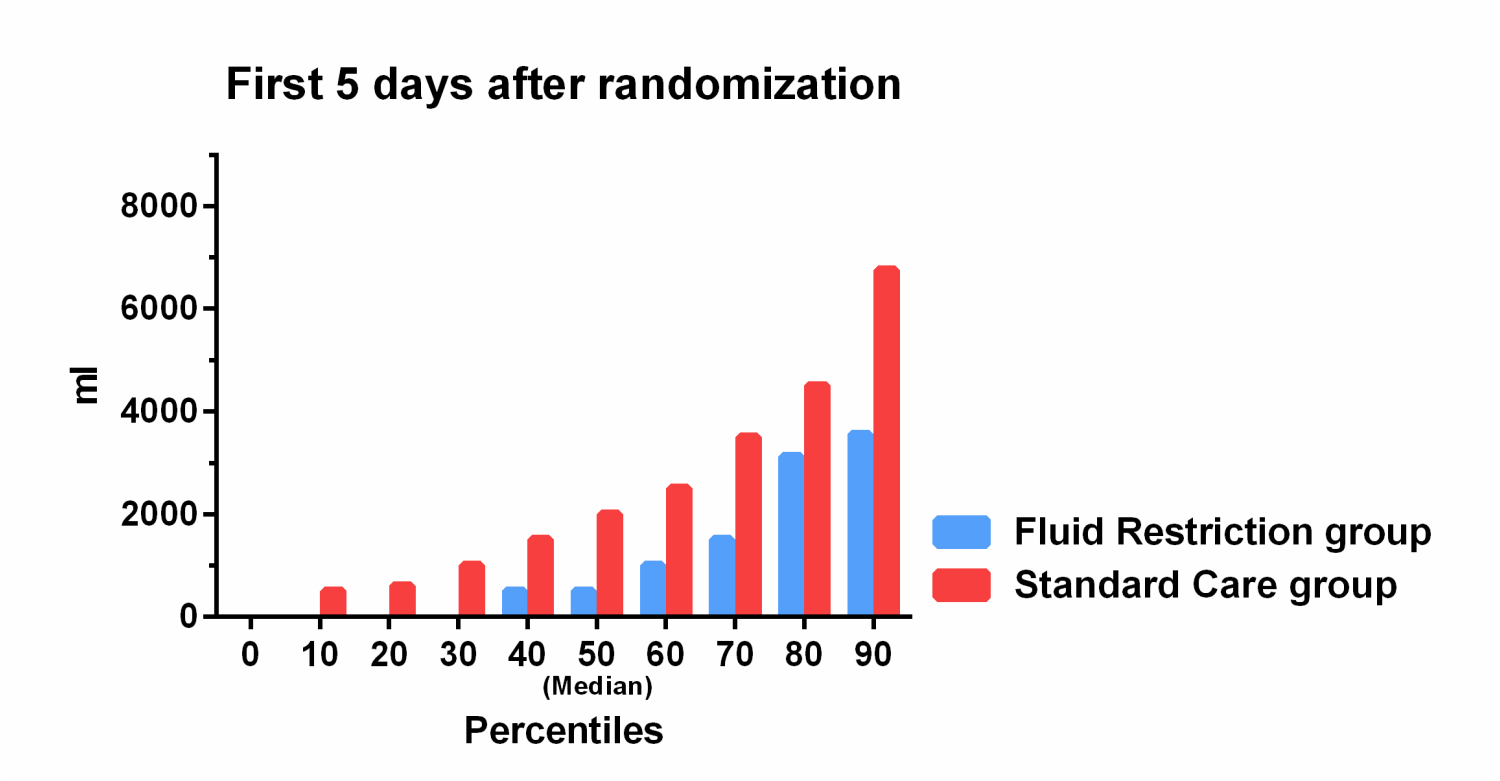

# Effects of restricting intravenous fluids vs. standard care fluid therapy in patients with septic shock

# The Conservative vs. Liberal Approach to fluid therapy of Septic Shock in Intensive Care (CLASSIC) Trial

# Resuscitation fluid in the pilot



Classic

# Why was resus fluid given?

**Lactate**
**Vasopressor/MAP**
**Oliguria**

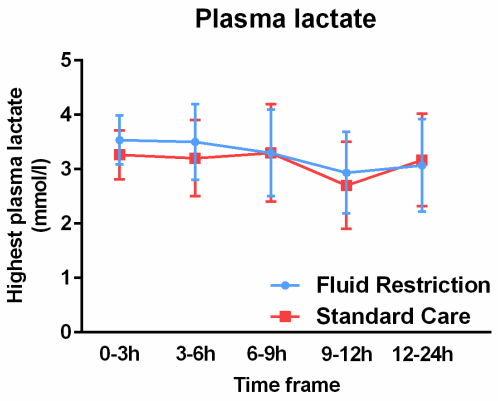
## Estimated differences

**0.1** (-0.7-0.9) mmol/l

**0.01** (-0.02-0.05) µg/kg/min

**-0.1** (-0.3-0.2) ml/kg/h

A

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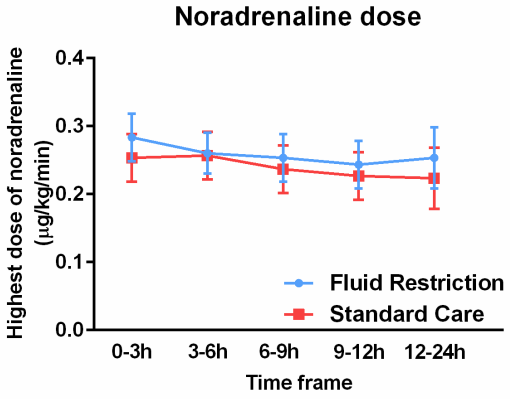


