37th Vicenza Course on AKI & CRRT

May 28-30, 2019

General management of the septic patient

M Ostermann

Disclosures

Speaker honoraria:	Alere, Fresenius
Advisory role:	Nxstage, Biomerieux, Fresenius
Research funding:	Fresenius, LaJolla Pharma

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

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Surviving Sepsis guideline recommendations

93 recommendations

- 32 **Strong** recommendations: ***"We recommend"***
- 39 **Weak** recommendations: ***"We suggest"***
- 18 Best Practice Statements

Source Control

A specific anatomic diagnosis of infection requiring emergent source control should be identified or excluded as rapidly as possible and any required source control intervention should be implemented.

(Best Practice Statement)

Antibiotics

- **administration of IV antimicrobials as soon as possible and within 1 h for both sepsis and septic shock**

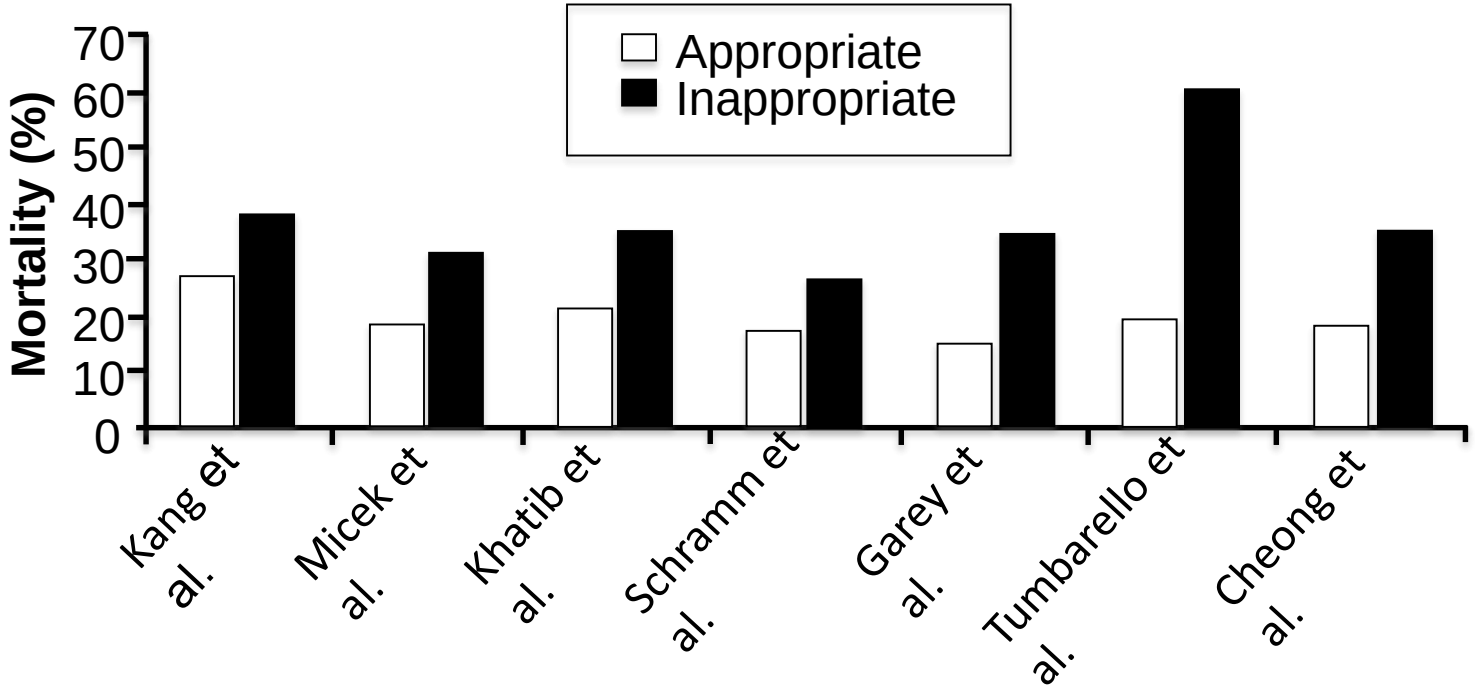
  (strong recommendation, moderate quality of evidence).

- **empiric broad-spectrum therapy with one or more antimicrobials to cover all likely pathogens**

  (strong recommendation, moderate quality of evidence).

