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

Azriel Perel

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Department of Anesthesiology and Intensive Care
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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.

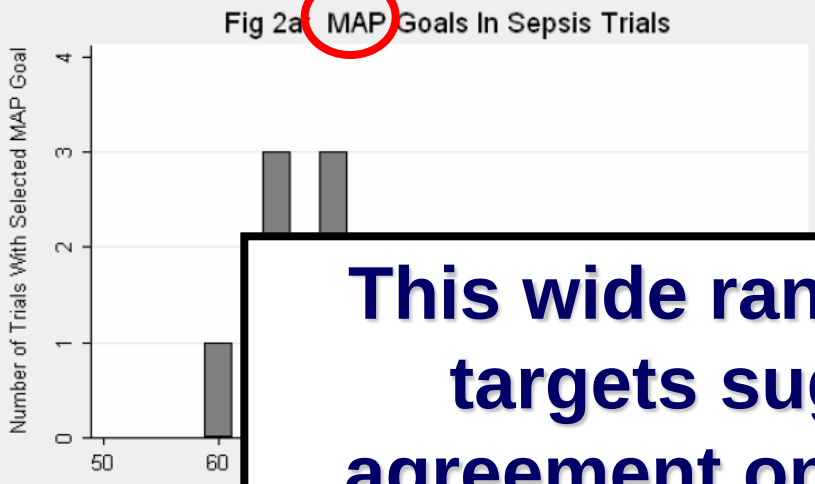
Practice parameters for hemodynamic support of sepsis in adult patients. 2004 update.

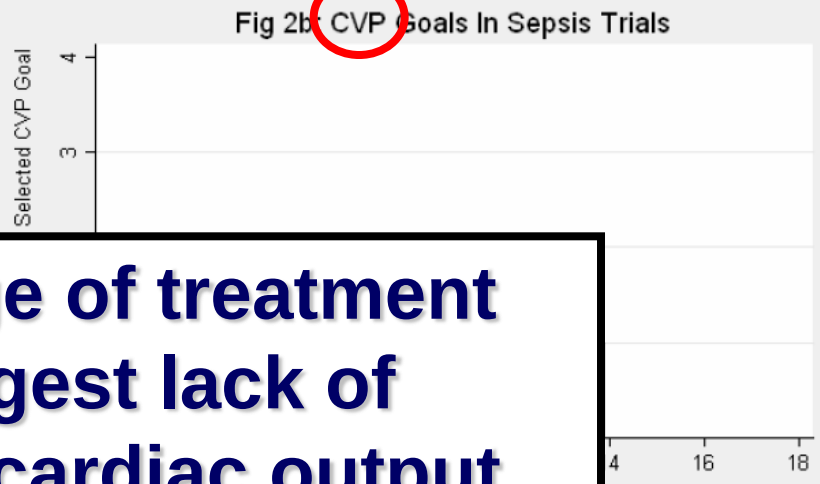
Hollenberg S et al. Crit Care Med 2004; 32:1928-48

"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."

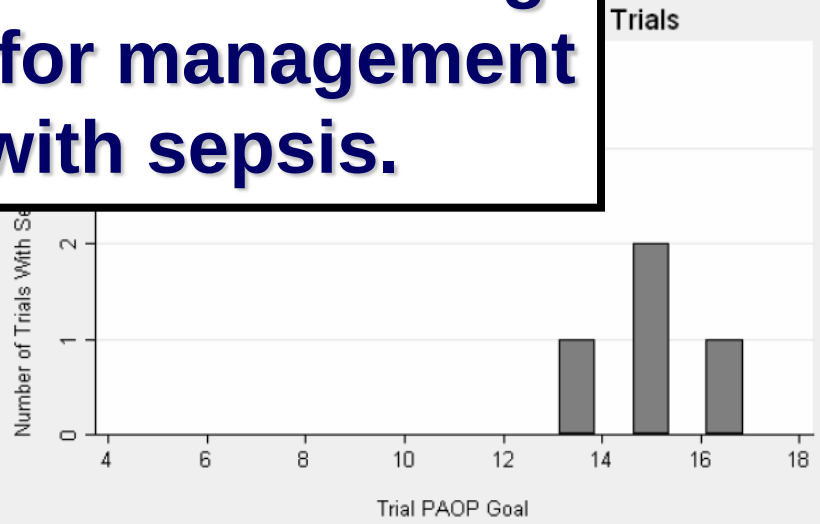
Hemodynamic goals in randomized clinical trials in patients with sepsis: a systematic review of the literature

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





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.



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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.

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Critical Care Congress

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

February 2013 • Volume 41 • Number 2

The NEW ENGLAND JOURNAL of MEDICINE

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

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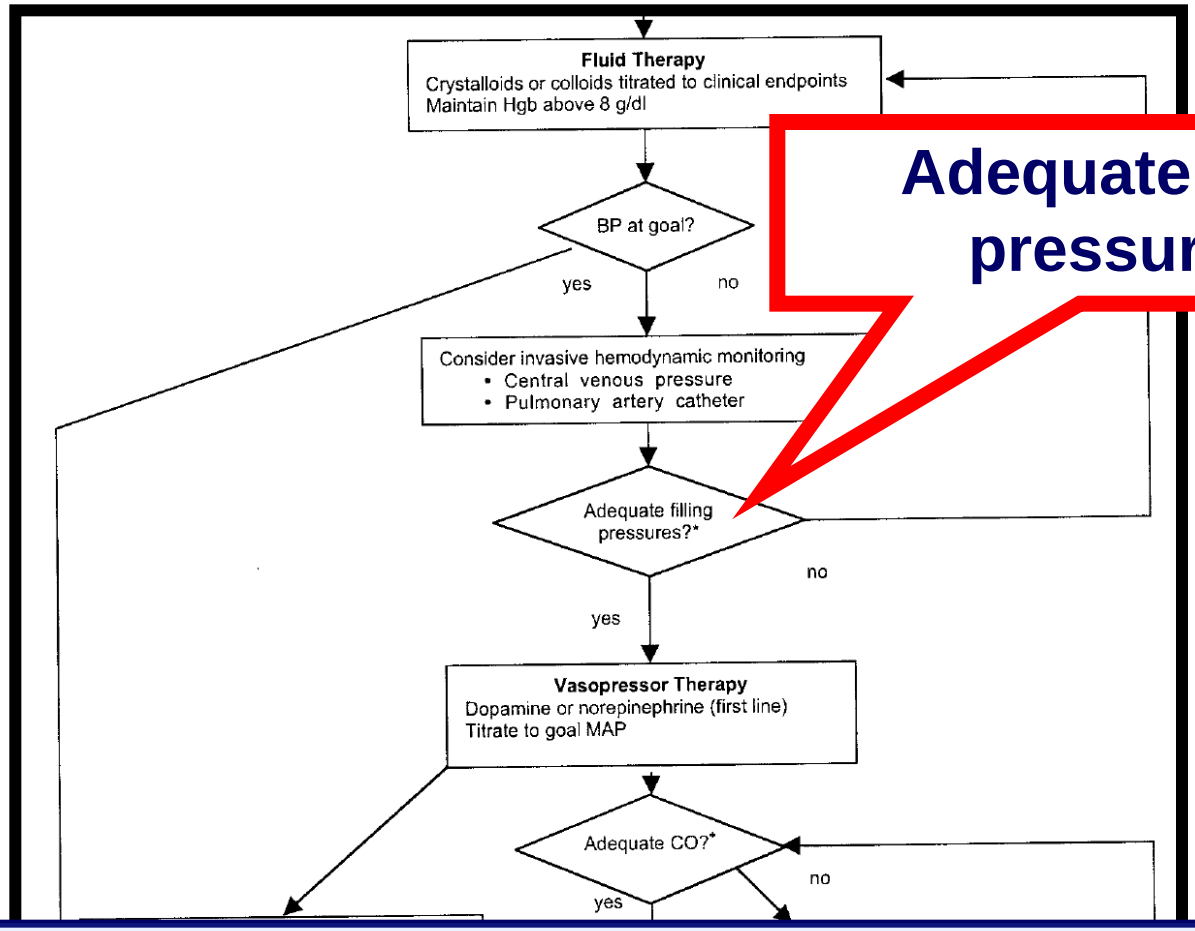
February 2013 • Volume 41 • Number 2

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) ≥ 65 mm Hg
Urine output ≥ 0.5 $mL.kg^{-1}.hr^{-1}$
Central venous (superior vena cava) or mixed venous oxygen saturation ≥ 70% or ≥ 65%, respectively

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

February 2013 • Volume 41 • Number 2

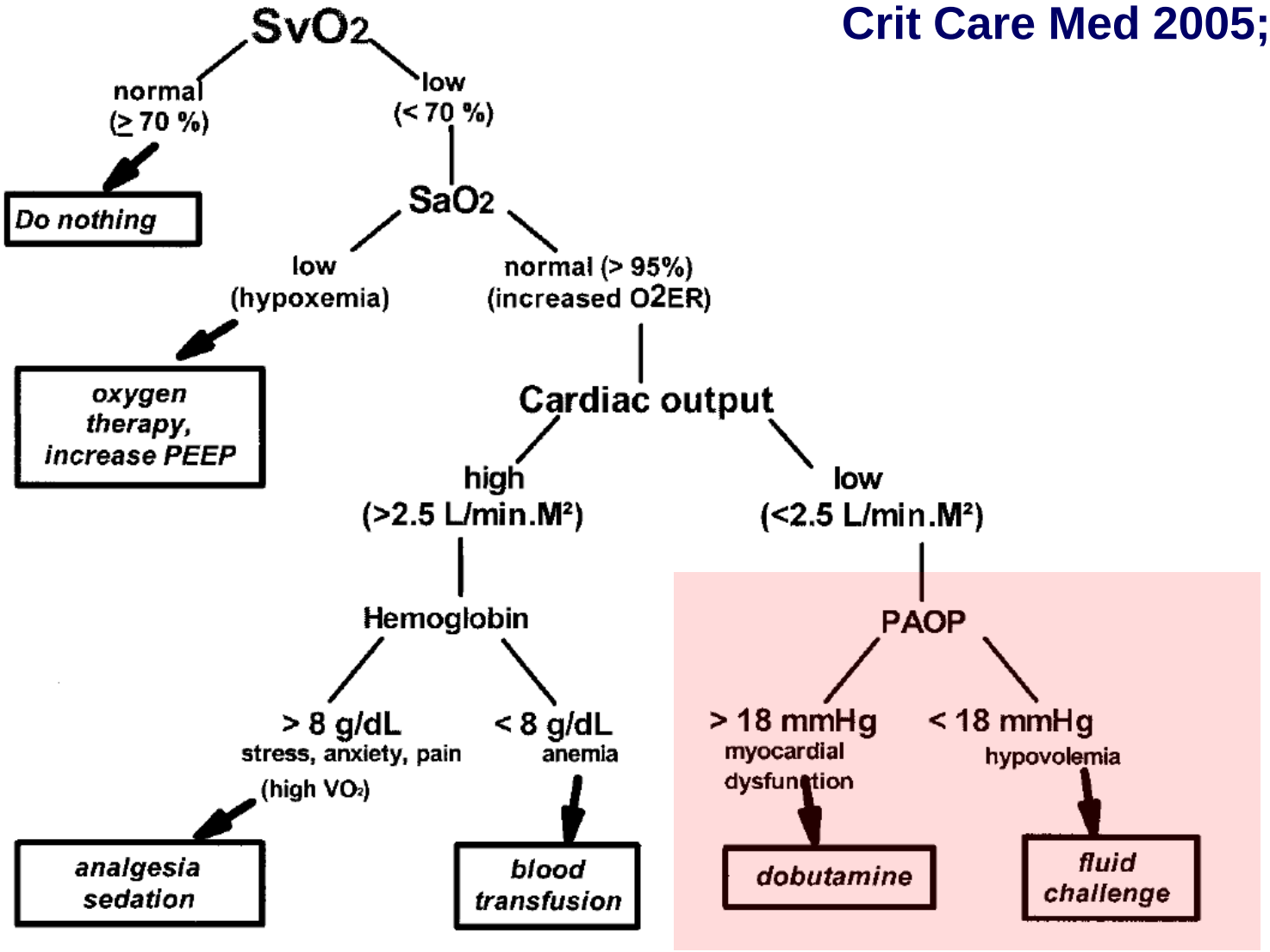
During the first 6 hrs of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as a part of a treatment protocol (grade 1C):

a) CVP 8–12 mm Hg
b) MAP ≥ 65 mm Hg
c) Urine output ≥ 0.5 mL·kg·hr
d) Superior vena cava oxygenation saturation ($Scvo_2$) or mixed venous oxygen saturation (Svo_2) 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 hemodynam… port of sepsis in adults patients. 20…