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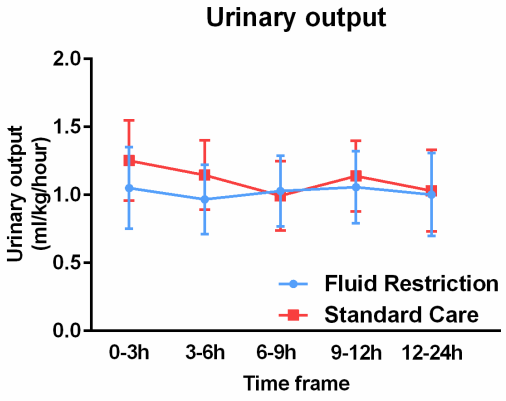
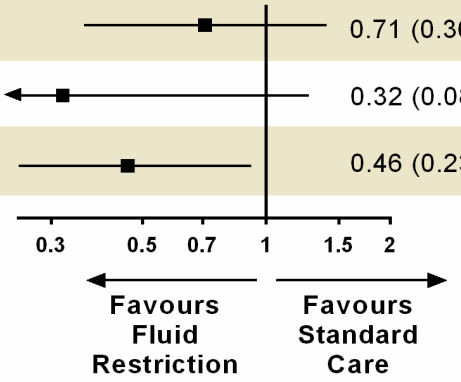



Hjortrup AAS 2017

# Exploratory outcome measures

**A Odds ratios of exploratory outcomes**

| | Fluid Restriction | Standard Care | Odds ratio (95% CI) | P value |
|---|---|---|---|---|
| | No. of events / No. at risk | | | |
| Death by day 90 | 25/75 (33%) | 31/76 (41%) | 0.71 (0.36-1.40) | 0.32 |
| Ischemic events in the ICU | 3/75 (4%) | 9/76 (12%) | 0.32 (0.08-1.27) | 0.11 |
| Worsening of AKI | 27/73 (37%) | 39/72 (54%) | 0.46 (0.23-0.92) | 0.03 |

