

Global variations in trauma outcomes

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Global trauma

- Variation in outcome
- Variation in practice
- Need for guidelines and consistent training
- Focus on individual quality improvement

Australian trauma fatalities in perspective

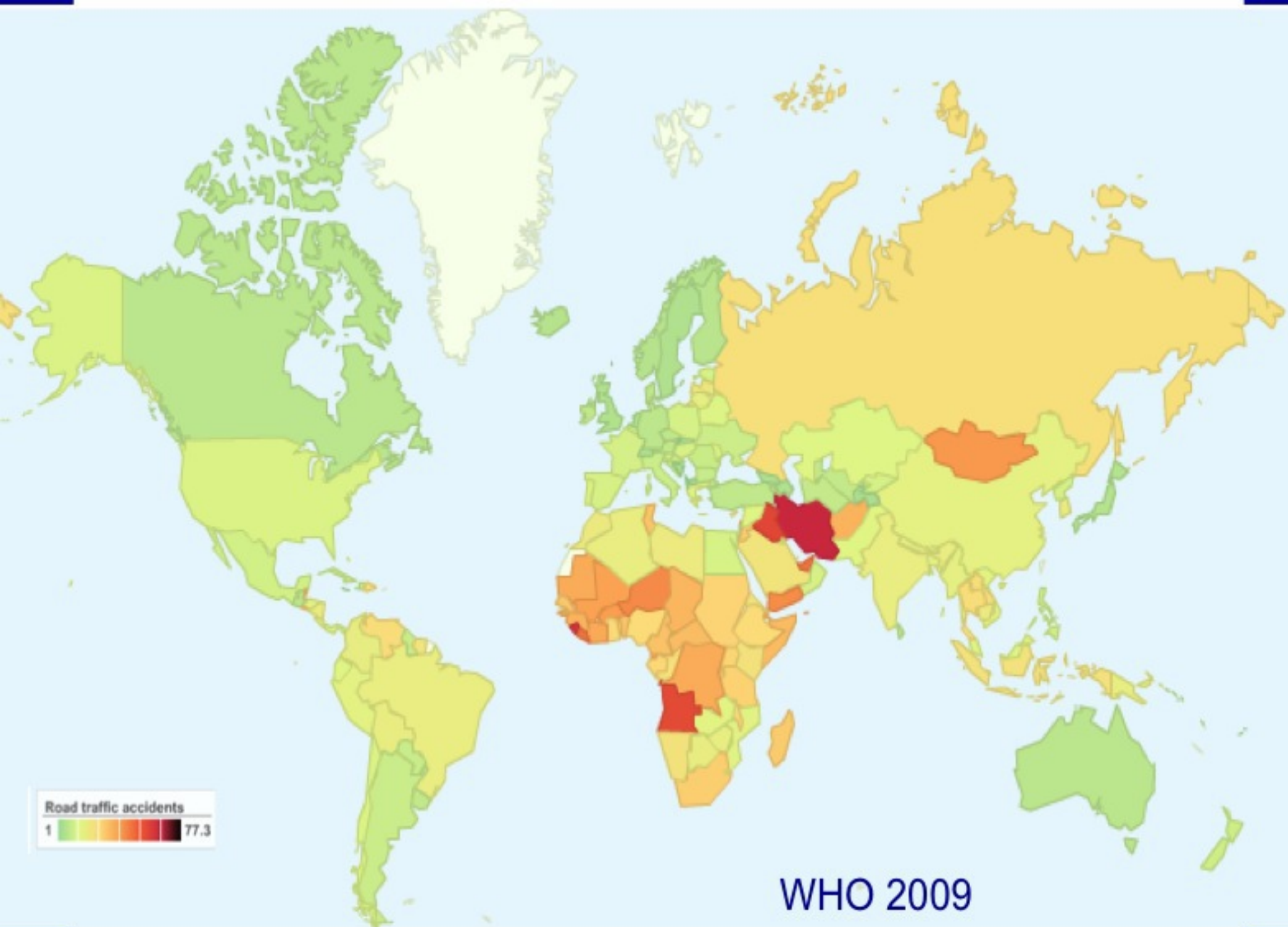
- Shark attack <1 death per year
- Box jellyfish <1 death per year
- Crocodile attacks <1 death per year
- Snake bite 2-4 deaths per year
- Lightning 5-10 deaths per year
- Road deaths 1756 in 2001



