SEPSIS UPDATE

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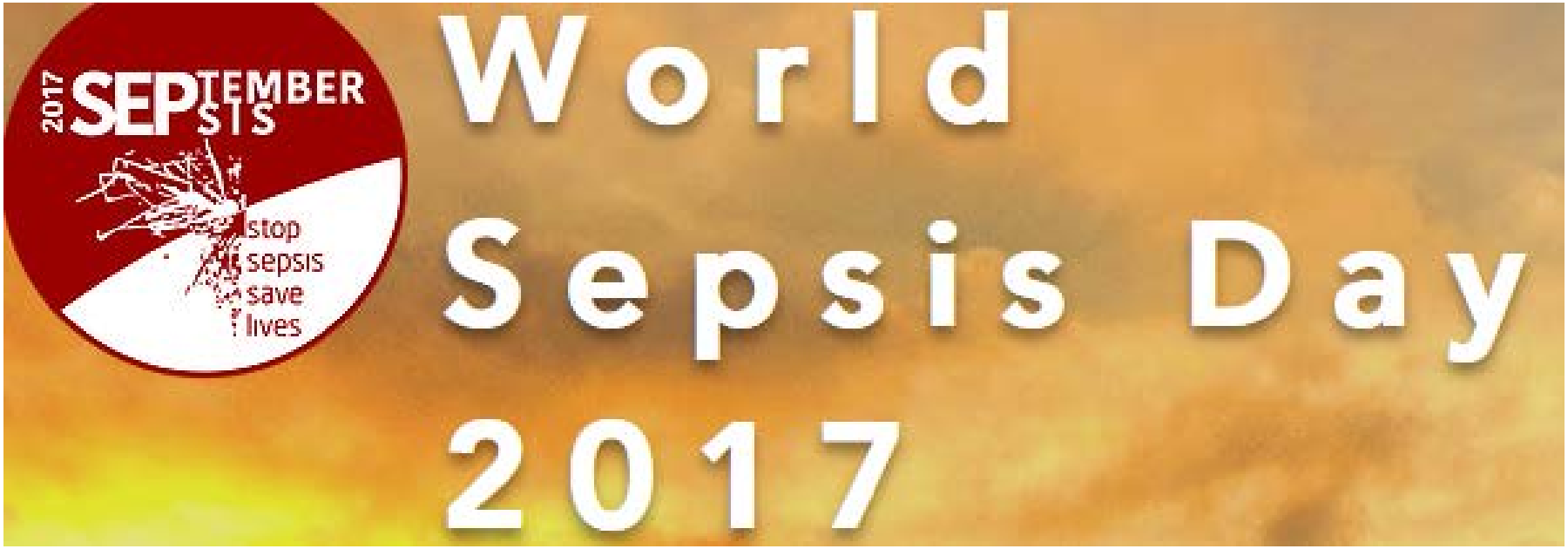
No Potential Financial COI


2017
SEPTEMBER
SEPSIS
stop
sepsis
save
lives
World
Sepsis Day
2017

Surviving Sepsis Campaign

- Phase 1
  - Barcelona Declaration
    [redacted]
- Phase 2
  - Guidelines
- Phase 3
  - ↓Mortality 25%

GUIDELINES TO BUNDLES - 2004

Special Articles

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock

R. Phillip Dellinger, MD; Jean M. Carlet, MD; Henry Masur, MD; Herwig Gerlach, MD, PhD; Thierry Calandra, MD; Jonathan Cohen, MD; Juan Gea-Banacloche, MD, PhD; Didier Keh, MD; John C. Marshall, MD; Margaret M. Parker, MD; Graham Ramsay, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; Mitchell M. Levy, MD; for the Surviving Sepsis Campaign Management Guidelines Committee

Sponsoring Organizations: American Association of Critical-Care Nurses, American College of Chest Physicians, American College of Emergency Physicians, American Thoracic Society, Australian and New Zealand Intensive Care Society, European Society of Clinical Microbiology and Infectious Diseases, European Society of Intensive Care Medicine, European Respiratory Society, International Sepsis Forum, Society of Critical Care Medicine, Surgical Infection Society.

Objective: In 2003, critical care and infectious disease experts representing 11 international organizations developed management guidelines for severe sepsis and septic shock that would be of practical use for the bedside clinician, under the auspices of the Surviving Sepsis Campaign, an international effort to increase awareness and improve outcome in severe sepsis.

Design: The process included a modified Delphi method, a consensus conference, several subsequent smaller meetings of subgroups and key individuals, teleconferences, and electronic-based discussion among subgroups and among the entire committee.

Methods: We used a modified Delphi methodology for grading recommendations, built on a 2001 publication sponsored by the International Sepsis Forum. We undertook a systematic review of the literature graded along five levels to create recommendation grades from A to E, with A being the highest grade. Pediatric considerations were provided to contrast adult and pediatric management.

Results: Key recommendations, listed by category and not by hierarchy, include early goal-directed resuscitation of the septic patient during the first 6 hrs after recognition; appropriate diagnostic studies to ascertain causative organisms before starting antibiotics; early administration of broad-spectrum antibiotic therapy; reassessment of antibiotic therapy with microbiology and clinical data to narrow coverage, when appropriate; a usual 7–10 days of antibiotic therapy guided by clinical response; source control with attention to the method that balances risks and benefits; equivalence of crystalloid and colloid resuscitation; aggressive fluid challenge to restore mean circulating filling pressure; vasopressor preference for norepinephrine and dopamine; cautious use of vasopressin pending further studies; avoiding low-dose dopamine administration for renal protection; consideration of dobutamine inotropic therapy in some clinical situations; avoidance of supranormal oxygen delivery as a goal of therapy; stress-dose steroid therapy for septic shock; use of recombinant activated protein C in patients with severe sepsis and high risk for death; with resolution of tissue hypoperfusion and in the absence of coronary artery disease or acute hemorrhage, targeting a hemoglobin of 7–9 g/dL; appropriate use of fresh frozen plasma and platelets; a low tidal volume and limitation of inspiratory plateau pressure strategy for acute lung injury and acute respiratory distress syndrome; application of a minimal amount of positive end-expiratory pressure in acute lung injury/acute respiratory distress syndrome; a semirecumbent bed position unless contraindicated; protocols for weaning and sedation/analgesia, using either intermittent bolus sedation or continuous infusion sedation with daily interruptions/lightening; avoidance of neuromuscular blockers, if at all possible; maintenance of blood glucose <150 mg/dL after initial stabilization; equivalence of continuous veno-veno hemofiltration and intermittent hemodialysis; lack of utility of bicarbonate use for pH ≥ 7.15; use of deep vein thrombosis/stress ulcer prophylaxis; and consideration of limitation of support where appropriate. Pediatric considerations included a more likely need for intubation due to low functional residual capacity; more difficult intravenous access; fluid resuscitation based on weight with 40–60 mL/kg or higher needed; decreased cardiac output and increased systemic vascular resistance as the most common hemodynamic profile; greater use of physical examination therapeutic end points; unsettled issue of high-dose steroids for therapy of septic shock; and greater risk of hypoglycemia with aggressive glucose control.

Conclusion: Evidence-based recommendations can be made regarding many aspects of the acute management of sepsis and septic shock that are hoped to translate into improved outcomes for the critically ill patient. The impact of these guidelines will be formally tested and guidelines updated annually and even more rapidly as some important new knowledge becomes available. (Crit Care Med 2004; 32:858–873)

Key Words: sepsis; severe sepsis; septic shock; sepsis syndrome; infection; guidelines; evidence-based medicine; Surviving Sepsis Campaign

DOI: 10.1097/01.CCM.0000117317.18092.E4

Severe Sepsis Bundles:

Sepsis Resuscitation Bundle — 6 hour
(To be accomplished as soon as possible and scored over first 6 hours):

1. Serum lactate measured.
2. Blood cultures obtained prior to antibiotic administration.
3. From the time of presentation, broad-spectrum antibiotics administered within 3 hours for ED admissions and 1 hour for non-ED ICU admissions.
4. In the event of hypotension and/or lactate > 4 mmol/L (36 mg/dl):
   a) Deliver an initial minimum of 20 ml/kg of crystalloid (or colloid equivalent*).
   b) Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) ≥ 65 mm Hg.
5. In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate > 4 mmol/L (36 mg/dl):
   a) Achieve central venous pressure (CVP) of ≥ 8 mm Hg.
   b) Achieve central venous oxygen saturation ($ScvO_2$) of ≥ 70%.**

Sepsis Management Bundle — 24 hour
(To be accomplished as soon as possible and scored over first 24 hours):

1. Low-dose steroids* administered for septic shock in accordance with a standardized ICU policy.
2. Drotrecogin alfa (activated) administered in accordance with a standardized ICU policy.
3. Glucose control maintained ≥ lower limit of normal, but < 150 mg/dl (8.3 mmol/L).
4. Inspiratory plateau pressures maintained < 30 cm H_2O for mechanically ventilated patients.

**See the individual chart measurement tool for an equivalency chart.*
***Achieving a mixed venous oxygen saturation (SvO_2) of 65% is an acceptable alternative.*

2012 SEPSIS BUNDLES

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION :

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

TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure (MAP) ≥65mmHg)
6. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36mg/dl):
   - Measure central venous pressure (CVP)
   - Measure central venous oxygen saturation (ScvO2)
7. Remeasure lactate if elevated.

