patients who received All of the following)

Within three hours of presentation of severe sepsis:

- Initial lactate level measurement
- Broad spectrum or other antibiotics administered
- Blood cultures drawn prior to antibiotics

AND received within six hours of presentation of severe sepsis. ONLY if the initial lactate is elevated:

- Repeat lactate level measurement

AND within three hours of initial hypotension:

- Resuscitation with 30 mL/kg crystalloid fluids

OR within three hours of septic shock:

- Resuscitation with 30 mL/kg crystalloid fluids

AND within six hours of septic shock presentation, ONLY if hypotension persists after fluid administration:

- Vasopressors are administered

AND within six hours of septic shock presentation, if hypotension persists after fluid administration or initial lactate >= 4 mmol/L:

- Repeat volume status and tissue perfusion assessment is performed

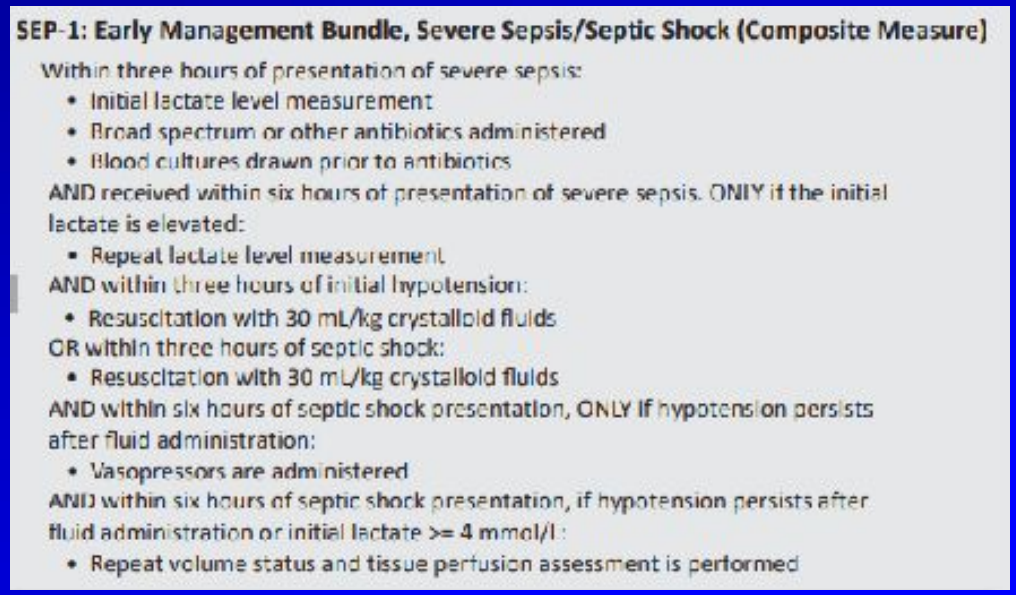
Denominator:

Inpatients age 18 and over with an ICD-10-CM Principal or Other Diagnosis Code of sepsis, severe sepsis or septic shock as defined in Appendix A, Table 4.01 and not equal to U07.1 (COVID-19)

CMS 2021

Sepsis, SEP-1

- ✧Rory's regulation introduced in NY State in 2013
- ✧SEP-1 measures introduced by CMS in 2015
- ✧Rules are pages long, very complicated, very difficult to meet all metrics
- ✧Measure steward is not CMS or AMA or a professional society, it is Henry Ford Hospital
- ✧Seven elements



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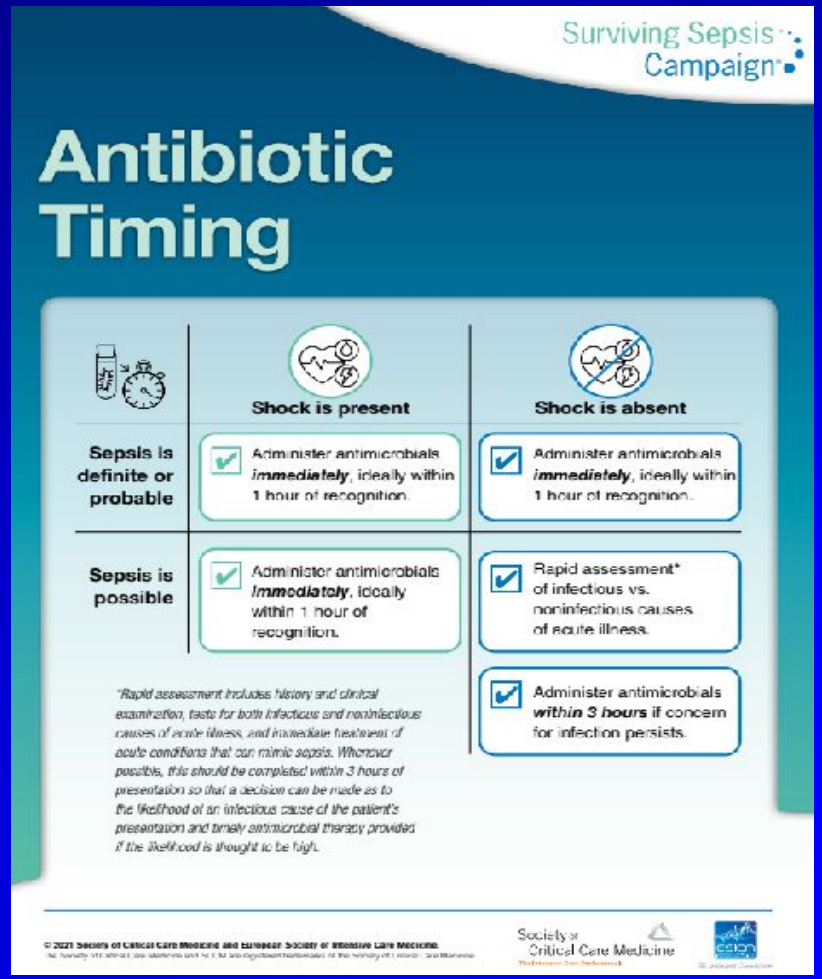
- Repeat volume status and tissue perfusion assessment is performed

