SEPSIS

Back to the Basics

Raymond Lee Kiser, MD
Associate Chief Medical Officer
Columbus Regional Health
September 13, 2017

SEPSIS
DEFINING THE PROBLEM

- **Historically**
  - The term “sepsis” has been around for over 2700 years
    - Greek, meaning, “putrefaction,”
    - Specifically pertained to bacteria-mediated decomposition of organic matter
  - Similarly, “shock” has been around for hundreds of year
    - French, from choquer, meaning “to collide with”

SEPSIS
DEFINING THE PROBLEM

- **Centers for Medicare and Medicaid Services**
  - Systemic Inflammatory Response Syndrome
    - T > 38.3 or < 36
    - P > 90
    - RR > 20
    - WBC > 12 or < 4, or >10% bands
  - Sepsis
    - 2 SIRS *PLUS*
    - **Suspected or Confirmed Infection**

SEPSIS
DEFINING THE PROBLEM

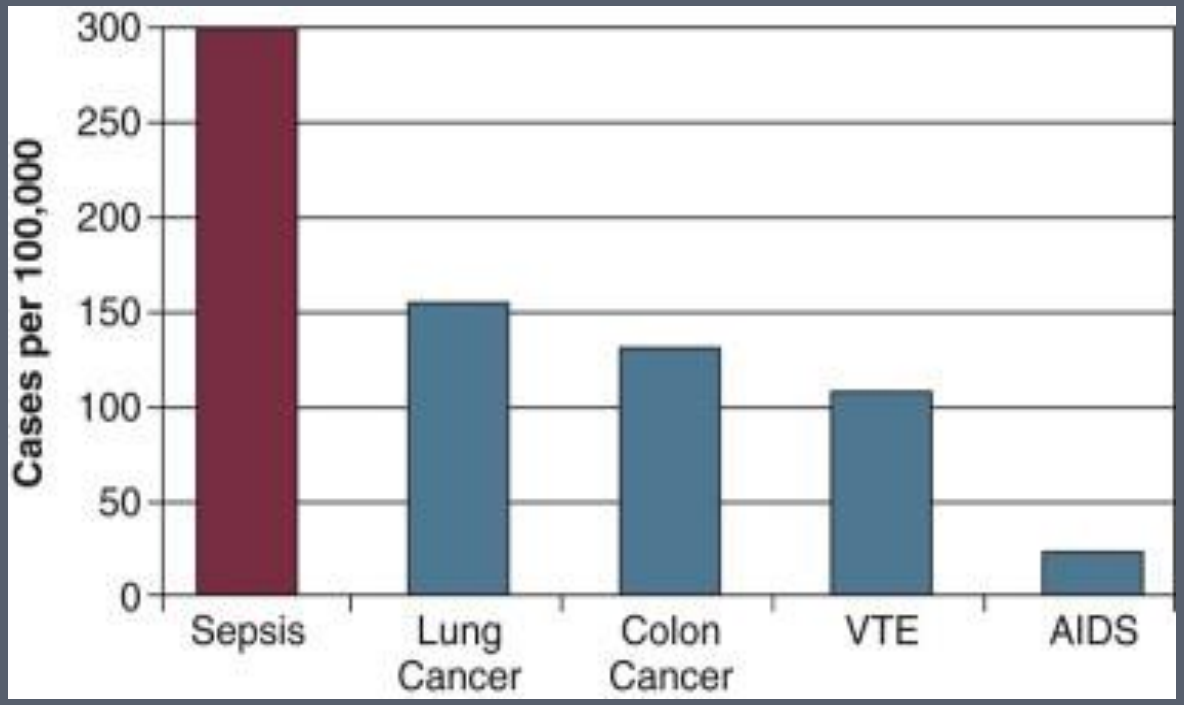
- **Centers for Medicare and Medicaid**
  - Severe Sepsis
    - Sepsis *PLUS*
    - Signs of end organ dysfunction or tissue hypoperfusion
      - SBP < 90 or MAP < 65
      - Cr > 2
      - Bilirubin > 2
      - Platelet < 100
      - INR > 1.5 or PTT > 60
      - Serum lactate > 2
  - Septic Shock
    - Severe Sepsis *PLUS*
    - SBP < 90 or MAP < 65 *AFTER* 30 ml/kg fluid OR
    - Serum lactate > 4

SEPSIS
DEFINING THE PROBLEM

- **Sepsis-3 (Third International Consensus Definitions for Sepsis and Septic Shock)**
  - Sepsis
    - Life-Threatening Organ Dysfunction caused by a Dysregulated Host Response to Infection
  - Septic Shock
    - Subset of patients with sepsis in which circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
    - Clinically defined as persistent hypotension requiring vasopressors to maintain a MAP > 65 and having a lactate > 2

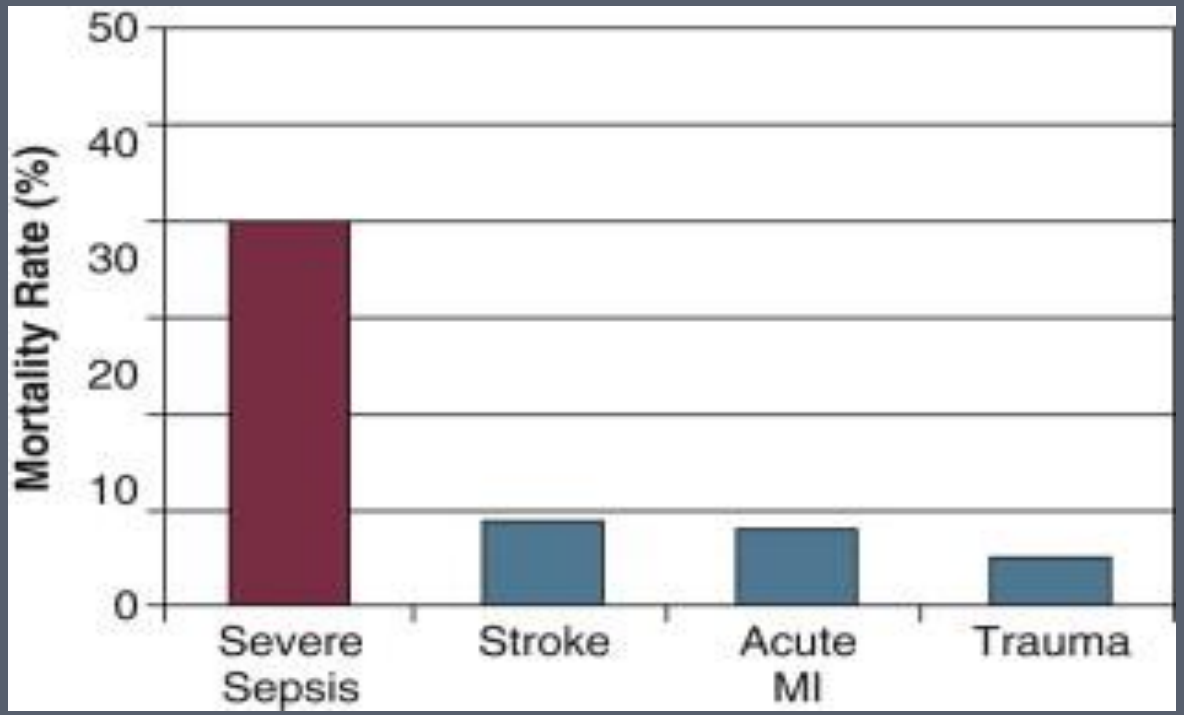
JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

SEPSIS AND SEPTIC SHOCK
THE EPIDEMIOLOGY



- **Incidence projected to increase by 1.5% per year**
- **Will likely exceed 1 million cases annually by 2020**

SEPSIS AND SEPTIC SHOCK
THE EPIDEMIOLOGY

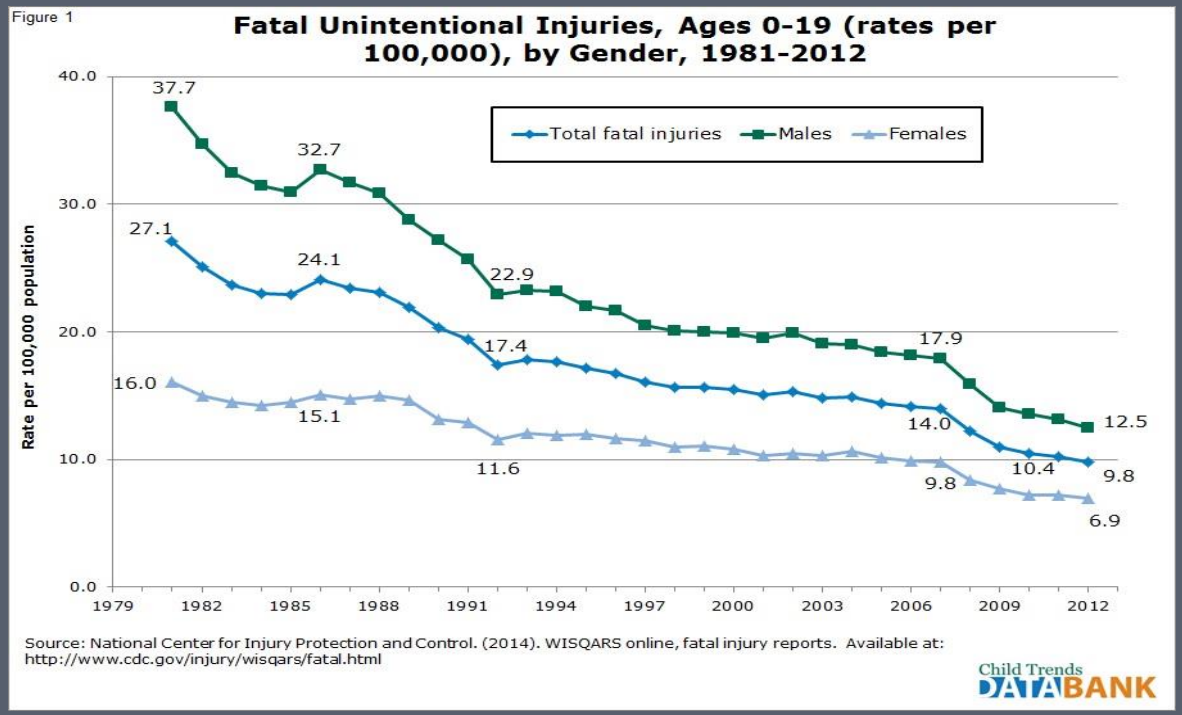


- Sepsis ranks 10th as the leading cause of death in the US
- Survivors have a diminished QOL, sharply reduced long term survival, and may have major cognitive impairment

