Fluid resuscitation in the ICU: colloids vs. crystalloids

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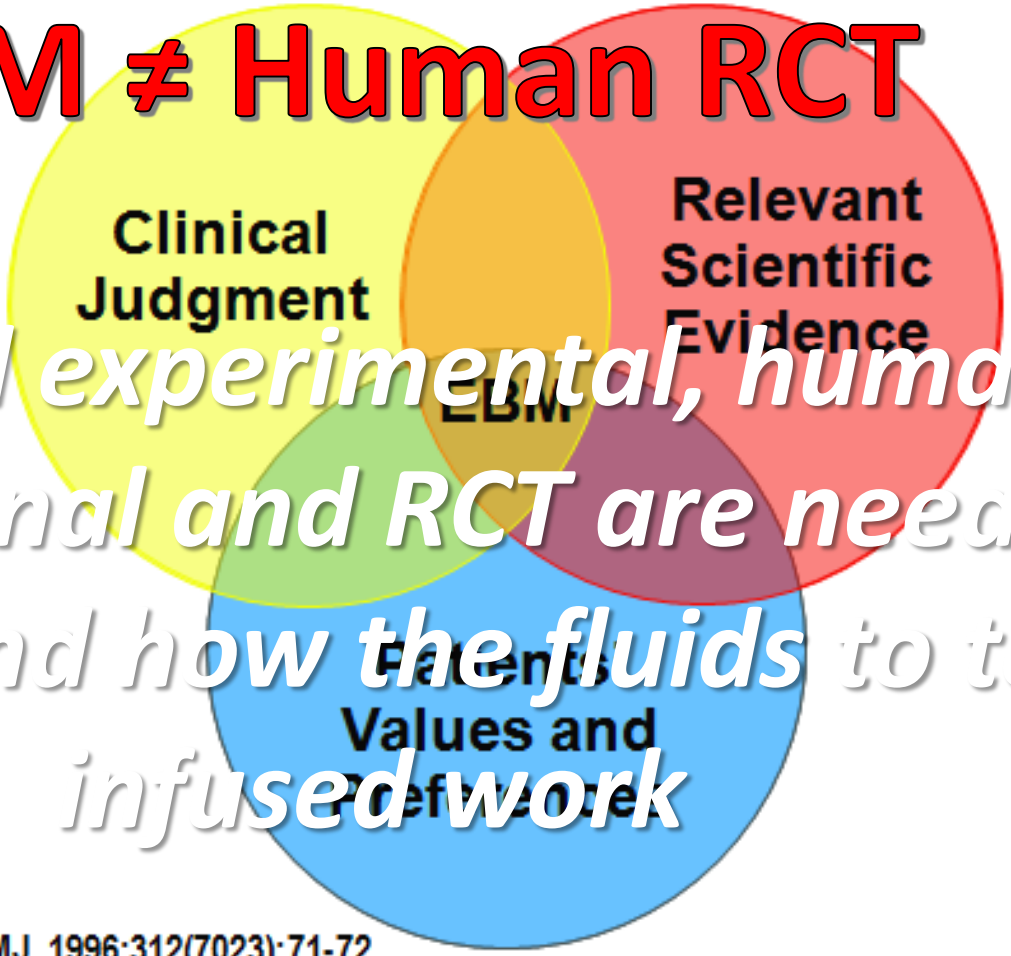
Where to find the evidence ?

What Is Evidence-Based Medicine?

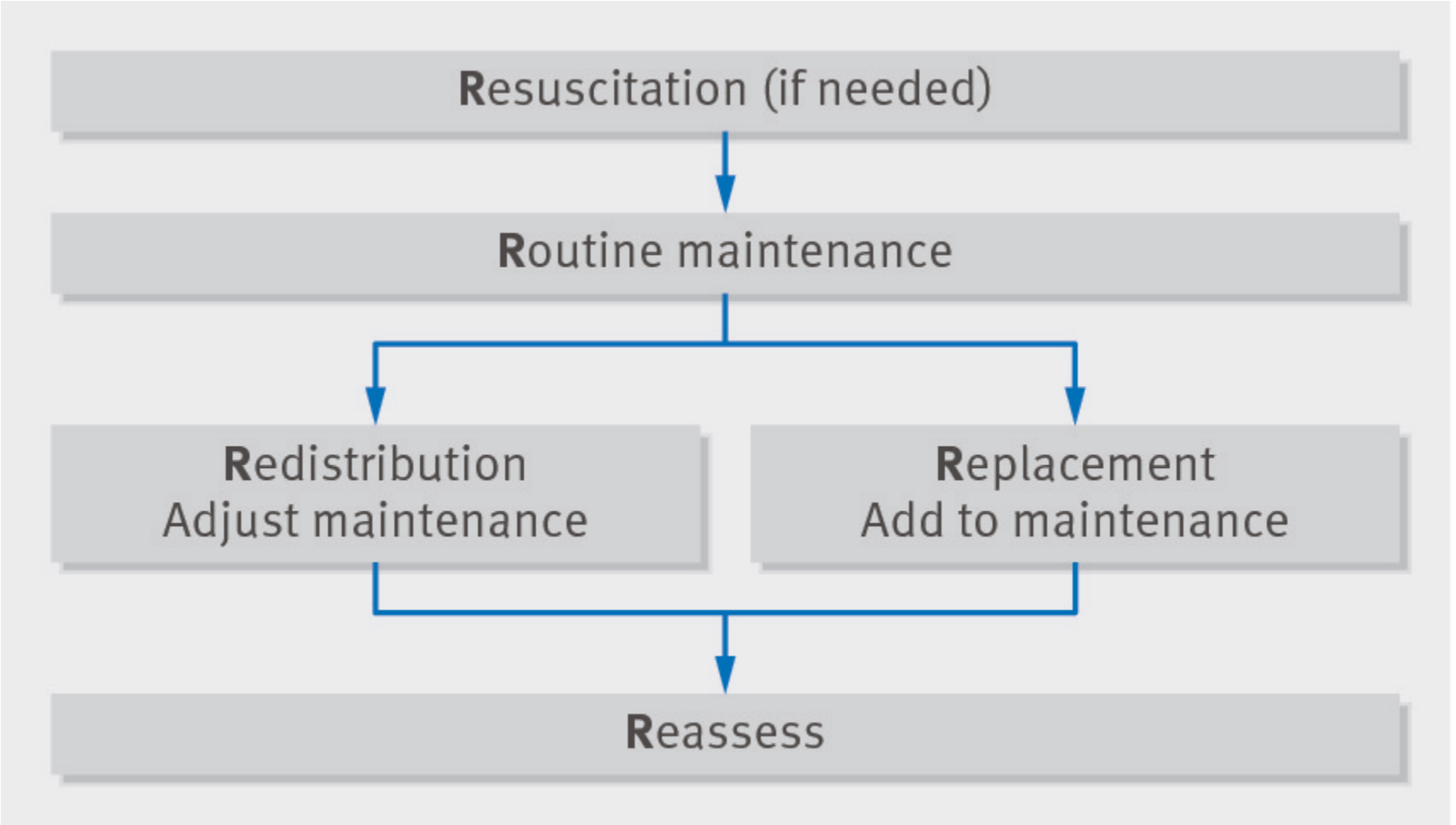
EBM ≠ Human RCT



Animal experimental, human observational and RCT are needed to understand how the fluids to to be infused work

Sackett DL, et al. BMJ. 1996;312(7023):71-72.

Prescribing intravenous fluids: the 5Rs



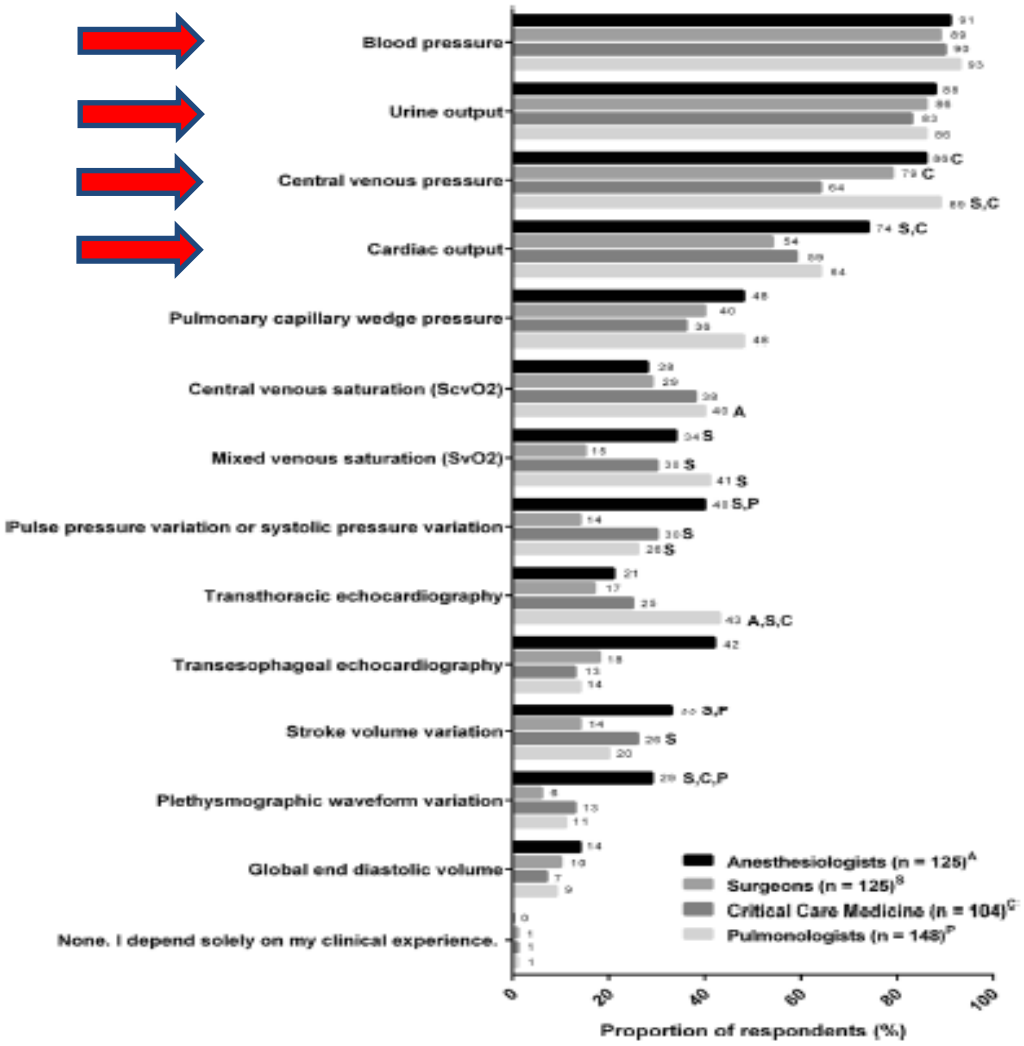
When to administer fluids?

