

# **The initial hemodynamic resuscitation of the septic patient – does one size fit all?**

**Azriel Perel**

Professor and Chairman

Department of Anesthesiology and Intensive Care

Sheba Medical Center, Tel Aviv University

Israel

**Ostrava 2013**

# **Disclosure**

**The speaker is a member of the  
Medical Advisory Board of  
Pulsion Medical Systems,  
Munich, Germany**

**Consulted until recently to BMEYE, FlowSense, iMDsoft**

**perelao@shani.net**

**New ways to reduce unnecessary variation and improve outcomes in the intensive care unit**

Barry W. Holcomb, MD, Arthur P. Wheeler, MD, FCCP, and E. Wesley Ely, MD, MPH, FCCP

Current Opinion In Critical Care 2001, 7:304–311

**A number of large, randomized, prospective trials have demonstrated that protocol-based strategies can reduce variation and cost of intensive care medicine and improve morbidity and mortality of critically ill patients.**

## **New ways to reduce unnecessary variation and improve outcomes in the intensive care unit**

Barry W. Holcomb, MD, Arthur P. Wheeler, MD, FCCP, and E. Wesley Ely, MD, MPH, FCCP

Current Opinion In Critical Care 2001, 7:304–311

- (1) Ventilatory management of acute lung injury (ALI)/acute respiratory distress syndrome (ARDS)
- (2) Ventilator-weaning protocols
- (3) Sedation and analgesia protocols in ICU care
- (4) Transfusion and blood product conservation protocols

# Functional hemodynamic monitoring

Mehrnaz Hadian and Michael R. Pinsky

Current Opinion in Critical Care 2007, 13:318–323

A systematic approach to an effective resuscitation effort can be incorporated into a **protocolized cardiovascular management algorithm**, which, in turn, can improve patient-centered outcomes and the cost of healthcare systems, by faster and more effective response in order to **diagnose and treat hemodynamically unstable patients** both inside and outside of intensive care units.

**Practice parameters for hemodynamic support of sepsis  
in adult patients. 2004 update.**

**Hollenberg S et al. Crit Care Med 2004; 32:1928-48**

**“Because of the complexity of hemodynamics in sepsis, the goals of therapy are much more difficult to define with certainty than in other forms of shock.”**

# Hemodynamic goals in randomized clinical trials in patients with sepsis: a systematic review of the literature

Sevransky JE et al. Critical Care 2007, 11:R67

Fig 2a MAP Goals In Sepsis Trials

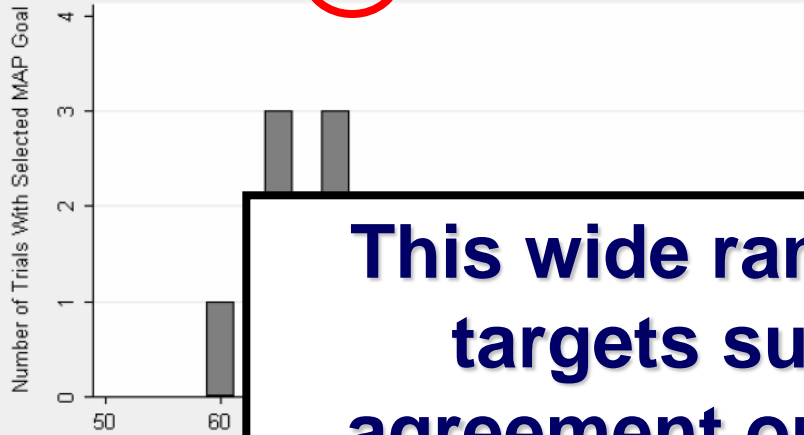
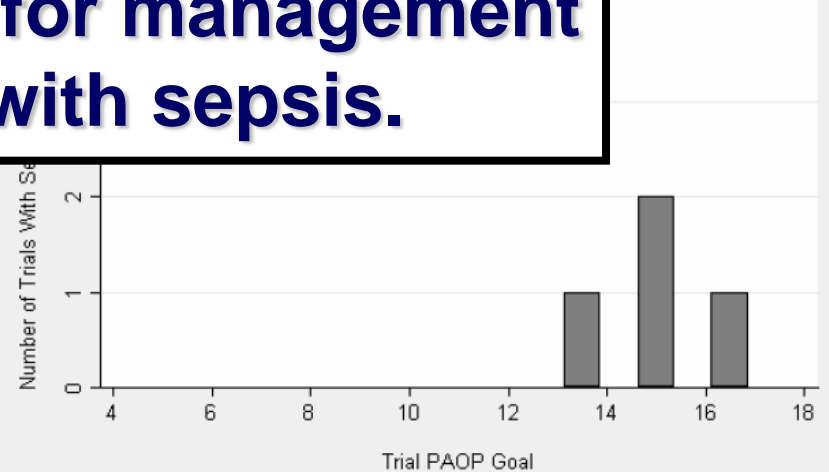


Fig 2b CVP Goals In Sepsis Trials



**This wide range of treatment targets suggest lack of agreement on cardiac output (CO), blood pressure and filling pressures goals for management of patients with sepsis.**

**Practice parameters for hemodynamic support of  
sepsis in adults patients. 2004 update.**

**Hollenberg et al. Crit Care Med 2004; 32:1928 –48**



**Practice parameters for hemodynamic support of sepsis in adults patients. 2004 update.**

**Hollenberg et al. Crit Care Med 2004; 32:1928 –48**

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

**Practice parameters for hemodynamic support of sepsis in adults patients. 2004 update.**

**Hollenberg et al. Crit Care Med 2004; 32:1928 –48**

JANUARY 21, 2013



**Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012** February 2013 • Volume 41 • Number 2



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## ORIGINAL ARTICLE

[◀ Previous](#)

Volume 345:1368-1377

November 8, 2001

Number 19

[Next ▶](#)

## Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock

*Emanuel Rivers, M.D., M.P.H., Bryant Nguyen, M.D., Suzanne Havstad, M.A., Julie Ressler, B.S., Alexandria Muzzin, B.S., Bernhard Knoblich, M.D., Edward Peterson, Ph.D., Michael Tomlanovich, M.D., for the Early Goal-Directed Therapy Collaborative Group*

**Early goal-directed therapy  
improves outcome in patients with  
severe sepsis and septic shock.**

# **Practice parameters for hemodynamic support of sepsis in adults patients. 2004 update.**

**Hollenberg et al. Crit Care Med 2004; 32:1928 –48**

JANUARY 21, 2013



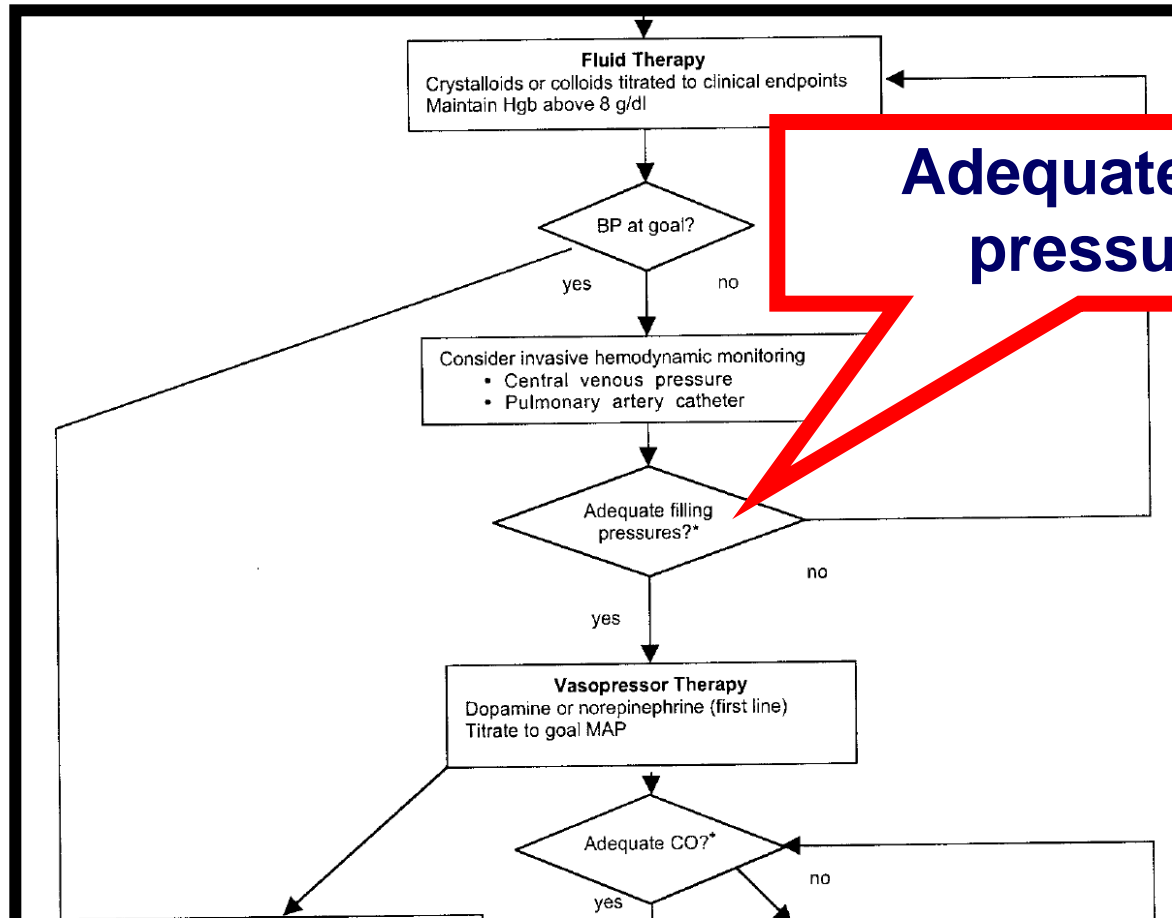
# **Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012**

February 2013 • Volume 41 • Number 2

**Let us use the pulmonary artery catheter correctly and only when we need it**

Michael R. Pinsky, MD, Dr hc, FCCM; Jean-Louis Vincent, MD, PhD, FCCM

**Crit Care Med 2005; 33:1119-22**



**Adequate filling pressures?**

**Practice parameters for hemodynamic support of sepsis in adults patients. 2004 update.**  
**Hollenberg et al. Crit Care Med 2004; 32:1928 –48**

# Surviving Sepsis Campaign Guidelines

Dellinger RP, et al. Crit Care Med 2004;32:858-73

(based on Rivers et al, NEJM 2001)

If the hypotension does not respond to fluid challenges or the lactate remains  $> 4$  mmol/L then the goals of initial resuscitation should include all of the following as one part of a treatment protocol: (= the “bundle”)

12-15 under MV

Central venous pressure (CVP): 8–12 mm Hg

Mean arterial pressure (MAP)  $\geq 65$  mm Hg

Urine output  $\geq 0.5$  mL.kg<sup>-1</sup>.hr<sup>-1</sup>

Central venous (superior vena cava) or mixed venous oxygen saturation  $\geq 70\%$  or  $\geq 65\%$ , respectively



**Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012** February 2013 • Volume 41 • Number 2

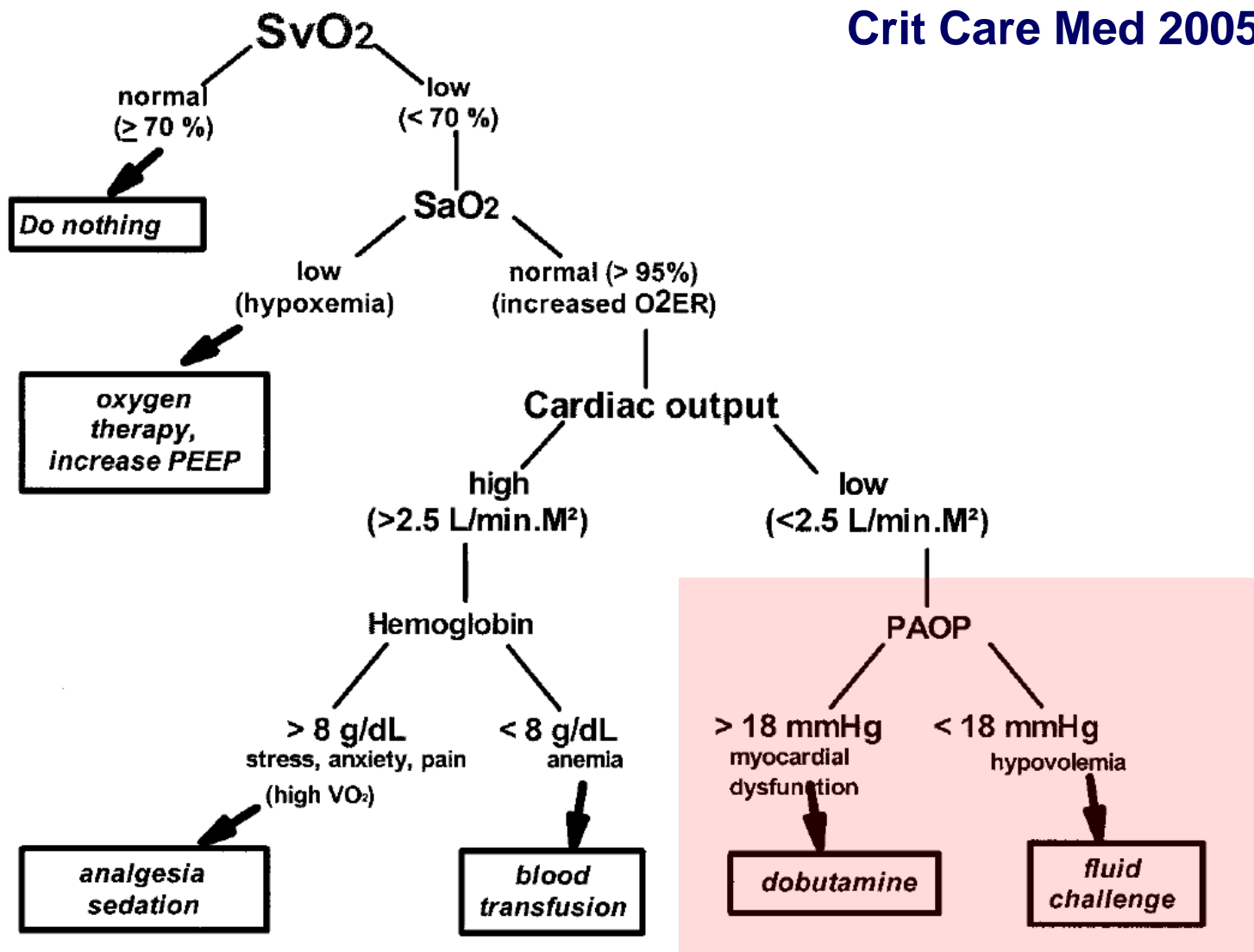
During the first 6 hrs of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as a part of a treatment protocol (grade 1C):

- a) CVP 8–12 mm Hg
- b) MAP  $\geq$  65 mm Hg
- c) Urine output  $\geq$  0.5 mL·kg·hr
- d) Superior vena cava oxygenation saturation (Scvo<sub>2</sub>) or mixed venous oxygen saturation (Svo<sub>2</sub>) 70% or 65%, respectively.

