

Transexamic Acid

M*A*S*H in an Ampule

Howard Mell, MD, MPH, CPE, FACEP
EMS Medical Director, Newark (OH) Division of Fire
Clinical Assistant Professor, Emergency Medicine,
Department of Surgery, University of Illinois
College of Medicine at Urbana

The Road to Progress is Paved in Tombstones...



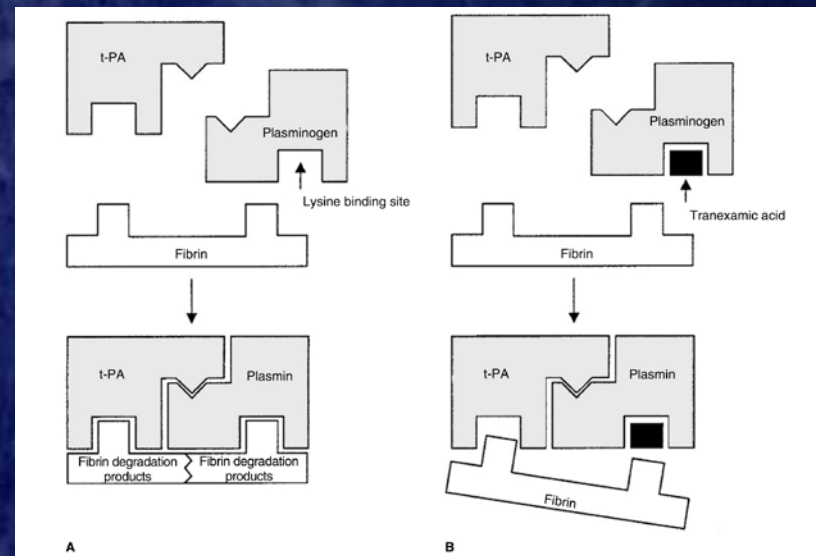
Disclosure

- **In accordance with the Accreditation Council for Continuing Medical Education (ACCME) Standards, the American Nurses Credentialing Center's Commission on Accreditation and the Continuing Education Coordinating Board for Emergency Medical Services and the policy of the ACEP, ENA and CECBEMS, presenters must disclose the existence of significant financial interests in or relationships with manufacturers or commercial products that may have a direct interest in the subject matter of the presentation, and relationships with the commercial supporter of this CME activity. These presenters do not consider that it will influence their presentation.**
- **Dr. Mell does not have a significant financial relationship to report.**



Tranexamic Acid (TXA)

- Stabilizes Fibrin Clot after trauma
- By mechanism it cannot be thrombogenic



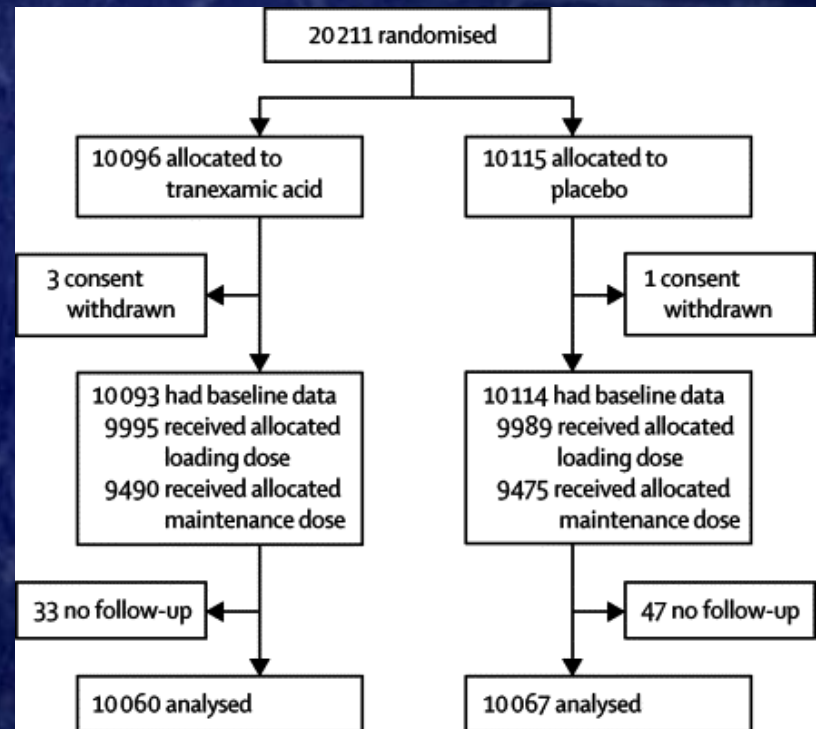
GOBSAAT

Good 'ol boys sitting
around a table



CRASH-2

- **Lancet 2010; 376: 23–32 *Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): a randomized, placebo-controlled trial*** CRASH-2 trial collaborators
 - Randomized, placebo controlled, double blind study,
 - N>20,000



