

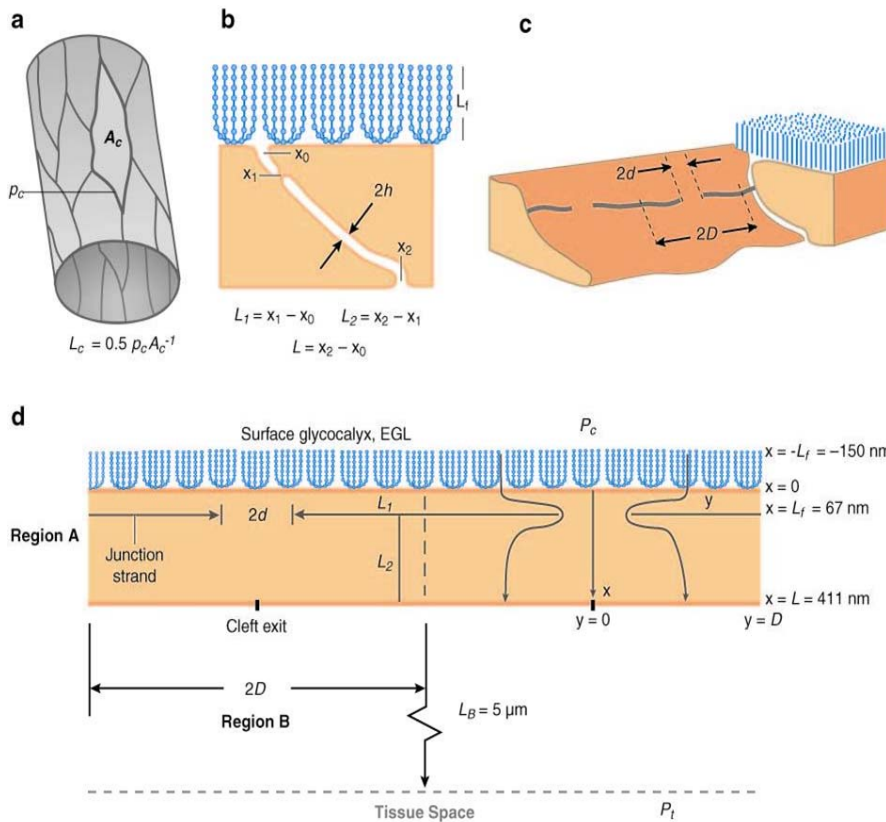
FACULTY OF MEDICINE, DENTISTRY AND HEALTH SCIENCES


# **Choice of Colloid Fluid Therapy in Septic Patients – A Comparative Cost-Effectiveness Analysis of Crystalloid, Albumin and Hydroxyethyl Starch**

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Megha Bansal, MA Econ

**ESICM LIVES 2013  
26<sup>th</sup> Annual Congress  
Paris, October 5-9, 2013**

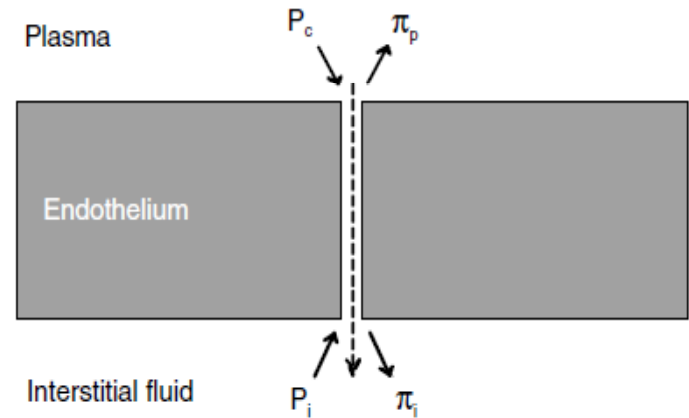
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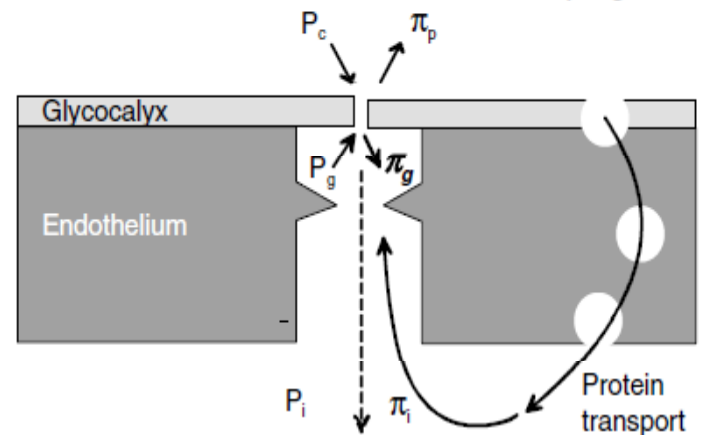
 Weinbaum S, et al. 2007.  
Annu. Rev. Biomed. Eng. 9:121-67