# Let us use the pulmonary artery catheter correctly and only when we need it

Michael R. Pinsky, MD, Dr hc, FCCM; Jean-Louis Vincent, MD, PhD, FCCM

Crit Care Med 2005; 33:1119-22





**Practice parameters for hemodynamic support of sepsis in adults patients. 2005**

Hollenberg et al. Crit Care Med 2005; 33:1119-22

JANUARY 21, 2013



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**Surviving Sepsis Campaign International Guidelines for Management of Severe Sepsis and Septic Shock**  
February 2013 • Volume 41 • Number 2

Let us use arterial catheter correctly and only when we need

Michael... CM; Jean-Louis Vincent, MD, PhD, FCCM

**Crit Care Med 2005; 33:1119-22**

**All three treatment protocols are based on filling pressures!**

**Practice parameters for hemodynamic support of sepsis  
in adult patients. 2004 update.**

Hollenberg S et al. Crit Care Med 2004; 32:1928-48

**“In most patients with septic shock, CO will  
be optimized at filling pressures between  
12-15 mmHg**

**Increases above this range...increase the  
risk for developing pulmonary edema.”**

**26. (III) Packman MJ, Rackow EC: Optimum left heart filling  
pressure during fluid resuscitation of patients with  
hypovolemic and septic shock. Crit Care Med 1983; 11:165-9**

*Level D recommendation*

# Optimum left heart filling pressure during fluid resuscitation of patients with hypovolemic and septic shock

MICHAEL I. PACKMAN, MD; ERIC C. RACKOW, MD

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CRITICAL CARE MEDICINE

MARCH, 1983

# Optimum left heart filling pressure during fluid resuscitation of patients with hypovolemic and septic shock

MICHAEL I. PACKMAN, MD; ERIC C. RACKOW, MD

166

CRITICAL CARE MEDICINE

MARCH, 1983

The data were analyzed for the 15 patients in whom at least 3 WP determinations were obtained and the final WP was  $\geq 15$  mm Hg. Four patients had only 2 data points (WP  $\geq 15$  mm Hg after 250 ml of fluid administration) and in 2 the protocol was terminated because of inability to increase the WP of 10 mm Hg, despite administration of 5 and 8 L, respectively, of normal saline solution.



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**Surviving Sepsis Campaign: International  
Guidelines for Management of Severe Sepsis  
and Septic Shock: 2012** February 2013 • Volume 41 • Number 2

**“Although there are limitations to CVP as a marker of intravascular volume status and response to fluids, a low CVP generally can be relied upon as supporting positive response to fluid loading.”**

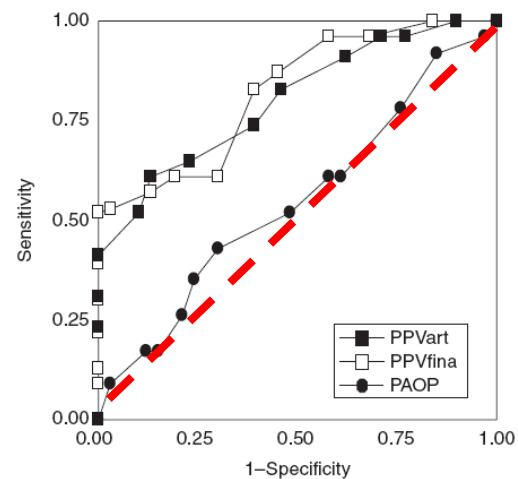
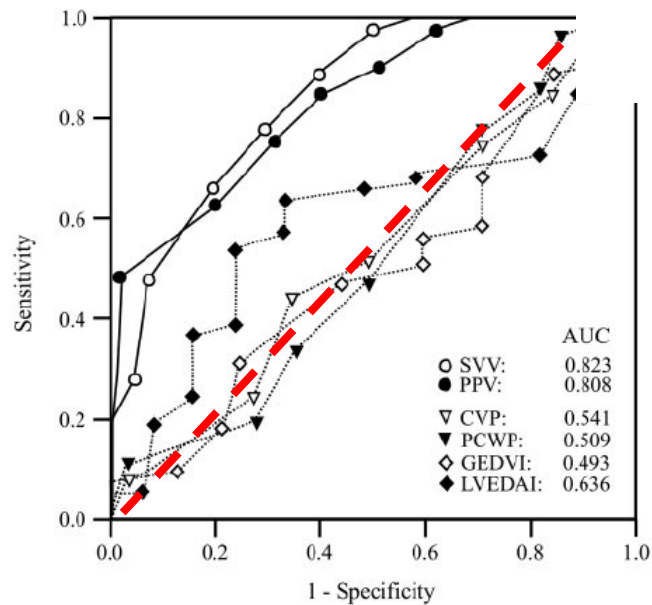
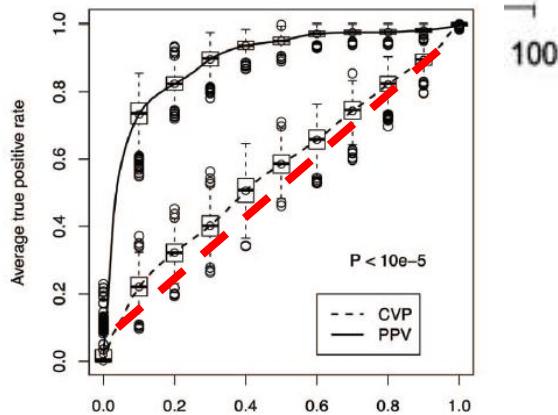
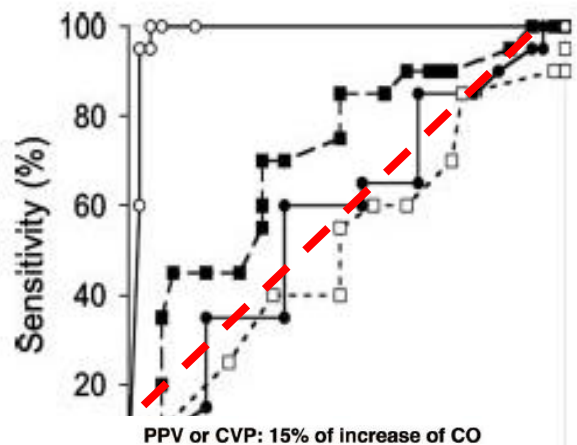
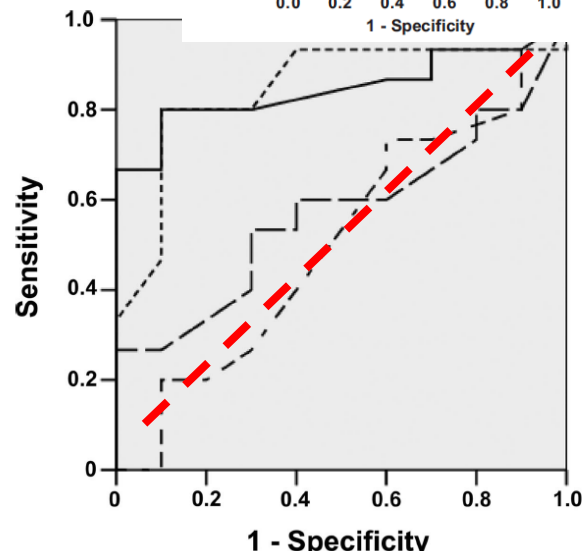
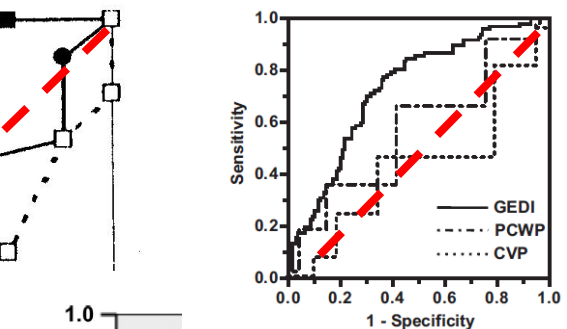
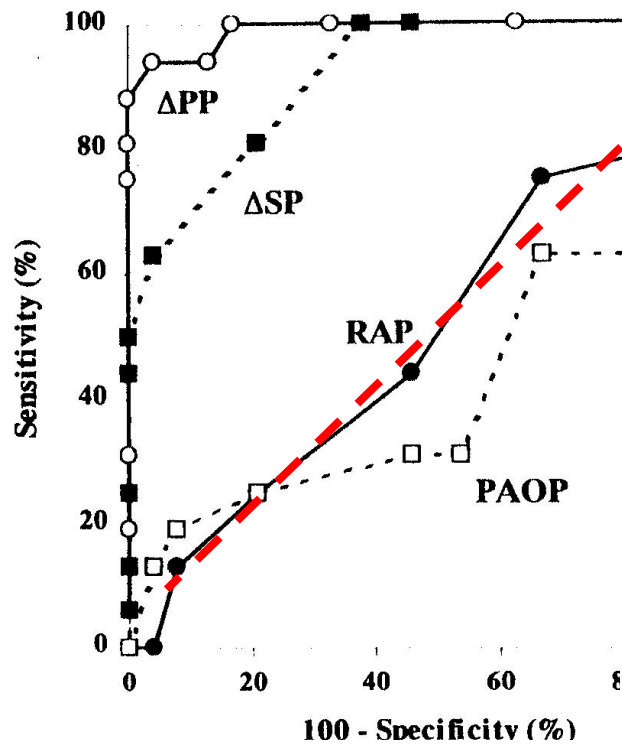
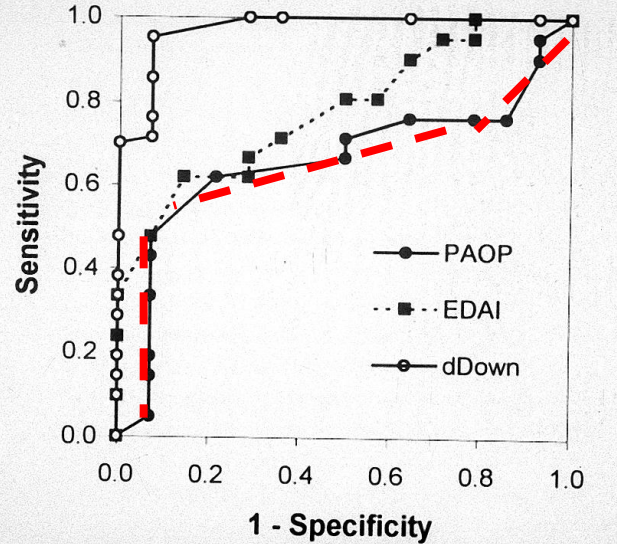


FIGURE 2. Prediction of fluid responsiveness: Areas under the

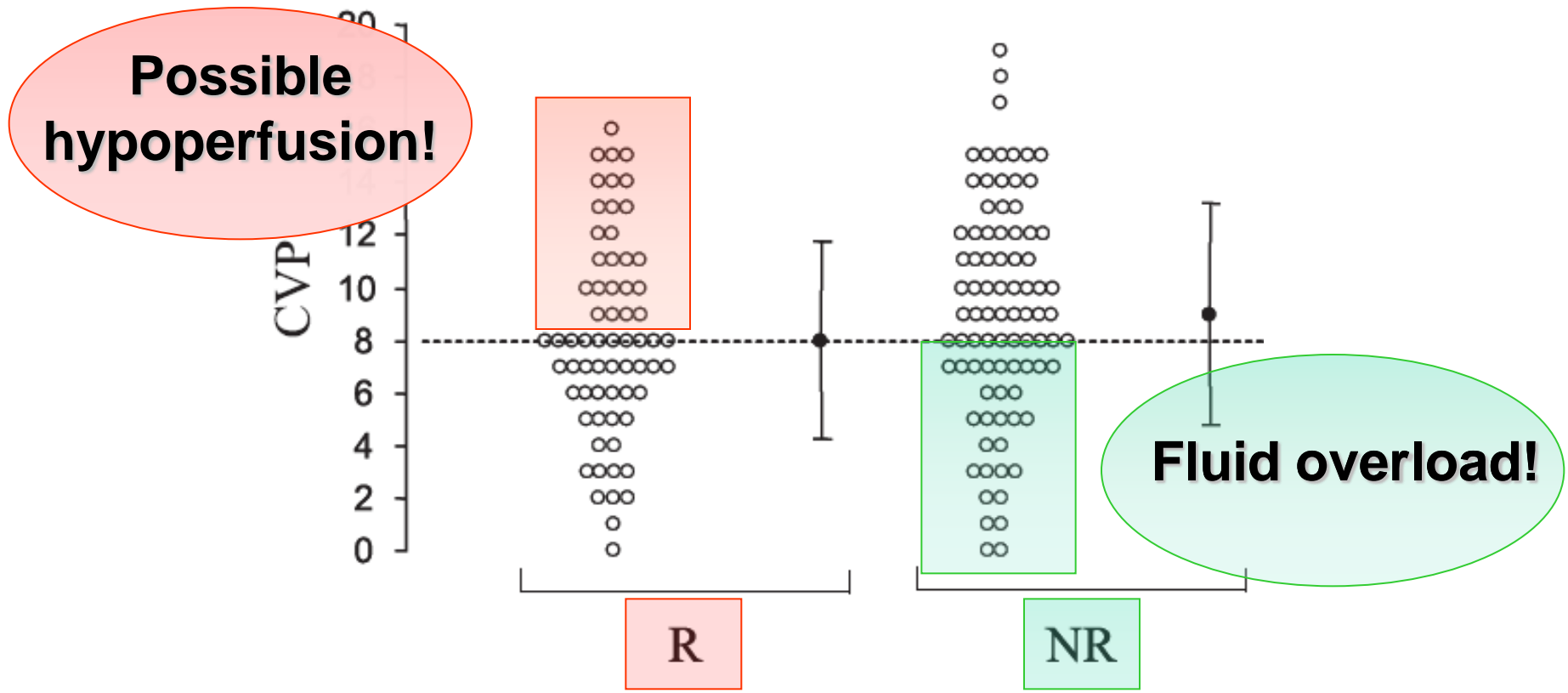
Fig 1 Receiver operating characteristic (ROC) curves for PPVart, PPVfina and PAOP.

# Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge\*

CCM 2007 35:64-8

David Osman, MD; Christophe Ridel, MD; Patrick Ray, MD; Xavier Monnet, MD, PhD; Nadia Anguel, MD; Christian Richard, MD; Jean-Louis Teboul, MD, PhD

Central venous pressure (CVP): 8–12 mm Hg



# A patient with head injury, severe ARDS and septic shock

## Initial resuscitation

*Begin resuscitation immediately in patients with hypotension or elevated serum lactate.*

### Resuscitation goals:

- ◆ Central venous pressure ~~8-12~~ mm Hg
- ◆ Mean arterial pressure  $\geq 65$  mm Hg
- ◆ Urine output  $\geq 0.5$  mL.kg<sup>-1</sup>.hr<sup>-1</sup>
- ◆ Central venous or mixed venous oxygen saturation  $\geq 70\%$

*If central venous oxygen saturation or mixed venous oxygen saturation of 70% is not achieved with a central venous pressure of 8-12 mm Hg, then transfuse packed red blood cells to achieve a haematocrit of  $\geq 30\%$  and/or administer a dobutamine infusion of up to a maximum of 20  $\mu\text{g.kg}^{-1}.\text{min}^{-1}$ .*

**BP** 70/40 mmHg

**HR** 155 bpm

**CVP** 5 cmH<sub>2</sub>O

**PaO<sub>2</sub>/FiO<sub>2</sub>** 80 (PEEP 16)

**Noradrenaline + aggressive diuresis!**

**Can this patient “afford” the price of a possible mistake?**



Fluid challenge revisited

CCM 2006;34:1333

Jean-Louis Vincent, MD, PhD, FCCM; Max Harry Weil, MD, PhD, ScD (Hon), FCCM

**“Filling pressure do not reliably predict a patient’s response to fluid administration.”**

Intensive Care Med  
DOI 10.1007/s00134-007-0531-4

INTERNATIONAL CONSENSUS CONFERENCE

Massimo Antonelli  
Mitchell Levy  
Peter J. D. Andrews  
Jean Chastre  
Leonard D. Hudson  
Constantine Manthous  
G. Umberto Meduri  
Rui P. Moreno  
Christian Putensen  
Thomas Stewart  
Antoni Torres

**Hemodynamic monitoring in shock and implications for management**

**International Consensus Conference, Paris, France,  
27–28 April 2006**

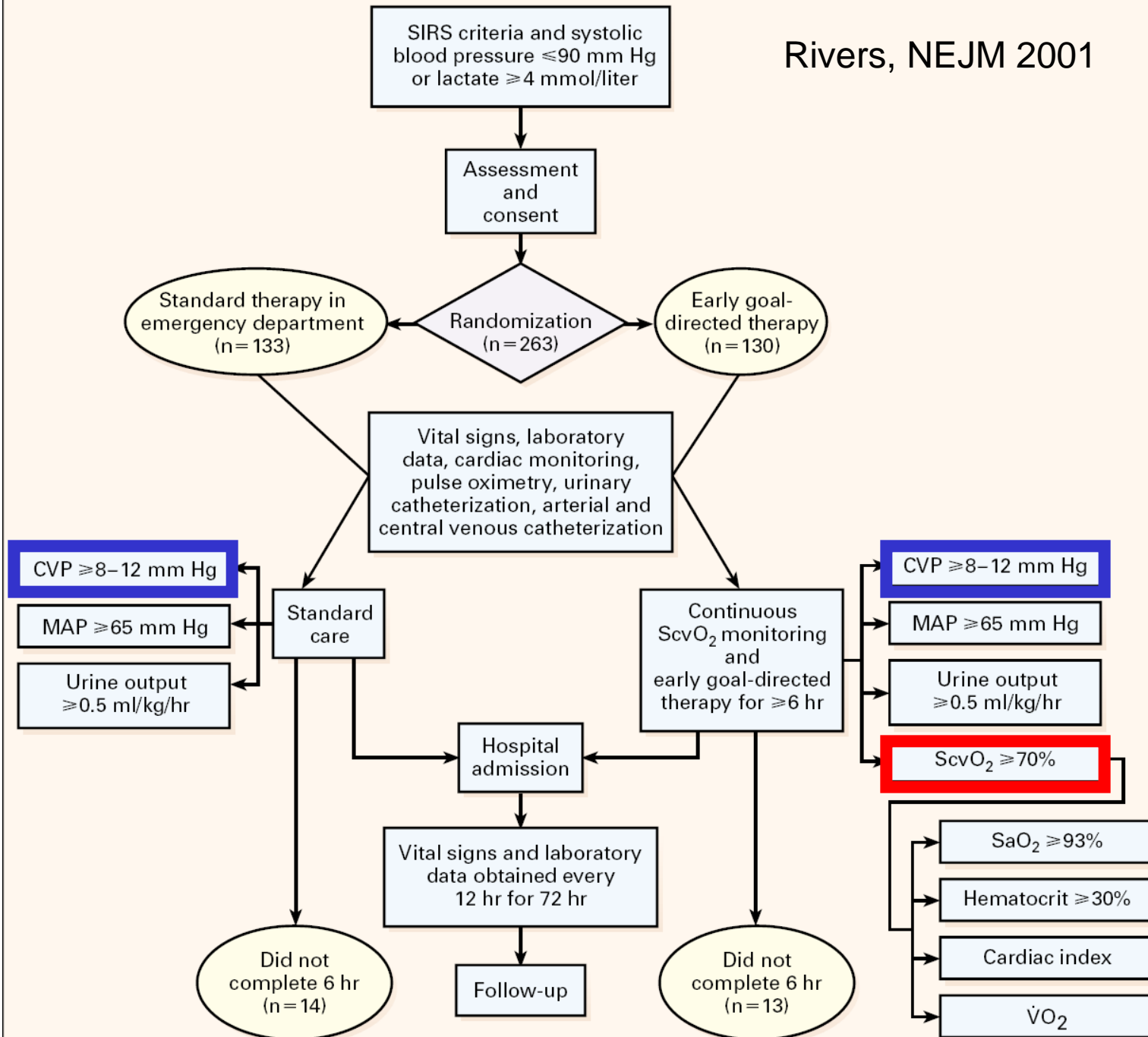
**“We recommend that preload measurement alone not be used to predict fluid responsiveness.”**

**Does Central Venous Pressure Predict Fluid Responsiveness?\***

*(CHEST 2008; 134:172–178)*

*Paul E. Marik, MD, FCCP; Michael Baram, MD, FCCP; and Bobbak Vahid, MD*

**“CVP should not be used to make clinical decisions regarding fluid management.”**



# Surviving Sepsis Campaign Guidelines

Dellinger RP, et al. Crit Care Med 2004;32:858-73

(based on Rivers et al, NEJM 2001)

If the hypotension does not respond to fluid challenges or the lactate remains  $> 4$  mmol/L then the goals of initial resuscitation should include all of the following as one part of a treatment protocol: (= the “bundle”)

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Let us use the pulmonary artery catheter correctly and only when we need it

**Crit Care Med 2005; 33:1119-22**

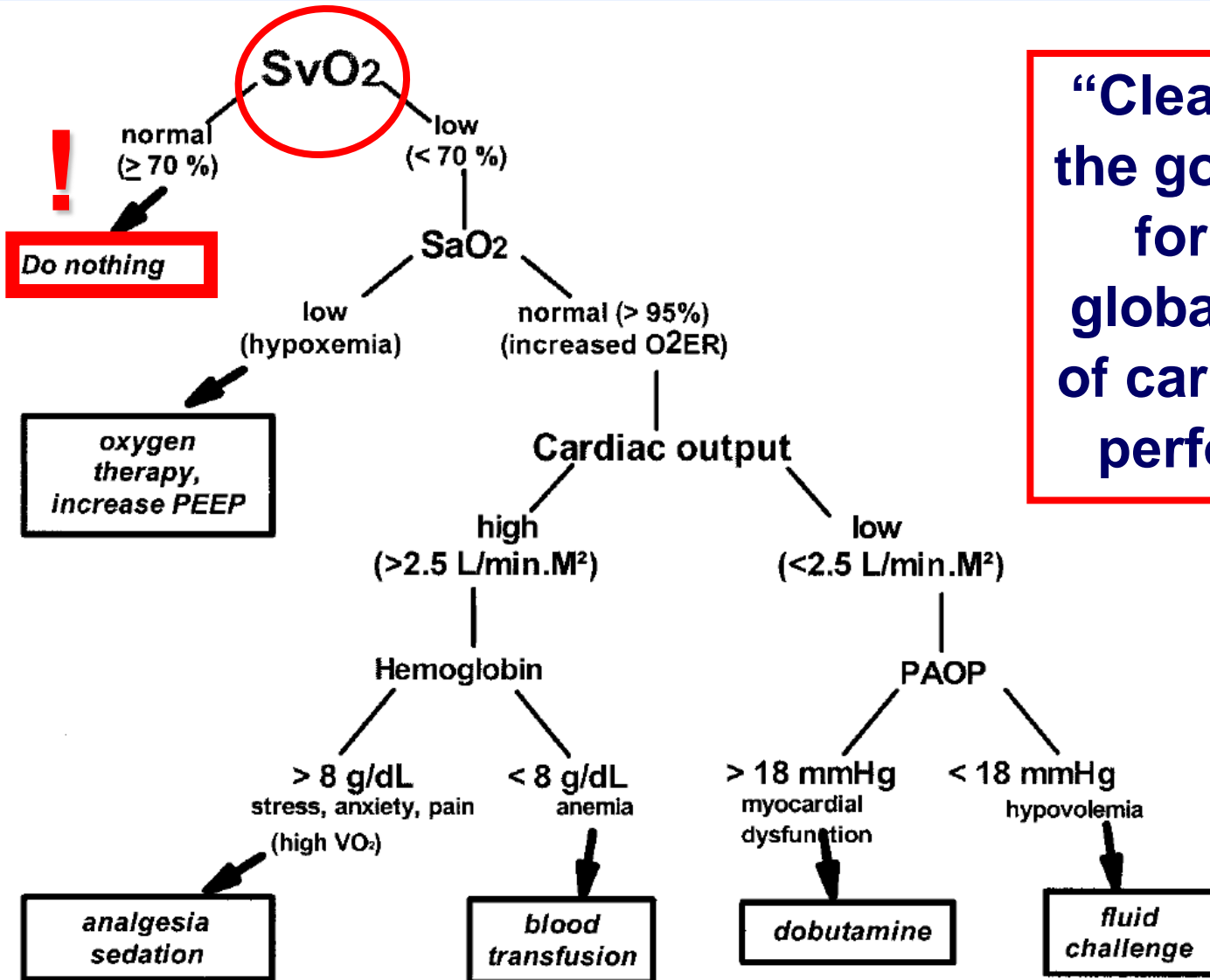
Michael R. Pinsky, MD, Dr hc, FCCM; Jean-Louis Vincent, MD, PhD, FCCM

**“Clearly, SvO<sub>2</sub> is the gold standard for defining global adequacy of cardiovascular performance.”**

Let us use the pulmonary artery catheter correctly and only when we need it

Crit Care Med 2005; 33:1119-22

Michael R. Pinsky, MD, Dr hc, FCCM; Jean-Louis Vincent, MD, PhD, FCCM



“Clearly, SvO<sub>2</sub> is the gold standard for defining global adequacy of cardiovascular performance.”

VARIABLE AND TREATMENT GROUP	BASE LINE (0 hr)	HOURS A 6
Heart rate (beats/min)		
Standard therapy	114±27	105±25
EGDT	117±31	103±19
P value	0.45	0.12
Central venous pressure (mm Hg)		
Standard therapy	6.1±7.7	11.8±6.8
EGDT	5.3±9.3	13.8±4.4
P value	0.57	0.007
Mean arterial pressure (mm Hg)		
Standard therapy	76±24	81±18
EGDT	74±27	95±19
P value	0.60	<0.001
Central venous oxygen saturation (%)		
Standard therapy	49.2±13.3	66.0±15.5
EGDT	48.6±11.2	77.3±10.0
P value	0.49	<0.001

**The normal ScvO<sub>2</sub> is ~70%**

**Rivers et al NEJM 2001**

**Krafft P et al, Chest 1993; 103:900-6**

**Mixed venous oxygen saturation in critically ill septic shock patients. The role of defined events**

- **A high incidence of short-term SvO<sub>2</sub> changes in a septic shock patient may be of diagnostic and prognostic significance.**
- **The SvO<sub>2</sub> of septic shock patients is mainly normal or even supra-normal.**

$$O_2ER \cong 1 - S_{\bar{v}}O_2$$

Am J Med. 1988 Oct;85(4):581-2.

