Centre for Perioperative Medicine and Critical Care Research

## **Obstetrics and Critical Care**

## Dr Stephen Brett





# Imperial College Healthcare NHS Trust

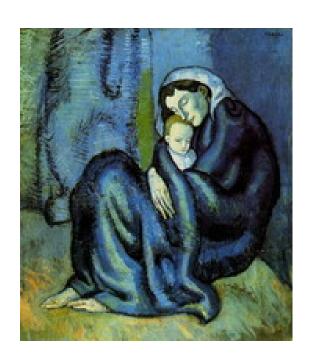


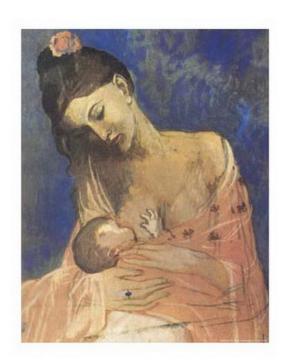






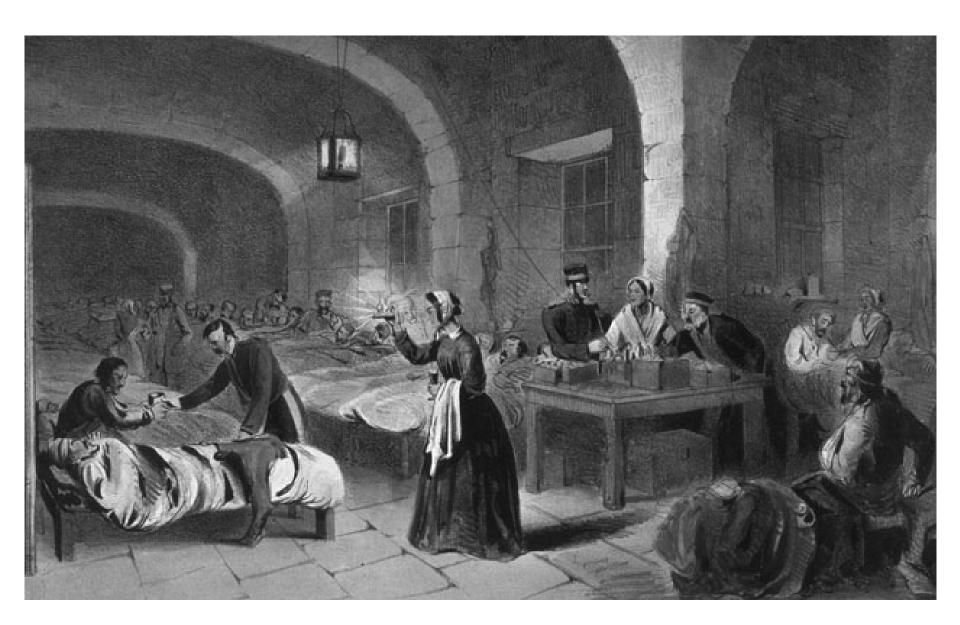








Théodore Géricault, 1791-1824, Musee du Louvre







## Objectives of intensive care?

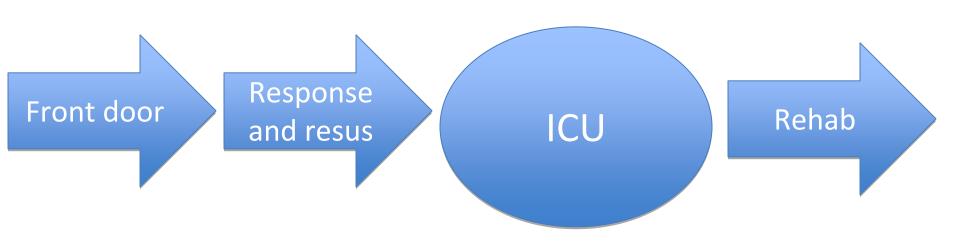
- Effective
- Humane

- When does intensive care start?
- When does critical illness finish?

- Current areas of research?
  - Born out of passion or frustration??









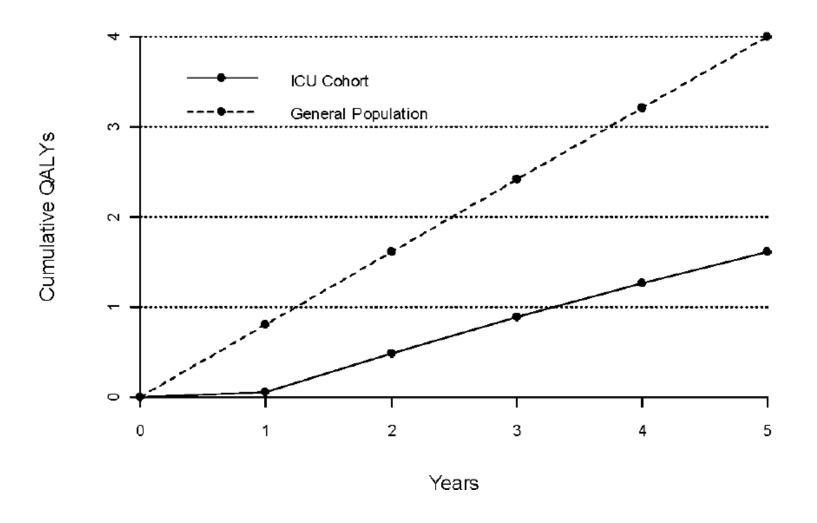
# Comprehensive Critical Care A REVIEW OF ADULT CRITICAL CARE SERVICES

#### ORIGINAL ARTICLE

#### A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators\* National Institute for Health and Clinical Excellence Issue date: March 2009 Rehabilitation after critical illness

## Quality of life in the five years after intensive care: a cohort study.



Cuthbertson B et al. Critical Care 2010;14(1):R6. [Epub]

## Clinical trial failure

- Useless treatments
- Useless diseases
- Useless trial design
- Noise>signal

## Issues

- Recognition
- Staffing
- Resuscitation
- Transfer
- Continuing treatment
- Issues around fluids

## Data sources

1985



## Data sources

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Updated: 02 Oct 2013 11:24

What We Do - by Methodology

Registers, Surveys and Cohorts

MBRRACE-UK

Topic proposals

FAQ's

IT FAQ's Internet browser

specification

Why we need identifiers

Newsletters

Programme of work

Collaboration

HQIP and the funding bodies

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#### THIS IS NOT THE MBRRACE-UK ONLINE REPORTING SYSTEM. IF YOU WISH TO REPORT A CASE PLEASE GO TO: www.mbrrace.ox.ac.uk

'MBRRACE-UK' is the collaboration appointed by the Healthcare Quality Improvement Partnership (HQIP) to continue the national programme of work investigating maternal deaths, stillbirths and infant deaths, including the Confidential Enquiry into Maternal Deaths.

The aim of MBRRACE-UK is to provide robust information to support the delivery of safe, equitable, high quality, patient-centred maternal, newborn and infant health services.

The MBRRACE-UK online reporting system for stillbirths, perinatal deaths and infant deaths is now live and available here: www.mbrrace.ox.ac.uk.

Guidelines for using the system can be downloaded here: MBRRACE online data entry guidebook.

Units are asked to review their access to the internet to ensure that the web browser they are using meets the specifications required to enter data via the MBRRACE-UK system once it is launched; older versions of software are not suitable. Please view the IT specification page to check this for your Unit.