Hollenberg et al. Crit Care Me… 48

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Surviving Sepsis … ternational Guidelines for M… of Severe Sepsis and Septic S…

…ebruary 2013 • Volume 41 • Number 2

Let us use … rtery 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

166 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 ≥15 mm Hg. Four patients had only 2 data points (WP ≥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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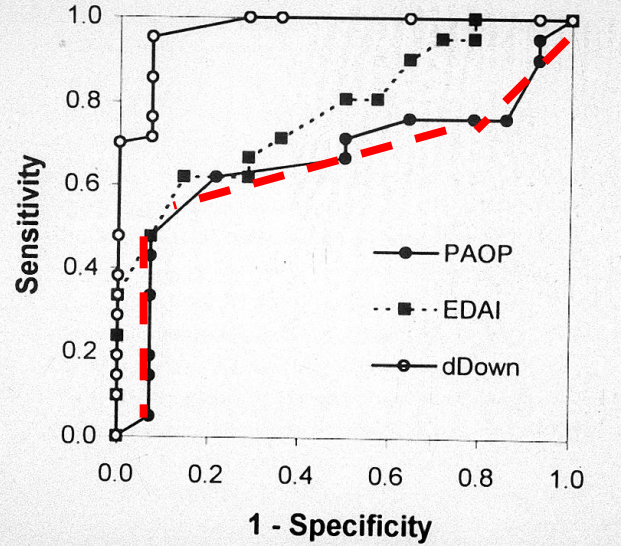
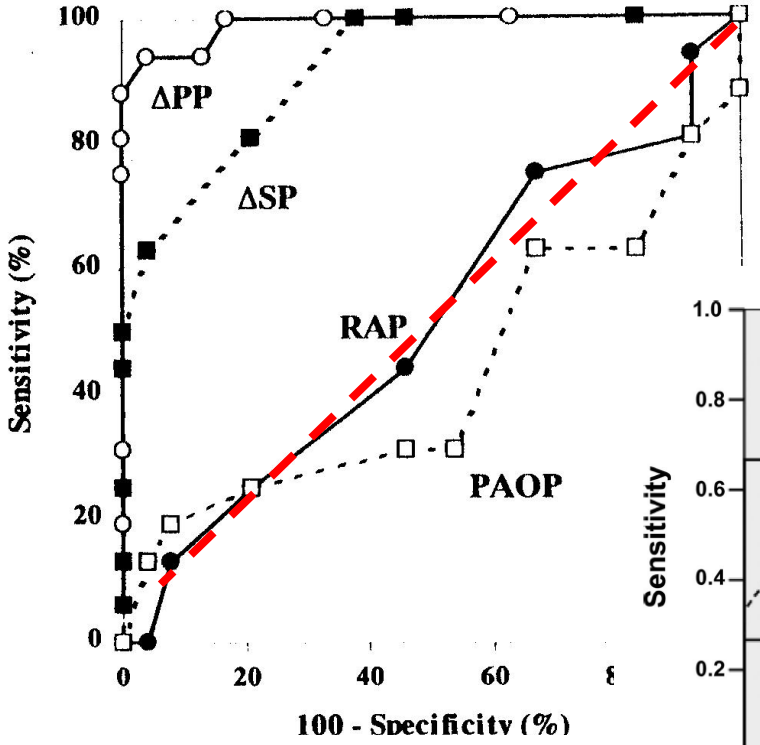
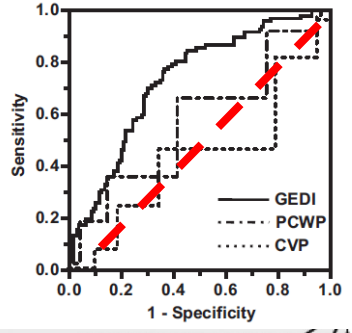
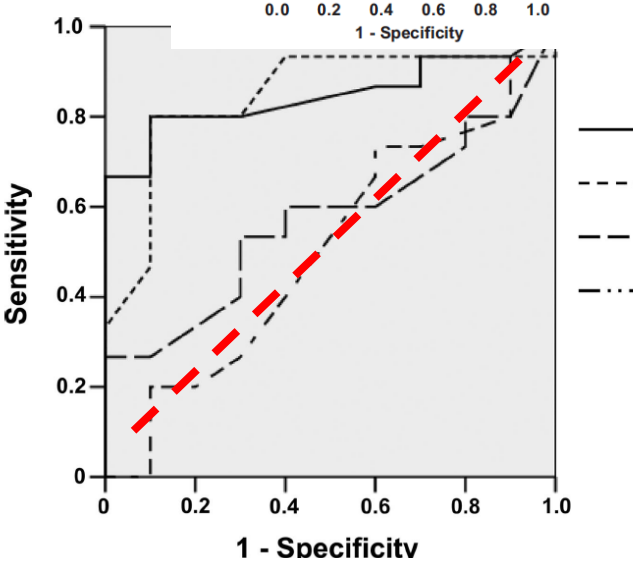
Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012 February 2013 • Volume 41 • Number 2

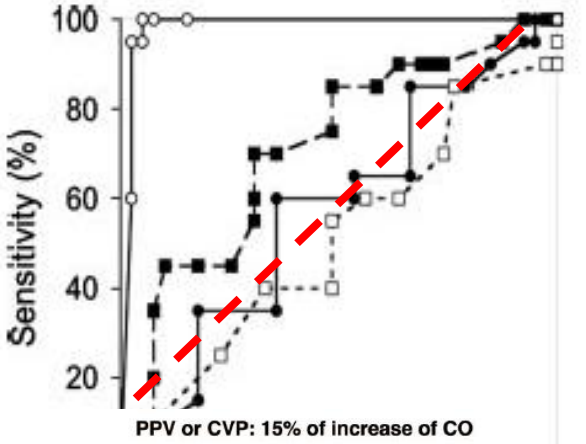
"Although there are limitations to CVP as a marker of intravascular volume status and response to fluids, a low CVP generally can be relied upon as supporting positive response to fluid loading."