SEPSIS BUNDLE PROJECT (SEP) NATIONAL HOSPITAL INPATIENT QUALITY MEASURES

SEP-1 EARLY MANAGEMENT BUNDLE, SEVERE SEPSIS/SEPTIC SHOCK

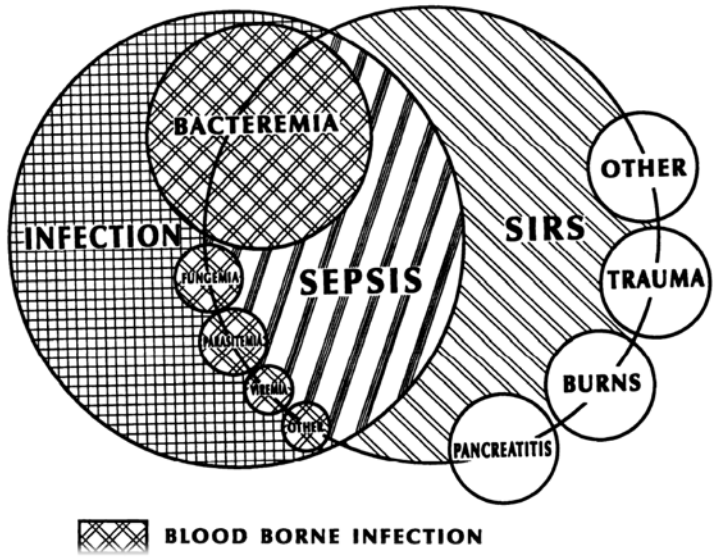
Discharges 10-01-2015 (4Q15)
through 06-30-16 (2Q16)

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

HISTORICAL PERSPECTIVE

accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis



SIRS Criteria (≥ 2)

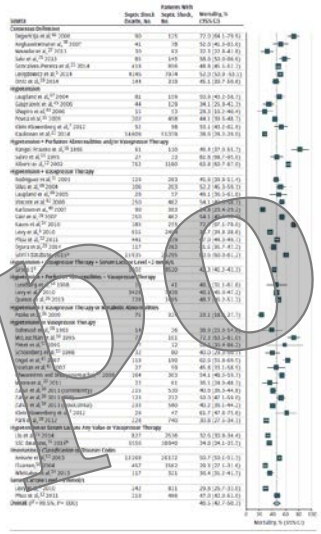
- Temperature > 38 C < 36 C
- Heart rate > 90 bpm
- Respiratory rate > 20 /min or a $PaCO_2$ < 32 mmHg
- White blood cell count > 12,000 / cu mm or < 4,000 / cu mm, or > 10 bands

CHEST 1992

Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

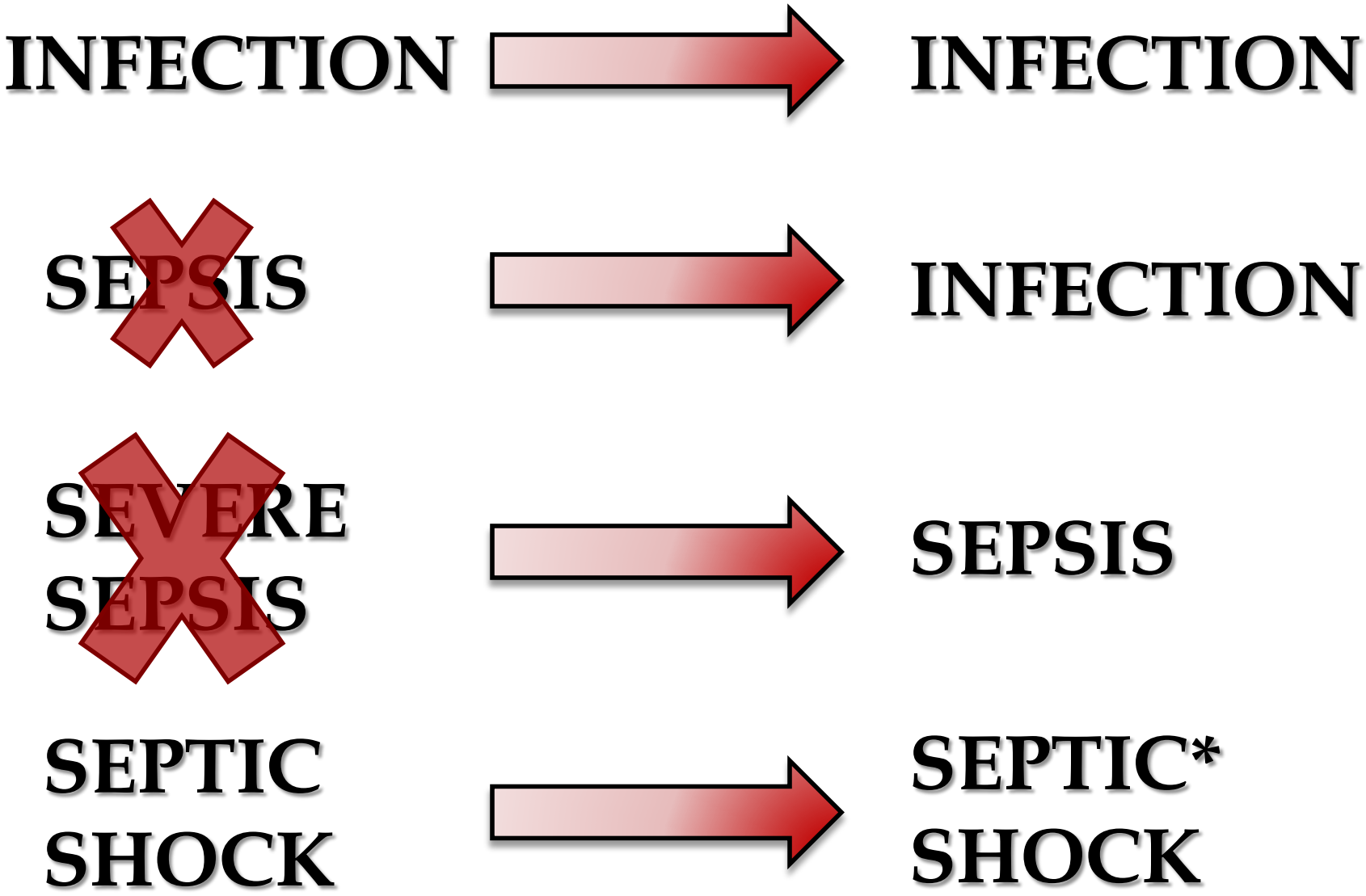
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)



Society of Critical Care Medicine
The Intensive Care Professionals

ESICM EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

JAMA 2016



* Elevated lactate

SEQUENTIAL [SEPSIS-RELATED] ORGAN FAILURE ASSESSMENT SCORE (SOFA)

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Acute change in total SOFA score $\geq$ 2 identifies organ failure
Mortality risk of approximately 10%

Quick SOFA or qSOFA

ALTERED MENTAL STATUS

FAST RESPIRATORY RATE

> 22/ min

LOW BLOOD PRESSURE

SBP ≦100mmHg

In patients with infection a qSOFA score $\geq$ 2 is associated with higher mortality and prolonged ICU stay.

The best available evidence

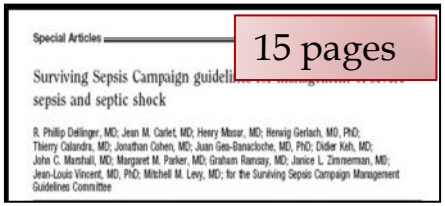
Intensive Care Med
DOI 10.1007/s00134-017-4683-6

CONFERENCE REPORTS AND EXPERT PANEL

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

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

2004 2008 2012 2016


Special Articles

Surviving Sepsis Campaign guideli… sepsis and septic shock

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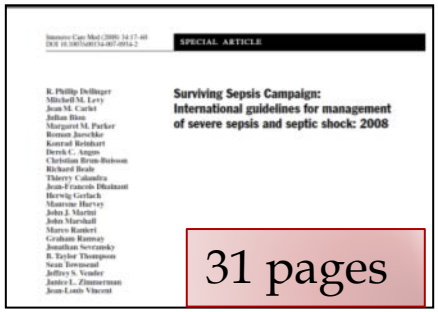
15 pages

Surviving Sepsis Campaign


SPECIAL ARTICLE

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, Mitchell M. Levy, Jean M. Carlet, Julian Bion, Margaret M. Parker, Roman Jaeschke, Konrad Reinhart, Derek C. Angus, Christian Brun-Buisson, Richard Beale, Thierry Calandra, Jean-Francois Dhainaut, Herwig Gerlach, Maurene Harvey, John J. Marini, John Marshall, Marco Ranieri, Graham Ramsay, Jonathan Sevransky, B. Taylor Thompson, Sean Townsend, Jeffrey S. Vender, Janice L. Zimmerman, Jean-Louis Vincent

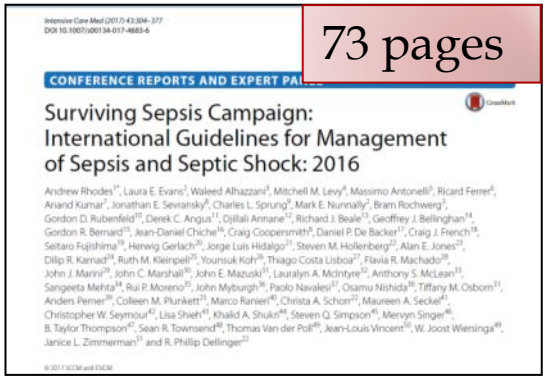
31 pages


Special Articles

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

57 pages


CONFERENCE REPORTS AND EXPERT PA…

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

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[11], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

73 pages

WHO HERE HAS FULLY READ THE 2016 SSC GUIDELINES?