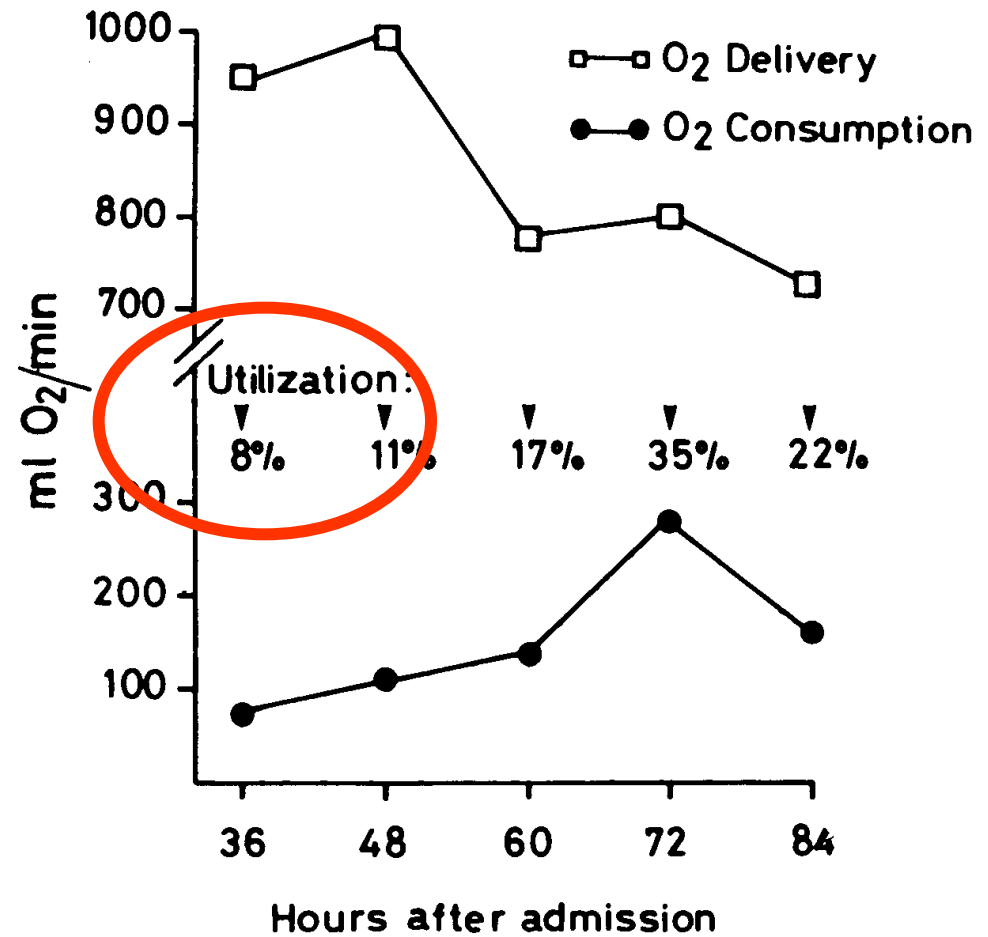
## Decreased oxygen utilization in epidemic typhus infection: case report with sequential hemodynamic studies.

Flugelman MY, Ephros M, Gotlieb S, Cotev S, Perel A.

Hadassah University Hospital, Jerusalem, Israel.

$SvO_2 \sim 1 - O_2ER$

$SvO_2 \sim 92\%$





# The mean initial ScvO<sub>2</sub> of Rivers' patients was 50%

## Implementation and outcomes of the Multiple Urgent Sepsis Therapies (MUST) protocol\*

Nathan I. Shapiro, MD, MPH; Michael D. Howell, MD; Daniel Talmor, MD, MPH; Dermot Lahey, BA; Long Ngo, PhD; Jon Buras, MD, PhD; Richard E. Wolfe, MD; J. Woodrow Weiss, MD; Alan Lisbon, MD

*Crit Care Med* 2006, 34:1025-1032

Initial ScvO<sub>2</sub> **72 ± 11%**

## Multicenter Study of Central Venous Oxygen Saturation (ScvO<sub>2</sub>) as a Predictor of Mortality in Patients With Sepsis

Jennifer V. Pope, MD  
Alan E. Jones, MD  
David F. Gaieski, MD  
Ryan C. Arnold, MD  
Stephen Trzeciak, MD, MPH  
Nathan I. Shapiro, MD, MPH

*Ann Emerg Med.* 2010;55:40-46

Initial ScvO<sub>2</sub> **73 ± 13%**

## The incidence of low venous oxygen saturation on admission to the intensive care unit: a multi-center observational study in The Netherlands

PA van Beest<sup>1,2</sup>, JJ Hofstra<sup>3</sup>, MJ Schultz<sup>3,4</sup>, EC Boerma<sup>1</sup>, PE Spronk<sup>3,4,5</sup> and MA Kuiper<sup>1,3,4</sup>

*Critical Care* 2008, 12:R33

Initial ScvO<sub>2</sub> **74 ± 10%**

## Early Lactate-Guided Therapy in Intensive Care Unit Patients

A Multicenter, Open-Label, Randomized Controlled Trial

Tim C. Jansen<sup>1</sup>, Jasper van Bommel<sup>1</sup>, F. Jeanette Schoonderbeek<sup>3</sup>, Steven J. Sleswijk Visser<sup>4</sup>, Johan M. van der Klooster<sup>5</sup>, Alex P. Lima<sup>1</sup>, Sten P. Willemsen<sup>2</sup>, and Jan Bakker<sup>1</sup>, for the LACTATE study group\*

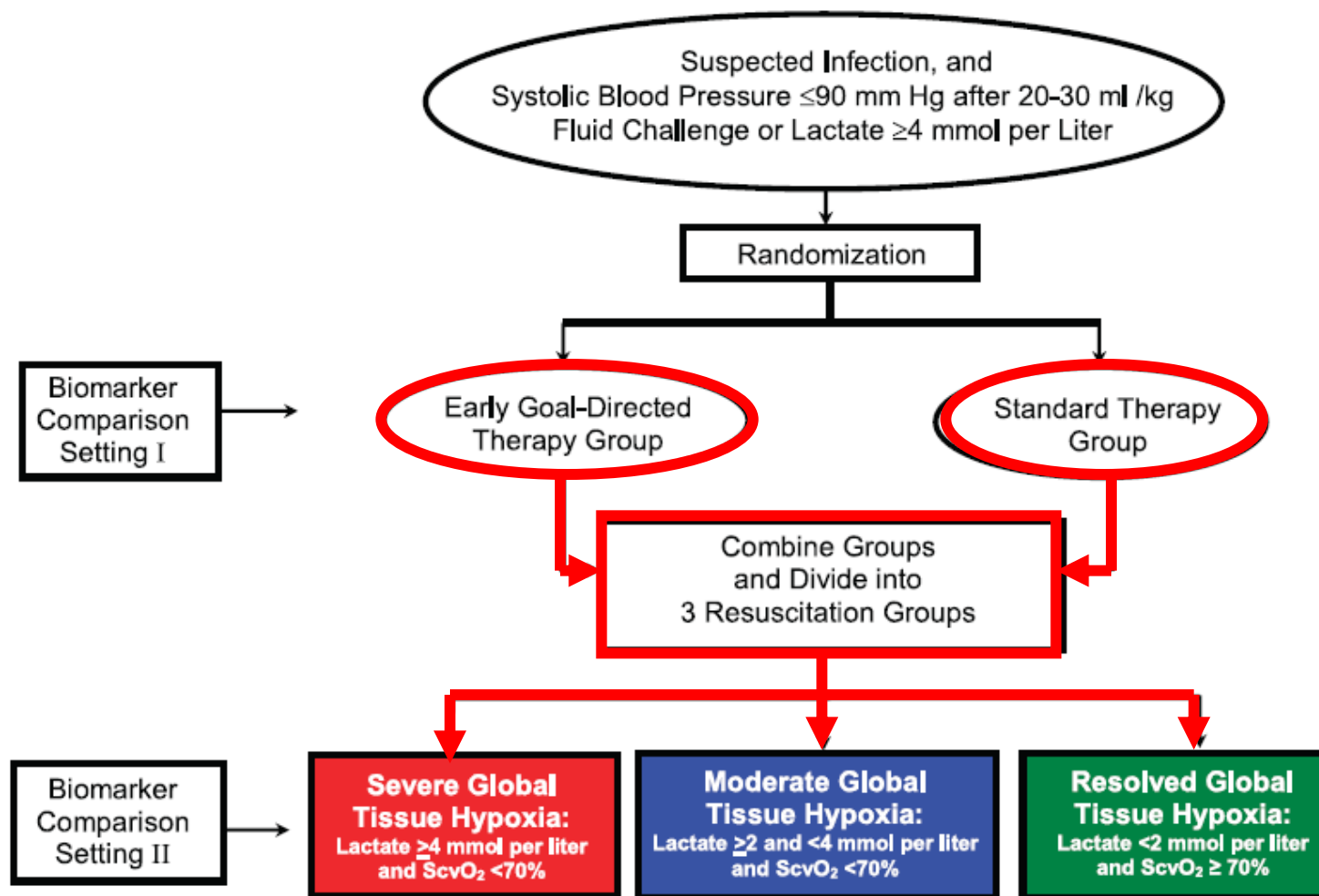
*Am J Respir Crit Care Med* Vol 182, pp 752-761, 2010

Initial ScvO<sub>2</sub> **73 ± 11%**

# The influence of early hemodynamic optimization on biomarker patterns of severe sepsis and septic shock\*

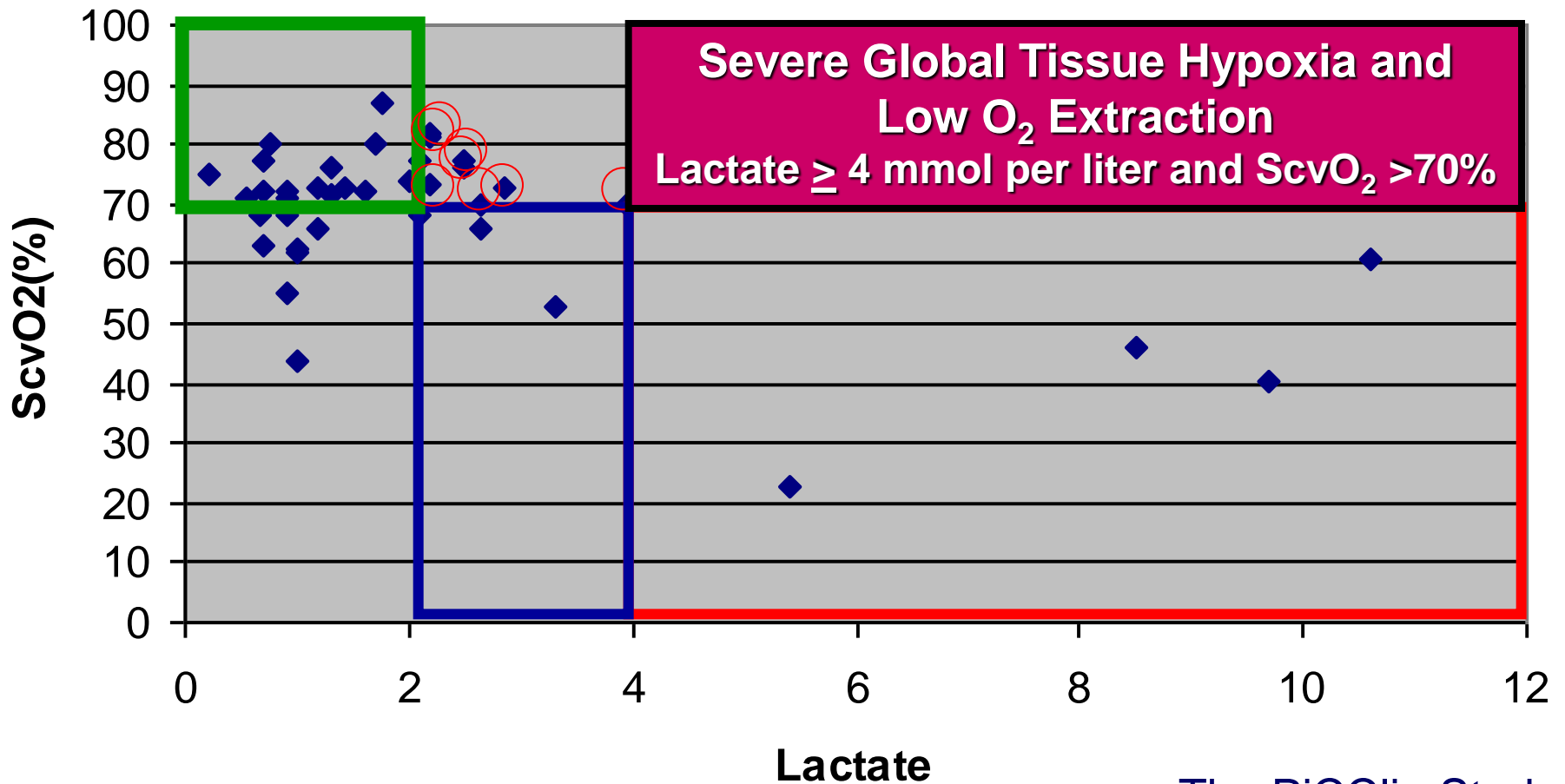
CCM 2007

Emanuel P. Rivers, MD, MPH; James A. Kruse, MD; Gordon Jacobsen, MS; Kant Shah, MD; Manisha Loomba, MD; Ronny Otero, MD; Ed W. Childs, MD



**Optimal hemodynamic management according to the surviving sepsis guidelines is not applicable to all ICU patients.**

**Perel A, et al. Crit Care 2008;12 (Suppl 2):S156.**



# Multicenter Study of Central Venous Oxygen Saturation (ScvO<sub>2</sub>) as a Predictor of Mortality in Patients With Sepsis

[Ann Emerg Med. 2010;55:40-46.]