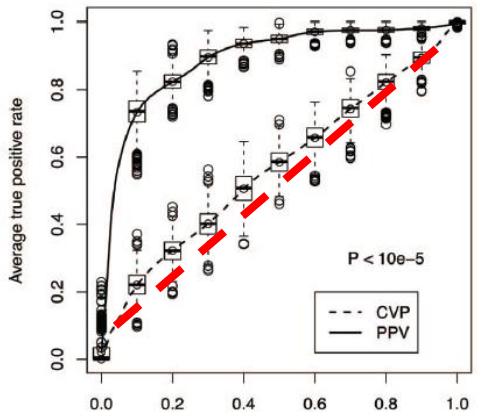


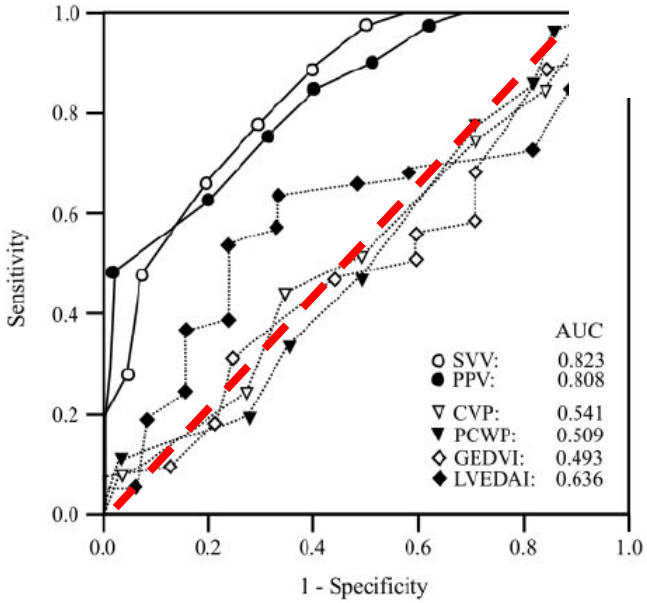












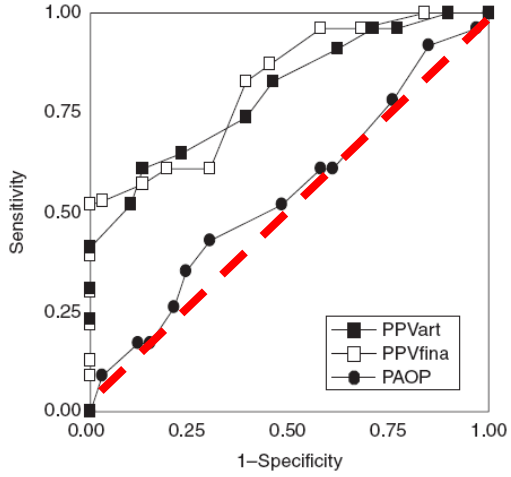


FIGURE 2. Prediction of fluid responsiveness: Areas under the

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

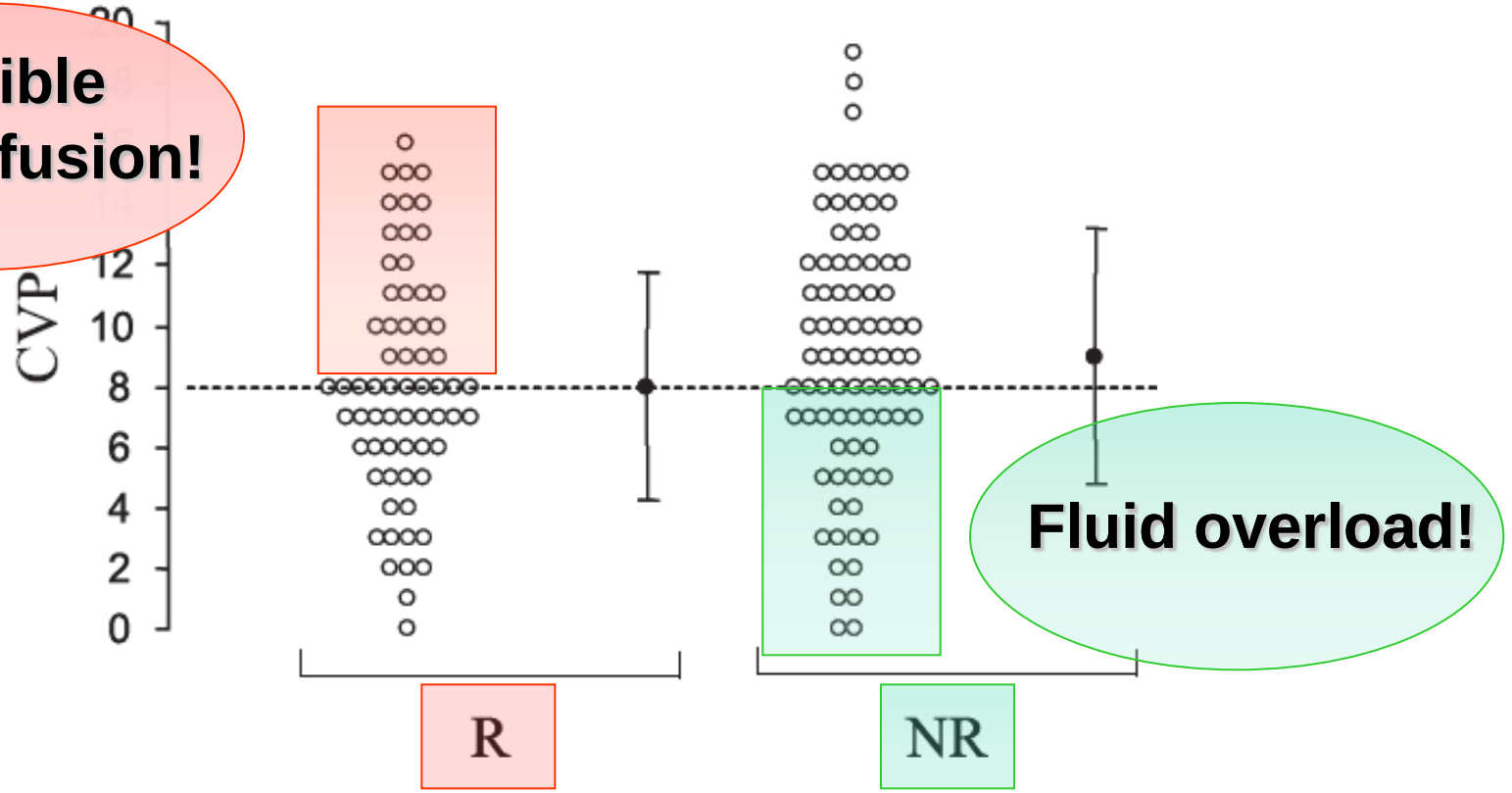
Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge*

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

Possible hypoperfusion!



Fluid overload!

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 ≥ 65 mm Hg*
- *Urine output ≥ 0.5 mL.kg-1.hr-1*
- *Central venous or mixed venous oxygen saturation ≥ 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 ≥ 30% and/or administer a dobutamine infusion of up to a maximum of 20 µg.kg-1.min-1.

BP	70/40 mmHg
HR	155 bpm
CVP	5 cmH_2O
PaO_2/FiO_2	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."

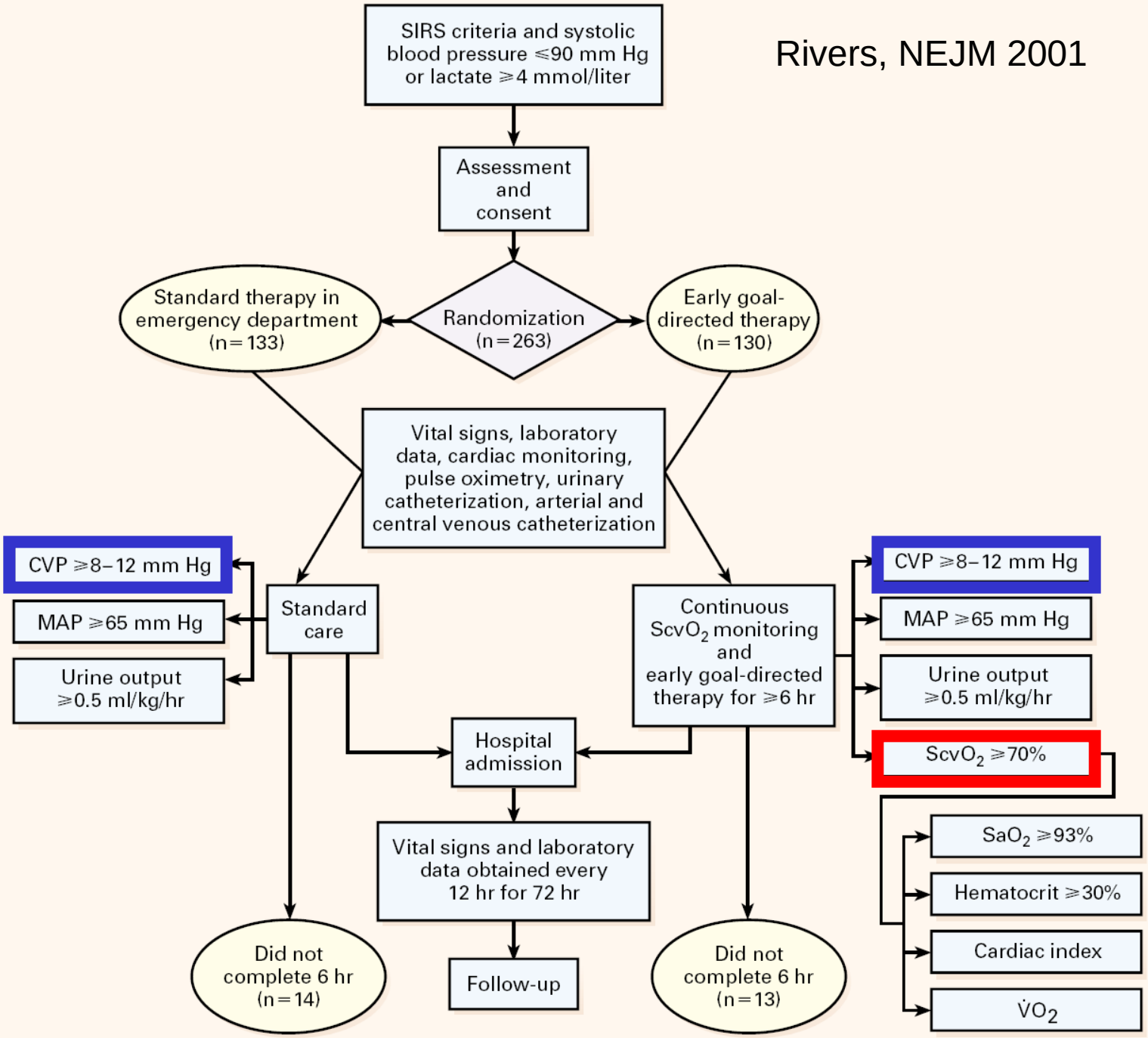
Does Central Venous Pressure Predict Fluid Responsiveness?*

(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."

Rivers, NEJM 2001



Surviving Sepsis Campaign Guidelines

Dellinger RP, et al. Crit Care Med 2004;32:858-73
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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_2 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

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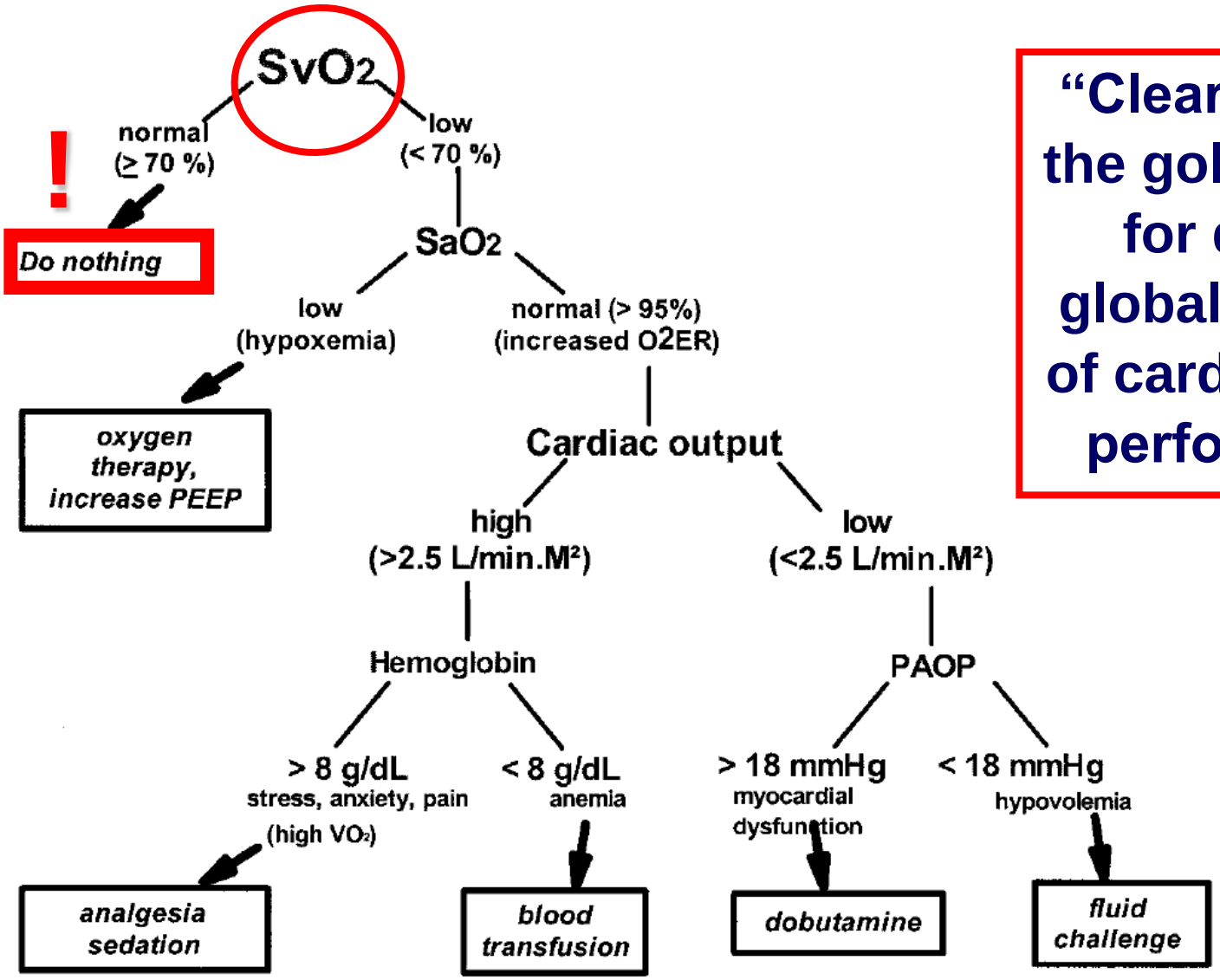
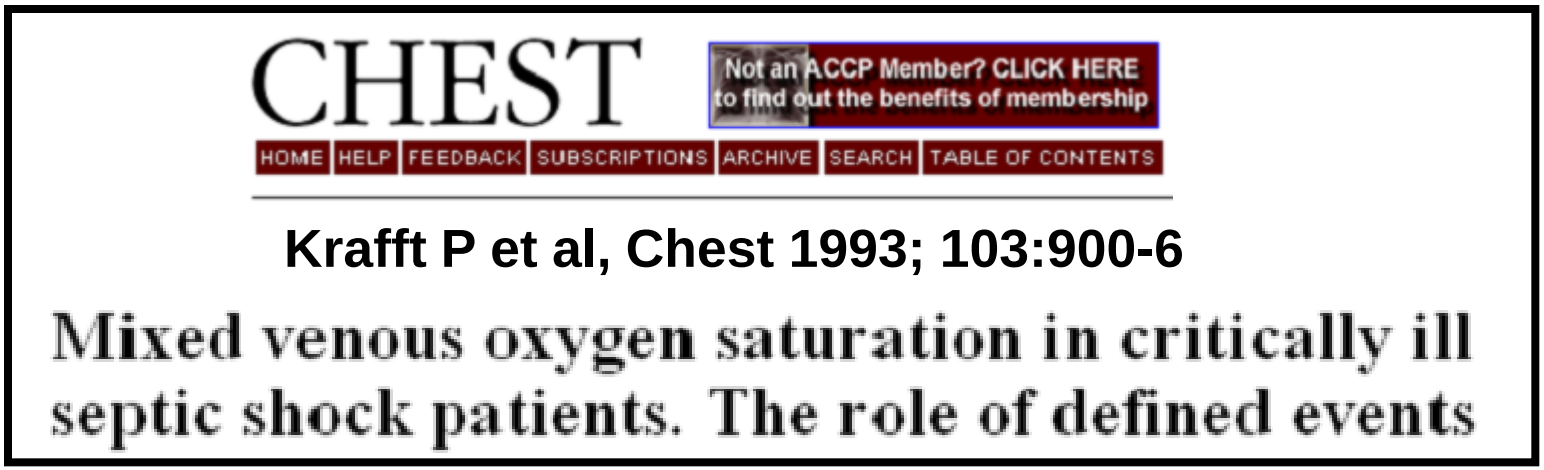


"Clearly, SvO_2 is the gold standard for defining global adequacy of cardiovascular performance."