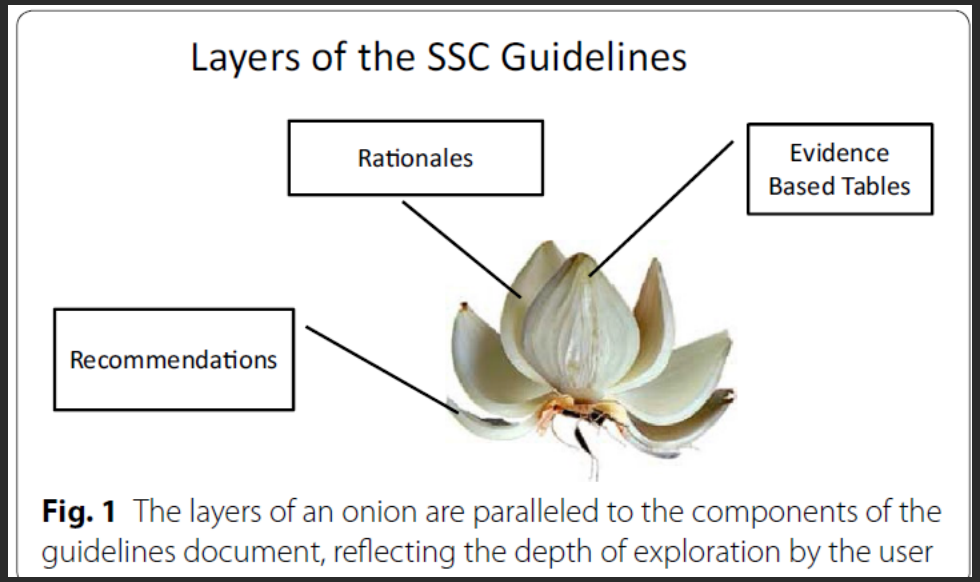
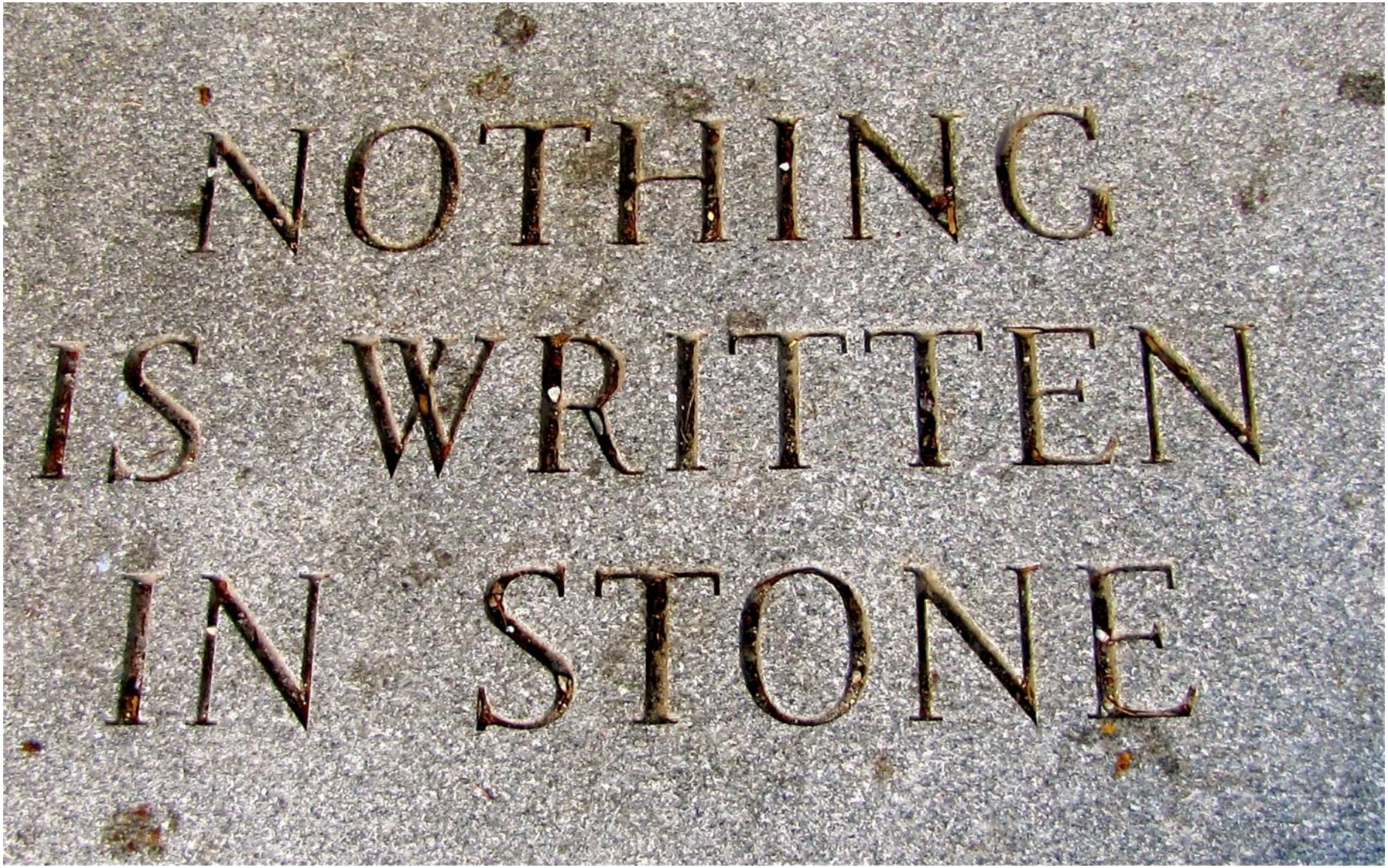


Fig. 1 The layers of an onion are paralleled to the components of the guidelines document, reflecting the depth of exploration by the user

SSC GUIDELINE TOOLS

A User's Guide to the 2016 Surviving Sepsis Guidelines

Dellinger, Schorr, Levy. Intensive Care Medicine 2017. 43(3);299-303.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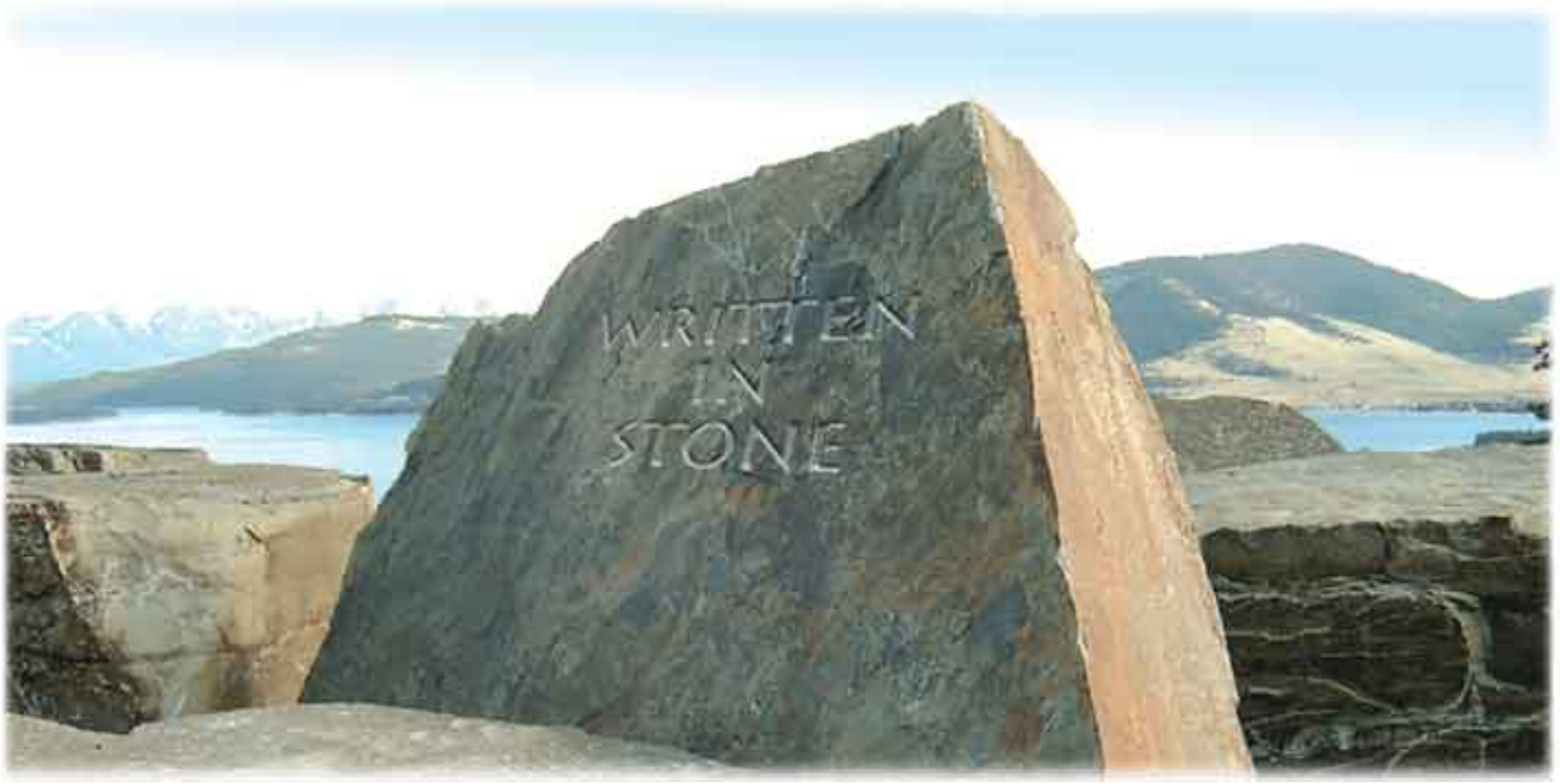
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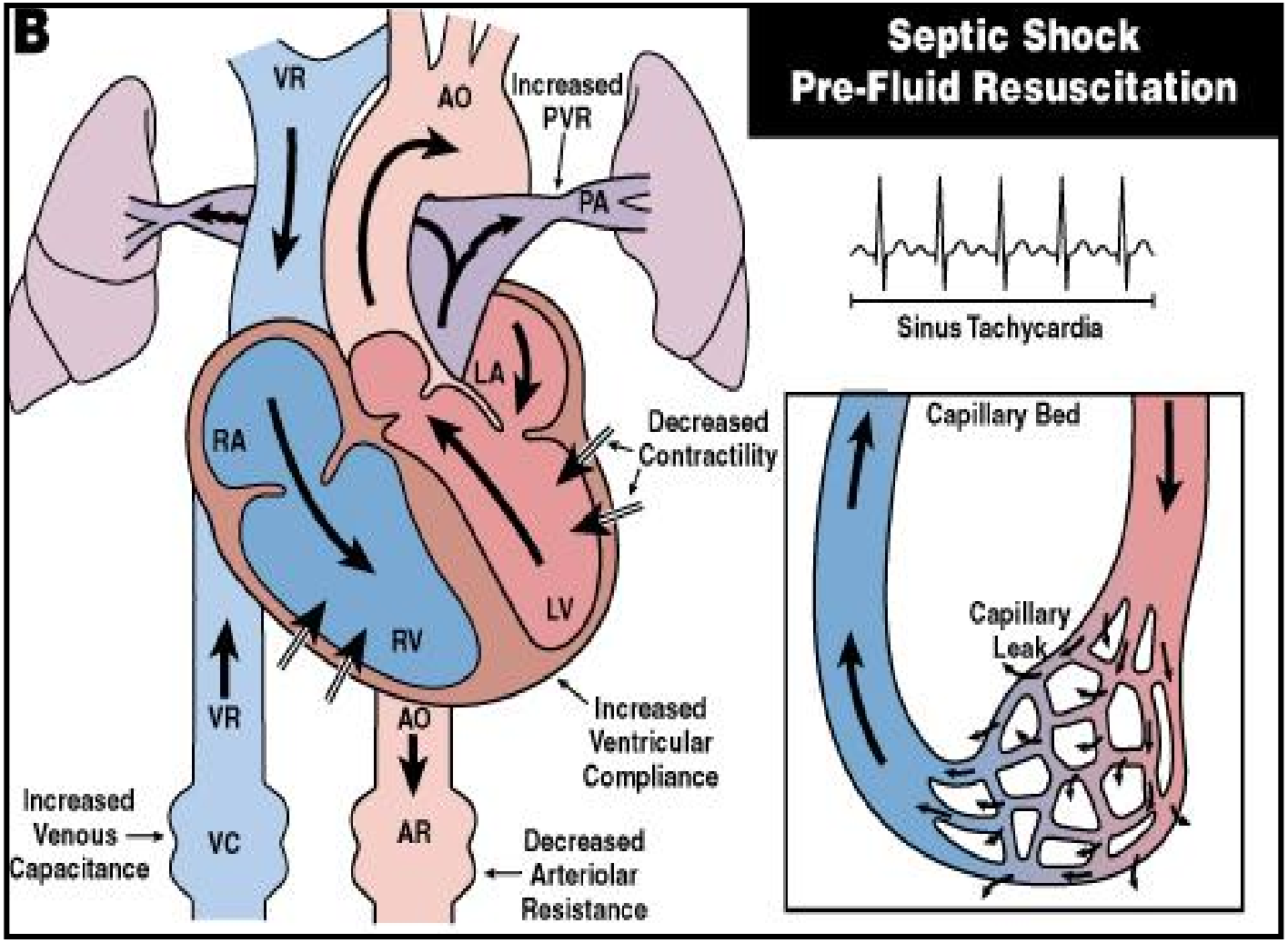
D. ANTIMICROBIAL THERAPY