SEPSIS AND SEPTIC SHOCK
THE EPIDEMIOLOGY

Trauma

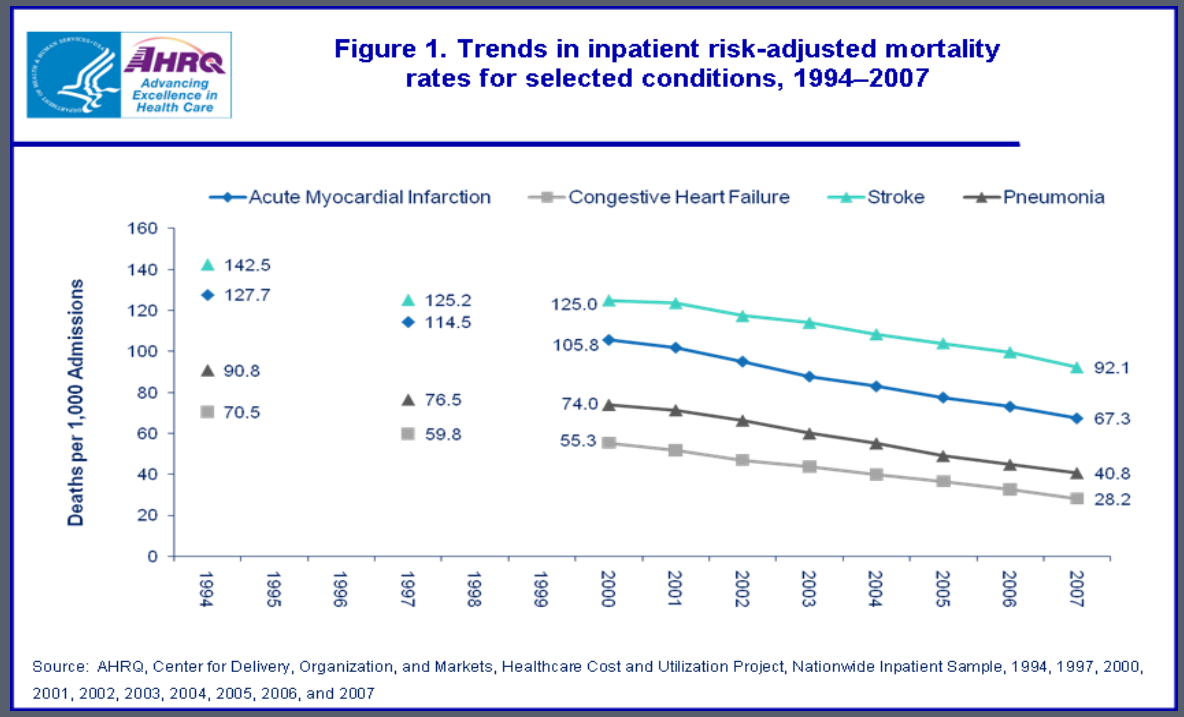
The Importance of "The Golden Hour"



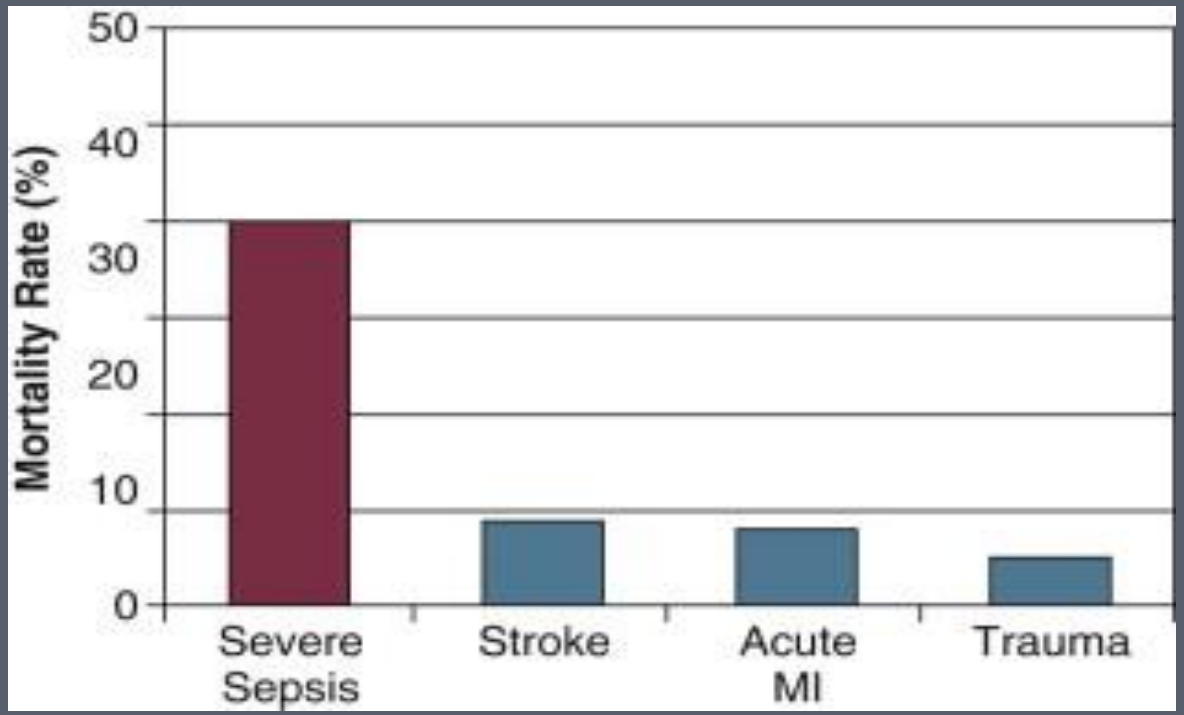
SEPSIS AND SEPTIC SHOCK
THE EPIDEMIOLOGY

MI and Stroke

The Importance of "The Golden Hour(s)"

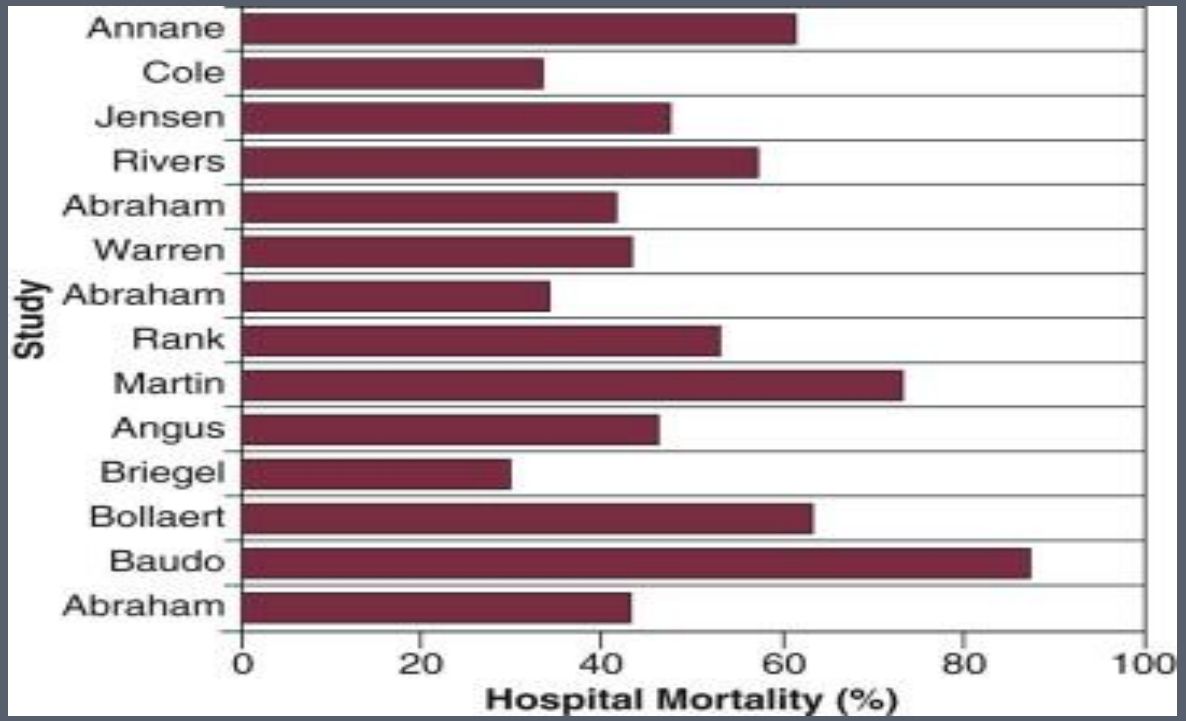


SEPSIS AND SEPTIC SHOCK
THE EPIDEMIOLOGY



- Sepsis ranks 10th as the leading cause of death in the US
- Survivors have a diminished QOL, sharply reduced long term survival, and may have major cognitive impairment