Road traffic injuries are a huge public health and development problem

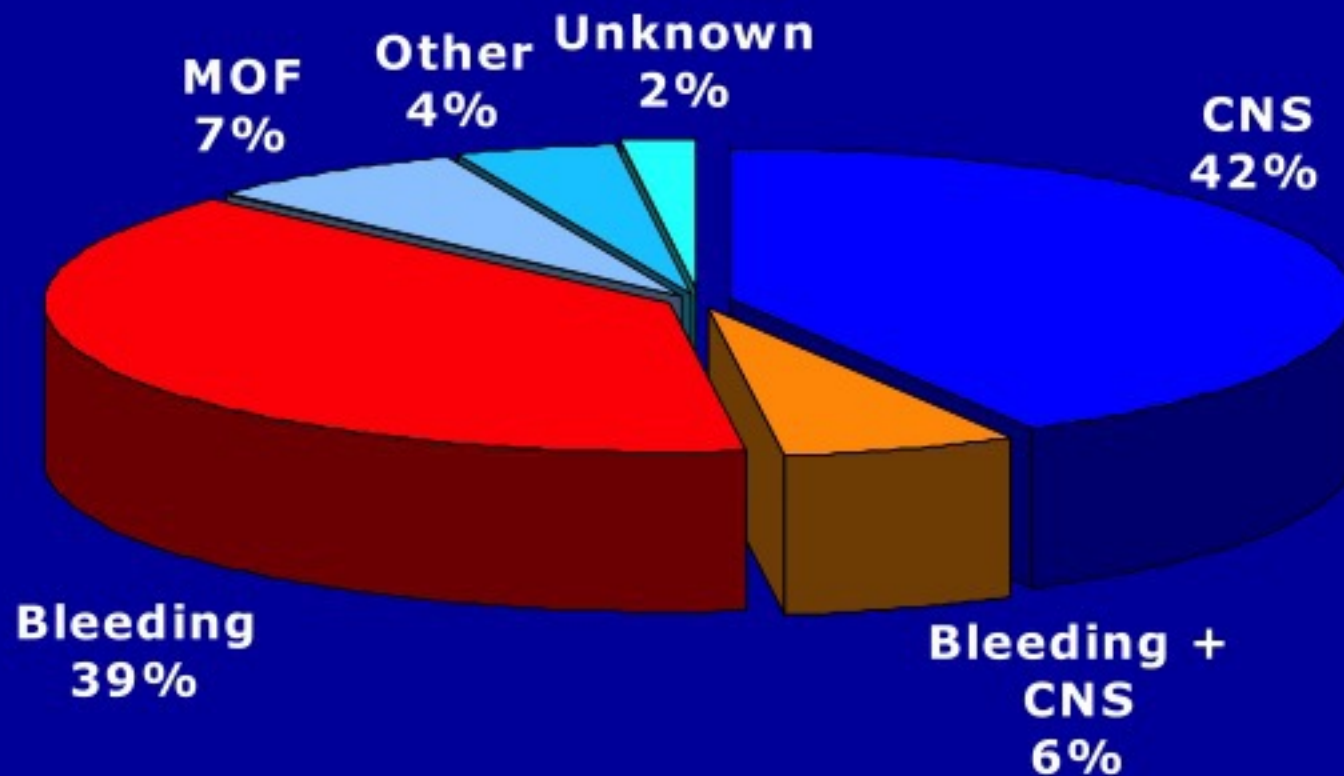
- > 1.2 million people die per year
- World mortality: 20.95 per 100,000 population
- Children, pedestrians, cyclists and the elderly are the most vulnerable
- 20-50 million more are injured or disabled





Patients dying in hospital within 48 hours of admission

Bleeding is a major cause of death



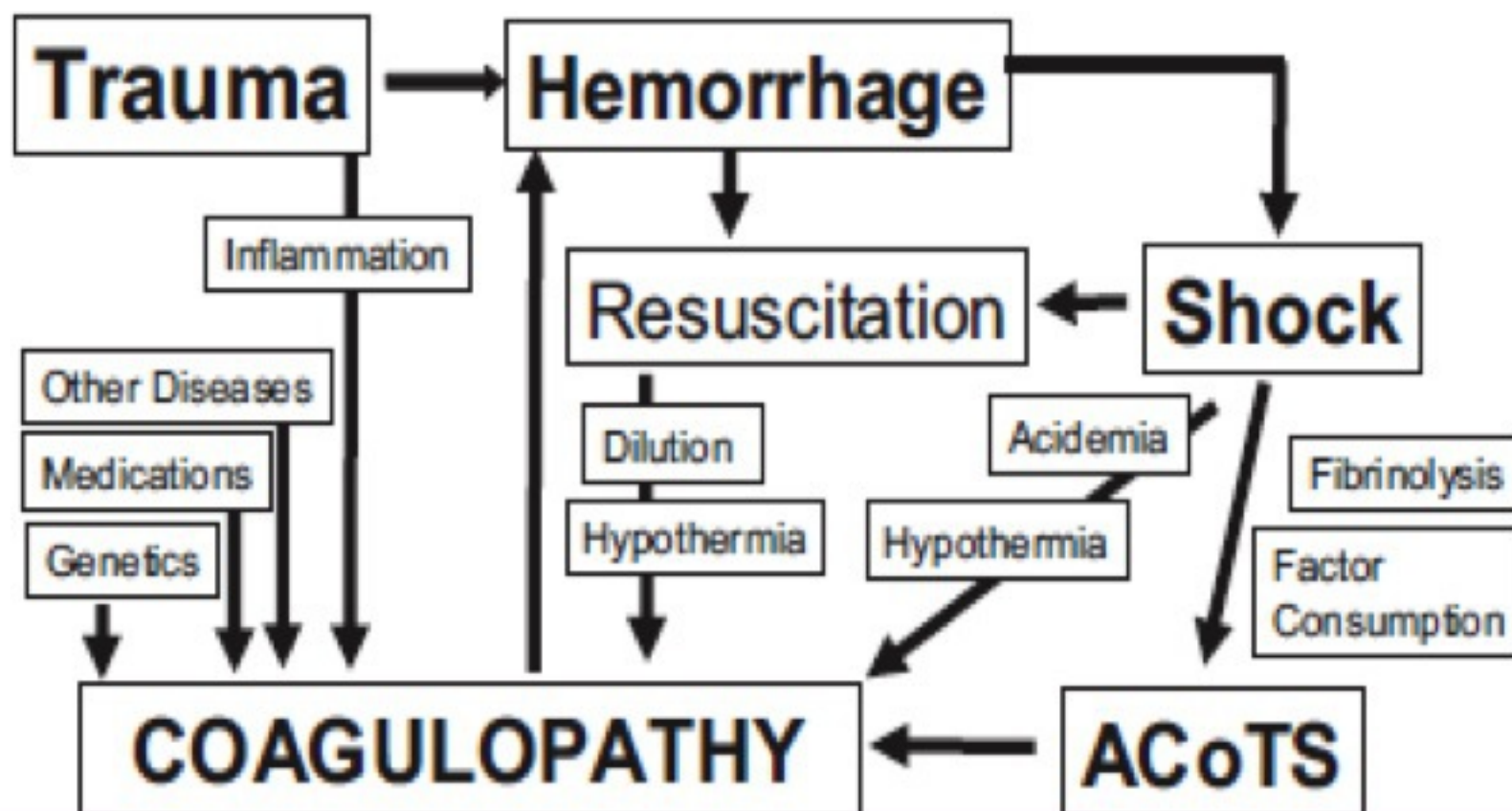
Management of Coagulopathy in the Patients With Multiple Injuries: Results From an International Survey of Clinical Practice