Potential parameters to start fluid administration

HR	MAP	SAP	Lactate
BE	CVP	LAP	PAOP
CI	SV	LVSWI	SVO2
	Diuresis	Medical judgement	

Hypovolemia is frequent in all types of shock

Fluid resuscitation practice patterns in intensive care units of the USA: a cross-sectional survey of critical care physicians



MAP
Diuresis
CVP
Cardiac Output

Miller *et al. Perioperative Medicine* (2016) 5:15

Fluid challenges in intensive care: the FENICE study

A global inception cohort study

Table 3 Indications and variables used to predict fluid responsiveness ($N = 2213$)

Indication	*n* (%)
Hypotension	1211 (58.7 [56.7–60.8])
Weaning vasopressor	146 (7.1 [6.0–8.2])
Cardiac output	62 (3.0) [2.3–3.7]
Oliguria	372 (18.0 [16.4–19.6])
Skin mottling	36 (1.7 [1.2–2.2])
Lactate	128 (6.2 [5.2–7.2])
$SvO_2/ScvO_2$	10 (0.5 [0.2–0.8])
SVV/PPV	37 (1.8 [1.3–2.4])
CVP/PAOP	60 (2.9 [2.2–3.6])

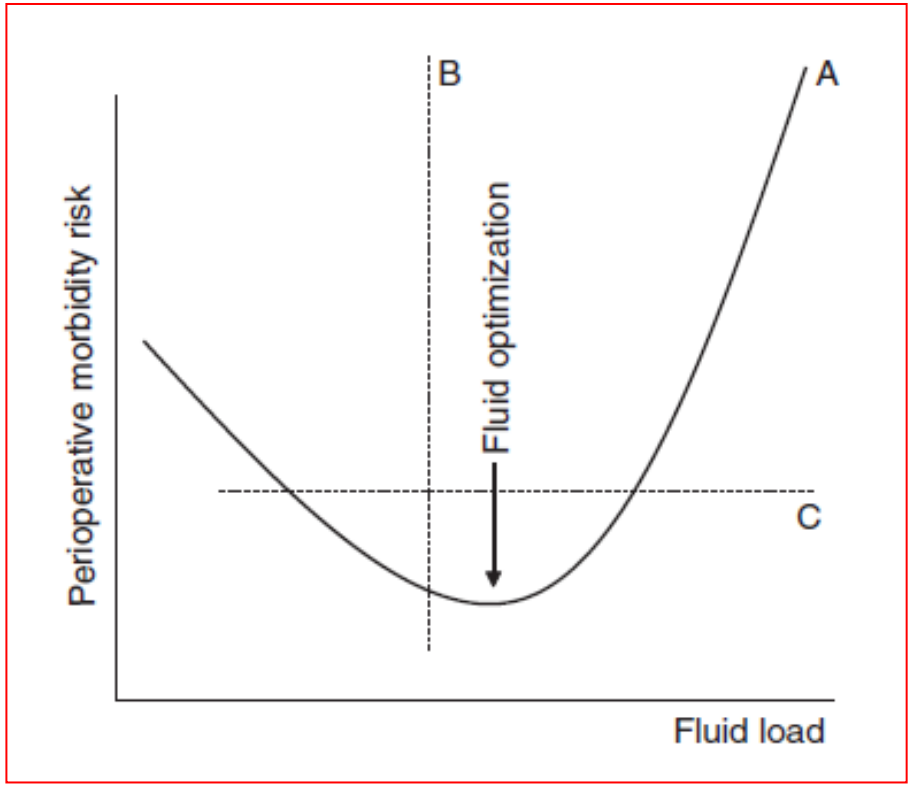
Cecconi et al, Intensive Care Medicine 2015 (41): 1529-37

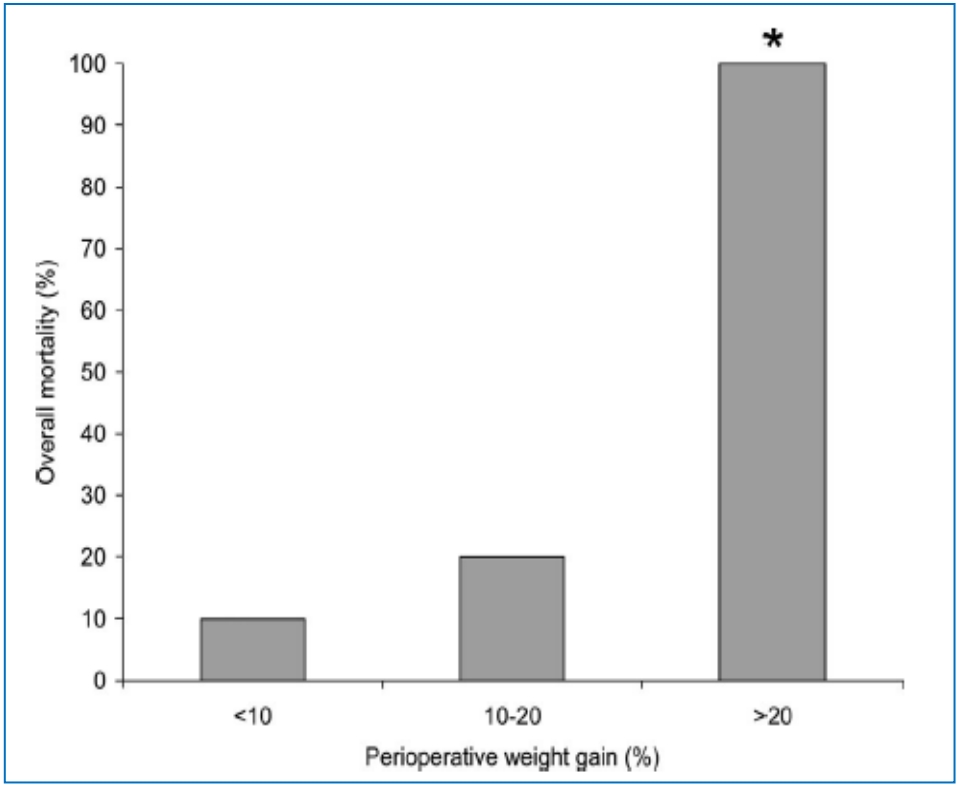
Hypotension is a late event in hypovolemic patients

In patients with suspected or confirmed hypovolemia, administration of fluids must be considered as an early strategy

How much to administer ?

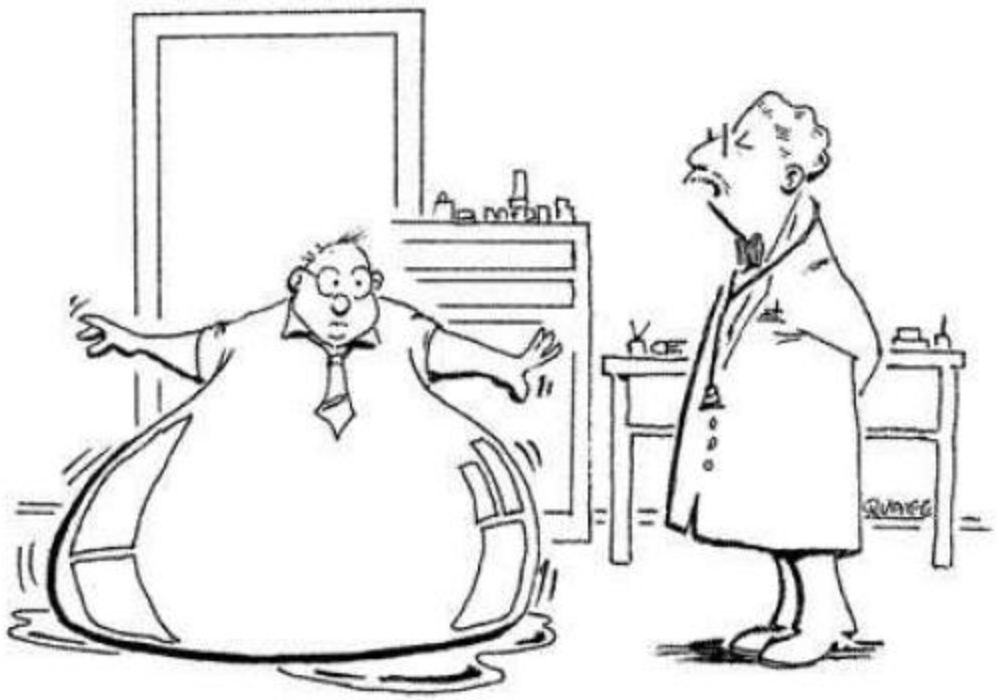
Hypovolemia and hypervolemia can both cause harm





Bellamy MC. Br J Anaesth. 2006; 97 (6): 755-7
Chappell D et al. Anesthesiology. 2008; 109: 723-40

