PREHOSPITAL TRANSFUSION ON THE BATTLEFIELD:

FROM PROOF OF CONCEPT TO FINE TUNING

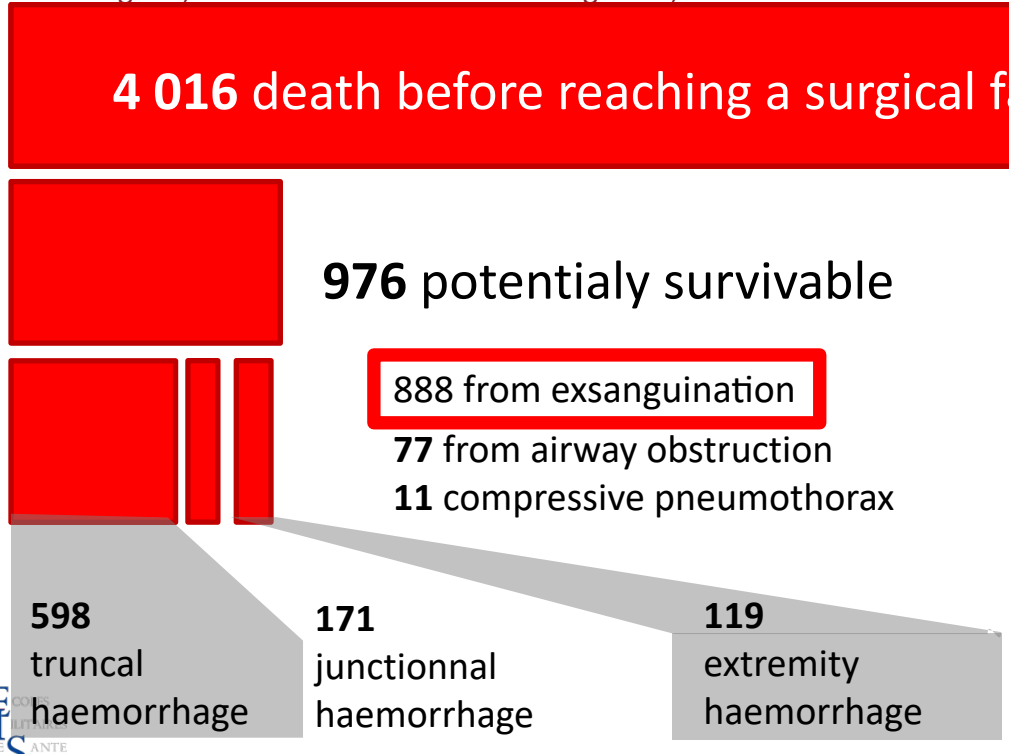
[redacted]

Paris SOF Combat Medical Care Conference
October 20th 2022

Proof of concept: 1 – Haemorrage 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



