



# How to Manage Fluids in AKI

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# Why do doctors give fluids to critically ill patients with AKI?

- **The urine output is low**
- The blood pressure is low
- The neck veins are low
- The CVP is low
- The cardiac output is low
- The patient is bleeding (typically they give blood)
- The pulse pressure variation, stroke volume variation, PAOP etc.) are abnormal



# Oliguria in ICU

- It is very common.
- If short-lived, the typical response is observation (but not always – see below).
- If sustained, the most common response is to give intravenous fluids



# EVIDENCE

- The giving intravenous fluids for oliguria is so common that there **must be strong evidence** to support the view that
- A) Fluids are efficacious (they achieve the physiological target variable)
- B) Fluids are effective (they improve clinical outcomes)
- C) Fluids are safe (they do not cause important adverse events)





# EVIDENCE

- Very strong historical control-based evidence that intravenous fluids are **life-saving** in
  - 1. Cholera
  - 2. Severe viral diarrhea
  - 3. Severe bacterial diarrhea
  - 4. Other states of profound dehydration (heat stroke, sun stroke, marathon runners etc.)
  - 5. Rhabdomyolysis

**All conditions with low UO, low BP, low CVP.**



# EVIDENCE

- By **analogy** with cholera, diarrhea, rhabdomyolysis, heat stroke, other states of volume depletion which are associated with low UO, low BP, low neck veins, low CVP, doctors respond in the same way **(give fluids)** to other states that carry similar physiological markers (post-surgical oliguria, oliguria during epidural infusion, septic oliguria, oliguria after cardiac surgery. AKI etc.)...**but where things are very different!**



# RCT of fluids in AKI

- PubMed identifies only 67 RCTs
- Most are irrelevant studies or contrast nephropathy studies
- Some evidence that steady hydration with isotonic fluid decreases the incidence of contrast nephropathy
- Several studies show possible renal toxicity of starch preparations
- No other relevant studies



## The emergence of a contrary view

# REVIEWS

## Fluid balance and acute kidney injury

*John R. Prowle, Jorge E. Echeverri, E. Valentina Ligabo, Claudio Ronco and Rinaldo Bellomo*

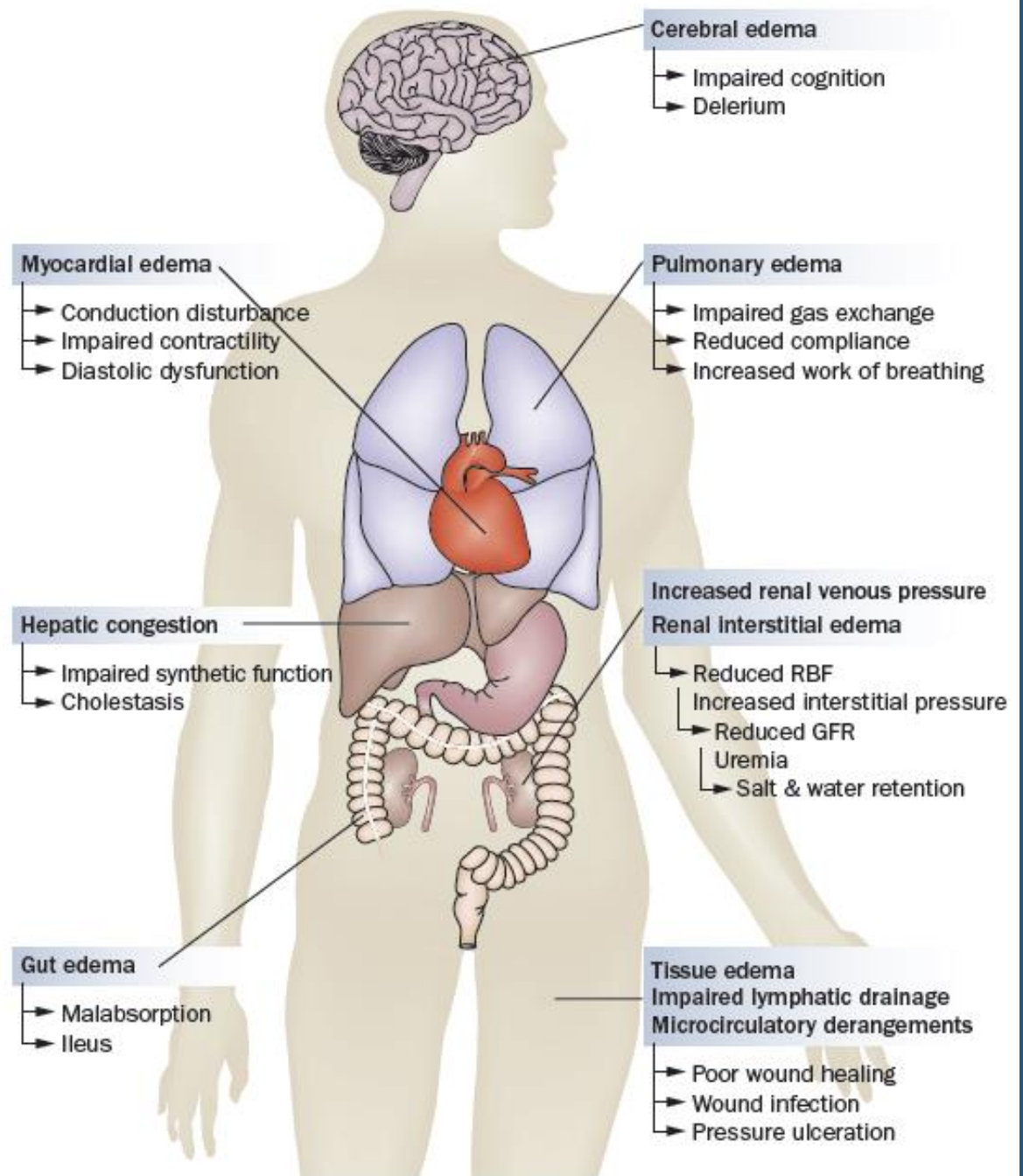
**Abstract** | Intravenous fluids are widely administered to patients who have, or are at risk of, acute kidney injury (AKI). However, deleterious consequences of overzealous fluid therapy are increasingly being recognized. Salt and water overload can predispose to organ dysfunction, impaired wound healing and nosocomial infection, particularly in patients with AKI, in whom fluid challenges are frequent and excretion is impaired. In this Review article, we discuss how interstitial edema can further delay renal recovery and why conservative fluid strategies are now being advocated. Applying these strategies in critical illness is challenging. Although volume resuscitation is needed to restore cardiac output, it often leads to tissue edema, thereby contributing to ongoing organ dysfunction. Conservative strategies of fluid management mandate a switch towards neutral balance and then negative balance once hemodynamic stabilization is achieved. In patients with AKI, this strategy might require renal replacement therapy to be given earlier than when more-liberal fluid management is used. However, hypovolemia and renal hypoperfusion can occur in patients with AKI if excessive fluid removal is pursued with diuretics or extracorporeal therapy. Thus, accurate assessment of fluid status and careful definition of targets are needed at all stages to improve clinical outcomes. A conservative strategy of fluid management was recently tested and found to be effective in a large, randomized, controlled trial in patients with acute lung injury. Similar randomized, controlled studies in patients with AKI now seem justified.