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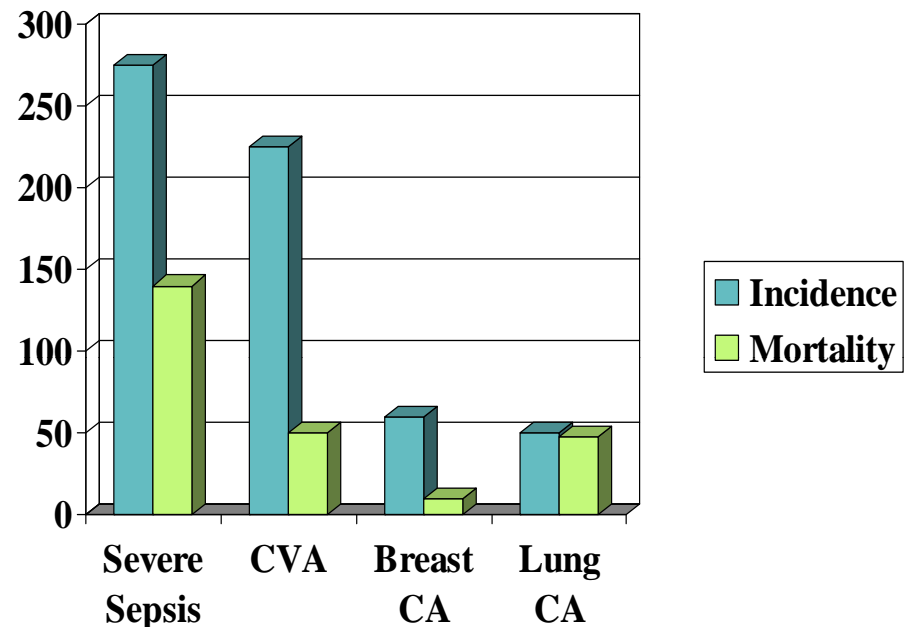
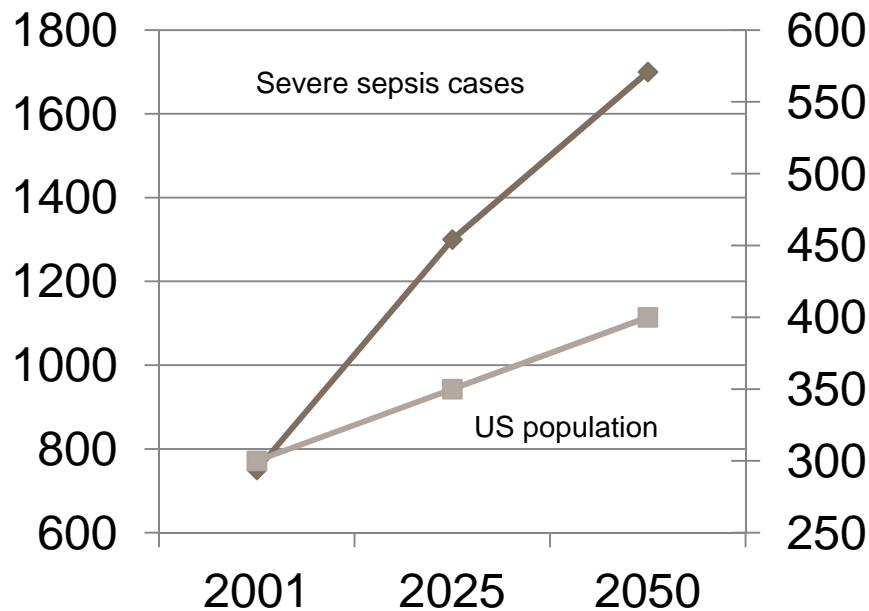
Classic Starling principle :  $F = (P_c - P_i) - \sigma (\pi_p - \pi_i)$