87% deaths are pre-hospital

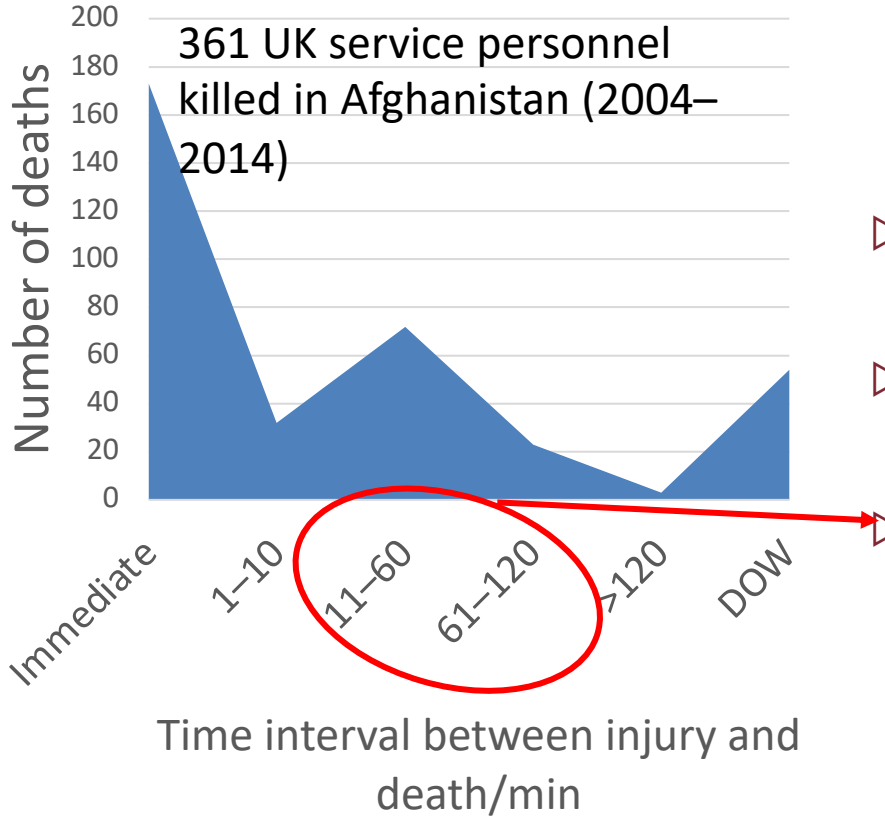
¼ avoidable

90% from haemorrage

Service de santé des armées

Proof of concept

2 – Death on the battlefield occurs early



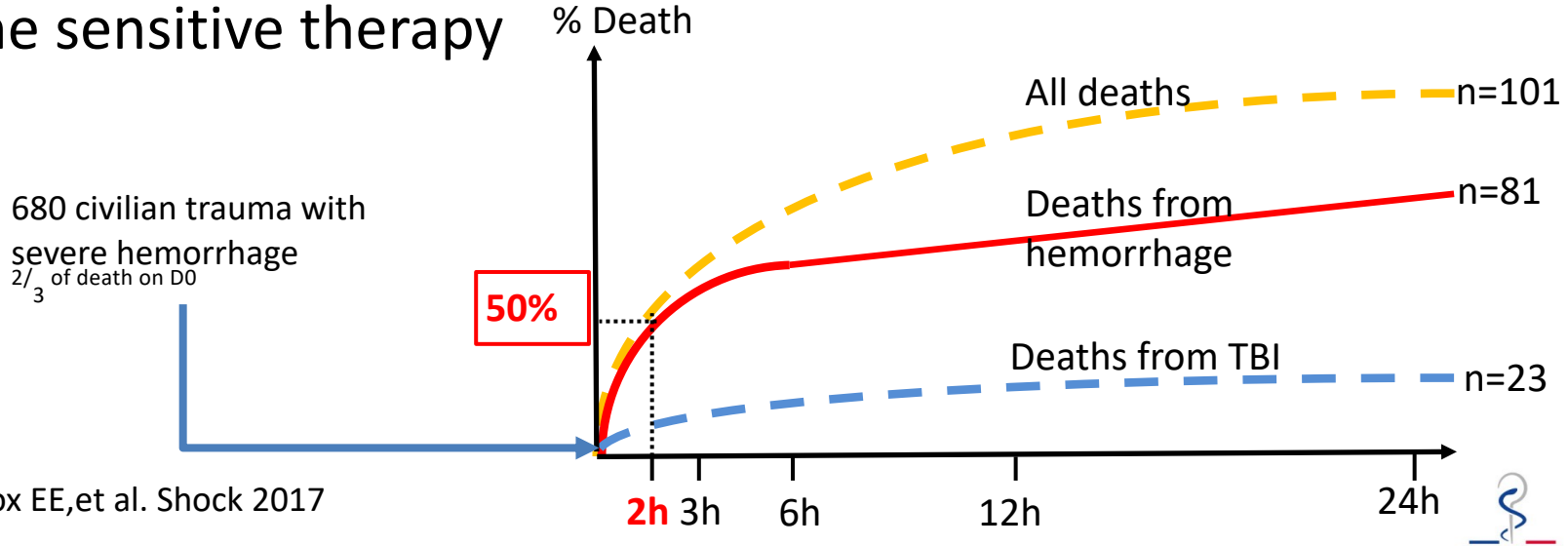
- Battlefield mortality follows a Trimodal distribution
- 2/3 occurred within 10 min of injury
- 1/3 is likely to benefit from a therapeutic intervention