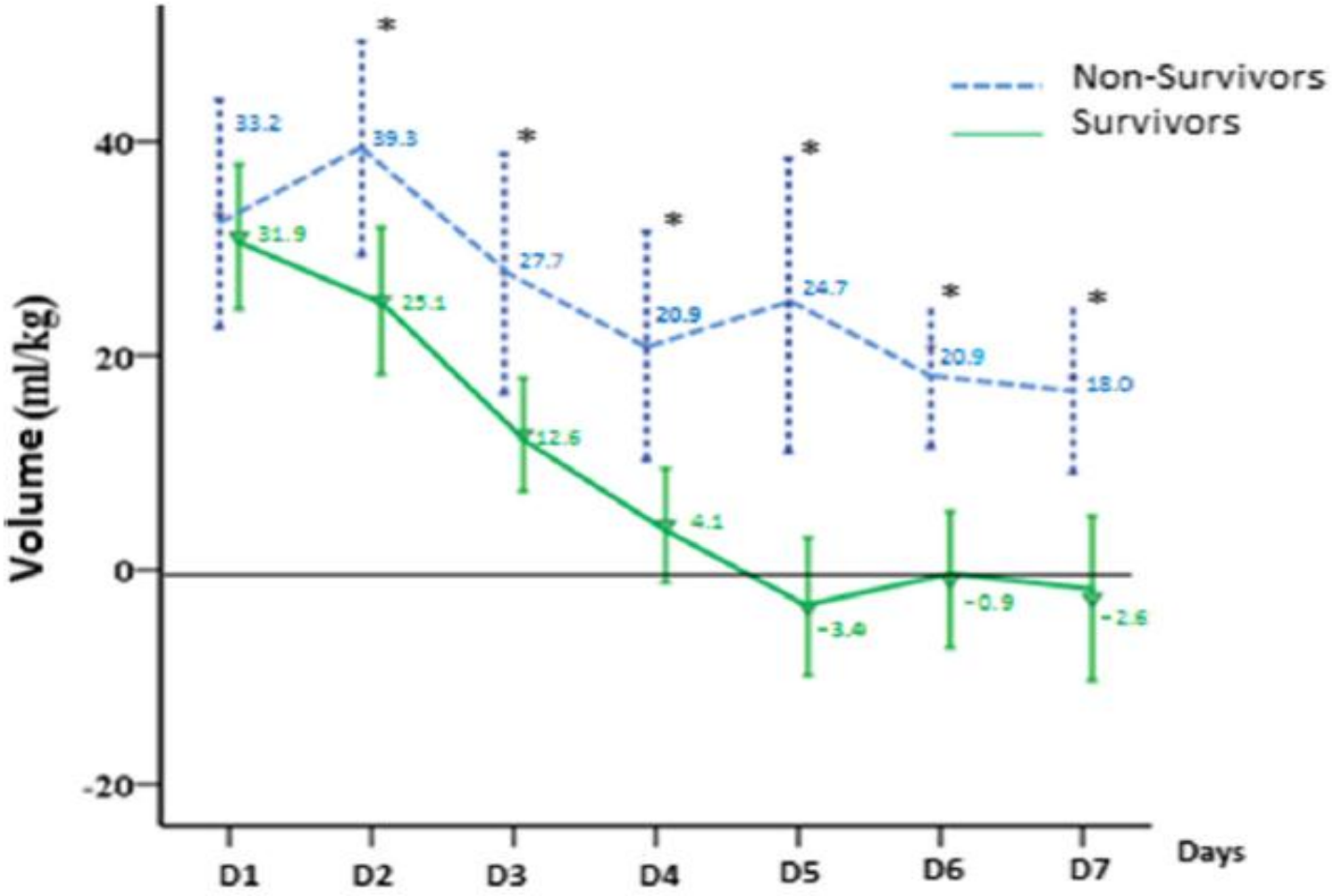
Is ed[illegible] sue ?



Your tests reveal that
you are retaining fluids!

A positive fluid balance is an independent prognostic factor in patients with sepsis

Angela Acheampong and Jean-Louis Vincent*

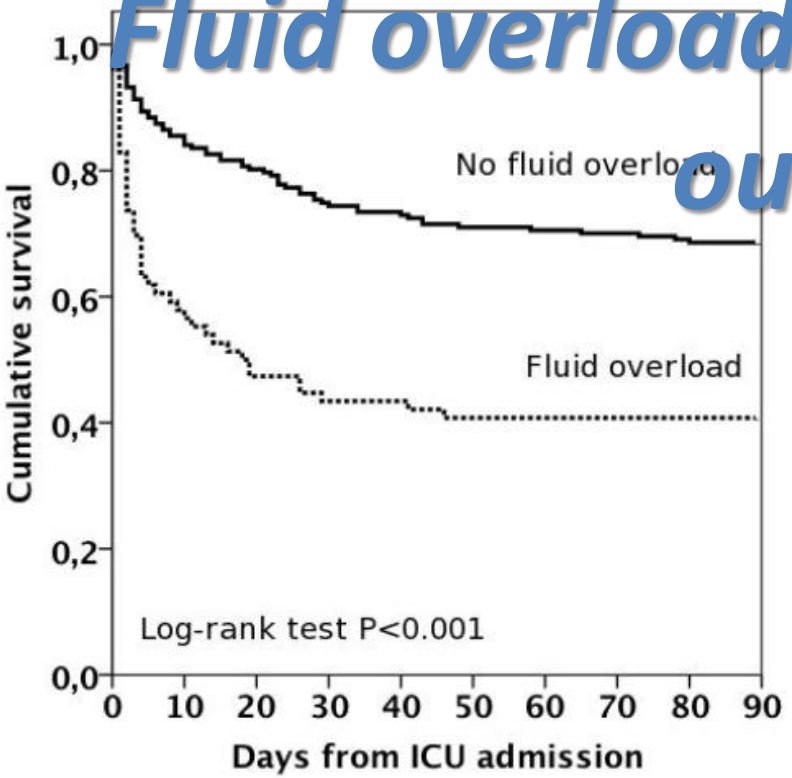


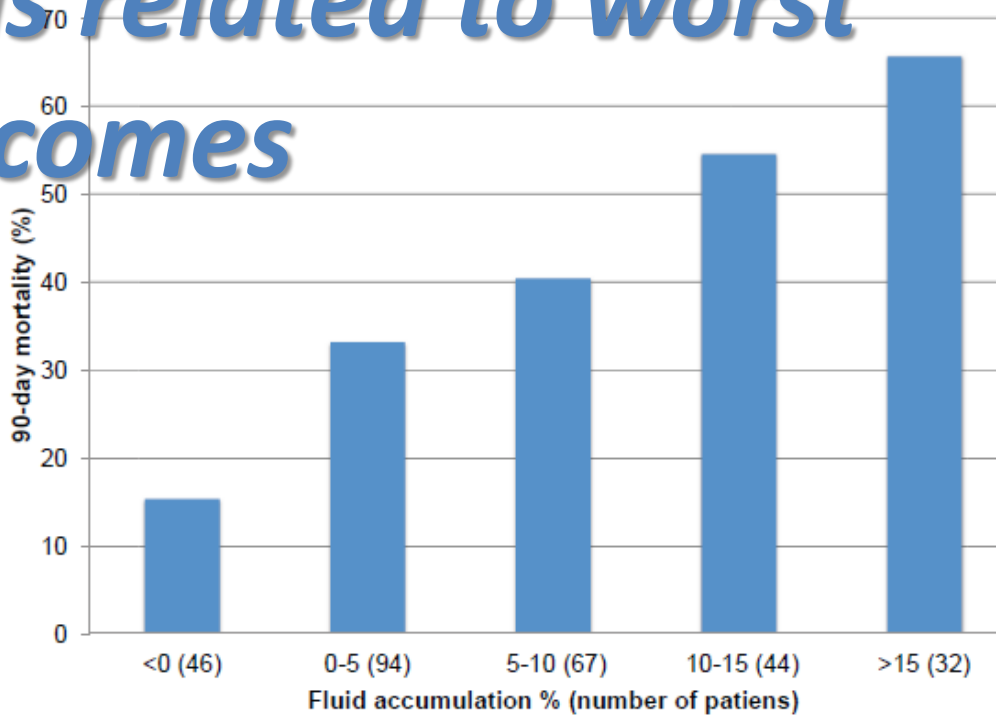
Critical Care (2015) 19:251

Fluid overload is associated with an increased risk for 90-day mortality in critically ill patients with renal replacement therapy: data from the prospective FINNAKI study

Suvi T Vaara[1*], Anna-Maija Korhonen[1], Kirsi-Maija Kaukonen[1], Sara Nisula[1], Outi Inkinen[2], Sanna Hoppu[3], Jouko J Laurila[4], Leena Mildh[1], Matti Reinikainen[5], Vesa Lund[6], Ilkka Parviainen[7] and Ville Pettilä[1,8], for The FINNAKI study group

Fluid overload is related to worst outcomes





Vaara *et al. Critical Care* 2012, **16**:R197

Which one to use?

TYPES OF FLUIDS

- Different types of solutions can have
  - specific capacity of volume expansion,
  - duration of effect,
  - impact on vascular integrity,
  - acid-base balance,
  - inflammatory response,
  - changes in red blood cell rheology and haemostasis

Isotonic Crystalloids

- Most common type of fluids used to replace bodily fluids
- Three main compositions:

*For each 1 ml increase in vasculature fluid, you need to give 3-4 mls of isotonic fluid

CRYSTALLOIDS

- Normal saline (0.9% NaCl) is considered an isotonic solution, with osmolality closer to the plasma osmolality
- Sodium 154mEq/L and Chloride 154mEq/L
- 1.5-fold higher than the physiologic serum concentration of chloride → (non-balanced solution)
- large volume infusions can promote hyperchloremic acidosis (dilution hyperchloremic acidosis), dilutional coagulopathy and renal dysfunction

Type	Plasma	N/S	R/L	R/A	Plasma-lyte
Osmo:	290	308	273	275	295
pH	7.4	5.7	6.5	6.7	7.4
Na	140	154	130	131	140
Cl	103	154	109	109	98
K	4	0	4	4	5
Ca	4	0	3	3	0
Mg	2	0	0	0	3
Buffer	HCO3	0	Lactate	Acetate	Acetate Gluconate

- Balanced solutions have been proposed as an alternative to normal saline
- Ringer Lactate, Ringer Acetate and Plasma-Lyte.
- A chloride-restrictive strategy in critically ill patients was associated with a significant decrease in the incidence of acute kidney injury and use of renal replacement therapy

COLLOIDS

- Higher oncotic pressure when compared to crystalloids
- Higher duration and capacity of intravascular expansion with lower volumes
- Colloids are not able to cross the semi impermeable vascular membrane due to their high molecular weight.