Please also view the MBRRACE-UK IT deployment page which outlines more information about the deployment of the MBRRACE-UK data collection system and may be helpful for IT staff in Units.

## Data sources



# A look into the nature and causes of human errors in the intensive care unit

Conclusions: A significant number of dangerous human errors occur in the ICU. Many of these errors could be attributed to problems of communication between the physicians and nurses. Applying human factor engineering concepts to the study of the weak points of a specific ICU may help to reduce the number of errors. Errors should not be considered as an incurable disease, but rather as preventable phenomena.

Donchin Y et al. Crit Care Med. 1995: 23: 294

# Design and internal validation of an obstetric early warning score: secondary analysis of the Intensive Care National Audit and Research Centre Case Mix Programme database

Table 4 New clinical obstetric early warning score. Score created by combining the statistical score derived using logistic regression analysis and clinical judgement.

	3	2	1	0	1	2	3
<b>Systolic blood pressure</b> (mmHg)	< 80	80–89		90–139	140–149	150–159	≥ 160
<b>Diastolic blood pressure</b> (mmHg)				< 90	90–99	100–109	≥ 110
Respiratory rate (min <sup>-1</sup> )	< 10			10–17	18–24	25–29	≥ 30
Heart rate (min <sup>-1</sup> )	< 60			60–110		111–149	≥ 150
% O₂ required to maintain SpO₂ ≥ 96%				Room alr	24–39%		≥ 40%
Temperature (°C)	< 34.0		34.0–35.0	35.1–37.9	38.0-38.9		≥ 39
Conscious level				Alert*			Not alert†

Urine output, pain score, F<sub>I</sub>O<sub>2</sub> and S<sub>p</sub>O<sub>2</sub> recorded elsewhere on chart. Alert\*, alert and orientated, equivalent to Glasgow Coma Score (GCS) 15 and A on Alert/Voice/Pain/Unresponsive (AVPU) scale; Not alert†, GCS 3–14 or V, P, U on AVPU scale.

Carle et al, Anaesthesia 2013; 68:354

#### OBSTETRICS

## Existing models fail to predict sepsis in an obstetric population with intrauterine infection

Justin R. Lappen, MD; Melissa Keene, MD; Marybeth Lore, MD; William A. Grobman, MD, MBA; Dana R. Gossett, MD

OBJECTIVE: Multiple scoring systems exist to identify inpatients who are at risk for clinical deterioration. None of these systems have been evaluated in an obstetric population. We examined the Systemic Inflammatory Response syndrome (SIRS) and Modified Early Warning score (MEWS) criteria in pregnant women with chorioamnionitis.

**STUDY DESIGN:** This was an 18-month retrospective analysis of patients with chorioamnionitis. SIRS and MEWS scores were calculated; clinical outcomes were ascertained, and test characteristics were calculated for the primary outcome of sepsis, intensive care unit transfer, or death.

RESULTS: Nine hundred thirteen women with chorioamnionitis were identified. Five women experienced sepsis; there was 1 death. Five hundred seventy-five of the 913 women (63%) met SIRS criteria (95% confidence interval, 59.8−66.2%; positive predictive value, 0.9%). Ninety-two of the 913 women (10.3%) had a MEWS score of ≥5 (95% confidence interval, 8.3−12.2%; positive predictive value, 0.05%).

**CONCLUSION:** SIRS and MEWS criteria do not identify accurately patients who are at risk for intensive care unit transfer, sepsis, or death among pregnant women with intrauterine infection and should not be used in an obstetric setting.

Key words: chorioamnionitis, intensive care unit, MEWS, sepsis

TABLE 2 Modified Early Warning sco	ore <sup>4</sup>						
Variable	3	2	1	0	1	2	3
Systolic blood pressure, mmHg	<70	71-80	81-100	101-199		≥200	
Heart rate, beats/min		<40	41-50		101-110	111-129	≥130
Respiratory rate, breaths/min		<9		9-14	15-20	21-29	≥30
Temperature, °C		<35		35-38.4		≥38.5	
Mental status				Alert	Reacts to voice	Reacts to pain	Unresponsive
Temperature, °C		<35		35-38.4 Alert	Reacts to voice	≥38.5 Reacts	to pain

FIGURE Distribution of maximal Modified Early Warning scores (MEWS) 300-200-Frequency 100-

Statistical challenge???

**MEWS Score** 

## Original Article

A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS)\*

S. Singh, A. McGlennan, A. England and R. Simons

1 Consultant Anaesthetist, Barnet Hospital, Herts, UK. 2 Consultant Anaesthetist, Royal Free Hospital, London, UK

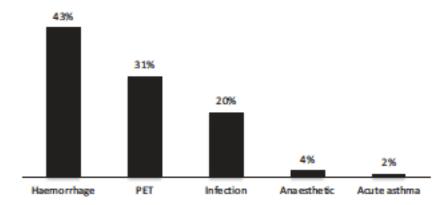
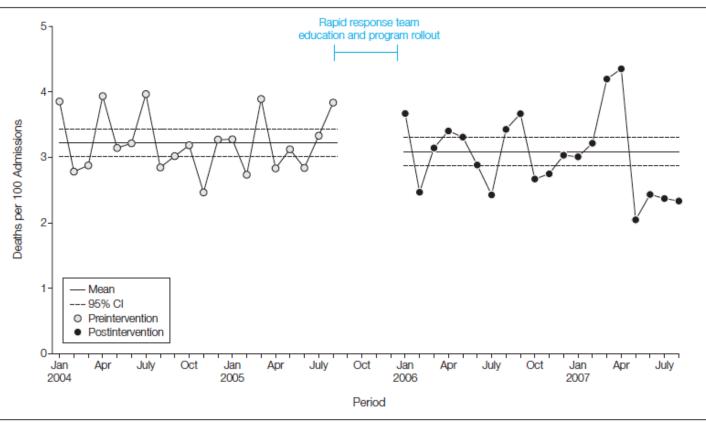


Figure 1 Distribution of maternal morbidity according to defined diagnostic criteria. Values are proportion. PET, pre-eclampsia.

## Hospital-wide Code Rates and Mortality Before and After Implementation of a Rapid Response Team

Figure 2. Hospital-Wide Mortality Rates per 100 Eligible Adult Patient Admissions by Month



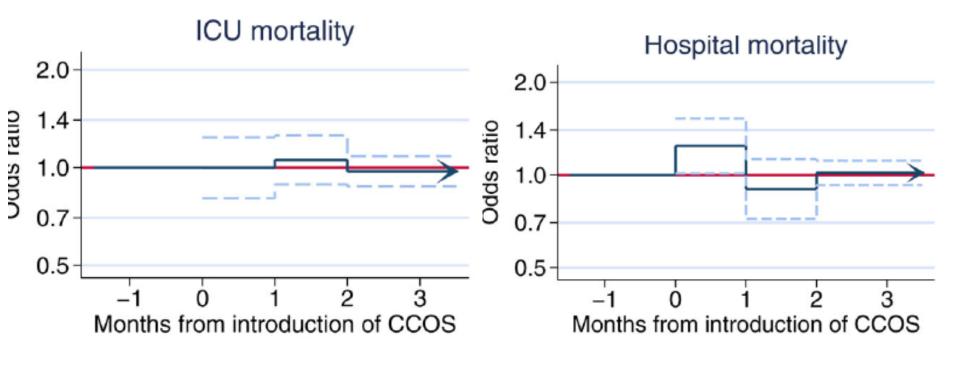
The preintervention period was between January 1, 2004, and August 31, 2005, and the postintervention period was between January 1, 2006, and August 31, 2007. Clindicates confidence interval.