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 $ScvO_2$ is ~70%

Rivers et al NEJM 2001



- A high incidence of short-term SvO_2 changes in a septic shock patient may be of diagnostic and prognostic significance.
- The SvO_2 of septic shock patients is mainly normal or even supra-normal.

$$\dot{O}_2ER \cong 1 - S_{\bar{v}}O_2$$

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

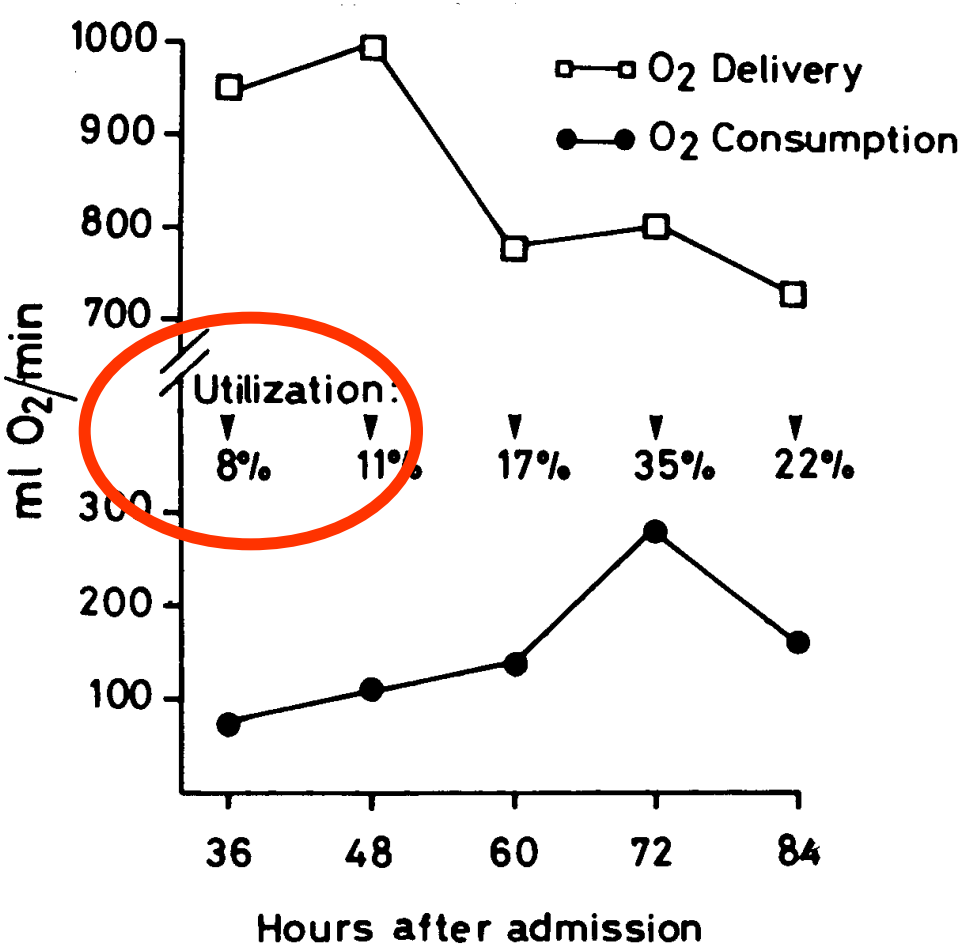
Decreased oxygen utilization in epidemic typhus infection: case report with sequential hemodynamic studies.

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

Hadassah University Hospital, Jerusalem, Israel.

$SvO_2 \sim 1\text{-}O_2ER$

$SvO_2 \sim 92\%$



The mean initial $ScvO_2$ 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 $ScvO_2$ 72 ± 11%

Multicenter Study of Central Venous Oxygen Saturation ($ScvO_2$) 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 $ScvO_2$ 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[1,2], JJ Hofstra[3], MJ Schultz[3,4], EC Boerma[1], PE Spronk[3,4,5] and MA Kuiper[1,3,4]

Critical Care 2008, **12**:R33

Initial $ScvO_2$ 74 ± 10%

Early Lactate-Guided Therapy in Intensive Care Unit Patients

A Multicenter, Open-Label, Randomized Controlled Trial

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

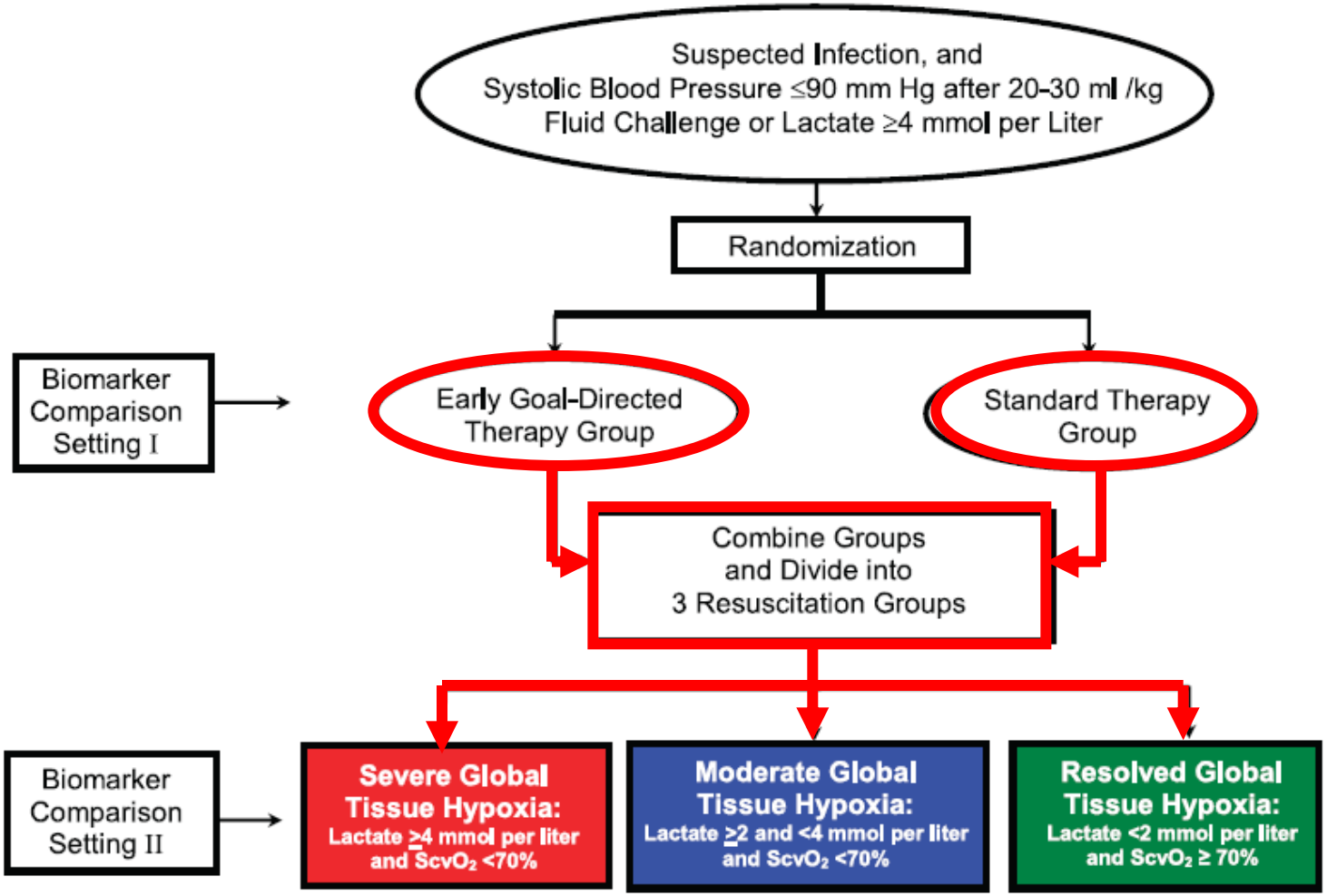
Am J Respir Crit Care Med Vol 182. pp 752–761, 2010

Initial $ScvO_2$ 73 ± 11%

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

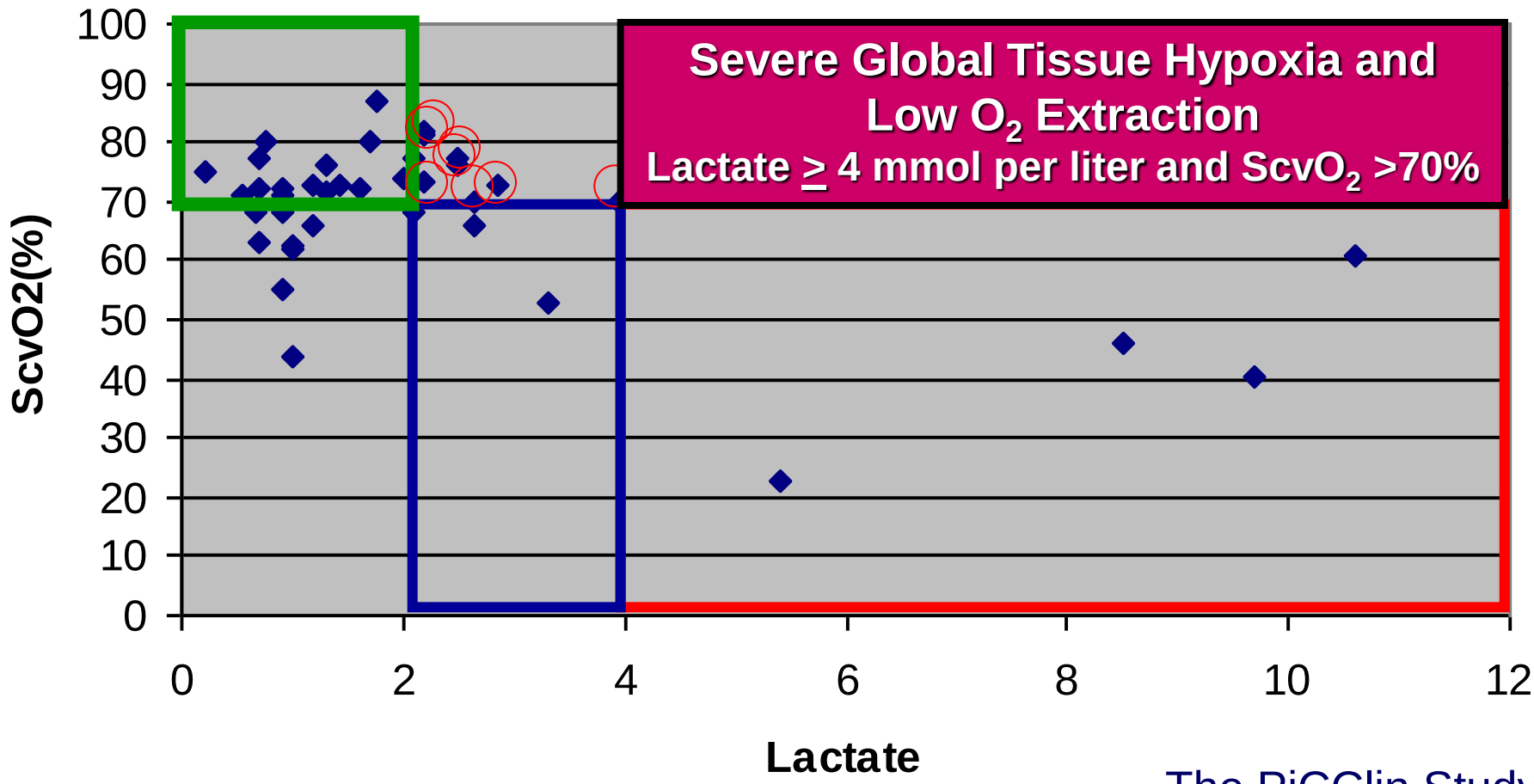
CCM 2007

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.