David B. Hoyt, MD, FACS, Richard P. Dutton, MD, MBA, Carl J. Hauser, MD, FACS, FCCM, John R. Hess, MD, MPH, FACP, FAAAS, John B. Holcomb, MD, FACS, Yoram Kluger, MD, Kevin Mackway-Jones, MD, FRCP, FRCS, FCEM, Michael J. Parr, MB, BS, FRCP, FRCA, FANZCA, FJFICM, Sandro B. Rizoli, MD, PhD, FRCSC, Tetsuo Yukioka, MD, and Bertil Bouillon, MD

- 25 countries: regional differences in the specialty responsible
 - 45% follow a massive transfusion protocol
 - 19% inconsistent protocol use and 34% do not use a protocol
 - management of hypothermia, acidosis, blood products, and adjuvant therapy was variable, few massive transfusion protocols specifically address these issues.
-
- Conclusions: need for a common definitions and standardized clinical protocols to ensure optimal patient care.

The Coagulopathy of Trauma: A Review of Mechanisms

John R. Hess, MD, MPH, FACP, FAAAS, Karim Brohi, MD, Richard P. Dutton, MD, MBA,
Carl J. Hauser, MD, FACS, FCCM, John B. Holcomb, MD, FACS, Yoram Kluger, MD,
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- Michael Parr was Chairman of an Australian NovoNordisk Advisory Board, member of a NovoNordisk International Trauma Education Advisory Board, and member of the CONTROL trial steering committee