Prowle, J. R. et al. *Nat. Rev. Nephrol.* 6, 107–115 (2010); published online 22 December 2009; [doi:10.1038/nrneph.2009.213](https://doi.org/10.1038/nrneph.2009.213)





# The risks of IV fluids



**Table 2** | Publications describing two groups of critically ill patients with differing fluid balances where a renal outcome was reported\*

Reference	Study type	Population	n	Average fluid balance in less-positive group	Average fluid balance in more-positive group	Renal function measure	Renal outcome with more-restrictive fluid balance strategy	Principal outcome with more-restrictive fluid balance strategy
ARDS Clinical Trials Network (2006) <sup>88</sup>	Multicenter RCT	ARDS	1,000	-136 ml on day 7	+6,992 ml on day 7	Need for RRT; change in creatinine	No difference	Shorter duration of ventilation and ICU stay
Martin <i>et al.</i> (2005) <sup>86</sup>	Single-center RCT	Mixed ALI	40	-5,480 ml on day 5	-1,490 ml on day 5	Change in creatinine	No difference	Improved oxygenation
Martin <i>et al.</i> (2002) <sup>85</sup>	Single-center RCT	ALI after trauma	37	-3,300 ml on day 5	+500 ml on day 5	Change in creatinine	No difference	Improved oxygenation
Mitchell <i>et al.</i> (1992) <sup>127</sup>	Single-center RCT	Mixed ICU needing PAC	102	+142 ml	+2,239 ml	Change in creatinine	Small rise in creatinine	Shorter duration of ventilation and ICU stay
Bouchard <i>et al.</i> (2009) <sup>25</sup>	Retrospective observational	Mixed ICU with AKI	542	<10% rise	>10% rise	Dialysis independence	Improved	Decrease in mortality
Payen <i>et al.</i> (2008) <sup>6</sup>	Retrospective observational	Mixed ICU with or without AKI	3,147	-1,000 ml	+3,000 ml	Renal SOFA score	Improved	Decrease in mortality in patients with AKI
Vidal <i>et al.</i> (2008) <sup>72</sup>	Prospective observational	Mixed ICU with elevated or normal IAP	83	+5,000 ml	+9,000 ml	Renal SOFA score	Improved	Normal IAP associated with less organ failure and shorter ICU stay
Adesanya <i>et al.</i> (2008) <sup>128</sup>	Retrospective observational	Surgical ICU	41	+5 kg	+8.3 kg	Change in creatinine	No difference	Shorter duration of ventilation and ICU stay
McArdle <i>et al.</i> (2007) <sup>87</sup>	Retrospective observational	Surgical ICU	100	+7,500 ml	+10,000 ml	Change in creatinine	No difference	Decrease in postoperative complications
Arlati <i>et al.</i> (2007) <sup>99</sup>	Prospective observational	Burns ICU	24	+7,500 ml	+12,000 ml	Urine output	No difference	Decrease in organ dysfunction score

\*See Supplementary Information online for systematic search strategy. Abbreviations: AKI, acute kidney injury; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; IAP, intra-abdominal pressure; ICU, intensive care unit; PAC, pulmonary artery catheter; RCT, randomized, controlled trial; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.



IV fluids always looks bad!!

37<sup>th</sup> Vicenza Course on AKI & CRRT – May 28-30, 2019

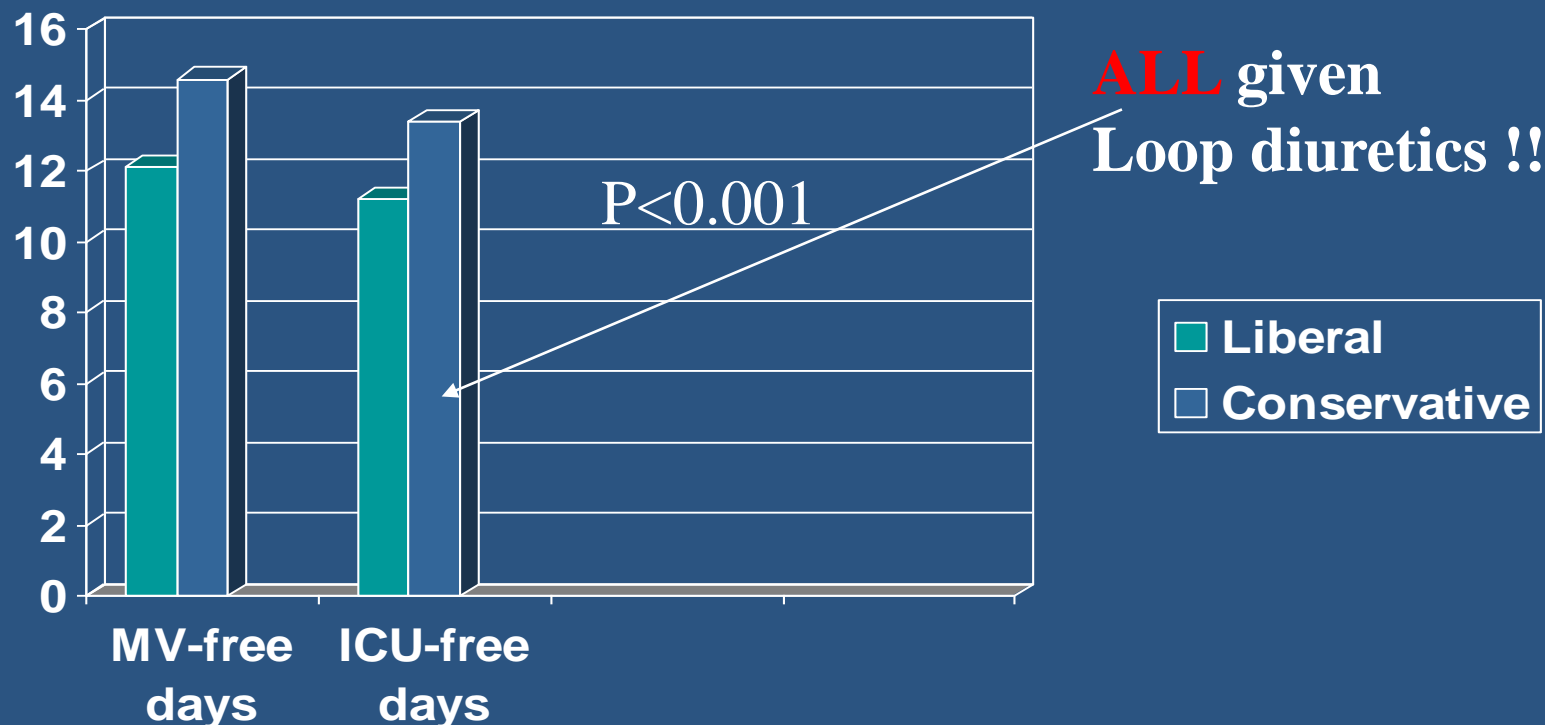
# The “FACTTs”

- **NEJM 2006; 354: 1-12**
- Comparison of two fluid-management strategies in acute lung injury
- NB: Pneumonia + sepsis >80% of patients
- 503 = conservative strategy
- 497 = liberal strategy