#### Research

#### Open Access

#### The impact of the introduction of critical care outreach services in England: a multicentre interrupted time-series analysis

Haiyan Gao<sup>1,2</sup>, David A Harrison<sup>1</sup>, Gareth J Parry<sup>3</sup>, Kathleen Daly<sup>4</sup>, Christian P Subbe<sup>5</sup> and Kathy Rowan<sup>1</sup>



#### Introduction of the medical emergency team (MET) system: $\rightarrow$ a cluster-randomised controlled trial



MERIT study investigators\*

Outcome	Control hospitals			MET hospit	MET hospitals				Control and MET hospitals combined			
	Baseline	Study	Weighted difference	Р	Baseline	Study	Weighted difference	Р	Baseline	Study	Weighted difference	Р
Primary outcome	7-07	5-86	-1.41	0.030	6-58	5-31	-0-39	0-612	6-82	5-57	-0.85	0.089
Cardiac arrest*	2.61	1.64	-0.98	0.004	1.60	1.31	-0-44	0-171	2-08	1-47	-0.68	0.003
Unplanned ICU admission	5-29	4-96	-0.53	0.280	4.68	4.19	-0-02	0-976	5-12	4-42	-0.23	0.577
Unexpected death*	1.61	1.18	-0.68	0.040	1.65	1.06	-0-31	0-132	1.63	1.11	-0.48	0.010

Outcome data are crude rate per 1000 admissions. \*Excludes events with pre-existing NFR orders. Differences are weighted by number of hospital admissions during study period. p values for weighted differences are derived. from the paired weighted t test. If the change in outcomes from baseline to study periods are compared (ie, the change over time in control hospitals vs change over time in MET hospitals), p values for weighted differences are: primary outcome, p=0-297; cardiac arrest, p=0-190; unplanned ICU admission, p=0-508; unexpected death p=0-288, p values for change over time are derived from the weighted t test.

Table 4: Primary and secondary outcomes during baseline and study periods

## Recognition.....

#### Physiological derangement

- Pregnancy "normal"
- Normal variation
- "Normal" pain

#### Diagnosis and specific Rx

- Default diagnostic settings
  - PET
  - Haemorrhage
  - PE
  - AFLP
  - (Sepsis)
- Intensivists defaults
  - Sepsis
  - Occult bleeding
  - Weird things
    - TTP



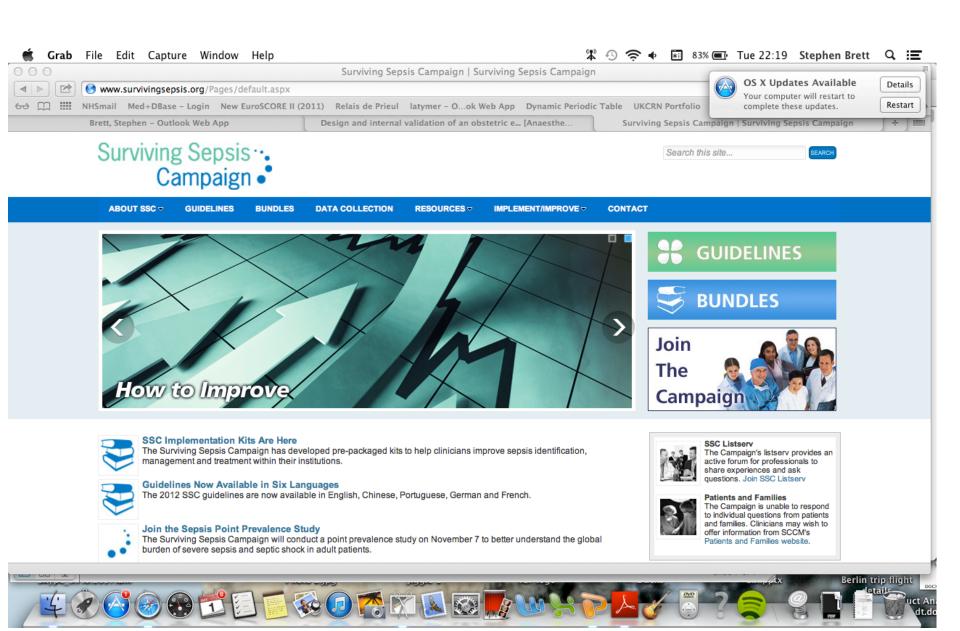


12 September 2013 Last updated at 22:58

## Sepsis lives can be saved, says ombudsman



Sepsis is a potentially fatal condition caused by the body's immune system overreacting to infection





#### Recommendations: Initial Resuscitation and Infection Issues\*

#### A. Initial Resuscitation

- Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood factate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:
- a) Central venous pressure 8-12 mm Hg
- b) Mean arterial pressure (MAP)≥ 65 mm Hg
- c) Urine output ≥ 0.5 mL/kg/hr
- d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).
- In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).

#### B. Screening for Sepsis and Performance Improvement

- Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C).
- 2. Hospital-based performance improvement efforts in severe sepsis (UG).

#### C. Diagnosis

- Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s) (grade 1C). At least 2 sets of blood cultures (both serobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted (grade 1C).</li>
- Use of the 1,3 beta-D-glucan assay (grade 2B), mannan and anti-mannan antibody assays (2C), if available, and invasive candidiasis is in differential diagnosis of cause of infection.
- Imaging studies performed promptly to confirm a potential source of infection (UG).

## Surviving Sepsis · . Campaign •

#### Recommendations: Hemodynamic Support and Adjunctive Therapy\*

#### G. Fluid Therapy of Severe Sepsis

- Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
- Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 18).
- Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
- 4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
- Fluid challenge technique be applied wherein fluid administration is continued as long as there
  is hemodynamic improvement either based on dynamic (eg. change in pulse pressure, stroke
  volume variation) or static (eg. arterial pressure, heart rate) variables (UG).

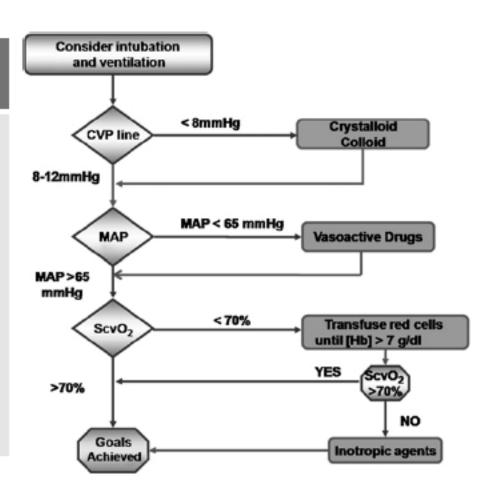
#### H. Vasopressors

- Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C).
- 2. Norepinephrine as the first choice vasopressor (grade 1B).
- Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B).
- Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).
- 5. Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents) (UG).
- Doparnine as an alternative vasopressor agent to norepittephrine only in highly selected patients (eg. patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (grade 2C).