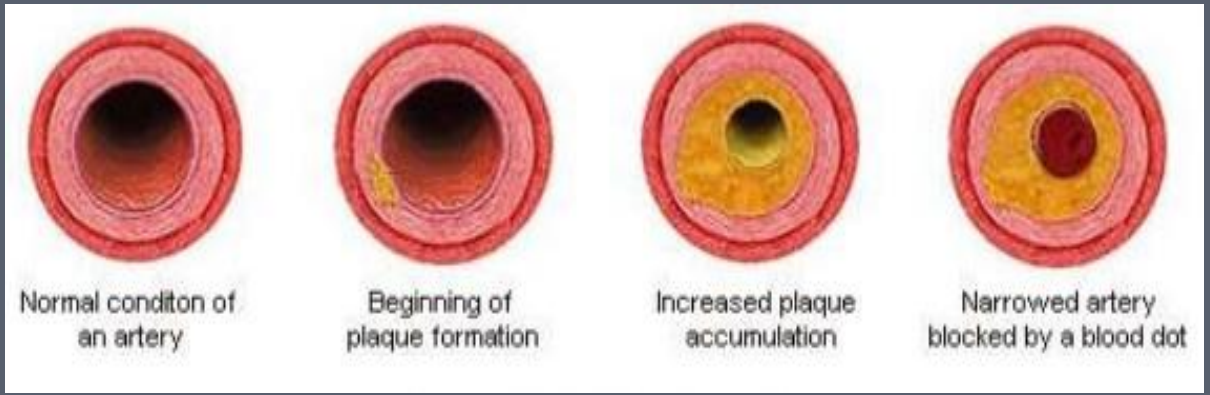
SEPSIS AND SEPTIC SHOCK
THE EPIDEMIOLOGY



- **Hospital mortality in septic shock from major studies over the last decade**

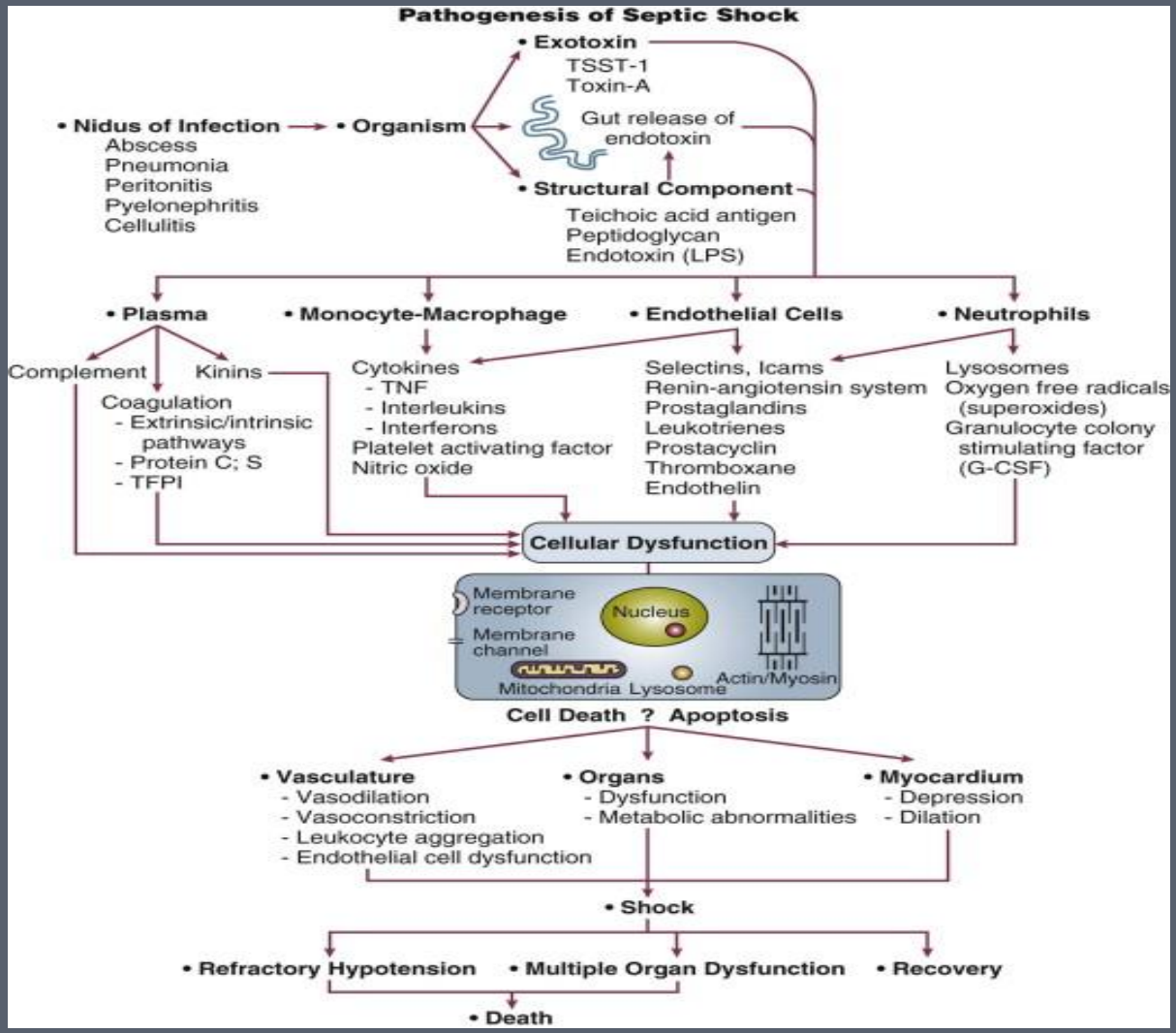
SEPSIS AND SEPTIC SHOCK

THE PATHOGENESIS MI AND STROKE



https://www.slideshare.net/ALPHAROMEO93/myocardial-infarction-case-presentation-and-an-overview

SEPSIS AND SEPTIC SHOCK
THE PATHOGENESIS



SEPSIS AND SEPTIC SHOCK
THE DIAGNOSIS

Sepsis - Septic Shock
Think 1-2-1 to identify sepsis

SEPSIS

1 Confirmed or suspected infection

2 or more systemic inflammatory response syndrome (SIRS)

1 or more new acute organ dysfunction

SEPTIC SHOCK

Sepsis + ongoing hypotension despite adequate resuscitation or

evidence of poor organ perfusion (lactate >/=4)

SEPSIS AND SEPTIC SHOCK
THE DIAGNOSIS

- **Confirmed or Suspected Infection**
- **SIRS – Systemic Inflammatory Response Syndrome**
  - Temperature <36.0 C (96.8 F) or >38.3 C (100.9)
  - Altered mental status
  - Heart rate >90
  - Respiratory rate >20
  - WBC <4000 or >12000 or >10% bands
- **Sepsis with Induced Organ Dysfunction**
  - Systolic Blood pressure <90 or decreased 40 points from baseline or MAP <65
  - Acute respiratory failure as evidenced by a new need for invasive or noninvasive ventilation (BIPAP or intubation)
  - Creatinine >2 or urine output <0.5ml/kg/hour for 2 hours
  - Bilirubin >2
  - Platelet count <100,000
  - Lactate >2
  - INR >1.5 or aPTT >60 seconds
- **Septic Shock**
  - Sepsis + ongoing hypotension ***despite*** adequate resuscitation or evidence of poor organ perfusion (lactate >/=4)

SEPSIS AND SEPTIC SHOCK
THE MANAGEMENT

TREATMENT GUIDELINES WITHIN 3 HOURS OF ONSET OF SYMPTOMS

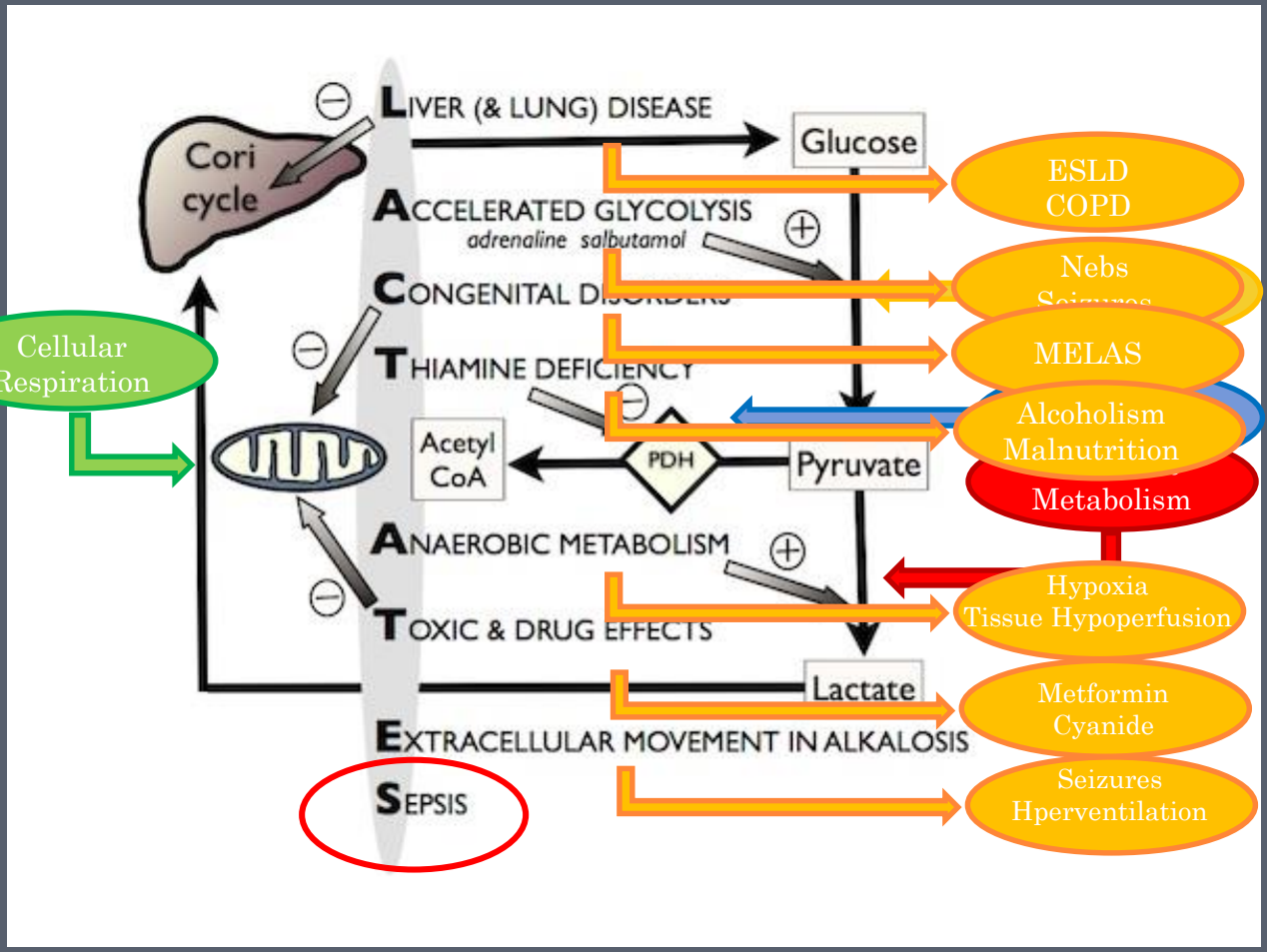
- **Measure lactate level (indicator of organ dysfunction)**
- **Obtain blood cultures prior to antibiotics**
  - Ideally urine also
- **Administer broad spectrum antibiotics**
  - TIME IS CRITICAL
  - If more than one antibiotic is prescribed, and IV access is limited, administer the broadest spectrum one first – usually Zosyn or Merem
- **Administer 30 ml/kg bolus of crystalloid for:**
  - Hypotension: SBP <90 or MAP <65
  - ***OR*** Lactate >/= 4mmol/L