1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within one hour for both sepsis and septic shock (strong recommendation, moderate quality of evidence).



Dellinger RP. Cardiovascular management of septic shock. *Crit Care Med* 2003;31:946-955.

FLUID THERAPY

We recommend that, in the resuscitation of sepsis induced hypoperfusion, at least 30 ml/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).

Choice of Fluids

- Crystalloids
  - Ringers Lactate
  - Normal Saline
- Colloids
  - Gelatins
  - ~~Hetastarch~~
  - Albumin

Crystalloids				
	mEq/L			
	Na+	Cl-	Lactate	Acetate
0.9% NaCl	**154**	**154**	**0**	**0**
Lactated Ringer's (LR)	**130**	**111**	**29**	**0**
Hartman's	**131**	**109**	**29**	**0**
Ringer's Acetate (RA)	**130**	**112**	**0**	**27**
Plasma-Lyte®/Normosol-R ®	**140**	**98**	**0**	**27**

Feature Articles

Association Between the Choice of IV Crystalloid and In-Hospital Mortality Among Critically Ill Adults With Sepsis*

Karthik Raghunathan, MD, MPH[1,2]; Andrew Shaw, MB, FRCA, FFICM, FCCM[1]; Brian Nathanson, PhD[3]; Til Stürmer, MD, PhD[4]; Alan Brookhart, PhD[4]; Mihaela S. Stefan, MD[5]; Soko Setoguchi, MD, DrPH[6]; Chris Beadles, MD, PhD[2]; Peter K. Lindenauer, MD, MSc[7]

Resuscitation 83 (2012) 767–773

Contents lists available at SciVerse ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Experimental paper

Balanced vs unbalanced crystalloid resuscitation in a near-fatal model of hemorrhagic shock and the effects on renal oxygenation, oxidative stress, and inflammation☆

Ugur Aksu[a,b,*], Rick Bezemer[a], Berna Yavuz[c], Asli Kandil[b], Cihan Demirci[b], Can Ince[a]

[a] Department of Translational Physiology, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands
[b] Department of Biology, Faculty of Science, University of Istanbul, Vezneciler, Istanbul, Turkey
[c] Department of Biochemistry, Cerrahpasa Medical School, University of Istanbul, Cerrahpasa, Istanbul, Turkey

Annals of Internal Medicine

Fluid Resuscitation in Sepsis

A Systematic Review and Network Meta-analysis

Bram Rochwerg, MD; Waleed Alhazzani, MD; Anees Sindi, MD; Diane Heels-Ansdell, MSc; Lehana Thabane, PhD; Alison Fox-Robichaud, MD; Lawrence Mbuagbaw, MSc; Wojciech Szczeklik, MD; Fayez Alshamsi, MD; Sultan Altayyar, MD; Wang-Chun Ip, MD; Guowei Li, MSc; Michael Wang, MD; Anna Włudarczyk, MD; Qi Zhou, PhD; Gordon H. Guyatt, MD; Deborah J. Cook, MD; Roman Jaeschke, MD; and Djillali Annane, MD, PhD, for the Fluids in Sepsis and Septic Shock Group

PRELIMINARY COMMUNICATION

Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

Nor'azim Mohd Yunos, MD
Rinaldo Bellomo, MD, FCICM
Colin Hegarty, BSc
David Story, MD
Lisa Ho, MClinPharm
Michael Bailey, PhD

Context Administration of traditional chloride-liberal intravenous fluids may precipitate acute kidney injury (AKI).

Objective To assess the association of a chloride-restrictive (vs chloride-liberal) intravenous fluid strategy with AKI in critically ill patients.

Design, Setting, and Patients Prospective, open-label, sequential period pilot study of 760 patients admitted consecutively to the intensive care unit (ICU) during the control period (February 18 to August 17, 2008) compared with 773 patients admitted

2278 Patients
Postoperative predominant
Median 2 liters fluid

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Plasma-Lyte 148® versUs Saline (PLUS) Study

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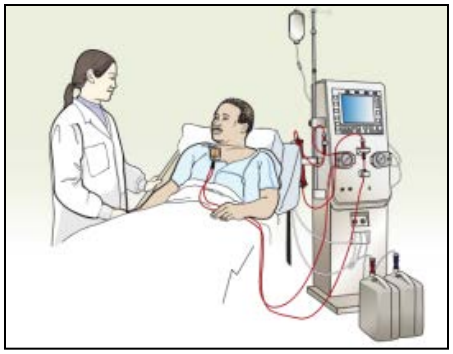
Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde

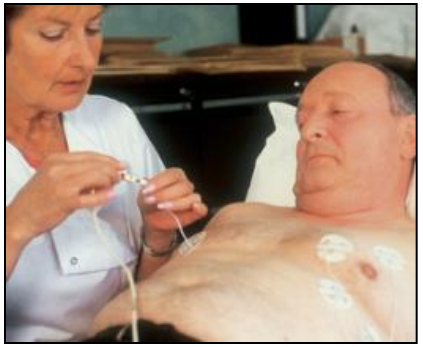
BRICNet
Brazilian Research in Intensive Care Network