# Liberal vs. conservative fluid use



**NB: need for RRT 2.8 vs. 1.9% ( $p=0.06$ )**  
**Mortality 28.4 vs. 25.5%.**  
**All in favour of "dry"**



# Positive fluid balance is bad in AKI

original article

<http://www.kidney-international.org>

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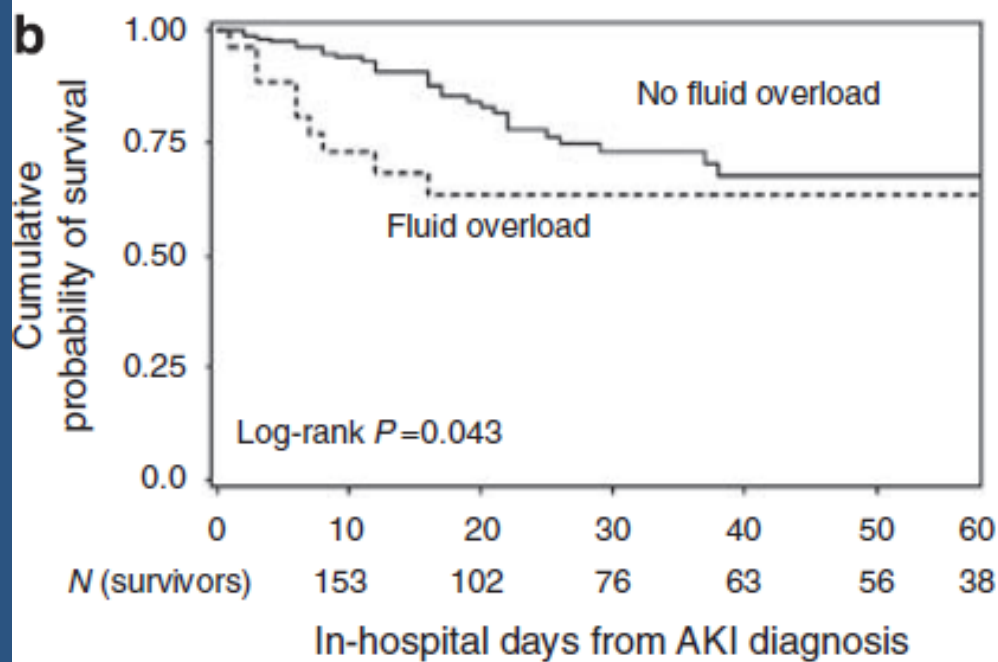
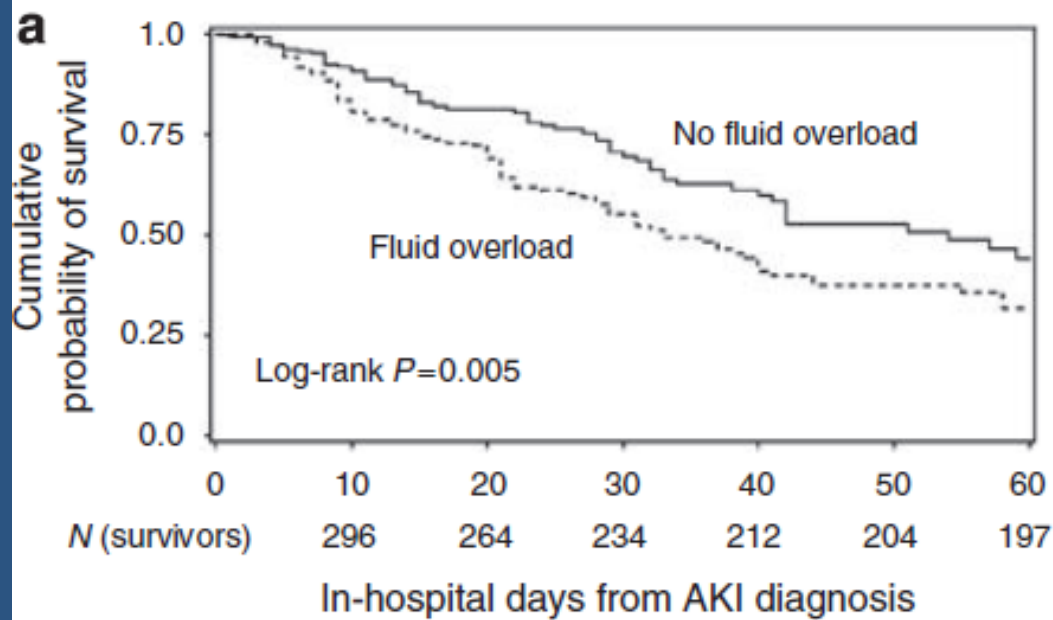
## Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury

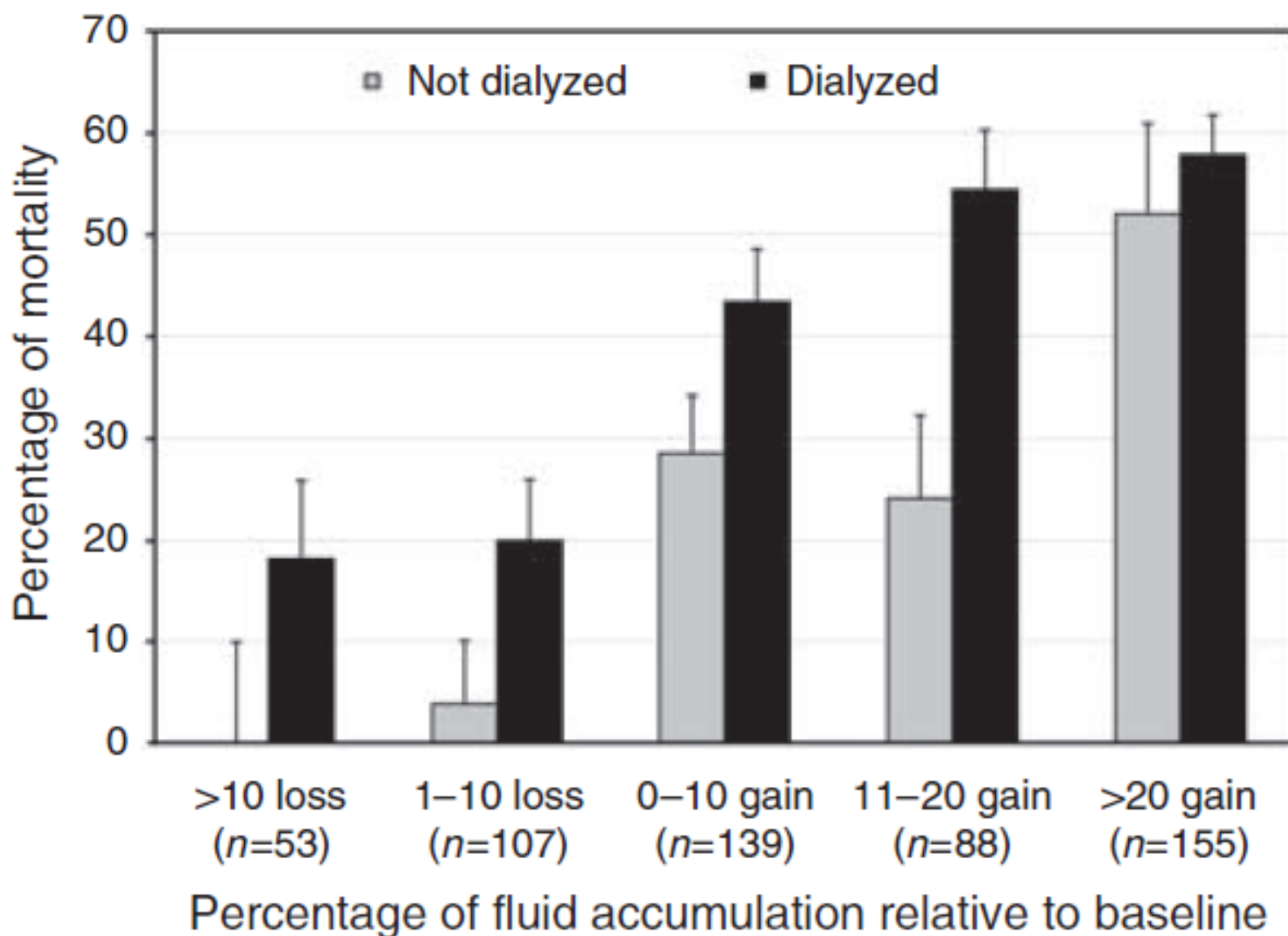
Josée Bouchard<sup>1</sup>, Sharon B. Soroko<sup>1</sup>, Glenn M. Chertow<sup>2</sup>, Jonathan Himmelfarb<sup>3</sup>, T. Alp Ikizler<sup>4</sup>, Emil P. Paganini<sup>5</sup> and Ravindra L. Mehta<sup>1</sup>, Program to Improve Care in Acute Renal Disease (PICARD) Study Group

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# A positive fluid balance is associated with a worse outcome in patients with acute renal failure

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**Table 2**

**Hazard ratios: results of multivariate Cox regression analysis for 60-day mortality in critically ill patients with acute renal failure**

Characteristic	Hazard ratio	95% CI	P value
Age	1.02	1.01–1.03	<0.001
SAPS II (per point)	1.03	1.02–1.04	<0.001
Heart failure	1.38	1.05–1.81	0.02
Medical admission	1.68	1.35–2.08	<0.001
Mean fluid balance, L/24 hours	1.21	1.13–1.28	<0.001
Mechanical ventilation	1.55	1.14–2.11	<0.001
Liver cirrhosis	2.73	1.88–3.95	<0.001

# The type of fluid matters

PRELIMINARY  
COMMUNICATION

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

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Colin Hegarty, BSc  
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Lisa Ho, MClInPharm  
Michael Bailey, PhD

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

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

**Design, Setting, and Patients** Prospective, open-label, sequential period pilot study of 760 patients admitted consecutively to the intensive care unit (ICU) during the control period (February 18 to August 17, 2008) compared with 773 patients admitted consecutively during the intervention period (February 18 to August 17, 2009) at a university-affiliated hospital in Melbourne, Australia.

**T**HE ADMINISTRATION OF INTRAVENOUS chloride is ubiquitous

**Interventions** During the control period, patients received standard intravenous fluids. After a 6-month phase-out period (August 18, 2008, to February 17, 2009), any use of chloride-rich intravenous fluids (0.9% saline, 4% succinylated gelatin solution, or 4% albumin solution) was restricted to attending specialist approval only during the intervention period; patients instead received a lactated solution (Hartmann solution), a balanced solution (Plasma-Lyte 148), and chloride-poor 20% albumin.