- **antibiotic stewardship**

Failure to treat with the right antibiotics increases mortality by 10-20%



Morell MR et al. *Infectious Disease Clinics of North America* 23 (3): 485-501, 2009

Initial Resuscitation

- **at least 30ml/kg of intravenous crystalloid fluid to be given within the first 3 hours**

  (Strong recommendation; low quality of evidence)

- **crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement**

  (Strong recommendation, moderate quality of evidence)

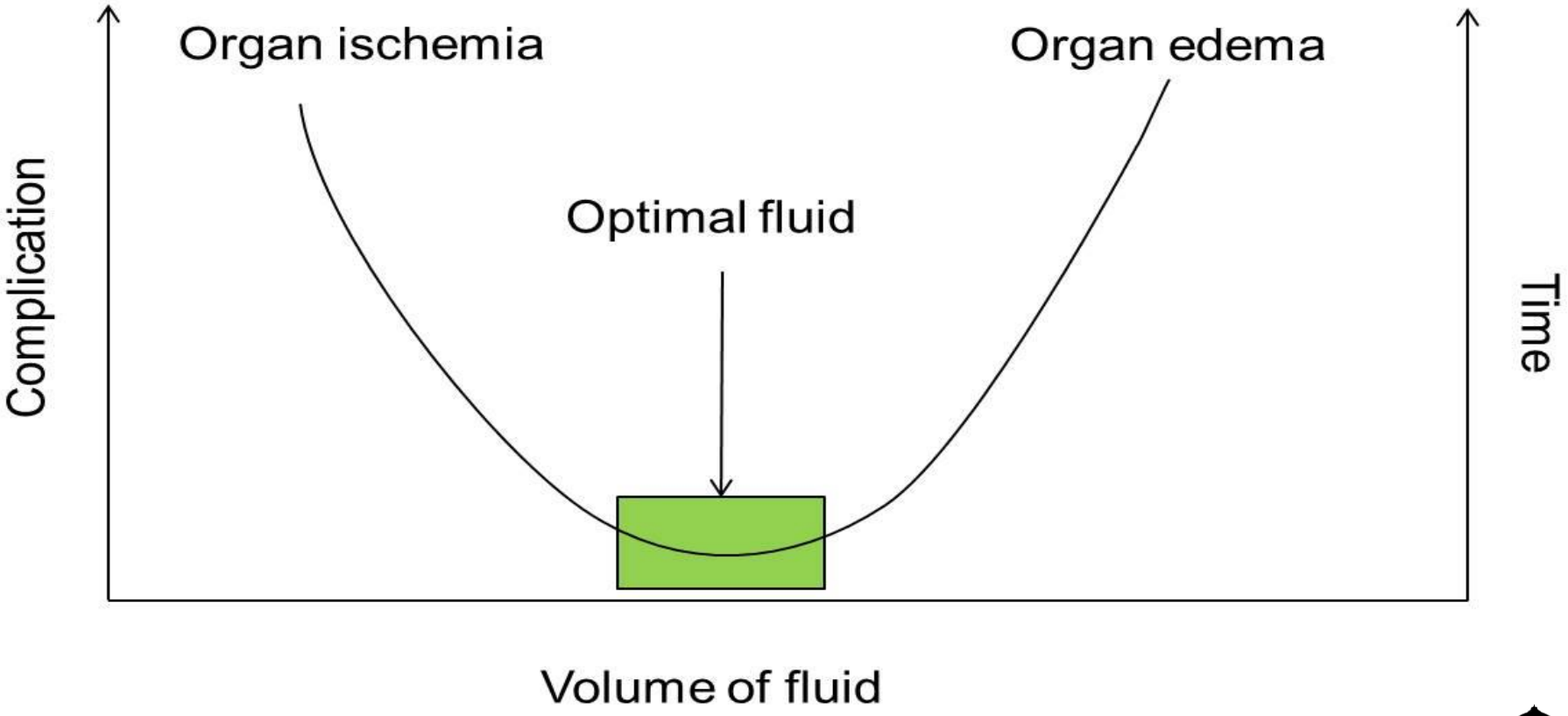
- **to avoid starches**

Fluid therapy

- **following initial fluid resuscitation: additional fluids to be guided by frequent reassessment of hemodynamic status**
  (Best Practice Statement)