Surviving sepsis campaign, Oct 21

https://www.sccm.org/Clinical-Resources/Guidelines/Guidelines/Surviving-Sepsis-Guidelines-2021

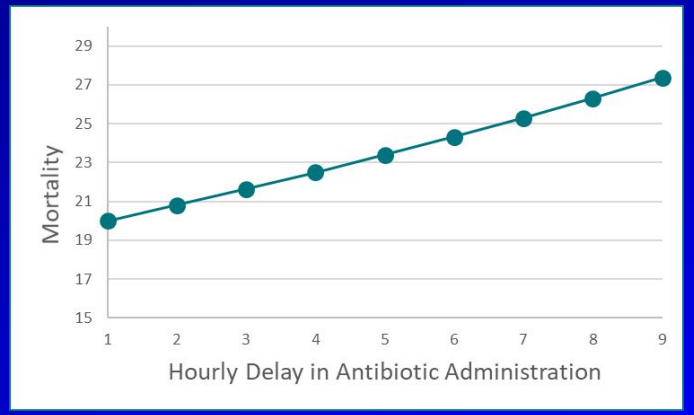
Sepsis, antibiotics

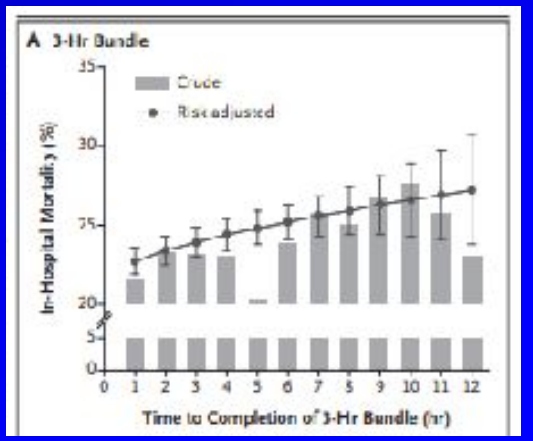
- Administration of antibiotics
  - Initiate as soon as possible and within 1 hour if shock is present
  - If sepsis is possible and shock is absent administer within 3 hours if concern for infection persists



Sepsis, antibiotics within 1-3 hours

- Benefit of very early administration (<1 hour) in ICU patients with hypotension
- Benefit in ED patients with hypotension
- Large NYS study in severe sepsis and hypotension
  - More rapid completion of the bundle and administration of IV antibiotics associated with improved mortality





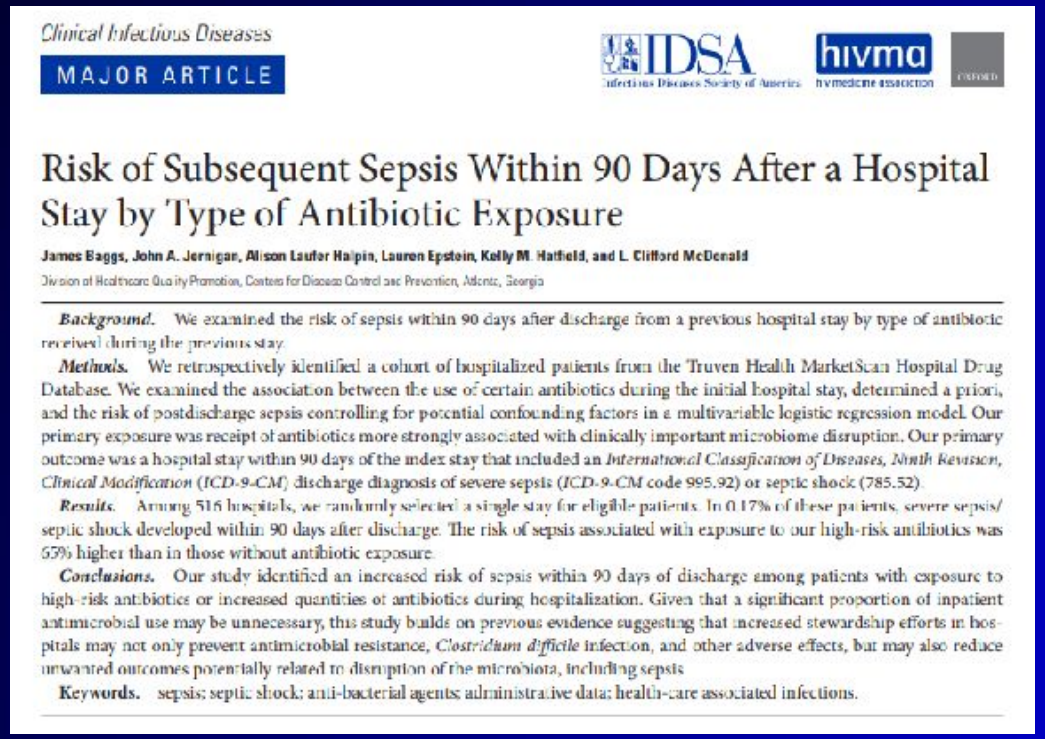
Liu VX, et al. Am J Resp Crit Care Med 2017; 196:856. Alam N, et al. Lancet Resp 2018; 6:40. Kumar A et al. Crit Care Med 2006; 34:1589. Seymour C, et al. N Eng J Med 2017; 376:2235

Sepsis, antibiotics within 1-3 hours

- Other studies have not found benefit
  - Meta-analysis of >16000 patients found no benefit
  - Large study in England of antibiotics in ambulances showed no benefit

Liu VX, et al. Am J Resp Crit Care Med 2017; 196:856. Alam N, et al. Lancet Resp 2018; 6:40. Kumar A et al. Crit Care Med 2006; 34:1589. Seymour C, et al. N Eng J Med 2017; 376:2235

Sepsis, harm with early administration of antibiotics for possible sepsis?



Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hivmedicine association · OXFORD

Risk of Subsequent Sepsis Within 90 Days After a Hospital Stay by Type of Antibiotic Exposure

James Baggs, John A. Jernigan, Alison Laufer Halpin, Lauren Epstein, Kelly M. Hatfield, and L. Clifford McDonald

Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

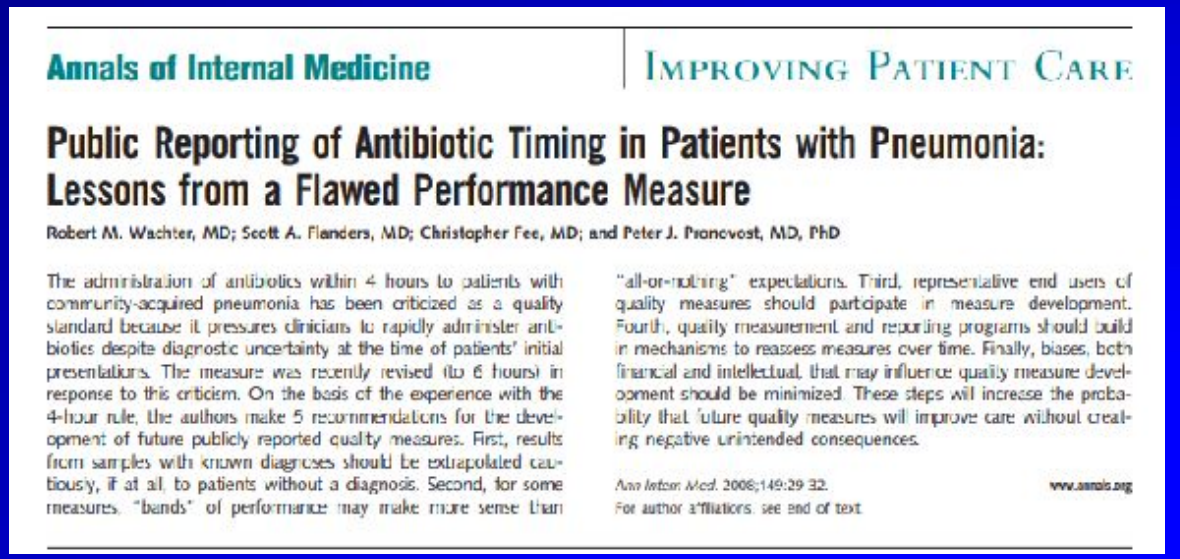
Background. We examined the risk of sepsis within 90 days after discharge from a previous hospital stay by type of antibiotic received during the previous stay.

Methods. We retrospectively identified a cohort of hospitalized patients from the Truven Health MarketScan Hospital Drug Database. We examined the association between the use of certain antibiotics during the initial hospital stay, determined a priori, and the risk of postdischarge sepsis controlling for potential confounding factors in a multivariable logistic regression model. Our primary exposure was receipt of antibiotics more strongly associated with clinically important microbiome disruption. Our primary outcome was a hospital stay within 90 days of the index stay that included an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) discharge diagnosis of severe sepsis (*ICD-9-CM* code 995.92) or septic shock (785.52).

Results. Among 516 hospitals, we randomly selected a single stay for eligible patients. In 0.17% of these patients, severe sepsis/septic shock developed within 90 days after discharge. The risk of sepsis associated with exposure to our high-risk antibiotics was 55% higher than in those without antibiotic exposure.

Conclusions. Our study identified an increased risk of sepsis within 90 days of discharge among patients with exposure to high-risk antibiotics or increased quantities of antibiotics during hospitalization. Given that a significant proportion of inpatient antimicrobial use may be unnecessary, this study builds on previous evidence suggesting that increased stewardship efforts in hospitals may not only prevent antimicrobial resistance, *Clostridium difficile* infection, and other adverse effects, but may also reduce unwanted outcomes potentially related to disruption of the microbiota, including sepsis.

Keywords. sepsis; septic shock; anti-bacterial agents; administrative data; health-care associated infections.



Annals of Internal Medicine | IMPROVING PATIENT CARE

Public Reporting of Antibiotic Timing in Patients with Pneumonia: Lessons from a Flawed Performance Measure

Robert M. Wachter, MD; Scott A. Flanders, MD; Christopher Fee, MD; and Peter J. Pronovost, MD, PhD

The administration of antibiotics within 4 hours to patients with community-acquired pneumonia has been criticized as a quality standard because it pressures clinicians to rapidly administer antibiotics despite diagnostic uncertainty at the time of patients' initial presentations. The measure was recently revised (to 6 hours) in response to this criticism. On the basis of the experience with the 4-hour rule, the authors make 5 recommendations for the development of future publicly reported quality measures. First, results from samples with known diagnoses should be extrapolated cautiously, if at all, to patients without a diagnosis. Second, for some measures, "bands" of performance may make more sense than "all-or-nothing" expectations. Third, representative end users of quality measures should participate in measure development. Fourth, quality measurement and reporting programs should build in mechanisms to reassess measures over time. Finally, biases, both financial and intellectual, that may influence quality measure development should be minimized. These steps will increase the probability that future quality measures will improve care without creating negative unintended consequences.