**Results** Chloride administration decreased by 144 504 mmol (from 694 to 496 mmol/patient) from the control period to the intervention period. Comparing the control period with the intervention period, the mean serum creatinine level increase while in the ICU was 22.6  $\mu\text{mol/L}$  (95% CI, 17.5-27.7  $\mu\text{mol/L}$ ) vs 14.8  $\mu\text{mol/L}$  (95% CI, 9.8-19.9  $\mu\text{mol/L}$ ) ( $P=.03$ ), the incidence of injury and failure class of RIFLE-defined AKI was 14% (95% CI, 11%-16%;  $n=105$ ) vs 8.4% (95% CI, 6.4%-10%;  $n=65$ ) ( $P<.001$ ), and the use of RRT was 10% (95% CI, 8.1%-12%;  $n=78$ ) vs 6.3% (95% CI, 4.6%-8.1%;  $n=49$ ) ( $P=.005$ ). After adjustment for covariates, this association remained for incidence of injury and failure class of RIFLE-defined AKI (odds ratio, 0.52 [95% CI, 0.37-0.75];  $P<.001$ ) and use of RRT (odds ratio, 0.52 [95% CI, 0.33-0.81];  $P=.004$ ). There were no differences in hospital mortality, hospital or ICU length of stay, or need for RRT after hospital discharge.

**Conclusion** The implementation of a chloride-restrictive strategy in a tertiary ICU was associated with a significant decrease in the incidence of AKI and use of RRT.





ORIGINAL ARTICLE

## Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D.,  
Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S.,  
Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D.,  
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Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,  
and Todd W. Rice, M.D., for the SALT-ED Investigators\*

### METHODS

We conducted a single-center, pragmatic, multiple-crossover trial comparing balanced crystalloids (lactated Ringer's solution or Plasma-Lyte A) with saline among adults who were treated with intravenous crystalloids in the emergency department and were subsequently hospitalized outside an ICU. The type of crystalloid that was administered in the emergency department was assigned to each patient on the basis of calendar month, with the entire emergency department crossing over between balanced crystalloids and saline monthly during the 16-month trial. The primary outcome was hospital-free days (days alive after discharge before day 28). Secondary outcomes included major adverse kidney events within 30 days — a composite of death from any cause, new renal-replacement therapy, or persistent renal dysfunction (defined as an elevation of the creatinine level to  $\geq 200\%$  of baseline) — all censored at hospital discharge or 30 days, whichever occurred first.

**Table 2. Crystalloids Received in the Emergency Department According to Assigned Treatment Group.\***

Variable	Balanced Crystalloids (N = 6708)	Saline (N = 6639)
Total crystalloid volume		
Mean — ml	1608±1095	1597±1105
Median (IQR) — ml	1089 (1000–2000)	1071 (1000–2000)
≥2000 ml — no. (%)	2207 (32.9)	2150 (32.4)
Median volume of balanced crystalloids (IQR) — ml	1000 (1000–2000)	0
Median volume of saline (IQR) — ml	0	1000 (1000–2000)
Percentage of crystalloid volume consistent with assigned group — no. (%)		
100%: per-protocol population	5620 (83.8)	6160 (92.8)
51–99%	514 (7.7)	270 (4.1)
1–50%	254 (3.8)	131 (2.0)
0%	320 (4.8)	78 (1.2)

\* Plus-minus values are means ±SD. Percentages may not sum to 100 because of rounding.

**Table 3. Clinical Outcomes According to Assigned Treatment Group in the Intention-to-Treat Analysis.**

Outcome	Balanced Crystalloids (N = 6708)	Saline (N = 6639)	Adjusted Odds Ratio (95% CI)*	Adjusted P Value
Median hospital-free days to day 28 (IQR)	25 (22–26)	25 (22–26)	0.98 (0.92–1.04)	0.11
Major adverse kidney event within 30 days — no. (%)	315 (4.7)	370 (5.6)	0.82 (0.70–0.95)	0.01
Death — no. (%)	94 (1.4)	102 (1.5)	0.89	
New renal-replacement therapy — no./total no. (%)†	18/6582 (0.3)	31/6530 (0.5)	0.56	
Final serum creatinine ≥200% of baseline — no./total no. (%)†	253/6582 (3.8)	293/6530 (4.5)	0.84	
Stage 2 or higher acute kidney injury — no./total no. (%)†	528/6582 (8.0)	560/6530 (8.6)	0.91 (0.80–1.03)	0.14
In-hospital death — no. (%)	95 (1.4)	105 (1.6)	0.88 (0.66–1.16)	0.36

ORIGINAL ARTICLE

## Balanced Crystalloids versus Saline in Critically Ill Adults

Matthew W. Semler, M.D., Wesley H. Self, M.D., M.P.H.,  
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Li Wang, M.S., Daniel W. Byrne, M.S., Joanna L. Stollings, Pharm.D.,  
Avinash B. Kumar, M.D., Christopher G. Hughes, M.D.,  
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Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,  
and Todd W. Rice, M.D., for the SMART Investigators  
and the Pragmatic Critical Care Research Group\*

### METHODS

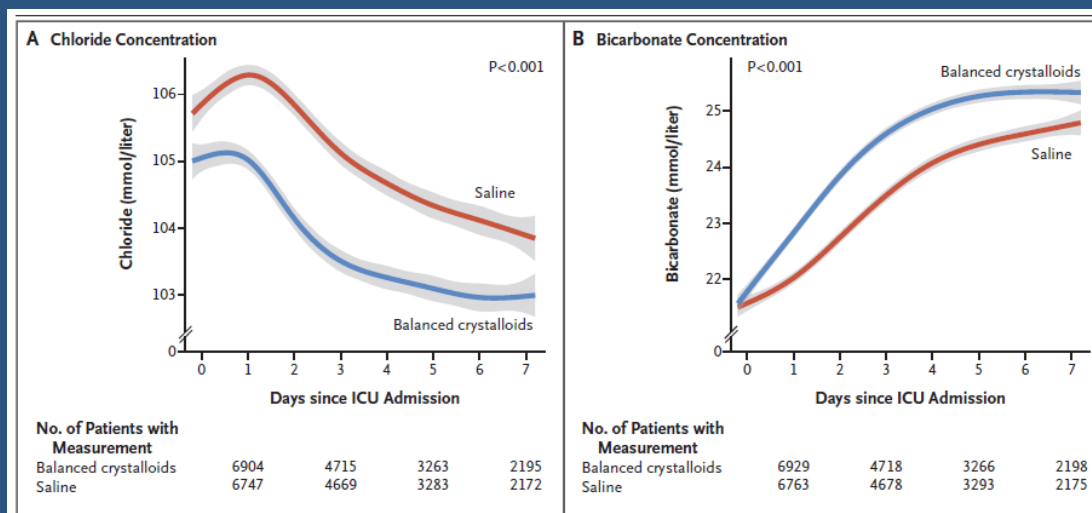
In a pragmatic, cluster-randomized, multiple-crossover trial conducted in five intensive care units at an academic center, we assigned 15,802 adults to receive saline (0.9% sodium chloride) or balanced crystalloids (lactated Ringer's solution or Plasma-Lyte A) according to the randomization of the unit to which they were admitted. The primary outcome was a major adverse kidney event within 30 days — a composite of death from any cause, new renal-replacement therapy, or persistent renal dysfunction (defined as an elevation of the creatinine level to  $\geq 200\%$  of baseline) — all censored at hospital discharge or 30 days, whichever occurred first.