FLUID THERAPY

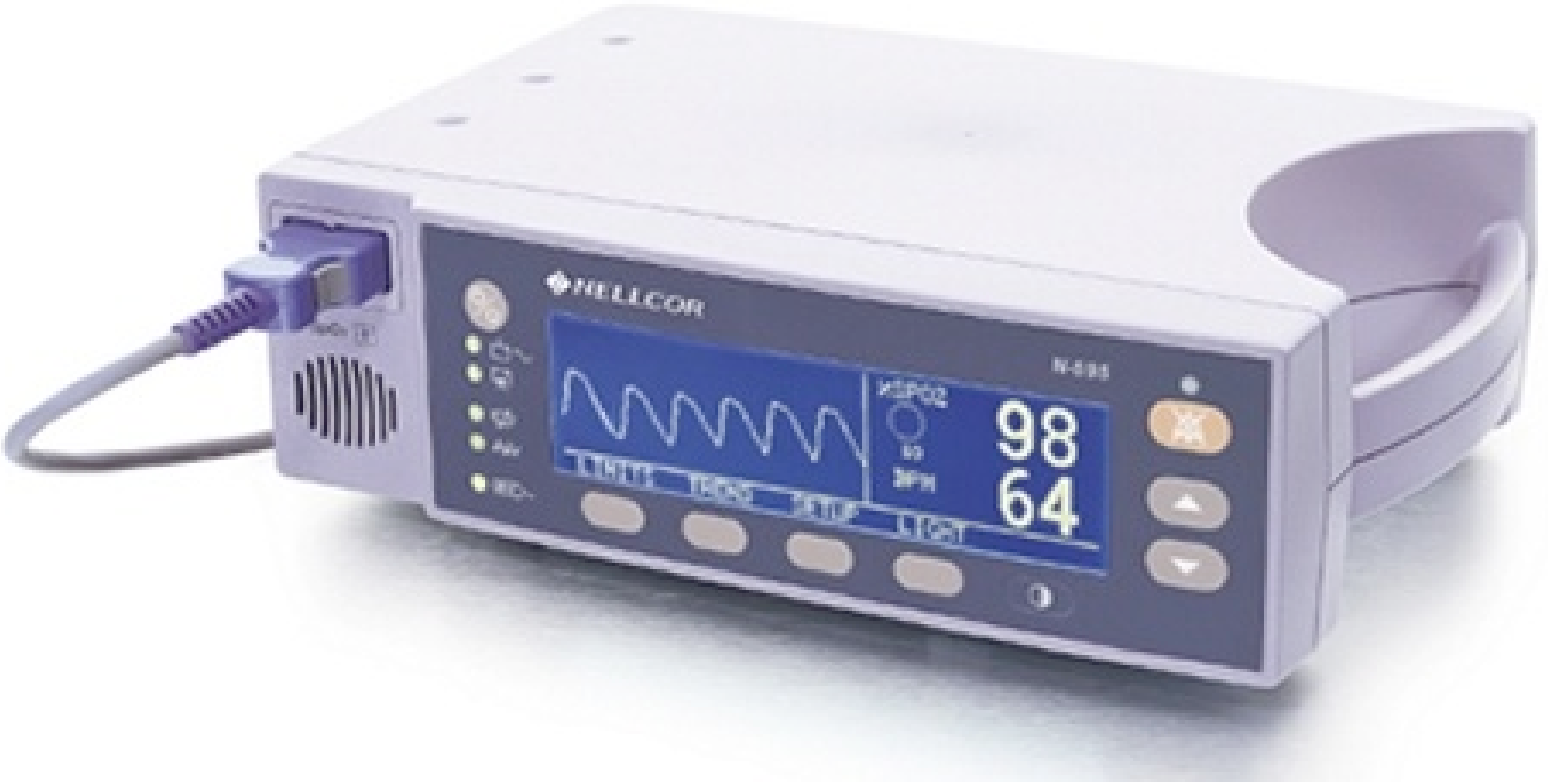
4. We suggest using albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with septic shock when patients require substantial amounts of crystalloids (weak recommendation, low quality of evidence)



End Stage Renal Disease on Dialysis



Compensated Congestive Heart failure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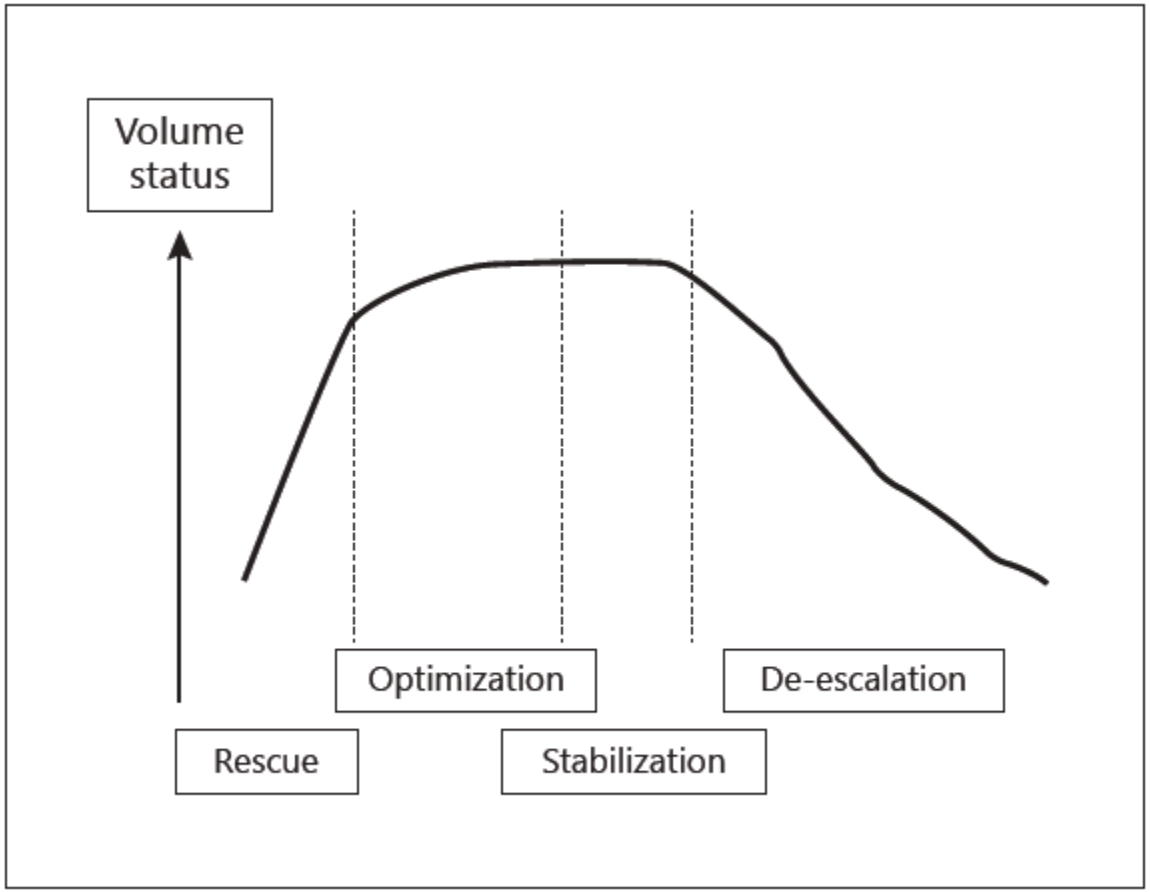
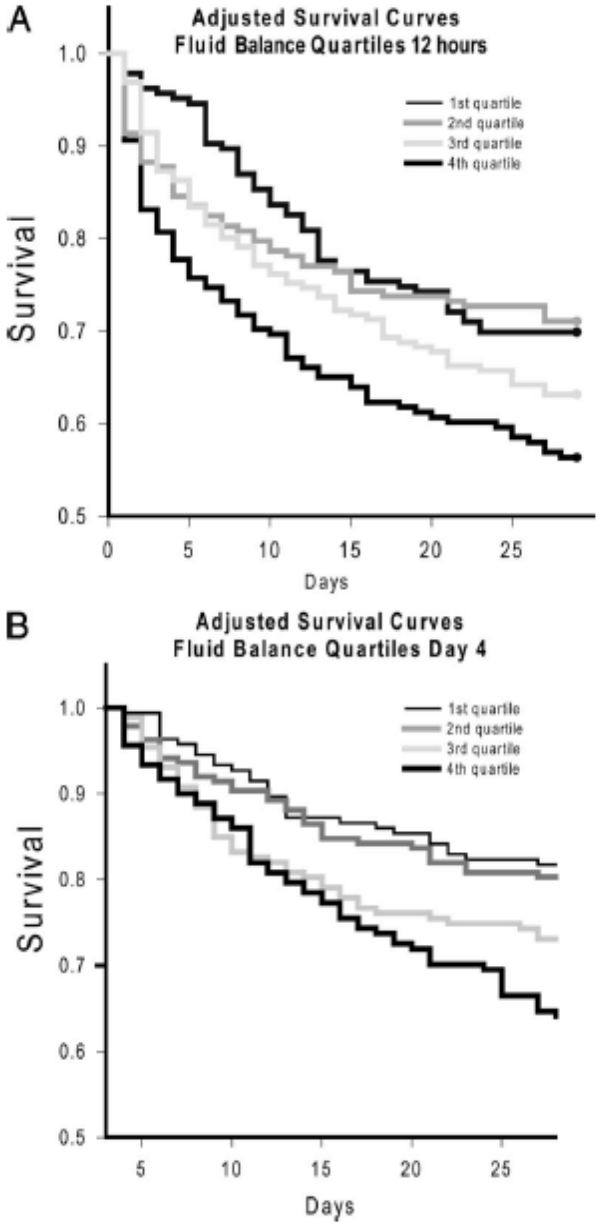
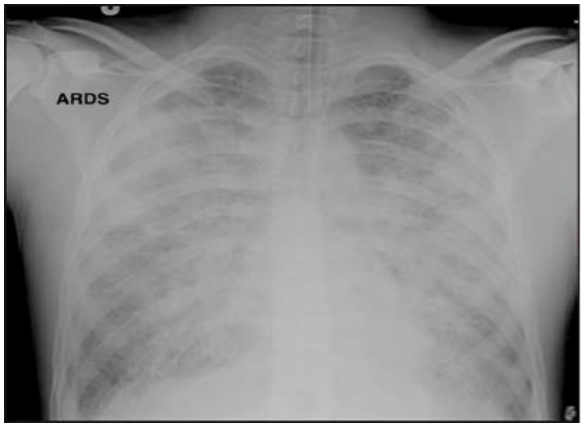


Kidney Dis (Basel). 2016 Jun;2(2):64-71.

