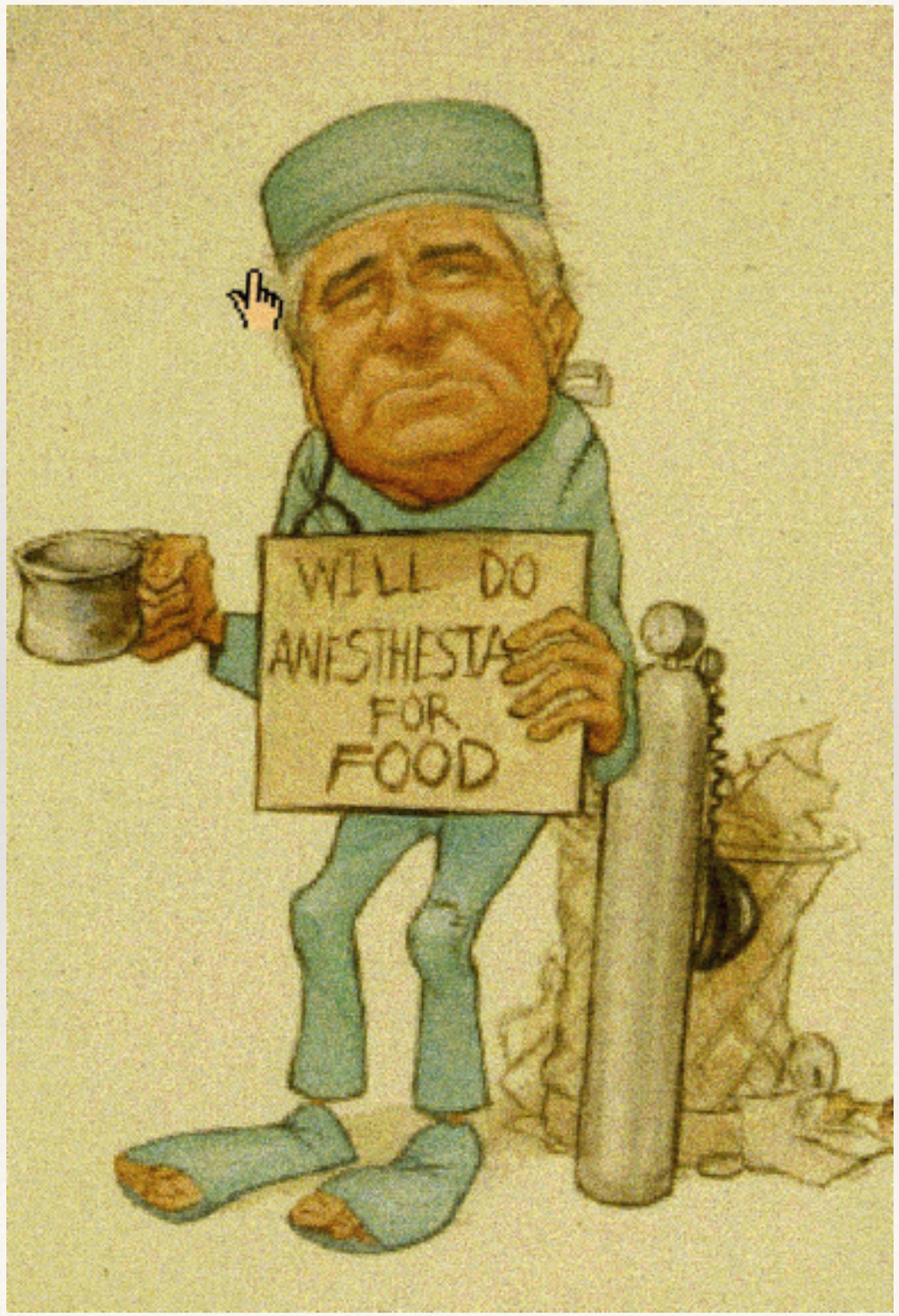
Best of Brussels-2016

Dr John Vogel

No conflict of interest



Best of Brussels 2016

- Acute fibrinolytic shutdown
- SEPSIS-3
- Urine output in AKI
- Timing of source control and mortality
- Early goal directed therapy
- Microbiota
- Measuring VAP rate as a quality measure
- ECC02R
- Haematological malignancy and ITU outcomes
- Coagulopathy in liver disease
- Neuro-imaging in ITU survivors
- Best use of ITU beds
- Odds and Sods

791 lectures over 4 days!

Fibrinolytic shutdown

Tranexamic Acid for all?

Acute Fibrinolysis Shutdown after Injury Occurs Frequently and Increases Mortality: A Multicenter Evaluation of 2,540 Severely Injured Patients

- **Fibrinolysis shutdown** is the **most common** phenotype and associated with **increased mortality**
- These findings may help explain the 2 recent retrospective studies that do not identify a survival benefit in using tranexamic acid as proposed by the CRASH II trial
- The optimal use of antifibrinolytics is likely in a **targeted** population.
- **Reconsideration** of the empiric use of antifibrinolytics in trauma

J Am Coll Surg.2016.01.006

Tranexamic Acid for all?

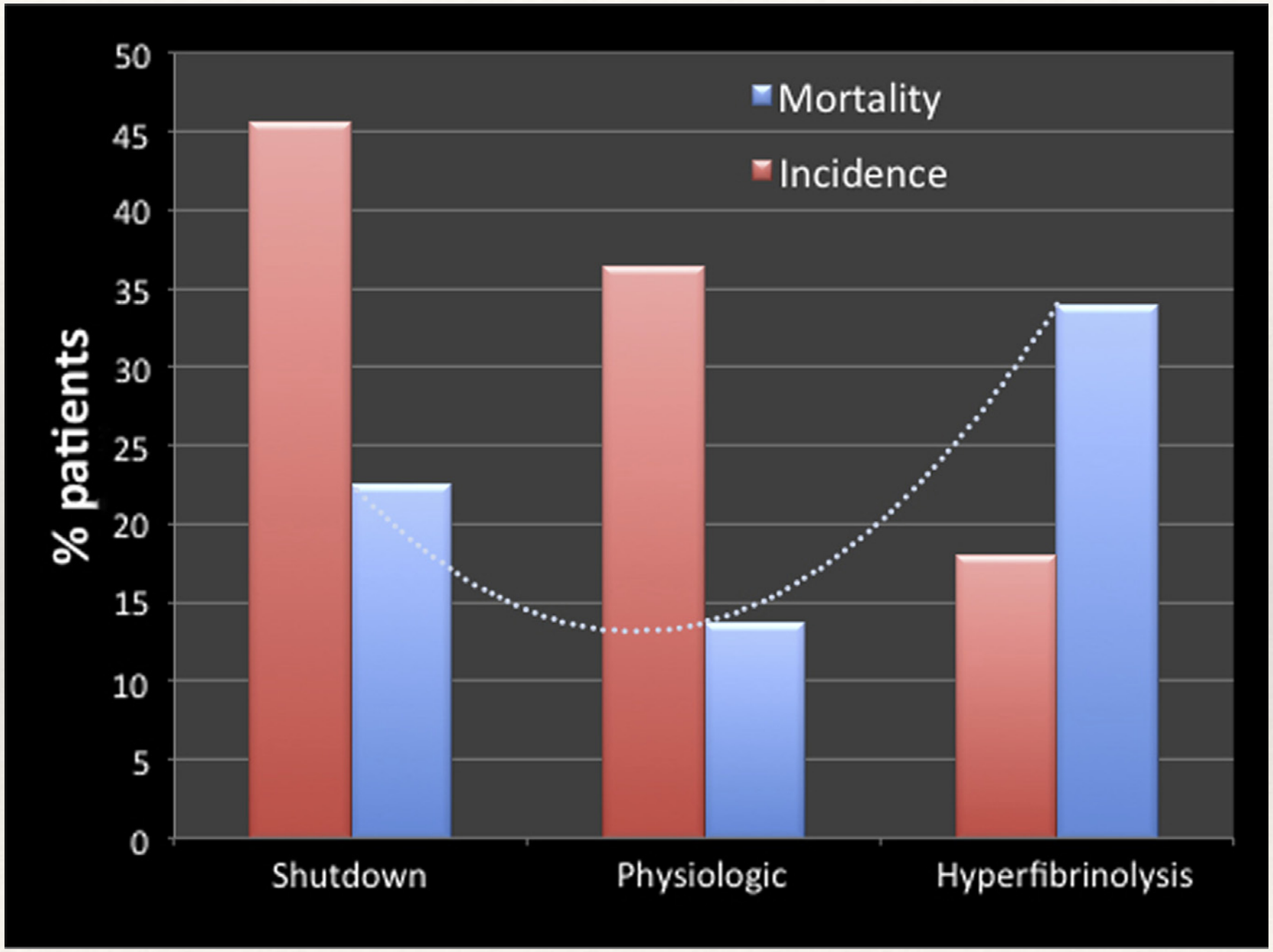
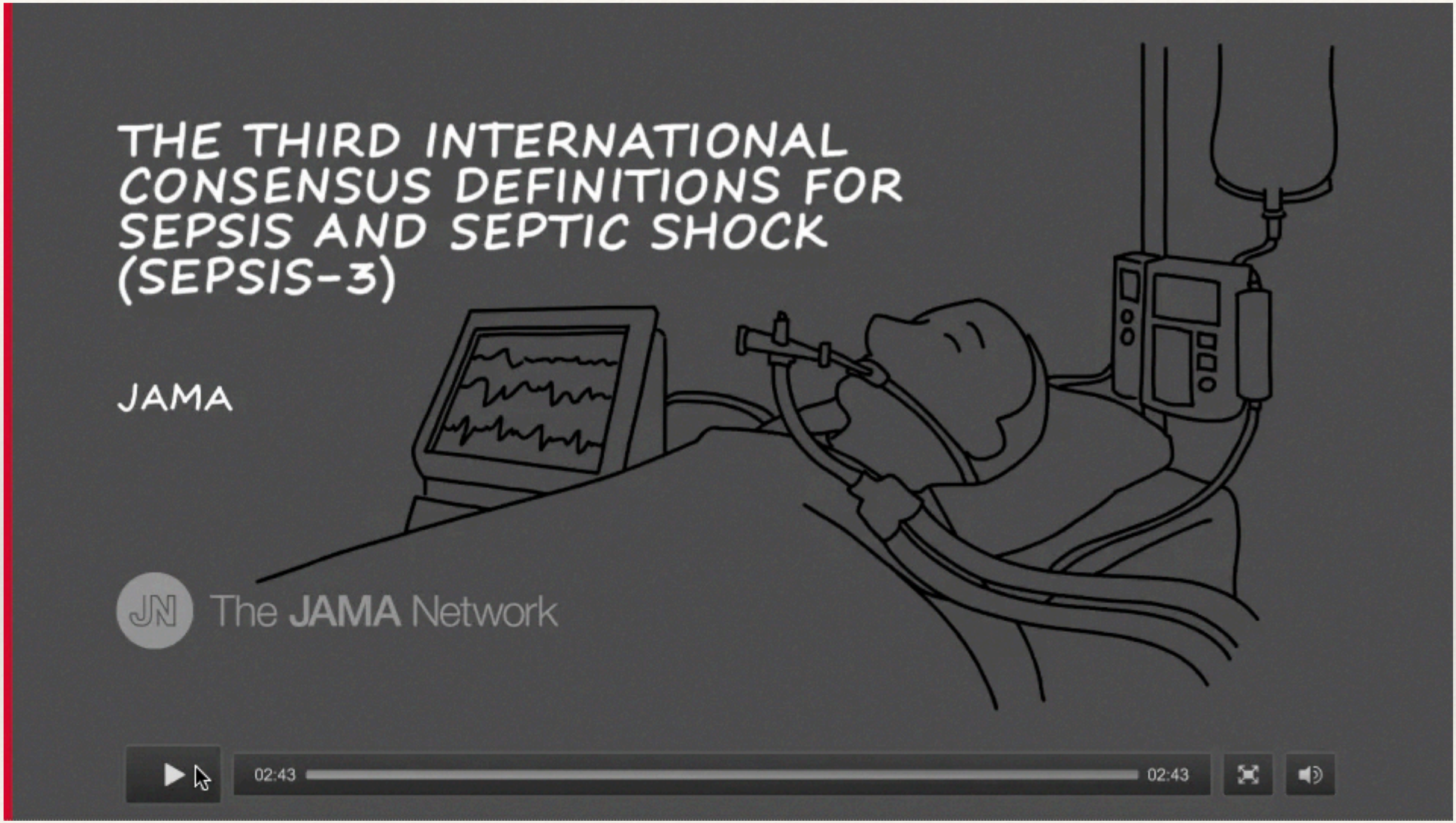


Figure 1. Incidence and mortality of severely injured trauma patients stratified by fibrinolysis phenotype.

J Am Coll Surg.2016.01.006

Sepsis 3


THE THIRD INTERNATIONAL CONSENSUS DEFINITIONS FOR SEPSIS AND SEPTIC SHOCK (SEPSIS-3)
JAMA
The JAMA Network
02:43
02:43

Sepsis 3 - but…

- “Big data” retrospective from a single US source
- Needs validation in other settings
- “qSOFA should not replace NEWS”
- Not really a definition of sepsis
- Not all agree with “dropping” SIRS

Urine output in AKI

Classifying AKI by Urine Output versus Serum Creatinine Level

John A. Kellum,*† Florentina E. Sileanu,*†‡ Raghavan Murugan,*† Nicole Lucko,*†
Andrew D. Shaw,*§ and Gilles Clermont*†

J Am Soc Nephrol 26: 2231–2238, 2015

8179 ITU patients	Mortality
No AKI by UO nor SCreat	6%
AKI -stage III S Creat only	12%
AKI -stage III UO only	18%
AKI -stage III S Creat + UO	**51%**

Even adding minor (stage 1) UO or S Creat criteria, to a stage 3 AKI based on only one criteria increased mortality by a factor of 2-3 !