SEPSIS AND SEPTIC SHOCK
THE MANAGEMENT

TREATMENT GUIDELINES WITHIN 3 HOURS OF ONSET OF SYMPTOMS

- **Measure *lactate* level (indicator of organ dysfunction)**
- **Obtain blood cultures prior to antibiotics**
  - Ideally urine also
- **Administer broad spectrum antibiotics**
  - TIME IS CRITICAL
  - If more than one antibiotic is prescribed, and IV access is limited, administer the broadest spectrum one first – usually Zosyn or Merem
- **Administer 30 ml/kg bolus of crystalloid for:**
  - Hypotension: SBP <90 or MAP <65
  - ***OR*** Lactate >/= 4mmol/L

SEPSIS AND SEPTIC SHOCK
THE MANAGEMENT



http://resus.me/tag/lactate/

SEPSIS AND SEPTIC SHOCK
THE MANAGEMENT

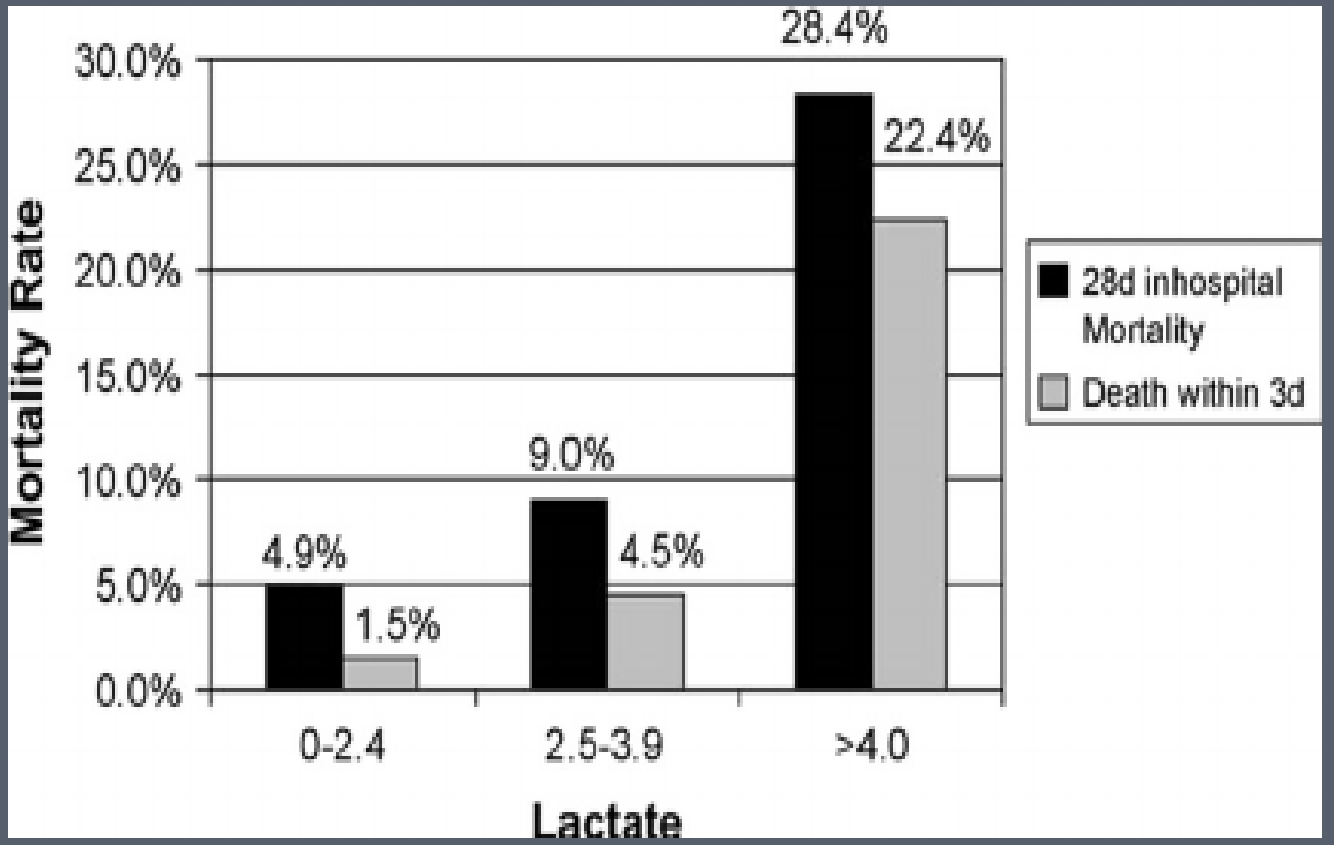


Figure 1 Serum lactate as a predictor of mortality in emergency... - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/269339822_fig1_Figure-1-Serum-lactate-as-a-predictor-of-mortality-in-emergency-department-ED-patients [accessed Sep 15, 2016]

SEPSIS AND SEPTIC SHOCK
THE MANAGEMENT

TREATMENT GUIDELINES WITHIN 3 HOURS OF ONSET OF SYMPTOMS

- **Measure lactate level (indicator of organ dysfunction)**
- **Obtain blood cultures prior to antibiotics**
  - Ideally urine also
- **Administer broad spectrum antibiotics**
  - TIME IS CRITICAL
  - If more than one antibiotic is prescribed, and IV access is limited, administer the broadest spectrum one first – usually Zosyn or Merem
- **Administer 30 ml/kg bolus of crystalloid for:**
  - Hypotension: SBP <90 or MAP <65
  - ***OR*** Lactate >/= 4mmol/L

SEPSIS AND SEPTIC SHOCK
THE MANAGEMENT

TREATMENT GUIDELINES WITHIN 3 HOURS OF ONSET OF SYMPTOMS

- **Measure lactate level (indicator of organ dysfunction)**
- **Obtain blood cultures prior to antibiotics**
  - Ideally urine also
- **Administer broad spectrum antibiotics**
  - TIME IS CRITICAL
  - If more than one antibiotic is prescribed, and IV access is limited, administer the broadest spectrum one first – usually Zosyn or Merem
- **Administer *30 ml/kg bolus* of crystalloid for:**
  - Hypotension: SBP <90 or MAP <65
  - ***OR*** Lactate >/= 4mmol/L

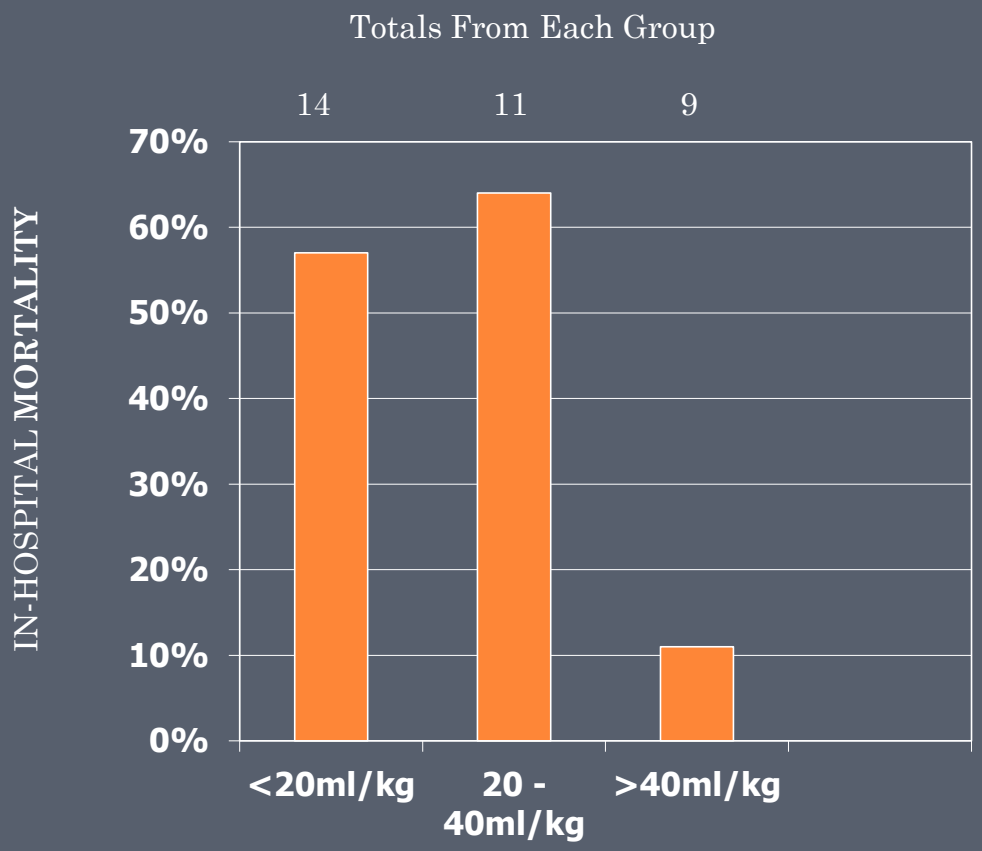
SEPSIS AND SEPTIC SHOCK WHAT ABOUT ALL THAT FLUID?