### RESULTS



**Table 1. Participant Characteristics at Baseline.\***

Characteristic	Balanced Crystalloids (N=7942)	Saline (N=7860)
Age — yr		
Median	58	58
Interquartile range	44–69	44–69
Male sex — no. (%)	4540 (57.2)	4557 (58.0)
White race — no. (%)†	6384 (80.4)	6322 (80.4)
Weight — kg‡		
Median	80	79
Interquartile range	69–96	68–95
Coexisting renal conditions — no. (%)		
Chronic kidney disease of stage 3 or higher§	1388 (17.5)	1360 (17.3)
Previous receipt of renal-replacement therapy — no. (%)	384 (4.8)	402 (5.1)
Source of admission to ICU — no. (%)		
Emergency department	3975 (50.1)	3997 (50.9)
Operating room	1732 (21.8)	1649 (21.0)
Transfer from another hospital	1038 (13.1)	1018 (13.0)
Hospital ward	788 (9.9)	780 (9.9)
Outpatient	363 (4.6)	359 (4.6)
Another ICU within hospital	46 (0.6)	57 (0.7)



**Table 2. Clinical Outcomes.\***

Outcome	Balanced Crystalloids (N=7942)	Saline (N=7860)	Adjusted Odds Ratio (95% CI)†	P Value‡
<b>Primary outcome</b>				
Major adverse kidney event within 30 days — no. (%)‡	1139 (14.3)	1211 (15.4)	0.90 (0.82 to 0.99)	0.04
<b>Components of primary outcome</b>				
In-hospital death before 30 days — no. (%)	818 (10.3)	875 (11.1)	0.90 (0.80 to 1.01)	0.06
Receipt of new renal-replacement therapy — no./total no. (%)§	189/7558 (2.5)	220/7458 (2.9)	0.84 (0.68 to 1.02)	0.08

Renal-replacement therapy-free days¶			1.11 (1.02 to 1.20)	0.01
Median	28.0	28.0		
Interquartile range	28.0 to 28.0	28.0 to 28.0		
Mean	25.0±8.6	24.8±8.9		



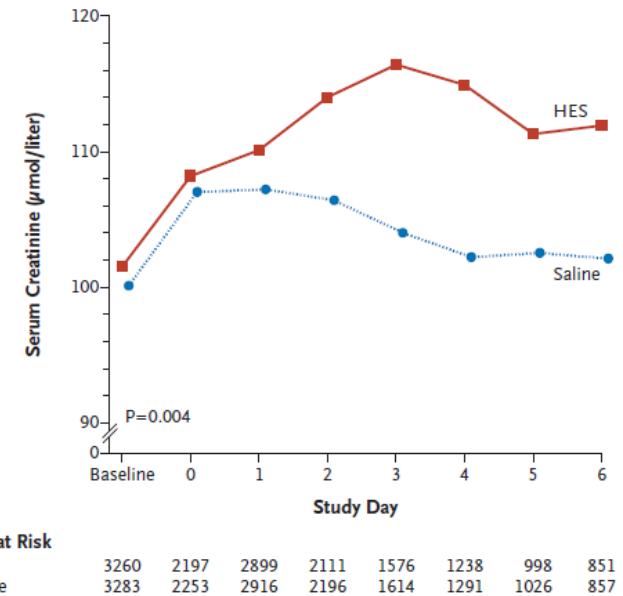


## ORIGINAL ARTICLE

## Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group\*

A Serum Creatinine



## METHODS

We randomly assigned 7000 patients who had been admitted to an intensive care unit (ICU) in a 1:1 ratio to receive either 6% HES with a molecular weight of 130 kD and a molar substitution ratio of 0.4 (130/0.4, Voluven) in 0.9% sodium chloride or 0.9% sodium chloride (saline) for all fluid resuscitation until ICU discharge, death, or 90 days after randomization. The primary outcome was death within 90 days. Secondary outcomes included acute kidney injury and failure and treatment with renal-replacement therapy.

Use of renal-replacement therapy

235/3352 (7.0)

196/3375 (5.8)

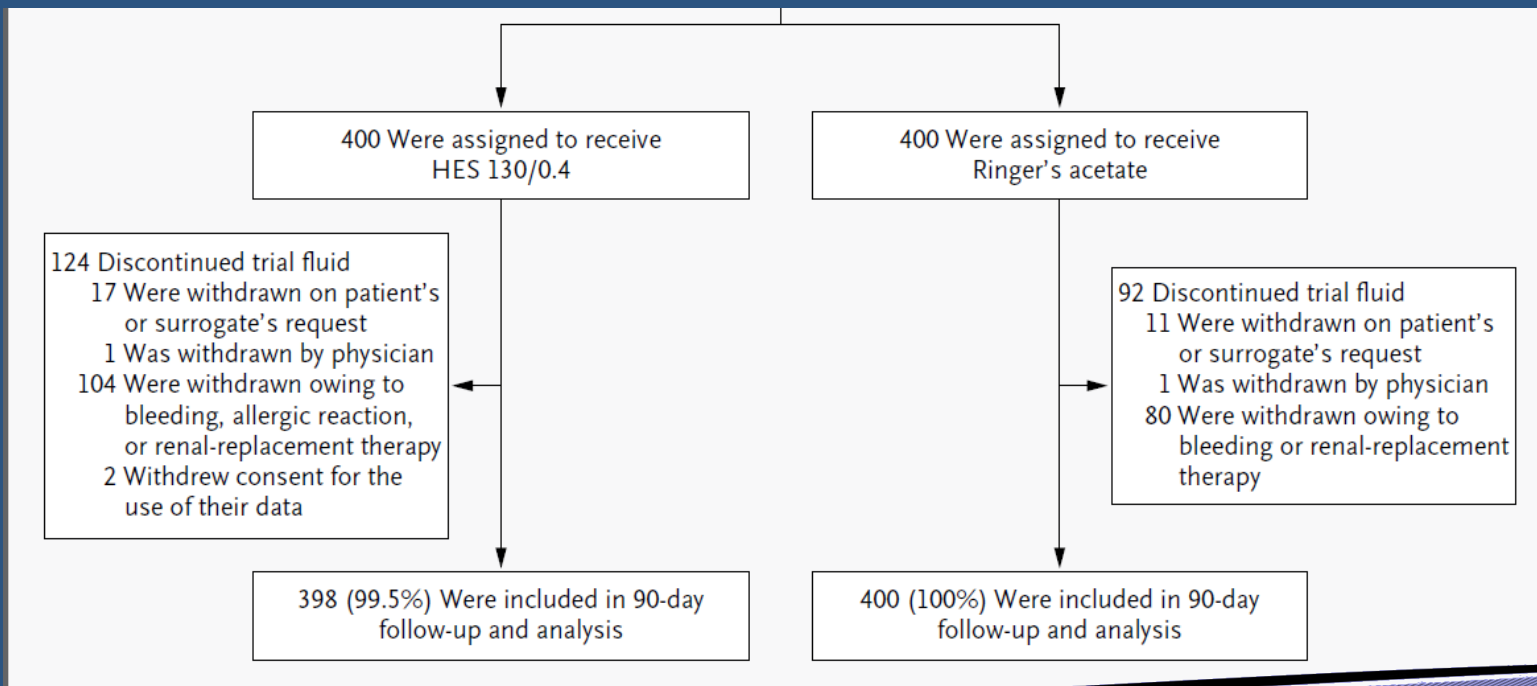
1.21 (1.00 to 1.45)

0.04

ORIGINAL ARTICLE

# Hydroxyethyl Starch 130/0.4 versus Ringer's Acetate in Severe Sepsis

Anders Perner, M.D., Ph.D., Nicolai Haase, M.D.,  
Anne B. Guttormsen, M.D., Ph.D., Jyrki Tenhunen, M.D., Ph.D.,





**Table 3. Primary and Secondary Outcomes.\***

Outcome	HES 130/0.4 (N = 398)	Ringer's Acetate (N = 400)	Relative Risk (95% CI)	P Value
<b>Primary outcome</b>				
Dead or dependent on dialysis at day 90 — no. (%)	202 (51)	173 (43)	1.17 (1.01–1.36)	0.03
Dead at day 90 — no. (%)	201 (51)	172 (43)	1.17 (1.01–1.36)	0.03
Dependent on dialysis at day 90 — no. (%)	1 (0.25)	1 (0.25)	—	1.00
<b>Secondary outcome measures</b>				
Dead at day 28 — no. (%)	154 (39)	144 (36)	1.08 (0.90–1.28)	0.43
Severe bleeding — no. (%) <sup>†</sup>	38 (10)	25 (6)	1.52 (0.94–2.48)	0.09
Severe allergic reaction — no. (%) <sup>†</sup>	1 (0.25)	0	—	0.32
SOFA score at day 5 — median (interquartile range)	6 (2–11)	6 (0–10)	—	0.64
Use of renal-replacement therapy — no. (%) <sup>‡</sup>	87 (22)	65 (16)	1.35 (1.01–1.80)	0.04