J Am Soc Nephrol 26: 2231–2238, 2015

Timing of source control and mortality

Bloos et al. Critical Care 2014, 18:R42
http://ccforum.com/content/18/2/R42

CRITICAL CARE

RESEARCH Open Access

Impact of compliance with infection management guidelines on outcome in patients with severe sepsis: a prospective observational multi-center study

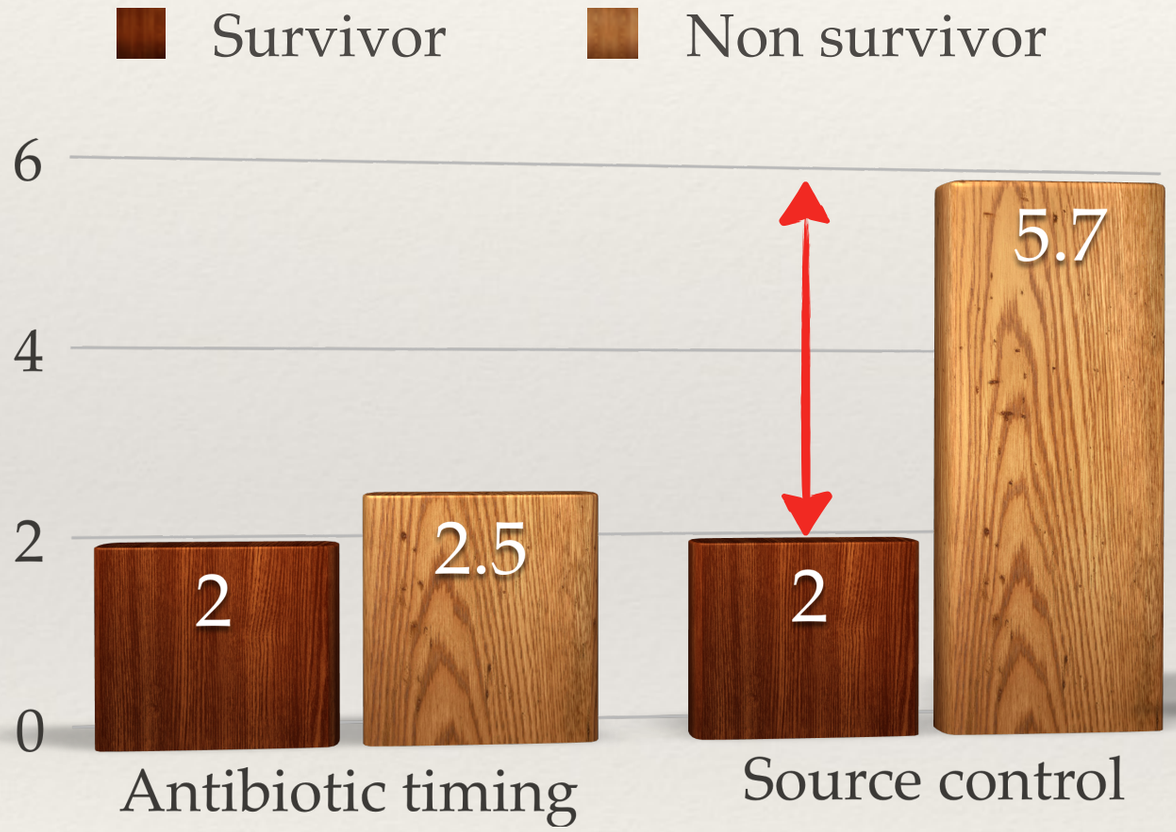
Azuhata et al. Critical Care 2014, 18:R87
http://ccforum.com/content/18/3/R87

CRITICAL CARE

RESEARCH Open Access

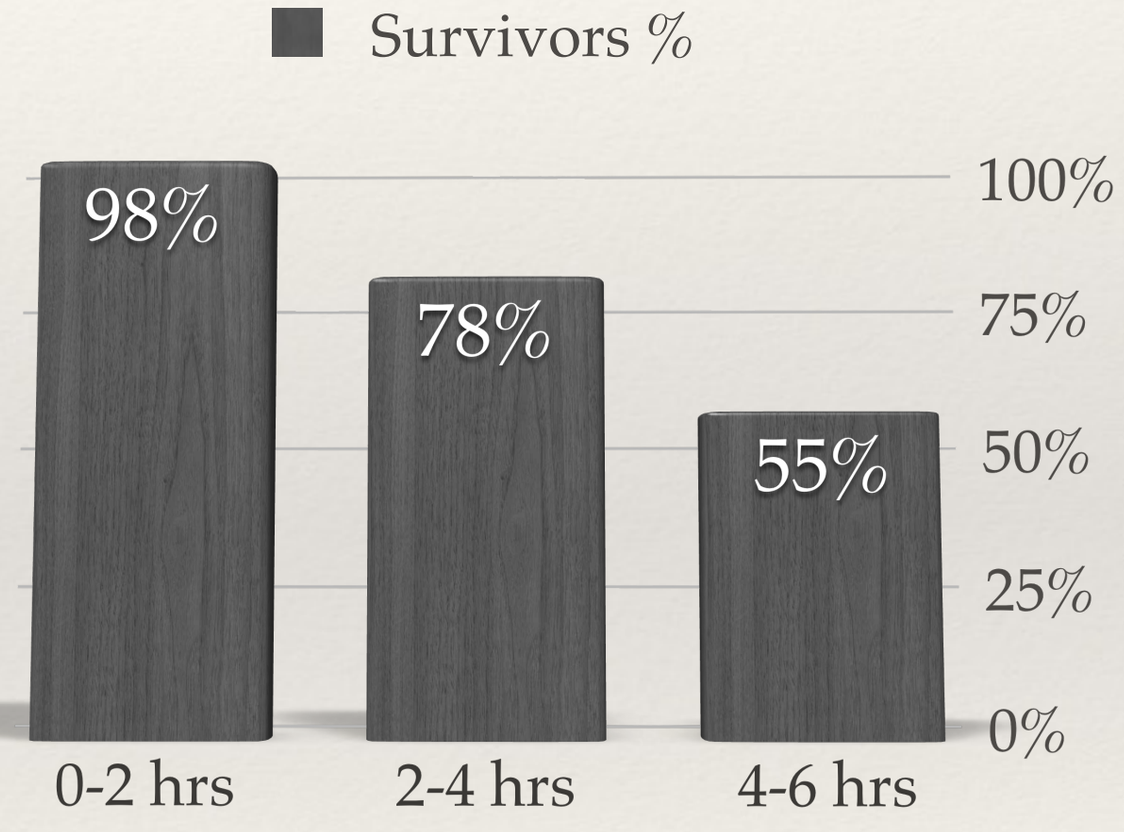
Time from admission to initiation of surgery for source control is a critical determinant of survival in patients with gastrointestinal perforation with associated septic shock

Time to treatment (hrs)



"A delay in source control **beyond 6 hours** may have a major impact on patient mortality "

60 day survival rate



"The target time for a favorable outcome … **within 6 hours**… do not delay in initiating EGDT assisted surgery"

Should “Goal Directed Therapy” be abandoned?

PROCESS / ARISE / PROMISE

Angus D et al
NEJM 2014

Peake S et al
NEJM 2014

Mouncey P et al
NEJM 2015

Excellent trials but ….

Imagine a trial on penic

- 80% of the pa
- Some patient
- Most patients

Limited power

lower tha

Limited externa

low inclusion rate

mostly office hours inclusions

Most of the screened patients were included in the Rivers trial but only 20–30 % included in the subsequent studies.

The patients enrolled in the recent multicenter trials were less severely ill than those in the Rivers study, being less often treated with mechanical ventilation and having a lower mortality rate.

Even patients with lactate levels between 3 and 4 mEq/l had higher mortality rates (30 %). There may be a bias towards including less severe patients in clinical trials.

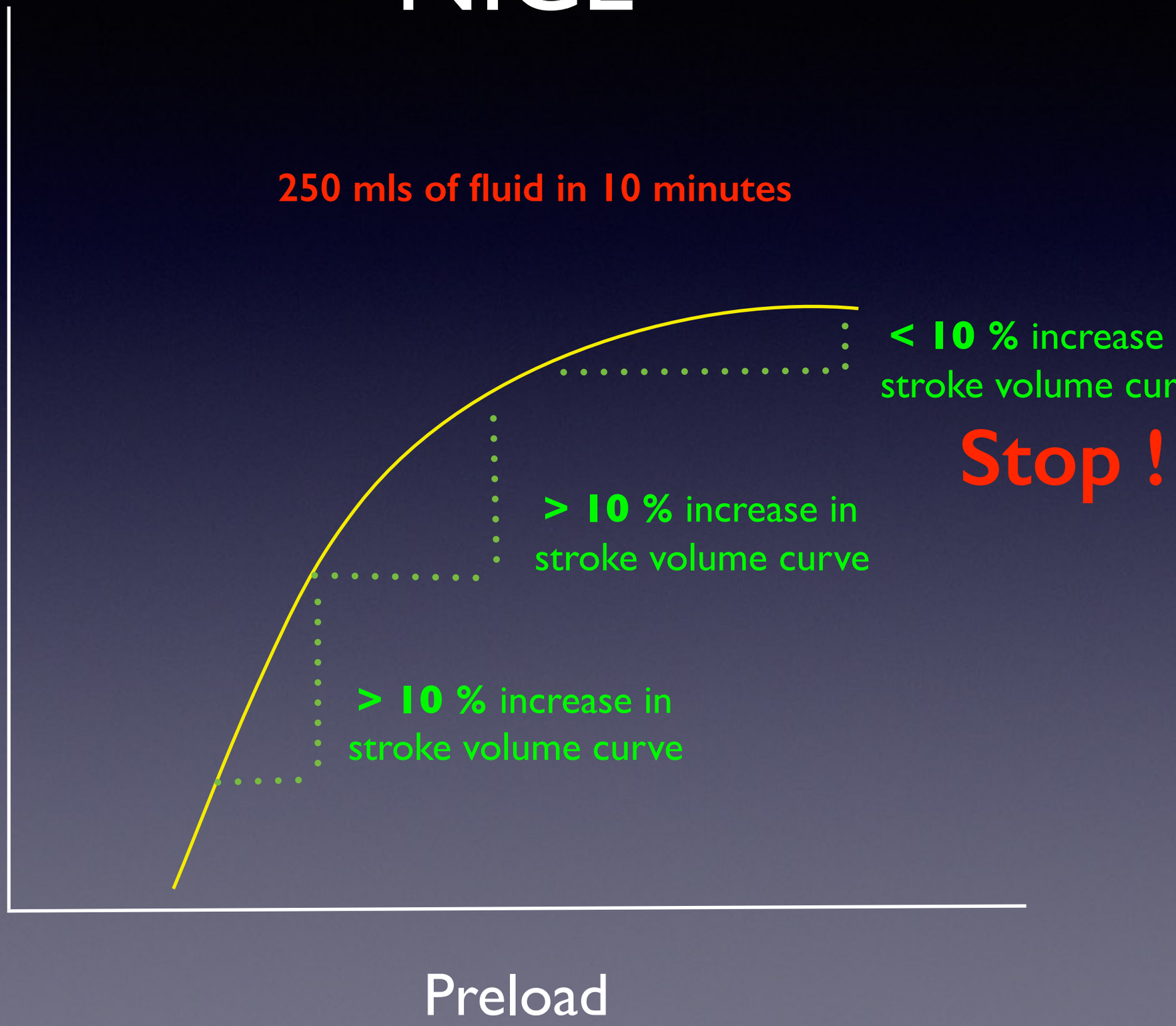
. The rate of admission of patients to the intensive care unit (ICU) was also remarkably low in the three large- scale randomized trials: Close to one patient in five (422/2324 = 18 %) in the control groups of these three trials was not even admitted to the ICU [14].

A final point suggesting a marked degree of patient selection in these trials is their inclusion primarily during office hours.In the ProMISe study 90 % of patients were included between 8 am and 8 pm on weekdays and less than 10 % during the night and at the weekend.

This may have been due to the restricted working hours of research assistants, but protocolized care may, in fact, be more useful when less experienced physicians are in charge, which is often during the night and at the weekend.

EGDT may still be beneficial in the most severely ill
patients, especially when less experienced staff who may appreciate using simple protocols are in charge.