- **Aggressive volume resuscitation associated with improved survival in septic children**
  - First study to show a beneficial intervention in pediatric septic shock – observational study
  - Recruited all pediatric sepsis patients to ER in Washington DC Childrens Hospital – PA catheter in situ by 6 hours
  - 34 patients – mean age 13.5 months
  - Divided into 3 groups by volume received in first hour (post hoc)

Group 1	<20ml/kg
Group 2	20 – 40ml/kg
Group 3	>40ml/kg

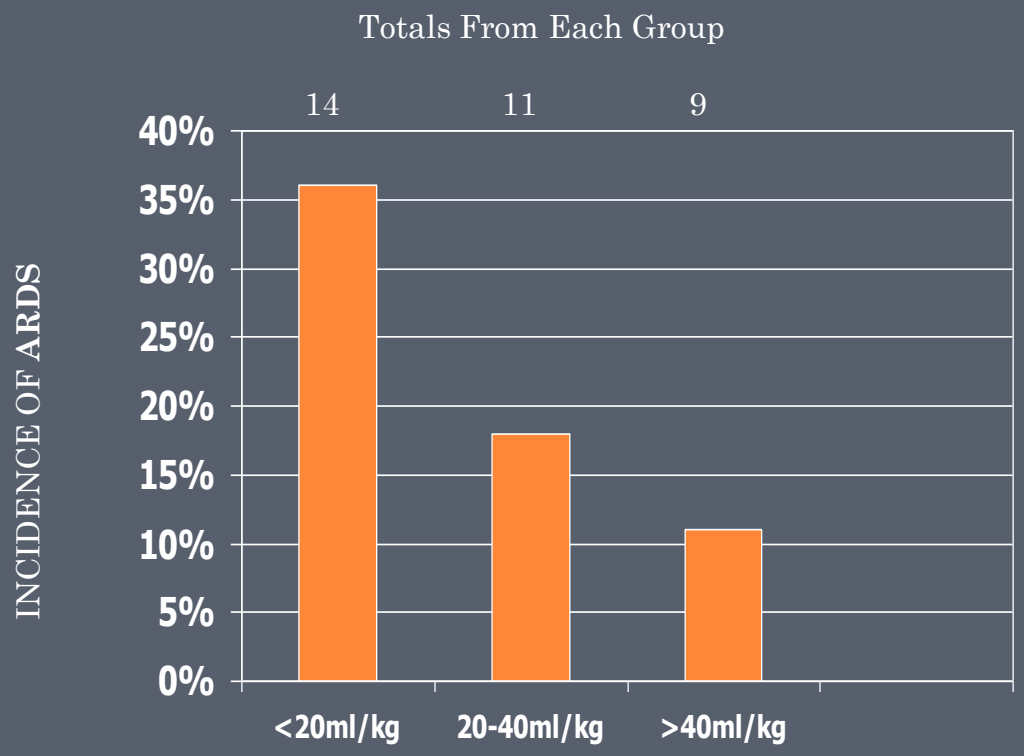
Carcillo et al. Role of early fluid resuscitation in pediatric septic shock. JAMA. **1991**;266:1242-1245

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?



Carcillo et al. Role of early fluid resuscitation in pediatric septic shock. JAMA. 1991;266:1242-1245

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?



Carcillo et al. Role of early fluid resuscitation in pediatric septic shock. JAMA. 1991;266:1242-1245

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?

TABLE 3. KAPLAN–MEIER ESTIMATES OF MORTALITY AND CAUSES OF IN-HOSPITAL DEATH.*

VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	29 (42.3)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03
Causes of in-hospital death‡				
Sudden cardiovascular collapse	25/119 (21.0)	12/117 (10.3)	—	0.02
Multiorgan failure	26/119 (21.8)	19/117 (16.2)	—	0.27

*CI denotes confidence interval. Dashes indicate that the relative risk is not applicable.

†Percentages were calculated by the Kaplan–Meier product-limit method.

‡The denominators indicate the numbers of patients in each group who completed the initial six-hour study period.

- Rivers et al NEJM 2001; 345: 1368-77

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

ABSTRACT

BACKGROUND

In a single-center study published more than a decade ago involving patients presenting to the emergency department with severe sepsis and septic shock, mortality was markedly lower among those who were treated according to a 6-hour protocol of early goal-directed therapy (EGDT), in which intravenous fluids, vasopressors, inotropes, and blood transfusions were adjusted to reach central hemodynamic targets, than among those receiving usual care. We conducted a trial to determine whether these findings were generalizable and whether all aspects of the protocol were necessary.

METHODS

In 31 emergency departments in the United States, we randomly assigned patients with septic shock to one of three groups for 6 hours of resuscitation: protocol-based EGDT; protocol-based standard therapy that did not require the placement of a central venous catheter, administration of inotropes, or blood transfusions; or usual care. The primary end point was 60-day in-hospital mortality. We tested sequentially whether protocol-based care (EGDT and standard-therapy groups combined) was superior to usual care and whether protocol-based EGDT was superior to protocol-based standard therapy. Secondary outcomes included longer-term mortality and the need for organ support.

RESULTS

We enrolled 1341 patients, of whom 439 were randomly assigned to protocol-based EGDT, 446 to protocol-based standard therapy, and 456 to usual care. Resuscitation strategies differed significantly with respect to the monitoring of central venous pressure and oxygen and the use of intravenous fluids, vasopressors, inotropes, and blood transfusions. By 60 days, there were 92 deaths in the protocol-based EGDT group (21.0%), 81 in the protocol-based standard-therapy group (18.2%), and 86 in the usual-care group (18.9%) (relative risk with protocol-based therapy vs. usual care, 1.04; 95% confidence interval [CI], 0.82 to 1.31; P=0.83; relative risk with protocol-based EGDT vs. protocol-based standard therapy, 1.15; 95% CI, 0.88 to 1.51; P=0.31). There were no significant differences in 90-day mortality, 1-year mortality, or the need for organ support.

CONCLUSIONS

In a multicenter trial conducted in the tertiary care setting, protocol-based resuscitation of patients in whom septic shock was diagnosed in the emergency department did not improve outcomes. (Funded by the National Institute of General Medical Sciences; ProCESS ClinicalTrials.gov number, NCT00510835.)

The members of the writing committee (Donald M. Yealy, M.D., John A. Kellum, M.D., David T. Huang, M.D., Amber E. Barnato, M.D., Lisa A. Weissfeld, Ph.D., and Francis Pike, Ph.D., University of Pittsburgh, Pittsburgh; Thomas Terndrup, M.D., Ohio State University, Columbus; Henry E. Wang, M.D., University of Alabama at Birmingham, Birmingham; Peter C. Hou, M.D., Brigham and Women's Hospital, Boston; Frank LoVecchio, D.O., Maricopa Medical Center, Phoenix; Michael R. Filbin, M.D., Massachusetts General Hospital, and Nathan I. Shapiro, M.D., Beth Israel Deaconess Medical Center— both in Boston; and Derek C. Angus, M.D., M.P.H., University of Pittsburgh, Pittsburgh) assume responsibility for the content and integrity of the article. Address reprint requests to Dr. Angus at the Department of Critical Care Medicine, University of Pittsburgh, 3550 Terrace St., 614 Scaife Hall, Pittsburgh, PA 15261, or at angusdc@upmc.edu.

*A complete list of investigators in the Protocolized Care for Early Septic Shock (ProCESS) study is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on March 18, 2014, at NEJM.org.

N Engl J Med 2014;370:1683-93.
DOI: 10.1056/NEJMoa1401602

- PROCESS Study N Engl J Med 2014;370:1683-93.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

ABSTRACT

BACKGROUND

Early goal-directed therapy (EGDT) has been endorsed in the guidelines of the Surviving Sepsis Campaign as a key strategy to decrease mortality among patients presenting to the emergency department with septic shock. However, its effectiveness is uncertain.

METHODS

In this trial conducted at 51 centers (mostly in Australia or New Zealand), we randomly assigned patients presenting to the emergency department with early septic shock to receive either EGDT or usual care. The primary outcome was all-cause mortality within 90 days after randomization.

RESULTS

Of the 1600 enrolled patients, 796 were assigned to the EGDT group and 804 to the usual-care group. Primary outcome data were available for more than 99% of the patients. Patients in the EGDT group received a larger mean (±SD) volume of intravenous fluids in the first 6 hours after randomization than did those in the usual-care group (1964±1415 ml vs. 1713±1401 ml) and were more likely to receive vasopressor infusions (66.6% vs. 57.8%), red-cell transfusions (13.6% vs. 7.0%), and dobutamine (15.4% vs. 2.6%) (P<0.001 for all comparisons). At 90 days after randomization, 147 deaths had occurred in the EGDT group and 150 had occurred in the usual-care group, for rates of death of 18.6% and 18.8%, respectively (absolute risk difference with EGDT vs. usual care, −0.3 percentage points; 95% confidence interval, −4.1 to 3.6; P=0.90). There was no significant difference in survival time, in-hospital mortality, duration of organ support, or length of hospital stay.

CONCLUSIONS

In critically ill patients presenting to the emergency department with early septic shock, EGDT did not reduce all-cause mortality at 90 days. (Funded by the National Health and Medical Research Council of Australia and the Alfred Foundation; ARISE ClinicalTrials.gov number, NCT00975793.)

ARISE Study **N Engl J Med 2014;371:1496-506.**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D., for the ProMISe Trial Investigators*

ABSTRACT

BACKGROUND

Early, goal-directed therapy (EGDT) is recommended in international guidelines for the resuscitation of patients presenting with early septic shock. However, adoption has been limited, and uncertainty about its effectiveness remains.

METHODS

We conducted a pragmatic randomized trial with an integrated cost-effectiveness analysis in 56 hospitals in England. Patients were randomly assigned to receive either EGDT (a 6-hour resuscitation protocol) or usual care. The primary clinical outcome was all-cause mortality at 90 days.