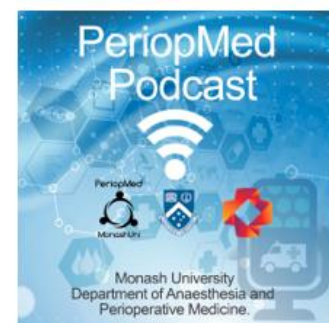
The NEW ENGLAND  
JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery

P.S. Myles, R. Bellomo, T. Corcoran, A. Forbes, P. Peyton, D. Story, C. Christophi, K. Leslie, S. McGuinness, R. Parke, J. Serpell, M.T.V. Chan, T. Painter, S. McCluskey, G. Minto, and S. Wallace, for the Australian and New Zealand College of Anaesthetists Clinical Trials Network and the Australian and New Zealand Intensive Care Society Clinical Trials Group\*

Monash Perioperative Medicine  
podcasts



# 3000 patients, 47 hospitals, 7 countries



## AUSTRALIA (1686 patients)

Alfred Hospital  
Royal Melbourne Hospital  
Austin Health  
St Vincent's Hospital  
Western Hospital  
Geelong Hospital  
Dandenong Hospital  
Monash Medical Centre  
Peter MacCallum  
Maroondah Hospital  
Epworth Hospital  
Coffs Harbour Health Campus  
Macquarie University Hospital  
Prince of Wales Hospital  
John Hunter Hospital  
Cairns Hospital  
Princess Alexandra Hospital  
Redcliffe Hospital  
Prince Charles Hospital  
Nepean Hospital  
Royal Hobart Hospital  
Launceston General Hospital  
Royal Adelaide Hospital  
Royal Perth Hospital

## USA (150 patients)

Cleveland Clinic  
Wake Forest  
Weill Medical College

## NEW ZEALAND (94 patients)

Auckland CVICU  
Auckland Hospital  
Wellington Hospital

## CANADA (471 patients)

Toronto General Hospital  
Royal Victoria Infirmary  
Royal Victoria Montreal  
Toronto Western  
Kingston General Hospital

## HONG KONG (231 patients)

Prince of Wales Hospital

## ITALY (64 patients)

Scientific Institute San  
Raffaele

## UK (304 patients)

Bassildon and Thurrock  
Plymouth NHS Trust  
St Georges Healthcare NHS Trust  
Kings College Hospital  
Kettering General Hospital  
Freeman Hospital  
Sunderland Hospital  
Russells Hall Hospital  
Royal Free Hospital  
University Hospital of North Durham





# Background

- Routine management of perioperative hypotension = IV fluid bolus +++
- Traditional IV fluid therapy
  - 6 L on day of surgery, then 3 L/day → 4-6 kg weight increase
- Can a restrictive fluid regimen improve outcome?
  - less tissue and pulmonary oedema, haemodilution ...
  - but more hypotension: vasopressor support (& need for ICU?)
    - metaraminol, noradrenaline, dopexamine





# Restrictive Fluid Therapy

1. Lobo D, et al. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. Lancet 2002
  - RCT, 20 colonic surgical patients
  - restrictive group: less complications (0 vs. 7,  $P=0.01$ ), shorter hospital stay (6 vs. 9 days,  $P=0.001$ )
2. Brandstrup B, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial Ann Surg 2003
  - RCT, 172 colorectal surgical patients
  - restrictive group: less complications (33% vs. 51%,  $P=0.013$ ), less deaths (0 vs. 4,  $P=0.12$ )
3. Nisanevich V, et al. Effect of intraoperative fluid management on outcome after intraabdominal surgery. Anesthesiology 2005
  - RCT, 152 abdominal surgical patients
  - restrictive group: less complications ( $P=0.046$ ), shorter hospital stay ( $P=0.01$ )





# Perioperative Fluid Management Strategies in Major Surgery: A Stratified Meta-Analysis

Tomas Corcoran, MB, BCh, BAO, MRCPI, FCARCSCI, MD, FCICM,\* Julia Emma Joy Rhodes, MBBS (Hons),\* Sarah Clarke, MBBS (Hons),† Paul S. Myles, MB, BS, MPH, MD, FCARCSCI, FANZCA, FRCA,‡ and Kwok M. Ho, MPH, PhD, FRCP, FCICMS

Anesth Analg 2012



## Scottish Intercollegiate Guidelines Network



### Postoperative management in adults

A practical guide to postoperative care for clinical staff

## British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients

### GIFTASUP

Jeremy Powell-Tuck (chair)<sup>1</sup>, Peter Gosling<sup>2</sup>, Dileep N Lobo<sup>1,3</sup>, Simon P Allison<sup>1</sup>, Gordon L Carlson<sup>3,4</sup>, Marcus Gore<sup>3</sup>, Andrew J Lewington<sup>5</sup>, Rupert M Pearse<sup>6</sup>, Monty G Mythen<sup>6</sup>

Thiele et al. *Perioperative Medicine* (2016) 5:24  
DOI 10.1186/s13741-016-0049-9

Perioperative Medicine

### CONSENSUS STATEMENT

Open Access



American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on perioperative fluid management within an enhanced recovery pathway for colorectal surgery

### Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice

A. Feldheiser<sup>1</sup>, O. Aziz<sup>2</sup>, G. Baldini<sup>3</sup>, B. P. B. W. Cox<sup>4</sup>, K. C. H. Fearon<sup>5</sup>, L. S. Feldman<sup>6</sup>, T. J. Gan<sup>7</sup>, R. H. Kennedy<sup>8</sup>, O. Ljungqvist<sup>9</sup>, D. N. Lobo<sup>10</sup>, T. Miller<sup>7</sup>, F. F. Radtke<sup>1</sup>, T. Ruiz Garces<sup>11</sup>, T. Schricker<sup>12</sup>, M. J. Scott<sup>13</sup>, J. K. Thacker<sup>14</sup>, L. M. Ytrebø<sup>15</sup> and F. Carli<sup>3</sup>

*Acta Anaesthesiologica Scandinavica* **60** (2016) 289–334

JAMA Surgery | Review

### 'Enhanced Recovery After Surgery A Review

Olle Ljungqvist, MD, PhD; Michael Scott, MD; Kenneth C. Fearon, MD, PhD\*

*"maintaining patients near zero-fluid balance in the perioperative period leads to a decrease in postoperative complications with a reduction in length of hospital stay"*



# The RELIEF Trial

[www.relief.org.au](http://www.relief.org.au)

## Hypothesis

A restrictive fluid regimen for adults undergoing major surgery leads to reduced complications and improved disability-free survival when compared with a liberal fluid regimen

- Study population: major abdominal surgery
- International, multicentre, randomised, single-blind, pragmatic trial