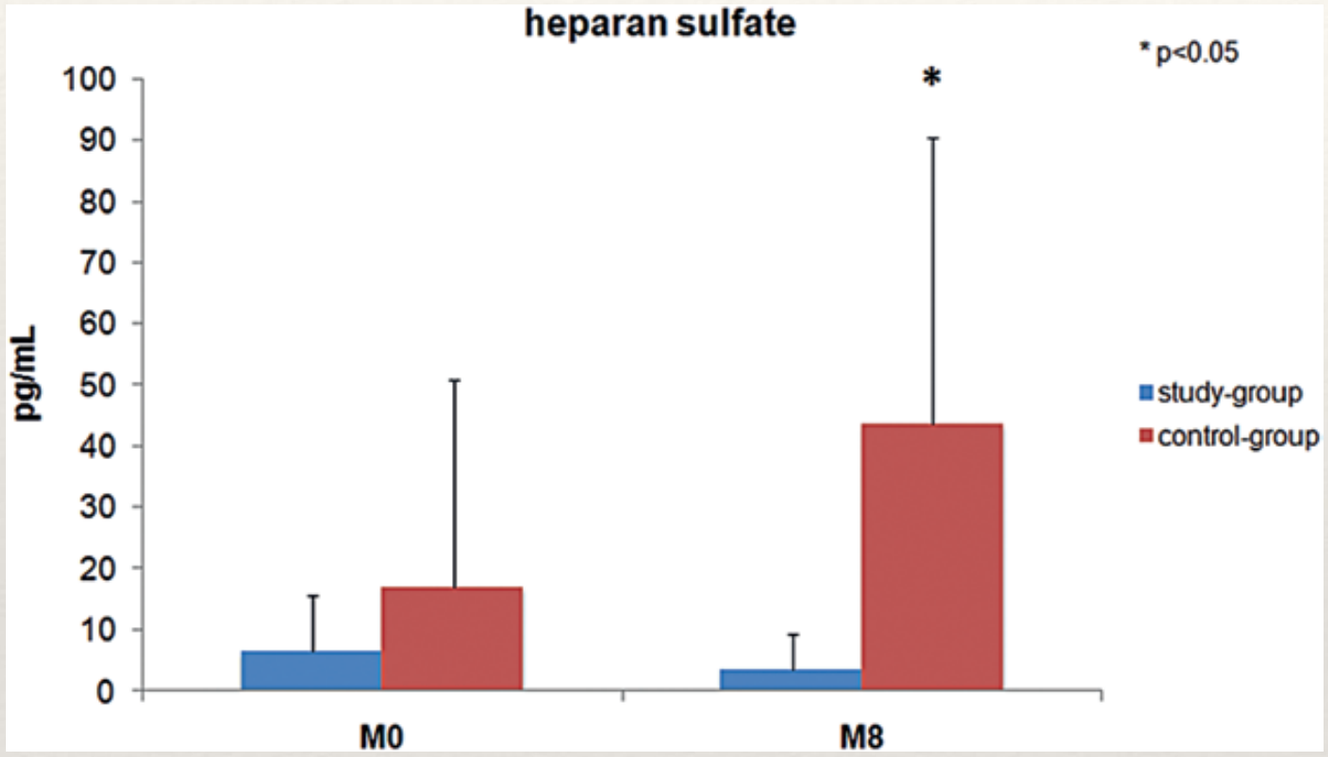
Protocol recommended by NICE

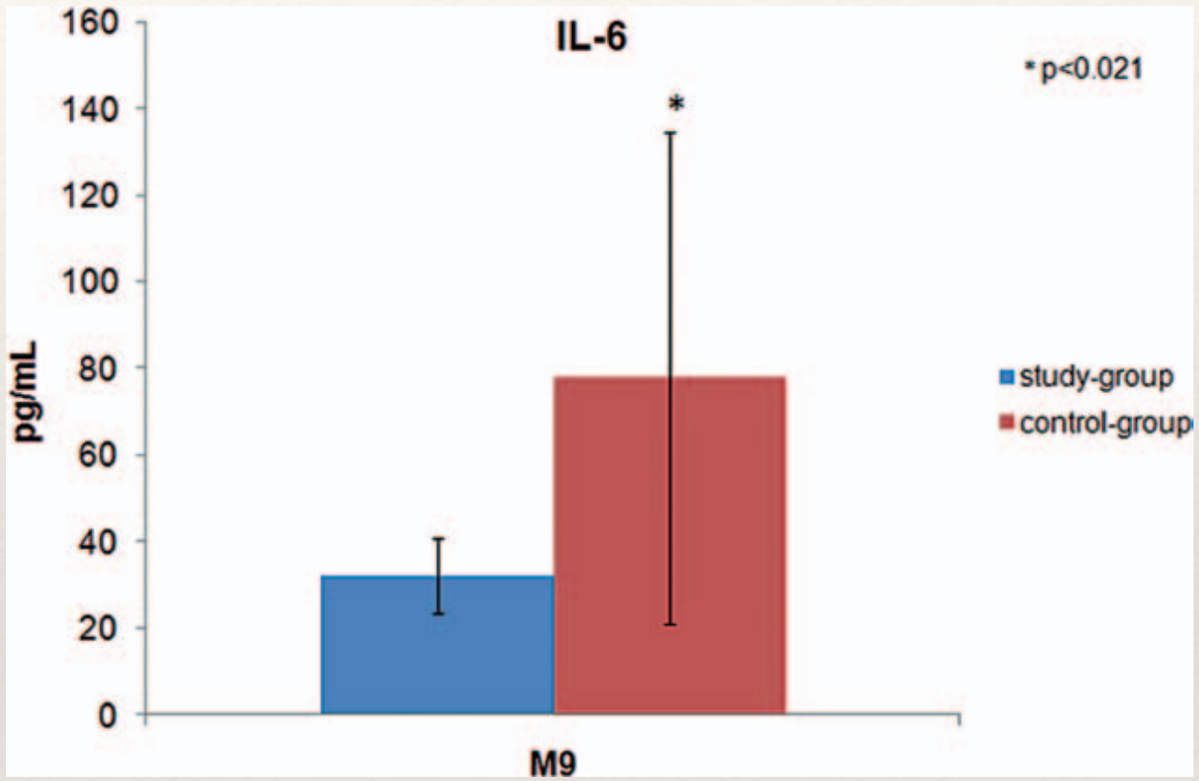


But.....

Individualized Early Goal-Directed Therapy in Systemic Inflammation: Is Full Utilization of Preload Reserve the Optimal Strategy?

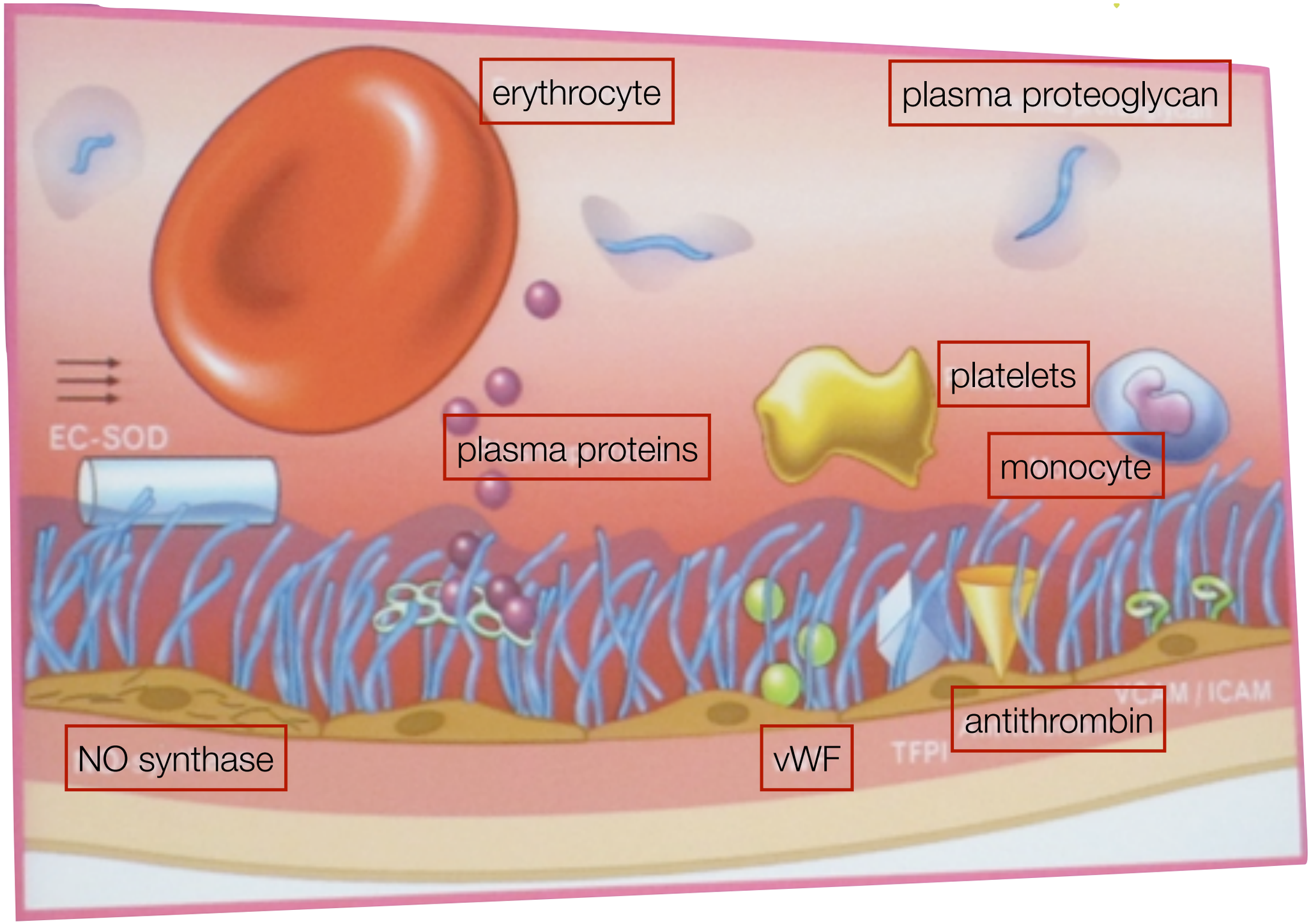
Crit Care Med 2014; 42:e741–e751





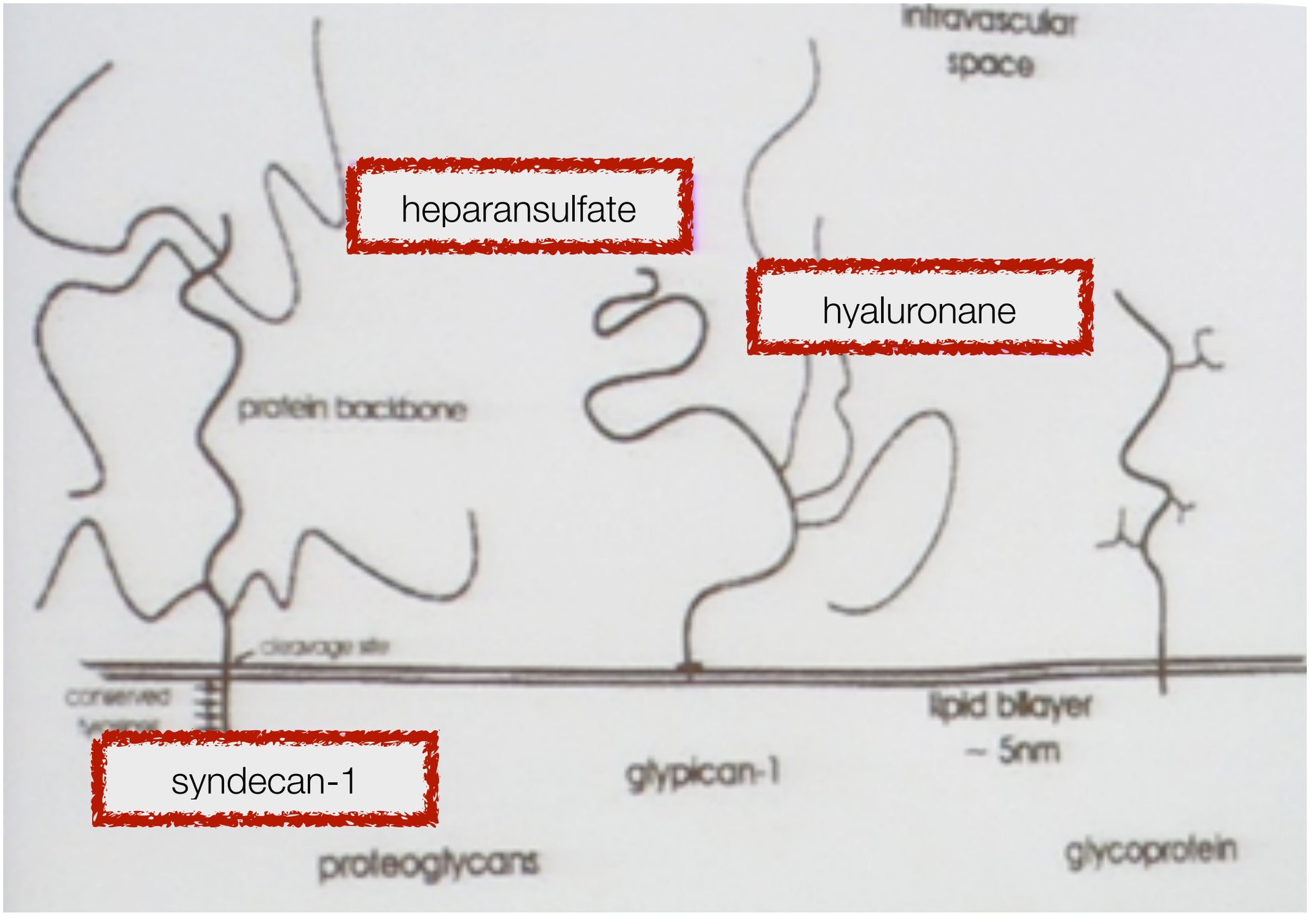
Maximizing SV leads to more severe **glycocalyx degradation** and **inflammatory response** and led to more **pancreatic edema** compared to maintaining individual, "normal" values of SVI in SAP.

