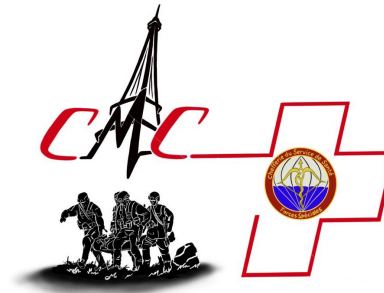
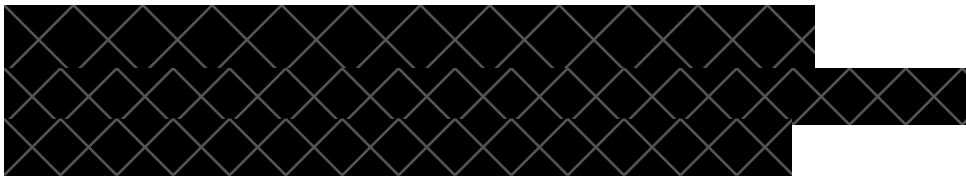


PREHOSPITAL TRANSFUSION ON THE BATTLEFIELD: FROM PROOF OF CONCEPT TO FINE TUNING



Paris SOF Combat Medical Care Conference
October 20th 2022

Proof of concept: 1 – Haemorrhage is the leading cause of avoidable deaths

Oct 2001 – June 2011, Afghanistan - Iraq : **4696 autopsies**

Eastridge BJ, et al. J Trauma Acute Care Surg 2012;73:S431-7

4 016 death before reaching a surgical facility

976 potentially survivable

888 from exsanguination

77 from airway obstruction

11 compressive pneumothorax

87% deaths are pre-hospital

1/4 avoidable

90% from haemorrhage

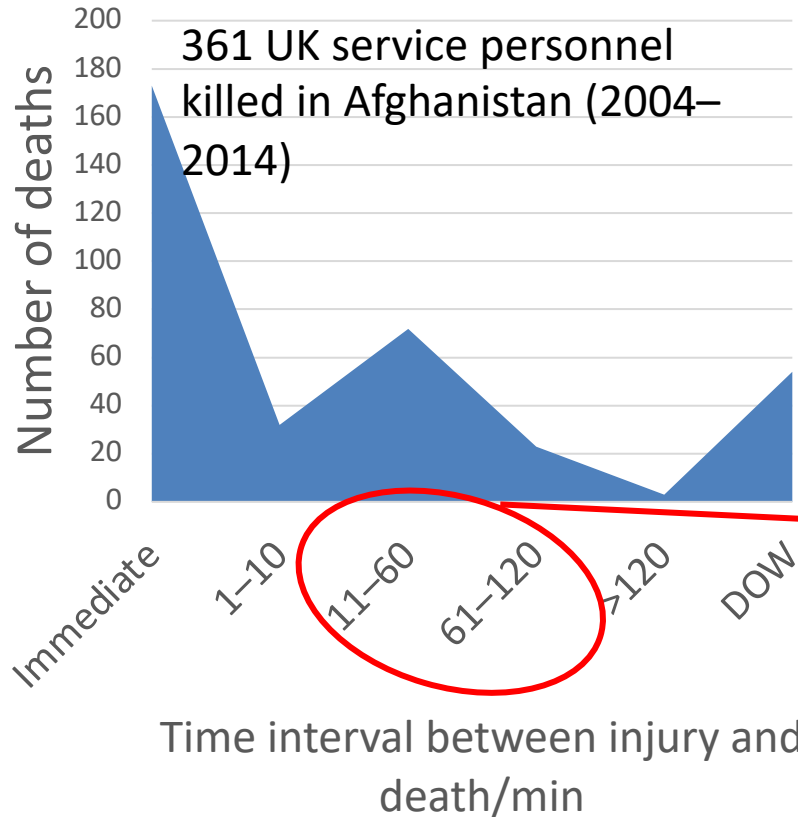