Main colloidal solutions and their composition

	Albumin		Hydroxyethyl Starch		Dextran		Gelatins
	4%,5%	20%,25%	6%, 10% pentastarch	6% hetastarch	10% Dex 40	3% Dex 60 6% Dex 70	
Molecular weight	69		100-450		40-70		30-35
Osmolality (mOsm/L)	300	1500	300-325		280-324		300-350
Oncotic pressure (mmHg)	19-30	74-120	23-82		20-60		25-42
Plasmatic expansion (%)	70-100	200-300	100-160		100-200	80-140	70-100
Duration of plasmatic expansion (h)	≤24		≤12	≤4-36	≤4-6	≤8-24	≤4-6
Plasma half-life (h)	16-24		2-12		2	24	2-9
Possible adverse effects	High cost, risk of infection & anaphyl reactions		Impairment coagulation, pruritus, acute kidney failure, and anaphylactic reactions		Changes in blood viscosity, coagulopathy, renal dysfunction, and anaphylactic reactions		Hypercalcemia and Anaphyl reactions

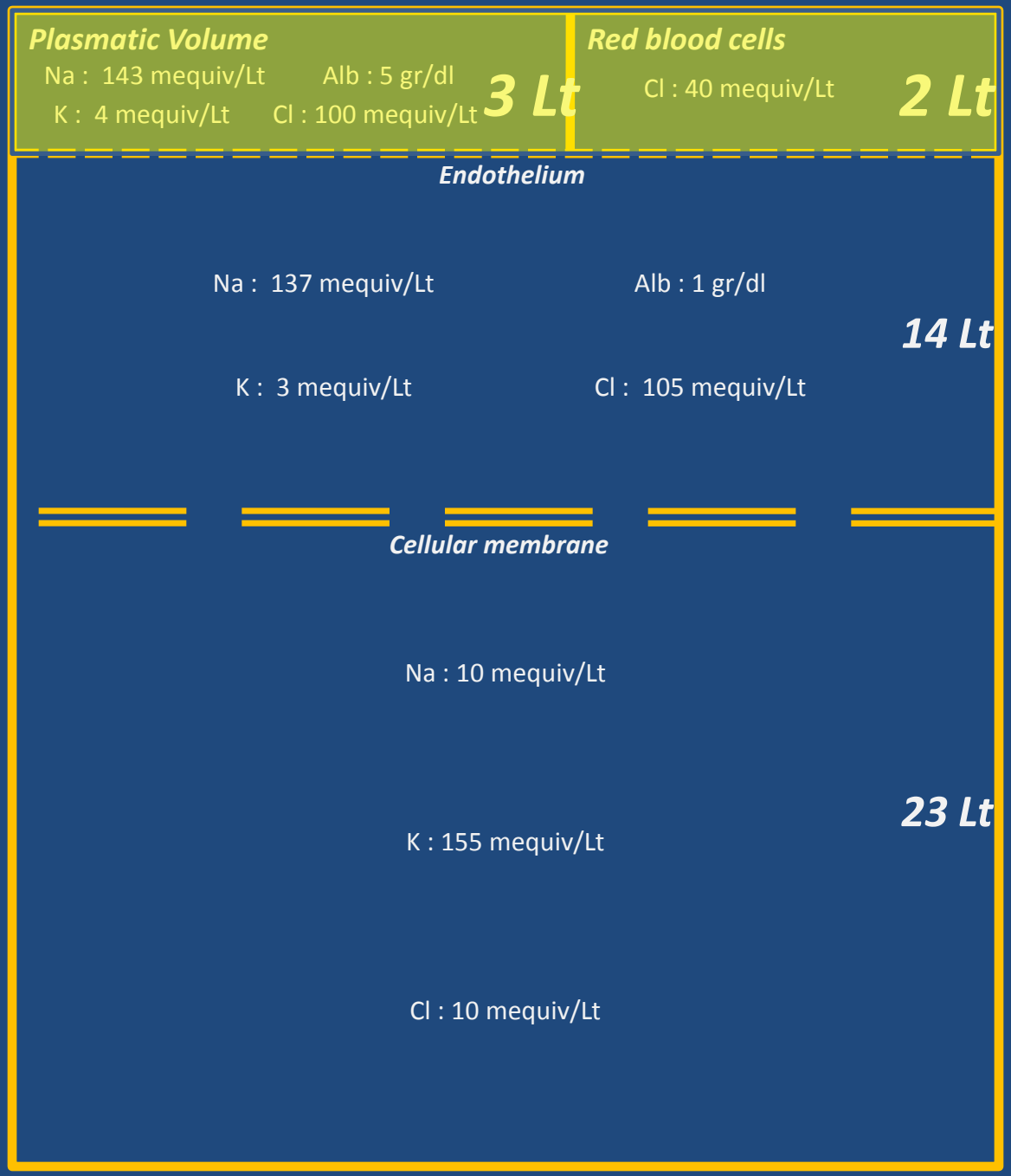
Hydroxyethyl starch (HES)

- One of the most frequently used colloidal plasma expanders worldwide, mainly due to their lower cost when compared to albumin
- avoided in the treatment of critically ill patients, specifically in those with sepsis
- 10% HES 200/0.5 or 6% HES 130/0.4
- solution concentration, mean mol. wt expressed in kilo Dalton (kDa), molar substitution (MS)

- In general, HES is used for restrictive fluid strategy due to a high plasma expansion capacity with lower volume administration
- Increase the risk of acute renal failure (Systematic review of RCT on the use of HES for fluid management in sepsis, BMC Emerg Med.2008)

Albumin

- Based on its physiological effects, primarily binding and transportation of various substances (drugs and hormones) in the blood; antioxidant properties, nitric oxide modulation; and buffer capacity, not only to regulate osmotic pressure
- limitations for a broader use of albumin : high cost, potential risk of microorganisms transmission and allergic effects
- Those with traumatic brain injury, can have an increased risk of death when receiving albumin solutions.

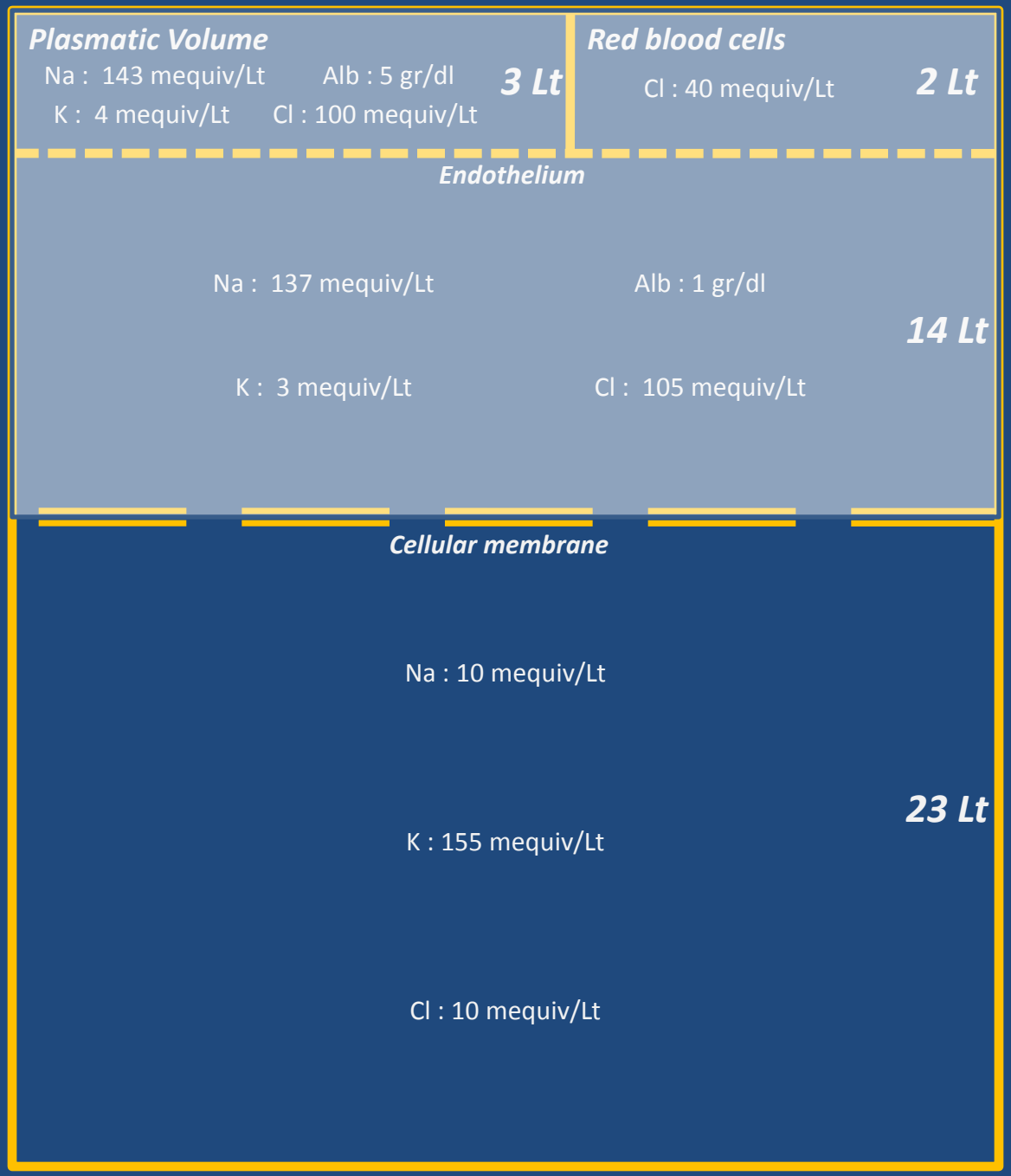


INTRAVASCULAR COMPARTMENT

INTERSTITIAL COMPARTMENT

INTRACELLULAR COMPARTMENT

De Backer and Orbegozo. Best Pract Res Clin Anaesthesiol. 2012 Dec; 26(4):441-51.