CONTROLTM

CLINICAL TRIAL ON THE EFFECT OF rFVIIa ON TRAUMATIC BLOOD LOSS

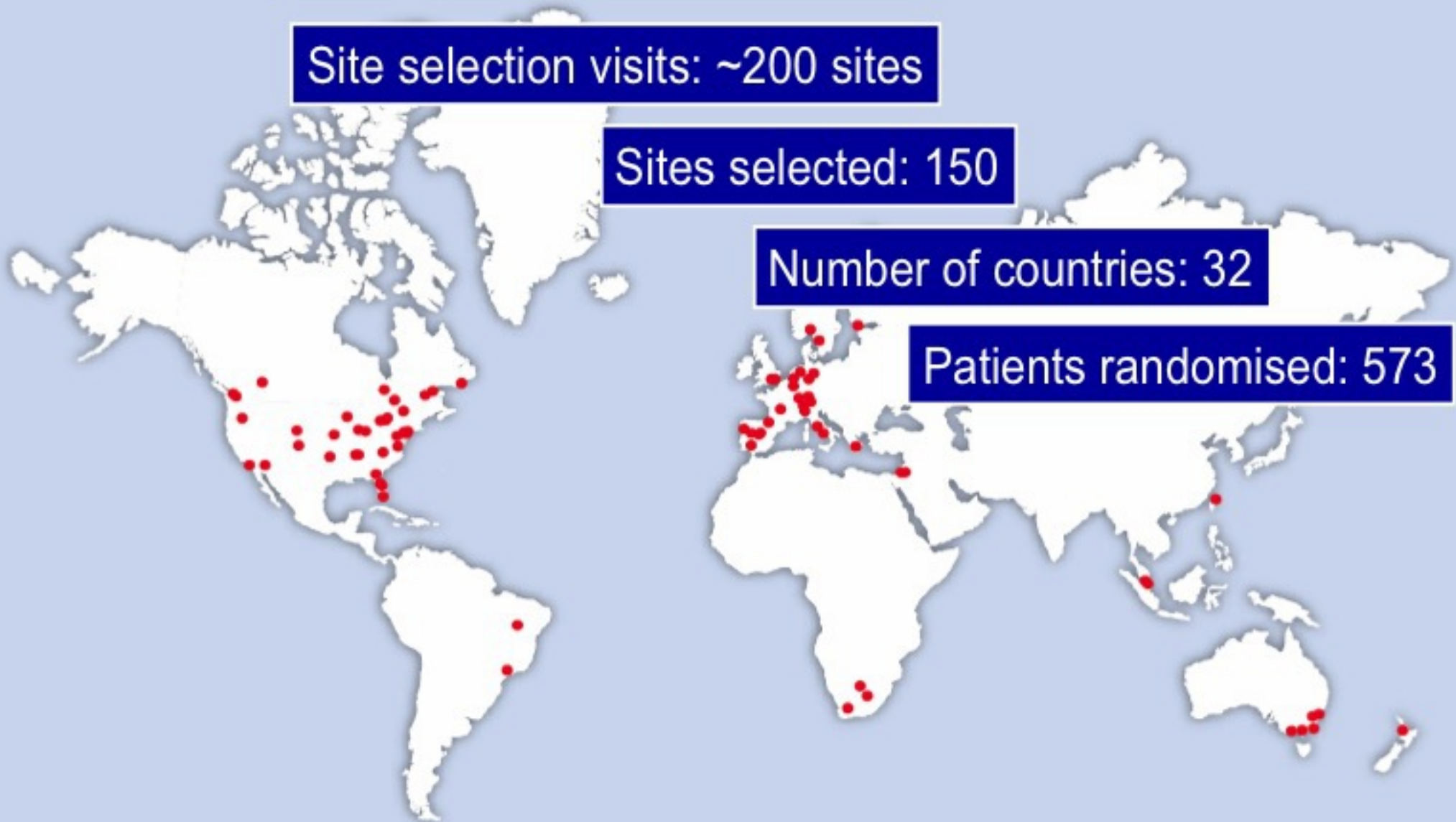
August 2005-Sept 2008

Site selection visits: ~200 sites

Sites selected: 150

Number of countries: 32

Patients randomised: 573



Summary

- Mortality and morbidity
 - No significant differences between placebo and rFVIIa
- Transfusion requirements: blunt patients (post-dosing to 24h)
 - Significant reduction in RBC (1.2 units), FFP (2.2 units) and total allogeneic blood (3.6 units)
 - No differences in platelets, fibrinogen concentrate or cryoprecipitate
- Safety
 - No statistical difference for total SAEs

Damage Control Guideline

- Definitive management for bleeding begins <2 hours after hospital arrival
- Operations and procedures within 24 hours = “damage control” controlling hemorrhage and contamination.
- No orthopaedic, maxillofacial, vertebral or complex gastrointestinal reconstructive surgery shall be performed until after the subject is outside this ‘window’.
- A “damage control” approach (i.e. no definitive surgical care for other than bleeding injuries) will be initiated when any of the below is present:
 - Temperature < 35 °C
 - Lactate > 4 mmol/l
 - Corrected pH < 7.3
- Active warming devices will be used to maintain core temperature of >35 °C

Transfusion Guideline

- *In patients hemodynamically unstable as defined by:*
- SBP \leq 90 mmHg or
- SBP is only maintained $>$ 90 mmHg with massive fluids or vasopressor support
- RBC should be administered as determined by "clinical necessity".

- *In patients hemodynamically stable as defined by:*
- No SBP \leq 90 mmHg for 1 hour and
- No resuscitation (or use of vasopressor support) (exception: use of low dose vasopressor support for neurogenic shock)
- Hemoglobin $<$ 7g/dL: RBC administered at the investigators discretion
- Hemoglobin 7-9 g/dL: RBC should only be administered at the discretion of the investigator, if evidence of hypoperfusion is present
- Hemoglobin $>$ 9 g/dL: No RBC transfusions

Ventilation weaning

Patients requiring mechanical ventilation will be ventilated to achieve:

- Decreasing PEEP and FiO_2 as early as possible.
- Limiting ventilation volumes to no greater than 6 ± 2 ml/kg predicted body weight as much as possible
- Limiting plateau pressures to ≤ 30 cm H_2O whenever possible
- Avoiding the use of muscle relaxants, except when specifically indicated.
- Attempting to wean on an ongoing basis, at least once daily when weaning criteria are met.

Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med. 2000; 342: 1301-1308.