Healthy endothelial glycocalyx



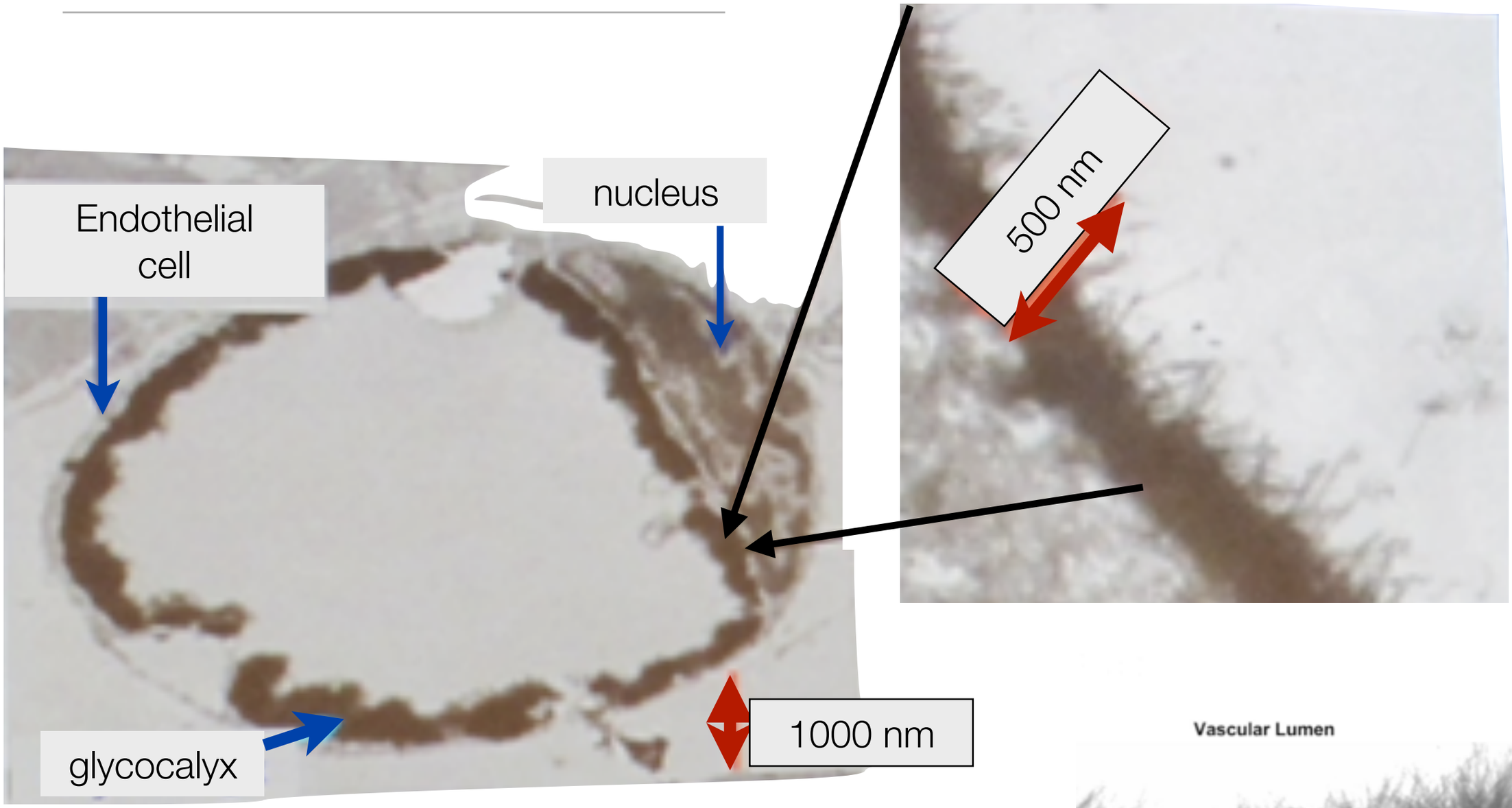
Nieuwdorp et al Curr Opin Lipidol 2005; 16:507