RESULTS

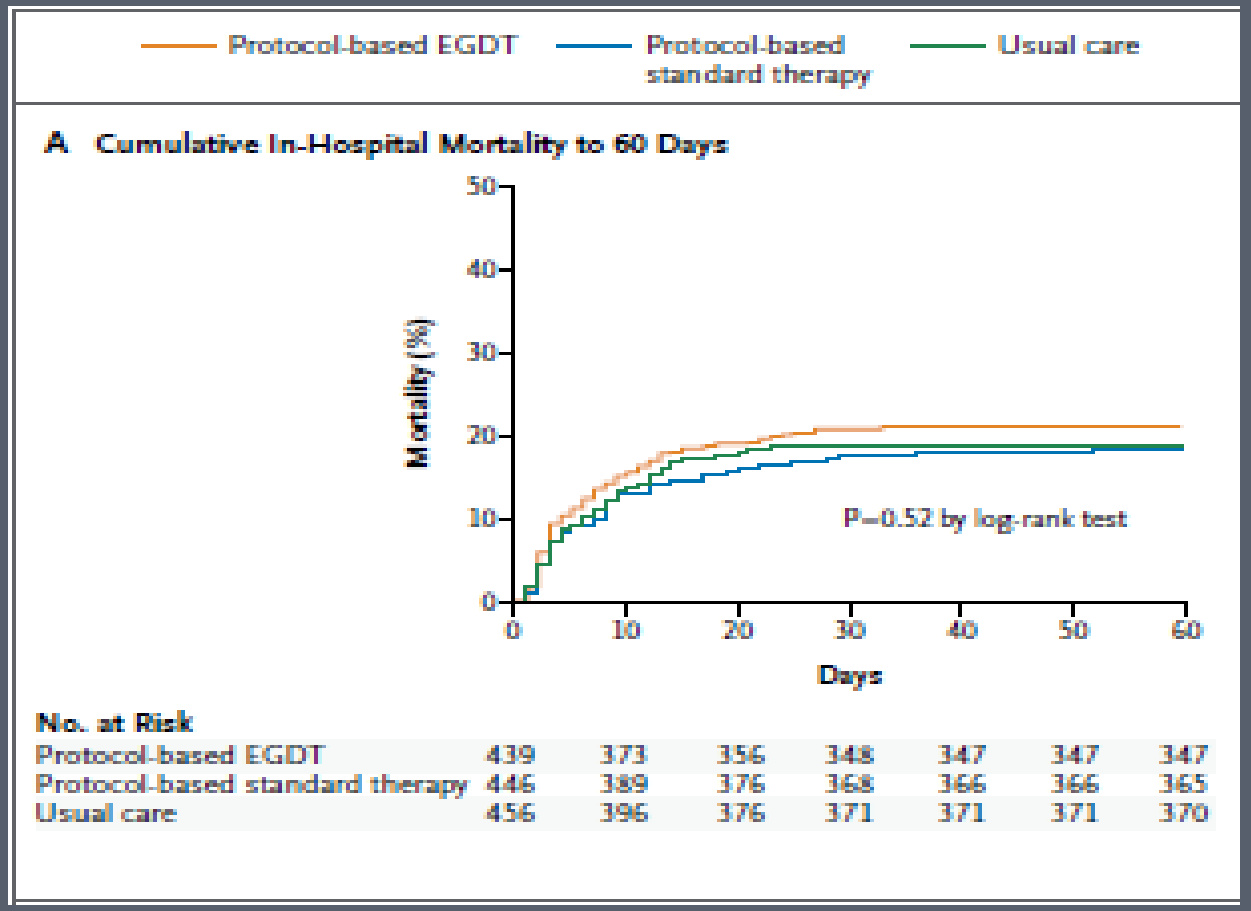
We enrolled 1260 patients, with 630 assigned to EGDT and 630 to usual care. By 90 days, 184 of 623 patients (29.5%) in the EGDT group and 181 of 620 patients (29.2%) in the usual-care group had died (relative risk in the EGDT group, 1.01; 95% confidence interval [CI], 0.85 to 1.20; P=0.90), for an absolute risk reduction in the EGDT group of −0.3 percentage points (95% CI, −5.4 to 4.7). Increased treatment intensity in the EGDT group was indicated by increased use of intravenous fluids, vasoactive drugs, and red-cell transfusions and reflected by significantly worse organ-failure scores, more days receiving advanced cardiovascular support, and longer stays in the intensive care unit. There were no significant differences in any other secondary outcomes, including health-related quality of life, or in rates of serious adverse events. On average, EGDT increased costs, and the probability that it was cost-effective was below 20%.

CONCLUSIONS

In patients with septic shock who were identified early and received intravenous antibiotics and adequate fluid resuscitation, hemodynamic management according to a strict EGDT protocol did not lead to an improvement in outcome. (Funded by the United Kingdom National Institute for Health Research Health Technology Assessment Programme; ProMISe Current Controlled Trials number, ISRCTN36307479.)

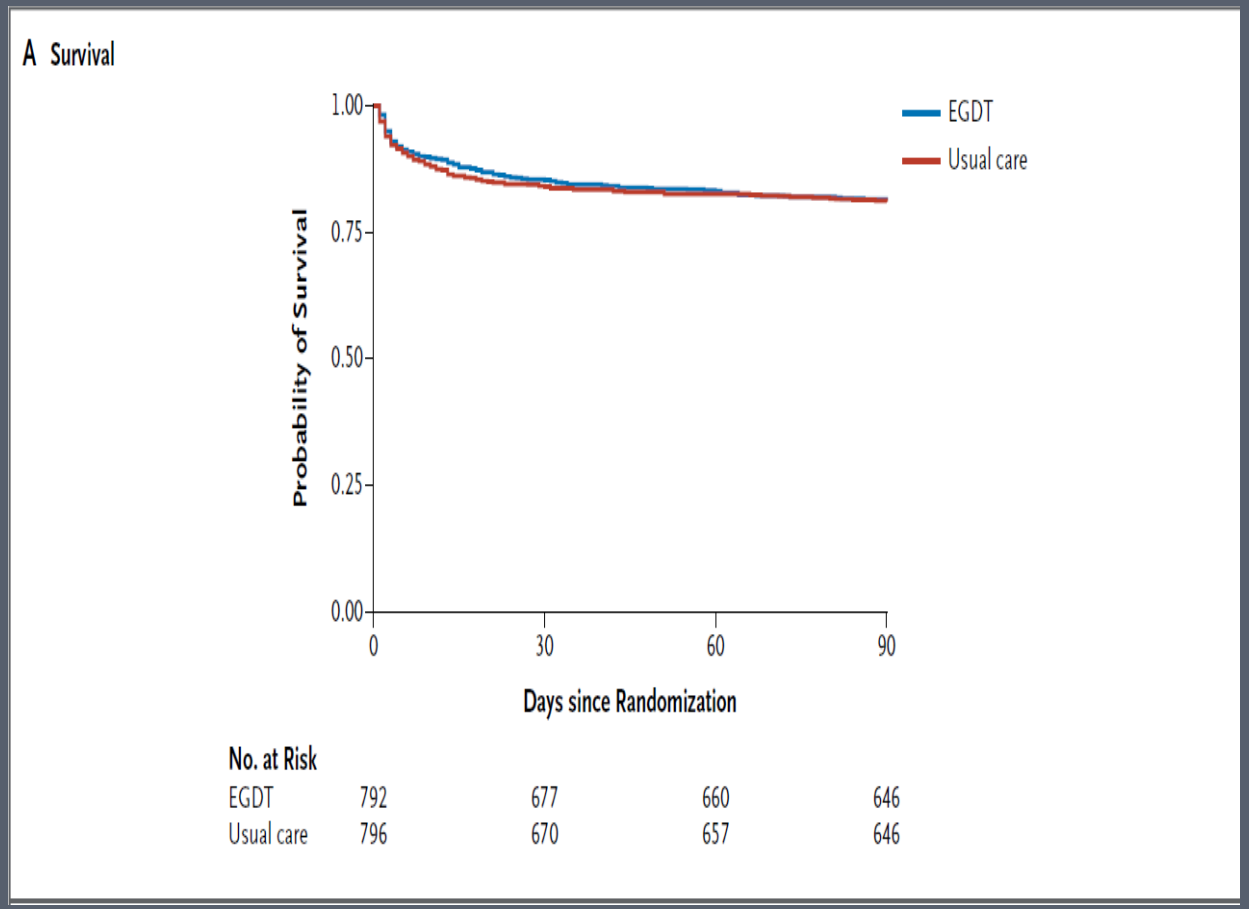
PROMISE Study. **N Engl J Med 2015;372:1301-11.**

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?