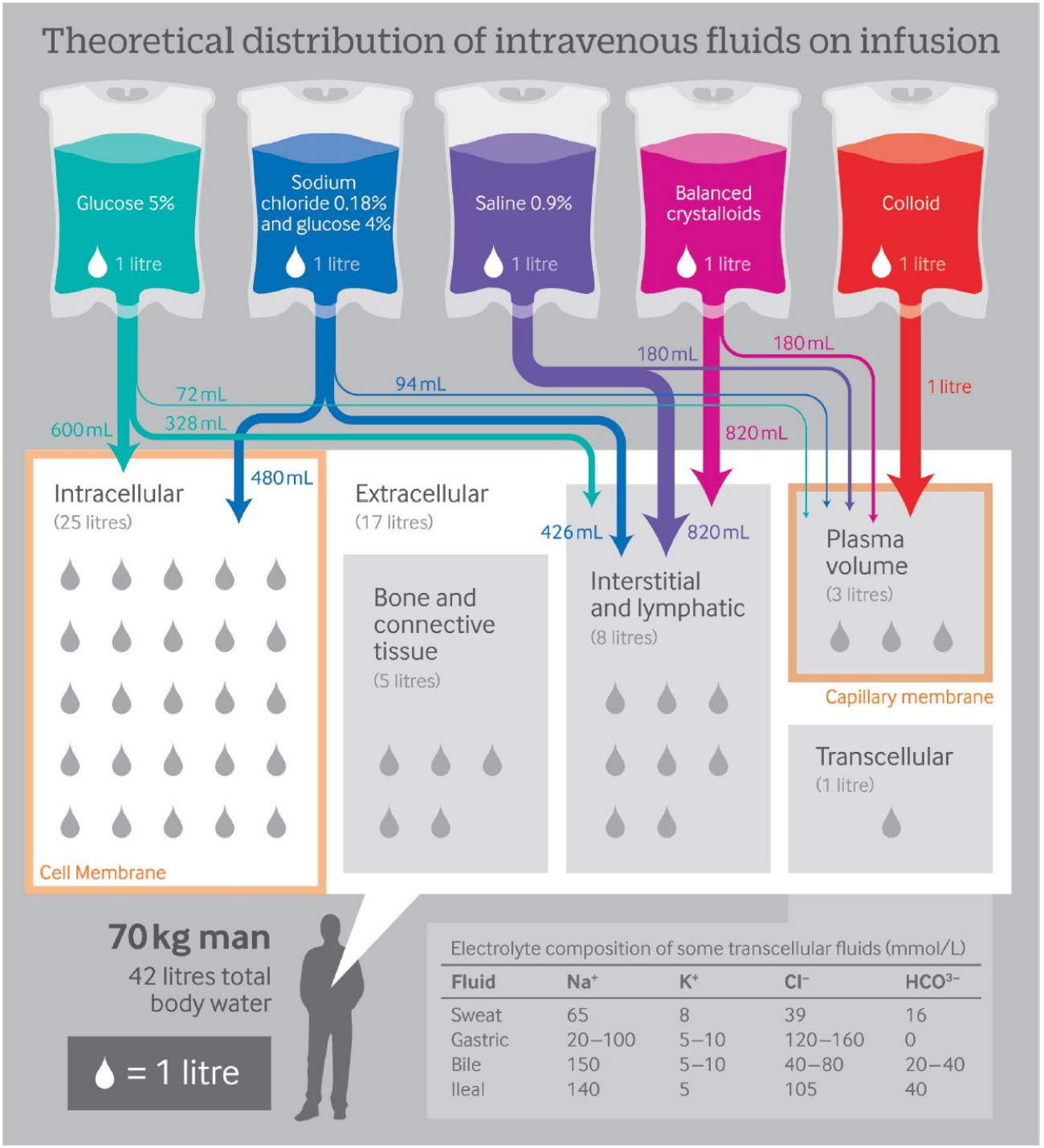
INTRAVASCULAR COMPARTMENT

INTERSTITIAL COMPARTMENT

INTRACELLULAR COMPARTMENT

De Backer and Orbegozo. Best Pract Res Clin Anaesthesiol. 2012 Dec; 26(4):441-51.

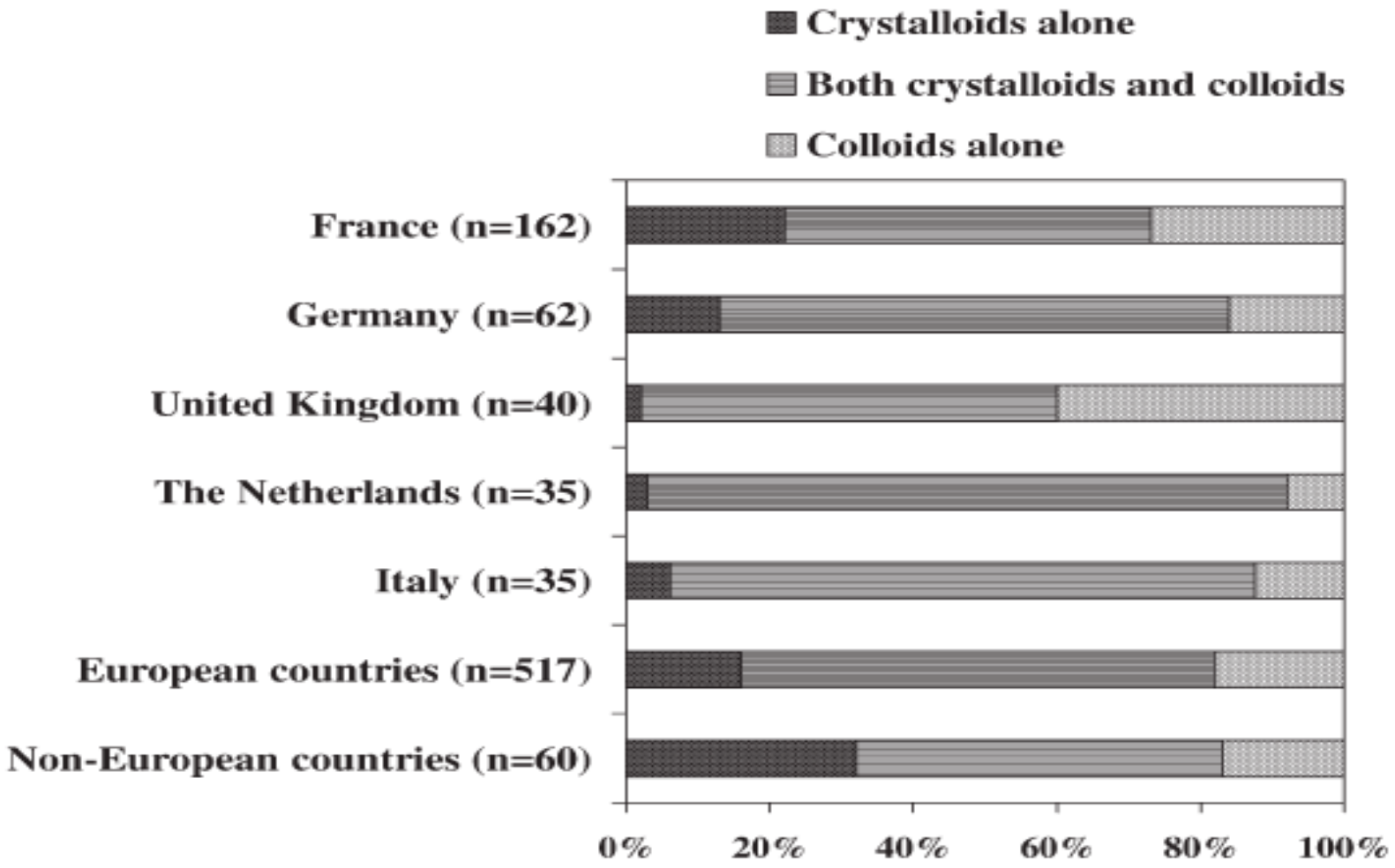
Body fluid compartment volumes and theoretical distribution of IV fluids in healthy people



Frost P. BMJ. 2015 Jan 6;350:g7620

Frédérique Schortgen
Nicolas Deye
Laurent Brochard
for the CRYCO Study Group

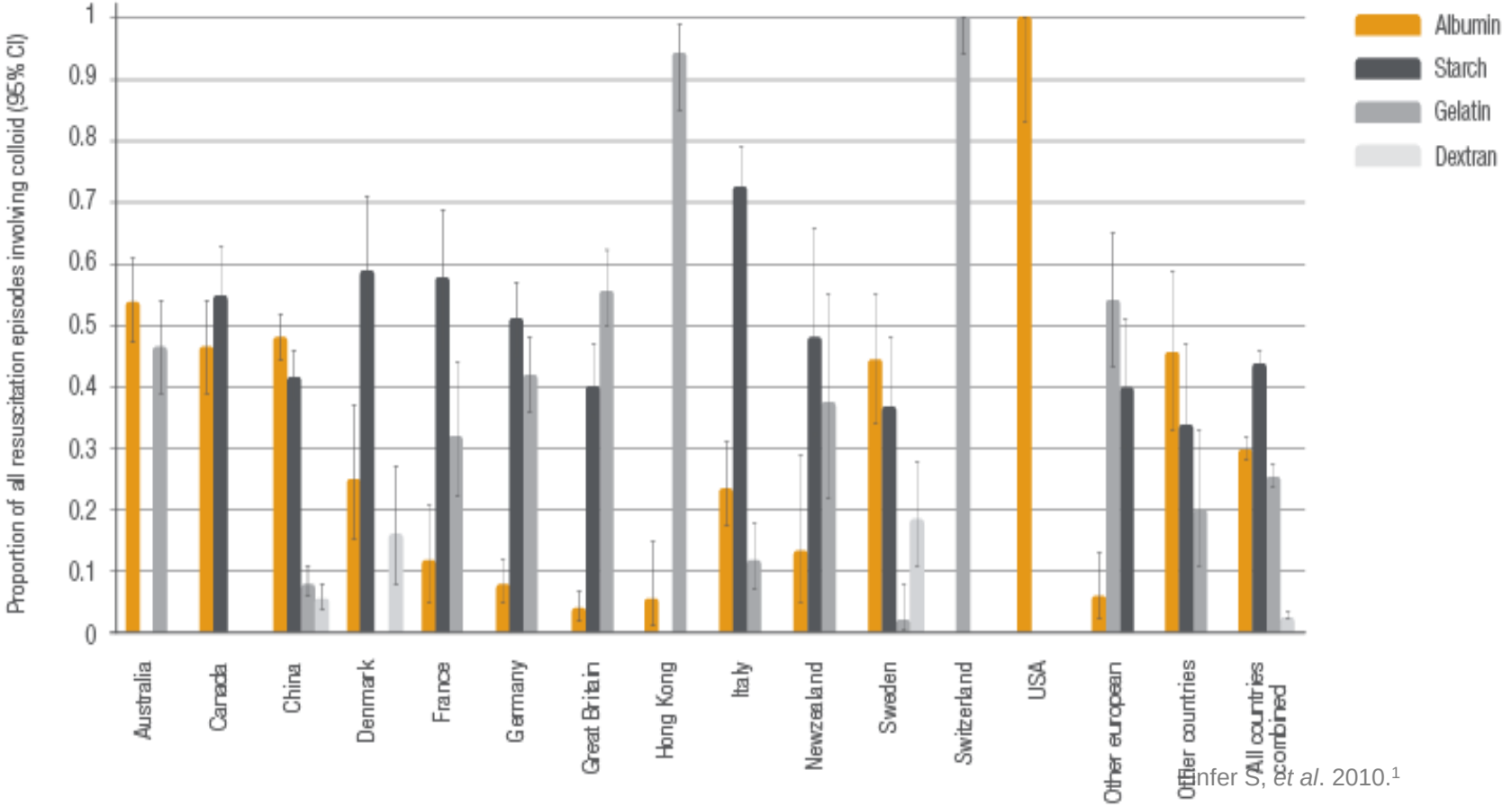
Preferred plasma volume expanders for critically ill patients: results of an international survey