ORIGINAL ARTICLE

Global Differences in Causes, Management, and Survival After
Severe Trauma: The Recombinant Activated Factor VII Phase 3
Trauma Trial

*Michael C. Christensen, MSc, MPA, DrPH, Michael Parr, MB, BS, FRCP, FRCA, FANZCA, FJFICM,
Bartholomew J. Tortella, MD, MBA, FACS, FCCM, Johan Malmgren, MD, Stephen Morris, BSc, MSc, PhD,
Todd Rice, MD, and John B. Holcomb, MD; for the CONTROL Study Group*

J Trauma August 2010

Mortality rate (%) by country and time period, unadjusted

	Adm-24h	24h-90d	Adm-90d
Australia	3.6	0.0	3.6
Brazil	12.0	18.2	28.0
Canada	8.1	14.7	21.6
Switzerland	12.5	3.6	15.6
Czech Republic	3.5	3.6	6.9
Germany	4.9	5.2	9.8
Spain	6.3	6.7	12.5
Italy	6.5	17.2	22.6
Singapore	4.0	0.0	4.0
USA	4.0	11.1	14.7
S Africa	8.8	16.1	23.5
Total	6.4	8.9	14.7

N=409

Between-country differences in mortality, Adm-24h

	Unadjusted		Adjusted for baseline characteristics ¹		Adjusted for baseline characteristics ¹ and case management variables	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
USA			(Base case)			
Australia	0.89	(0.16–4.97)	0.23	(0.02–3.09)	0.16	(0.01–4.33)
Brazil	3.27*	(1.20–8.94)	5.84	(0.53–64.83)	6.48	(0.00–10028.35)
Canada	2.12	(0.64–7.00)	1.05	(0.04–28.74)	1.02	(0.01–133.45)
Switzerland	3.43†	(1.45–8.09)	0.94	(0.09–9.69)	0.53	(0.00–190.35)
Czech Republic	0.86	(0.11–6.62)	1.98	(0.08–46.96)	10.97	(0.08–1600.40)
Germany	1.24	(0.35–4.36)	0.25	(0.03–2.35)	0.01	(0.00–10.27)
Spain	1.60	(0.35–7.22)	0.27	(0.04–1.72)	0.06	(0.00–4.80)
Italy	1.66	(0.46–5.91)	0.10	(0.00–6.67)	0.09	(0.00–219.16)
Singapore	1.00	(0.12–8.07)	6.79	(0.64–71.95)	23.92	(0.22–2652.23)
South Africa	2.32	(0.81–6.64)	1.10	(0.05–23.61)	1.61	(0.00–664.78)
Observations		409		402		398
Pseudo- R^2		0.0278		0.388		0.5646
C-statistic		0.6304		0.9141		0.9714
Joint test P		0.0246		0.0109		<0.0001

¹ Including type and mechanism of injury

OR: odds ratio. CI: confidence interval.

ORs > 1 indicate that the likelihood of mortality is higher in that country compared with the base category, US., < 1, lower

* $P < 0.05$, † $P < 0.01$.

Between-country differences in mortality, Adm-90d

	Unadjusted		Adjusted for baseline characteristics ¹		Adjusted for baseline characteristics ¹ and case management variables	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
USA			(Base case)			
Australia	0.22	(0.04–1.07)	0.34	(0.05–2.54)	0.28	(0.03–2.79)
Brazil	2.26*	(1.01–5.06)	0.27	(0.05–1.55)	1.52	(0.06–37.47)
Canada	1.61	(0.70–3.70)	2.04	(0.39–10.61)	1.04	(0.03–34.31)
Switzerland	1.08	(0.58–1.99)	0.84	(0.11–6.47)	1.12	(0.05–24.39)
Czech Republic	0.43	(0.19–1.00)	0.80	(0.14–4.64)	0.45	(0.04–5.55)
Germany	0.63	(0.28–1.43)	0.59	(0.10–3.60)	0.14	(0.01–2.55)
Spain	0.83	(0.20–3.54)	0.03†	(0.00–0.17)	0.03†	(0.00–0.43)
Italy	1.70	(0.74–3.88)	0.83	(0.12–5.76)	0.62	(0.06–6.29)
Singapore	0.24	(0.03–1.77)	0.48	(0.05–4.64)	0.13	(0.00–5.55)
S Africa	1.79	(0.98–3.27)	1.90	(0.51–7.05)	3.25	(0.45–23.61)
Observations		409		401		397
Pseudo- R^2		0.0509		0.3600		0.4664
C-statistic		0.6602		0.8924		0.9267
Joint test P		<0.0001		0.0172		0.0712

¹ Including type and mechanism of injury

OR: odds ratio. CI: confidence interval.

ORs > 1 indicate that the likelihood of mortality is higher in that country compared with the base category, US., < 1, lower

* $P < 0.05$, † $P < 0.01$.

Predictors of Mortality

	Admission–24h		24h–90d		Admission–90d	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
RBC ≥8 units Adm–24h	3.80*	(1.24–11.64)			3.75†	(2.02–6.97)
Lactate ≥5 mmol/L at adm	7.85†	(2.82–21.86)	3.56*	(1.29–9.88)	4.37†	(2.19–8.74)
Chest injury AIS ≥4	3.56*	(1.14–11.12)				
Highest AIS score =5			2.65*	(1.11–6.33)		
Overall patient care compliance: does not meet guidelines	4.52*	(1.14–17.98)	5.90*	(1.48–23.54)	3.19*	(1.25–8.19)
Male			9.09	(0.97–99.98)	3.70*	(1.16–12.48)
Age ≥60 years			5.61†	(1.80–17.51)	3.78†	(1.48–9.62)
Hemaglobin <10 g/dL at adm			4.55*	(1.39–14.29)	2.44*	(1.08–5.56)

* $P<0.05$, † $P<0.01$.