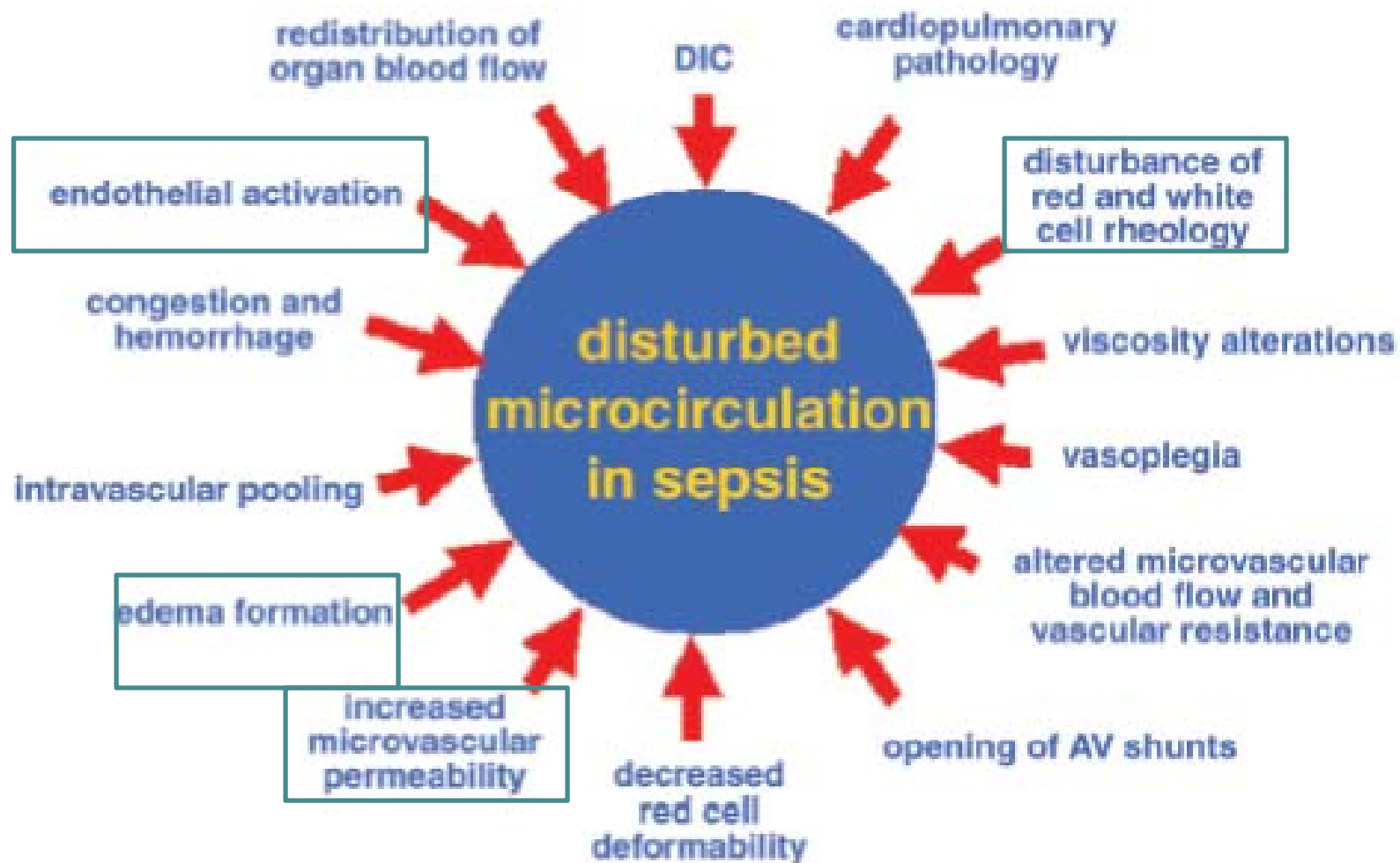
Revised Starling principle :  $F = (P_c - P_g) - \sigma (\pi_p - \pi_g)$



J Physiol 557.3 (3004) p704



- **More than 750,000 cases/Y of severe sepsis in US**
- **Estimated annual healthcare costs due to severe sepsis in U.S. exceed \$16 billion**
- **Leading cause of death in non-coronary ICU**



## Crystalloid Solutions

*(universally used for initial volume resuscitation)*

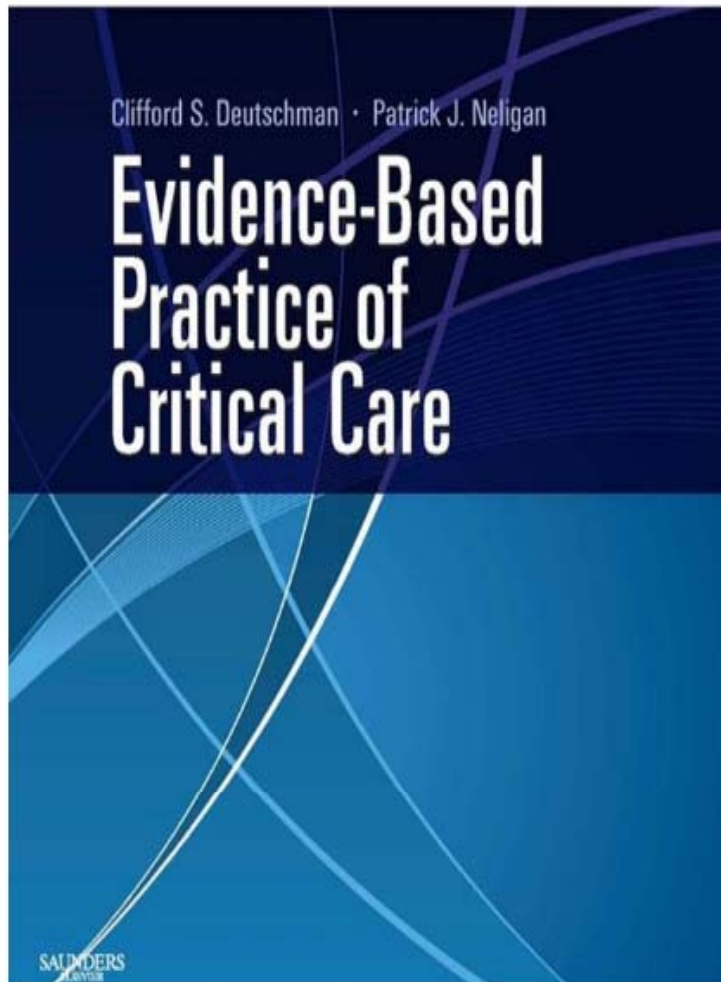
- “Normal” saline
- “Balanced” solutions
  - Ringers Lactate solution
  - Plasmalyte