Ann Intern Med. 2008;149:29-32. www.annals.org

For author affiliations, see end of text.

Sepsis, harm with early administration of antibiotics for possible sepsis?

- Antibiotics for patients without sepsis
  - Overdiagnosis is common
  - Broad spectrum antibiotics and inappropriate duration
  - *C. difficile*, AKI, liver toxicity, rash, hematologic
  - Selection of MDRO, changes in microbiome, increase in risk of sepsis in future

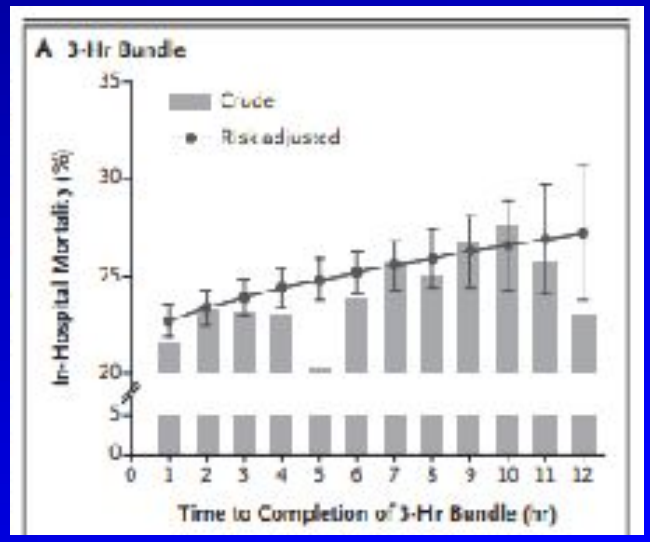
- Many experts believe that modest delays may not affect outcomes if the diagnosis is not clear and the patient is stable

Sepsis, IV fluids

- In sepsis-induced hypoperfusion
  - 30 ml/Kg IV crystalloid within the first 3 hours (weak recommendation)
  - Balanced crystalloids are suggested (LR)

Sepsis, IV fluids

- No RCT
- Retrospective studies suggest benefits from using a bundle that includes IV fluids and antibiotics
- Some studies have found balanced solutions were associated with better outcomes



IV fluids, harms?

- Morbidity, longer hospital stay, even mortality
- Hyponatremia, hyperchloremic metabolic acidosis, AKI, coagulation abnormalities, volume overload, increased need for transfusions, outcomes in ARDS

Hoste EA, et al. Br J Anaesthesia 2014; 113:740

IV fluids, how much? Harms?

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

ABSTRACT

BACKGROUND

Optimal fluid management in patients with acute lung injury is unknown. Diuresis or fluid restriction may improve lung function but could jeopardize extrapulmonary organ perfusion.

METHODS

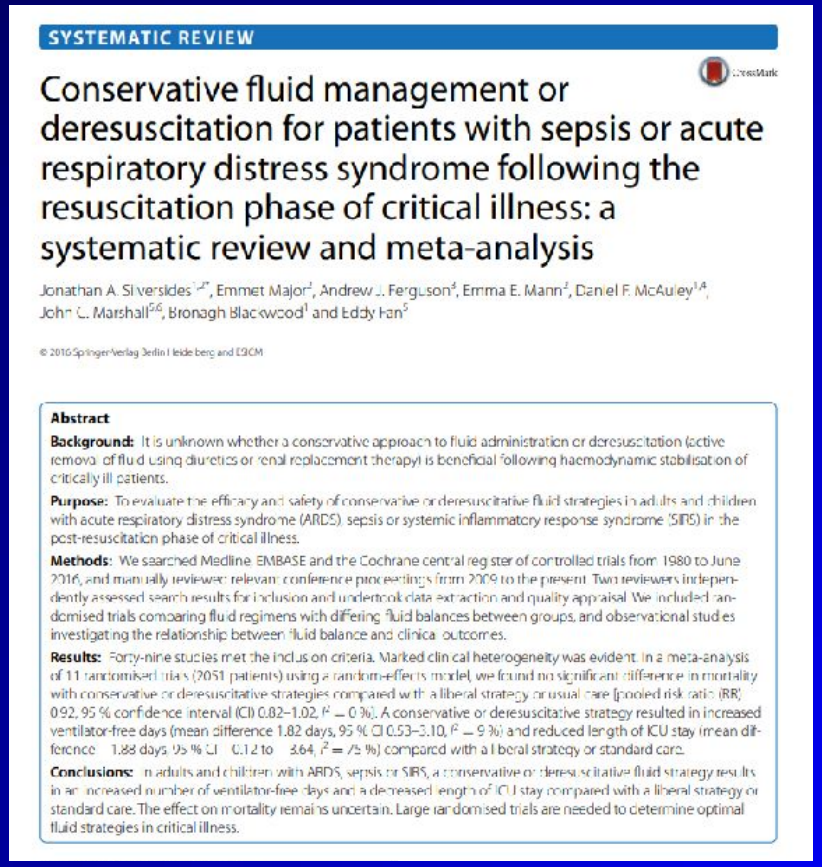
In a randomized study, we compared a conservative and a liberal strategy of fluid management using explicit protocols applied for seven days in 1000 patients with acute lung injury. The primary end point was death at 60 days. Secondary end points included the number of ventilator-free days and organ-failure–free days and measures of lung physiology.