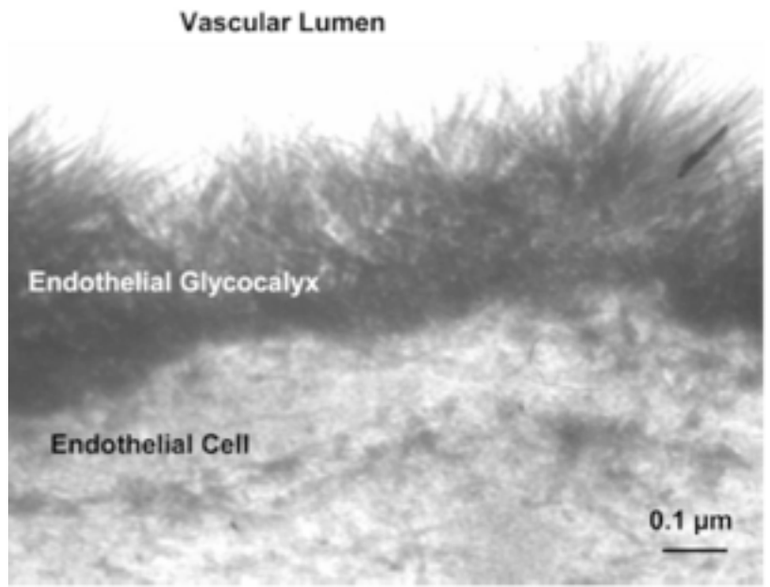
Glycocalyx - components



Pries et al Eur J Physiol; 440:653-666, 2000

Electron microscopy - glycocalyx



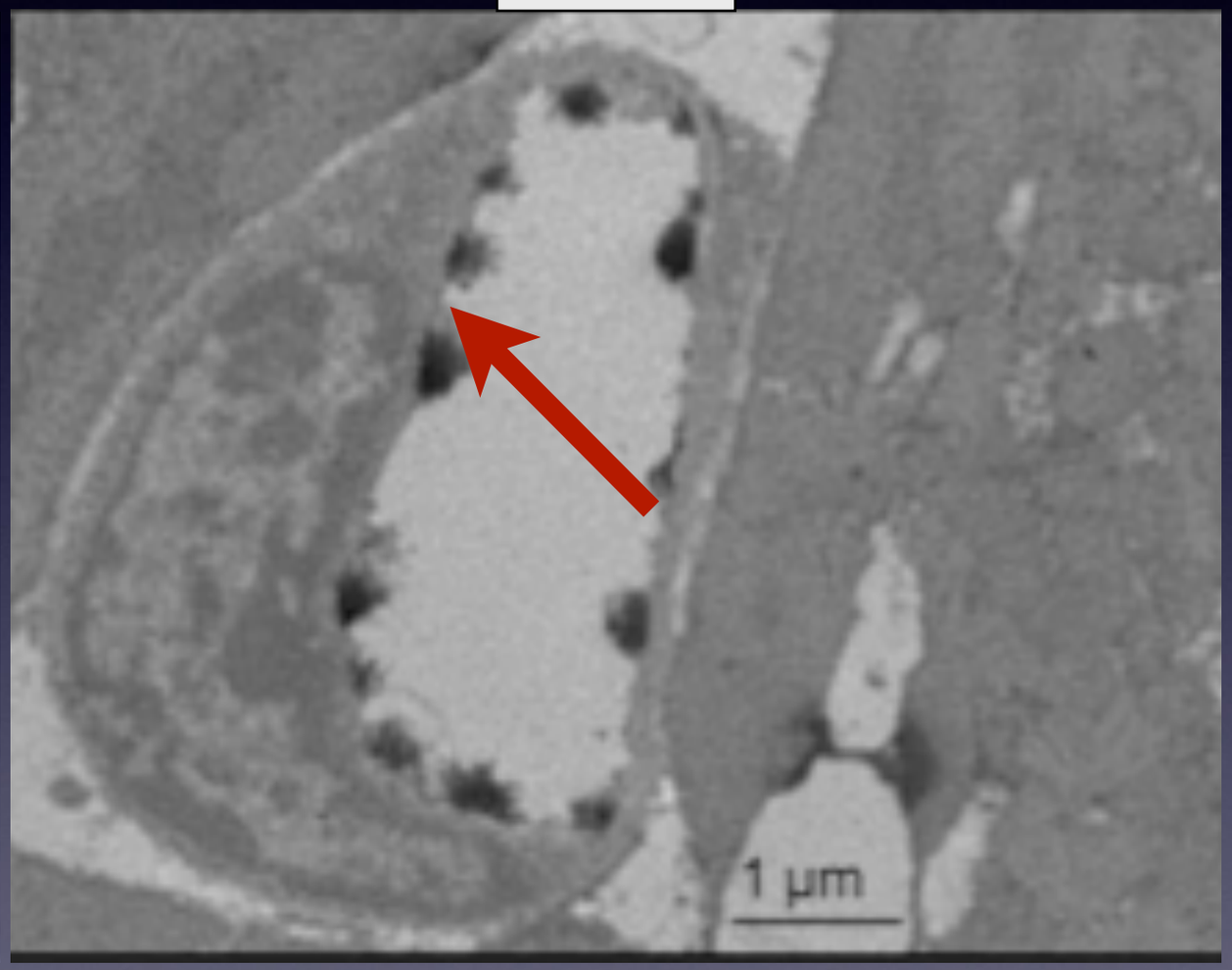


Rehm et al Anesthesiology 2004;100:1211

“Protect” the glycocalyx

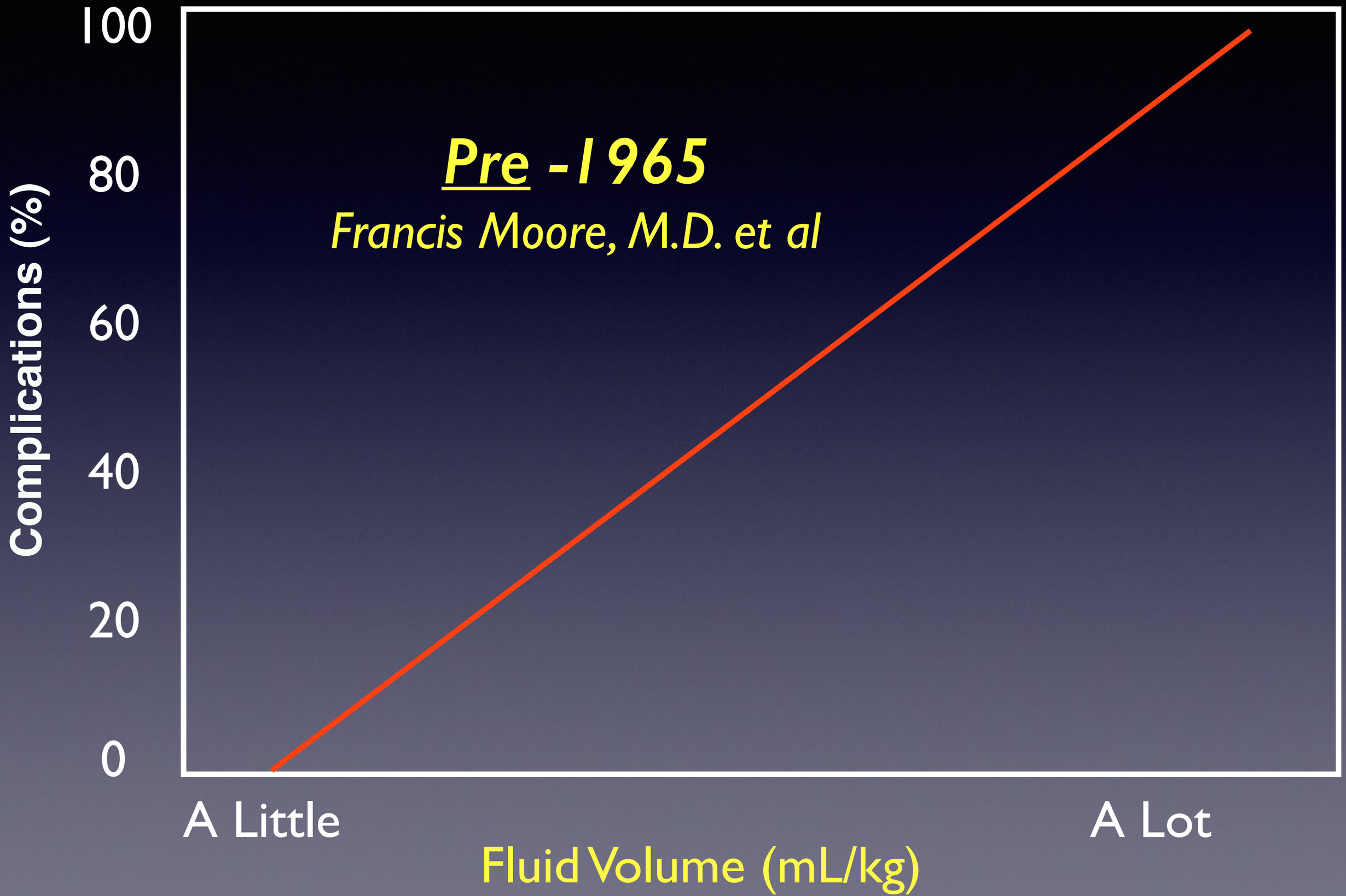
Control

ANP

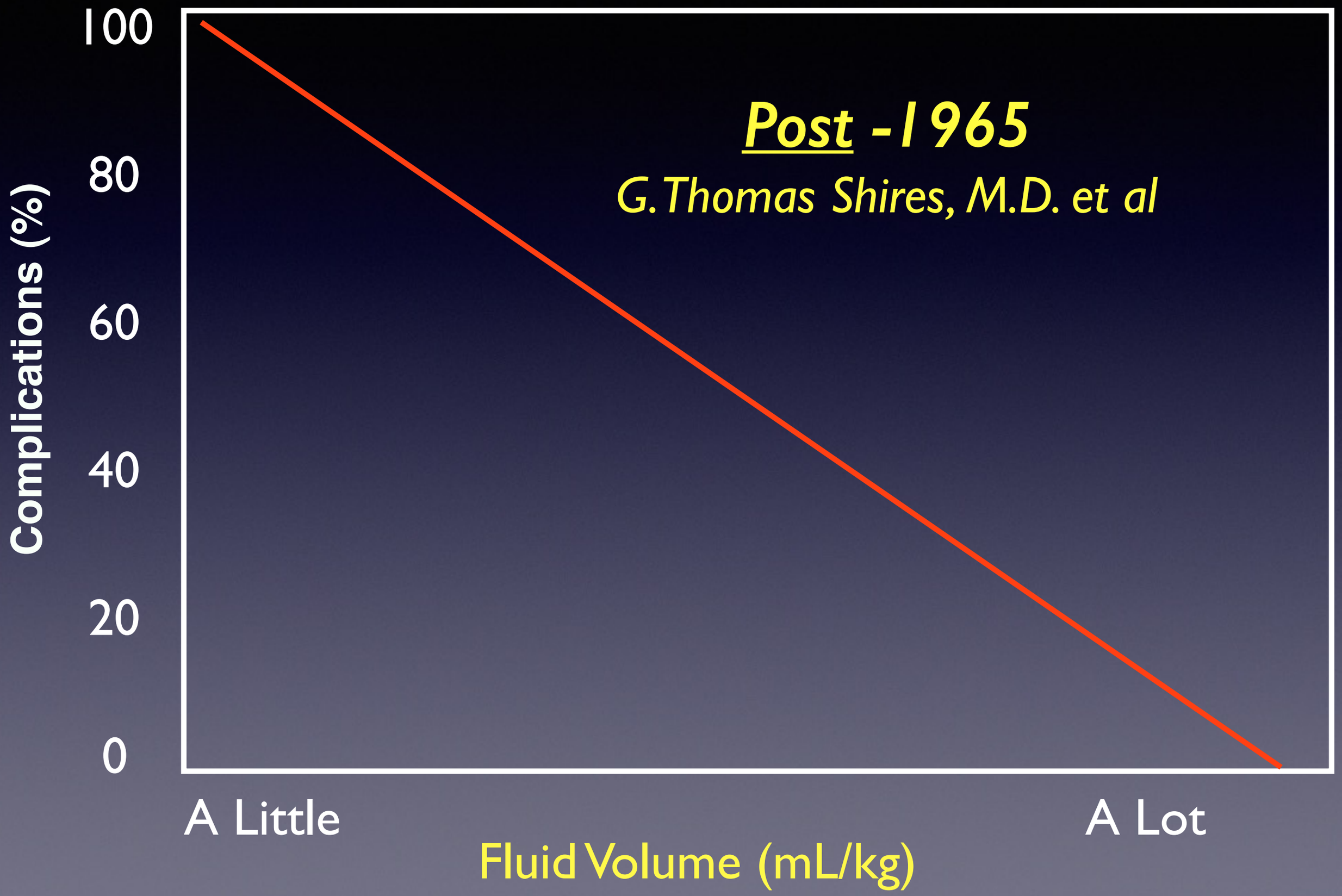


Am J Physiol Heart Circ Physiol 289: H1993–H1999, 2005

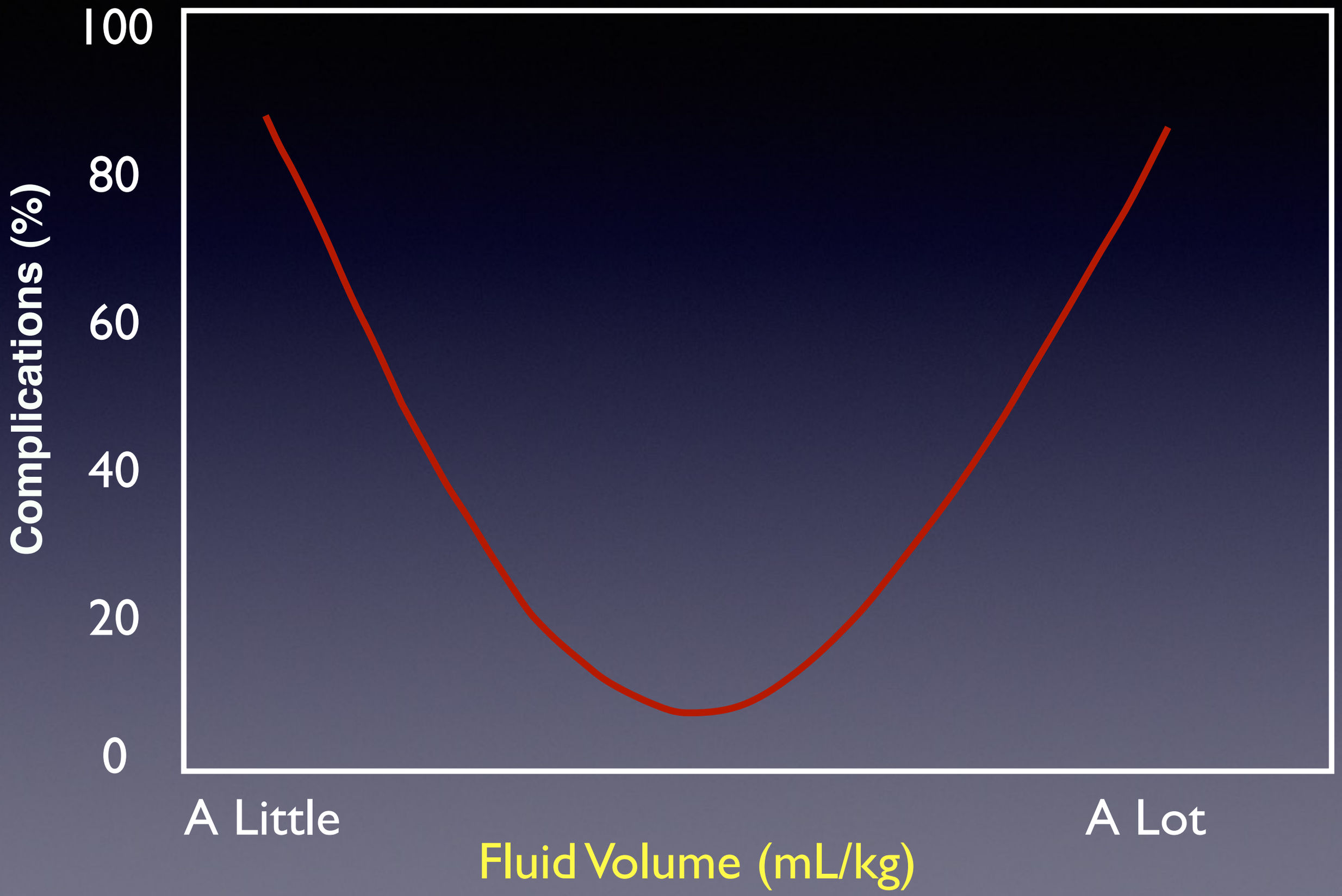
"Fluid Restriction"



"Fill that Third Space"



The True Picture ?



CONCLUSIONS

- **Should we abandon Early Goal directed therapy ?**

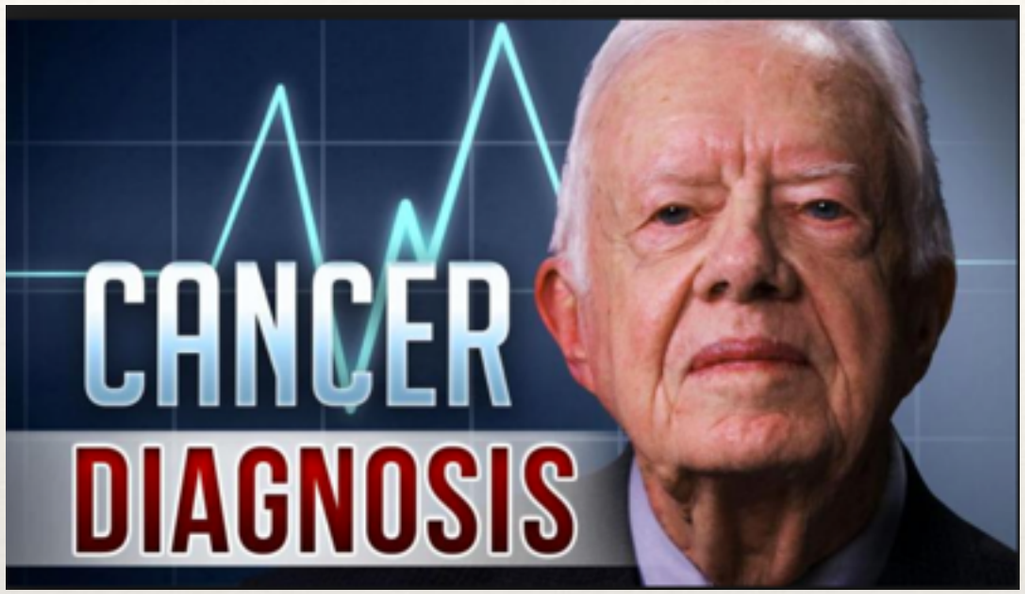
- **No but it should be adapted using more physiologic variables and endpoints.**

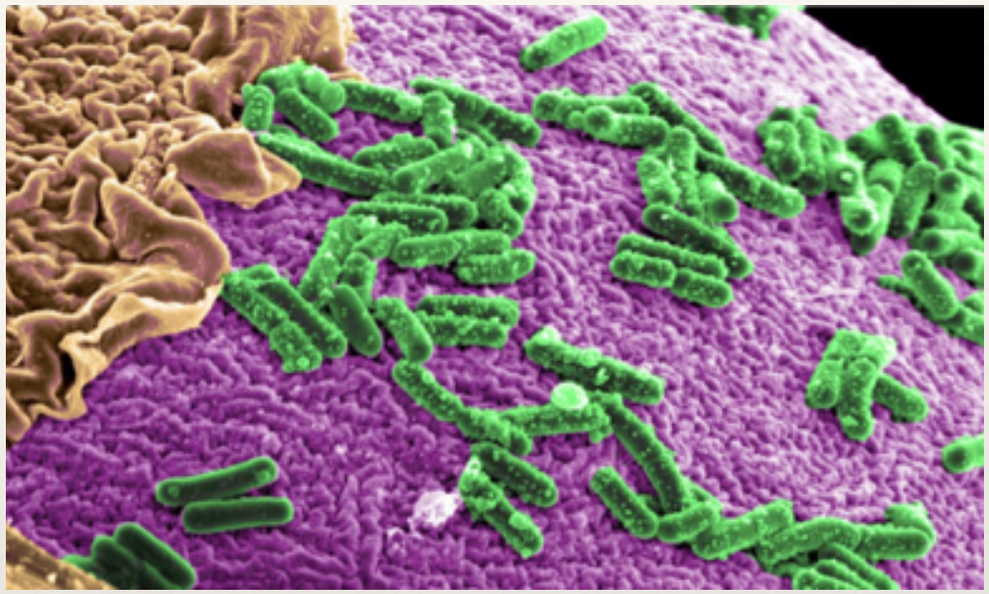
- **Individualisation of therapy is probably preferred than standardization to common minimal endpoints**

Microbiota

Gut Bacteria Are Linked to Success of Cancer Treatment

The new studies could pave the way for anti-cancer therapies that control the makeup of these bacterial communities.





"transferred gut microbes from the treated humans to mice, they found that mice with higher amounts of transplanted *Bacteroides fragilis* responded better to ipilimumab"

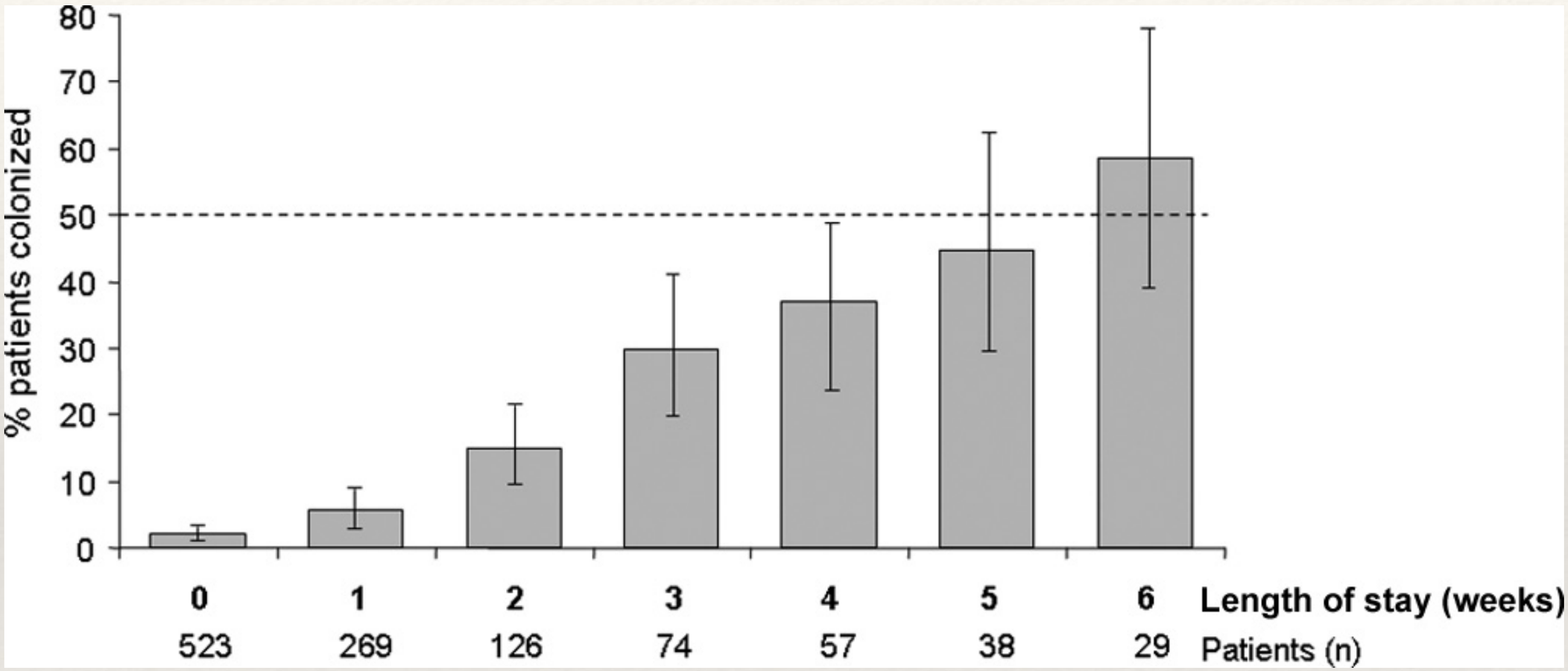
"the **gut microbiome** could play an important role in **facilitating immunotherapy for cancer**"

5 November 2015 issue of *Science*

AAC
Journals.ASM.org

Emergence of Imipenem-Resistant Gram-Negative Bacilli in Intestinal Flora of Intensive Care Patients

Antimicrobial Agents and Chemotherapy p. 1488–1495 March 2013 Volume 57 Number 3



Rates of intestinal colonisation by imipenem resistant GNB in ITU patients

"…**even a few days of imipenem exposure** can promote collateral damage by altering intestinal flora in favor of **colonization with MDR bacteria**"