## The sepsis six and the severe sepsis resuscitation bundle: a prospective observational cohort study

### Box 1 The Surviving Sepsis Campaign severe sepsis resuscitation bundle

- Measure serum lactate within first 6 h after presentation.
- Obtain blood cultures before antibiotic administration.
- From the time of presentation, give broad-spectrum antibiotics within 1 h.
- Source of infection to be identified and controlled within 6 h.
- ▶ In the event of hypotension and/or lactate >4 mmol/1 (36 mg/dl):
  - Deliver an immediate minimum of 20 ml/kg crystalloid (or colloid equivalent).
  - Give vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure ≥65 mm Hg.
- In the event of persistent arterial hypotension despite volume resuscitation (septic shock) and/or initial lactate >4 mmol/l (36 mg/dl):
  - Achieve central venous pressure of ≥8 mm Hg within 6 h.
  - Achieve central venous oxygen saturation ≥70% within 6 h.



## Maternal & Staffing issues

- Mother
  - Co-morbidities
  - Social exclusion
- Staff recruitment and training trajectories
  - Midwives
  - Obstetricians
  - Anaesthetists
  - Intensivists
- Clear need for curriculum acknowledgement of this

## Resuscitation

Avoid by identification, pessimism and planning

## **Transfers**

Labour ward

Operating theatre

Interventional radiology

Critical care unit

Reason for Admission	No. of Admissions	Mean Age	Mean LOS (days)	No. of Level 3 Days	No. of Level 2 Days
Pregnant				, -	
Epidural management post oopherectomy surgery for ovarian cyst	1	28	0.9	0	0
Respiratory failure secondary to Charcot Marie Tooth Disease	1	28	3.5	0	2
Sepsis secondary to pneumonia	1	18	2.5	0	3
GI Surgery for neoplasm (Large bowel and hepatic tumours)	1	38	4.9	2	4
Postpartum					
Acute Kidney Injury secondary to pre-eclampsia	1	33	1.5	0	2
Metabolic Acidosis post C Section	1	34	1.3	1	1
Cardiac Arrest	2	29.5	1	3	1
Cardiogenic shock	1	26	5.2	3	3
Cardiac insufficiency secondary to hypotension	1	42	0.9	0	0
Post partum Cardiomyopathy	2	30.5	7.8	6	11
Pulmonary Artery Hypertension	2	28.5	5.3	0	4
Craniotomy for Neoplasm	1	28	1	0	2
Intracerebral AVM	1	32	1	0	2
Pituitary Haemmothage	1	35	3.8	0	5
Seizures (Hyponatraemia and Pre-eclampsia)	2	29	2.4	5	1
Subarachnoid Haemorrhage	2	29.5	14.9	12	19
GI Haemorrhage (Hepatic subcapsular)	1	34	8.2	5	4
Haemorrhagic shock-postpartum bleed	25	32.8	2	47	27
Acute Cholecystitis	1	30	1.9	0	3
Respiratory insufficiency secondary to Oedema	2	37.5	4.2	8	2
Respiratory Insufficiency secondary to Sickle Cell Crisis	1	39	0.9	2	0
Respiratory Insufficiency secondary to Infection (3 x H1N1)	4	27	4.8	9	12
Sepsis	15	30.3	4.4	38	38
Multiple Trauma	1	32	7.13	6	2
Termination of Pregnancy					
Haemorrhagic shock post termination	1	33	0.8	1	0
Pulmonary Artery Hypertension	2	19.5	0.3	0	2
Total	74	31.1	3.4	148	150

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Postpartum		22	4.5		-
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## Clinical Characteristics and Outcomes of Obstetric Patients Requiring ICU Admission

Characterístics	All	Hypertensive Disease	Major Hemorrhage	Septic Abortion	CAP	ICH
Patients, No.	161	68	26	19	9	5
Age, yr	$28 \pm 9$	$26 \pm 9$	$33 \pm 7 \dagger$	$31 \pm 7$	$28 \pm 8$	$25 \pm 8$
APACHE II score	$14 \pm 8$	$10 \pm 6$	$13 \pm 7$	$21 \pm 76$	19 ± 61	$23 \pm 96$
APACHE II predicted mortality, %	24	15	24	45	35	535
Mortality	18(11)	5 (8)	1(4)	4(21)	1(11)	4 (80)§¶
TISS 24-h score	$25 \pm 9$	$20 \pm 5$	$30 \pm 9$ §	31 ± 8§	$27 \pm 5$	$34 \pm 86$
Presence of comorbidities	54 (34)	18 (28)	5 (19)	3(16)	5 (56)	1(20)
SOFA score on admission	$5 \pm 3$	$3 \pm 3$	5 ± 3	$8 \pm 35$	5 ± 2	$8 \pm 3$
Any organ fatlure	77 (48)	17 (27)	12 (46)	16 (84) §	7 (78)†	5 (100)†
Cestational age, wk	$29 \pm 9$	33 ± 5 **	35 ± 6 **	$12 \pm 4$	28 ± 7**	$25 \pm 8#$
Antenatal care	48 (30)	27 (42)	9 (33)	0	2 (22)	0
MV	66 (41)	10 (16)	14 (54)†	13 (68) §	7 (78)§	5 (100)
ARDS	30 (19)	4 (6)	4 (15)	3(16)	5 (56)§	4 (80) §
Shoek	40 (25)	2 (3)	18 (69)§	7 (37)5	3 (33)	1(20)
ICU LOS, d	6 (3-11)	5 (3-7)	4 (3-10)	7 (4-14)	18 (10-20)§¶	10 (7-20)

## Clinical Characteristics and Outcomes of Obstetric Patients Requiring ICU Admission

Obstetric	121 (75 <u>)</u>	Nonobstetric	40 (25)
Hypertensive disease	64 (40)	Nonobstetric sepsis	15 (10)
Preeclampsia	32 (20)	CAP	9 (6)
Eclampsia	24 (15)	Urinary tract infection	3 (2)
HELLP	3 (2)	Others	3 (2)
AFLP	3 (2)	Respiratory failure	6 (4)
Gestational hypertension	2 (1)	ICH	5 (3)
Major hemorrhage	26 (16)	Immunologic diseases	3 (2)
Sepsis of pelvic origin	26 (16)	Chronic hypertension	2 (1)
Septic abortion	19 (12)	Endocrine disorders	2 (1)
Intrauterine fetal death	4 (2)	Others	7 (4)
Puerperal sepsis	3 (2)		
Others	5 (3)		

Vasquez et al CHEST 2007; 131:718-724

## Continuing treatment

- Standard critical care
  - Protective ventilation
  - Metabolic stability
- Liaison
  - Management of
    - uterus- contracted and evacuated
    - pre-eclamptic phenomena
    - Haemostasis and thromboprophylaxis
  - Interaction with baby
  - Bereavement
  - Long term consequences- psychology