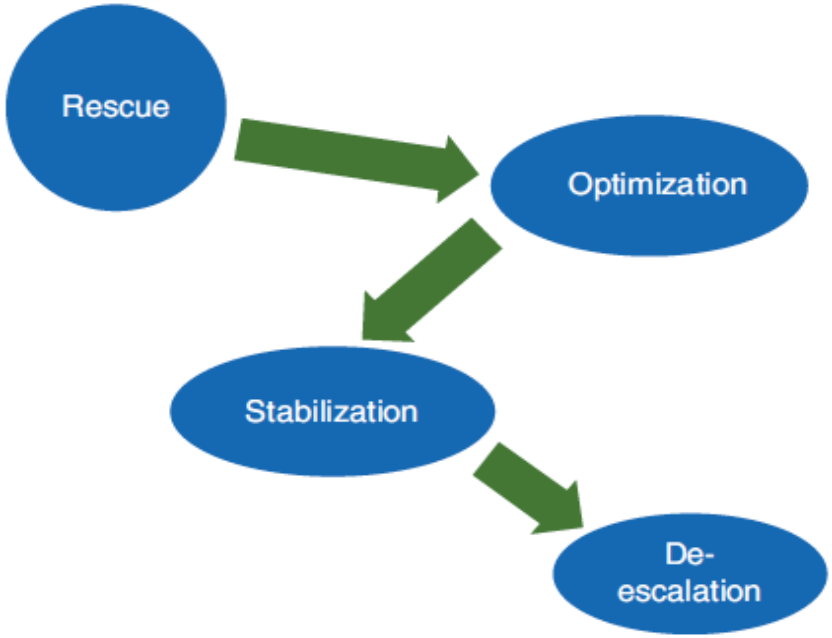
How much fluid and for how long?

- **Individualised Rx**
- **According to dynamic signs of fluid responsiveness**
  (Physical exam, straight leg raise, IVC ultrasound, etc)
- **Without causing fluid overload**

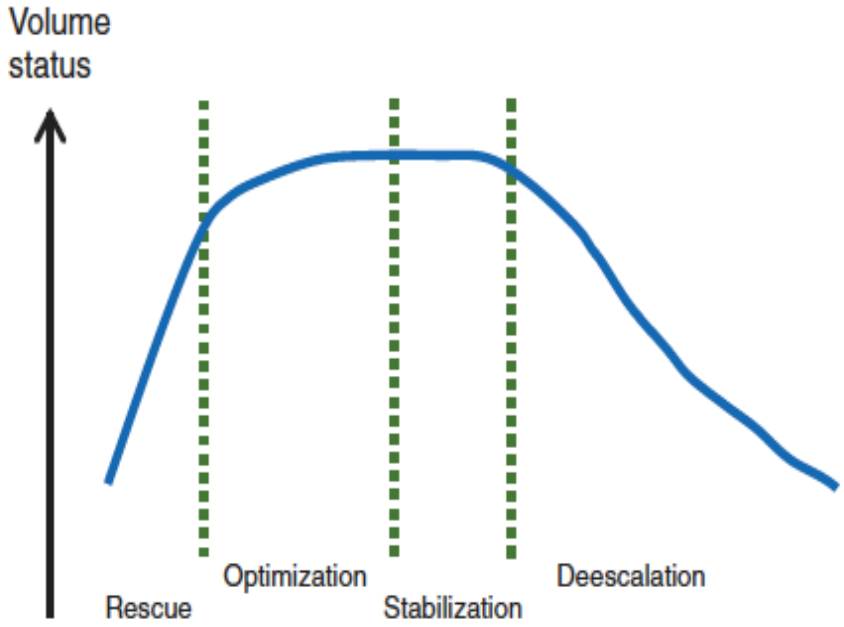


Critical Care Medicine 2012;40(6)

Resuscitation phases



Relationship between different stages of resuscitation



Volume status of different stages of resuscitation

Vasopressor therapy

- **Target mean arterial pressure of 65 mmHg in patients with septic shock requiring vasopressors**
  (Strong recommendation; moderate quality of evidence)

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High versus Low Blood-Pressure Target in Patients with Septic Shock