Intensive Care Med (2004) 30:2222–2229

International resuscitation fluid use – Safe TRIPS

Type of colloid used as a percentage of all colloid episodes by country



Finfer S, *et al*. 2010.[1]

2007: Colloid choice varied **among countries**, artificial colloids prevailed[1]

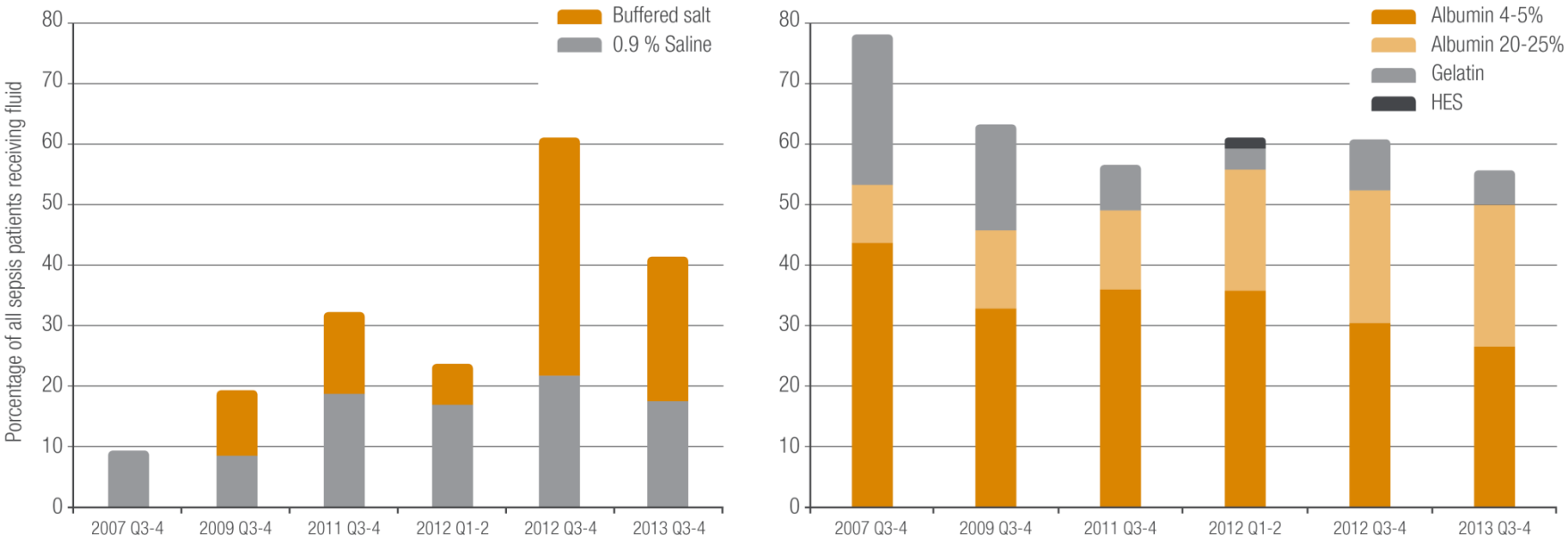
1. Finfer S. *et al.* Crit Care. 2010;14(5):R185.

Resuscitation fluid use – evolution in 6 yrs in Australia - New Zealand

Cross-sectional point prevalence studies on the use of resuscitation fluids[1]

- Pending publication of international trends (Fluid-TRIPS), changes in fluid preferences, including an **increase of albumin use,** were **observed in Australia and New Zealand**
  - In particular, a significant increase in the use of crystalloids and decrease in the use of colloids, specifically gelatin was observed

Proportion of all patients receiving selected types of crystalloid (a) and colloid (b) solutions between 2007 and 2013



Adapted from Hammond NE *et al*. 2015.[1]

1. Hammond NE. *et al.* Intensive Care Med. 2015;41(9):1611-9.

Even if fluids administration practices are highly variable and subjective, physiology is exactly the same everywhere

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

Nor'azim Mohd Yunos, MD

Rinaldo Bellomo, MD, FCICM

Colin Hegarty, BSc

David Story, MD

Lisa Ho, MClinPharm

Michael Bailey, PhD

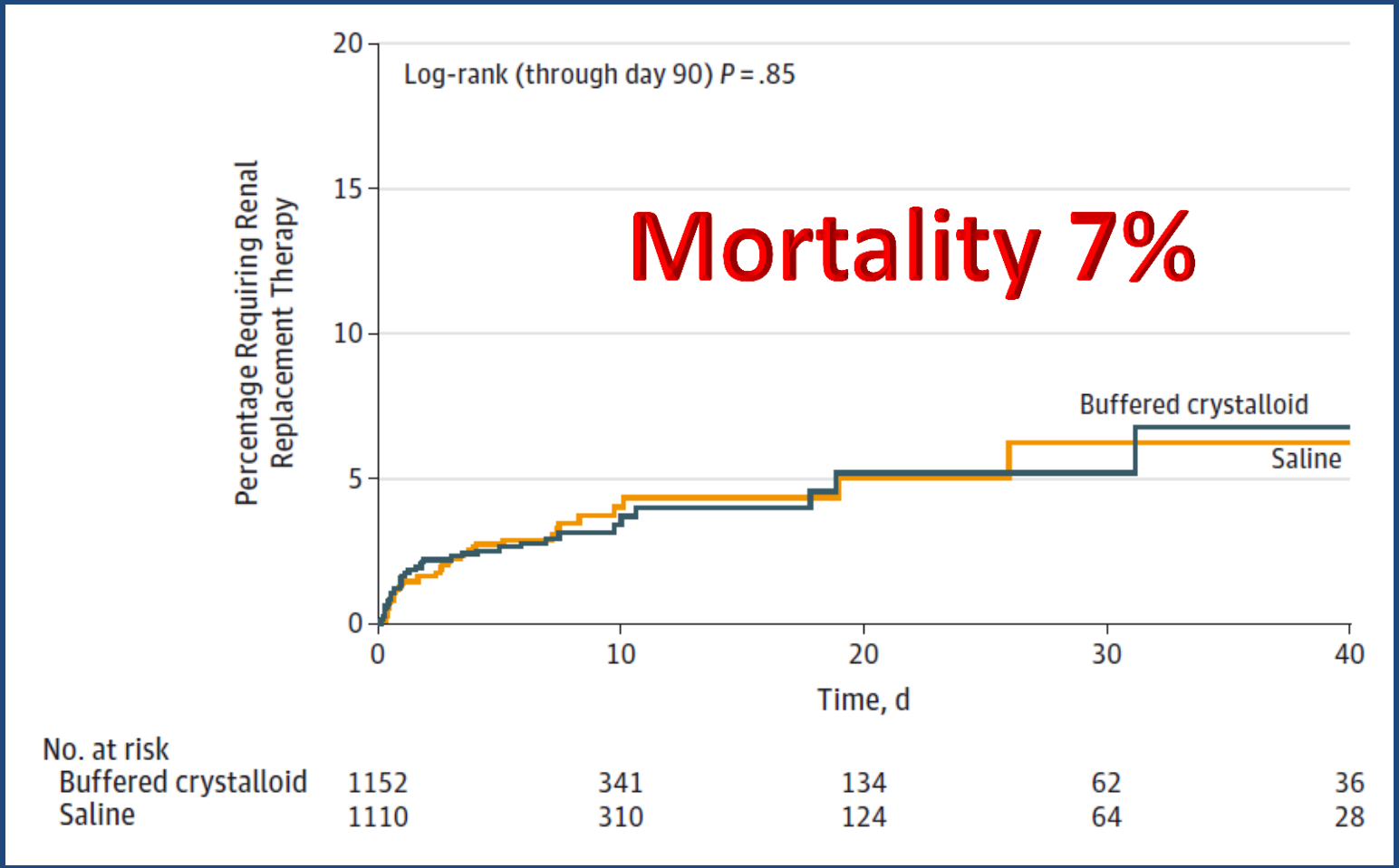
Table 3. Incidence of Acute Kidney Injury Stratified by Risk, Injury, Failure, Loss, and End-Stage (RIFLE) Serum Creatinine Criteria

	No. (%) [95% CI] of Patients[a]		
	Control Period (n = 760)	Intervention Period (n = 773)	*P* Value
RIFLE class			
Risk	71 (9.0) [7.2-11.0]	57 (7.4) [5.5-9.0]	.16
Injury	48 (6.3) [4.5-8.1]	23 (3.0) [1.8-4.2]	.002
Failure	57 (7.5) [5.6-9.0]	42 (5.4) [3.8-7.1]	.10
Injury and failure	105 (14) [11-16]	65 (8.4) [6.4-10.0]	<.001

[a] The control period was from February 18 through August 17, 2008, and the intervention period was from February 18 through August 17, 2009.

Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit

The SPLIT Randomized Clinical Trial



Young et al. JAMA. 2015 Oct 27;314(16):1701-10

Crystalloids

Colloids and crystalloids

Renal effects of synthetic colloids and crystalloids in patients with severe sepsis: A prospective sequential comparison*

Ole Bayer, MD; Konrad Reinhart, MD; Yasser Sakr, MD, PhD; Bjoern Kabisch, PhD; Matthias Kohl, PhD; Niels C. Riedemann, MD; Michael Bauer, MD; Utz Settmacher, MD; Khosro Hekmat, MD; Christiane S. Hartog, MD

Table 3. Primary and secondary outcomes

	Hydroxyethyl Starch Group (n = 118)	p	Adjusted p	Gelatin Group ((n = 87)	p	Adjusted p	Crystalloid Group ((n = 141)
RIFLE risk, n (%)[a]	15 (13)	.698	1.000	10 (11)	.831	1.000	15 (11)
RIFLE injury, n (%)[b]	12 (10)	.842	1.000	14 (16)	.319	1.000	16 (11)
RIFLE failure, n (%)[c]	56 (47)	<.001	0.002	35 (40)	.018	.162	35 (25)
AKI, n (%)[d]	83 (70)	<.001	0.002	59 (68)	.003	.025	66 (47)
Renal replacement therapy, n (%)	40 (34)	.011	0.086	30 (34)	.019	.162	28 (20)
Sequential Organ Failure score maximum, median (IQR)[e]	11 (9–14)	.355	1.000	13 (10–15)	.332	1.000	12 (9–14)
Sequential Organ Failure score mean, median (IQR)[e]	7 (6–10)	.032	.227	8 (6–10)	.122	.853	8 (6–11)
Intensive care unit mortality, n (%)	41 (35)	.506	1.000	23 (26)	.550	1.000	43 (30)
Hospital mortality, n (%)	51 (43)	.311	1.000	27 (31)	.393	1.000	52 (37)
Intensive care unit length of stay, days, median (IQR)	14 (6–28)	.070	.421	13 (6–26)	.167	1.000	10 (5–20)

IQR, interquartile range.

[a]Five-fold increase in serum creatinine levels and/or urine output <0.5 mL/kg/hr for ≥24 hrs; [b]two-fold increase in serum creatinine levels and/or urine output <0.3 mL/kg/hr for ≥24 hrs; [c]three-fold increase in serum creatinine levels and/or renal replacement therapy, serum creatinine ≥354 μmol/L with an acute increase of at least 44 μmol/L, and/or urine output <0.3 mL/kg/hr ≥24 hrs or anuria ≥12 hrs for ≥24 hrs; [d]defined by any RIFLE category; [e]within 28 days of admission to the intensive care unit. The *p* values were calculated with the Mann-Whitney test and Fisher's exact test, as appropriate. For *p* value adjustment, the Bonferroni-Holm method was used.

Crit Care Med 2011 Vol. 39, No. 6

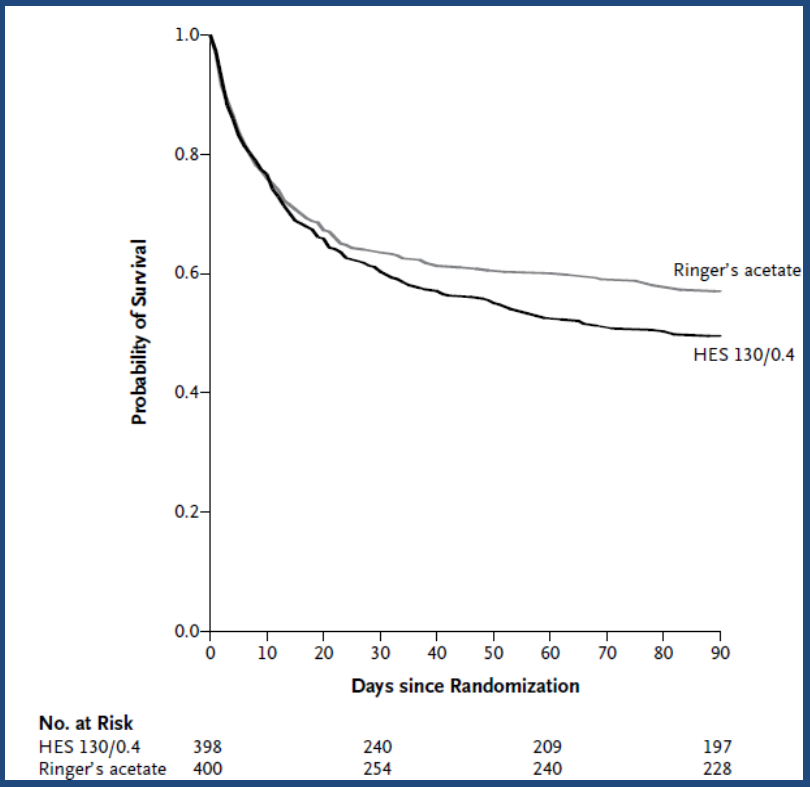
Fluid resuscitation with only crystalloids was equally effective, resulted in a more positive fluid balance only on the first 2 days , and was associated with a lesser incidence of AKI

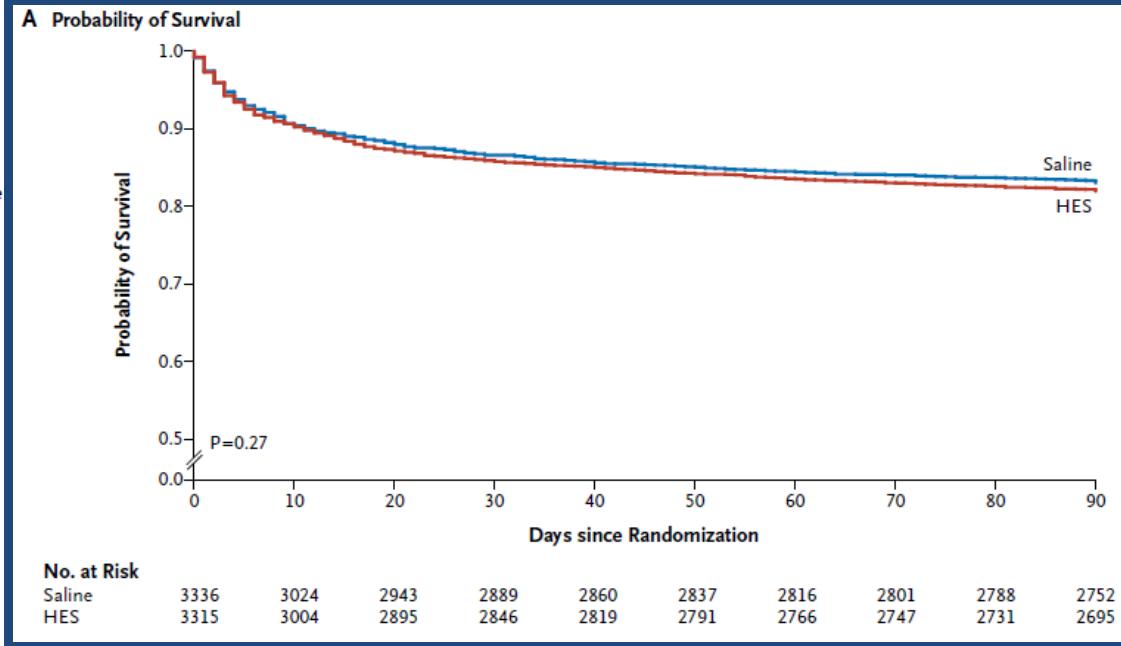
(Critical Care Med 2011 Vol, No.6)

Other recent trials in fluid therapy

- **6S** (n = 800 [severe sepsis])
- **CHEST** (n = 7,000 [ICU-admitted])

RRT at 90-d: more need for HES (p = 0.04)



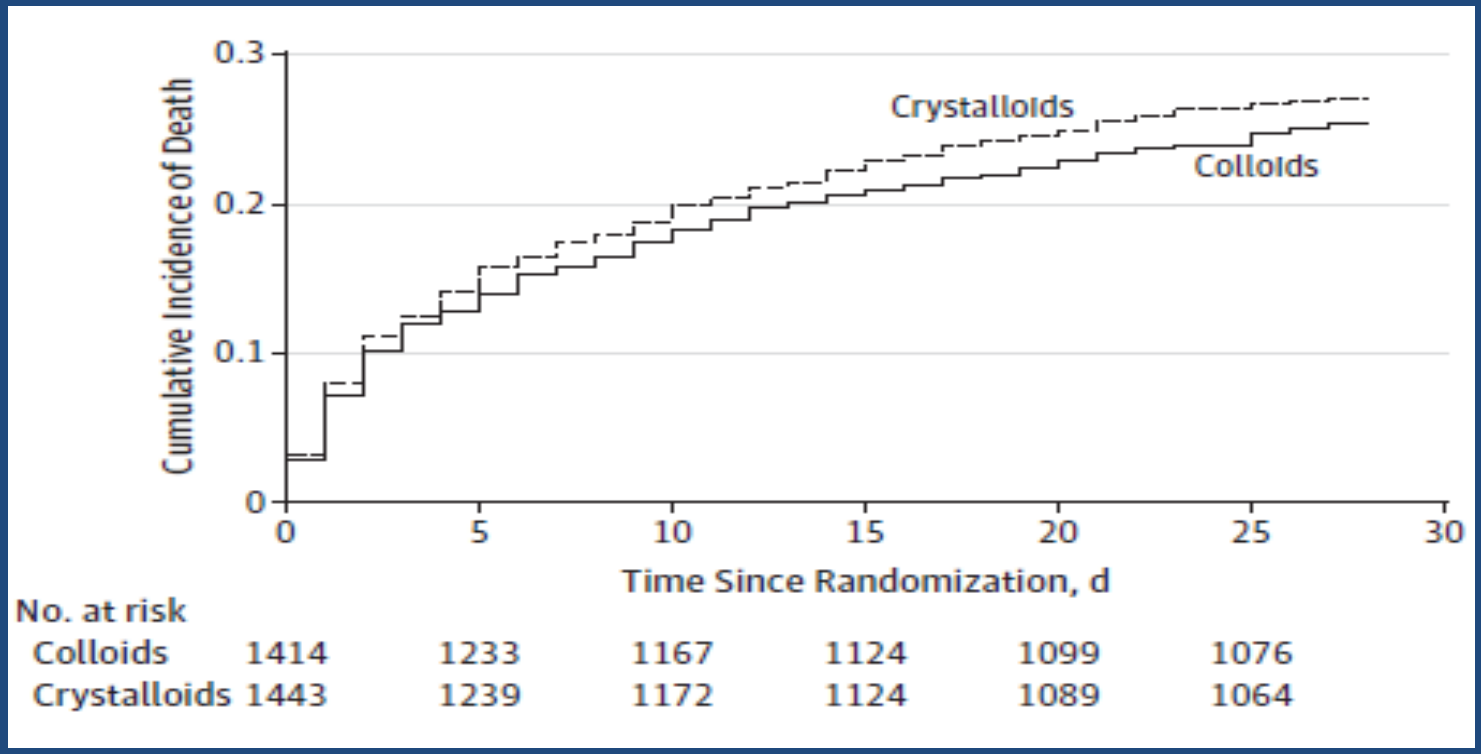


Perner A, *et al*. N Engl J Med. 2012 Jul 12;367(2):124-34.