# Clinical review: Special populations - critical illness and pregnancy

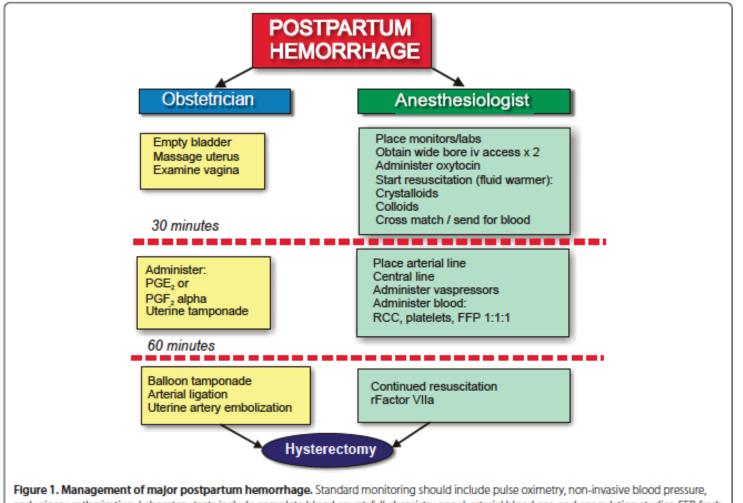
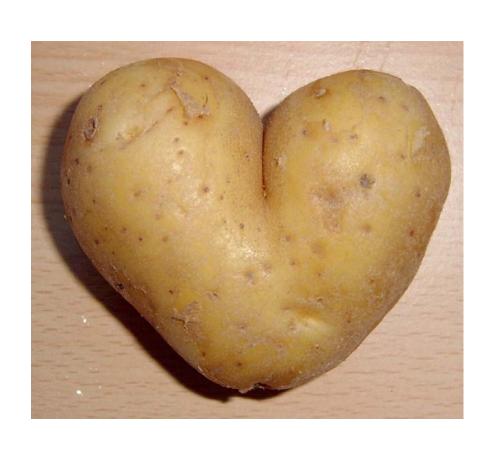


Figure 1. Management of major postpartum hemorrhage. Standard monitoring should include pulse oximetry, non-invasive blood pressure, and urinary catherization. Laboratory tests include complete blood count, full chemistry panel, arterial blood gas, and coagulation studies. FFP, fresh frozen plasma; PGE<sub>2</sub>, prostaglandin E<sub>2</sub>; PGF<sub>2</sub> alpha, prostaglandin F<sub>2a</sub>; RCC, red cell concentrate.

# Fluids- HES





#### 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

The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

### Hydroxyethyl Starch 130/0.42 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.,
Gudmundur Klemenzson, M.D., Anders Åneman, M.D., Ph.D.,
Kristian R. Madsen, M.D., Morten H. Møller, M.D., Ph.D., Jeanie M. Elkjær, M.D.,
Lone M. Poulsen, M.D., Asger Bendtsen, M.D., M.P.H., Robert Winding, M.D.,
Morten Steensen, M.D., Pawel Berezowicz, M.D., Ph.D., Peter Søe-Jensen, M.D.,
Morten Bestle, M.D., Ph.D., Kristian Strand, M.D., Ph.D., Jørgen Wiis, M.D.,
Jonathan O. White, M.D., Klaus J. Thornberg, M.D., Lars Quist, M.D.,
Jonas Nielsen, M.D., Ph.D., Lasse H. Andersen, M.D., Lars B. Holst, M.D.,
Katrin Thormar, M.D., Anne-Lene Kjældgaard, M.D., Maria L. Fabritius, M.D.,
Frederik Mondrup, M.D., Frank C. Pott, M.D., D.M.Sci., Thea P. Møller, M.D.,
Per Winkel, M.D., D.M.Sci., and Jørn Wetterslev, M.D., Ph.D.,
for the 6S Trial Group and the Scandinavian Critical Care Trials Group\*

### CRITICALLY ILL PATIENT

## Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically III Patients Requiring Volume Resuscitation

A Systematic Review and Meta-analysis

Ryan Zarychanski, MD, MSc

Ahmed M. Abou-Setta, MD, PhD

Alexis F. Turgeon, MD, MSc

Brett L. Houston, BSc

Lauralyn McIntyre, MD, MSc

John C. Marshall, MD

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the resuscitation of critically ill patients and the relative superiority and safety of different re**Importance** Hydroxyethyl starch is commonly used for volume resuscitation yet has been associated with serious adverse events, including acute kidney injury and death. Clinical trials of hydroxyethyl starch are conflicting. Moreover, multiple trials from one investigator have been retracted because of scientific misconduct.

**Objectives** To evaluate the association of hydroxyethyl starch use with mortality and acute kidney injury.

**Data Sources** Randomized controlled trials from MEDLINE, EMBASE, CENTRAL, Global Health, HealthStar, Scopus, Web of Science, the International Clinical Trials Registry Platform (Inception to October 2012), reference lists of relevant articles, and gray literature.

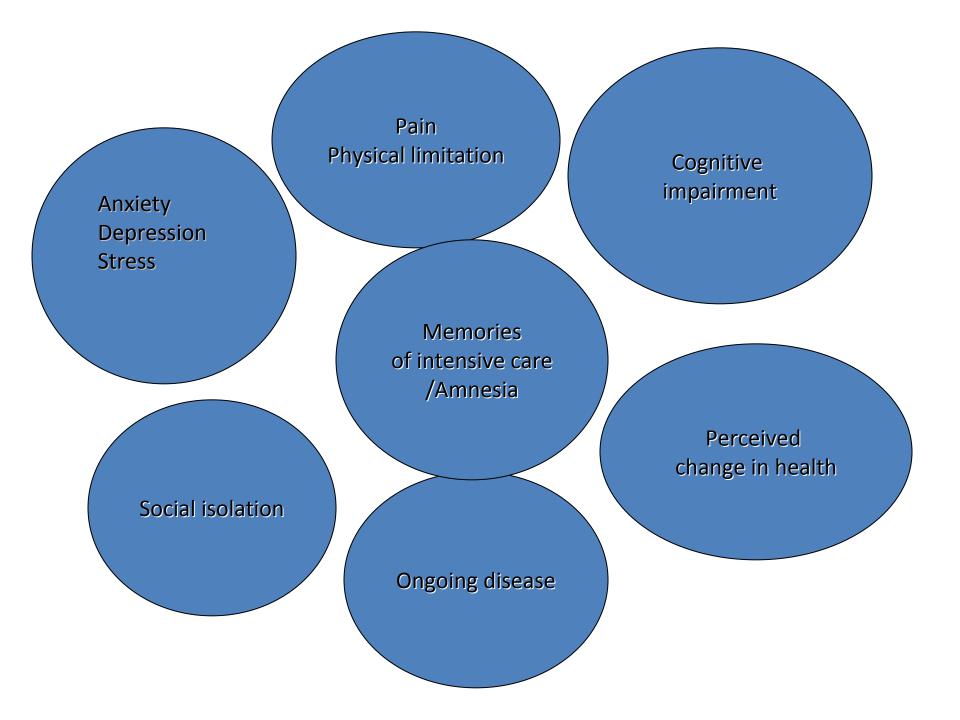
**Study Selection** Two reviewers independently identified randomized controlled trials comparing hydroxyethyl starch with other resuscitation fluids in critically ill patients receiving acute volume resuscitation.