598
truncal
haemorrhage

171
junctional
haemorrhage

119
extremity
haemorrhage

Proof of concept

2 – Death on the battlefield occurs early



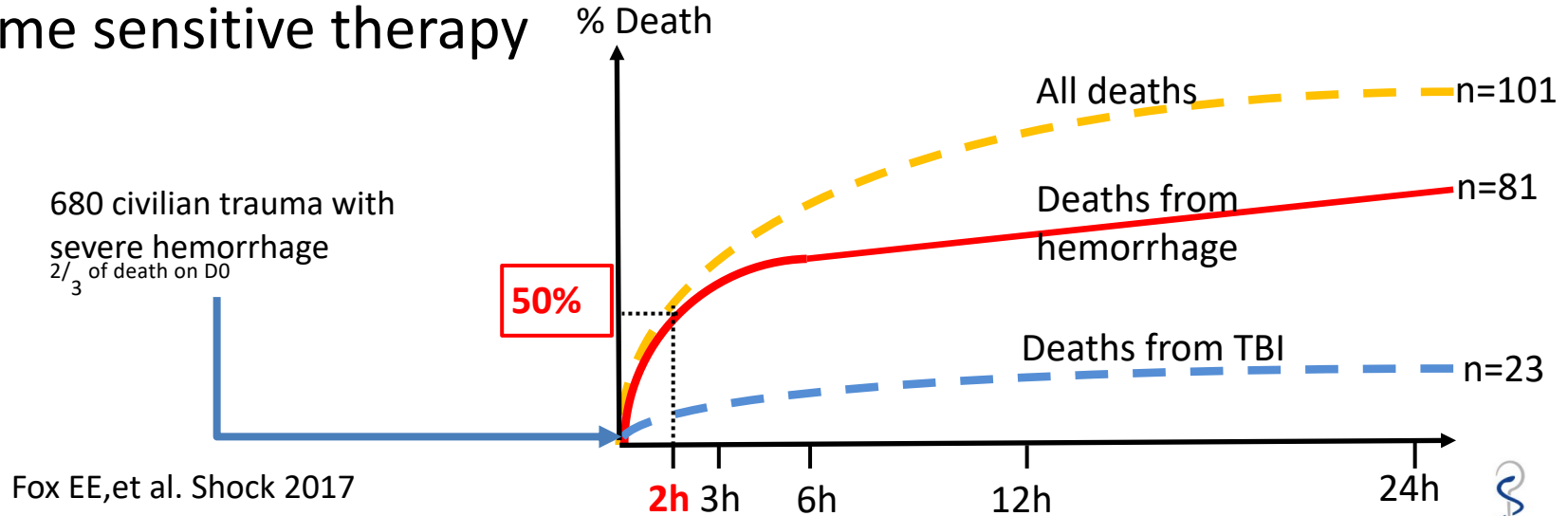
- ▷ Battlefield mortality follows a Trimodal distribution
- ▷ 2/3 occurred within 10 min of injury
- ▷ 1/3 is likely to benefit from a therapeutic intervention

Proof of concept

3 – Transfusion save lives, if started Early

- An hemostatic transfusion regimen
 - A high **plasma**/pRbc ratio ($>1/2$) \searrow 50% in mortality
Bhangu A, et al. *Injury*. 2013;44(12):1693–1699
 - A high **Platelets**/pRbc ratio (1/6) \searrow 20% in mortality
Johansson PI, et al. *J Emerg Trauma Shock* 2012 ; 5 : 120-5