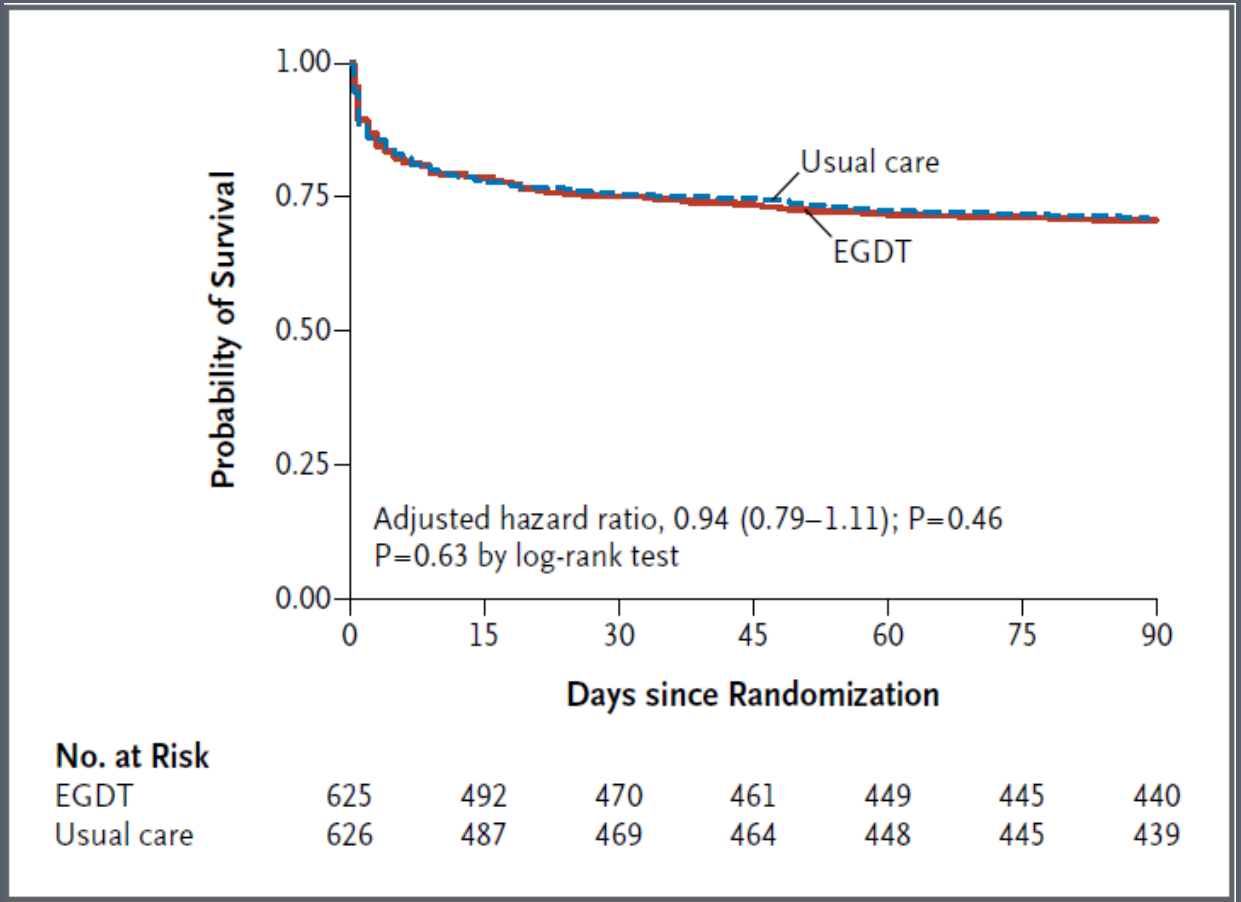
- **PROCESS Study N Engl J Med** 2014;**370:1683-93.**

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?



ARISE Study **N Engl J Med 2014;371:1496-506.**

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?



PROMISE Study. **N Engl J Med 2015;372:1301-11.**

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?

Table S7. Ancillary Interventions Delivered.*

	Baseline		*Hour 0 to hour 6*		*Hour 6 to hour 72*		*Hour 0 to hour 72*	
	EGDT (N = 625)	Usual resuscitation (N= 626)	EGDT (N = 625)	Usual resuscitation (N= 626)	EGDT (N = 608)	Usual resuscitation (N= 607)	EGDT (N = 625)	Usual resuscitation (N= 626)
Total intravenous fluid† - no./total no. (%)	612/625 (97.9)	606/625 (97.0)	609/623 (97.8)	604/625 (96.6)	546/603 (90.5)	548/603 (90.9)	615/623 (98.7)	618/625 (98.9)
Total intravenous fluid - mL	1890±1105	1965±1149	2226±1443	2022±1271	4215±3068	4366±3114	5946±3740	5844±3651
Median total intravenous fluid (IQR) - mL	1950 (1000, 2500)	2000 (1000, 2500)	2000 (1150, 3000)	1784 (1075, 2775)	3623 (1800, 6060)	3981 (1895, 6291)	5587 (2915, 8150)	5410 (3000, 7970)
Intravenous colloid‡ - no./total no. (%)	--	---	197/623 (31.6)	180/625 (28.8)	174/603 (28.4)	150/603 (24.9)	260/623 (41.7)	240/625 (38.4)
Intravenous colloid - mL	--	---	1062±801	913±627	1207±1042	1093±1012	1598±1391	1369±1150
Median intravenous colloid (IQR) - mL	--	---	1000 (500, 1500)	750 (500, 1000)	750 (500, 1750)	750 (500, 1500)	1000 (575, 2000)	1000 (500, 1750)
Intravenous crystalloid‡ - no./total no. (%)	--	---	584/623 (93.7)	597/625 (95.5)	537/603 (89.1)	543/603 (90.0)	609/623 (97.8)	617/625 (98.7)
Intravenous crystalloid - mL	--	---	1963±1357	1767±1178	3909±2869	4136±2914	5323±3518	5317±3435
Median intravenous crystalloid (IQR) - mL	--	---	1750 (999, 2750)	1500 (900, 2380)	3403 (1576, 5647)	3694 (1832, 5911)	4864 (2520, 7241)	4900 (2700, 7408)
Vasopressors - no./total no. (%)	15/625 (2.4)	21/626 (3.4)	332/623 (53.3)	291/625 (46.6)	349/603 (57.9)	317/603 (52.6)	377/623 (60.5)	344/625 (55.0)
Red cell transfusion - no./total no. (%)	--	---	55/623 (8.8)	24/625 (3.8)	76/603 (12.6)	51/603 (8.5)	107/623 (17.2)	65/625 (10.4)
Red cells transfusion- mL	--	---	426±209	540±294	487±335	606±403	565±393	674±506
Median red cell transfusion (IQR) - mL	--	---	309 (285, 577)	535 (305, 607)	351 (291, 579)	552 (317, 620)	529 (298, 602)	562 (317, 660)
Dobutamine - no./total no. (%)	2/625 (0.3)	0/626 (0.0)	113/623 (18.1)	24/625 (3.8)	107/603 (17.7)	39/603 (6.5)	139/623 (22.3)	44/625 (7.0)

PROMISE Study. **N Engl J Med 2015;372:1301-11.**

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?

Intervention	0 to 6 hours			6 to 72 hours[b]		
	EGDT (N = 793)	Usual care (N = 798)	P Value	EGDT (N = 782)	Usual care (N = 778)	P Value
Supplemental oxygen - no./total no. (%)	629/687 (91.6)	554/609 (91.0)	0.71	533/610 (87.4)	494/569 (86.8)	0.78
Mechanical ventilation - no./total no.						
Invasive	176/793 (22.2)	179/798 (22.4)	0.91	211/782 (27.0)	210/778 (27.0)	1.00
Non-invasive	100/793 (12.6)	84/798 (10.5)	0.19	91/782 (11.6)	106/778 (13.6)	0.24
Intravenous fluids,[c]						
Total - ml	1964 ±1415	1713 ± 1401	<0.001	4274 ± 3071	4382 ± 3136	0.51
Total - ml/kg	26.8 ± 20.6	23.2 ± 21.2	<0.001	58.9 ± 46.2	59.2 ± 45.1	0.87
Crystalloids - ml	1547 ± 1351	1374 ± 1335	0.01	3520 ± 2792	3608 ± 2783	0.54
Crystalloids - ml/kg	21.1 ± 19.8	18.7 ± 19.9	0.02	48.7 ± 42.3	48.8 ± 39.1	0.93
Colloids - ml	323 ± 672	249 ± 552	0.02	345 ± 777	328 ± 808	0.68
Colloids - ml/kg	4.4 ± 8.9	3.3 ± 7.5	0.01	4.8 ± 10.6	4.5 ± 11.2	0.63

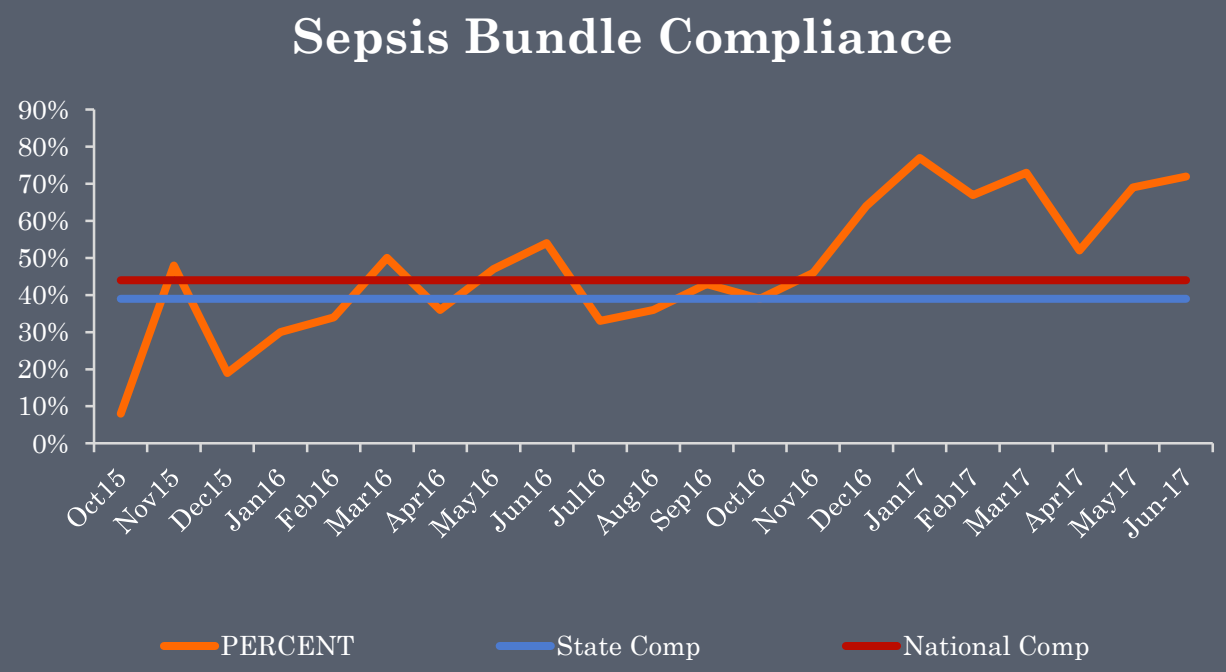
ARISE Study **N Engl J Med 2014;371:1496-506.**

SEPSIS AND SEPTIC SHOCK
WHAT ABOUT ALL THAT FLUID?