Figure 2. Mortality and Hydroxyethyl Starch

	Н	E8	Cor	trol	•		
Trials excluding those published by Boldt et al	No. of Events	Total	No. of Events	Total	FIR (95% CI)	Favors Favors Control HES Intervention	Waight %
Haupt and Rackow, 24 1982	5	9	12	17	0.79 (0.41-1.52)	<del></del>	1.0
Rackow et al. 50 1989	5	10	5	10	1.00 (0.42-2.40)	<del></del>	0.6
Nagy et al, <sup>23</sup> 1993	4	21	4	20	0.95 (0.27-3.30)	<del></del>	0.3
Beards et al. 49 1964	4	13	6	15	0.77 (0.28-2.14)	<del></del>	0.4
Berard et al. 26 1995	32	146	31	153	1.08 (0.70-1.68)	<del></del>	2.2
Younes et al. (6) 1998	2	12	3	11	0.61 (0.12-3.00)	<del></del>	0.2
Astar at al, <sup>67</sup> 2000	10	16	12	18	0.94 (0.57-1.56)	<del></del>	1.7
Carli et al,51 2000	9	85	4	79	2.09 (0.67-6.52)	<del>-  </del>	0.3
Schortgen et al, <sup>3</sup> 2001	28	65	29	64	0.95 (0.64-1.40)	<del>-</del>	2.8
Vanoman et al, 6 2004	18	30	13	31	1.43 (0.86-2.38)	<del>  = </del>	1.7
Moinar et al, 45 2004	12	15	10	15	1.20 (0.77-1.86)	<del>- =-</del>	2.2
Li et al, <sup>42</sup> 2008	14	30	20	30	0.70 (0.44-1.11)	<del>!</del>	2.0
Mointyre at at, <sup>22</sup> 2008	9	21	6	19	1.36 (0.59-3.10)	<del>-   •</del>	0.6
Brunkhorst et al. 44 2008	107	297	200	303	1.17 (0.94-1.47)	<del> ■</del> -	8.3
Haljdan at al, <sup>62</sup> 2009	4	12	8	36	1.50 (0.55-4.11)	<del>-   •</del>	0.4
Dolecek et al. 41 2009	6	26	4	30	1.73 (0.55-5.47)	<del></del>	0.3
Gondos et al, <sup>™</sup> 2010	15	50	38	150	1.18 (0.71-1.96)	<del>- i=</del>	1.7
hal et al, <sup>40</sup> 2010	5	15	5	15	1.00 (0.36-2.76)	<del></del>	0.4
Viadhou et al, <sup>37</sup> 2010	2	12	2	17	1.42 (0.23-8.70)	<del>- !</del>	0.1
Horadstvolt et al. 39 2010	2	10	2	9	0.90 (0.16-5.13)	<del></del>	0.1
Dubin et al. 35 2010	3	12	T	13	0.46 (0.15-1.40)	<del></del>	0.4
Zhao et al,21 2011	3	20	5	20	0.60 (0.17-2.18)	<del></del>	0.3
Zhu et al,22 2011	3	90	4	45	0.38 (0.09-1.60)		0.2
Du et al, 25 2011	2	21	2	21	1.00 (0.16-6.45)	<del></del>	0.1
James et al.4 2011	12	58	6	57	1.97 (0.79-4.88)	<del> </del>	0.5
Myburgh et al, <sup>54</sup> 2012	5007	3500	566	3500	1.05 (0.95-1.17)		38.9
Perner et al. 50 2012	201	400	172	400	1.17 (1.01-1.36)	<u> </u>	19.3
Guidat at al. <sup>52</sup> 2012	40	100	32	96	1.20 (0.83-1.74)	<del>- =-</del>	3.1
Subtotal (95% CI)		5096		5194	1.00 (1.02-1.17)	Þ	90.3
Total events Hatarogenalty: $\tau^2 = 0.00$ ; $\chi_{22}^{-2} = 19.16$ ; $(P = .86)$ ; $I$ Test for overall effect: $Z = 2.39$ , $(P = .02)$	1154 P=0%		1101				

Amit Patel Umeer Waheed Stephen J. Brett Randomised trials of 6 % tetrastarch (hydroxyethyl starch 130/0.4 or 0.42) for severe sepsis reporting mortality: systematic review and meta-analysis

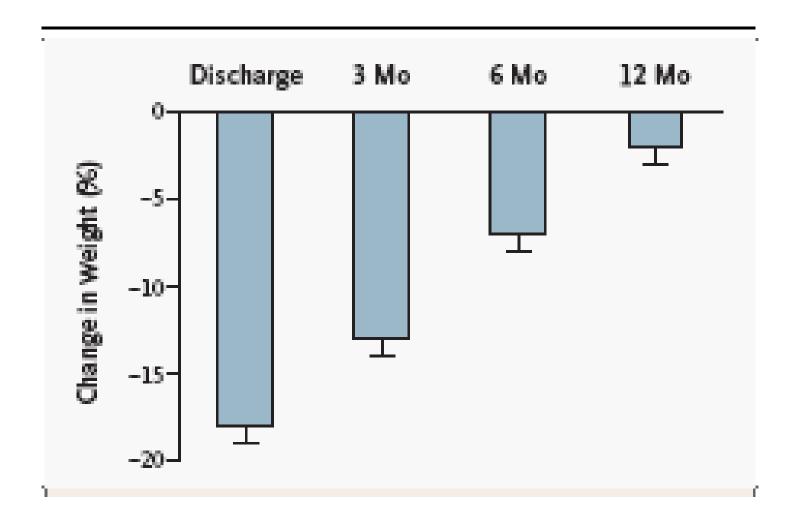
	6% tetras	6% tetrastarch Co		ntrol fluid		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
CHEST trial 2012	248	976	224	945	43.7%	1.07 [0.92, 1.25]	-
6S trial 2012	201	398	172	400	48.5%	1.17 [1.01, 1.36]	<b>■</b>
CRYSTMAS trial 2012	40	99	32	95	7.9%	1.20 [0.83, 1.74]	+-
Total (95% CI)		1473		1440	100.0%	1.13 [1.02, 1.25]	<b>•</b>
Total events	489		428				
Heterogeneity: Tau2 =	0.00; Chi <sup>2</sup>	= 0.81,	df = 2 (P	= 0.67	); $I^2 = 0\%$		0.1 0.2 0.5 1 2 5 10
Test for overall effect:	Z = 2.32 (P	= 0.02	)				Favours 6% tetrastarch Favours control fluid



### Memories of intensive care

- Homicidal nurse
- Drug dealing in the intensive care unit
- Trips to a bar every evening
- Visiting band
- Alien abduction
- The fiery furnace

# One-year outcomes in survivors of the acute respiratory distress syndrome



Herridge M. et al NEJM 2003;348:683

# One-year outcomes in survivors of the acute respiratory distress syndrome

Outcome	3 Months	6 Months	12 Months
Distance walked in 6 min No. evaluated Median — m Interquartile range — m Percentage of predicted value∫	80* 281 55–454 49	78† 396 244–500 64	81‡ 422 277–510 66
Returned to work— no./total no. (%)¶	13/83 (16)	26/82 (32)	40/82 (49)
Returned to original work — no./total no. (%)	10/13 (77)	23/26 (88)	31/40 (78)

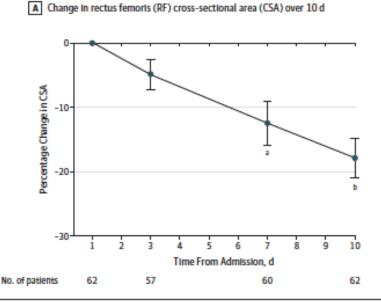
Herridge M. et al NEJM 2003;348:683

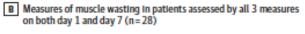
#### Research

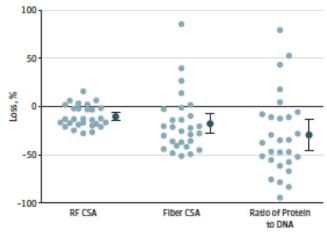
### Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