- A time sensitive therapy



Cohort studies

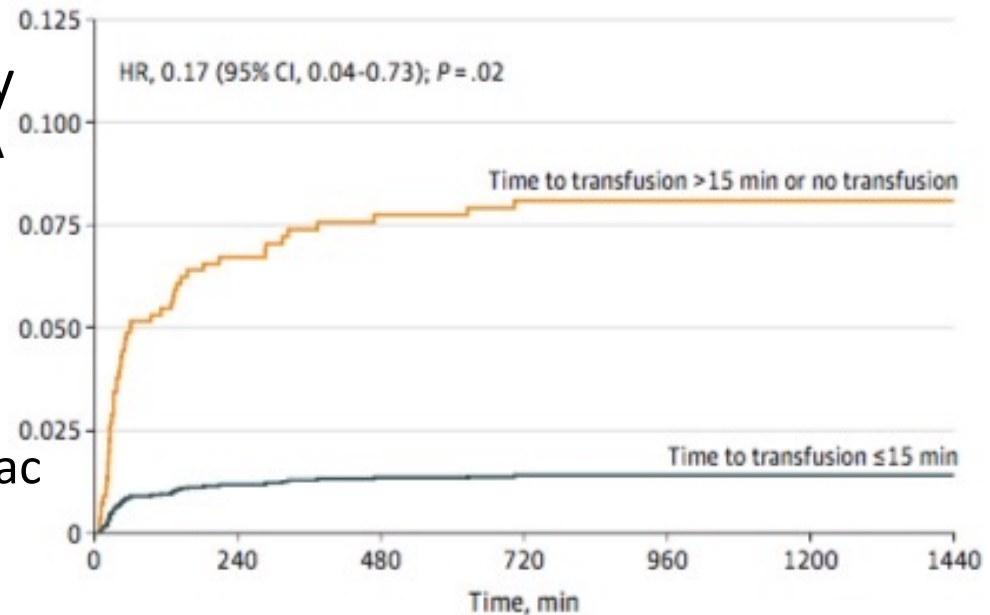
1 – Early intervention works

- British Army medical emergency response teams (MERT)
- Associated with lower mortality for severely injured patients (ISS 20 – 29) compared with traditional MEDEVAC platforms - Apodaca A et al. J Trauma Acute Care Surg. 2013
 - 2009-2011: 975 coalition patients injured in Southern Afghanistan, transported from the point of injury to a military hospital,
- **Early use of blood product associated with mortality ↓ by 50% after propensity scored analysis** - O'Reilly DJ, et al. J Trauma Acute Care Surg. 2014
 - 1,592 patients from 2006 to 2011 - 310 transfused after 2008

Cohort studies

2 – Early transfusion works

- 38% decrease in mortality for prehospital transfusions: 1,692 patients fully documented records (Iraq - Afgha) - Kotwal R et al. J Trauma 2018
- 400/502 patients matched by propensity score - Shackelford SA et al. JAMA 2017
 - 30d mortality decreased from 23% to 11% with prehospital transfusion
 - Only observed with very early transfusion (<15mn of Medevac rescue)



Randomized controlled studies

1 – Early transfusion works

	Study size	Intervention	Delay injury - tranfusion	Receipt of full dose of BP	Mortality rate (control)	Mortality rate (BP)
Combat (US) Moore HB. Lancet. 2018	125 patients 1 urban center	2 plasma units	24 mn	32%	10%	15%
PAMPER (US) Sperry JL. N Engl J Med. 2018	501 patients 27 helicopter bases	2 plasma units	30 mn	90%	33%	22%

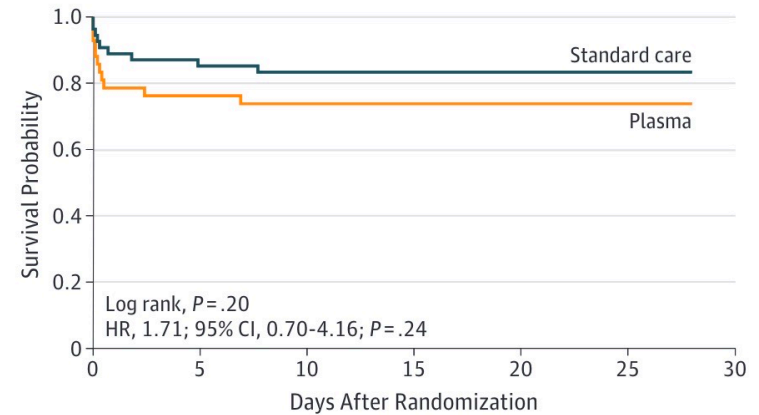


Fine tuning:

1 – Secondary analysis

	Study size	Intervention
Combat (US) Moore HB. Lancet. 2018	125 patients 1 urban center	2 plasma units
PAMPER (US) Sperry JL. N Engl J Med. 2018	501 patients 27 helicopter bases	2 plasma units

B Plasma vs standard care in ≤20-min transport time group



- Grouped analysis:

1. Prehospital resuscitation AND prehospital time: decisive but not independent roles. Pusateri A. JAMA Surg 2019

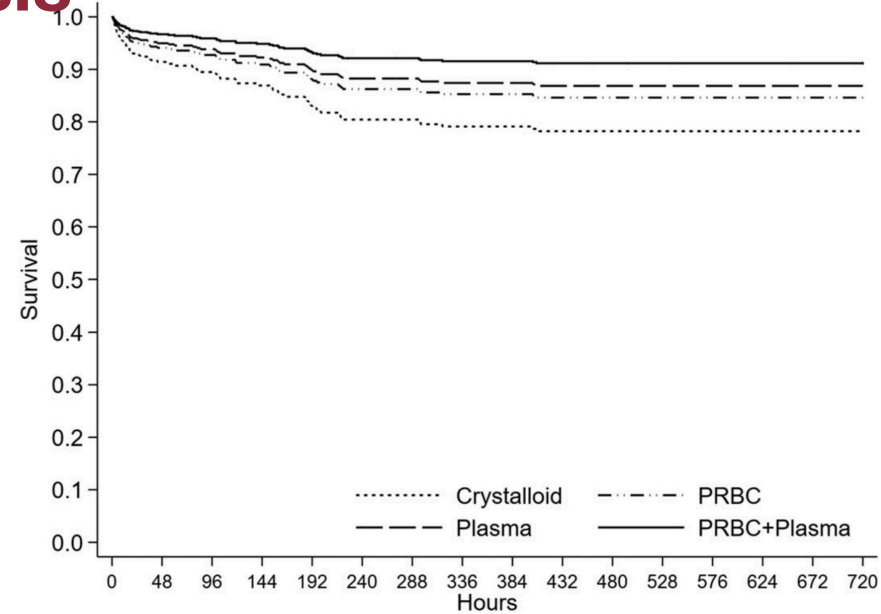
- Prehospital resuscitation has no benefit for transport time < 20 mn
- Prehospital resuscitation basically allows to « buy time »



Fine tuning:

2 – Secondary analysis

	Study size	Intervention
Combat (US) Moore HB. Lancet. 2018	125 patients 1 urban center	2 plasma units
PAMPER (US) Sperry JL. N Engl J Med. 2018	501 patients 27 helicopter bases	2 plasma units



- Predefined secondary analysis:
 1. Nature of resuscitation. Guyette FX. Ann Surg 2019
 - PRBC + Plasma > Plasma alone OR PRBC alone
 - Any blood product > Crystalloids
 2. Nature of injury? Reitz KM. J Trauma 2019
 - Benefit only for blunt trauma?

Fine tuning:

3 – Further randomized controlled trials

	Study size	Intervention	Delay injury - tranfusion	Receipt of full dose of BP	Mortality rate (control)	Mortality rate (BP)
Combat (US) Moore HB. Lancet. 2018	125 patients 1 urban center	2 plasma units	24 mn	32%	10%	15%
PAMPER (US) Sperry JL. N Engl J Med. 2018	501 patients 27 helicopter bases	2 plasma units	30 mn	90%	33%	22%
PreHoPlyo (Fr) Jost D. JAMA network open. 2022	134 patients 10 ground ambulances network	4 plasma units	51 mn	25%	15%	18%
Rephill (UK) Crombie N. Lancet Haematol. 2022	432 patients 4 ground/air ambulances network	2 plasma units 2 red blood cells units	56 mn	40%	45%	43%

○ Fine tuning:

Summary of available data

- Most of fatalities (up to 90%) occur out of hospital
- ¼ is avoidable and hemorrhage is, by far, the leading cause
- In the military, an aggressive and an early transfusion policy has proven to be effective in reducing mortality
- Although somewhat confusing, civilian data are consistent and for severely bleeding patients suggest that:
 - Any blood product is beneficial **if transfused early**
 - Prbc + Plasma (Whole blood?) > any blood product alone > Crystalloids

Fine tuning: The devil is in the details

- Blood products for everyone?
 - ↳ If not for which patients?
- What sort of blood products?
 - ↳ Plasma?
 - ↳ Packed red blood cells?
 - ↳ Whole blood?

○ — Fine tuning: The devil is in the details

- Blood products for everyone?
↳ If not **for wich patients?**

→ Patients severely enough injured to benefit from transfusion
↳ « ROC » criteria : SBP < 70 or <90 and HR > 110
↳ ≥1 traumatic limb amputation with at least 1 located above the knee or elbow

Fine tuning: The devil is in the details

- What sort of blood products?
 - ↳ Plasma?
 - Thawed? Dried?
 - AB type? → **A type**
 - ↳ Packed red blood cells?
 - Type O?
 - Rh neg?
 - ↳ Whole blood?
 - WFWB? FWB? CSWB?

Conclusion

For patients severely enough injured to benefit from transfusion

↳ « ROC » criteria : SBP < 70 or <90 and HR > 110

↳ ≥1 traumatic limb amputation with at least 1 located above the knee or elbow

- Dried plasma (type A of Flyp) is based on the best available evidence and is logistically the most sustainable solution
- The use of cold stored whole blood is the most promising option, but requires an extremely robust supply chain

Fine tuning is still in process...