## Colloid Solutions

*(achieve hemodynamic goals more quickly with significantly less volume)*

- Hydroxyethyl Starch(es)
- Blood products (albumin, RBC, plasma)

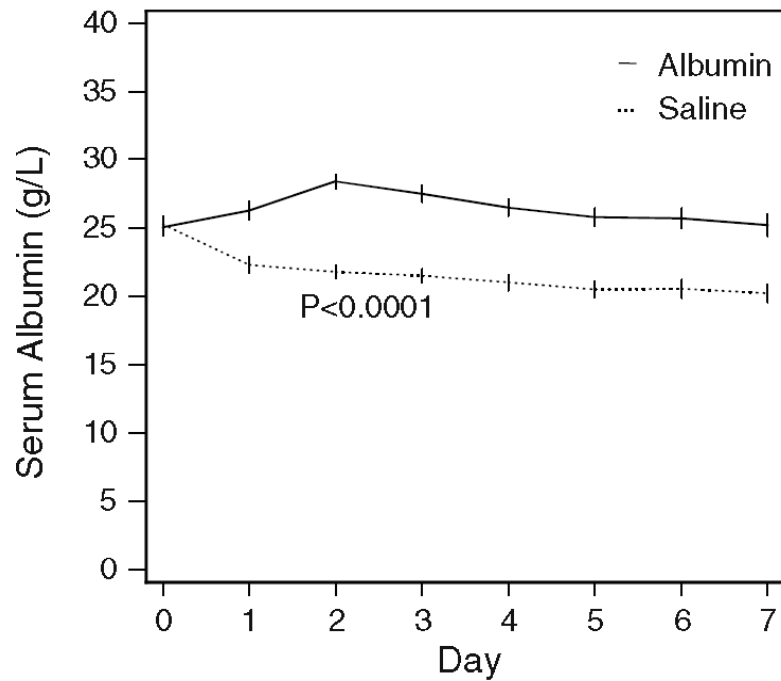
*As sepsis proceeds, ...significant tissue accumulation of resuscitation fluid occurs, resulting in adverse effects..*



**Elsevier 2010**

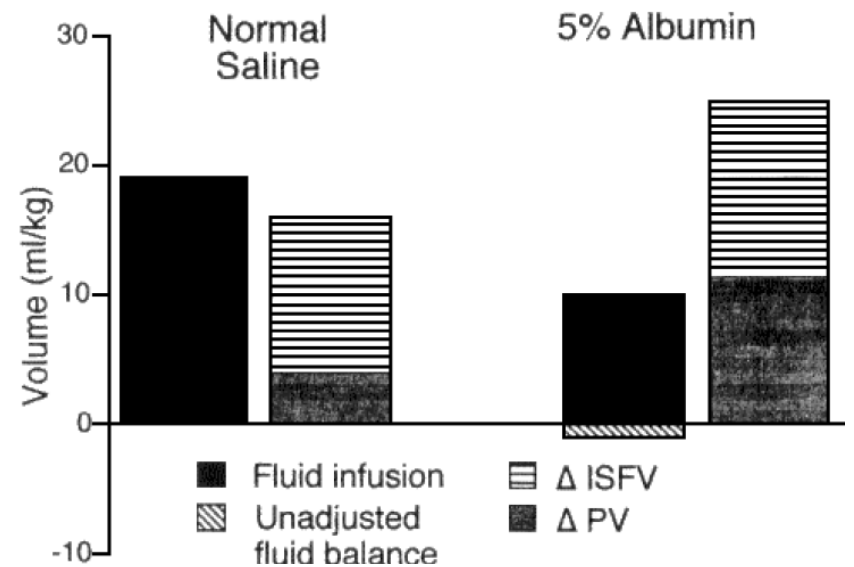
- ↘ *An ideal resuscitative fluid would maintain intravascular volume without expanding the interstitial space.*
- ↘ *Crystalloid solutions are universally used for initial volume resuscitation in sepsis and septic shock.....*
- ↘ *Colloid solutions achieve hemodynamic goals more quickly than crystalloids with significantly less volume.*
- ↘ *As sepsis proceeds,.....significant tissue accumulation of resuscitation fluid occurs, and this may result in adverse effects..*

Albumin is retained intravascularly...