Intervention	Protocol-based EGDT (N=439)	Protocol-based Standard Therapy (N=446)	Usual care (N=456)	p-value[g]
Pre-randomization				
Intravenous fluids[b] – mL	2254 ± 1472	2226 ± 1363	2083 ± 1405	0.15
Fluids per body weight (mL/kg)	30.5 ± 22.3	29.2 ± 19.1	28 ± 21	
Vasopressor use[c]	84 (19.1)	75 (16.8)	69 (15.1)	0.28
Dobutamine use	0 (0)	0 (0)	0 (0)	
Blood transfusion	5 (1.1)	7 (1.6)	9 (2.0)	0.63
Mechanical ventilation	60 (13.7)	65 (14.6)	63 (13.8)	0.93
Intravenous antibiotics	332 (75.6)	343 (76.9)	347 (76.1)	0.91
Corticosteroids	41 (9.3)	42 (9.4)	38 (8.3)	0.82
Activated protein C	0 (0)	0 (0)	0 (0)	

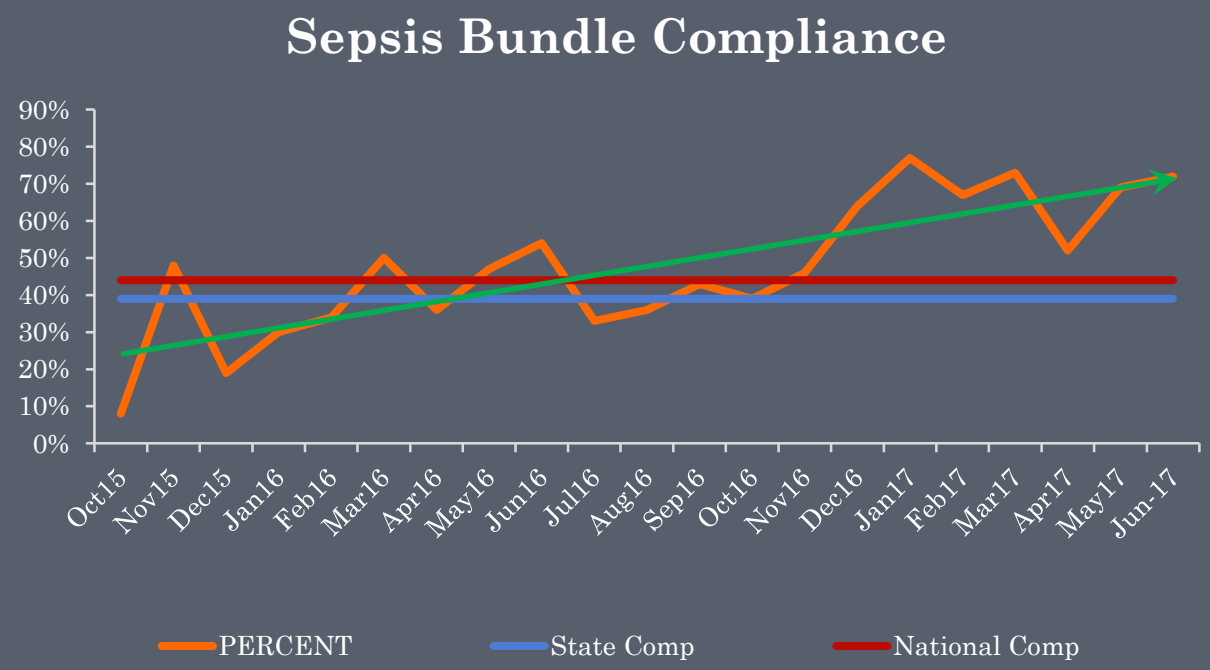
- **PROCESS Study N Engl J Med 2014;370:1683-93.**

SEPSIS AND SEPTIC SHOCK
WHY WE DO THIS

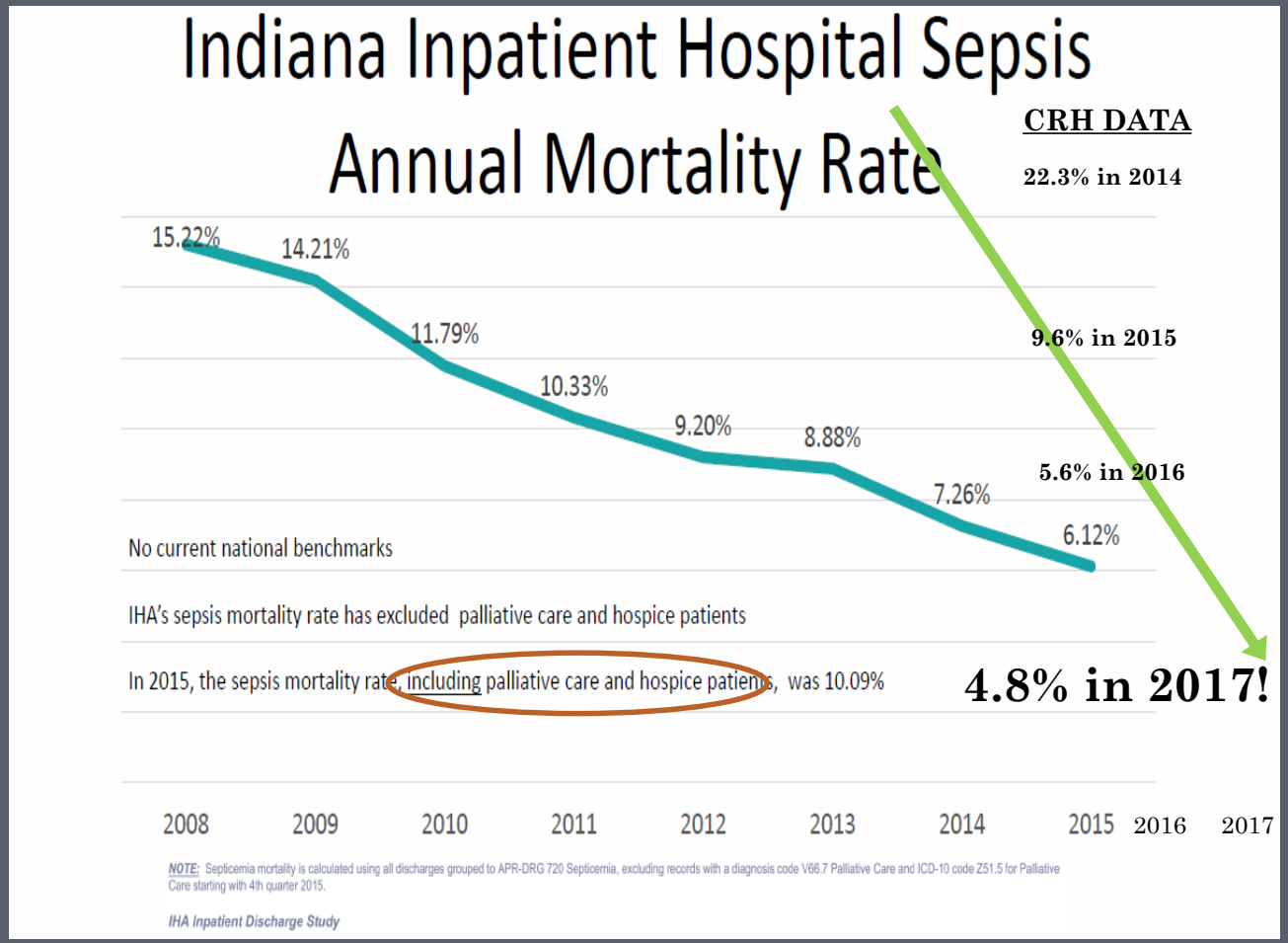


SEPSIS AND SEPTIC SHOCK

HOW WE WERE DOING WITH COMPLIANCE



SEPSIS AND SEPTIC SHOCK
WHY WE DO THIS



- *SurvivingSepsis.Org*

Post-Sepsis Syndrome or Post-ICU Syndrome

- **PTSD up to 30%:**
  - Insomnia, difficulty getting to or staying asleep Nightmares
  - Vivid hallucinations
  - Panic attacks
  - Depression (up to 50%, lasting several years)
  - Anxiety
- **Prolonged cognitive impairments**
  - up to 80%, lasting months to several years
- **Disabling muscle and joint pains**
  - up to 30%, takes up to a year of therapy to recover
- **Organ dysfunction**
  - kidney failure, respiratory problems, etc.
- **Amputations (loss of limb(s)**

Post-Sepsis Syndrome or Post-ICU Syndrome

- **Changes in ICU standards of care**
  - Routine breathing trials
  - Avoiding over sedation
  - Frequently assess for delirium
  - Sleep protocols
  - Early mobilization
- **Start rehabilitation in the hospital with early and frequent mobilization and continue post-discharge**
  - Consider a rehabilitation pathway specific to post-ICU to better recognize cognitive impairment and PTSD and ensure they are appropriately treated
- **Post-ICU rehabilitation**
  - Occupational Therapy
  - Physical Therapy
  - Nutritional consults
  - Social Services
  - Psychology

SEPSIS AND SEPTIC SHOCK
CASE PRESENTATION

- 84 year old male presents to PCP with c/o cold symptoms and persistent cough – oral antibiotics initiated
- One week later, presents to OSH with persistent symptoms
- Diagnosed with pneumococcal pneumonia and started on antibiotics
- Improving and discharge anticipated in a few days
- Day before discharge, his family is notified of sepsis and subsequent death

SEPSIS AND SEPTIC SHOCK
CASE PRESENTATION

- 34 year old male presents to PCP with c/o cold symptoms and persistent cough – oral antibiotics initiated
- One week later, presents to OSH with persistent symptoms
- Diagnosed with pneumococcal pneumonia and started on antibiotics
- Improving and discharge anticipated in a few days
- Day before discharge, his family, including his wife, his 17 year old daughter and his 11 year old son are notified of sepsis and subsequent death


SEE IT. STOP IT. SURVIVE IT.
SEPTEMBER IS SEPSIS AWARENESS MONTH