Multicenter open-label RCT

776 patients with septic shock undergoing resuscitation

Comparison: target MAP 80-85mmgHg versus 65-70mmHg

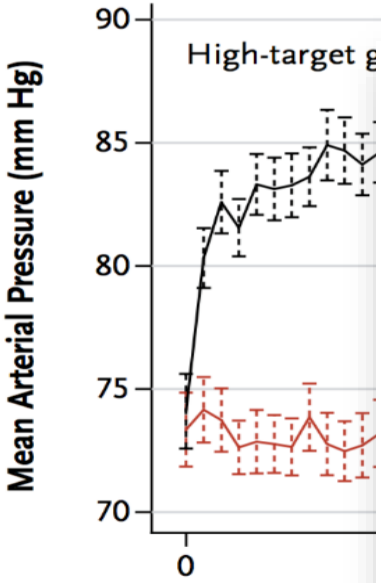
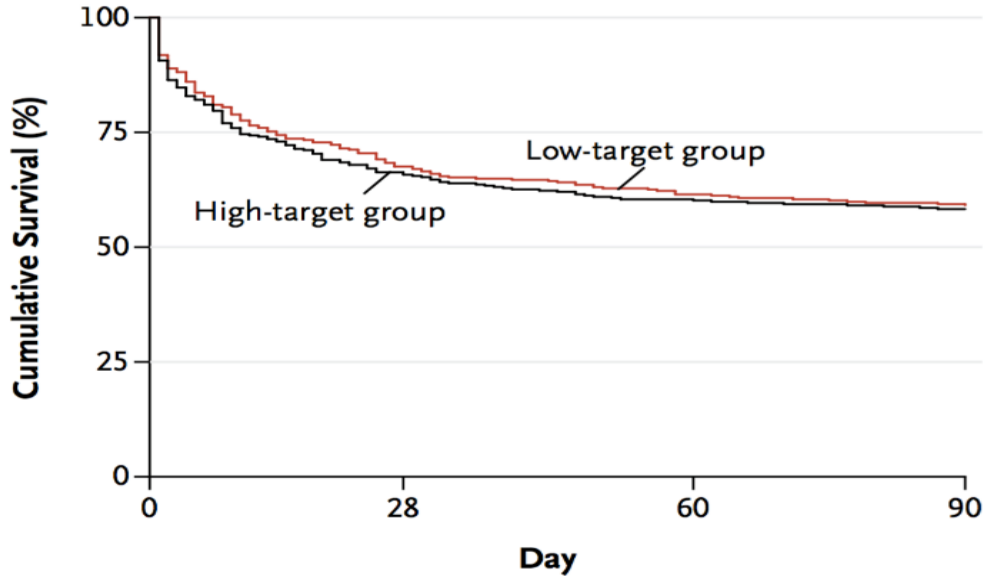


Figure 2. Mean Arteria



No. at Risk				
Low target	379	256	233	225
High target	375	249	227	219

Figure 3. Kaplan–Meier Curves for Cumulative Survival.

Additional results:

in patients with chronic hypertension (n=340):

significantly less RRT in high target group

(31.7% vs 42.2%, p=0.046)

Vasoactive agents

- **norepinephrine as the first choice vasopressor**
  (strong recommendation, moderate quality of evidence)

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Vasoactive agents

- **Norepinephrine as the first choice vasopressor**
  (strong recommendation, moderate quality of evidence)

- **To add vasopressin or epinephrine to norepinephrine to achieve MAP target**
  (weak recommendation, low quality of evidence)

- **Regular clinical assessment if shock does not resolve**
  (Best Practice Statement)

Corticosteroids

- **Not to use intravenous hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability.**
- **If not achievable, iv hydrocortisone 200 mg per day.**

(Weak recommendation; low quality of evidence)