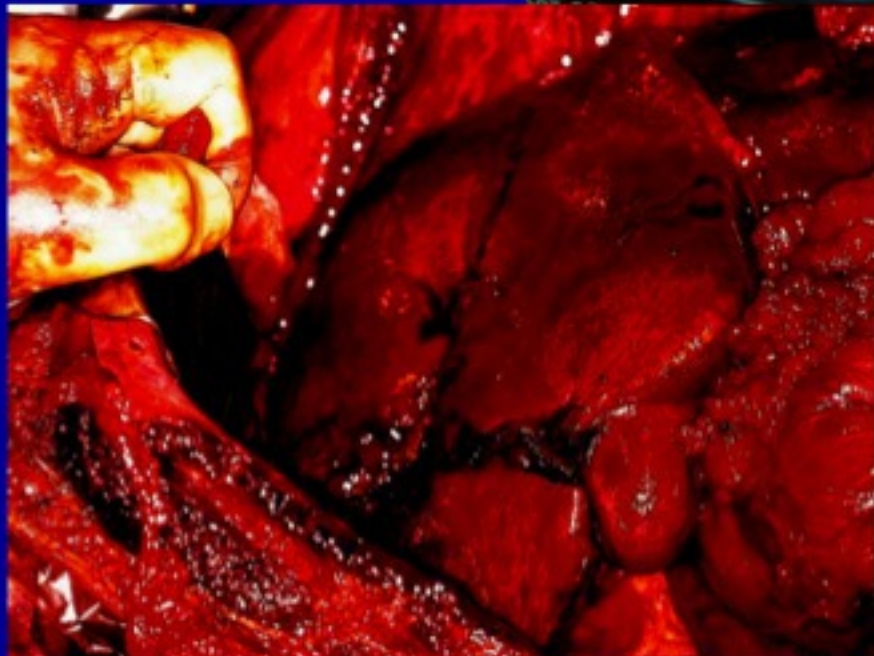
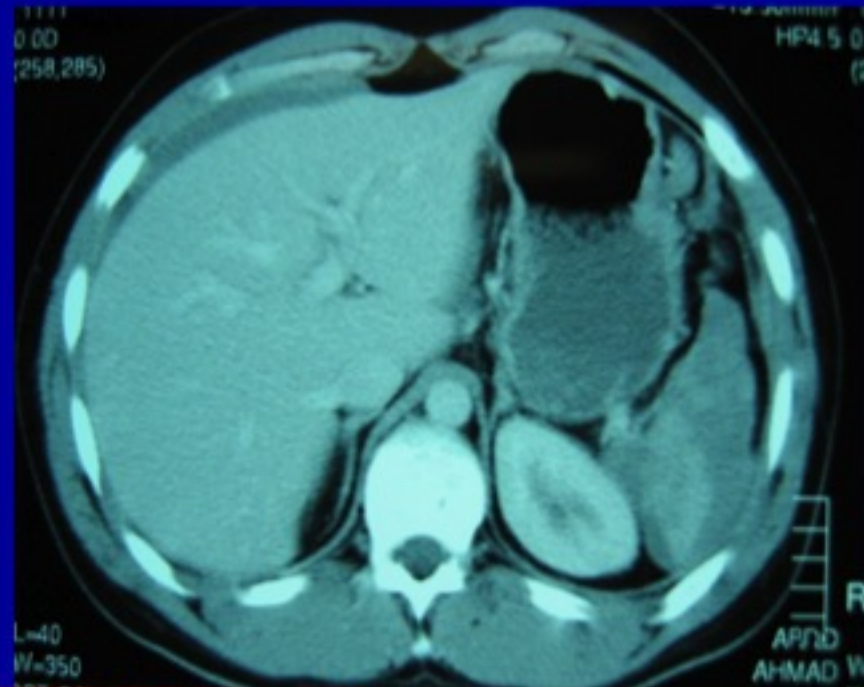
Conclusions

- Significant survival differences persisted between patients from different countries after case mix and management adjustment
- International variation may be important when designing or interpreting results from multinational trauma studies
- Stratification, case mix adjustment and the use of standard practice guidelines on damage control surgery, transfusion and ventilation may mitigate country-driven variation in outcomes
- Damage control saves lives!