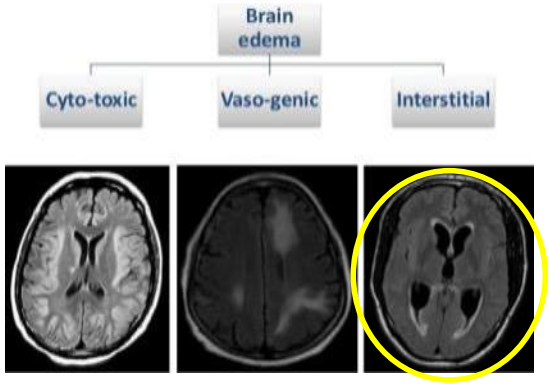


Boyd et al. Crit Care Med 2011;39:259-265

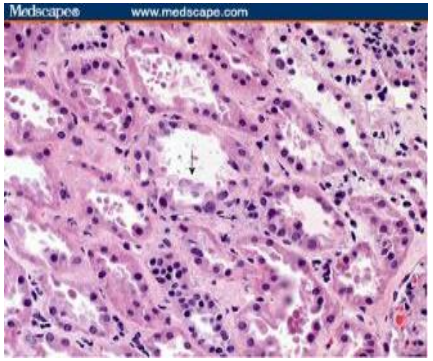
Interstitial Edema



Lungs



Brain

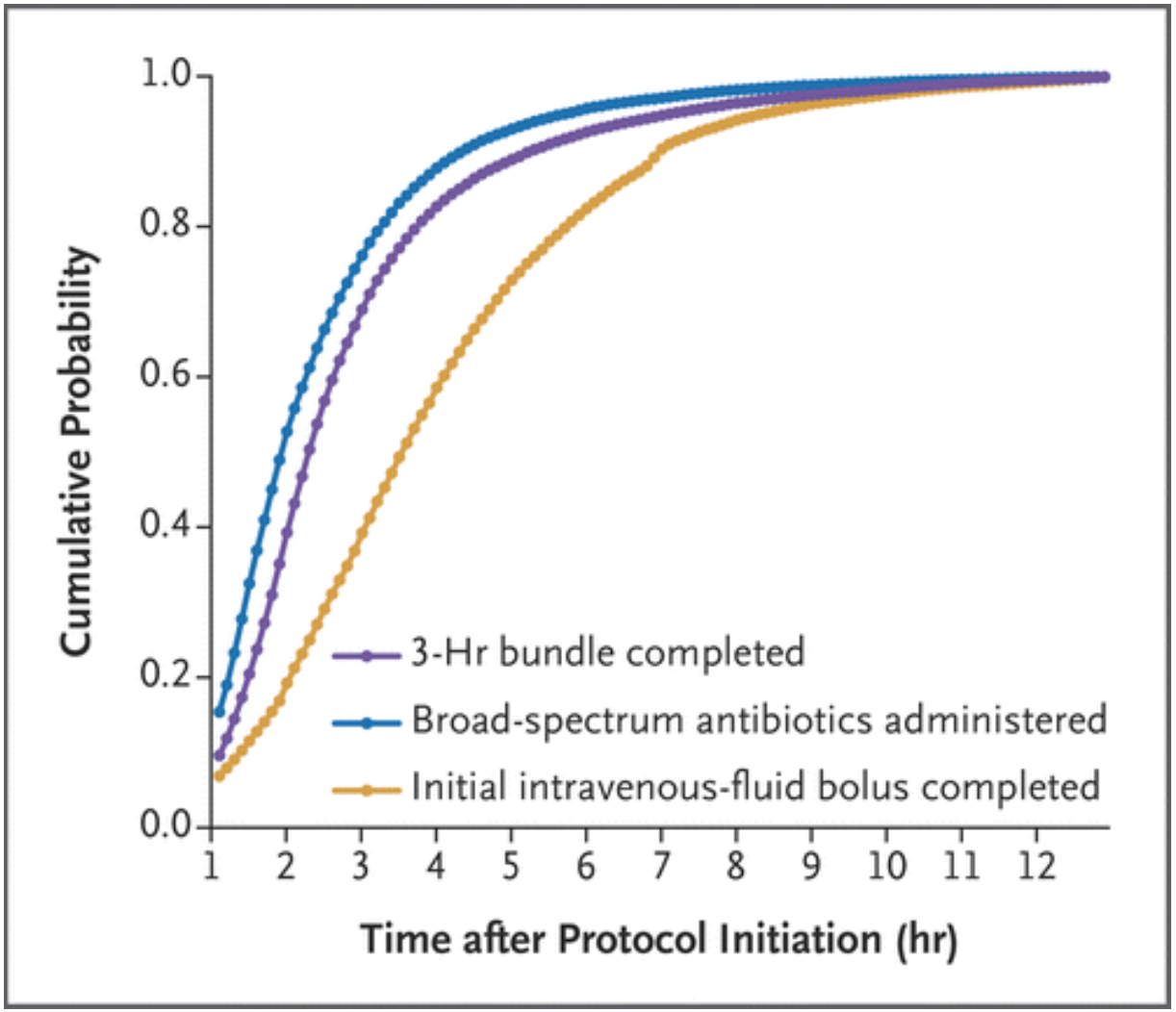


Kidney

Correct balance of fluids and vasopressors during rescue and optimization phase is goal

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

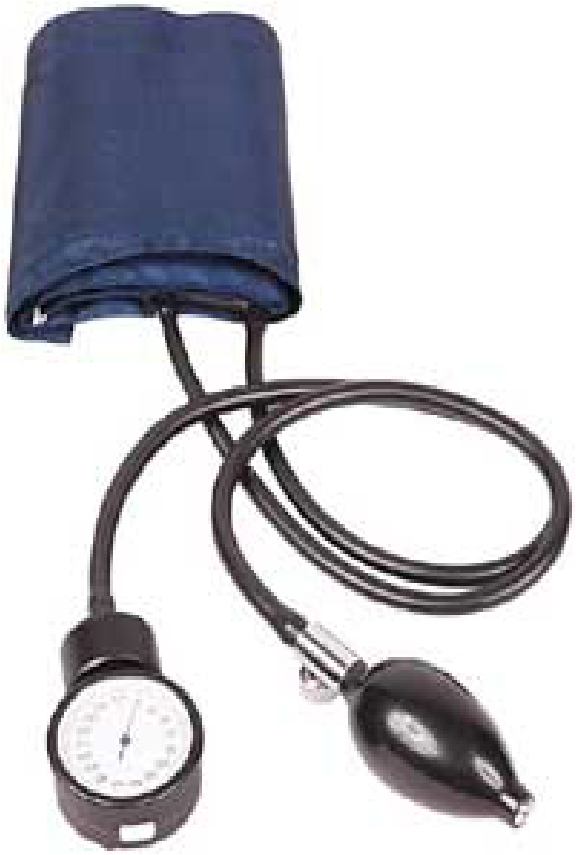
Seymour, Gesten, Prescott et al. **N Engl J Med 2017**; 376:2235-2244