SAFE investigators Int Care Med 2011, 37 (1), 86-96

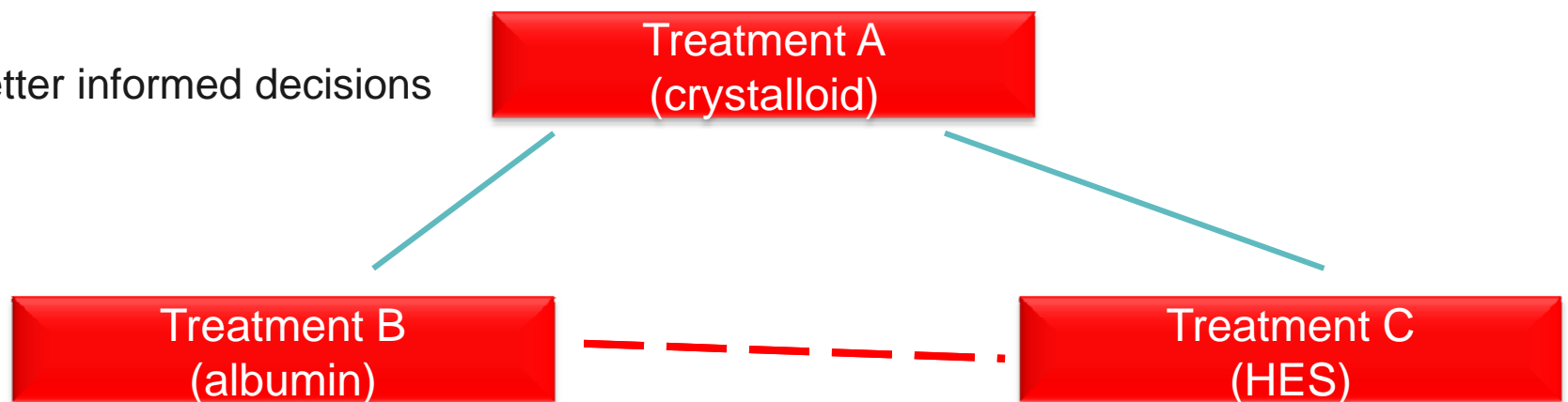
...and expands plasma volume



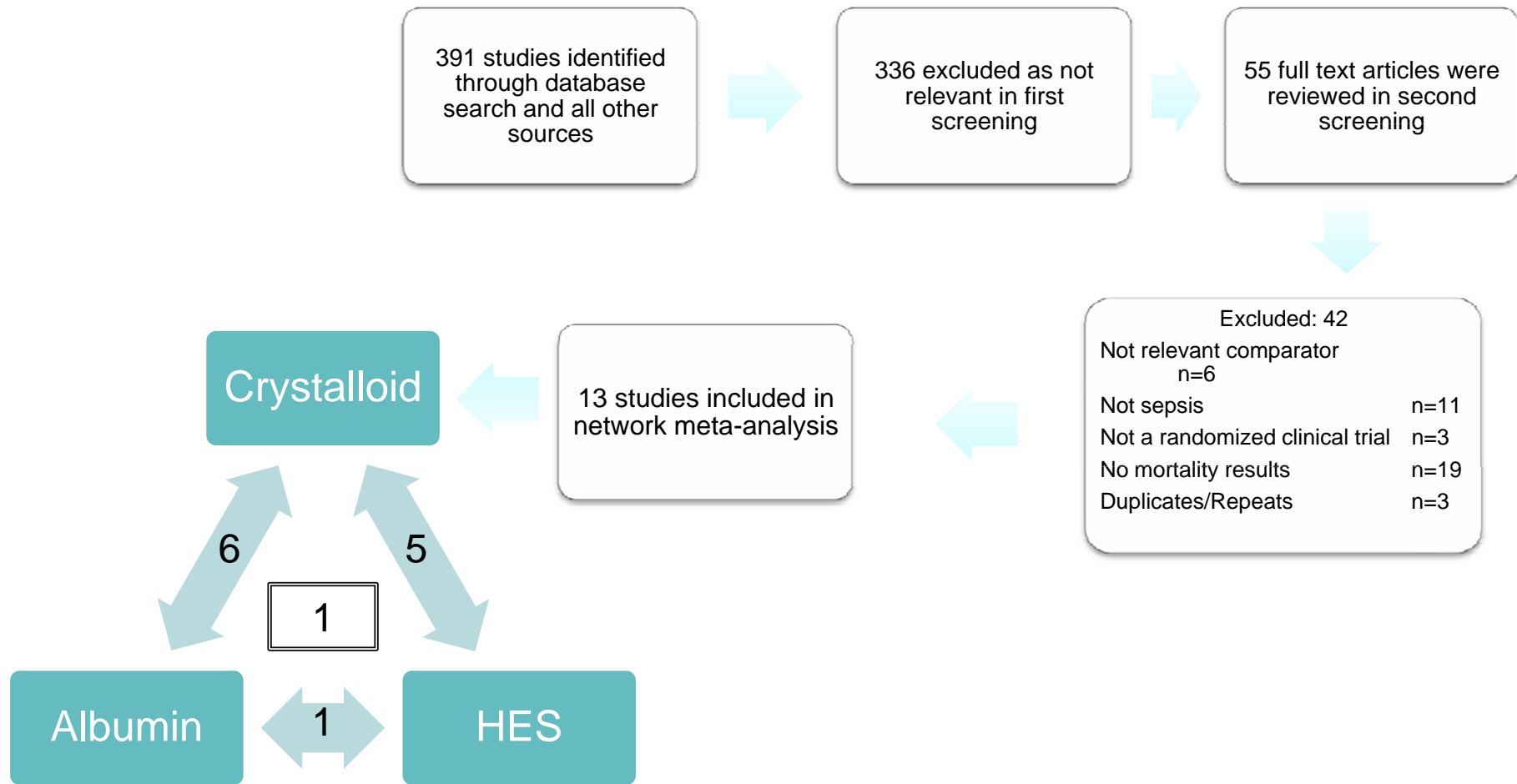
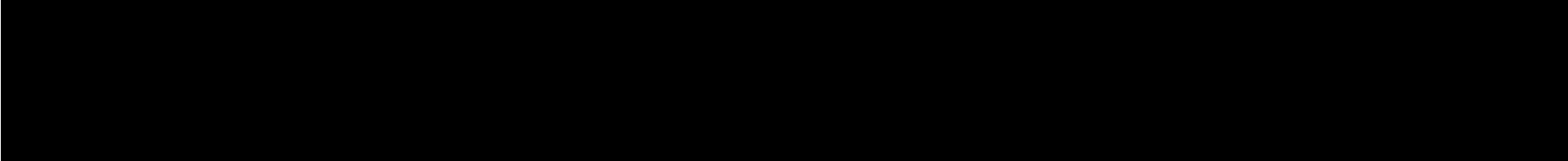
Ernest et al Critical Care Medicine:Volume 27(1)January 1999 pp 46-50

## NETWORK meta analysis / mixed treatment comparisons

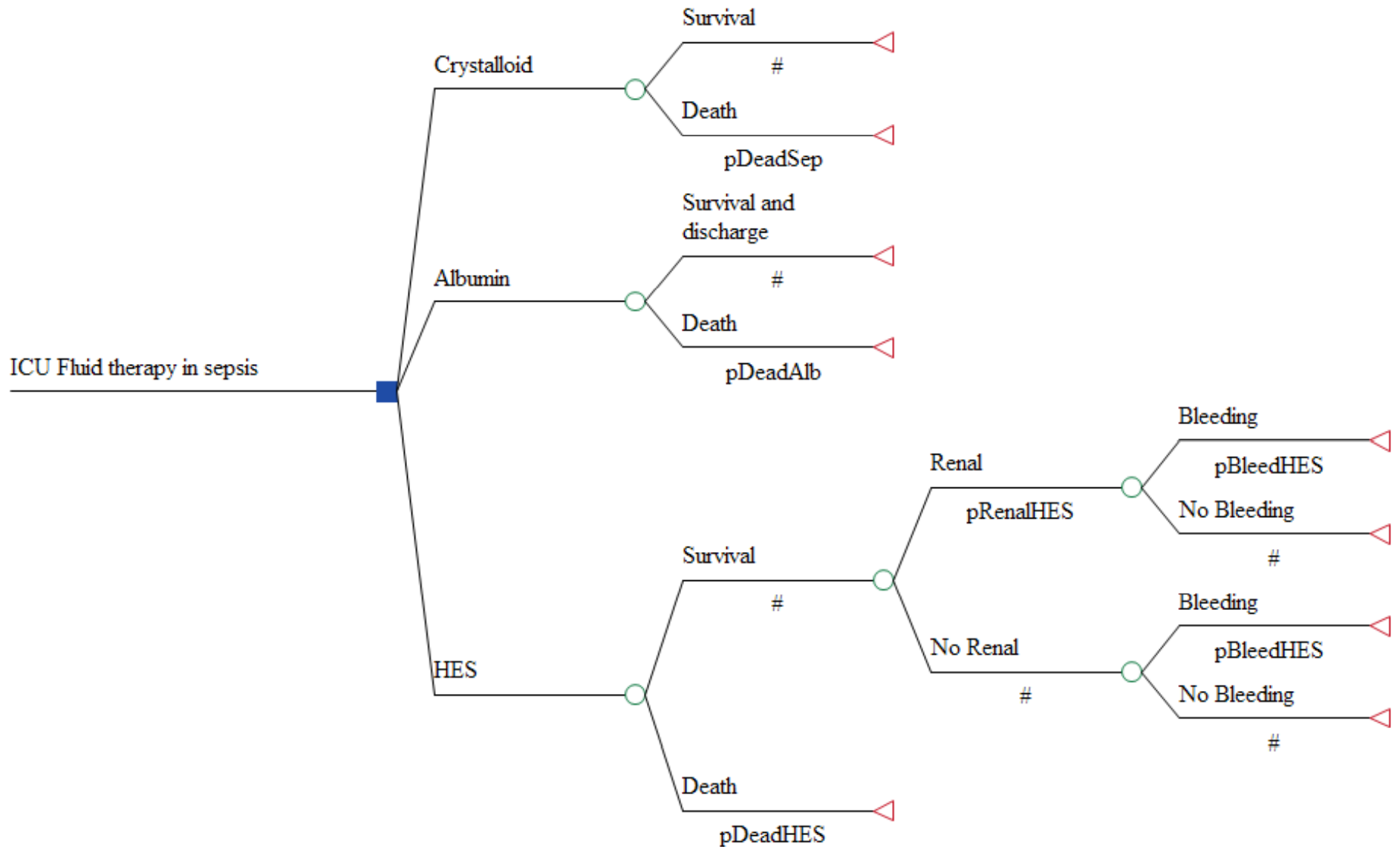
- Evidence from head to head comparison trials is often limited or unavailable
- Using evidence from A vs B and A vs C trials to draw conclusions about the effect of B relative to C
- It allows **all** evidence to be combined in a single analysis
  - Inference based on more evidence can (usually) provide more precision
  - Treatments can be ranked
  - Better informed decisions