Jennifer V. Pope, MD

Alan E. Jones, MD

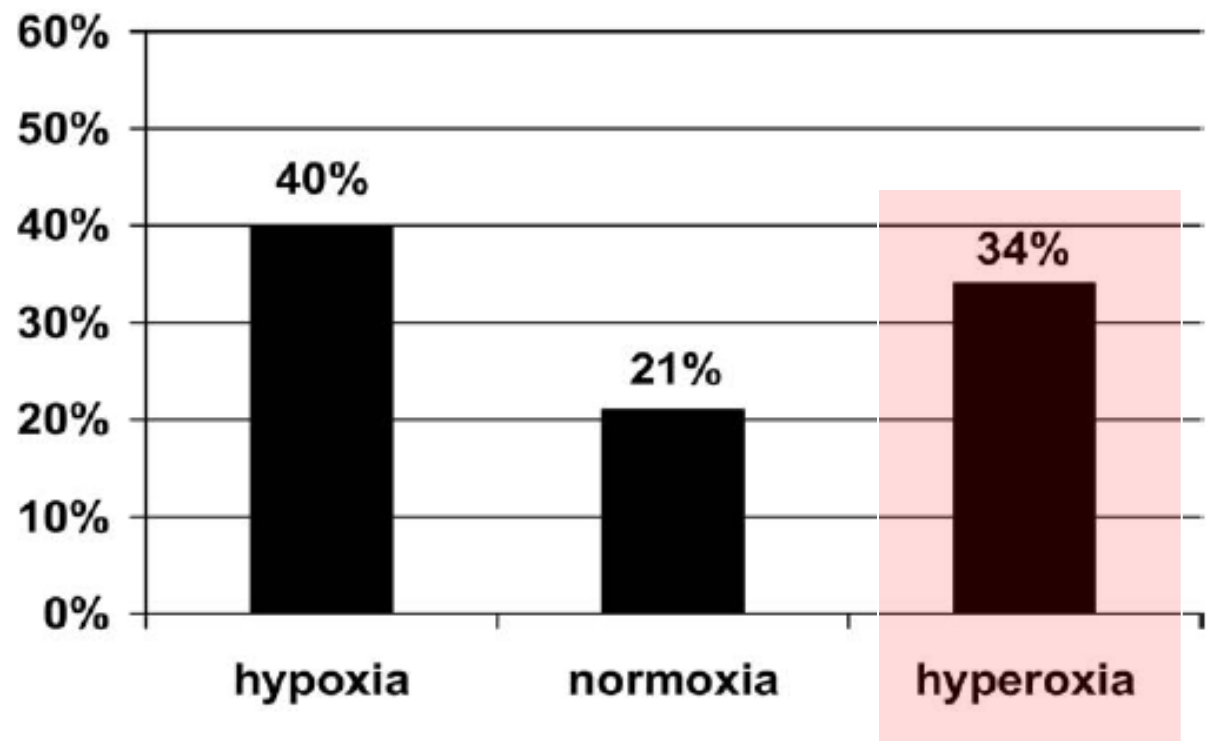
David F. Gaieski, MD

Ryan C. Arnold, MD

Stephen Trzeciak, MD, MPH

Nathan I. Shapiro, MD, MPH

On behalf of the Emergency  
Medicine Shock Research  
Network (EMShockNet)  
Investigators



The NEW ENGLAND JOURNAL of MEDICINE

**CORRESPONDENCE**

Volume 356:1178-1182

March 15, 2007

Number 11

**“The reported improved survival following the adoption of these (SSC) Guidelines....cannot be viewed as justification of the initial hemodynamic resuscitation protocol.**

**Physiologically and clinically this protocol may be wrong for many septic patients.”**

Azriel Perel, M.D.  
Eran Segal, M.D.  
*Sheba Medical Center  
Tel Aviv 52621, Israel*

New Therapy for Sepsis Infection  
Raises Hope but Many Questions

## Editorials

CAN J ANESTH 2007 / 54: 10 / pp 779-785

### Severe sepsis: a bundle still under construction?

Robert N. Sladen MB ChB MRCP(UK) FRCP(C)

### Bench-to-bedside review: The initial hemodynamic resuscitation of the septic patient according to Surviving Sepsis Campaign guidelines – does one size fit all?

Azriel Perel

*Critical Care* 2008, 12:223

Daniel A. Sweeney  
Robert L. Danner  
Peter Q. Eichacker  
Charles Natanson

### Once is not enough: clinical trials in sepsis

*Intensive Care Med* (2008) 34:1955–1960

Anaesthesia, 2006, 61, pages 313–315

### Early goal-directed therapy: on terminal life support? ☆

Paul E. Marik MD<sup>a,\*</sup>, Joseph Varon MD<sup>b</sup> *American Journal of Emergency Medicine* (2009)

## Editorial

The Surviving Sepsis  
Campaign and Sepsis Care  
Bundles: substance or  
sophistry?

### Why we should be wary of single-center trials

(*Crit Care Med* 2009; 37:3114–3119)

Rinaldo Bellomo, MD, FRACP, FJFICM; Stephen J. Warrillow, MBBS, FRACP, FJFICM;  
Michael C. Reade, MBBS, MPH, DPhil, FANZCA, FJFICM

Commentary

### The pursuit of a high central venous oxygen saturation in sepsis: growing concerns

*Critical Care* 2008, 12:130

Rinaldo Bellomo, Michael C Reade and Stephen J Warrillow



## Counterpoint: Adherence to Early Goal-Directed Therapy : Does It Really Matter? No. Both Risks and Benefits Require Further Study

Gregory A. Schmidt

*Chest* 2010;138;480-483

**Skepticism arises from the single-center nature of the only positive, prospective trial; uncertainty regarding the individual components of a complex, bundled protocol; and concern about the appropriateness of drawing general inferences from an unusual subject pool.**

# Surviving sepsis: going beyond the guidelines

Paul E Marik

*Annals of Intensive Care* 2011, 1:17

- **Most of the Surviving Sepsis Campaign recommendations are not evidence-based and the major components of the 6-hour bundle are based on a single-center study whose validity has been recently under increasing scrutiny.**
- **The end-points of resuscitation of patients with severe sepsis should be based on validated physiologic variables that are individualized based on each patients' co-morbidities and unique clinical circumstances.**
- **It is unlikely that a “one-size fits all” approach will be appropriate for all patients.**



**The Surviving Sepsis Campaign: robust  
evaluation and high-quality primary  
research is still needed**

Simon Finfer

Published online: 13 January 2010

**Increased awareness as a result of the campaign may be partly or even predominantly responsible for reduced mortality observed around the world.**

**A beneficial effect of the guidelines on patient outcomes is currently unproven, and the primary evidence is not yet of sufficient quality to promote the guidelines as a global standard of care.**

**The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis**

Levy M, et al. Crit Care Med. 2010 Feb;38(2):367-74

**The adjusted odds ratio for mortality improved by 5.4% over 2 yrs.**

**If the goals of the Rivers protocol have questionable pathophysiological rationale, how does the SSC save lives?**

**mortality fell from 37% to 30.6% during this 2-year performance improvement programme.**

## **Do the Rivers' patients represent all septic patients?**

- **Very recent literature from the US emphasizes the effects of race and socio-economic conditions on sepsis outcome.**
- **The Rivers study was done in the Department of Emergency Medicine which serves “metro Detroit’s largely poor, largely minority population, having poor health status and high chronic disease incidence”**  
[Ann Emerg Med Dec. 2008](#)
- **“Outcome of Americans without insurance who are admitted to the ICU is worse, possibly because they are sicker when they seek care.”**  
[Danis M, et al. Crit Care Med 2006; 34:2043](#)



TUESDAY, OCTOBER 16, 2012 | **7**

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**Paul  
Krugman**

## Death by ideology

if you go to an emergency room you will be billed, and the size of that bill can be shockingly high. Some people can't or won't pay, but fear of huge bills can deter the uninsured from visiting the emergency room even when they should. And sometimes they die as a result.



August 14, 2008

**PAGE ONE**

**New Therapy for Sepsis Infections  
Raises Hope but Many Questions**

- **The reported death rates in the standard treatment group in the Rivers study was 46.5%, compared to death rates of 30% or lower in Australia and the Netherlands.**
- **Dr. Rivers's explanation is that his patients were sicker, hence a higher death rate for those on conventional care.**

# Bench-to-bedside review: The initial hemodynamic resuscitation of the septic patient according to Surviving Sepsis Campaign guidelines – does one size fit all?

Azriel Perel

*Critical Care* 2008, 12:223

Comparison of comorbidities of the patients in studies by Rivers and colleagues [2] and Sprung and colleagues (CORTICUS) [23]

	Rivers <i>et al.</i> (n = 263)	Sprung <i>et al.</i> (n = 499)	Chi-square test
Caucasian (%)	Not reported	93	
Age (years)	65.7	63	
Male/Female (%)	50.6/49.4	66.5/33.5	0.0000
Hypertension (%)	67.3	37.7 <sup>a</sup>	0.0000
Coronary artery disease (%)	25.0	16.9 <sup>a</sup>	0.0080
Congestive heart failure (%)	33.4	6.0 <sup>a</sup>	0.0000
Diabetes (%)	31.4	21.6 <sup>a</sup>	0.0030
Chronic obstructive pulmonary disease (%)	15.7	11.3 <sup>a</sup>	0.0900
Chronic renal failure (%)	21.7	8.7 <sup>a</sup>	0.0000
Liver disease (%)	23.3	8.1 <sup>a</sup>	0.0000
Neurologic disease (%)	33.0	11.7 <sup>a</sup>	0.0000
Cancer (%)	11.4	16.9 <sup>a</sup>	0.0580
Alcohol use (%)	38.6	Not reported	

<sup>a</sup>n = 496. CORTICUS, Corticosteroid Therapy of Septic Shock.



**THE WALL STREET JOURNAL.**  
ONLINE

August 14, 2008

**PAGE ONE**

**New Therapy for Sepsis Infections  
Raises Hope but Many Questions**

- **The hospital held patents on a medical device critical to the therapy, and one of the groups that later endorsed the treatment had financial backing from the maker of the device.**
- **Rivers et al report that a total of 288 patients were "evaluated" of whom 25 "were excluded". A relatively high proportion of the 25 patients not included in the final analysis were either conventional-therapy patients who survived or patients on EGDT who died.**

**Bench-to-bedside review: The initial hemodynamic resuscitation of the septic patient according to Surviving Sepsis Campaign guidelines – does one size fit all?**

Azriel Perel

*Critical Care* 2008, 12:223

- **The extremely low ScvO<sub>2</sub> values seen in Rivers' patients on admission to the ED indicate that these patients had very low cardiac outputs.**
- **The most probable cause for their low CO was a combination of pre-existing co-morbidities and hypovolemia, which may have developed due to a late arrival to the hospital (black, low socioeconomic status, no insurance).**
- **The very significant hypovolemic element of their septic shock was successfully corrected by aggressive fluid loading which was guided by a very simple protocol that is unsuitable to most ICU septic patients.**





Critical Care Congress

JANUARY 21, 2013

Society of  
Critical Care Medicine  
The Intensive Care Professionals



**Surviving Sepsis Campaign: International  
Guidelines for Management of Severe Sepsis  
and Septic Shock: 2012** February 2013 • Volume 41 • Number 2

**A large number of other observational studies using similar forms of early quantitative resuscitation in comparable patient populations have shown significant mortality reduction compared to the institutions' historical controls (Supplemental Digital Content and references 19–24).**

**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**

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

**The revised SSC guidelines include  
85 recommendations (instead of the  
original 52 that appeared in 2004)**



**A. Initial Resuscitation**

**B. Diagnosis**

**C. Antibiotic Therapy**

**D. Source Control**

**E. Fluid Therapy**

**F. Vasopressors**

**G. Inotropic Therapy**

**H. Steroids**

**I. Recombinant Human  
Activated Protein C (rhAPC)**

**J. Blood Product Administration**

**K. Mechanical Ventilation**

**L. Sedation, Analgesia, and  
Neuromuscular Blockade**

**M. Glucose Control**

**N. Renal Replacement**

**O. Bicarbonate Therapy**

**P. DVT Prophylaxis**

**Q. Stress Ulcer Prophylaxis**

**R. Limitation of Support**

**S. Pediatric Considerations**

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

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

**Crit Care Med 2006; 34:1589–1596**

## **Initiation of Inappropriate Antimicrobial Therapy Results in a Fivefold Reduction of Survival in Human Septic Shock**

Anand Kumar, Paul Ellis, Yaseen Arabi, Dan Roberts, Bruce Light, Joseph E. Parrillo, Peter Dodek, Gordon Wood, Aseem Kumar, David Simon, Cheryl Peters, Muhammad Ahsan, Dan Chateau and the Cooperative Antimicrobial Therapy of Septic Shock Database Research Group

*Chest* 2009;136;1237-1248

## Bundled care for septic shock: An analysis of clinical trials\*

Amisha V. Barochia, MBBS; Xizhong Cui, MD, PhD; David Vitberg, MD; Anthony F. Suffredini, MD; Naomi P. O'Grady, MD; Steven M. Banks, PhD;† Peter Minneci, MD; Steven J. Kern, BS; Robert L. Danner, MD; Charles Natanson, MD; Peter Q. Eichacker, MD

Crit Care Med 2010; 38:668–678

- **As administered and studied to date, only antibiotics meet the stated criteria of proof for bundle inclusion.**
- **Current sepsis bundles may force physicians to provide unproven or even harmful care.**

Implementation and outcomes of the Multiple Urgent Sepsis Therapies (MUST) protocol\*

Crit Care Med 2006; 34:1025-32

Nathan I. Shapiro, MD, MPH; Michael D. Howell, MD; Daniel Talmor, MD, MPH; Dermot Lahey, BA; Long Ngo, PhD; Jon Buras, MD, PhD; Richard E. Wolfe, MD; J. Woodrow Weiss, MD; Alan Lisbon, MD

**Our septic patients were seemingly less critically ill compared with Rivers et al:**

- **Lower mortality in the control groups (29% vs. 57%)**
- **Lower initial serum lactate level (4.4 vs. 7.7 mmol/L)**
- **Higher initial ScvO<sub>2</sub> (72% vs. 49%)**

# Shapiro N, et al.

(Crit Care Med 2009; 37:819–824)

	Before Group (n = 200)	After Group (n = 200)	<i>p</i>
IV fluids given in first 12 hrs (mL)	1627 ± 1862	2054 ± 2237	0.04
Emergency department	0–6	3548 ± 2977	1.00
Intensive care unit		1477 ± 1193	0.45
Ward		1327 ± 1480	0.69
First antibiotic dose		131 (65.5)	0.01
Emergency department		48 (77.4)	0.01
Intensive care unit		32 (56.1)	0.58
Ward		51 (63.0)	0.40
Time to appropriate antibiotic coverage (min)	995 ± 1270	737 ± 1089	0.04
Emergency department	652 ± 1223	346 ± 921	0.19
Intensive care unit	1132 ± 1226	916 ± 1155	0.32
Ward	991 ± 1326	927 ± 1097	0.75
Steroids given in first 24 hrs, n (%)	34 (17.0)	42 (21.0)	0.31
Sepsis goals			
MAP goal achieved, n (%)	162 (81.0)	169 (84.5)	0.41
Requiring vasopressors <sup>a</sup>	137 (68.5)	105 (52.5)	<0.01
CVP monitored, n (%)	21 (10.5)	31 (15.5)	0.14
ScvO <sub>2</sub> monitored, n (%)	2 (1.0)	15 (7.5)	<0.01
Documented central venous pressure of >8 mm Hg in ED, n (%)	3 (5.0)	29 (48.3)	<.001
Central venous oxygen saturation assessment in the ED, n (%)	1 (1.7)	29 (48.3)	<.001

Rivers, NEJM, 2001

Total fluids (ml)

Standard therapy

EGDT

CCM, 2006;34:2707

## **The end of the line for the Surviving Sepsis Campaign, but not for early goal-directed therapy**

Patrick A Nee and Emanuel P Rivers

*Emerg Med J* published online November 9, 2010

- **Early interventions found to be independently associated with survival benefit were timely antibiotics and blood cultures prior to administration ( $p < 0.0001$ ).**
- **Attainment of a CVP of  $>8$  mmHg and ScvO<sub>2</sub> of  $>70\%$  did not influence survival in patients with septic shock.**