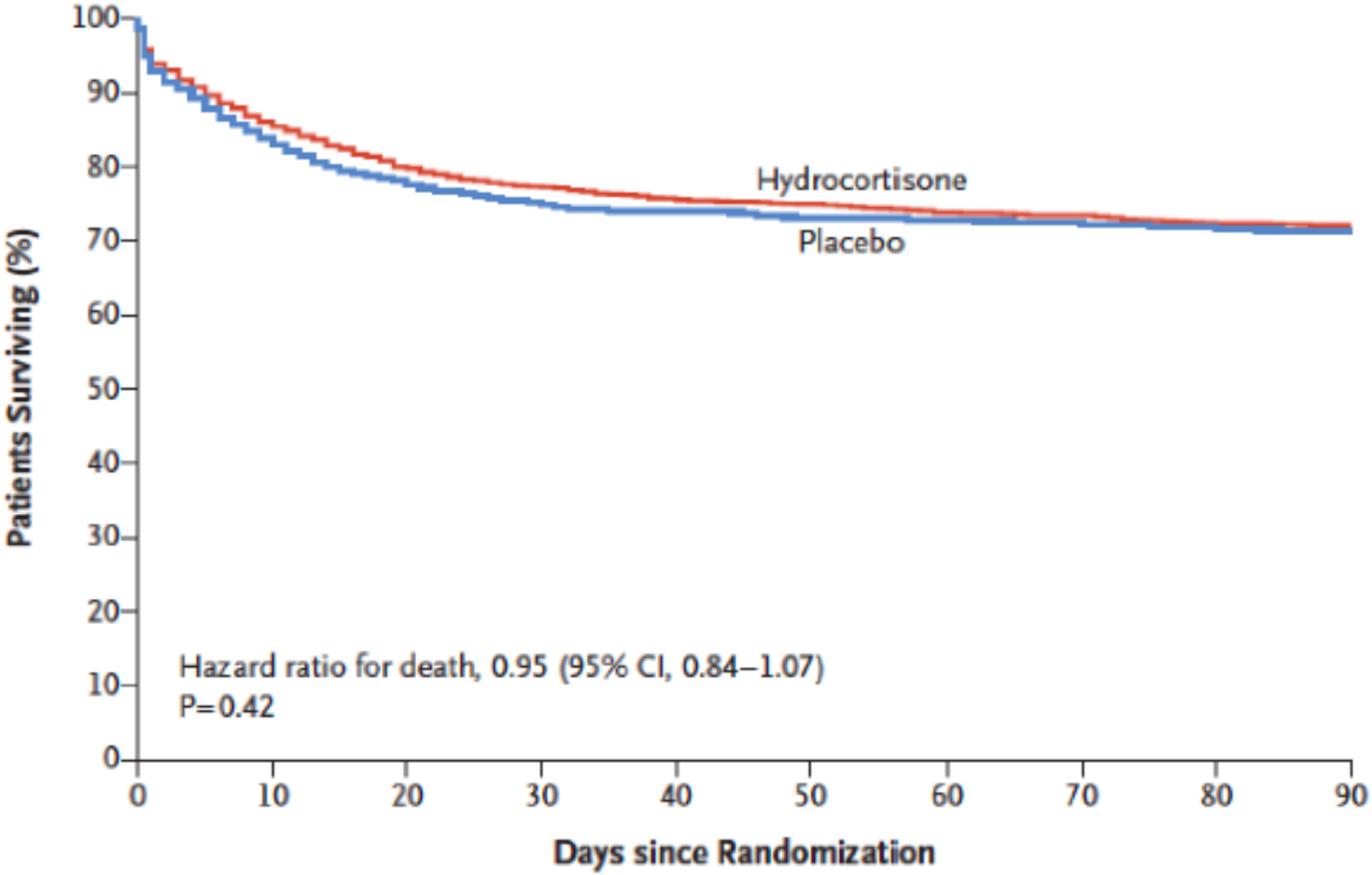
ORIGINAL ARTICLE

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass, M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh, for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

Aim: To determine whether hydrocortisone therapy reduces mortality in patients admitted to ICU with septic shock

Randomisation: Hydrocortisone 200mg/day vs placebo


Patients Surviving (%)
100
90
80
70
60
50
40
30
20
10
0
Hydrocortisone
Placebo
Hazard ratio for death, 0.95 (95% CI, 0.84–1.07)
P=0.42
0
10
20
30
40
50
60
70
80
90
Days since Randomization

Secondary outcomes

- Hydrocortisone - more rapid resolution of shock (3 vs 4 days**)
- Hydrocortisone - shorter duration of initial episode of IPPV (6 vs 7 days**)
- Hydrocortisone – earlier time to ICU discharge (10 vs 12 days**)
- Hydrocortisone – reduced frequency of blood transfusion (37% vs 42%**)