RESULTS

The rate of death at 60 days was 25.5 percent in the conservative-strategy group and 28.4 percent in the liberal-strategy group (P=0.30; 95 percent confidence interval for the difference, −2.6 to 8.4 percent). The mean (±SE) cumulative fluid balance during the first seven days was 136±491 ml in the conservative-strategy group and 6992±502 ml in the liberal-strategy group (P<0.001). As compared with the liberal strategy, the conservative strategy improved the oxygenation index ([mean airway pressure × the ratio of the fraction of inspired oxygen to the partial pressure of arterial oxygen] ×100) and the lung-injury score and increased the number of ventilator-free days (14.6±0.5 vs. 12.1±0.5, P<0.001) and days not spent in the intensive care unit (13.4±0.4 vs. 11.2±0.4, P<0.001) during the first 28 days but did not increase the incidence or prevalence of shock during the study or the use of dialysis during the first 60 days (10 percent vs. 14 percent, P=0.06).

CONCLUSIONS

Although there was no significant difference in the primary outcome of 60-day mortality, the conservative strategy of fluid management improved lung function and shortened the duration of mechanical ventilation and intensive care without increasing nonpulmonary-organ failures. These results support the use of a conservative strategy of fluid management in patients with acute lung injury. (ClinicalTrials.gov number, NCT00281268.)



SYSTEMATIC REVIEW

Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis

Jonathan A. Silversides[1,4*], Emmet Major[2], Andrew J. Ferguson[3], Emma E. Mann[2], Daniel F. McAuley[1,4], John G. Marshall[5,6], Bronagh Blackwood[1] and Eddy Fan[5]

Abstract

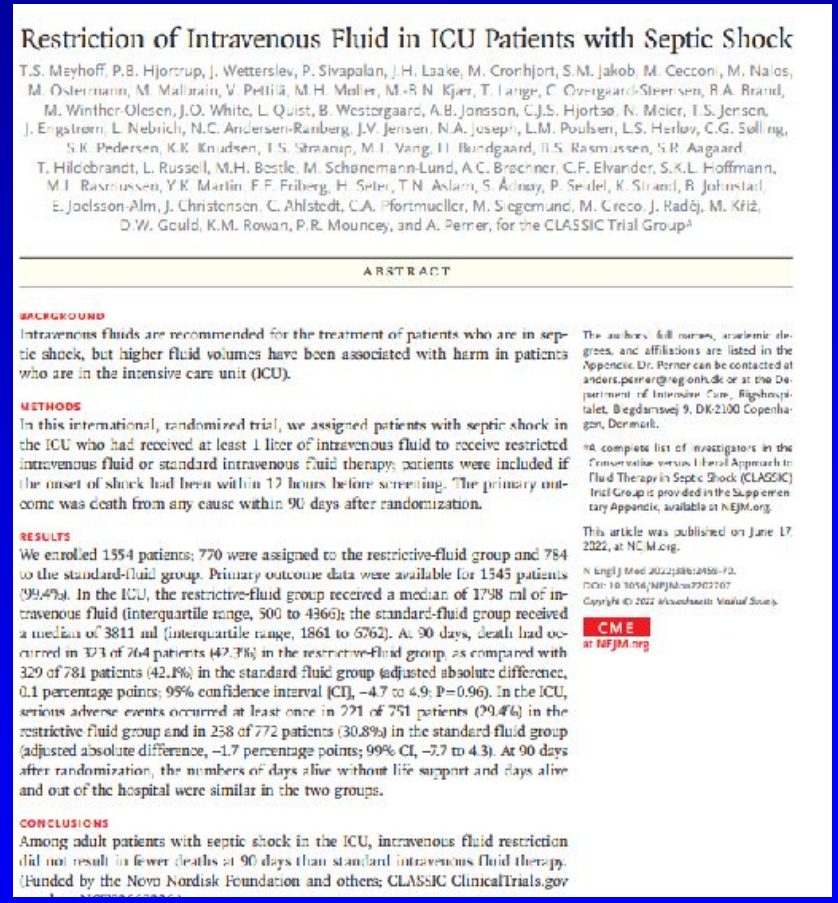
Background: It is unknown whether a conservative approach to fluid administration or deresuscitation (active removal of fluid using diuretics or renal replacement therapy) is beneficial following haemodynamic stabilisation of critically ill patients.

Purpose: To evaluate the efficacy and safety of conservative or deresuscitative fluid strategies in adults and children with acute respiratory distress syndrome (ARDS), sepsis or systemic inflammatory response syndrome (SIRS) in the post-resuscitation phase of critical illness.

Methods: We searched Medline, EMBASE and the Cochrane central register of controlled trials from 1980 to June 2016, and manually reviewed relevant conference proceedings from 2009 to the present. Two reviewers independently assessed search results for inclusion and undertook data extraction and quality appraisal. We included randomised trials comparing fluid regimens with differing fluid balances between groups, and observational studies investigating the relationship between fluid balance and clinical outcomes.

Results: Forty-nine studies met the inclusion criteria. Marked clinical heterogeneity was evident. In a meta-analysis of 11 randomised trials (2051 patients) using a random-effects model, we found no significant difference in mortality with conservative or deresuscitative strategies compared with a liberal strategy or usual care [pooled risk ratio (RR) 0.92, 95 % confidence interval (CI) 0.82–1.02, $I^2 = 0$ %]. A conservative or deresuscitative strategy resulted in increased ventilator-free days (mean difference 1.82 days, 95 % CI 0.53–3.10, $I^2 = 9$ %) and reduced length of ICU stay (mean difference −1.88 days, 95 % CI −3.12 to −0.64, $I^2 = 75$ %) compared with a liberal strategy or standard care.