N Engl J Med 2017; 376:2235-2244

SEPTIC SHOCK

- **Recommend MAP ≥ 65 mm Hg**

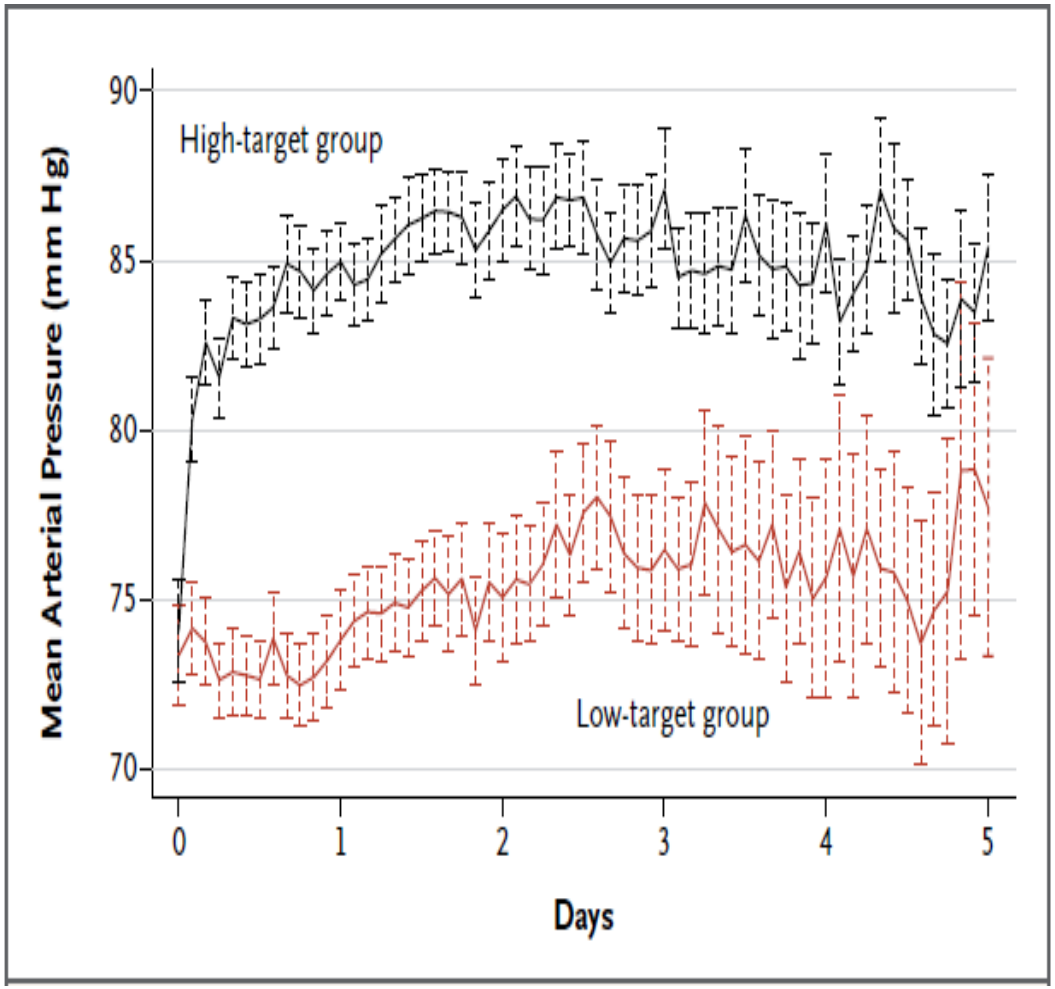


Mean Arterial Pressure

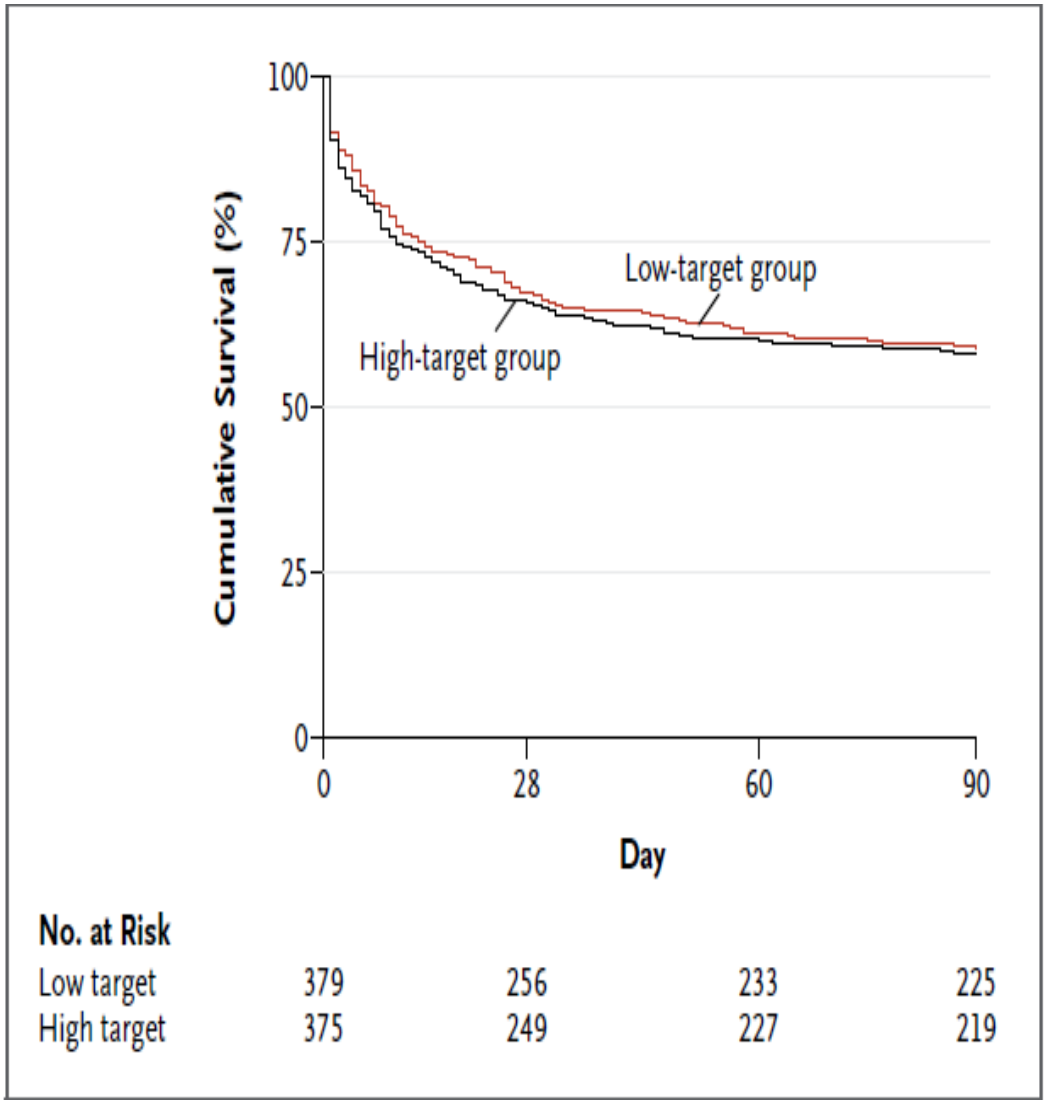
	65 mm Hg	75 mm Hg	85 mm Hg	F/LT
Urinary output (mL)	49 ±18	56 ± 21	43 ±13	.60/.71
Capillary blood flow (mL/min/100 g)	6.0 ± 1.6	5.8 ± 11	5.3 ± 0.9	.59/.55
Red Cell Velocity (au)	0.42 ± 0.06	0.44 ±016	0.42 ± 0.06	.74/.97
$Pico_2$ (mm Hg)	41 ± 2	47 ± 2	46 ± 2	.11/.12
Pa-$Pico_2$ (mm Hg)	13 ± 3	17 ± 3	16 ± 3	.27/.40

Adapted from Table 4, page 2731, from LeDoux, Astiz ME, Carpati CM, Rackow ED. Effects of perfusion pressure on tissue perfusion in septic shock. *Crit Care Med* 2000; 28:2729-2732

Asfar P, Meziani F, Hamel JF, Grelon F, et al. High versus Low Blood-Pressure Target in Patients with Septic Shock. N Engl J Med. 2014 Mar 18.



Asfar P, et al. N Engl J Med. 2014 Apr 24;370(17):1583-93.

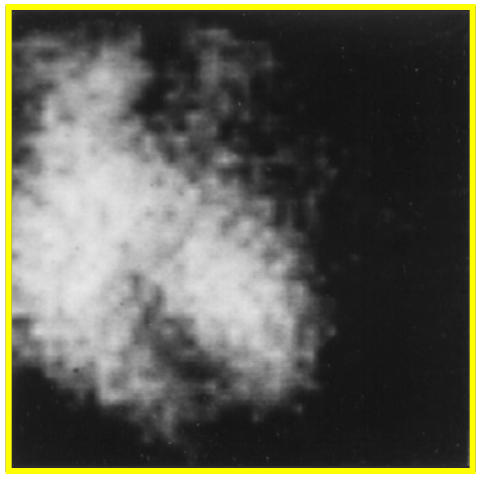


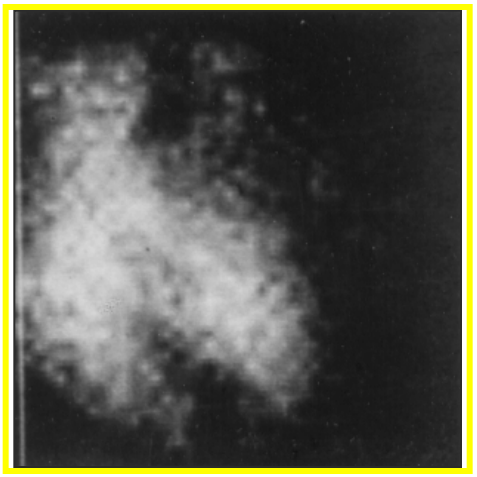
Asfar P, et al. N Engl J Med. 2014 Apr 24;370(17):1583-93.

CHOICE OF VASOPRESSOR

During Septic Shock

End Diastole

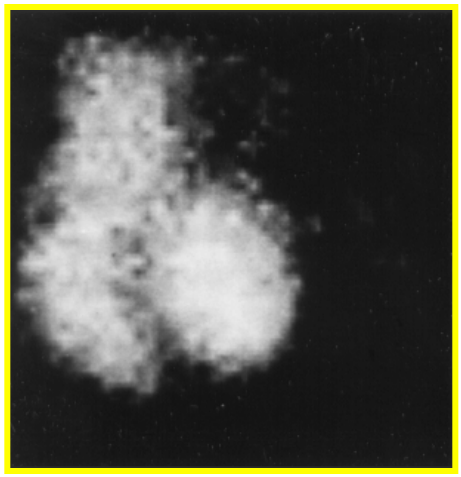


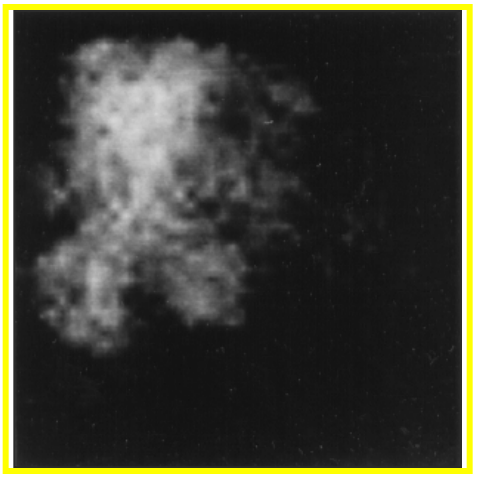


End Systole

10 Days Post Shock

End Diastole





End Systole

VASOPRESSORS IN SEPTIC SHOCK

First Line

Norepinephrine

Second Line

Epinephrine

Low Dose Vasopressin

(.01-.03 units/min**)**

Niche Drugs

Dopamine
(sinus bradycardia)

Phenylephrine
(high cardiac output or serious tachyarrhythmias and salvage)