### Acute Skeletal Muscle Wasting in Critical Illness

Zudin A. Puthucheary, MRCP; Jaikitry Rawal, MRCS; Mark McPhail, PhD; Bronwen Connolly, BSc; Gamunu Ratnayake, MRCP; Pearl Chan, MBBS; Nicholas S. Hopkinson, PhD; Rahul Padhke, PhD; Tracy Dew, MSc; Paul S. Sidhu, PhD; Cristiana Velloso, PhD; John Seymour, PhD; Chibeza C. Agley, MSc; Anna Selby, PhD; Marie Limb, PhD; Lindsay M. Edwards, PhD; Kenneth Smith, PhD; Anthea Rowlerson, PhD; Michael John Rennie, PhD; John Moxham, PhD; Stephen D. R. Harridge, PhD; Nicholas Hart, PhD; Hugh E. Montgomery, MD



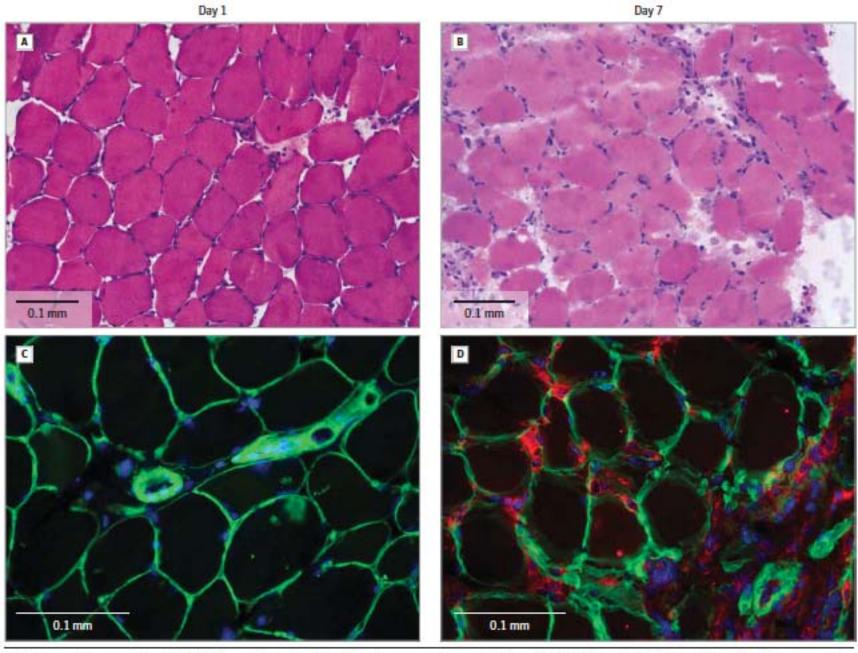




Summary data (dark circles) are expressed as medians and 95% confidence intervals.

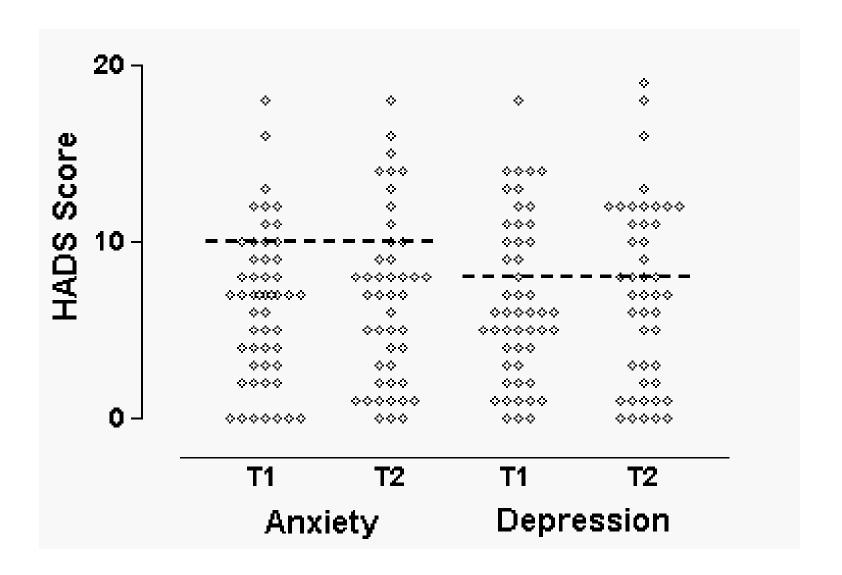
<sup>&</sup>lt;sup>a</sup> P=.002 for change from day 1 to day 7 by repeated measures 2-way analysis of variance.

b P<.001 for change from day 1 to day 10.</p>

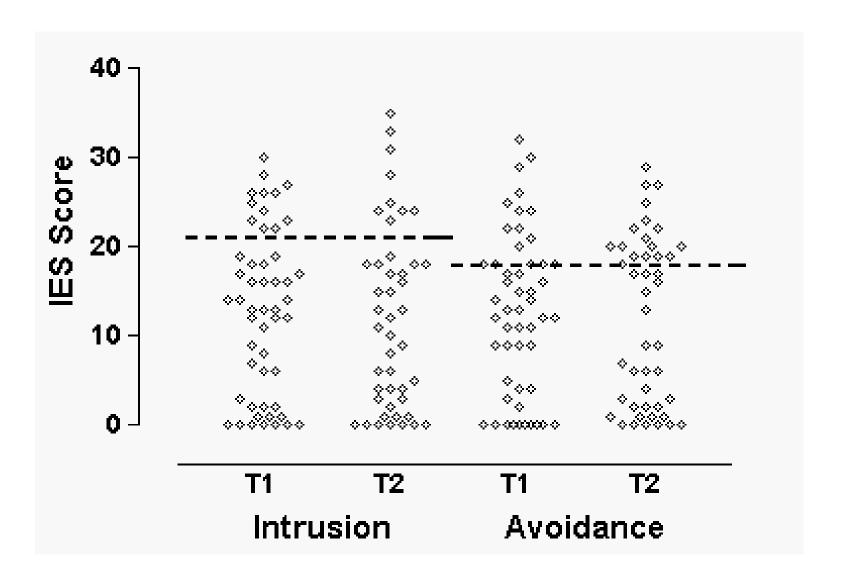


Healthy muscle is seen on day 1 (A, C) with necrosis and a cellular infiltrate on day 7 (B, D). This infiltrate was CD68 positive on immunostaining, indicating macrophage origin (red). A, B are hematoxylin and eosin stain, and C, D was

immunostaining, with CD68 for red, laminin (myofiber outline) for green, and 4',6-diamidion-2-pheylidole (a nuclear marker) for blue.



Sukantarat K. et al. Br J Health Psychol 2007;12:65



Sukantarat K. et al. Br J Health Psychol 2007;12:65

John Griffiths Gillian Fortune Vicki Barber J. Duncan Young

# The prevalence of post traumatic stress disorder in survivors of ICU treatment: a systematic review

30 studies included

### Prevalence

- ♦ By interview 0-64%
- ◆By self report measure 5-64%

# Investigating risk factors for psychological morbidity three months after intensive care: a prospective cohort study

#### Abstract

**Introduction:** There is growing evidence of poor mental health and quality of life among survivors of intensive care. However, it is not yet clear to what extent the trauma of life-threatening illness, associated drugs and treatments, or patients' psychological reactions during intensive care contribute to poor psychosocial outcomes. Our aim was to investigate the relative contributions of a broader set of risk factors and outcomes than had previously been considered in a single study.