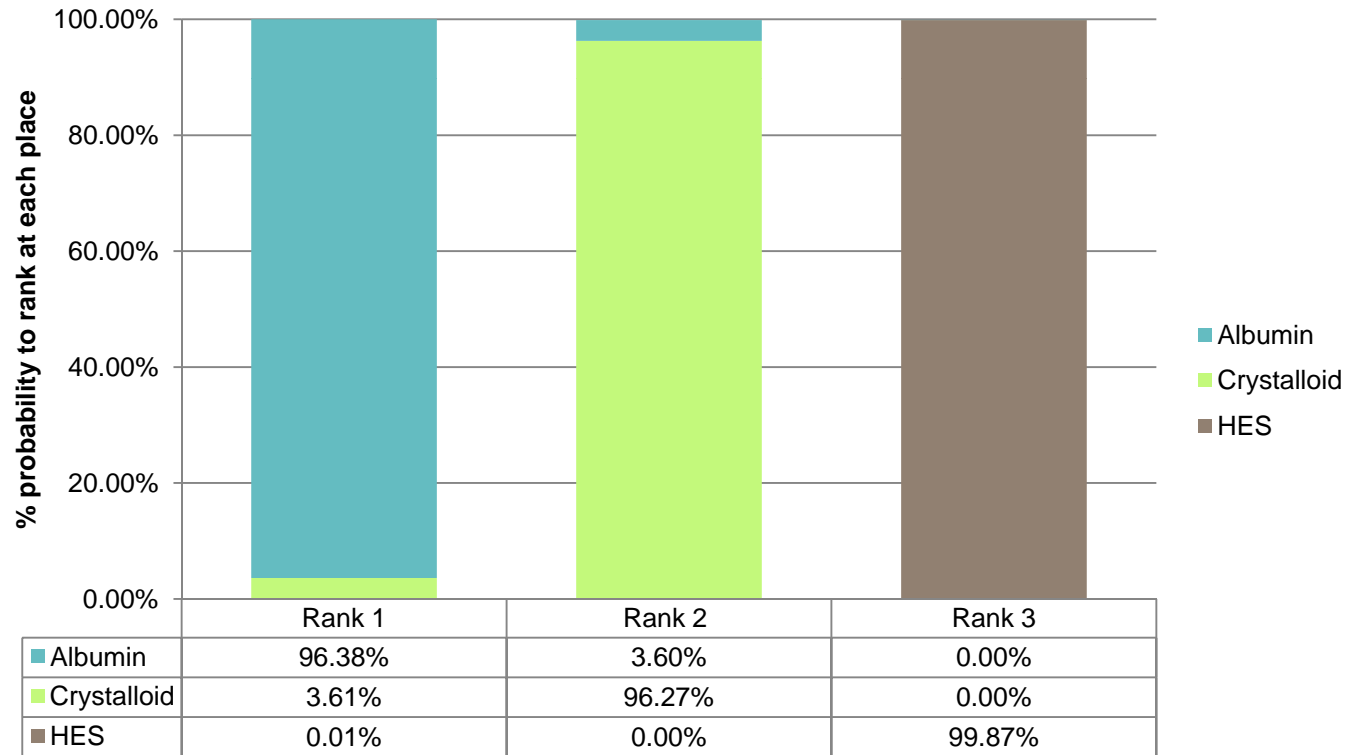


# Fluids in sepsis



Variable (Abbreviation in the model)	Base case value	One-way sensitivity analysis values	Probability Distribution
Cost of albumin US\$ (cAlb)	270	250 – 1,000	Not applied
Cost of hydroxyethyl starch US\$ (cHES)	269	±20%	Not applied
Cost of sepsis standard of care US\$ (cSepsisGen)	20,133	±20%	Gamma~ (55.56, 0.003)
Cost of renal replacement therapy US\$ (cRenal)	142,404	76,540 – 30,616	Normal~ (142404, 146792)
Cost of treatment for bleeding US\$ (cBleeding)	1,732	1,044 – 2,366	Normal~ (1732, 705.6)
Life expectancy – general population at 65 years (LEgenpop)	18.60	Not applied	Not applied
In-hospital or 28 day mortality with crystalloid (pDeadSep)	33.27%	Not applied	Beta~ (16.52, 33.14)
In-hospital or 28 day mortality with albumin (pDeadAlb)	30.95%	Not applied	Beta~ (14.78, 32.98)
In-hospital or 28 day mortality with hydroxyethyl starch (pDeadHES)	38.54%	Not applied	Beta~ (20.45, 32.60)
90-day excess mortality with hydroxyethyl starch (pDeadHES90)	13.6%	Not applied	Not applied
Excess probability of renal replacement therapy with hydroxyethyl starch (pRenalHES)	6.5%	3.5% - 19.5%	Uniform~(0.035, 0.195)
Excess probability of bleeding with hydroxyethyl starch (pBleeding)	3.29%	Not applied	Not applied
Prob. of mortality in bleeding episodes (pDeadBleed)	7.3%	Not applied	Beta~ (45.6, 579.1)
Prob. of mortality after RRT (pDeadRenal)	54.1%	50.8% - 60.8%	Uniform (0.508, 0.608)

# Ranking probabilities of competing fluid treatments



	Total Medical Cost	Effectiveness *
Crystalloid	\$18,199	Reference
Albumin	\$18,469	0.23
HES	\$24,196	-0.45

\* Years saved/lost compared to crystalloid.

Variable	Range (\$)	Fluid Treatment	Total Cost/Life Year (Low) \$	Total Cost/Life Year (High) \$
Cost of Renal Replacement Therapy	76,540 – 306,160	Crystalloid	9,086	9,086
		Albumin	8,259	8,259
		Hydroxyethyl Starch	13,775	19,639