Myburgh J, *et al*. N Engl J Med. 2012; 367(20): 1901-11.

CRISTAL trial

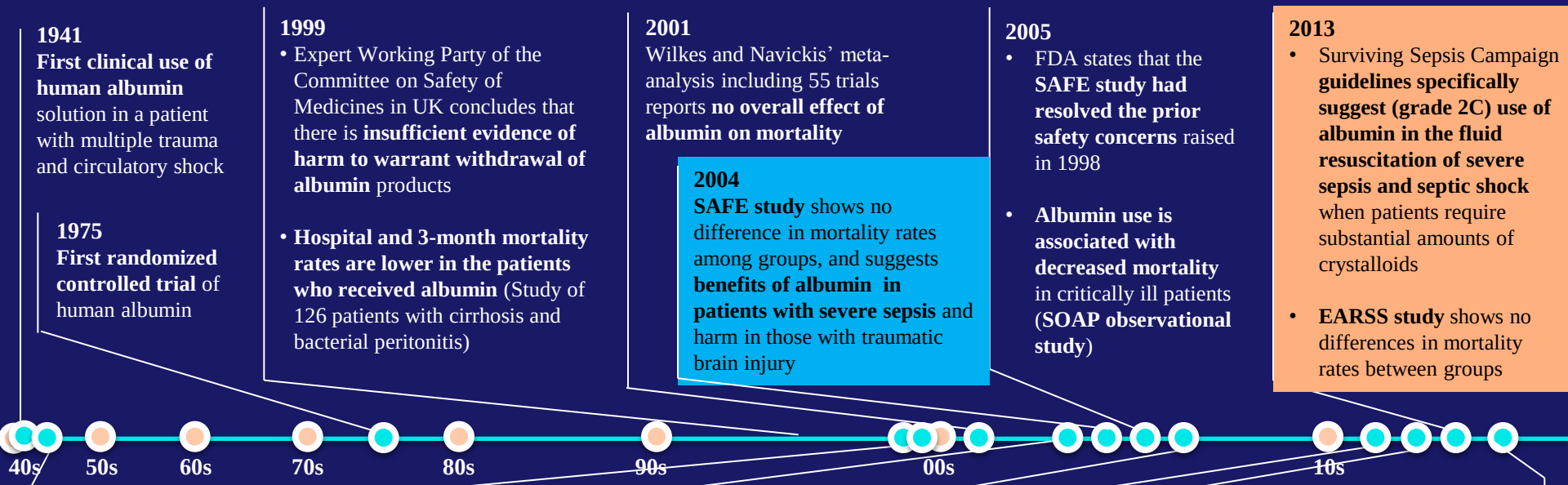
- **2,857 ICU-admitted patients**
  - 28 day mortality: 25.4% colloids *vs.* 27% crystalloids (p = 0.26)



Annane D. *et al.* JAMA. 2013; 310(17):1809-17.

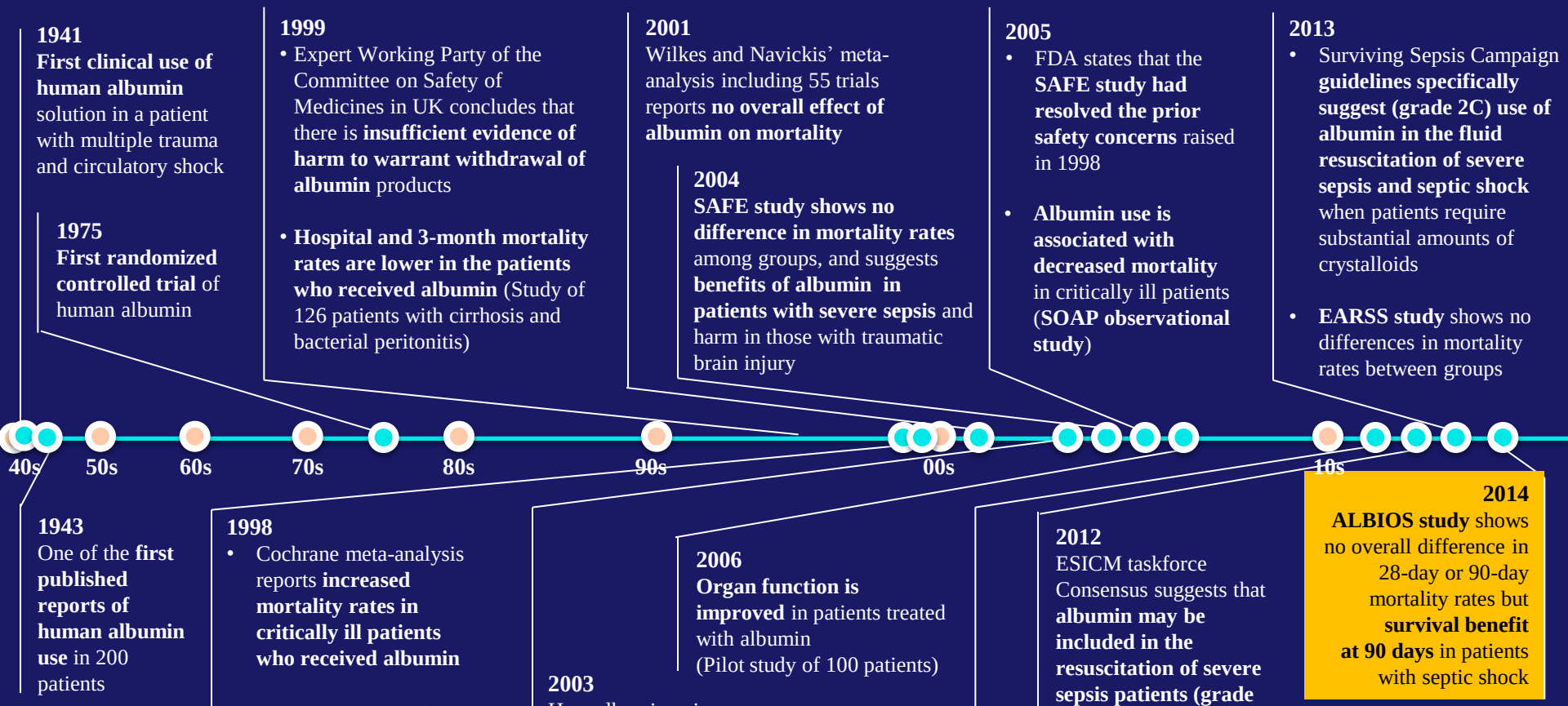
Synthetic colloids are not a good option in septic patients considering their side effects on renal and coagulation systems

Key milestones in the history of albumin



Adapted from Vincent, *et al*. 2014.

Key milestones in the history of albumin

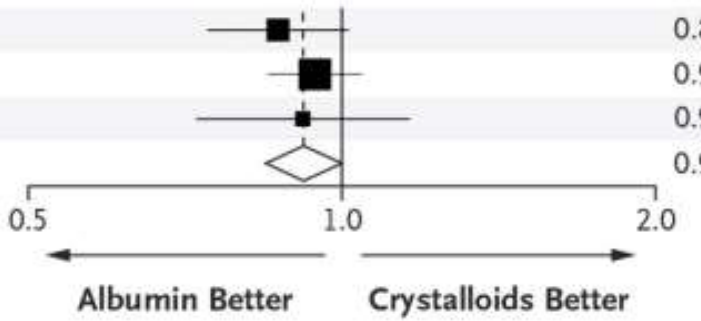


Adapted from Vincent, *et al*. 2014.

Meta-Analysis of Mortality in Large-Scale Randomized Trials Comparing Albumin with Crystalloids in Adult Patients with Severe Sepsis

Wiedermann CJ, Joannidis M. N Engl J Med. 2014;371(1):83.

Trial	Albumin	Crystalloids	Relative Weight	Relative Risk (95% CI)	P Value
	no. of patients who died/total no.		%		
SAFE[2]	185/603	217/615	30.41	0.87 (0.74–1.02)	
ALBIOS[1]	365/888	389/893	54.90	0.94 (0.85–1.05)	
EARSS[3]	96/399	103/393	14.69	0.92 (0.72–1.17)	
All trials	646/1890	709/1901	100.00	0.92 (0.84–1.00)	0.046



ALBUMIN

Authors suggest that there is a survival advantage associated with albumin use in patients with severe sepsis.

Initial fluid resuscitation with crystalloid,followed by albumin if needed

Fluid therapy

1. We recommend that a **fluid challenge technique** be applied where fluid administration is continued **as long as hemodynamic factors continue to improve** (BPS*).
2. We recommend **crystalloids as the fluid of choice**** for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).
3. We suggest using **either balanced crystalloids or saline** for fluid resuscitation of patients with sepsis or septic shock (weak recommendation, low quality of evidence).
4. We suggest using **albumin** in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock **when patients require substantial amounts of crystalloids** (weak recommendation, low quality of evidence).
5. We recommend **against using hydroxyethyl starches (HESs)** for intravascular volume replacement in patients with sepsis or septic shock (strong recommendation, high quality of evidence).
6. We suggest **using crystalloids over gelatins** when resuscitating patients with sepsis or septic shock (weak recommendation, low quality of evidence).

*BPS: best practice statement

** Initial resuscitation recommendation: We recommend that, in the resuscitation from sepsis induced hypoperfusion, **at le**
mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).

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1. Rhodes A, *et al.* Crit Care Med 2017;45(3):486-552.

Surviving Sepsis Campaign

Thank you