**The GENESIS Project (GENERALized Early Sepsis Intervention Strategies) : A Multicenter Quality Improvement Collaborative**

Chad M. Cannon, Christopher V. Holthaus, Marc T. Zubrow, Pat Posa, Satheesh Gunaga, Vipul Kella, Ron Elkin, Scott Davis, Bonnie Turman, Jordan Weingarten, Truman J. Milling, Jr, Nathan Lidsky, Victor Coba, Arturo Suarez, James J. Yang and Emanuel P. Rivers

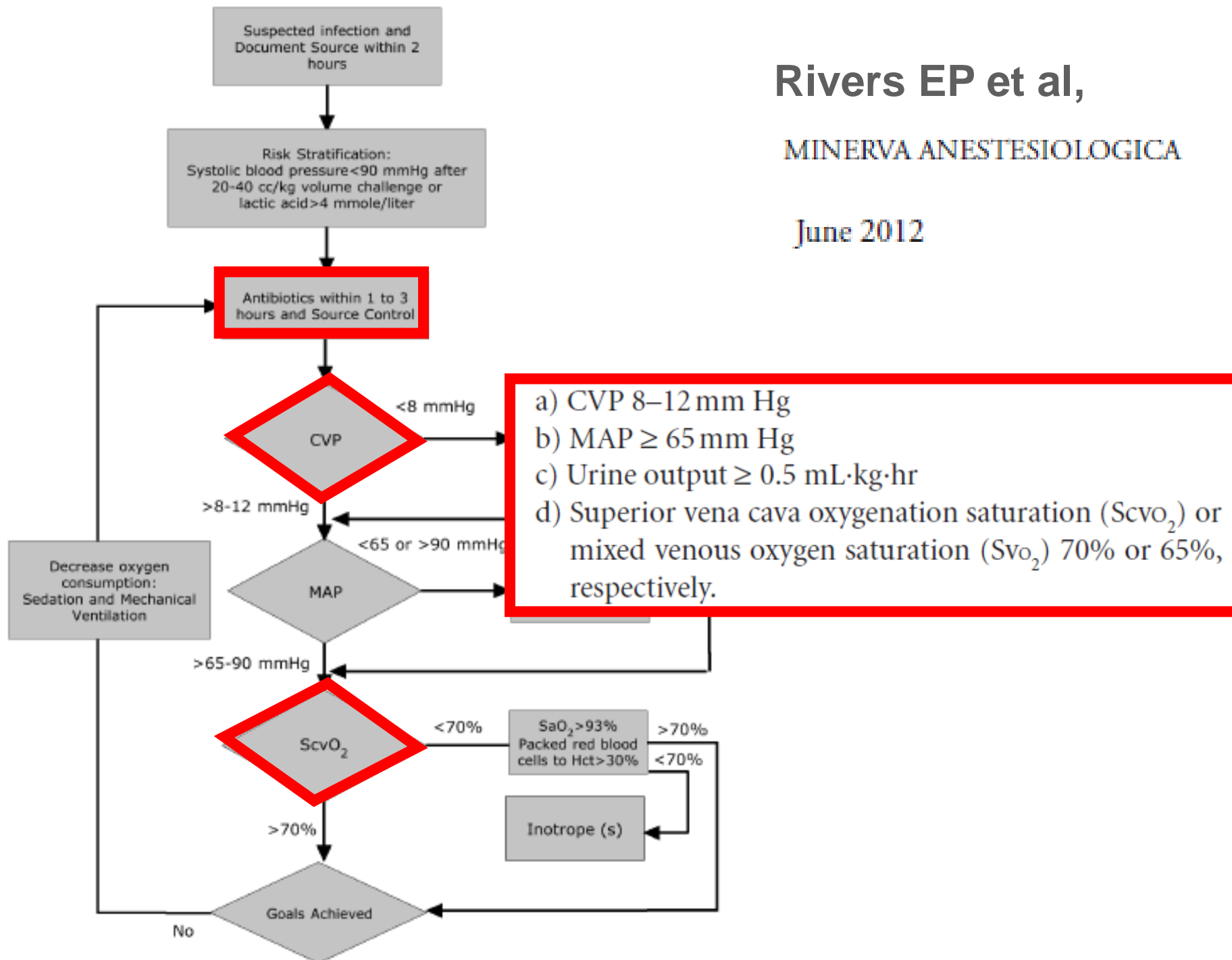
*J Intensive Care Med* published online 17 August 2012

**Patients with severe sepsis and septic shock receiving the Resuscitation Bundle in community and tertiary hospitals experience similar and significant reductions in mortality and hospital length of stay.**

Rivers EP et al,

MINERVA ANESTESIOLOGICA

June 2012



**“Medicine has become complex. Details have become overwhelming for clinicians to process at the bedside...”**

**M. Levy, SCCM 2009**

**Sepsis change bundles: Converting guidelines into meaningful change in behavior and clinical outcome**

Crit Care Med 2004 Vol. 32, No. 11 (Suppl.)

Mitchell M. Levy, MD; Peter J. Pronovost, MD, PhD; R. Phillip Dellinger, MD, FCCM; Sean Townsend, MD; Roger K. Resar, MD; Terry P. Clemmer, MD, FCCM; Graham Ramsay, MD

## **The 3 phases of the Surviving Sepsis Campaign**

- 1. Introduction at several major international critical care medicine conferences.**
- 2. Creating evidence-based guidelines for the management of severe sepsis and septic shock.**
- 3. To operationalize the SSC guidelines into a set of practical yet valid performance measure.**



*C.H. PhD, IHI Vice President  
and patient safety expert*

**Q. What makes the bundle so special?**

**The bundle is well-established, proven in scientific tests and based on randomized controlled trials, what we call Level 1 evidence.**

**The bundle must be followed for every patient, every single time. There should be no controversy involved, no debate or discussion of bundle elements.**



**“For every patient, every single time”**

**“No controversy involved, no debate or discussion”**

Zhongguo Wei Zhong Bing Ji Jiu Yi Xue. 2008 Mar;20(3):155-8.

**[Analysis of a survey of SSC guideline implemented among Chinese intensivists].**

[Article in Chinese]

Li J, Xi XM, Luo X.

**While only 47% of surveyed intensivists believed that CVP should guide resuscitation, 86% used it because of the Surviving Sepsis Campaign Guidelines.**

# Reassessment of Clinical Practice Guidelines

Go Gently Into That Good Night

---

Terrence M. Shaneyfelt, MD, MPH

---

Robert M. Centor, MD

---

**868** JAMA, February 25, 2009—Vol 301, No. 8

- **Some consensus statements are being turned into performance measures and other tools to critique the quality of physician care.**



UNLESS THE WORD SPECIFIC IS WRITTEN AFTER A DRUG ORDER BY TRADE NAME, A GENERIC EQUIVALENT DRUG APPROVED BY THE PHARMACY AND THERAPEUTICS COMMITTEE MAY BE DISPENSED IN ACCORDANCE WITH THE MEDICAL STAFF BYLAWS.

PLEASE CHECK (4) THE APPROPRIATE BOX  AND FILL IN THE BLANK(S) AS NEEDED. IF YOU DO NOT NEED ORDER, DRAW A LINE THROUGH IT AND INITIAL.

INITIATE THE FOLLOWING STANDARDIZED ORDERS FOR ALL PATIENTS IN SEVERE SEPSIS OR SEPSIS-INDUCED HYPOPERFUSION (SYSTOLIC BLOOD PRESSURE < 90 MMHG [AFTER A CRYSTALLOID FLUID CHALLENGE OF 20 ML/KG OVER 30 MINUTES] OR A BLOOD LACTATE CONCENTRATION OF ≥ 4 MMOL/L)



DATE	TIME	ORDERS
------	------	--------

Admission Status:  Inpatient  
 Recommended Admit Location: 83ICU or 89ICU or 84ICU if surgical patient

Diagnosis:  
 1.) \_\_\_\_\_  
 2.) \_\_\_\_\_  
 3.) \_\_\_\_\_

**Early Goal-Directed Therapy (To be initiated within 6 hours of presentation)**

- Procedures:**
- 1.) Arterial Catheterization
  - 2.) Central Venous Catheterization (subclavian or internal jugular)
  - 3.) Central Venous Pressure Transducer Set-up

**IV Fluids**  
 Choose One:

- 0.9 NS 500 ml IV over 30 minutes, repeat until central venous pressure (CVP) 8-12 mmHg or 12-15 in mechanically ventilated patients
- Other \_\_\_\_\_

**Vasopressors:** If the mean arterial pressure remains < 65 mmHg despite achieving a CVP of 8-15 mmHg, initiate vasopressor therapy. It may be necessary to employ vasopressors early as an emergency measure in patients with septic shock

- Dopamine 10 mcg/kg/min, titrate to a mean arterial pressure (MAP) of 65-90 mmHg
- Norepinephrine 5 mcg/min, titrate to a mean arterial pressure (MAP) of 65-90 mmHg

**Tissue Perfusion Assessment**

- Obtain central venous oxygen saturation (S<sub>CV</sub>O<sub>2</sub>) q 30 minutes until ≥ 70%
- Continuous central venous oxygen saturation (S<sub>CV</sub>O<sub>2</sub>) monitoring until ≥ 70%

**Transfusion Therapy:** If central venous oxygen saturation is < 70% despite a CVP of 8-15 mmHg and the addition of vasopressors, the patient should be transfused with packed red blood cells to achieve a hematocrit ≥ 30%. Separate order should be written.

**Inotropic Therapy:** If central venous pressure, mean arterial pressure and hematocrit have been optimized, and the central venous oxygen saturation remains < 70%, consider inotropic therapy.

- Dobutamine 2.5 mcg/kg/min, titrate by 2.5 mcg/kg/min to a central venous oxygen saturation (S<sub>CV</sub>O<sub>2</sub>) q 30 minutes until ≥ 70% (max dose 20 mcg/kg/min)



**Are you compliant?**

: \_\_\_\_\_ Telephone #/Pager # \_\_\_\_\_

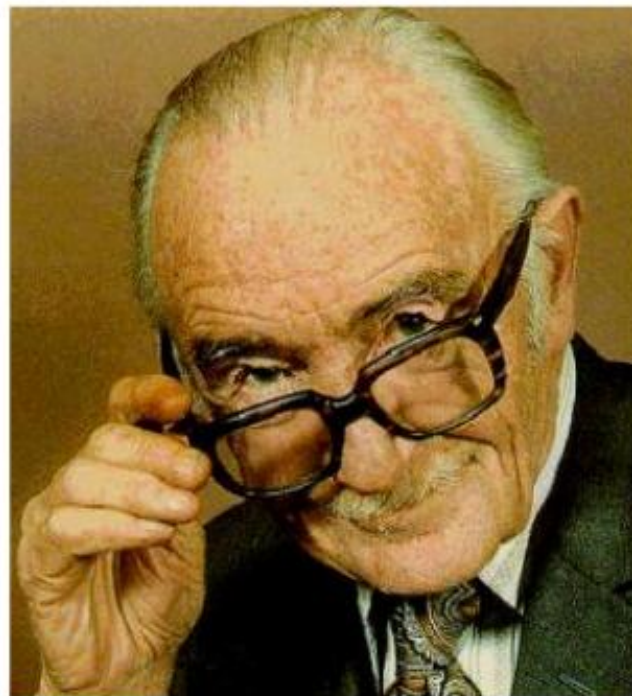
Rawlins MR: De Testimonio.  
Harveian oration 2008, Royal College of Physicians

# Archie Cochrane

*(1908-1988)*

---

"Between measurements based on randomised controlled trials and benefit in the community there is a gulf which has been much under-estimated".





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**Early Goal-Directed Therapy in the  
Treatment of Severe Sepsis and Septic Shock**  
E. Rivers and Others

[Abstract](#) | [FREE Full Text](#) | [PDF](#)



# The top cited clinical research articles on sepsis: a bibliometric analysis

Tao T, et al

*Critical Care* 2012, **16**:R110

Table 1 The top 50 cited clinical trials on sepsis

Ratings	Article	No. of citations
1	Bernard GR, Vincent JL, Laterre P, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, Steingrub JS, Garber GE, Helterbrand JD, Ely EW, Fisher CJ Jr: Efficacy and safety of recombinant human activated protein C for severe sepsis. <i>New England Journal of Medicine</i> 2001, <b>344</b> :699-709.	2932
2	Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M: Early Goal-Directed Therapy C: Early goal-directed therapy in the treatment of severe sepsis and septic shock. <i>New England Journal of Medicine</i> 2001, <b>345</b> :1368-1377.	2538
3	Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR: Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. <i>Critical Care Medicine</i> 2001, <b>29</b> (7):1303-1310.	2158
4	Martin GS, Mannino DM, Eaton S, Moss M: The epidemiology of sepsis in the United States from 1979 through 2000. <i>New England Journal of Medicine</i> 2003, <b>348</b> :1546-1554.	1551

# Severe Sepsis/Septic Shock Bundles

## 24 hours

*Efforts to accomplish these goals should begin immediately, but these items may be completed within 24 hours of presentation for patients with severe sepsis or septic shock.*

1. Administer low-dose steroids for septic shock in accordance with a standardized ICU policy. *If not administered*, document why the patient did not qualify for low-dose steroids based upon the standardized protocol.
2. Administer drotrecogin alfa (activated) in accordance with a standardized ICU policy. *If not administered*, document why the patient did not qualify for drotrecogin alfa (activated).
3. Maintain glucose control  $\geq 70$ , but  $< 150$  mg/dl
4. Maintain a median inspiratory plateau pressure (IPP)\*  $< 30$  cm H<sub>2</sub>O for mechanically ventilated patients



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

Press Release - **25 October 2011**

Xigris (drotrecogin alfa (activated)) to be withdrawn due to lack of efficacy

PROWESS-SHOCK study shows no gain in 28-day survival of septic shock patients

Bernard GR, Vincent J-L, Laterre P-F, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med 2001;344:699-709.

*The NEW ENGLAND JOURNAL of MEDICINE*

N Engl J Med 2012.

## **Septic Shock — Evaluating Another Failed Treatment**

Richard P. Wenzel, M.D., and Michael B. Edmond, M.D., M.P.H.

Bernard GR, Vincent J-L, Laterre P-F, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med 2001;344:699-709.