Conclusions: In adults and children with ARDS, sepsis or SIRS, a conservative or deresuscitative fluid strategy results in an increased number of ventilator-free days and a decreased length of ICU stay compared with a liberal strategy or standard care. The effect on mortality remains uncertain. Large randomised trials are needed to determine optimal fluid strategies in critical illness.



Restriction of Intravenous Fluid in ICU Patients with Septic Shock

T.S. Meyhoff, P.B. Hjortrup, J. Wetterslev, P. Sivapalan, J.H. Laake, M. Cronhjort, S.M. Jakob, M. Cecconi, M. Nalos, M. Ostermann, M. Mallaran, V. Pettilä, M.H. Møller, M.-R.N. Kjær, T. Lange, C. Overgaard-Steensen, R.A. Brand, M. Winther-Olesen, J.O. White, L. Quist, B. Westergaard, A.B. Jonsson, C.J.S. Hjortsø, N. Meier, T.S. Jensen, J. Engstrøm, L. Nebrich, N.C. Andersen-Ranberg, J.V. Jensen, N.A. Joseph, L.M. Poulsen, L.S. Herlov, C.G. Sølling, S.K. Pedersen, K.K. Knudsen, T.S. Strøm, M.L. Vang, H. Bundgaard, B.S. Rasmussen, S.R. Aagaard, T. Hildebrandt, L. Russell, M.H. Bestle, M. Schønemann-Lund, A.C. Brochner, C.F. Elvander, S.K.L. Hoffmann, M.I. Rasmussen, Y.K. Martin, F.F. Friberg, H. Seter, T.N. Aslam, S. Ádány, P. Seidel, K. Strand, B. Johnstad, E. Joelsson-Alm, J. Christensen, C. Ahlstedt, C.A. Þormundsdóttir, M. Siegemund, M. Creco, J. Radej, M. Kříž, D.W. Gould, K.M. Rowan, P.R. Mouncey, and A. Perner, for the CLASSIC Trial Group*

ABSTRACT

BACKGROUND

Intravenous fluids are recommended for the treatment of patients who are in septic shock, but higher fluid volumes have been associated with harm in patients who are in the intensive care unit (ICU).

METHODS

In this international, randomized trial, we assigned patients with septic shock in the ICU who had received at least 1 liter of intravenous fluid to receive restricted intravenous fluid or standard intravenous fluid therapy; patients were included if the onset of shock had been within 12 hours before screening. The primary outcome was death from any cause within 90 days after randomization.

RESULTS

We enrolled 1554 patients; 770 were assigned to the restrictive-fluid group and 784 to the standard-fluid group. Primary outcome data were available for 1545 patients (99.4%). In the ICU, the restrictive-fluid group received a median of 1798 ml of intravenous fluid (interquartile range, 500 to 4366); the standard-fluid group received a median of 3811 ml (interquartile range, 1861 to 6762). At 90 days, death had occurred in 323 of 764 patients (42.3%) in the restrictive-fluid group, as compared with 329 of 781 patients (42.1%) in the standard fluid group (adjusted absolute difference, 0.1 percentage points; 95% confidence interval [CI], −4.7 to 4.9; P=0.96). In the ICU, serious adverse events occurred at least once in 221 of 751 patients (29.4%) in the restrictive fluid group and in 258 of 772 patients (30.8%) in the standard fluid group (adjusted absolute difference, −1.7 percentage points; 99% CI, −7.7 to 4.3). At 90 days after randomization, the numbers of days alive without life support and days alive and out of the hospital were similar in the two groups.

CONCLUSIONS

Among adult patients with septic shock in the ICU, intravenous fluid restriction did not result in fewer deaths at 90 days than standard intravenous fluid therapy. (Funded by the Novo Nordisk Foundation and others; CLASSIC ClinicalTrials.gov

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Perner can be contacted at anders.perner@regionh.dk or at the Department of Intensive Care, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark.

*A complete list of investigators in the Conservative versus Liberal Approach to Fluid Therapy in Septic Shock (CLASSIC) Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