Cost of Albumin	250 – 1,000	Crystalloid	9,086	9,086
		Albumin	8,259	8,259
		Hydroxyethyl Starch	15,457	15,457
Cost of treatment of bleeds	1,193 – 2,693	Crystalloid	9,086	9,086
		Albumin	8,259	8,259
		Hydroxyethyl Starch	15,450	15,470



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### Hydroxyethyl Starch Solutions: FDA Safety Communication - Boxed Warning on Increased Mortality and Severe Renal Injury and Risk of Bleeding

- Do not use HES solutions in critically ill adult patients including those with sepsis, and those admitted to the ICU.
- Avoid use in patients with pre-existing renal dysfunction.
- Discontinue use of HES at the first sign of renal injury.
- Need for renal replacement therapy has been reported up to 90 days after HES administration.
- Continue to monitor renal function for at least 90 days in all patients.
- Avoid use in patients undergoing open heart surgery in association with cardiopulmonary bypass due to excess bleeding.
- Discontinue use of HES at the first sign of coagulopathy.



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

14 June 2013  
EMA/349341/2013

**PRAC recommends suspending marketing authorisations  
for infusion solutions containing hydroxyethyl-starch**

12 July 2013  
EMA/349341/2013

**Recommendation to suspend marketing authorisations for  
hydroxyethyl-starch solutions to be re-examined**



- ↘ Colloids are required after initial crystalloid infusion
- ↘ Albumin has been shown to improve outcomes in sepsis
- ↘ HES has been shown to increase mortality and renal damage
- ↘ Network meta-analysis and Decision Modeling allow direct comparison between fluid therapies
- ↘ In decision-making, a focus on total, long term costs needs to supersede short term considerations of individual interventions

Disclosure:

The authors provide services to the pharmaceutical and biotechnology industry, including the manufacturers of therapies described in this presentation.