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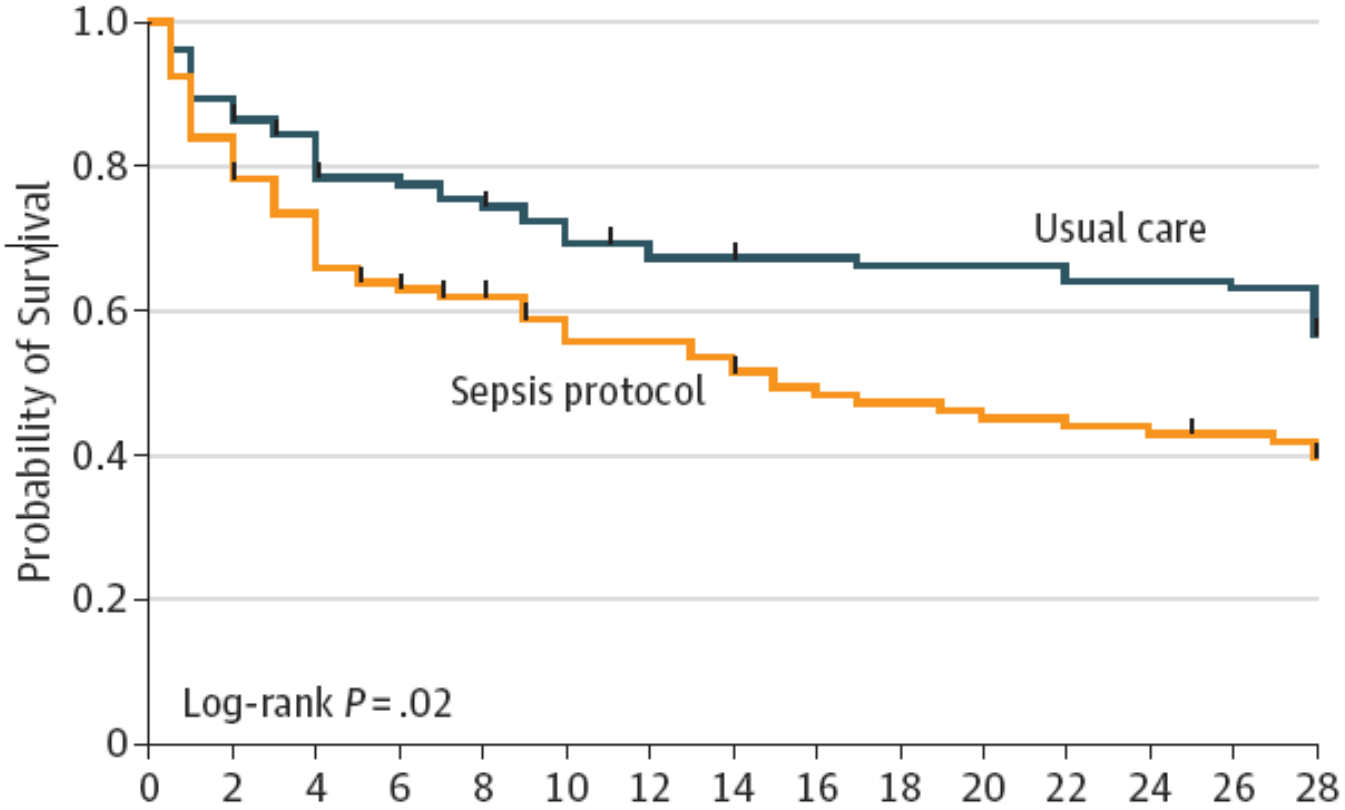
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

# Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension

## A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwango Bwalya, MBChB; Gordon R. Bernard, MD



*Intensive Care Med*
DOI 10.1007/s00134-016-4573-3

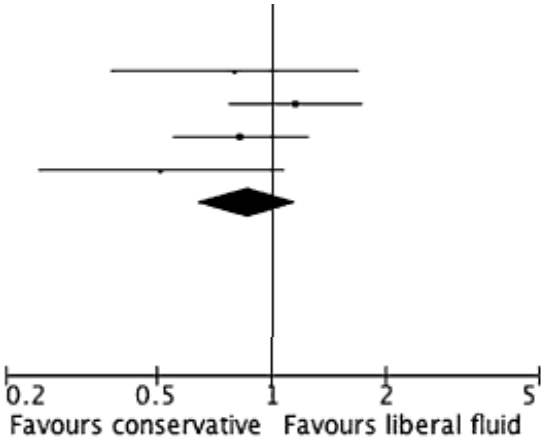
SYSTEMATIC REVIEW

# Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis

Jonathan A. Silversides[1,2*], Emmet Major[2], Andrew J. Ferguson[3], Emma E. Mann[2], Daniel F. McAuley[1,4], John C. Marshall[5,6], Bronagh Blackwood[1] and Eddy Fan[5]

| | | | | | | |
|---|---|---|---|---|---|---|
| **Sepsis or SIRS** | | | | | | |
| Benakatti et al. 2014 | 10 | 54 | 11 | 47 | 2.1% | 0.79 [0.37, 1.70] |
| Chen and Kollef. 2015 | 23 | 41 | 20 | 41 | 7.0% | 1.15 [0.76, 1.74] |
| Hjortrup et al. 2016 | 25 | 75 | 31 | 76 | 6.9% | 0.82 [0.54, 1.24] |
| Richard et al. 2015 | 7 | 30 | 14 | 30 | 2.1% | 0.50 [0.24, 1.06] |
| **Subtotal (95% CI)** | | **200** | | **194** | **18.1%** | **0.86 [0.62, 1.17]** |
| Total events | 65 | | 76 | | | |

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 4.06$, df = 3 (P = 0.26); $I^2 = 26\%$
Test for overall effect: Z = 0.98 (P = 0.33)



# Design

CLASSIC is a multicentre, parallel-grouped, open-labelled, centrally randomised, stratified, outcome assessor- and analyst-blinded trial

Classic

**Patients: Pts with septic-3 shock who have received 1 l of fluid and can be enrolled within 12 h**

**Intervention: Restriction of all IV fluids; may be given in extenuating circumstances: severe shock, losses or GI failure**

**Comparator: Standard care IV fluids**

**Outcomes: 90-day mortality, SAEs, SARs, days alive wo life support and days alive out of hospital, 1-yr mortality, HRQoL and cognition**