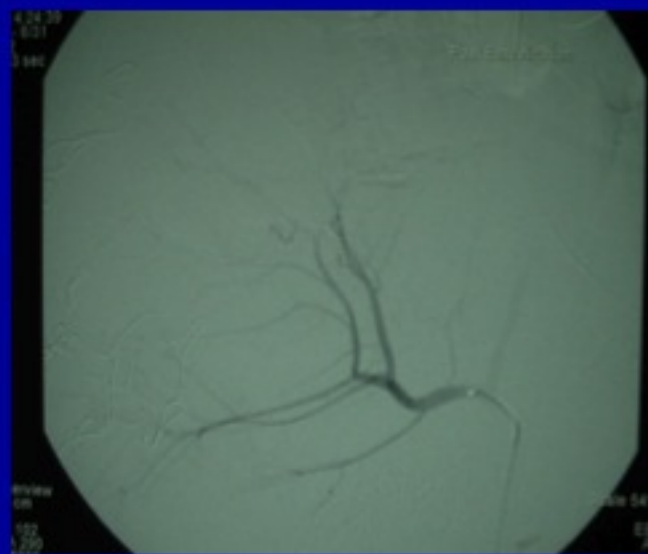
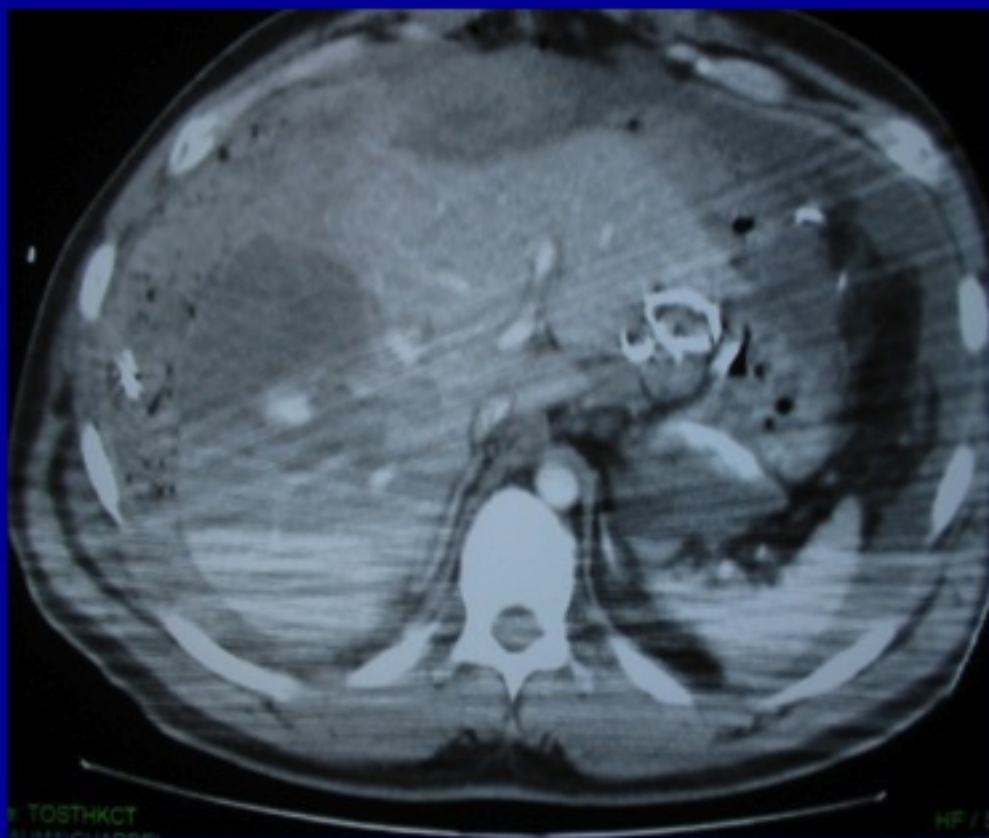
Damage control

- Originally a Naval term
“the capacity of a ship to absorb damage and maintain mission integrity”
- Originally for laparotomies to control contamination and stop bleeding
- Now also described for orthopaedics, thoracic, head and neck and major vascular injuries and resuscitation in general

Identify and manage surgical bleeding (i.e. surgery, angiographic embolisation)



Identify and manage surgical bleeding (i.e. surgery, angiographic embolisation)



Kushimoto S, Arai M, Aiboshi J et al. The Role of Interventional Radiology in Patients Requiring Damage Control Laparotomy. J Trauma 2003;54:171-176.

System approach to damage control in exsanguination

- Damage control resuscitation:
 - ≈ haemostatic resuscitation with early 1:1:1 transfusion of packed red blood cells, fresh frozen plasma and platelets (freshest blood, pre-thawed plasma)

Damage control Resuscitation

- Retrospective chart review, median ISS 18
- 246 patients in US combat hospital
- Received >10units blood in 24hours
- 3 groups by Plasma : RBC ratio
- Plasma: RBC ratio 1:8
 1:2.5
 1:1.4

Borgman MA et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007;63:805-813.