**The outcomes of the trial were also clouded by..... ethical questions surrounding the sponsor's hiring of a public relations firm to assemble a task force (consisting of many members with conflicts of interest) to promote sepsis-treatment bundles that would include the drug — despite a single positive study and lingering controversies.**





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[Abstract](#) | [FREE Full Text](#) | [PDF](#)



# Glucose in the ICU — Evidence, Guidelines, and Outcomes

Brian P. Kavanagh, M.B., F.R.C.P.C.

*The NEW ENGLAND JOURNAL of MEDICINE*

2012 Sep 7

**Perhaps the most important question from a decade of studying glucose control in the ICU is how influential practice guidelines were developed yet turned out to be harmful.**

# Critical Care Clinical Trials

## Getting Off the Roller Coaster

*Andrew J. Goodwin, MD*

*CHEST 2012; 142(3):563–567*

- Tremendous time and resources have been expended in implementing new protocols that incorporate emerging evidence from the medical literature, only to remove them a few years later when validation trials fail to confirm the initial results.
- The net effects of these “positive-negative” cycles are frustration and, more importantly, exposure of patients to costly treatments that may not be of benefit but, rather, could cause harm.

## Limitations of clinical trials in acute lung injury and acute respiratory distress syndrome

John J. Marini

Current Opinion in Critical Care 2006, 12:25–31

## Evidence should not be viewed in isolation

Rui Moreno, MD, PhD; Andrew Rhodes, FRCP, FRCA

Crit Care Med 2010 Vol. 38, No. 10 (Suppl.)

## We should abandon randomized controlled trials in the intensive care unit

Jean-Louis Vincent, MD, PhD, FCCM

The randomized controlled trial is seen by many as the summit of evidence-based medicine, yet, in the intensive care unit, randomized controlled trials can be challenging to conduct, and results are often difficult to interpret and apply. Many randomized controlled trials in intensive care patients have not demonstrated beneficial effects of the intervention under investigation often despite good preclinical and even previous randomized controlled

trial evidence. There are many reasons for these negative results including problems with timing, end point selection, and heterogeneous populations. In this article, we will discuss the limitations of randomized controlled trials in the intensive care unit population and highlight the importance of considering other study designs in the challenging intensive care unit environment. (Crit Care Med 2010; 38[Suppl.]:S534–S538)

# Evidence-Based Medicine

## A New Approach to Teaching the Practice of Medicine

Evidence-Based Medicine Working Group

JAMA, November 4, 1992—Vol 268, No. 17

A NEW paradigm for medical practice is emerging. Evidence-based medicine **de-emphasizes** intuition, unsystematic clinical experience, and **pathophysiologic rationale** as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research. Evidence-based medicine requires new skills of the physician, including efficient literature searching and the application of formal rules of evidence evaluating the clinical literature.

# **The Role of a Journal in a Scientific Controversy**

MARTIN J. TOBIN

*Editor*

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 168 2003

- **The developers of EBM wrote that “EBM deemphasizes reasoning based on pathophysiologic rationale”.**
- **As such, we are talking about a practice of medicine divorced from the scientific principles that are its foundation.**

# **An Official Multi-Society Statement: The Role of Clinical Research Results in the Practice of Critical Care Medicine**

THIS OFFICIAL STATEMENT OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS (ACCP), THE AMERICAN THORACIC SOCIETY (ATS), AND THE SOCIETY OF CRITICAL CARE MEDICINE (SCCM) WAS APPROVED BY THE ACCP BOARD OF REGENTS, JUNE 2011, BY THE ATS BOARD OF DIRECTORS, NOVEMBER 2011, AND BY THE SCCM COUNCIL, SEPTEMBER 2011

**Am J Respir Crit Care Med Vol 185, Iss. 10, pp 1117–1124, May 15, 2012**

- The results of clinical research, pathophysiologic reasoning, and clinical experience represent different kinds of medical knowledge crucial for effective clinical decision making.

# **Surviving Sepsis Campaign:**

**Requirements for fluid infusion are not easily determined so that repeated fluid challenges should be performed.**



# Surviving Sepsis Campaign:

Requirements for fluid infusion are not easily determined so that repeated fluid challenges should be performed.

Rivers et al NEJM 2001

TREATMENT	HOURS AFTER THE START OF THERAPY		
	0-6	7-72	0-72
Total fluids (ml)			
Standard therapy	3499 ± 2138	10,602 ± 6,216	13,358 ± 7,729
EGDT	4981 ± 2984	8,625 ± 5,162	13,443 ± 6,390
P value	<0.001	0.01	0.73

Australasian resuscitation of sepsis evaluation (ARISE): A multi-centre, prospective, inception cohort study<sup>☆</sup>

Resuscitation 80 (2009) 811-818

Sandra L. Peake<sup>a,b,\*</sup>, Michael Bailey<sup>c</sup>, Rinaldo Bellomo<sup>d,e,f</sup>, Peter A. Cameron<sup>g</sup>, Anthony Cross<sup>h</sup>, Anthony Delaney<sup>i,j</sup>, Simon Finfer<sup>k,l,m</sup>, Alisa Higgins<sup>c</sup>, Daryl A. Jones<sup>c</sup>, John A. Myburgh<sup>l,n,o</sup>, Gillian A. Syres<sup>c</sup>, Steven A.R. Webb<sup>p,q</sup>, Patricia Williams<sup>b</sup>, the ARISE Investigators, for the Australian and New Zealand Intensive Care Society Clinical Trials Group

ED to 0 h <sup>a</sup>	0-6 h	6-72 h
1224 (1224)	2218 (1887)	4914 (3533)

**Rivers et al NEJM 2001**

TREATMENT	HOURS AFTER THE START OF THERAPY		
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Total fluids (ml)			
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EGDT	4981 ± 2984	8,625 ± 5,162	13,443 ± 6,390
P value	<0.001	0.01	0.73

# Fluid Therapy in Resuscitated Sepsis

Less Is More

(*CHEST* 2008; 133:252–263)

Lakshmi Durairaj, MD; and Gregory A. Schmidt, MD, FCCP

Table 1—Studies of Fluid Responsiveness in Septic Patients\*

Study	Fluid Challenges, No.	Responders, %	Test Used
Tavernier et al, <sup>33</sup> 1998	35	60	dDown (SPV)
Sakka et al, <sup>35</sup> 1999	57	46	ITBVI
Michard et al, <sup>32</sup> 2000	40	40	PPV
Feissel et al, <sup>34</sup> 2001	19	53	$\Delta V_{\text{peak}}$
Michard et al, <sup>36</sup> 2003	66	48	GEDVI
Feissel et al, <sup>37</sup> 2004	39	41	$\Delta IVC$
Vieillard-Baron et al, <sup>39</sup> 2004	66	30	SVC collapsibility
Barbier et al, <sup>40</sup> 2004	20	50	$\Delta IVC$
Perner and Faber, <sup>41</sup> 2006	30	47	SVV
Feissel et al, <sup>38</sup> 2007	28	64	$\Delta P_{\text{plet}}$
Osman et al, <sup>31</sup> 2007	150	43	CVP/PAOP

**More than 50% of septic patients in which fluid administration was “clinically indicated” are being loaded with fluids unnecessarily!**

**High tidal volume and positive fluid balance are associated with worse outcome in ALI**

**Sakr Y and the SOAP Investigators. Chest 2005; 128: 3098-108**

**Sepsis in European intensive care units:  
results of the SOAP study.**

**Vincent JL, et al; Sepsis Occurrence in Acutely Ill Patients Investigators.  
Crit Care Med. 2006 Feb;34(2):344-53**

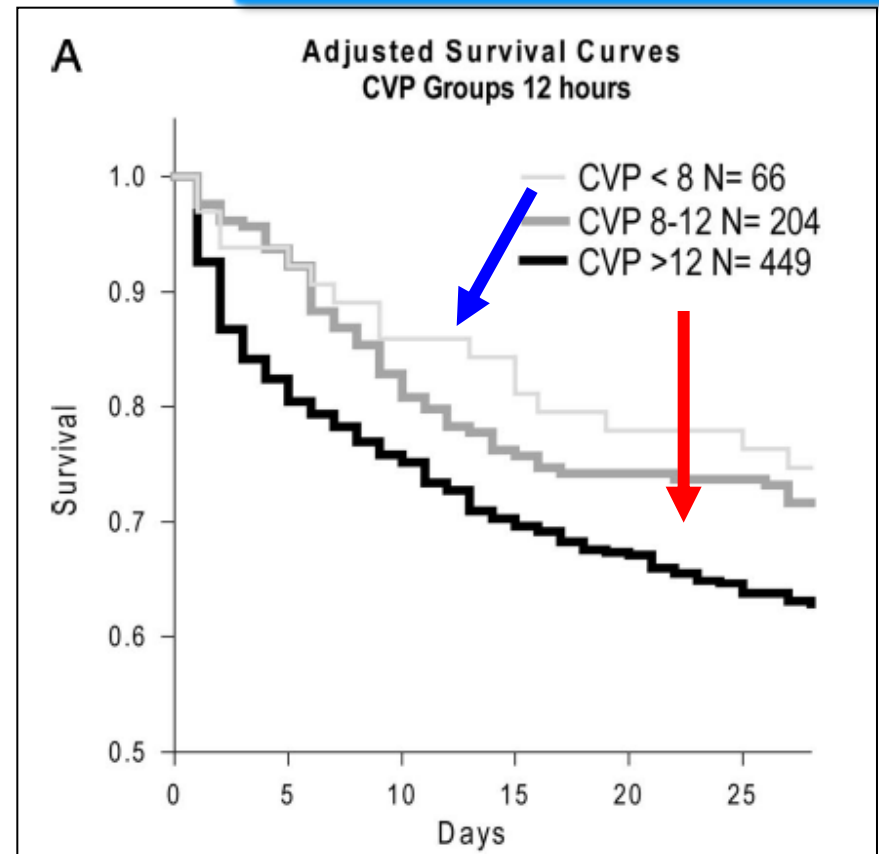
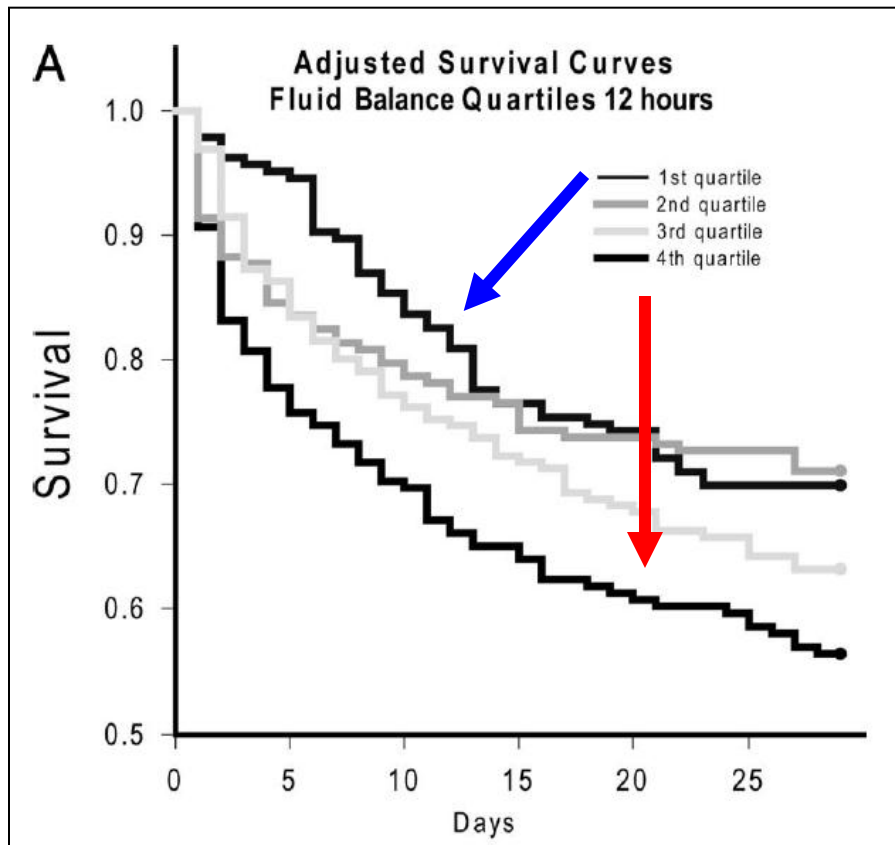
- **A positive fluid balance is associated with a worse outcome.**
- **A threshold may exist beyond which, after acute resuscitation, additional fluid therapy may cause harm.**

# Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality

**Crit Care Med 2011; 39:259-65**

John H. Boyd, MD, FRCP(C); Jason Forbes, MD; Taka-aki Nakada, MD, PhD; Keith R. Walley, MD, FRCP(C); James A. Russell, MD, FRCP(C)

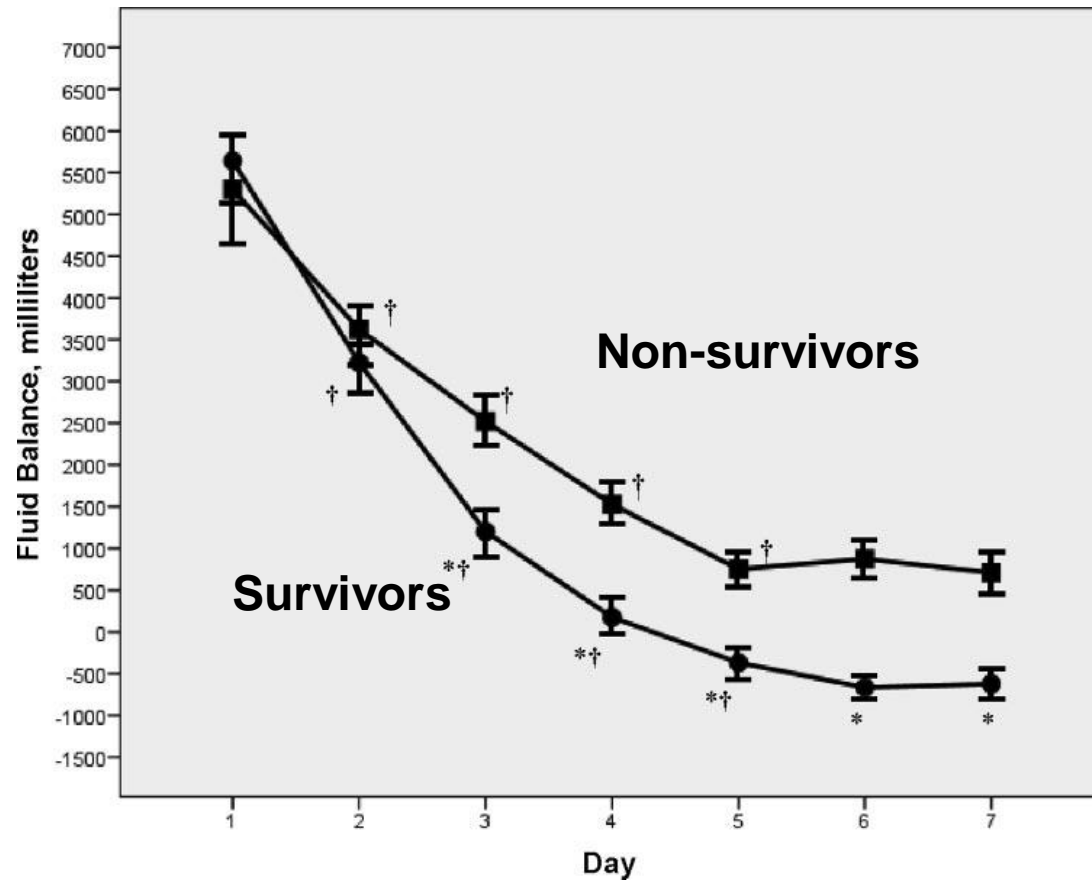
778 septic shock pts from the VASST study