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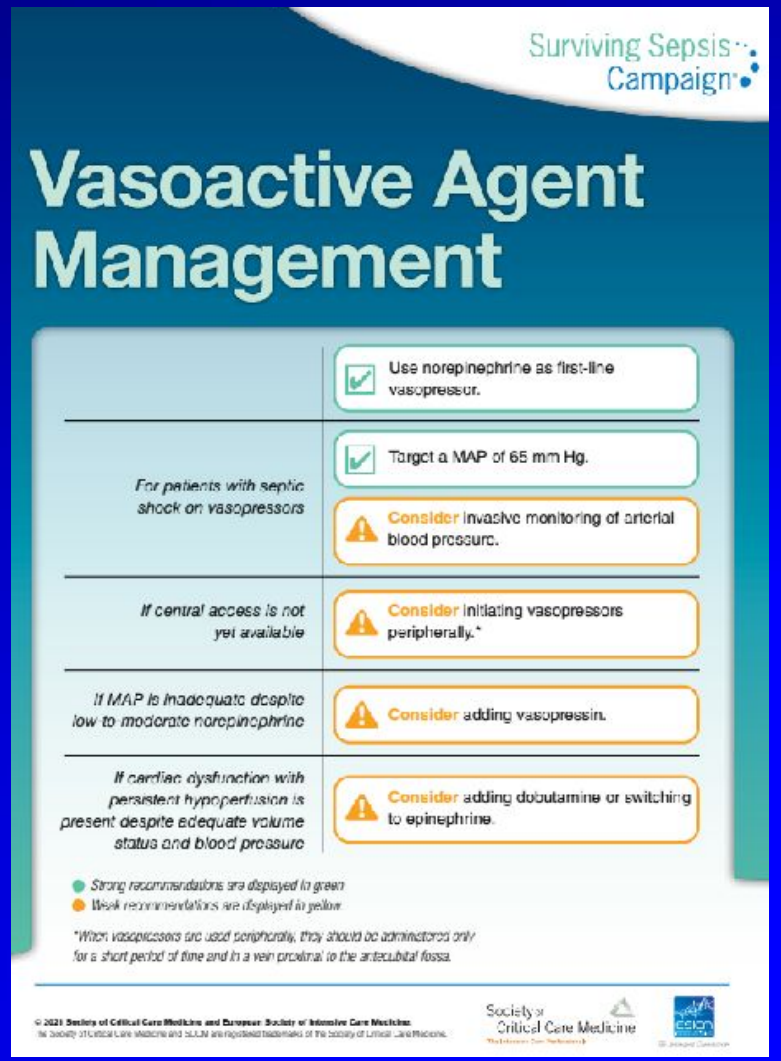
CME at NEJM.org

Sepsis, IV fluids

- In sepsis-induced hypoperfusion
  - 30 ml/Kg IV crystalloid within the first 3 hours
- Balanced crystalloids (LR vs NS)?
- After initial resuscitation
  - Small bloused as needed for persistent hypoperfusion?
  - Restriction of fluids?
  - How to evaluate for fluid needs? CO, capillary refill, lactate, dynamic maneuvers?
  - Role for albumin?

Septic shock, pressors

- Target MAP of 65 mmHg
- Norepinephrine should be first line
- Target MAP 65, if no response with low/moderate dose add vasopressin
- If no adequate response add epinephrine
- Dobutamine can be considered in individual cases if cardiac dysfunction
- Dopamine no longer recommended as standard care



Sepsis, evaluation

- Cultures
  - Appropriate cultures (including blood) before antibiotics if no delay (<45 min)
- Measure blood lactate (Quality of evidence: low)
  - Follow levels to guide resuscitation

Lactate Level	Mortality
0-2.5 mmol/L	4.9 percent mortality
2.5-4.0 mmol/L	9.0 percent mortality
> 4.0 mmol/L	28.4 percent mortality

Nguyen, et al., 2004; Shapiro, et al., 2005

Sepsis, other treatments

- Steroids
  - Mixed results, positive, negative neutral
  - Suggested if ongoing requirement for vasopressors (4 hours)
- Respiratory support
  - ARDSnet protocol (6 mg/Kg tidal volume)
- Glucose control
  - Try to keep <180 mg/dL but don’t be too aggressive

Sepsis, other treatments

- Blood transfusion
  - Goal 7 gm/dL
- Nutrition
  - Early initiation of enteral nutrition if possible (within 72 hours)
- DVT prophylaxis
- Stress ulcer prophylaxis if risk factors for GI bleed

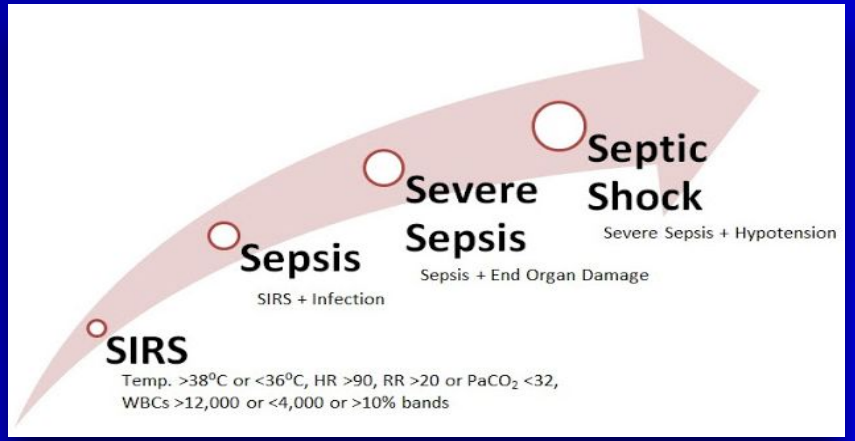
Sepsis, other treatments

- Lots of basic science studies have suggested additional therapies for sepsis, unfortunately they don't work
  - Drocrecogin alpha (Xigris®)
  - TNF alpha monoclonal antibody
  - Monoclonal antibody against endotoxin
  - IL-1 receptor antagonist
  - Immunoglobulins
  - Vitamin C
  - Cyclooxygenase inhibition
  - Inhibition of nitrous oxide synthesis