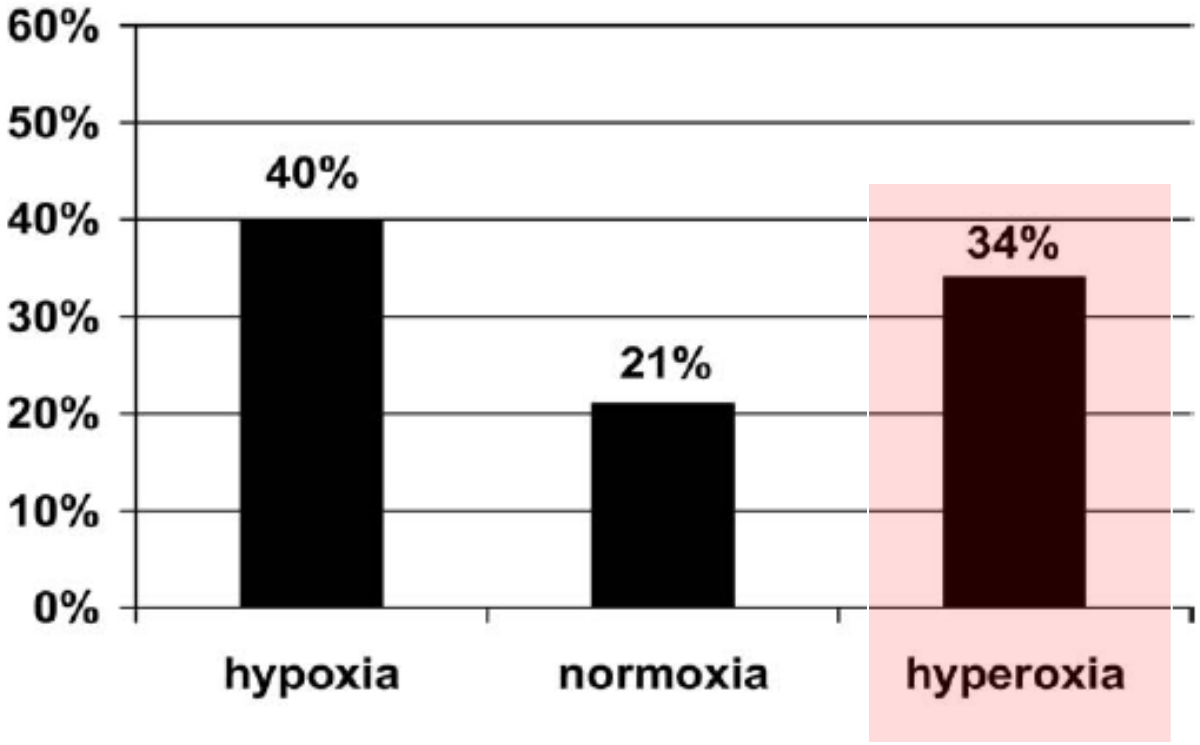


The PiCClin Study

Multicenter Study of Central Venous Oxygen Saturation ($ScvO_2$) 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

WSJ.com THE WALL STREET JOURNAL. ONLINE

August 14, 2008

PAGE ONE

New Therapy for Sepsis Infectio
Raises Hope but Many Question

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

Editorial

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

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

Paul E. Marik MD[a,*], Joseph Varon MD[b] American Journal of Emergency Medicine (2009)

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 30.8% 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.**

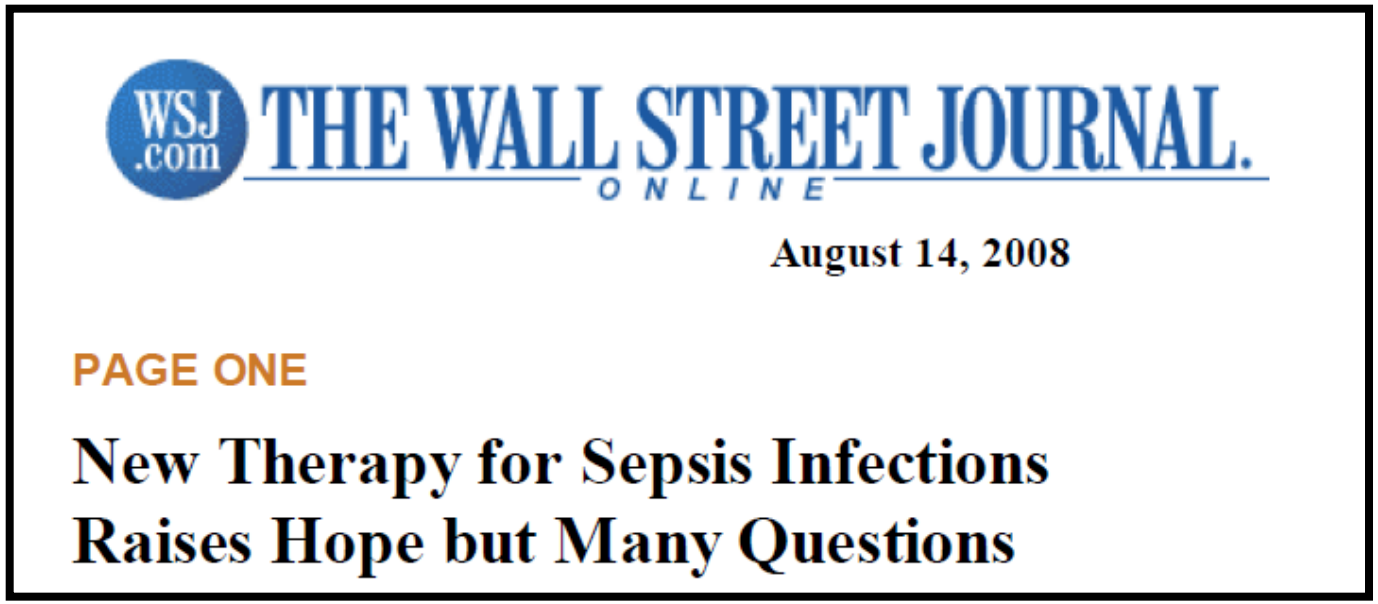
- **The Rivers study was done in the Department of Emergency Medicine which serves "metro Detroit's largely poor, largely minority population, having poor health status and high chronic disease incidence"**
  Ann Emerg Med Dec. 2008

- **"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

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.



WSJ.com THE WALL STREET JOURNAL. ONLINE

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?

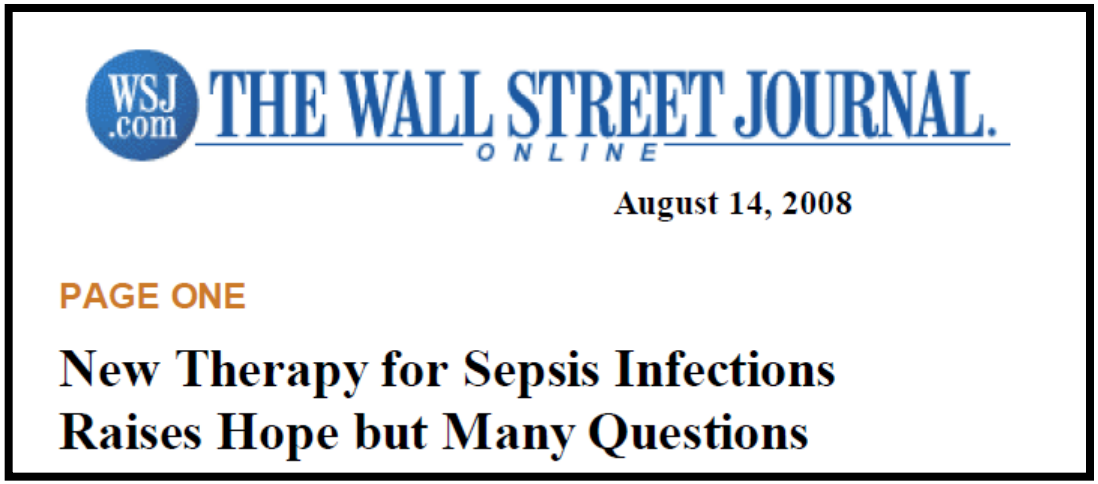
Azriel Perel

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 *et al.* (n = 263)	Sprung *et al.* (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[a]	0.0000
Coronary artery disease (%)	25.0	16.9[a]	0.0080
Congestive heart failure (%)	33.4	6.0[a]	0.0000
Diabetes (%)	31.4	21.6[a]	0.0030
Chronic obstructive pulmonary disease (%)	15.7	11.3[a]	0.0900
Chronic renal failure (%)	21.7	8.7[a]	0.0000
Liver disease (%)	23.3	8.1[a]	0.0000
Neurologic disease (%)	33.0	11.7[a]	0.0000
Cancer (%)	11.4	16.9[a]	0.0580
Alcohol use (%)	38.6	Not reported	

[a]n = 496. CORTICUS, Corticosteroid Therapy of Septic Shock.



WSJ.com 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 $ScvO_2$ 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).