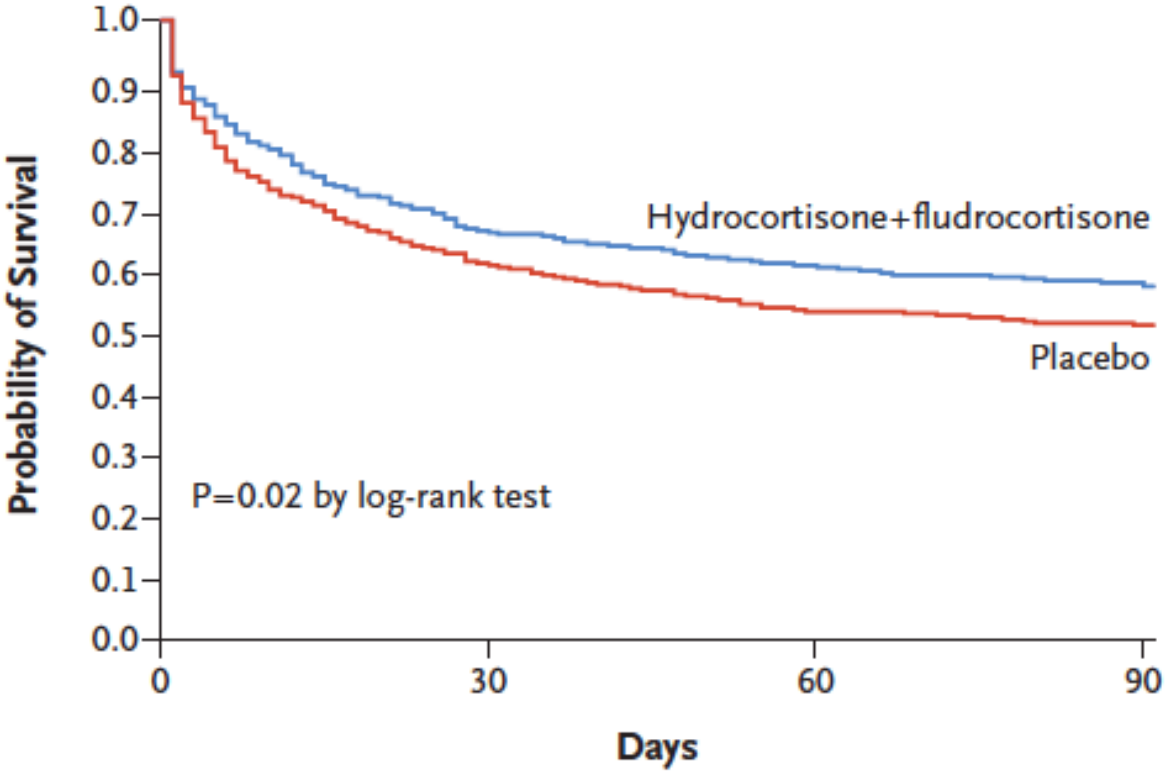
** significant after adjustment for multiplicity

ORIGINAL ARTICLE

Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

D. Annane, A. Renault, C. Brun-Buisson, B. Megarbane, J.-P. Quenot, S. Siami, A. Cariou, X. Forceville, C. Schwebel, C. Martin, J.-F. Timsit, B. Misset, M. Ali Benali, G. Colin, B. Souweine, K. Asehnoune, E. Mercier, L. Chimot, C. Charpentier, B. François, T. Boulain, F. Petitpas, J.-M. Constantin, G. Dhonneur, F. Baudin, A. Combes, J. Bohé, J.-F. Loriferne, R. Amathieu, F. Cook, M. Slama, O. Leroy, G. Capellier, A. Dargent, T. Hissem, V. Maxime, and F. Bellissant, for the CRICS-TRIGGERSEP Network*

Hypothesis:
hydrocortisone + fludrocortisone improves the outcome of patients with septic shock



No. at Risk

Hydrocortisone+ fludrocortisone	614	405	372	353
Placebo	627	381	333	319

Renal Replacement Therapy

Renal Replacement Therapy

- **Not to use RRT for increase in creatinine or oliguria without other definitive indications for RRT.**

  (Weak recommendation; low quality of evidence)

- **No specific recommendation for intermittent or continuous RRT unless need for large volume removal**

Nutrition

- **Early initiation of enteral feeding in critically ill patients who can be fed enterally**

  (Weak recommendation; low quality of evidence)

Others

No role for routine iv immunoglobulins

No role for erythropoetin

No $ScvO_2$ and lactate targets

Conclusions

The most important components of sepsis care are:

i) timely source control

ii) rapid administration of the right antibiotic(s)

iii) aggressive haemodynamic resuscitation with fluids +/- vasopressors within first 6 hours

Need for individualised approach