Clinical Trials Unit

LSHTM

Worldwide research and
postgraduate education in
global health

Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage

A large randomised placebo controlled trial among trauma patients with, or at risk of, significant haemorrhage, of the effects of antifibrinolytic treatment on death and transfusion requirement

ISRCTN86730102

FINAL RESULTS PUBLISHED ON LANCET ONLINE ON 15 JUNE 2010

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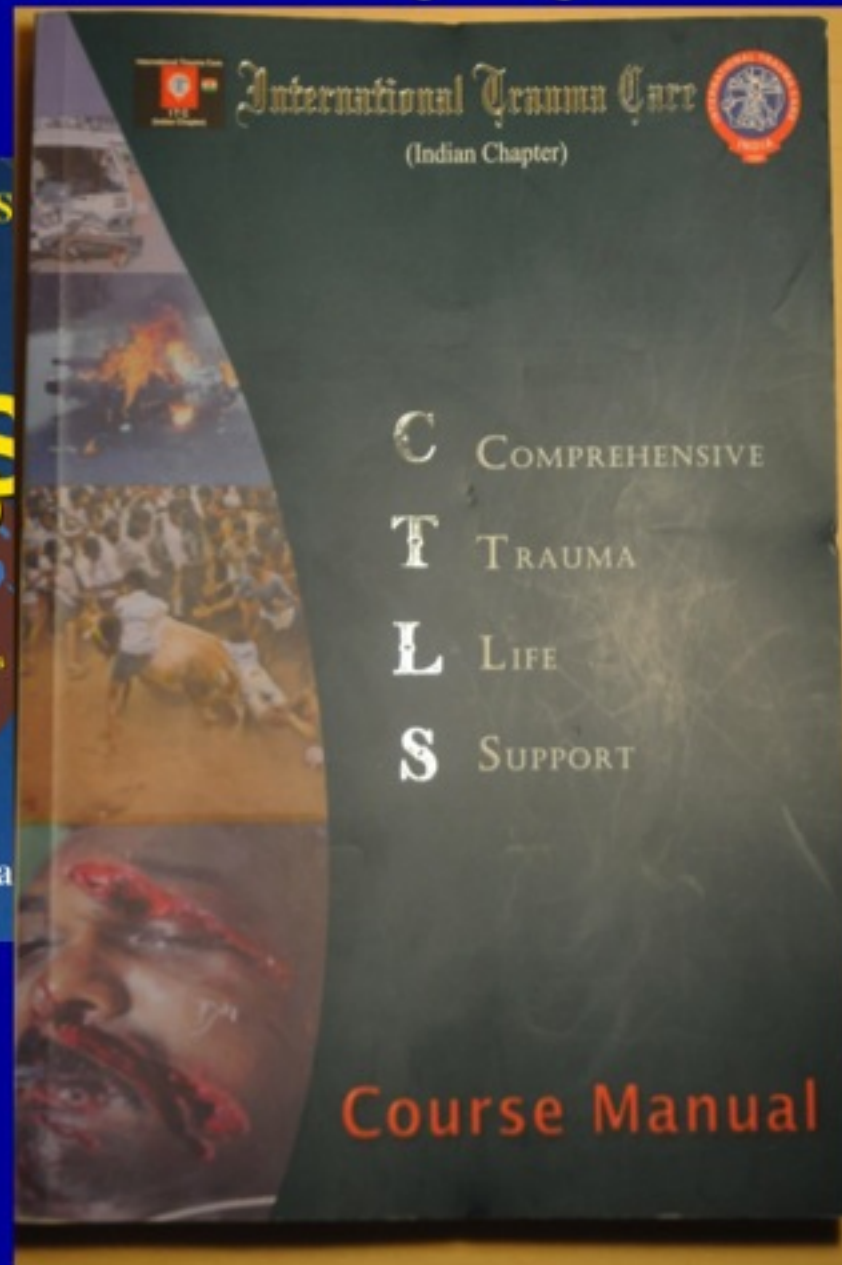
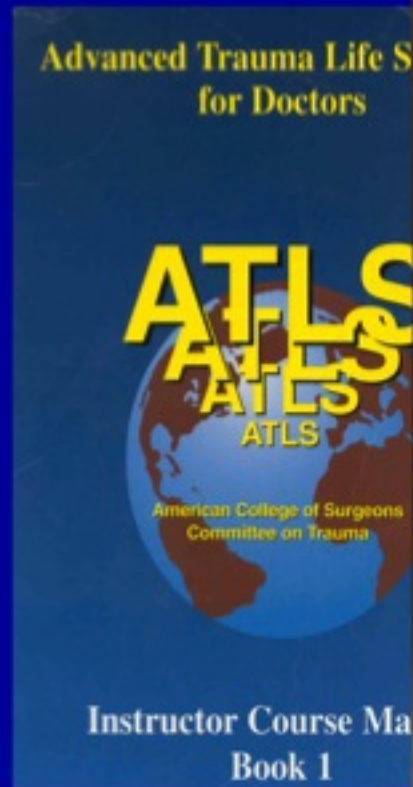
What did the collaborators think? See their comments [HERE](#)

20,000 PATIENTS RANDOMISED

Congratulations to all our 274 collaborating hospitals in 40 countries for completing the randomisation of 20,000 patients!

Last updated 16 June 2010

A common language is essential



Surviving Trauma Guidelines

- Tranexamic acid
- Damage Control (including transfusion protocol)
- Feeding
- Analgesia
- Sedation
- Thrombo-prophylaxis
- Head of bed elevated
- Ulcer prophylaxis
- Glucose management
- Tertiary survey
- Ventilation weaning
- Blood transfusion

Global trauma

- Variation in outcome
- Variation in practice
- Need for guidelines and consistent training
- Focus on individual quality improvement

Liverpool Hospital in 2010