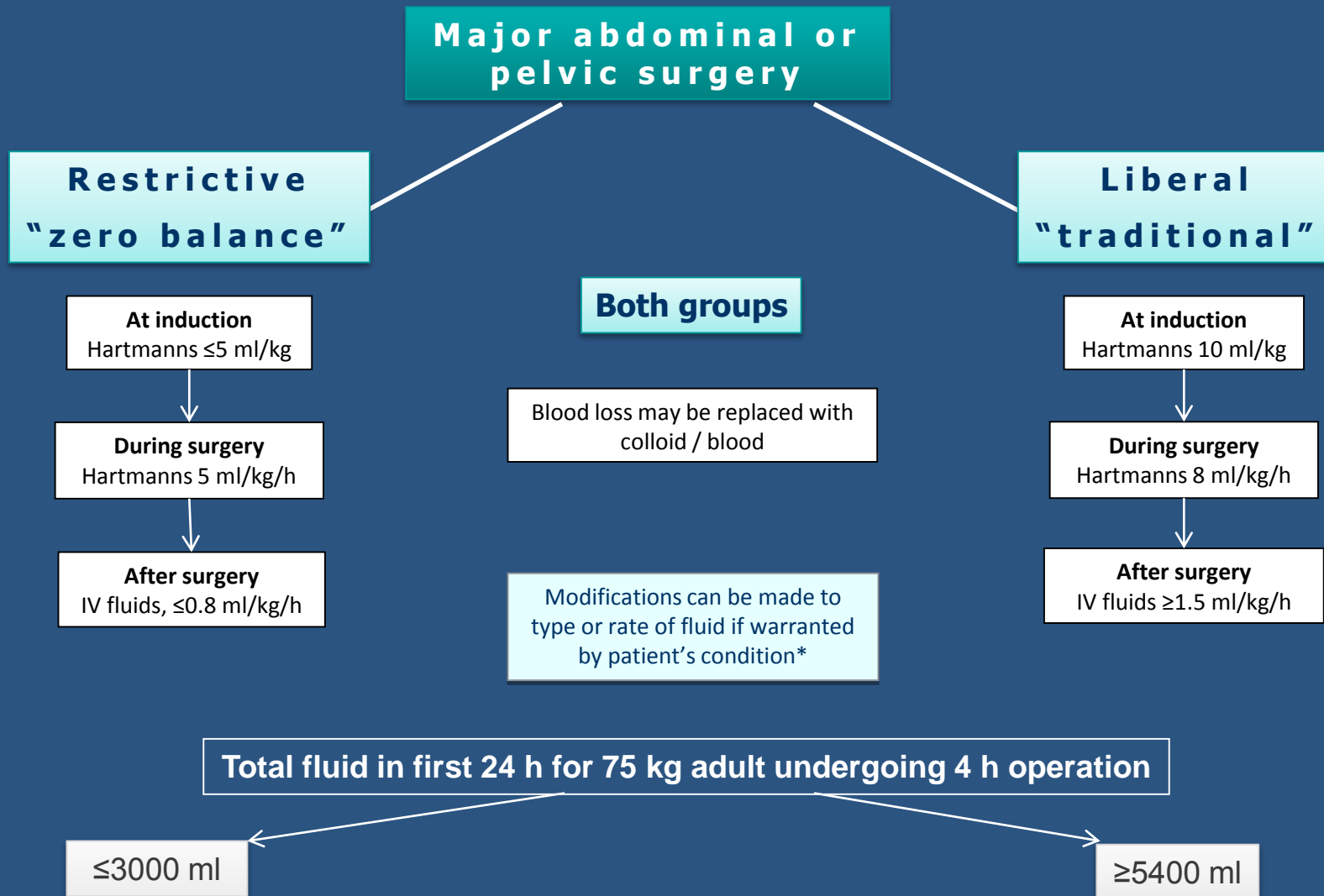
### First 24 h

Liberal group  $\approx$  5-6 litres

Restrictive group  $\approx$  2-3 litres







\*analysis by ITT





# Primary Endpoint of the Trial

## PERIOPERATIVE MEDICINE

Anesthesiology 2015

### Measurement of Disability-free Survival after Surgery

Mark A. Shulman, M.B., B.S., M.P.H., F.A.N.Z.C.A.,  
Paul S. Myles, M.B., B.S., M.P.H., M.D., F.A.N.Z.C.A., F.R.C.A.,  
Matthew T. V. Chan, M.B., B.S., F.A.N.Z.C.A., David R. McIlroy, M.B., B.S., M.Clin.Epi, F.A.N.Z.C.A.,  
Sophie Wallace, M.P.H., Jennie Ponsford, B.A.(Hons), M.A.(Clin Neuropsych), Ph.D.





# Secondary Endpoints

- Acute kidney injury
- Major septic complications (composite, plus individual) = any of:
  - sepsis, surgical site infection, anastomotic leak, pneumonia
- Also:
  - mortality (30 and 90 days, 1 year)
  - unplanned admission to ICU
  - quality of recovery (QoR-15)
  - ICU and hospital stay



# Results

## Group (IV fluid) Separation

Fluids	"Liberal" (traditional)	"Restrictive" (zero balance)	P value
<i>Duration of surgery</i>	3.3 h	3.3 h	
<b>Intraoperative</b> , ml	3000 (2100-3850)	1680 (1200-2300)	<0.001
<b>Total fluids</b> (0-24 h)	6146 (5000-7410)	3671 (2885-4880)	<0.001
Fluid balance, ml	3092 (2010-4241)	1380 (540-2338)	<0.001
Weight gain, kg	1.6 (0.0 – 3.6)	0.3 (-1.0 – 1.9)	<0.001

median (IQR)



## RELIEF Trial: Surgery

	<b>Liberal (n=1493)</b>	<b>Restrictive (n=1490)</b>
<b>Type of surgery – no. (%)</b>		
Oesophageal/gastric	257 (17)	286 (19)
Hepatobiliary	139 (9.3)	133 (8.9)
Colorectal	651 (44)	646 (43)
Urological/renal	223 (15)	220 (15)
Gynaecological	139 (9.3)	135 (9.1)
Other	84 (5.6)	70 (4.7)
Open	788 (53)	818 (55)
Laparoscopic	463 (31)	458 (31)
Laparoscopic-assisted	242 (16)	214 (14)
Duration of surgery - hour	3.3 (2.5-4.5)	3.3 (2.4-4.6)