Clinical Infectious Diseases February 9, 2016

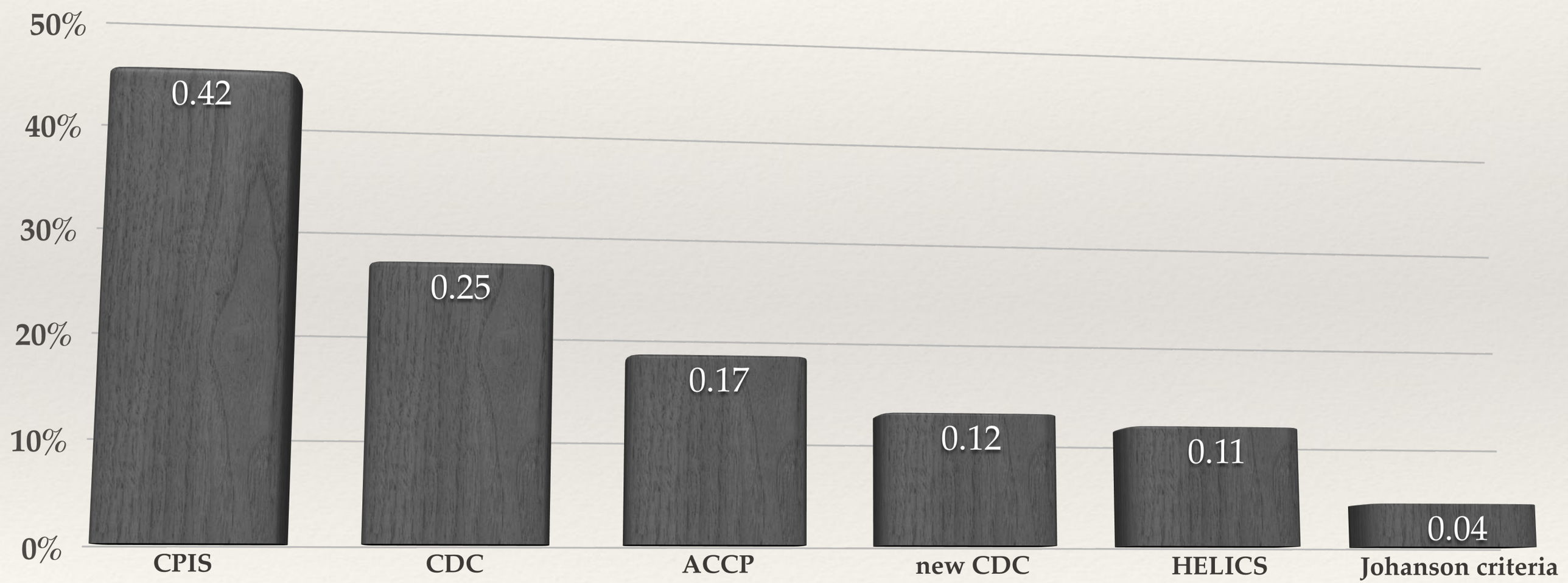
Measuring VAP rates as a quality measure

Impact of Diagnostic Criteria on the Incidence of Ventilator-Associated Pneumonia

Amédée Ego, MD; Jean-Charles Preiser, MD, PhD; and Jean-Louis Vincent, MD, PhD, FCCP

CHEST 2015; 147(2):347-355

Incidence of VAP according to the diagnostic criteria



ECCO2R

Professors Gattinoni and Brochard

"We do not know indications or when to use ECCO2R"

"It is still an **experimental** technique"

"Do not underestimate the dangers of anticoagulation in this vascular population"

"Beware"

Do we really understand the physiology?

COMMENTARY Open Access

Ultra-protective ventilation and hypoxemia

Luciano Gattinoni

Gattinoni *Critical Care* (2016) 20:130

Feasibility and safety of low-flow extracorporeal carbon dioxide removal to facilitate ultra-protective ventilation in patients with moderate acute respiratory distress syndrome

"The price of attaining this goal, however, appears quite high ~ 40 % with initially moderate ARDS experienced life-threatening hypoxemia and required extracorporeal membrane oxygenation (ECMO)…."

- **Gravitational atelectasis**
  - Whenever ventilation decreases (reduction of TV and/or respiratory rate) the mean airway pressure decreases, and the lungs tend to collapse
- **Absorption atelectasis**
  - when ventilation is very low the amount of oxygen provided to some pulmonary units may be lower than the amount removed by the blood perfusing those units
- **Opening pressures**
  - Sufficient pressure must be applied to reopen the atelectatic areas. Studies show that at least one normal TV every 2 min is needed
- **Alveolar PaO_2 and respiratory quotient (RQ)**

Do we really understand the physiology?

Alveolar air equation

PAO2 = PiO2-PACO2 / **RQ** **(=CO2/O2)**

FiO2 = 0.3

164 mm Hg = 214 - 40 / **0.8**

FiO2 = 0.3

114 mm Hg = 214 - 40 / **0.4**

FiO2 = 0.3

14 mm Hg = 214 - 40 / **0.2**

Haematological malignancy and ITU outcomes

Blood Reviews 29 (2015) 359–367

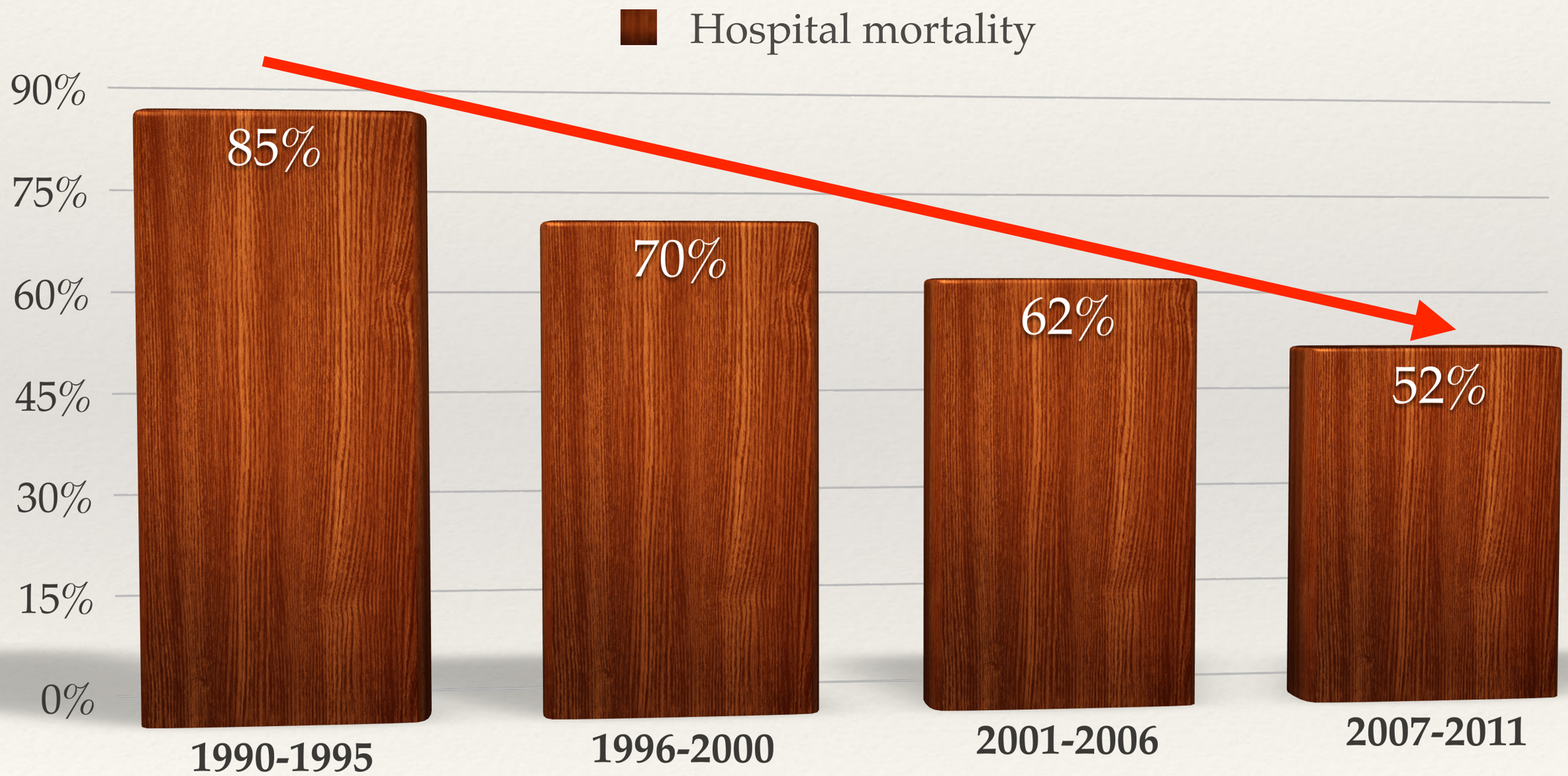
Contents lists available at ScienceDirect

Blood Reviews

journal homepage: www.elsevier.com/locate/blre

REVIEW

Managing critically Ill hematology patients: Time to think differently



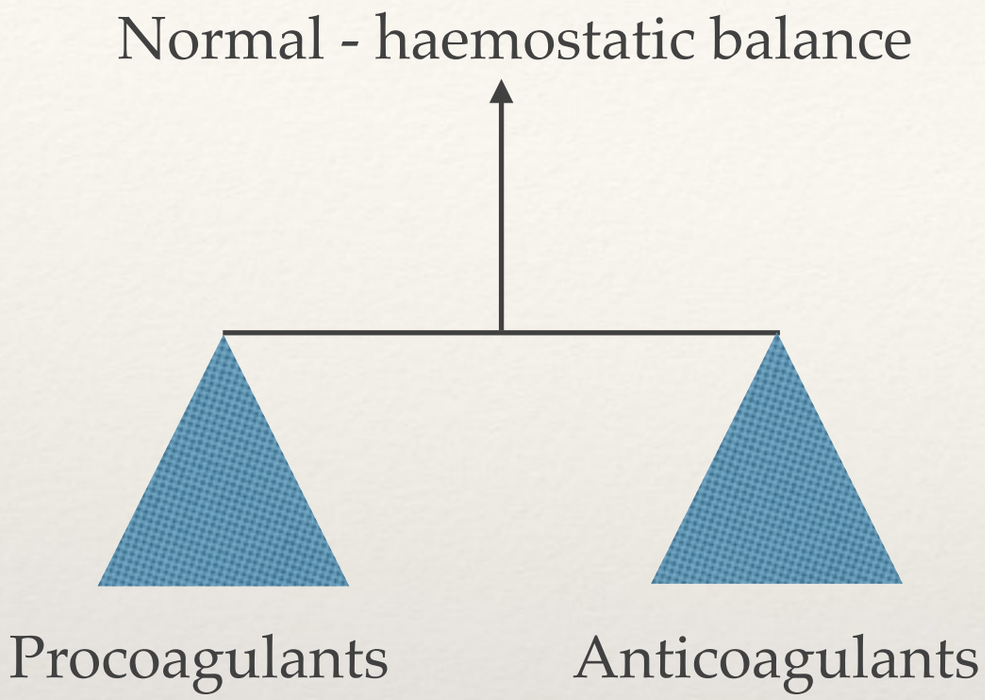
Hospital mortality in 1004 patients with ARDS according to period of ITU admission