# The Importance of Fluid Management in Acute Lung Injury Secondary to Septic Shock

(*CHEST* 2009; 136:102–109)

*Claire V. Murphy, PharmD; Garrett E. Schramm, PharmD;  
Joshua A. Doherty, BS; Richard M. Reichley, RPh; Ognjen Gajic, MD, FCCP;  
Bekele Afessa, MD, FCCP; Scott T. Micek, PharmD; and  
Marin H. Kollef, MD, FCCP*



**Both early and late fluid management of septic shock complicated by ALI can influence patient outcomes.**

# **Fluid balance as a biomarker: impact of fluid overload on outcome in critically ill patients with acute kidney injury**

Sean M Bagshaw<sup>1</sup>, Patrick D Brophy<sup>2</sup>, Dinna Cruz<sup>3</sup> and Claudio Ronco<sup>3</sup>

*Critical Care* 2008, 12:169

*The NEW ENGLAND JOURNAL of MEDICINE*

## **Fluid Resuscitation in Acute Illness — Time to Reappraise the Basics**

John A. Myburgh, M.B., B.Ch., Ph.D.

May 26, 2011

## **A critique of fluid bolus resuscitation in severe sepsis**

Andrew K Hilton<sup>1</sup> and Rinaldo Bellomo<sup>2\*</sup>

*Critical Care* 2012, 16:302

**Practice parameters for hemodynamic support of sepsis  
in adult patients. 2004 update.**

**Hollenberg S et al. Crit Care Med 2004; 32:1928-48**

**Pulmonary edema may occur as a  
complication of fluid resuscitation  
and necessitates monitoring of  
arterial oxygenation.**



The Surviving Sepsis guidelines:  
evidence-based ... or evidence-biased?

Singer M, Critical Care and Resuscitation 2006, 8:244-5

**Would it be more sensible to give guidelines as to when to use more sophisticated hemodynamic monitoring to better titrate fluid input, rather than react post-drowning?**



**Surviving Sepsis Campaign: International  
Guidelines for Management of Severe Sepsis  
and Septic Shock: 2012** February 2013 • Volume 41 • Number 2

- **Targeting dynamic measures of fluid responsiveness during resuscitation, including flow (CO) and possibly volumetric indices and microcirculatory changes, may have advantages.**

Vasopressor and inotropic support in septic shock: An evidence-based review

(Crit Care Med 2004; 32[Suppl.]:S455–S465)

Richard J. Beale, MBBS; Steven M. Hollenberg, MD, FCCM; Jean-Louis Vincent, MD, PhD, FCCM; Joseph E. Parrillo, MD, FCCM

**Because of the complexity of assessment of clinical variables in septic patients, direct measurement of cardiac output is advisable.**



**Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012** February 2013 • Volume 41 • Number 2

- Targeting dynamic measures of fluid responsiveness during resuscitation, including flow (CO) and possibly volumetric indices and microcirculatory changes, may have advantages.
- However, the efficacy of these monitoring techniques to influence clinical outcomes from early sepsis resuscitation remains incomplete and requires further study before endorsement.

# **The Importance of Fluid Management in Acute Lung Injury Secondary to Septic Shock**

*(CHEST 2009; 136:102–109)*

*Claire V. Murphy, PharmD; Garrett E. Schramm, PharmD;  
Joshua A. Doherty, BS; Richard M. Reichley, RPh; Ognjen Gajic, MD, FCCP;  
Bekele Afessa, MD, FCCP; Scott T. Micek, PharmD; and  
Marin H. Kollef, MD, FCCP*

- **Recent studies have suggested that both early goal-directed resuscitation of patients with septic shock (based on aggressive fluid resuscitation) and conservative fluid management of patients with acute lung injury (ALI) can improve outcomes.**
- **These may be seen as potentially conflicting practices.**

**Bench-to-bedside review: The initial hemodynamic resuscitation of the septic patient according to Surviving Sepsis Campaign guidelines – does one size fit all?**

Azriel Perel

*Critical Care* 2008, 12:223

- **Fluid resuscitation in severe sepsis should always be perceived as a therapeutic conflict.**
- **A therapeutic conflict is a situation where each of the possible therapeutic decisions carries some potential harm.**
- **Therapeutic conflicts (e.g., heart vs. lung) are the biggest challenge for protocolized care in critically ill patients.**

**YES**

**We need to  
stabilize the  
hemodynamic  
status**



**NO**

**We need to  
prevent  
respiratory  
deterioration**

**The conflict in administering fluids  
to a patient with sepsis and ARDS**

# Clinical review: Update on hemodynamic monitoring - a consensus of 16

Jean-Louis Vincent<sup>1\*</sup>, Andrew Rhodes<sup>2</sup>, Azriel Perel<sup>3</sup>, Greg S Martin<sup>4</sup>, Giorgio Della Rocca<sup>5</sup>, Benoit Vallet<sup>6</sup>, Michael R Pinsky<sup>7</sup>, Christoph K Hofer<sup>8</sup>, Jean-Louis Teboul<sup>9</sup>, Willem-Pieter de Boode<sup>10</sup>, Sabino Scolletta<sup>11</sup>, Antoine Vieillard-Baron<sup>12</sup>, Daniel De Backer<sup>1</sup>, Keith R Walley<sup>13</sup>, Marco Maggiorini<sup>14</sup> and Mervyn Singer<sup>15</sup>

*Critical Care* 2011, 15:229

## **Principle 4: we need to combine and integrate variables**

Any variable on its own provides relatively little information - it is just one piece of a large puzzle. We need rather to integrate all the available data from multiple sources.



**Clinical examination, vital signs, urine output, Hb, lactate...**

**Preload &  
Fluid responsiveness**

**EVLW**

**Cardiac Output**

**ScvO<sub>2</sub>**

**An old patient with chronic heart failure, sepsis, severe respiratory failure and hemodynamic instability.**

<b>CO</b>	<b>1.8 l/min</b>	<b>Low</b>
<b>ITBVi</b>	<b>600 ml/m<sup>2</sup></b>	<b>Low</b>
<b>EVLWi</b>	<b>15 ml/kg</b>	<b>High</b>
<b>SVV</b>	<b>25-30%</b>	<b>High</b>

## Question: What would you do now?

- A. Fluids
- B. Inotropes
- C. Vasopressors
- D. Diuretics
- E. I need more information

<b>CO</b>	<b>1.8 l/min</b>
<b>ITBVi</b>	<b>600 ml/m<sup>2</sup></b>
<b>EVLWi</b>	<b>15 ml/kg</b>
<b>SVV</b>	<b>25-30%</b>

## Question 4: What would you do now?

22% Fluids

A horizontal bar chart with a dark blue background. The bars are dark red. The categories and their percentages are: Fluids (22%), Inotropes (48%), Vasopressors (7%), Diuretics (6%), I need more information (16%), and Wrong answer (1%).

48% Inotropes

7% Vasopressors

6% Diuretics

16% I need more information

1% Wrong answer

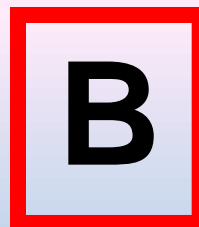
CO	1.8 l/min
ITBVi	600 ml/m <sup>2</sup>
EVLWi	15 ml/kg
SVV	25-30%

**RIGHT**

**WRONG**

**WRONG**

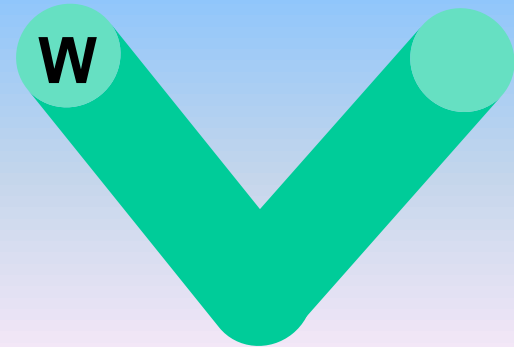
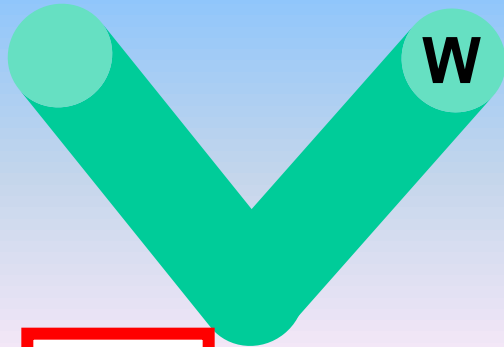
**RIGHT**



**Persistent  
tissue  
hypoperfusion**

**W**

**Worsening of  
pulmonary  
edema**

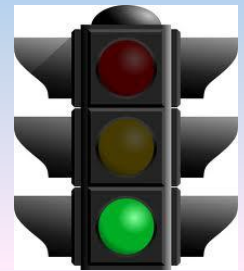
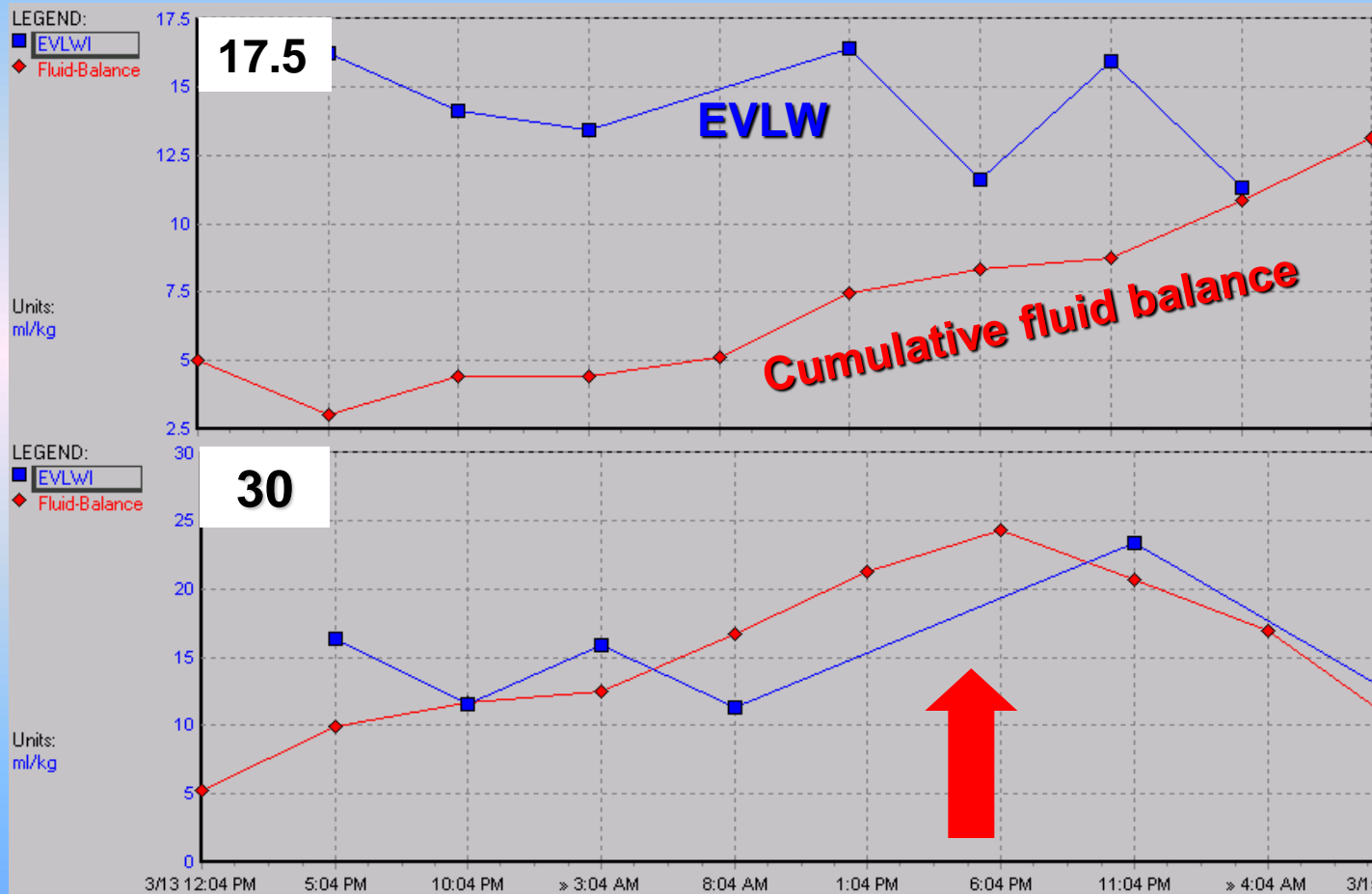


**Inotropes**

**Fluids**



# Cumulative fluid balance and EVLW during the resuscitation of a septic patient with chronic heart failure



## Conclusions:

- Rivers et al have started a most important process in modern intensive care medicine, and the SSC is saving lives as we speak.
- **And yet**, the physiological variables used in the SSC Guidelines to direct the initial hemodynamic resuscitation are not suitable for all septic patients and may be misleading in many instances.
- Attempts to protocolize care in critically ill patients have to leave room for clinical judgment especially during therapeutic conflicts.
- More comprehensive hemodynamic monitoring approaches may improve care in severe sepsis and septic shock.