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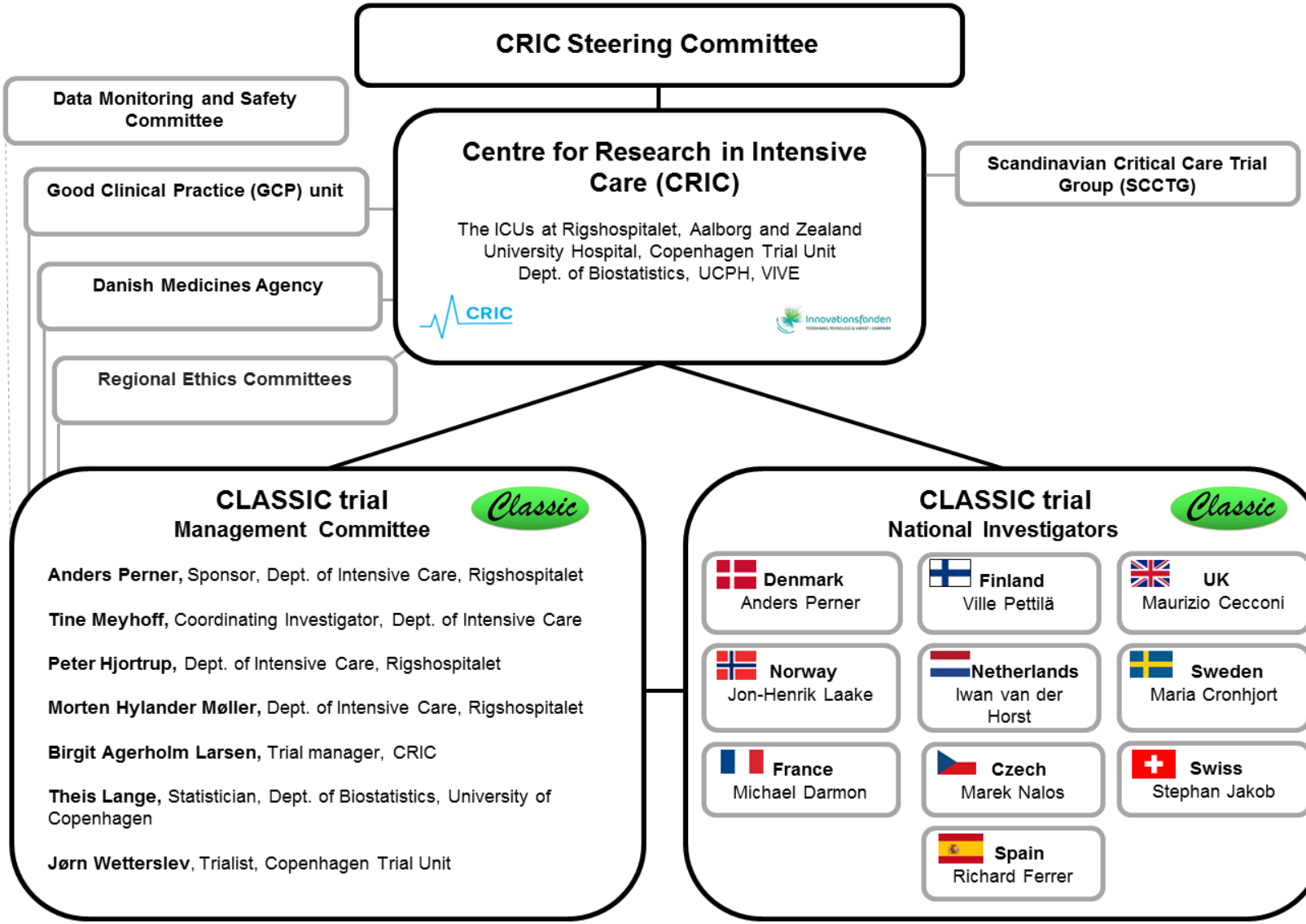
Classic

# Sample size

1554 (2 x 777) patients to show a 7% absolute reduction in 90-day mortality in the fluid restriction group vs standard care (est. 45% mortality) with 80% power


CRIC Steering Committee
Data Monitoring and Safety Committee
Good Clinical Practice (GCP) unit
Danish Medicines Agency
Regional Ethics Committees
Centre for Research in Intensive Care (CRIC)
The ICUs at Rigshospitalet, Aalborg and Zealand University Hospital, Copenhagen Trial Unit
Dept. of Biostatistics, UCPH, VIVE
CRIC
Innovationsfonden
Scandinavian Critical Care Trial Group (SCCTG)
CLASSIC trial
Management Committee
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Iwan van der Horst
Sweden
Maria Cronhjort
France
Michael Darmon
Czech
Marek Nalos
Swiss
Stephan Jakob
Spain
Richard Ferrer

Classic

**50 sites in 10 countries**

**31 patients per site**

**2 pts/site/ month**

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