Intensive Care Med
DOI 10.1007/s00134-007-0934-2

SPECIAL ARTICLE

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 $ScvO_2$ (72% vs. 49%)

Shapiro N, et al.
(Crit Care Med 2009: 37:819–824)

	Before Group (n = 200)	After Group (n = 200)	p
IV fluids given in first 12 hrs (mL)	1627 ± 1862	2054 ± 2237	0.04
Emergency depa	0–6	3548 ± 2977	1.00
Intensive care u		1477 ± 1193	0.45
Ward		1327 ± 1480	0.69
First antibiotic dos		131 (65.5)	0.01
Emergency depa		48 (77.4)	0.01
Intensive care unit	47 (52.8)	32 (56.1)	0.58
Ward	44 (55.7)	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[a]	137 (68.5)	105 (52.5)	<0.01
CVP monitored, n (%)	21 (10.5)	31 (15.5)	0.14
$ScvO_2$ 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 3499±2438
EGDT 4981±2984

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 ($p<0.0001$).**

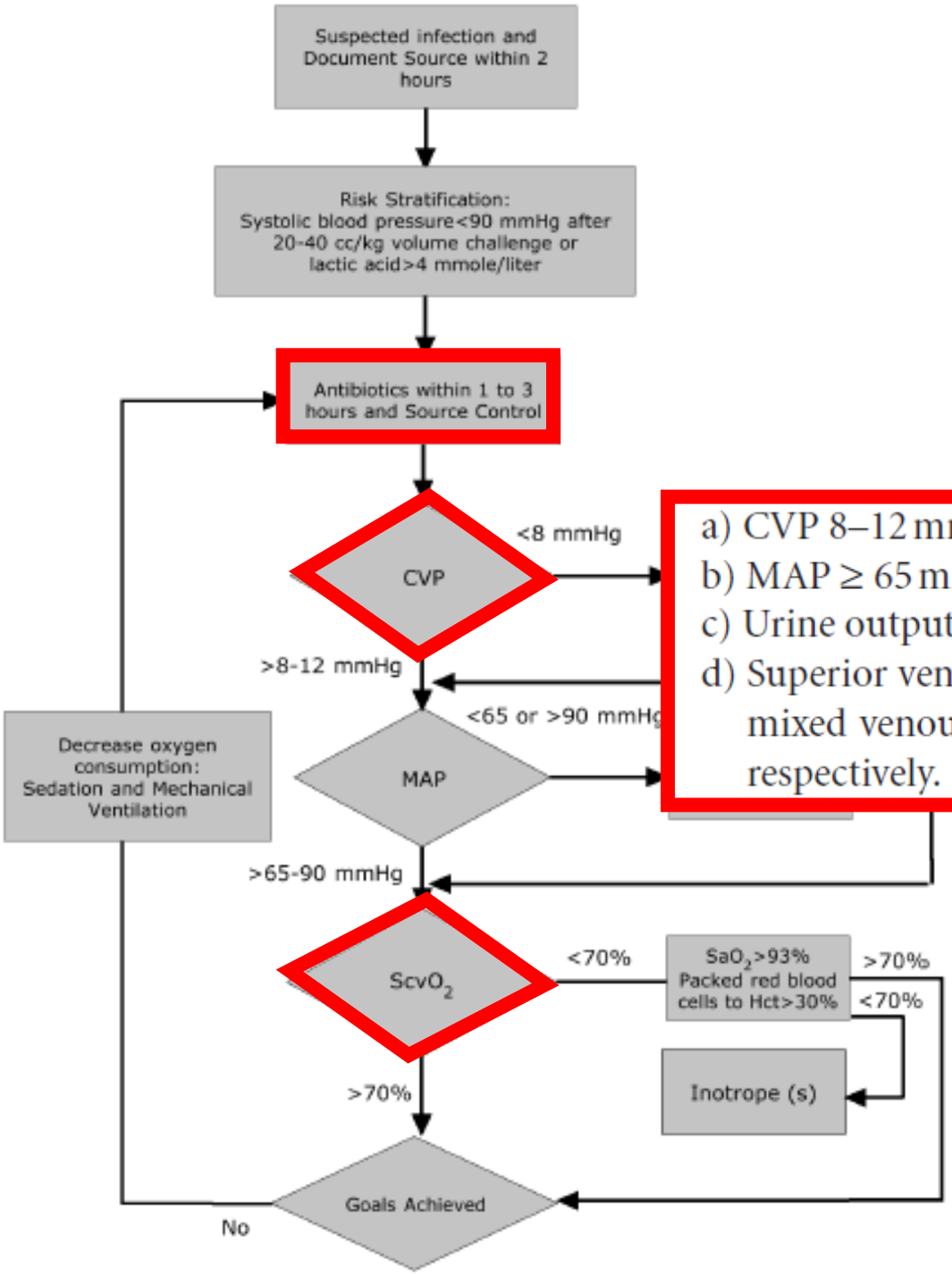
- **Attainment of a CVP of >8 mmHg and ScvO2 of >70% did not influence survival in patients with septic shock.**

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.



a) CVP 8–12 mm Hg
b) MAP ≥ 65 mm Hg
c) Urine output ≥ 0.5 mL·kg·hr
d) Superior vena cava oxygenation saturation ($ScvO_2$) or mixed venous oxygen saturation (SvO_2) 70% or 65%, respectively.

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.

INSTITUTE FOR HEALTHCARE IMPROVEMENT

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 ($S_{CV}O_2$) q 30 minutes until ≥ 70% □ Continuous central venous oxygen saturation ($S_{CV}O_2$) 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 ($S_{CV}O_2$) q 30 minutes until ≥ 70% (max dose 20 mcg/kg/min)
		:_____ **Telephone #/Pager #** _____

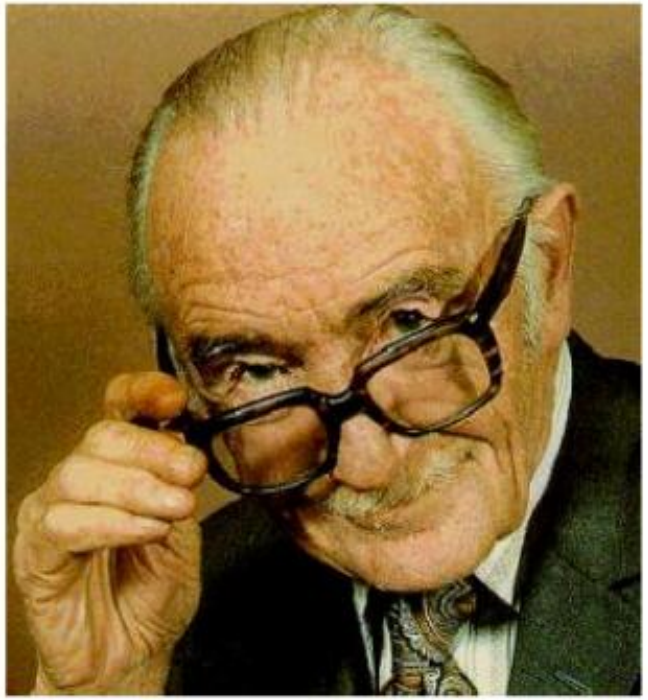
Are you compliant?

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".



The NEW ENGLAND JOURNAL of MEDICINE

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THIS WEEK IN THE JOURNAL

Article Summaries

Summaries | PDF

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.** *New England Journal of Medicine* 2001, 344:699-709.	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.** *New England Journal of Medicine* 2001, 345:1368-1377.	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.** *Critical Care Medicine* 2001, 29(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.** *New England Journal of Medicine* 2003, 348:1546-1554.	1551

Surviving Sepsis Campaign

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 H2O 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.

The NEW ENGLAND JOURNAL of MEDICINE

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E. Rivers and Others

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±2438	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☆

Resuscitation 80 (2009) 811–818

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

ED to 0 h[a]	0–6 h	6–72 h
1224 (1224)	2218 (1887)	4914 (3533)

Rivers et al NEJM 2001

TREATMENT	HOURS AFTER THE START OF THERAPY		
	0–6	7–72	0–72
Total fluids (ml)			
Standard therapy	3499±2438	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

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,[33] 1998	35	60	dDown (SPV)
Sakka et al,[35] 1999	57	46	ITBVI
Michard et al,[32] 2000	40	40	PPV
Feissel et al,[34] 2001	19	53	ΔVpeak
Michard et al,[36] 2003	66	48	GEDVI
Feissel et al,[37] 2004	39	41	ΔIVC
Vieillard-Baron et al,[39] 2004	66	30	SVC collapsibility
Barbier et al,[40] 2004	20	50	ΔIVC
Perner and Faber,[41] 2006	30	47	SVV
Feissel et al,[38] 2007	28	64	ΔPplet
Osman et al,[31] 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

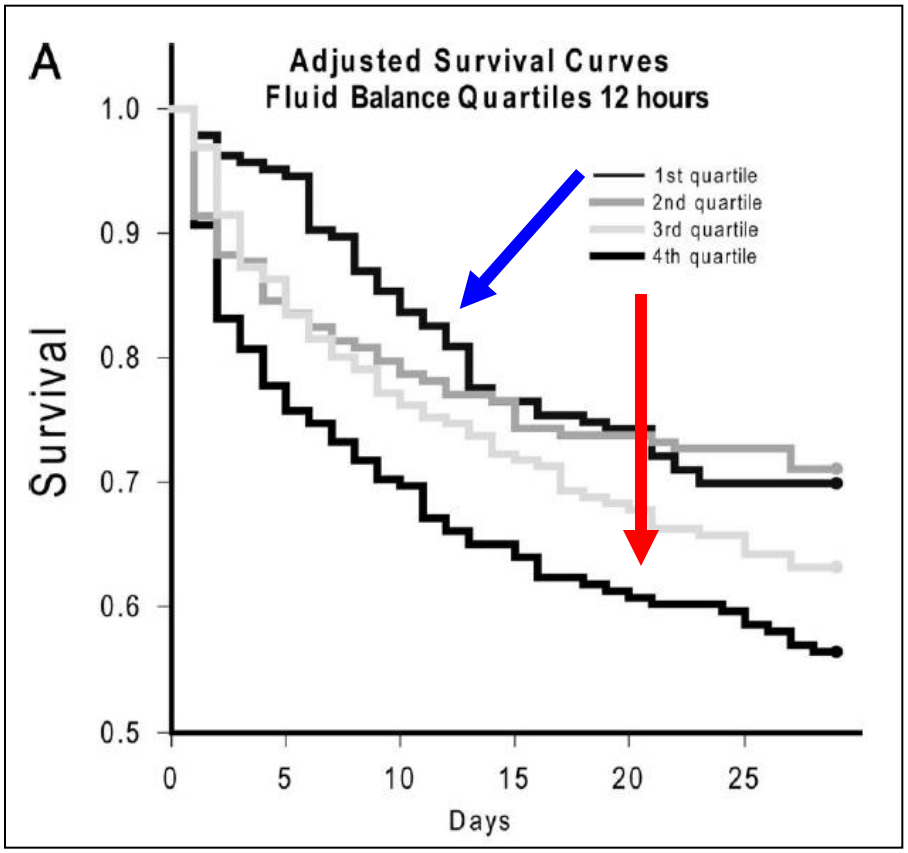
- **A positive fluid balance is associated with a worse outcome.**
- **A threshold may exist beyond which, after acute resuscitation, additional fluid therapy may cause harm.**

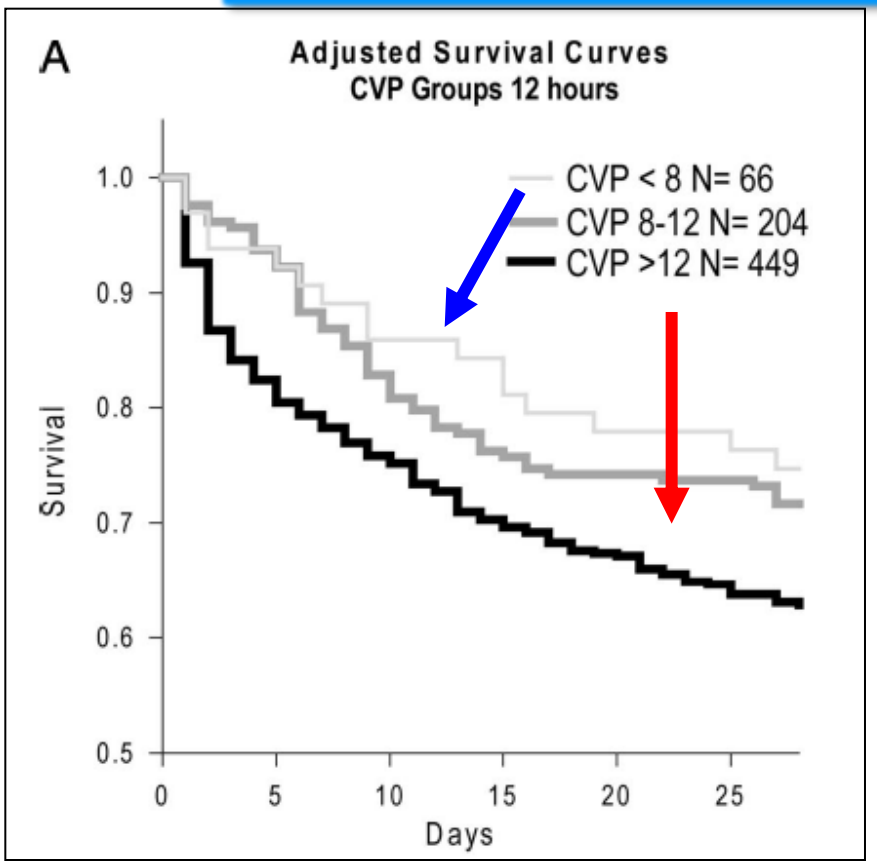
Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality

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

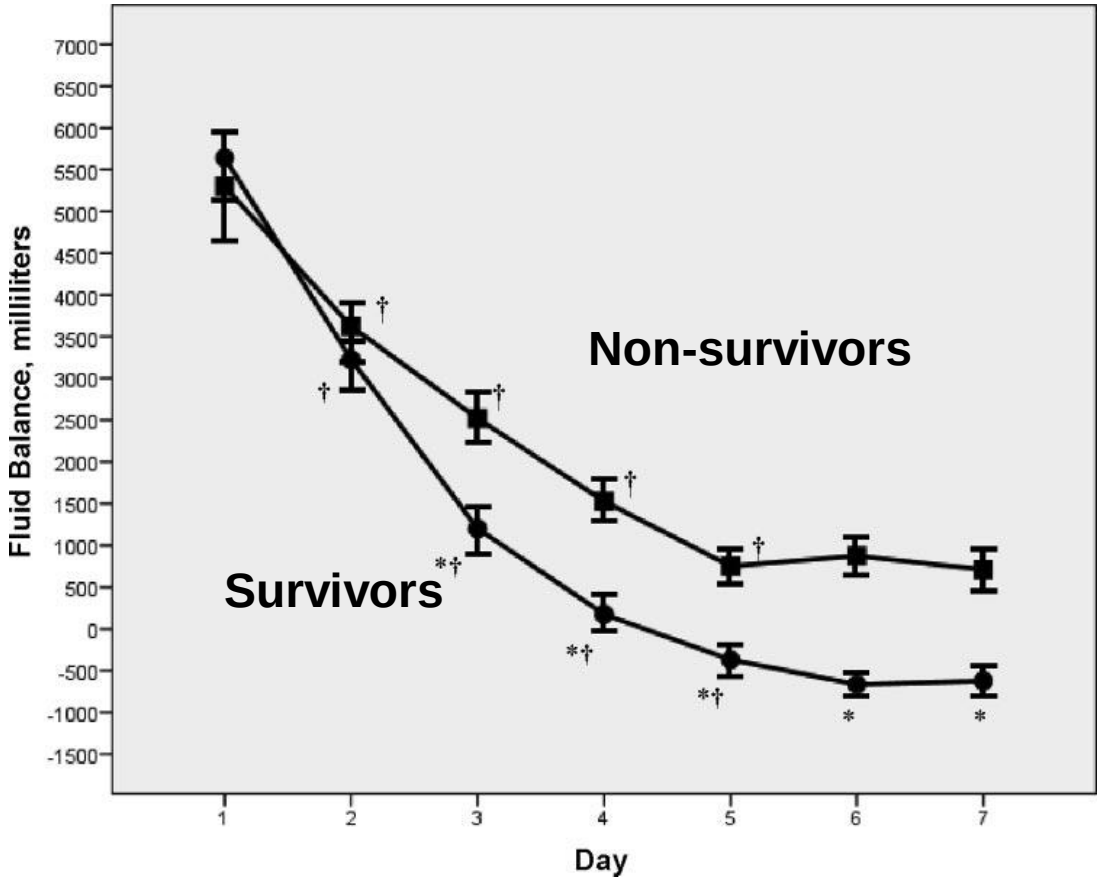




The Importance of Fluid Management in Acute Lung Injury Secondary to Septic Shock

(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[1], Patrick D Brophy[2], Dinna Cruz[3] and Claudio Ronco[3]

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[1] and Rinaldo Bellomo[2]*

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

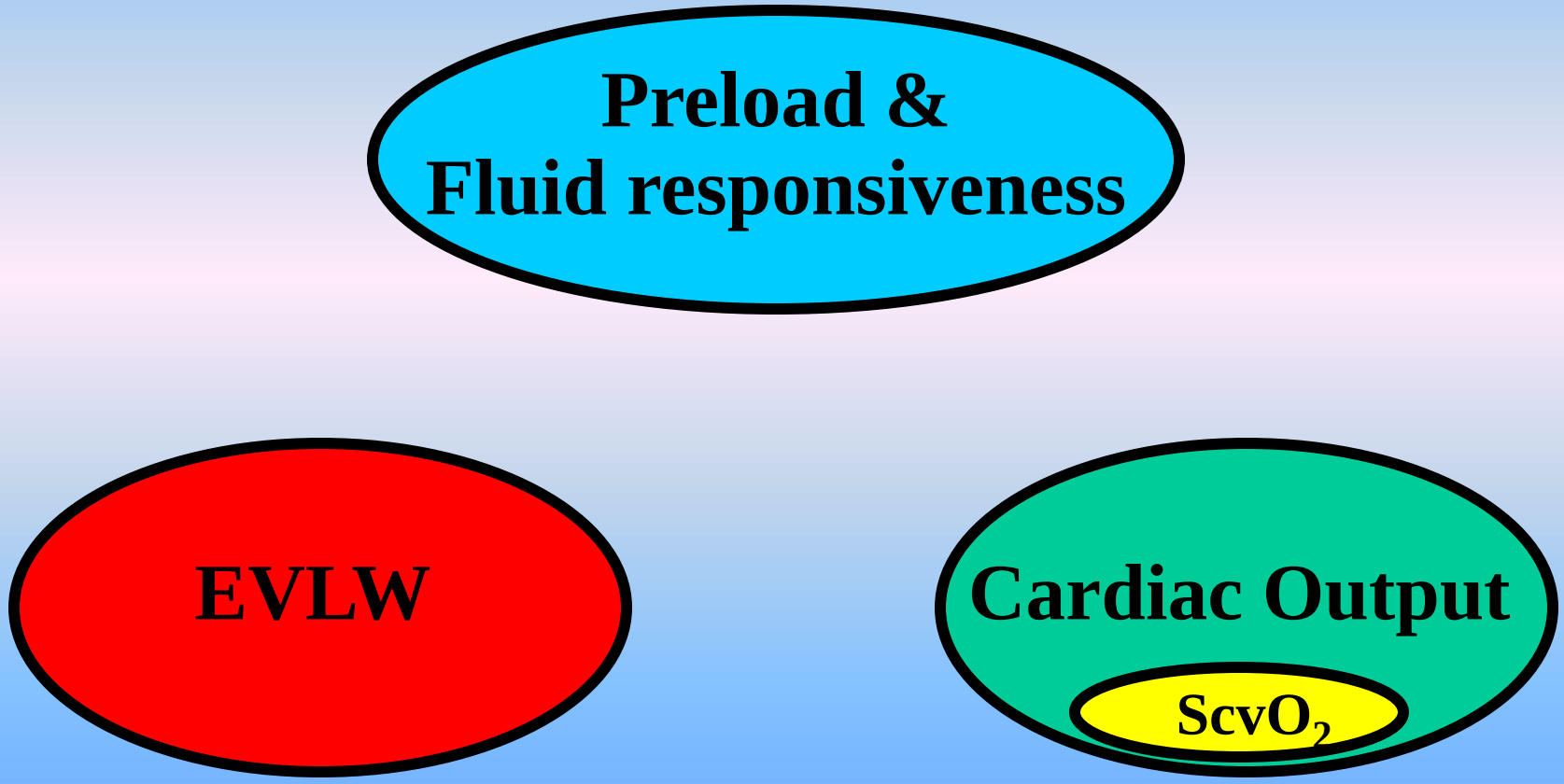
Jean-Louis Vincent[1]*, Andrew Rhodes[2], Azriel Perel[3], Greg S Martin[4], Giorgio Della Rocca[5], Benoit Vallet[6], Michael R Pinsky[7], Christoph K Hofer[8], Jean-Louis Teboul[9], Willem-Pieter de Boode[10], Sabino Scolletta[11], Antoine Vieillard-Baron[12], Daniel De Backer[1], Keith R Walley[13],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

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...



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

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

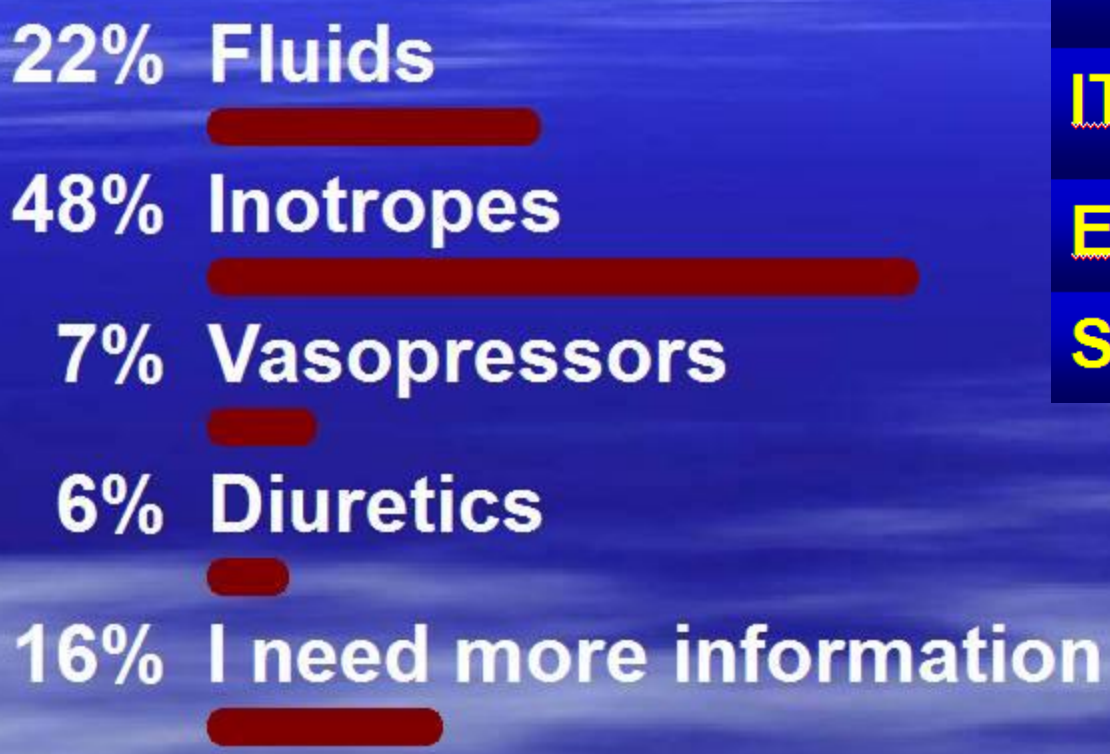
Question: What would you do now?