**Methods:** A prospective cohort study of 157 mixed-diagnosis highest acuity patients was conducted in a large general intensive care unit (ICU). Data on four groups of risk factors (clinical, acute psychological, sociodemographic and chronic health) were collected during ICU admissions. Post-traumatic stress disorder (PTSD), depression, anxiety and quality of life were assessed using validated questionnaires at three months (n =100). Multivariable analysis was used.

**Results:** At follow-up, 55% of patients had psychological morbidity: 27.1% (95% CI: 18.3%, 35.9%) had probable PTSD; 46.3% (95% CI: 36.5%, 56.1%) probable depression, and 44.4% (95% CI: 34.6%, 54.2%) anxiety. The strongest clinical risk factor for PTSD was longer duration of sedation (regression coefficient = 0.69 points (95% CI: 0.12, 1.27) per day, scale = 0 to 51). There was a strong association between depression at three months and receiving benzodiazepines in the ICU (mean difference between groups = 6.73 points (95% CI: 1.42, 12.06), scale = 0 to 60). Use of inotropes or vasopressors was correlated with anxiety, and corticosteroids with better physical quality of life. The effects of these clinical risk factors on outcomes were mediated (partially explained) by acute psychological reactions in the ICU. In fully adjusted models, the strongest independent risk factors for PTSD were mood in ICU, intrusive memories in ICU and psychological history. ICU mood, psychological history and socio-economic position were the strongest risk factors for depression.

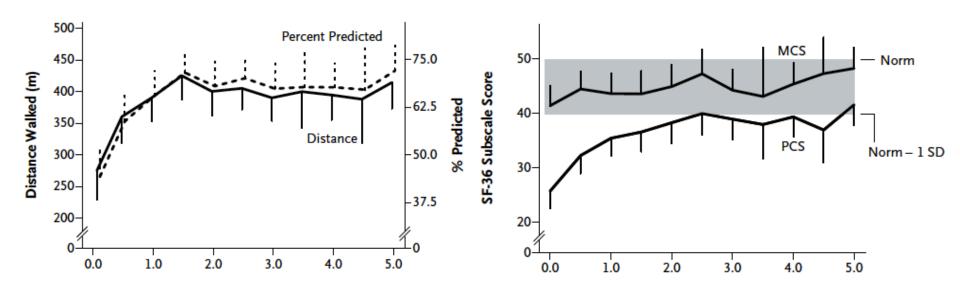
**Conclusions:** Strikingly high rates of psychological morbidity were found in this cohort of intensive care survivors. The study's key finding was that acute psychological reactions in the ICU were the strongest modifiable risk factors for developing mental illness in the future. The observation that use of different ICU drugs correlated with different psychological outcomes merits further investigation. These findings suggest that psychological interventions, along with pharmacological modifications, could help reduce poor outcomes, including PTSD, after intensive care.

# Functional capacity 5 years after acute respiratory distress syndrome

Distance walked in 6 min§					
Median — m	422	416	418	406	436
Interquartile range	277-510	285-496	311-474	314-488	324-512
Percent of predicted¶	66	68	67	71	76
Median SF-36 score					
Physical functioning	60	70	70	75	75
Role, physical	25	50	100	75	88
Bodily pain	62	62	72	74	74
General health	52	62	55	59	62
Vitality	55	55	50	50	55
Social functioning	63	75	75	69	75
Role, emotional	100	100	100	100	100
Mental health	72	76	72	76	76
Returned to work — no. of patients (%)*	40 (48)	45 (65)	50 (70)	46 (73)	49 (77)
Returned to original work — no. of patients/ total no. (%)	31/40 (78)	36/45 (80)	46/50 (92)	41/46 (89)	46/49 (94)

Herridge et al. N Engl J Med 2011;364:1293-304.

# Functional capacity 5 years after acute respiratory distress syndrome



### Non –physical-conclusions

- Neuropsycholgical problems occur
  - ➤ Depression
  - **≻**Anxiety
  - **>PTSD**
- Uncertain relationship to magnitude of acute illness

### Physical Consequences

- Unfixed underlying disease
- New chronic health issues
- Loss of muscle mass and strength
- Cosmetic problems
- Sexual dysfunction

- ➤ Stiff joints
- Heterotopic ossification
- Entrapment neuropathy
- Tracheal problems

### Oiling the wheels of intensive care to reduce "machine friction": The best way to improve outcomes?

Susanna Walker, MRCP, FRCA; Stephen Brett, MD, FRCA

Introduction: A number of costly trials of interventions for the critically III have had results that are initially positive, and then subsequent trials are less positive. This has led to uncertainty and a feeling that our scientific approach may need reevaluation. What are we missing when performing these trials? Are there simple, less costly ways of improving outcomes for patients?

simple, less costly ways of improving outcomes for patients?

Discussion: Many of the large interventional trials have included patients on the basis of syndromic enrollment criteria. This inevitably leads to a heterogeneous profile of patients, precipitating conditions, and chronic health. The realistic effect of an intervention may vary depending on the individual circumstances of a particular patient, contributing to trial "noise." The assumption that trial size and randomization will deal with this may not hold true and in some circumstances may be biologically questionable. Perhaps we should consider alternatives? In common with other areas of medicine, it is well-known that intensive care outcomes are variable, reflecting differing performance. Until

recently, little attention has been focused on a detailed understanding of variation in performance and delivery of care and how such knowledge might be used to improve patient outcomes. A number of recent efforts that have demonstrated positive improvements have been based around understanding and reducing individual and organizational underperformance. This human and organizational factors-based research does not conflict with more pharmacologic-based research and may be compilmentary.

Canclusion: By property understanding the way we do things and the optimal local balance of protocolized and individualized care, we may deliver greater improvements to the outcome of intensive care unit patients than many of the more expensive, pharmacologic, and technological attempts of recent years. (Crit Care Med 2010; 38[Suppl.]:S642–S648)

Key Wozes: communication; patient safety; teamwork; intensive care unit; nontechnical skills; human factors; quality improvement; evidence-based guidelines; quality of care; clinical trials

### The Doctor



Tate Britain

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

### **RECOMMENDATION:**

Patients should be aware of the risks associated with the use of HES solutions and discuss these risks with their healthcare provider (refer to the FDA Safety Communication for detailed recommendations for patients).

**Recommendations for Health Professionals include the following:** 

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.



14 June 2013 EMA/349341/2013

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

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded following a review of the available evidence that the benefits of infusion solutions containing hydroxyethyl-starch (HES) no longer outweigh their risks and therefore recommended that the marketing authorisations for these medicines be suspended.



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### Press release: MHRA suspends use of hydroxyethyl starch (HES) drips

### Press release

Date: 27 June 2013

Time: 12:30

MHRA suspends use of hydroxyethyl starch (HES) drips Subject:

Contact: Press Office 020 3080 7651

or press.office@mhra.gsi.gov.uk Out-of-hours 07770 446 189

The use of starch drips to treat critically ill patients and those undergoing surgery is to be suspended in the UK because their benefits no longer outweigh the risk of using them, the Medicines and Healthcare products Regulatory Agency (MHRA) announced today.

The drips are currently used in a range of clinical settings for treatment and prevention of low blood volume (hypovolaemia) and a steep drop in blood pressure (hypovolaemic shock), as well as for maintenance of adequate circulation during surgical procedures, should no longer be used.

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