Criticisms over the Surviving Sepsis Campaign and the CMS bundle

Criticisms

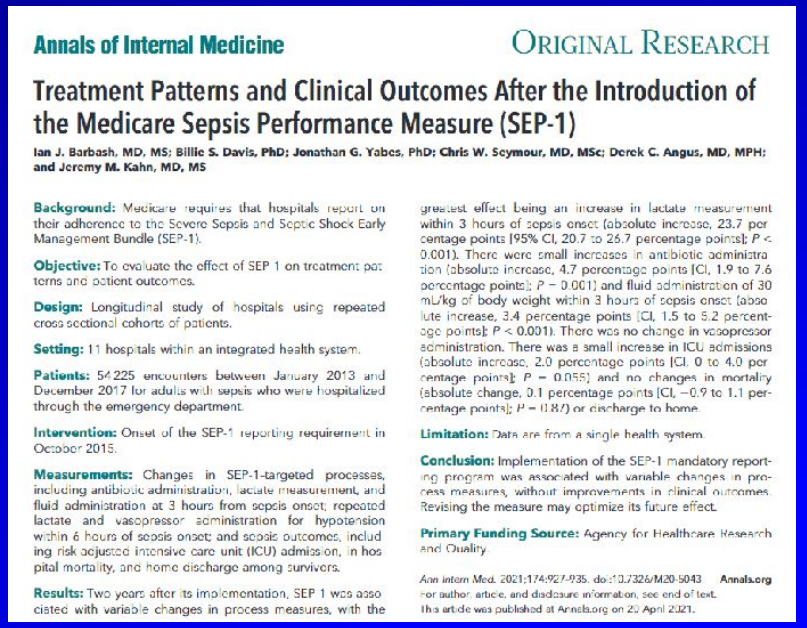
- Failure to acknowledge the practical difficulties clinicians face when trying to diagnose sepsis
  - Over and underdiagnosis
- One-size-fits-all approach
  - No differentiation in the management of patients with suspected sepsis or septic shock
  - There is time for better decisions in stable patients
  - Not balancing benefits and harms
  - Curtail the clinicians' ability to adjust treatments to the individual patient



https://doi.org/10.1093/cid/cix997

Criticisms

- ✧Concerns about timing, excessive fluids and antibiotics
- ✧Specific components are controversial
  - ✔ Lactate is not specific and checking it does not change prognosis
- ✧A third of patients are found to have alternative diagnosis
- ✧ NQF re-endorsed the measure in 2021
  - IDSA, ACEP, SHP filed an appeal with NQF expressing concerns



Annals of Internal Medicine ORIGINAL RESEARCH

Treatment Patterns and Clinical Outcomes After the Introduction of the Medicare Sepsis Performance Measure (SEP-1)

Ian J. Barbash, MD, MS; Billie S. Davis, PhD; Jonathan G. Yabes, PhD; Chris W. Seymour, MD, MSc; Derek C. Angus, MD, MPH; and Jeremy M. Kahn, MD, MS

Background: Medicare requires that hospitals report on their adherence to the Severe Sepsis and Septic Shock Early Management Bundle (SEP-1).

Objective: To evaluate the effect of SEP 1 on treatment patterns and patient outcomes.

Design: Longitudinal study of hospitals using repeated cross sectional cohorts of patients.

Setting: 11 hospitals within an integrated health system.

Patients: 54 225 encounters between January 2013 and December 2017 for adults with sepsis who were hospitalized through the emergency department.

Intervention: Onset of the SEP-1 reporting requirement in October 2015.

Measurements: Changes in SEP-1–targeted processes, including antibiotic administration, lactate measurement, and fluid administration at 3 hours from sepsis onset; repeated lactate and vasopressor administration for hypotension within 6 hours of sepsis onset; and sepsis outcomes, including risk adjusted intensive care unit (ICU) admission, in hospital mortality, and home discharge among survivors.

Results: Two years after its implementation, SEP 1 was associated with variable changes in process measures, with the greatest effect being an increase in lactate measurement within 3 hours of sepsis onset (absolute increase, 23.7 percentage points [95% CI, 20.7 to 26.7 percentage points]; $P < 0.001$). There were small increases in antibiotic administration (absolute increase, 4.7 percentage points [CI, 1.9 to 7.6 percentage points]; $P = 0.001$) and fluid administration of 30 mL/kg of body weight within 3 hours of sepsis onset (absolute increase, 3.4 percentage points [CI, 1.5 to 5.2 percentage points]; $P < 0.001$). There was no change in vasopressor administration. There was a small increase in ICU admissions (absolute increase, 2.0 percentage points [CI, 0 to 4.0 percentage points]; $P = 0.055$) and no changes in mortality (absolute change, 0.1 percentage points [CI, −0.9 to 1.1 percentage points]; $P = 0.87$) or discharge to home.

Limitation: Data are from a single health system.

Conclusion: Implementation of the SEP-1 mandatory reporting program was associated with variable changes in process measures, without improvements in clinical outcomes. Revising the measure may optimize its future effect.

Primary Funding Source: Agency for Healthcare Research and Quality.

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For author, article, and disclosure information, see end of text.

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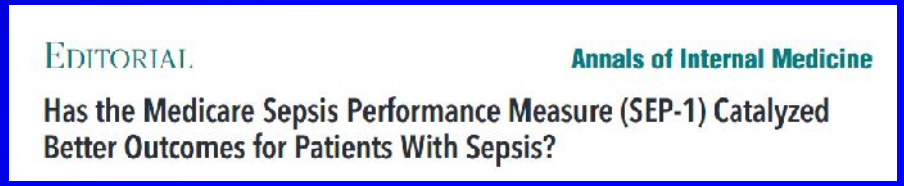

EDITORIAL Annals of Internal Medicine

Has the Medicare Sepsis Performance Measure (SEP-1) Catalyzed Better Outcomes for Patients With Sepsis?

Conclusions

- Sepsis is a very common problem
- Little RCT data to guide therapy
- Timely and appropriate management is key
  - Sepsis vs septic shock
  - Urgency of initiating interventions vs time to think about the case and getting more data
- CMS bundle and sepsis guidelines are controversial

Questions?