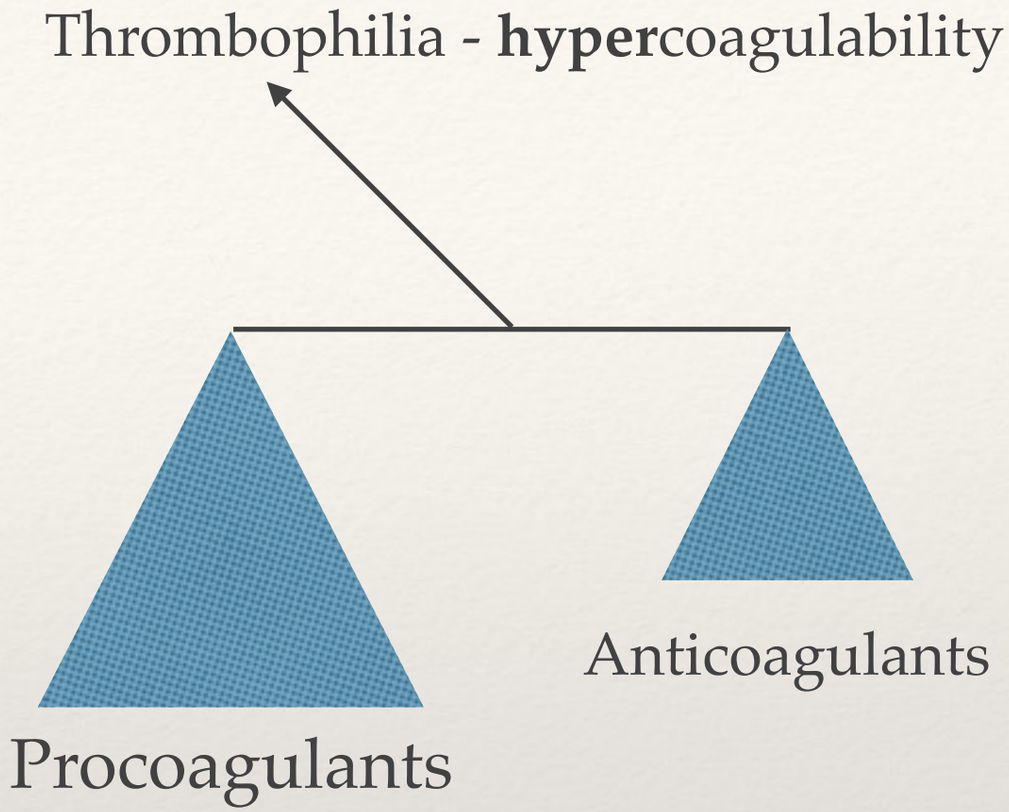
Coagulopathy in Liver disease

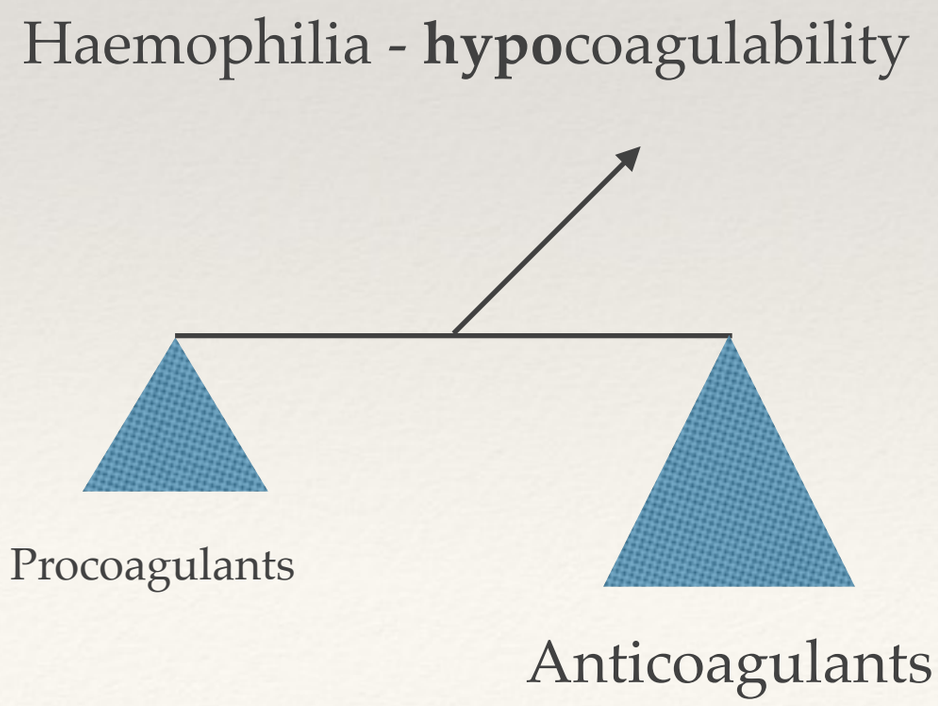
Meeting report

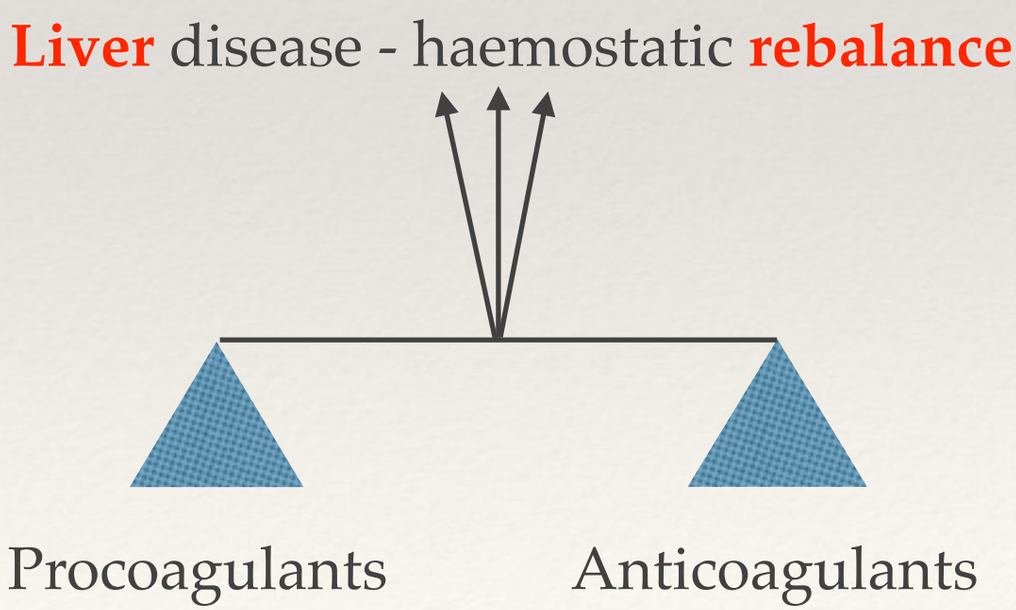
EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Hemostasis and thrombosis in patients with liver disease: The ups and downs



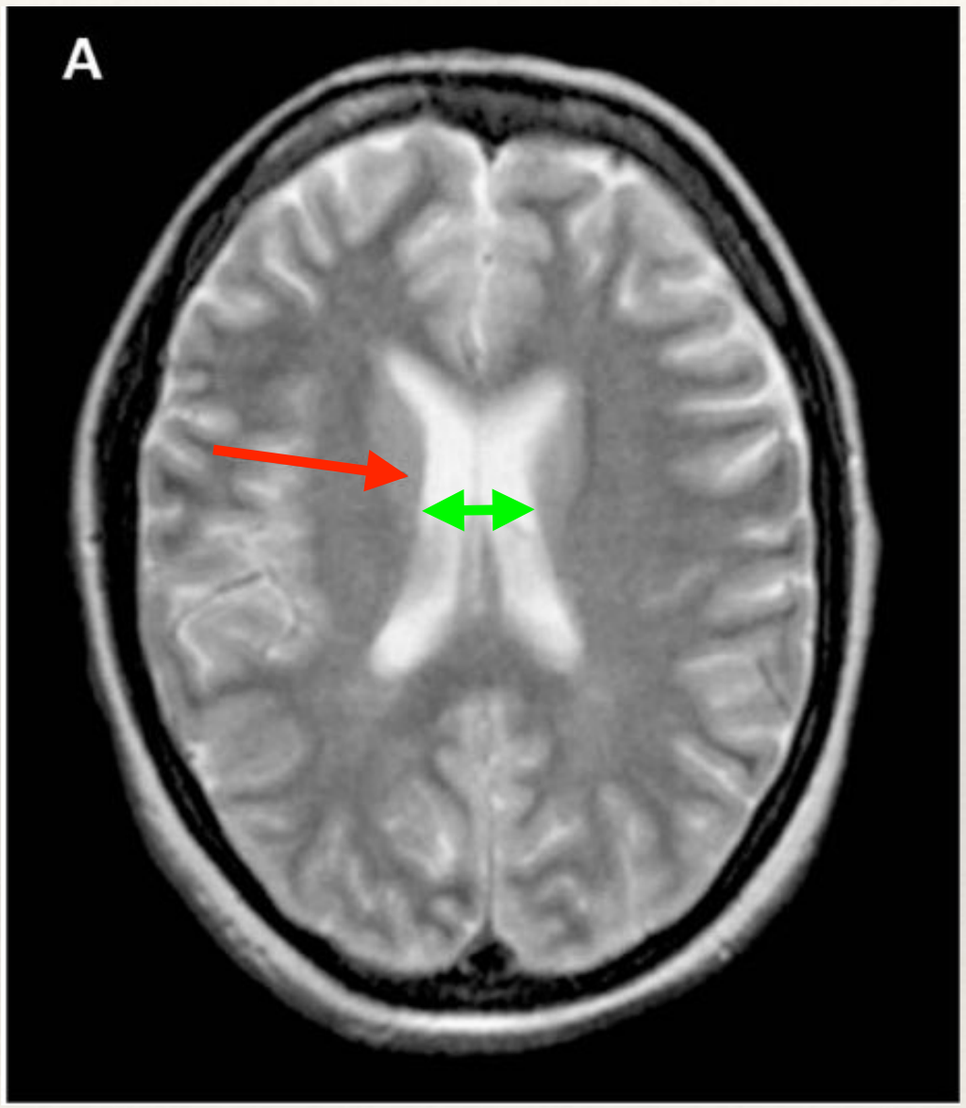






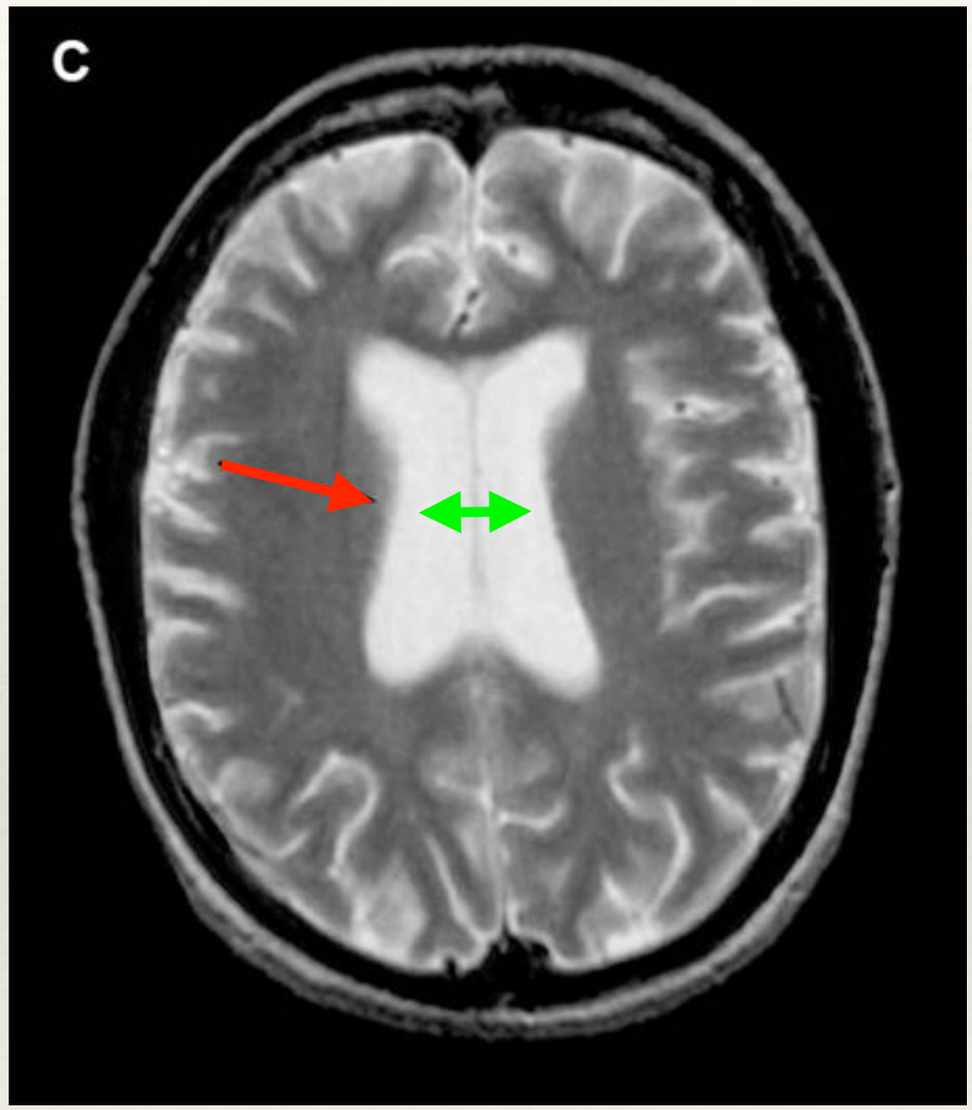
Neuro-imaging in ITU survivors

Neuro-imaging in ITU survivors



Normal baseline axial MR scan just prior to hospital discharge

Post ITU survivors have cognitive impairment equivalent to mild to moderate Alzheimers or moderate TBI

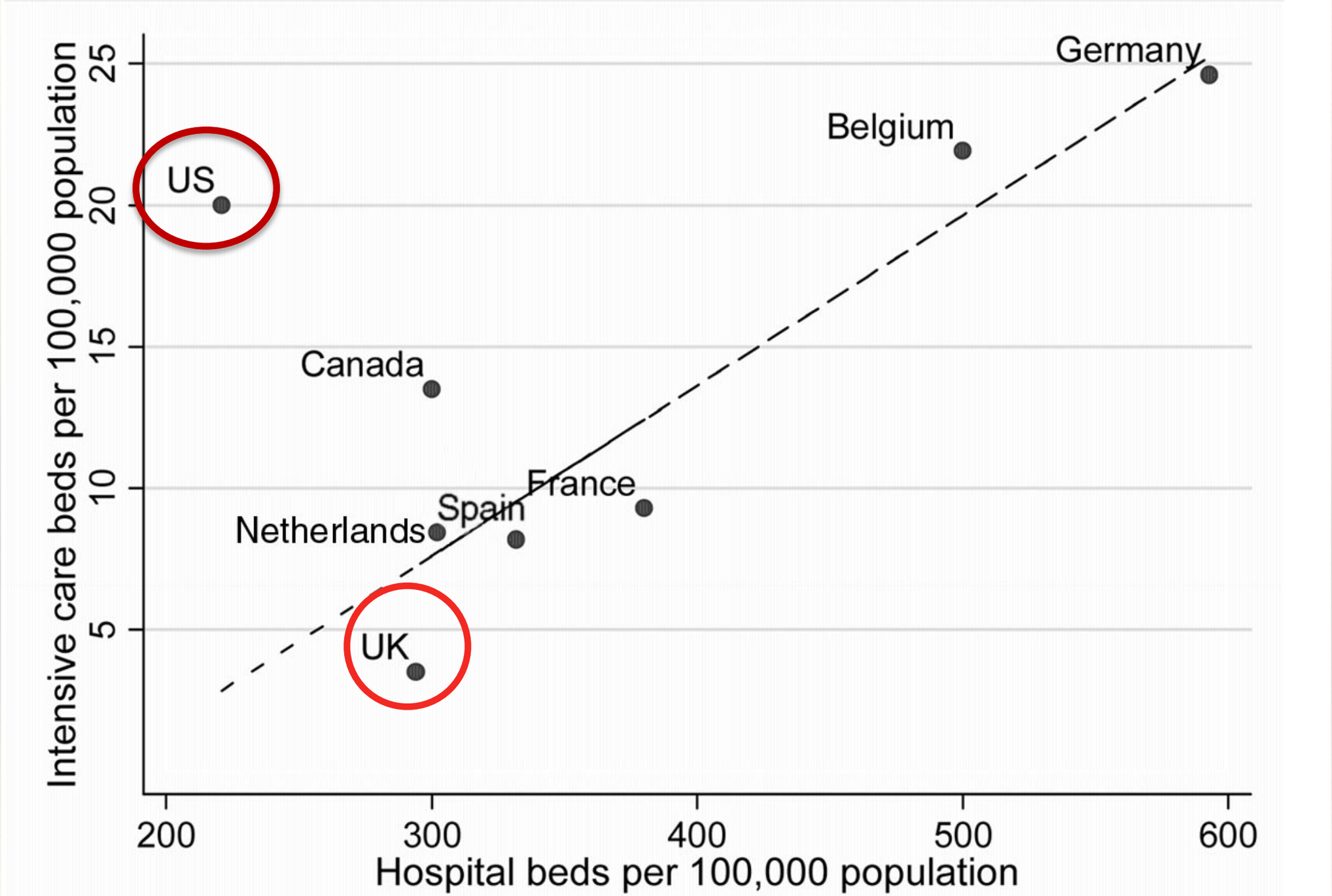


Enlargement of the lateral ventricles which have increased in size from one to two years, indicating some additional **atrophy**.