Stacey Webster et al. BMJ Mil Health 2021;167:84-88

Proof of concept

3 –Transfusion save lives, if started Early

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



Fox EE,et al. Shock 2017

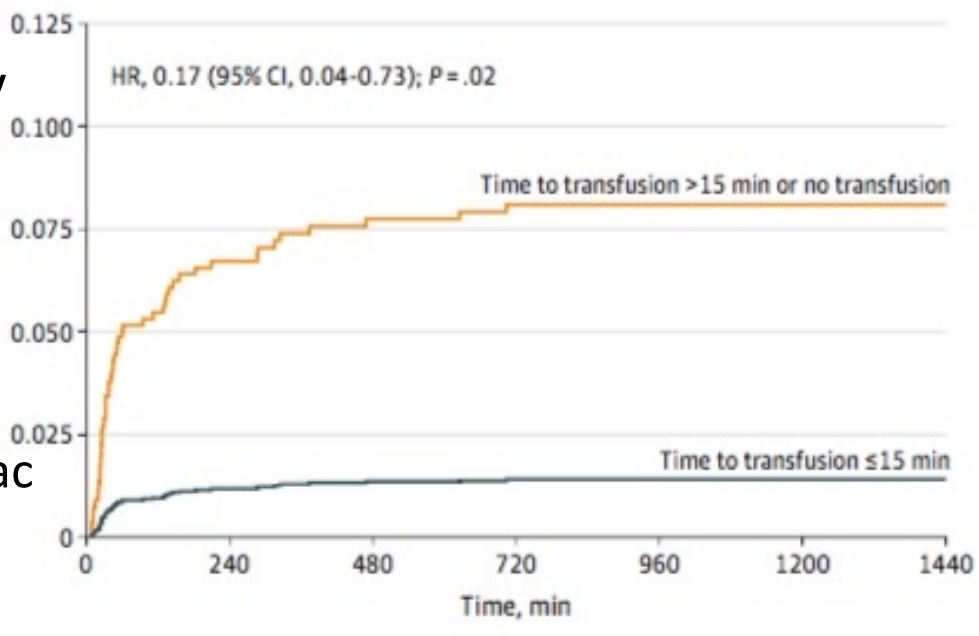
Cohort studies

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
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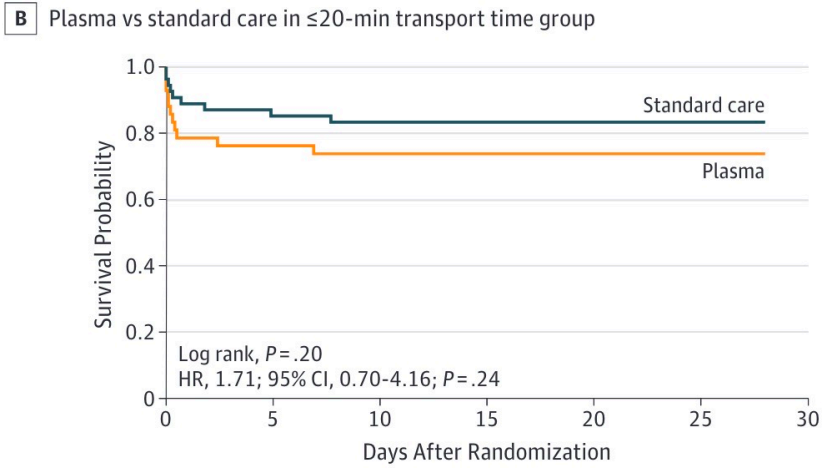

- Grouped analysis:
  1. Prehospital resucitation AND prehospital time: decisive but not independent roles. Pusateri A. JAMA Surg 2019
     - Prehospital resucitation has no benefit for transport time < 20 mn
     - Prehospital resucitation basically allows to « buy time »

Fine tuning:

2 – Secondary analysis

	Study size	Intervention
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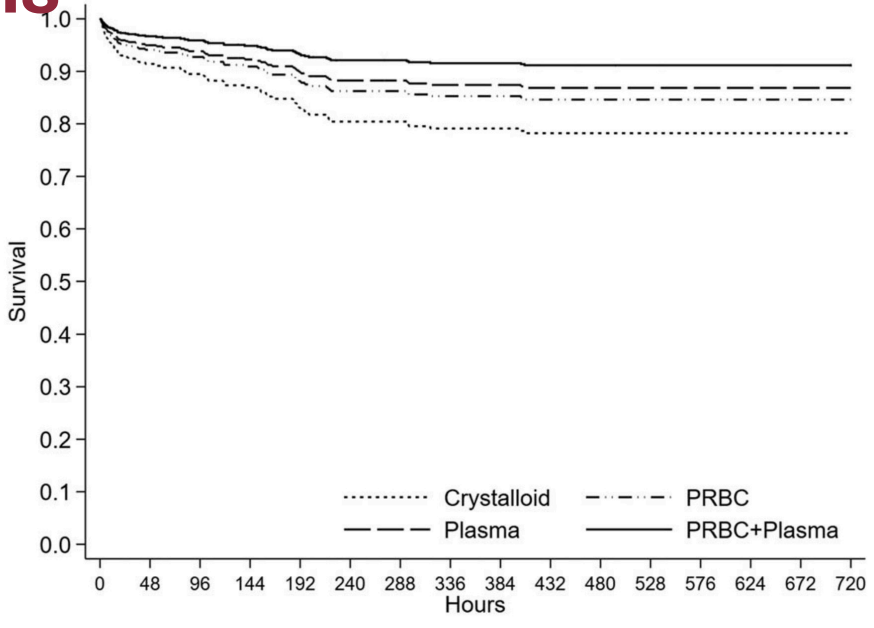

- Predefined secondary analysis:
  1. Nature of resucitation. Guyette FX. Ann Surg 2019
     - PRBC + Plasma > Plasma alone OR PRBC alone
     - Any blood product > Cristalloids
  2. Nature of injury? Reitz KM. J Trauma 2019
     - Benefit only for blunt trauma?

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)
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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 wich 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…