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

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

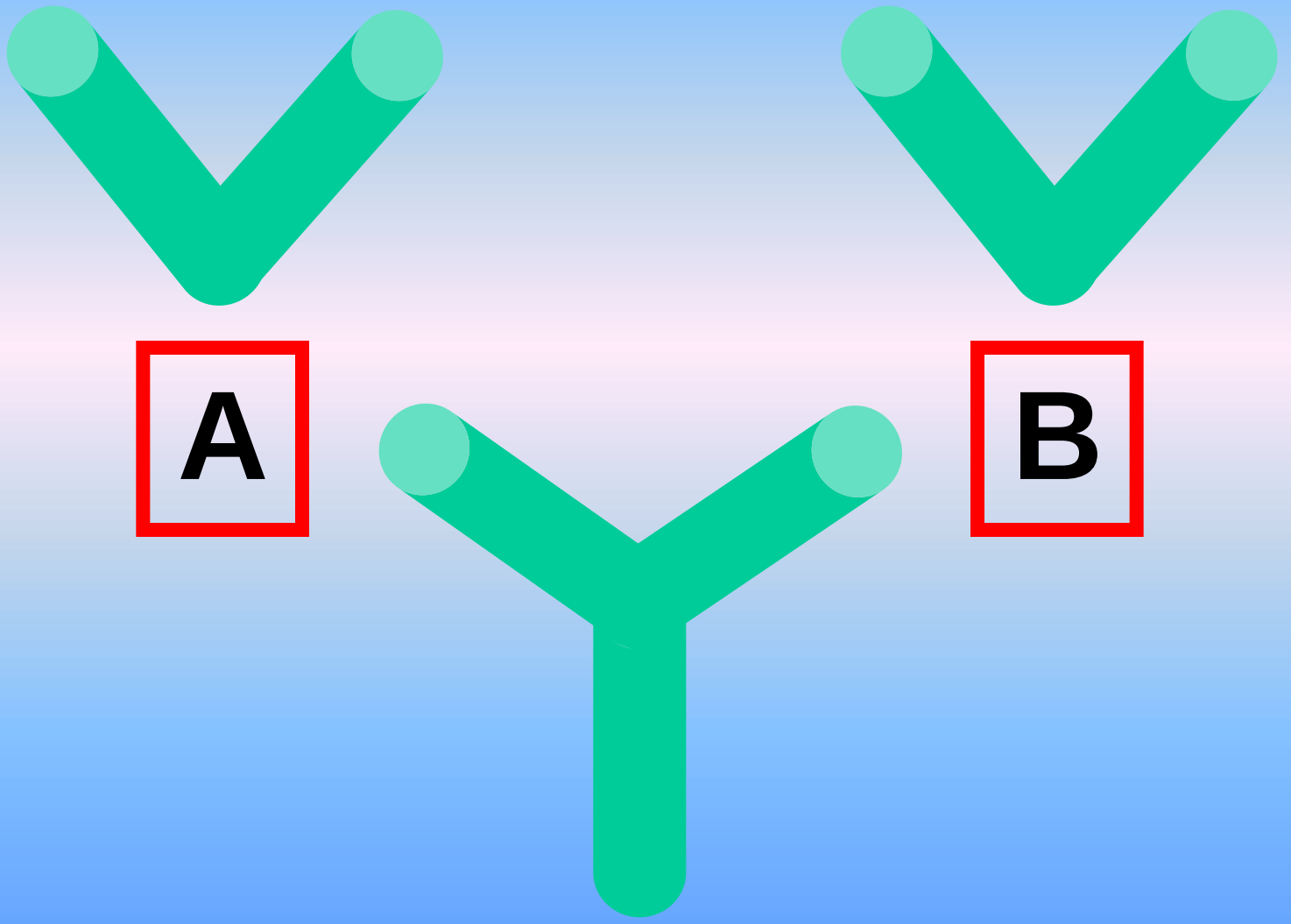
Question 4: What would you do now?

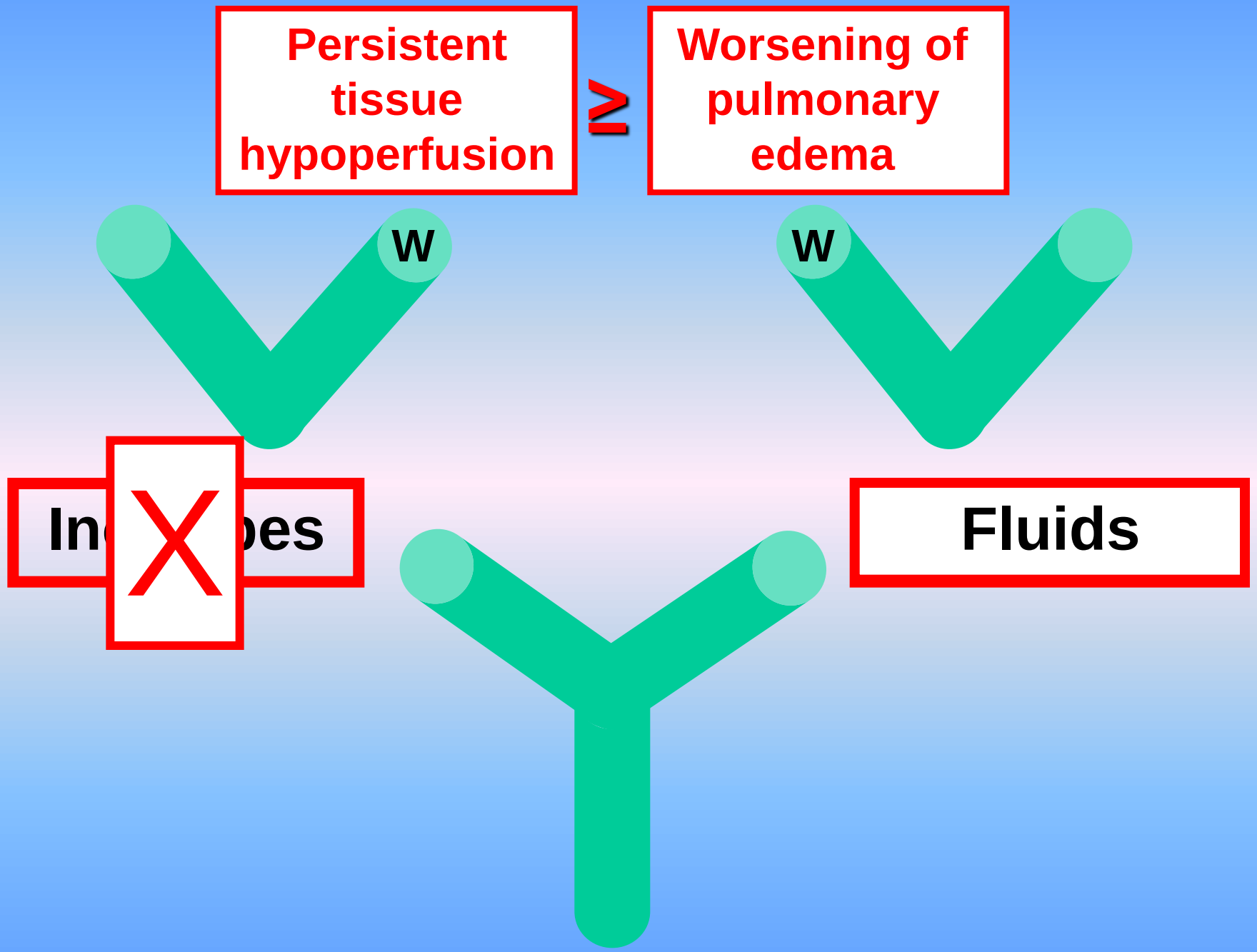
CO	1.8 l/min
ITBVi	600 ml/m^2
EVLWi	15 ml/kg
SVV	25-30%



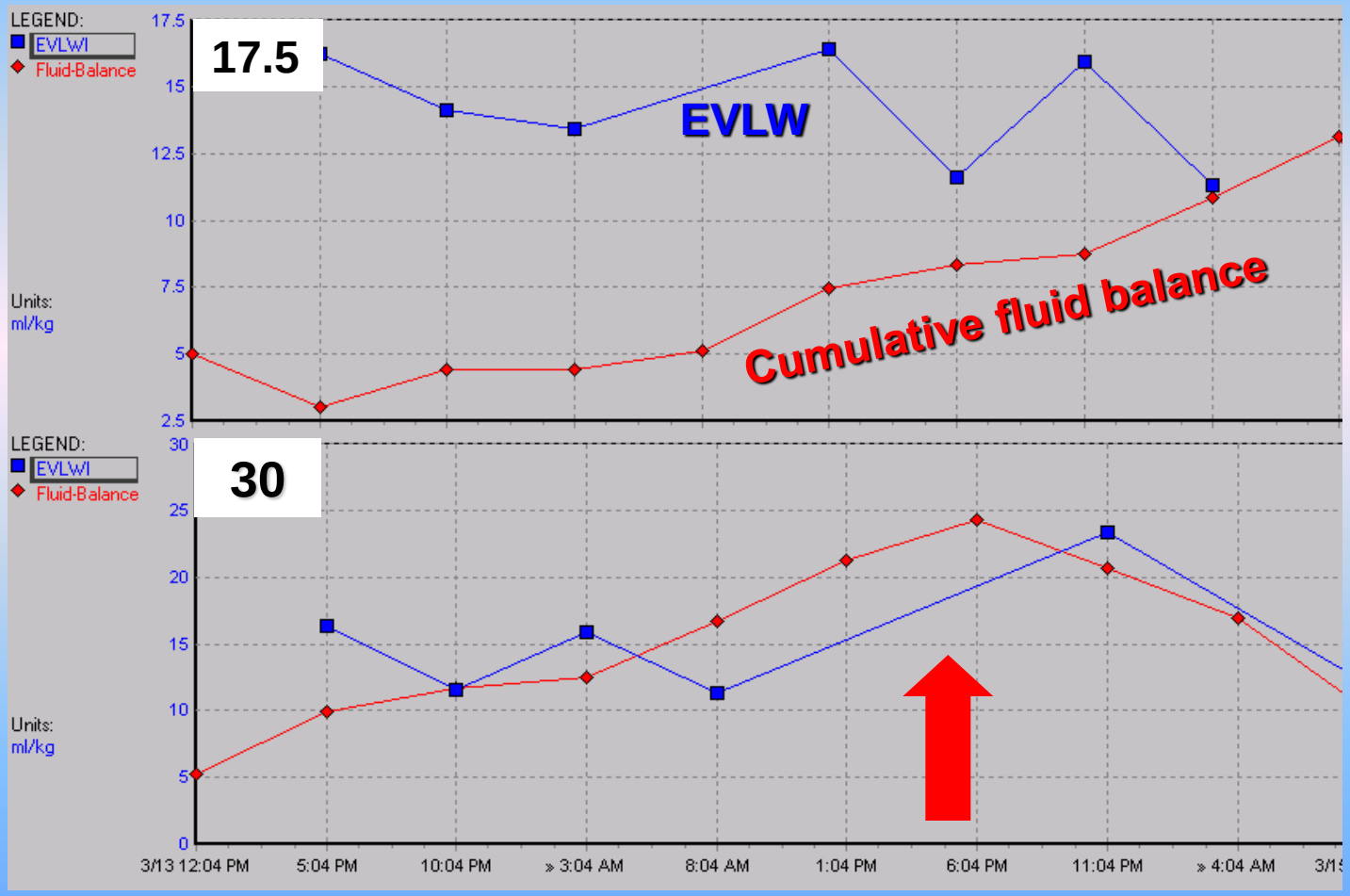
1% Wrong answer

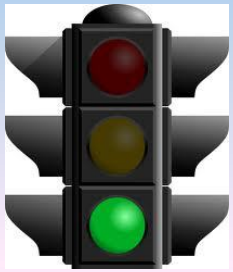
RIGHT WRONG WRONG RIGHT




Persistent tissue hypoperfusion
≥
Worsening of pulmonary edema
W
W
X
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.

Thank you for your attention!

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