Neuro Rehabilitation. 2012 ; 31(3): 311–318

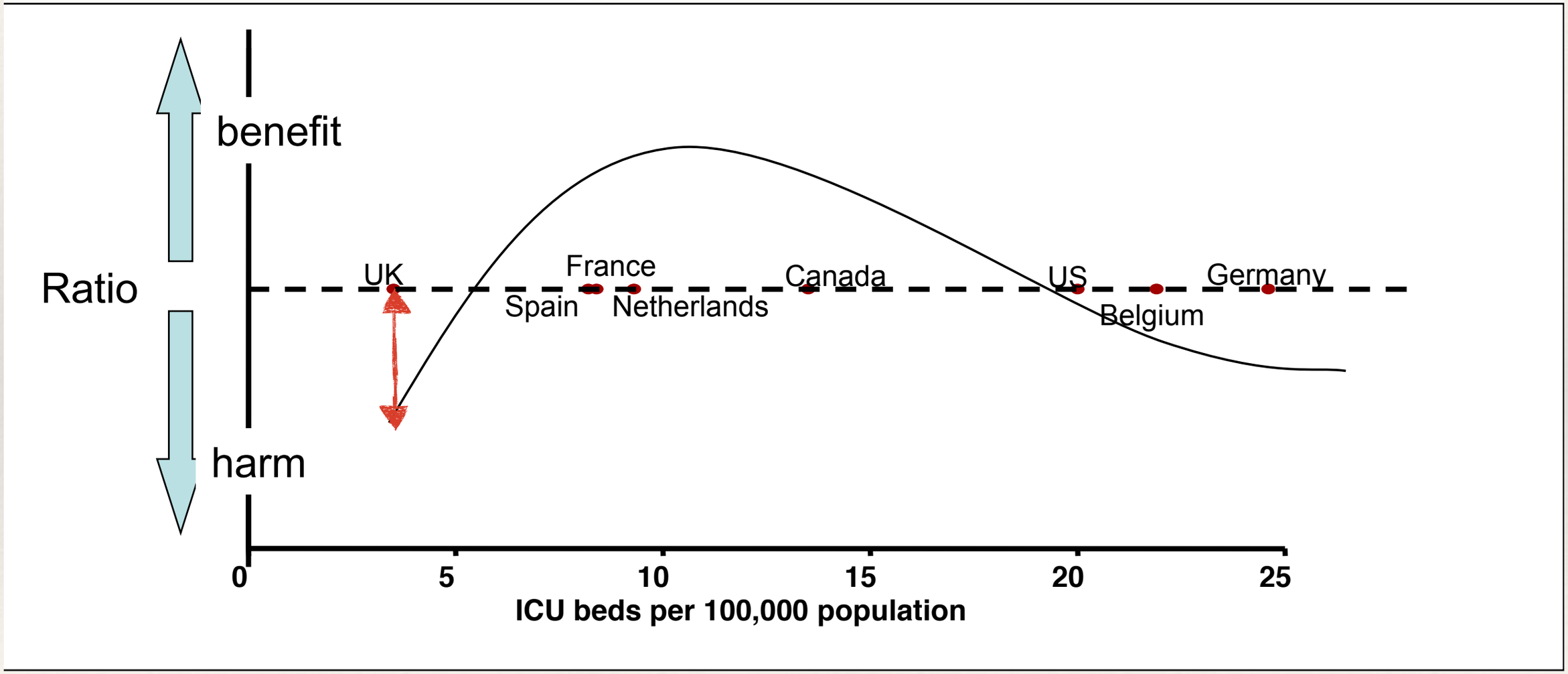
Best use of ICU beds

Ratio of ICU beds to hospital beds



Wunsch et al CCM 2008

Is there a "Starling Curve" for ITU beds



Wunsch et al Chest 2012

Odds and Sods

Checklists- really that good?

'Outcome' vs. 'Implementation'

Table 5. Outcomes before and after Checklist Implementation, According to Site.*

Site No.	No. of Patients Enrolled		Surgical-Site Infection		Unplanned Return to the Operating Room		Pneumonia		Death		Any Complication		All Six Safety Indicators Performed (N=7688)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
							percent							
1	524	598	**4.0**	**2.0**	**4.6**	**1.8**	0.8	1.2	**1.0**	**0.0**	**11.6**	**7.0**	94.1	94.2
2	357	351	2.0	1.7	0.6	1.1	3.6	3.7	1.1	0.3	7.8	6.3	3.6	55.3
3	497	486	5.8	4.3	4.6	2.7	1.6	1.7	0.8	1.4	13.5	9.7	30.8	51.0
4	520	545	3.1	2.6	2.5	2.2	0.6	0.9	1.0	0.6	7.5	5.5	67.1	63.7
5	370	330	**20.5**	**3.6**	1.4	1.8	0.3	0.0	**1.4**	**0.0**	**21.4**	**5.5**	0.0	0.0
6	496	476	4.0	4.0	3.0	3.2	2.0	1.9	3.6	1.7	10.1	9.7	1.4	18.1
7	525	585	**9.5**	**5.8**	**1.3**	**0.2**	1.0	1.7	2.1	1.7	**12.4**	**8.0**	46.7	92.1
8	444	584	4.1	2.4	0.5	1.2	0.0	0.0	1.4	0.3	6.1	3.6	0.0	51.7
Total	3733	3955	**6.2**	**3.4**	**2.4**	**1.8**	1.1	1.3	**1.5**	**0.8**	**11.0**	**7.0**	34.2	56.7
P value			<0.001		0.047		0.46		0.003		<0.001		<0.001	

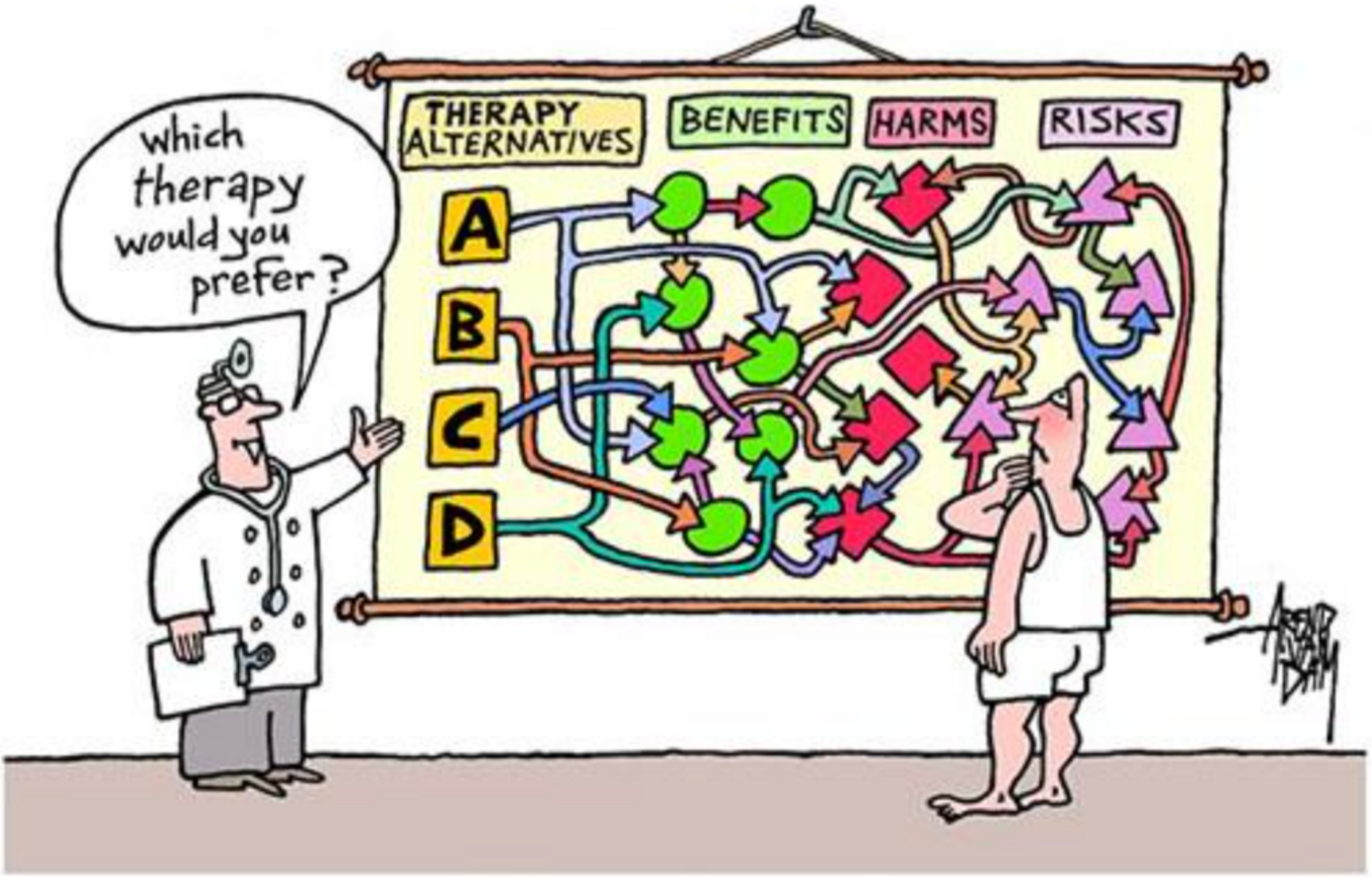
Less complications

More Implementation

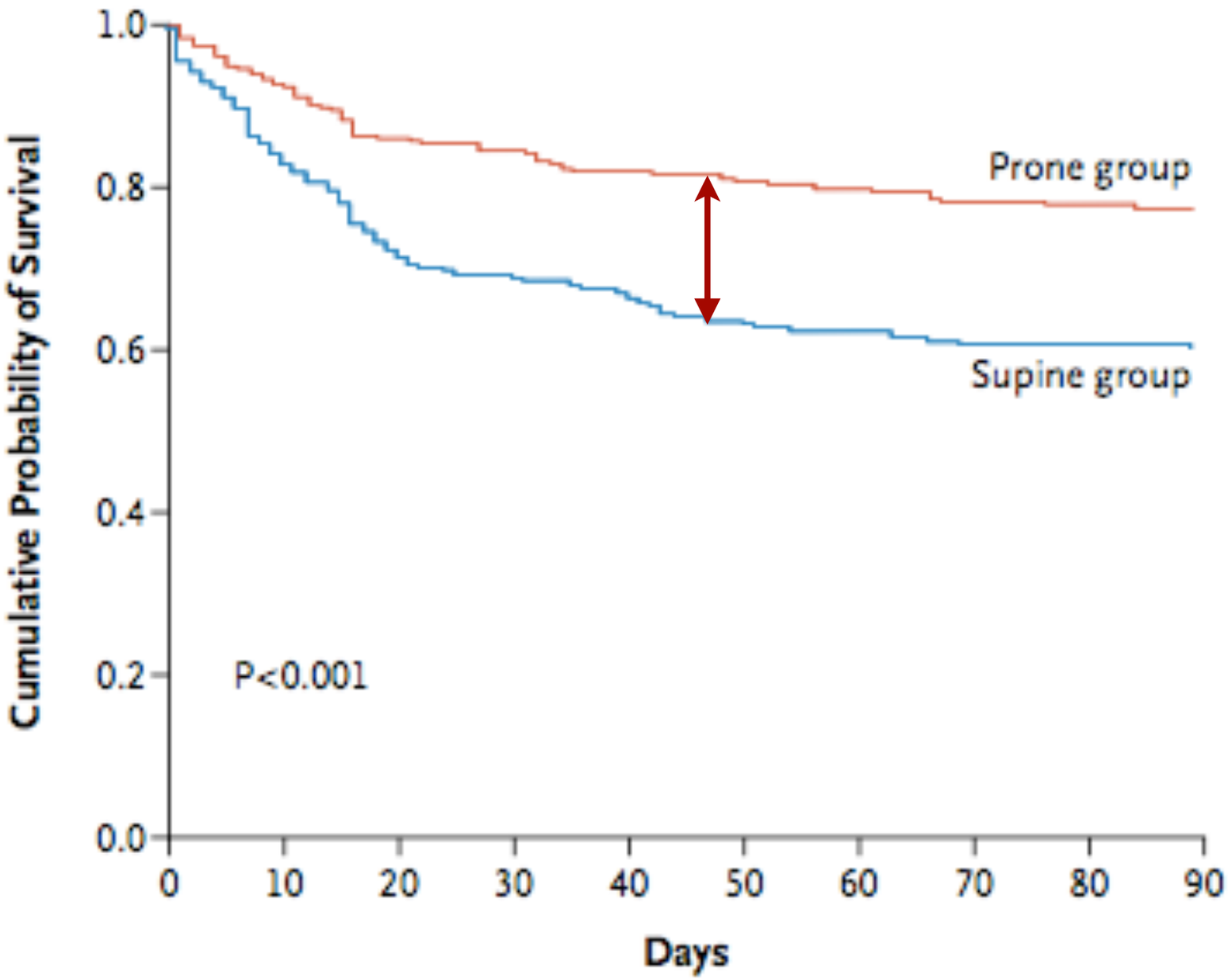
More Implementation & Less Complications

Hayes *et al*
N Engl J Med, 2009

Informed consent



Prone Positioning in Severe Acute Respiratory Distress Syndrome



N Engl J Med 2013; 368:2159-2168

Beware the dangers of proning

Unwary
house officer

???

Welcome to Ealing

13 novembre... 22 mars...