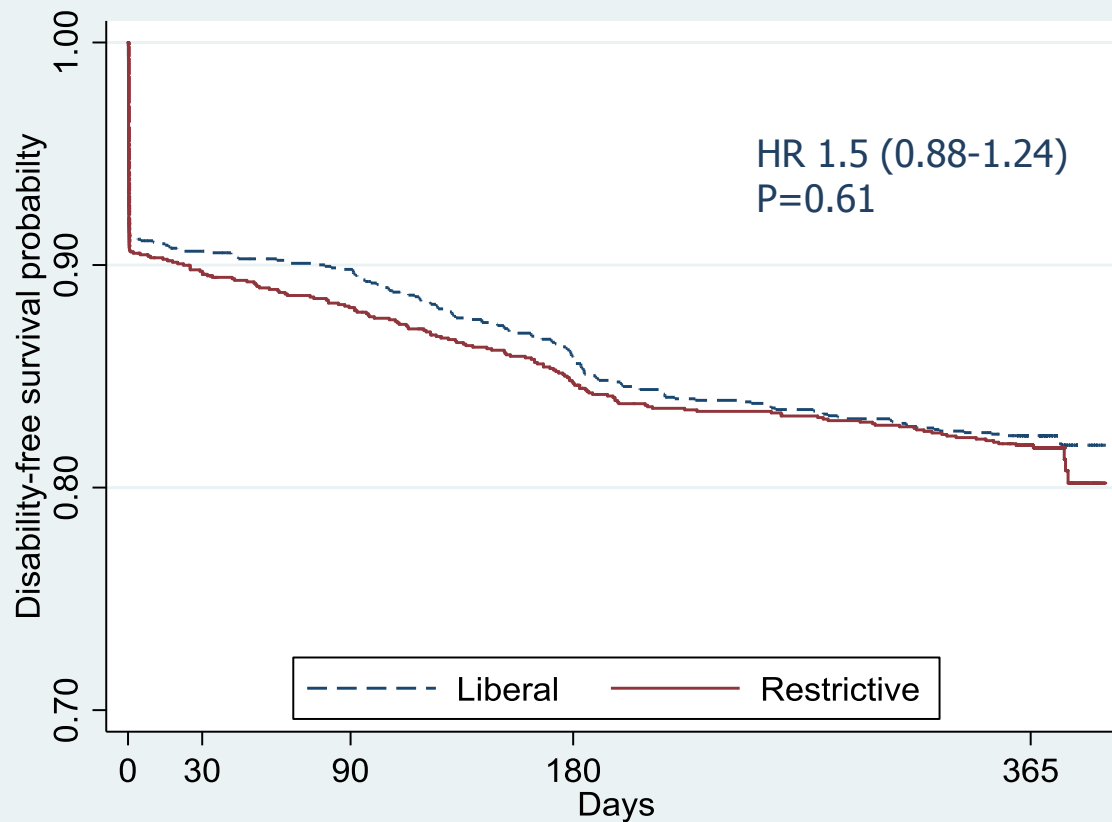




Factor	Liberal (N=1493)	Restrictive (N=1490)
Patient age - years	66 ± 13	66 ± 13
Male/female – no. (%male)	783/710 (52)	771/719 (52)
Body weight – kg	83 (69 -102)	84 (68-102)
<b>ASA physical status</b>		
1	21 (1.4)	25 (1.7)
2	540 (36)	542 (36)
3	868 (58)	849 (57)
4	64 (4.3)	74 (5.0)
Preoperative WHODAS score - median (IQR)	15 (13-21)	15 (13-21)
<b>Country – no. (%)</b>		
Australia	841 (56)	836 (56)
New Zealand	48 (3.2)	46 (3.1)
Canada	247 (17)	250 (17)
Hong Kong	116 (7.8)	111 (7.4)
United Kingdom	134 (9.0)	141 (9.5)
Italy	32 (2.1)	32 (2.1)
United States	75 (5.0)	74 (5.0)
<b>Medical conditions – no. (%)</b>		
Hypertension	908 (61)	899 (60)
Coronary artery disease	250 (17)	212 (14)
Heart failure	47 (3.1)	57 (3.8)
Previous MI	146 (9.8)	122 (8.2)
Peripheral vascular disease	92 (6.2)	95 (6.4)
Current smoker	204 (14)	194 (13)
History of stroke or TIA	115 (7.7)	105 (7.0)
COPD	254 (17)	244 (16)
Moderate or severe renal disease	108 (7.2)	101 (6.8)
<b>Preoperative investigations – no. (%)</b>		
Creatinine - µmol/L	83 ± 29	82 ± 28
Albumin – g/L	39 (35-42)	39 (35-42)
<b>Perioperative care</b>		
Neuraxial block - no. (%)	385 (26)	409 (27)
PPV/SVV or Oes. Doppler monitor- no. (%)	201 (14)	210 (14)
<b>Surgery – no. (%)</b>		
Clean	557 (38)	531 (36)
Clean-contaminated	836 (57)	862 (59)
Contaminated	58 (4.0)	56 (3.8)
Dirty	12 (0.8)	14 (1.0)



# Primary Outcome



Number at risk

Liberal	1493	1343	1320	1249	859
Restrictive	1490	1323	1292	1228	835

value



# Secondary Outcomes

Outcome	Liberal (n=1493)	Restrictive (n=1490)	RR (95% CI)	P value
Acute kidney injury				
Septic outcome or death				
Surgical site infection				
Sepsis				
Anastomotic leak				
Pneumonia				
Renal replacement therapy to 90 days				
QoR-15 score (day 1)				
Hospital stay - days				
Mortality				
at 90 days				
at 1 year				



# Acute Kidney Injury

Outcome	Liberal (n=1493)	Restrictive (n=1490)	RR (95% CI)	P value
Preop. Creatinine, $\mu\text{mol/L}$	$83 \pm 29$	$82 \pm 28$	-	-
Lowest systolic BP, mmHg intraoperative recovery room	$88 \pm 15$ $119 \pm 22$	$86 \pm 15$ $116 \pm 22$	-	<b>0.020</b> <b>0.002</b>
Urine output, ml (intraop.)	350 (200-600)	250 (140-440)	-	<b>&lt;0.001</b>
Oliguria/anuria (intraop.)	347 (27)	486 (39)	1.42 (1.26 - 1.59)	<b>&lt;0.001</b>
Acute kidney injury	72 (5.0)	124 (8.6)	1.71 (1.29 - 2.27)	<b>&lt;0.001</b>
Renal replacement therapy to 90 days	4 (0.3)	13 (0.9)	3.27 (1.01 - 13.8)	<b>0.048</b>





# Acute Kidney Injury

Outcome	Liberal (n=1493)	Restrictive (n=1490)	Odds Ratio	P value
<b>KDIGO</b>				
Stage 1	15.1%	19.6%	1.43	<b>&lt;0.001</b>
Stage 2	2.5%	4.5%	1.96	<b>0.002</b>
Stage 3	1.3%	2.3%	1.95	<b>0.022</b>
Stages 1-3 (all)	19.0%	26.4%	1.39	<b>&lt;0.001</b>
Stages 2 or 3	3.8%	6.8%	1.78	<b>&lt;0.001</b>
KDIGO Stage 2 or 3 <b>without</b> adjustment for fluid balance	3.2%	6.4%	2.0	<b>&lt;0.001</b>

\*KDIGO without urine output criteria



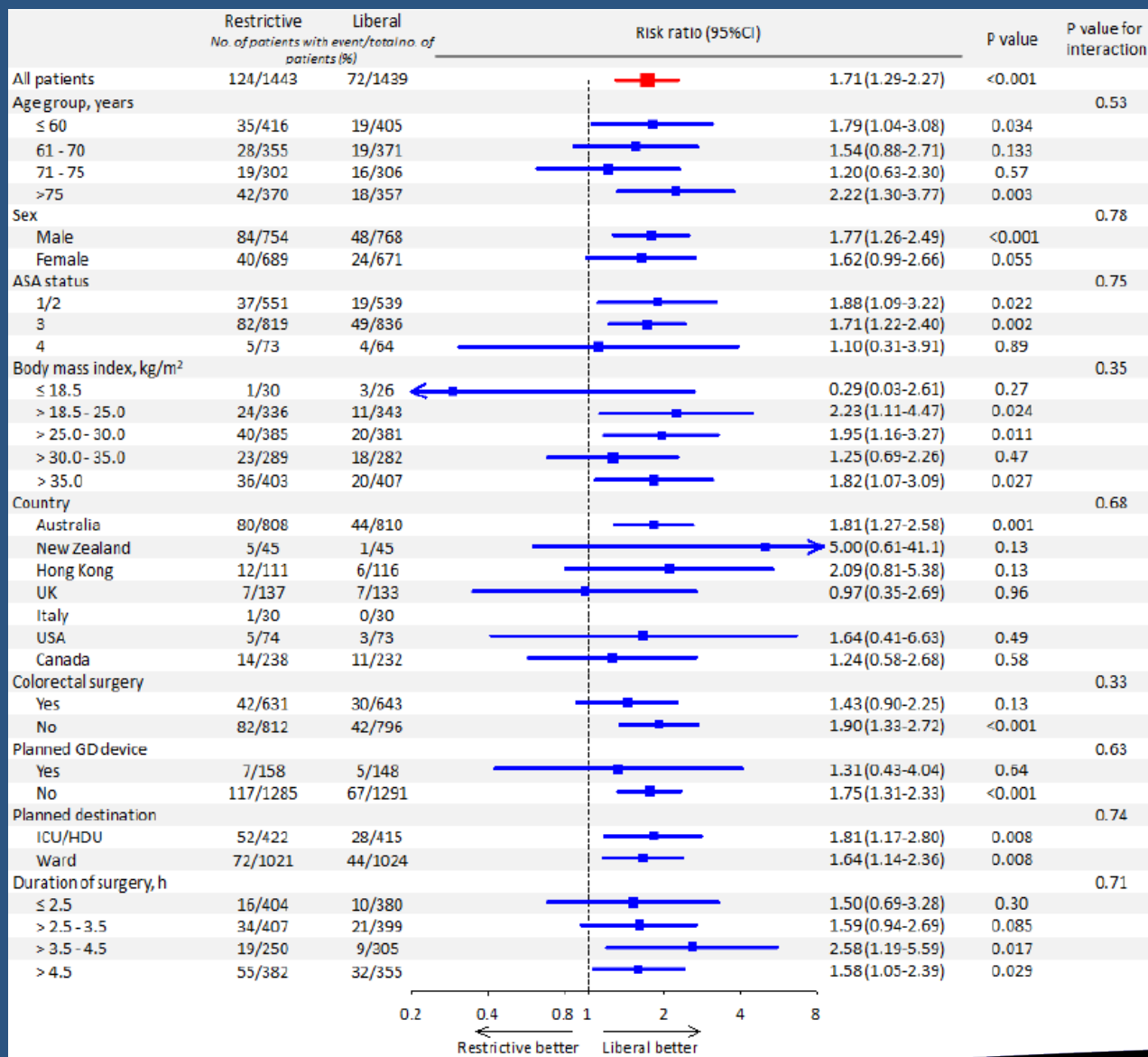
# Surgical Site Infection

Outcome	Liberal (n=1493)	Restrictive (n=1490)	P value
Superficial incisional	116 (7.8)	134 (9.0)	0.22
Deep incisional	56 (3.8)	62 (4.2)	0.56
Organ space	44 (3.0)	72 (4.9)	<b>0.007</b>





# acute kidney injury



# Conclusions

- Monitor fluid balance
- Assess regularly for adequacy of fluid status
- Avoid fluid depletion
- Avoid fluid overload
- Do not use starch or other synthetic colloids
- Do not use chloride rich fluids
- In major surgery patients apply the “liberal” fluid protocol of the RELIEF study