Vasopressin History

Circulating Vasopressin Levels in Septic Shock

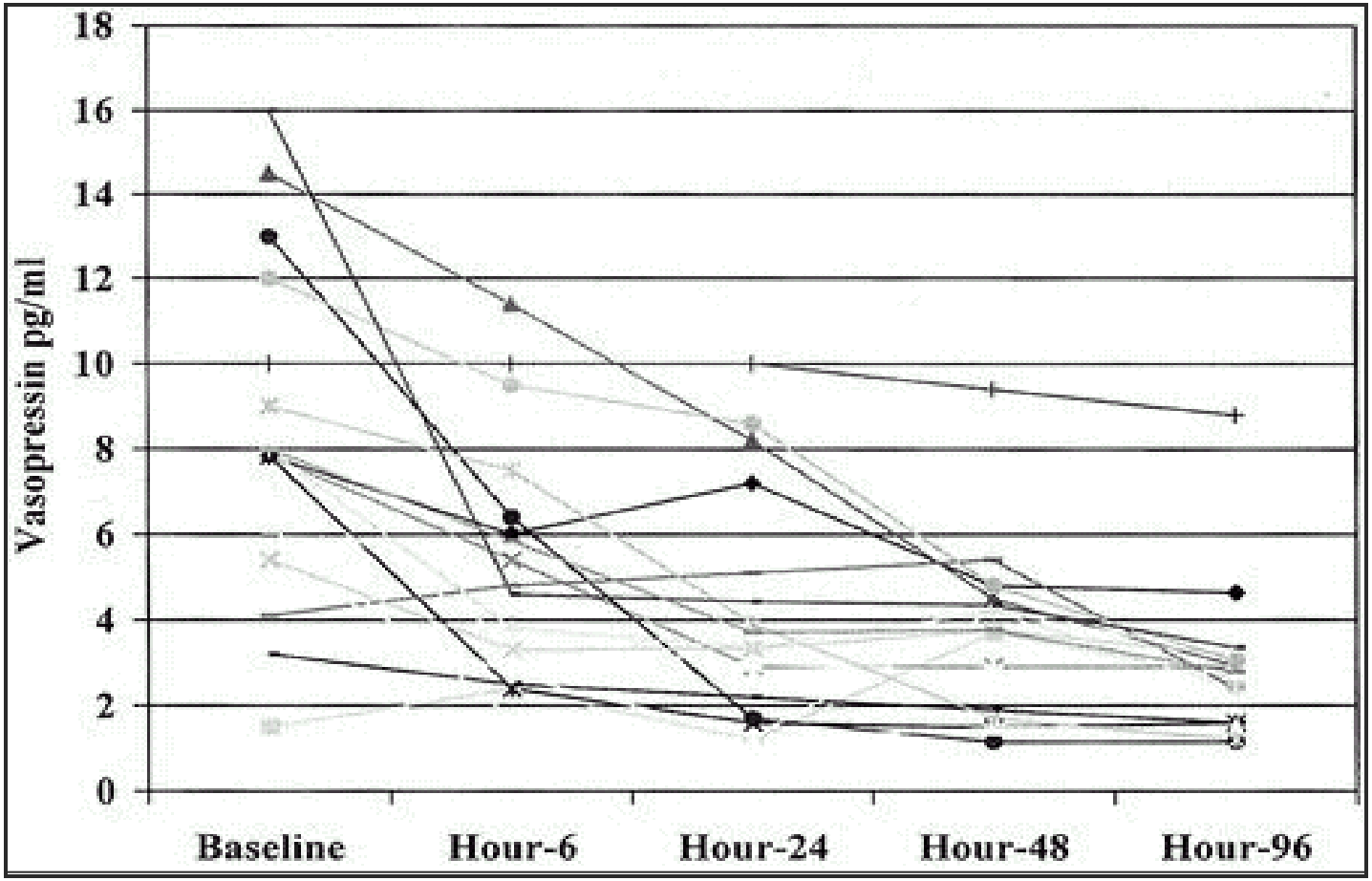
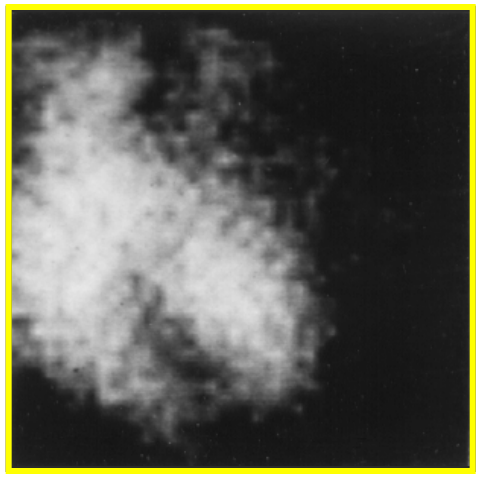


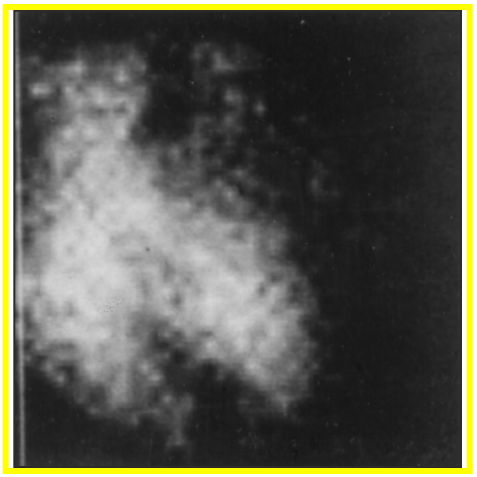
Figure 2, page 1755 reproduced with permission from Sharshar T, Blanchard A, Paillard M, et al. Circulating vasopressin levels in septic shock. *Crit Care Med* 2003; 31:1752-1758

VASST Trial

Septic Shock

End Diastole





End Systole

In a patient with septic shock, what if?

- Adequate fluid resuscitation
- MAP target achieved
- Depressed ejection fraction on bedside ECHO
- Persistent evidence of tissue hypoperfusion

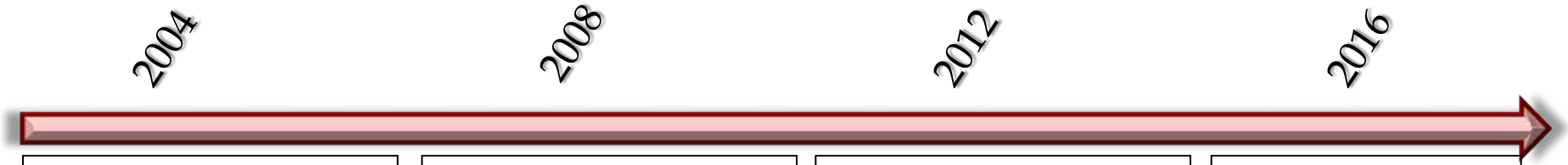
G. Vasoactive Medications

5. We suggest using dobutamine in patients who show evidence of persistent tissue hypoperfusion despite adequate fluid loading and the use of vasopressor agents (weak recommendation, low quality of evidence).


Steroids

What do we know?

- Low dose steroid therapy reduces time to reversal of septic shock
- Still controversial as to whether or not there is a meaningful reduction in mortality.
- The more severely ill and hemodynamically unstable the patient is the more likely to benefit from stress-dose steroids.



2004

1. Intravenous corticosteroids (hydrocortisone 200–300 mg/day, for 7 days in three or four divided doses or by continuous infusion) are recommended in patients with septic shock who, despite adequate fluid replacement, require vasopressor therapy to maintain adequate blood pressure.
2. Some experts would use a 250-µg ACTH stimulation test to identify responders (>9µg/dL increase in cortisol 30–60 mins post- ACTH administration) and discontinue therapy in these patients. Clinicians should not wait for ACTH stimulation results to administer corticosteroids.
3. Some experts would decrease dosage of steroids after resolution of septic shock.
4. Some experts would consider tapering the dose of corticosteroids at the end of therapy.
5. Some experts would add fludrocortisone (50 µg orally four times per day) to this regimen.
6. Doses of corticosteroids >300 mg hydrocortisone daily should not be used in severe sepsis or septic shock for the purpose of treating septic shock.
7. In the absence of shock, corticosteroids should not be administered for the treatment of sepsis. There is, however, no contraindication to continuing maintenance steroid therapy or to using stress dose steroids if the patient's history of Corticosteroid administration or the patient's endocrine history warrants.

2008

1. We suggest that intravenous hydrocortisone be given only to adult septic shock patients after it has been confirmed that their blood pressure is poorly responsive to fluid resuscitation and vasopressor therapy
2. We suggest that the ACTH stimulation test not be used to identify the subset of adults with septic shock who should receive hydrocortisone
3. We suggest that patients with septic shock should not receive dexamethasone if hydrocortisone is available
4. We suggest the daily addition of oral fludrocortisone (50µg) if hydrocortisone is not available and the steroid that is substituted has no significant mineralocorticoid activity. Fludrocortisone is considered optional if hydrocortisone is used
5. We suggest that clinicians wean the patient from steroid therapy when vasopressors are no longer required
6. We recommend that doses of corticosteroids comparable to >300 mg of hydrocortisone daily not be used in severe sepsis or septic shock for the purpose of treating septic shock
7. We recommend that corticosteroids not be administered for the treatment of sepsis in the absence of shock. There is, however, no contraindication to continuing maintenance steroid therapy or to using stress-dose steroids if the patient's endocrine or corticosteroid administration history warrants

2012

1. We suggest not using intravenous hydrocortisone as a treatment of adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). If this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day
2. We suggest not using the ACTH stimulation test to identify the subset of adults with septic shock who should receive hydrocortisone
3. We suggest that clinicians taper the treated patient from steroid therapy when vasopressors are no longer required
4. We recommend that corticosteroids not be administered for the treatment of sepsis in the absence of shock
5. When low-dose hydrocortisone is given, we suggest using continuous infusion rather than repetitive bolus injections

2016

1. We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day

Surviving Sepsis Campaign 2016

- We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day

[Original Research **Critical Care**]

CHEST

Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock

A Retrospective Before-After Study

PODCAST

Paul E. Marik, MD, FCCP; Vikramjit Khangoora, MD; Racquel Rivera, PharmD; Michael H. Hooper, MD; and John Catravas, PhD, FCCP

BACKGROUND: The global burden of sepsis is estimated as 15 to 19 million cases annually, with a mortality rate approaching 60% in low-income countries.

METHODS: In this retrospective before-after clinical study, we compared the outcome and clinical course of consecutive septic patients treated with intravenous vitamin C, hydrocortisone, and thiamine during a 7-month period (treatment group) with a control group treated in our ICU during the preceding 7 months. The primary outcome was hospital survival. A propensity score was generated to adjust the primary outcome.

RESULTS: There were 47 patients in both treatment and control groups, with no significant differences in baseline characteristics between the two groups. The hospital mortality was 8.5% (4 of 47) in the treatment group compared with 40.4% (19 of 47) in the control group ($P < .001$). The propensity adjusted odds of mortality in the patients treated with the vitamin C protocol was 0.13 (95% CI, 0.04-0.48; $P = .002$). The Sepsis-Related Organ Failure

Take Home Message

ORIGINAL ARTICLE

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

The ProCESS Investigators*

N Engl J Med. 2014 May 1;370(18):1683-93.

21.0/18.2/18.9% Mortality

Over 1500 Patients

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

N Engl J Med. 2014 Oct 16;371(16):1496-506.

18.6/18.7 % Mortality

1600 Patients

	ProCESS	ARISE
Enrollment	<2 hours from detection of shock	2.8 hours (median) from presentation to ED
Antibiotics	75% received prior to enrollment	70 minutes (median) from presentation to ED
Fluids	>2 liters prior ot enrollment	2515ml (mean) prior to enrollment


THE
BOTTOM
LINE

TO SAVE LIVES.....

Early identification

Early antibiotics

Early **appropriate** fluid resuscitation

THANK YOU