CRASH-2

- **Lancet 2010; 376: 23–32 Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): a randomized, placebo-controlled trial** CRASH-2 trial collaborators
 - Randomized, placebo controlled, double blind study,
 - N>20,000

Table 2: Death by cause

Cause of death	Tranexamic acid [n = 10,060]	Placebo [n = 10,067]	RR (95% CI)	p value (two-sided)
Any cause of death	1463 (14.5%)	1613 (16.0%)	0.91 (0.85 – 0.97)	0.0035
Bleeding	489 (4.9%)	574 (5.7%)	0.85 (0.76 – 0.96)	0.0077
Vascular occlusion*	33 (0.3%)	48 (0.5%)	0.69 (0.44 – 1.07)	0.096
Multiorgan failure	209 (2.1%)	233 (2.3%)	0.90 (0.75 – 1.08)	0.25
Head injury	603 (6.0%)	621 (6.2%)	0.97 (0.87 – 1.08)	0.60
Other causes	129 (1.3%)	137 (1.4%)	0.94 (0.74 – 1.20)	0.63

Data are number (%), unless otherwise indicated. RR = relative risk.

*Includes myocardial infarction, stroke and pulmonary embolism.

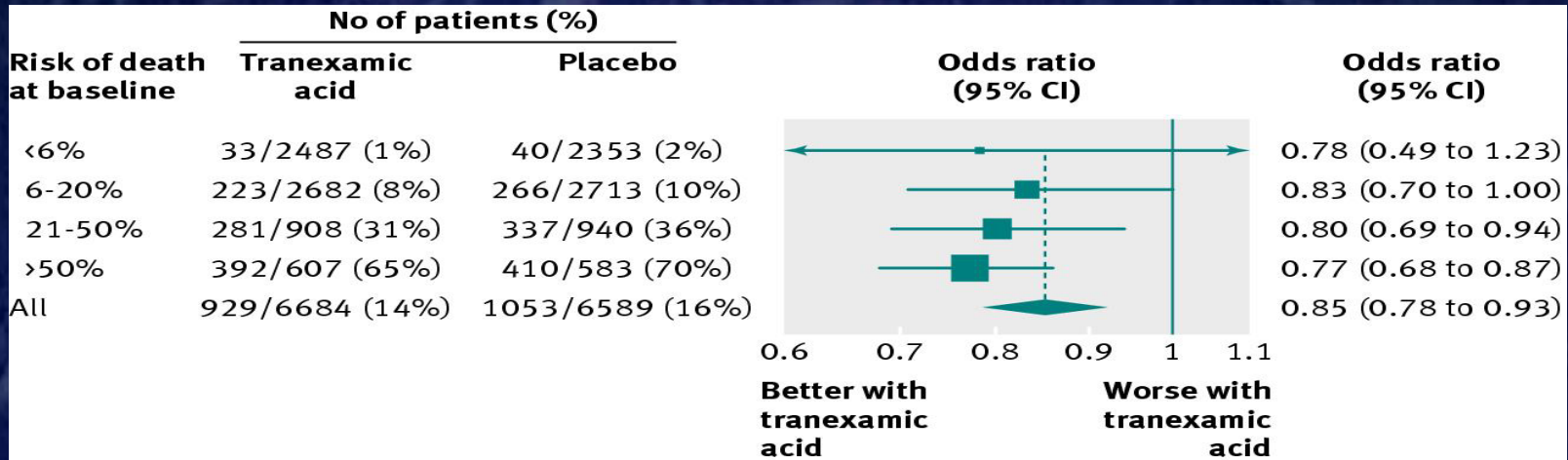


MATTERs

- **ARCH SURG Vol 147 (NO. 2), Feb 2012**
Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study
Morrison, JJ; Dubose, JJ; Rasmussen, TE; Midwinter, MJ
- **Observational Study**
 - Military, incl prehospital
 - NNT = 7 in the worst injured



Crash-2 M&M



Tranexamic acid can be administered safely to a wide spectrum of patients with traumatic bleeding and should not be restricted to the most severely injured.

BMJ. 2012 Sep 11; 345: e5839. *Effect of tranexamic acid on mortality in patients with traumatic bleeding: prespecified analysis of data from randomised controlled trial.* Roberts, I; Perel, P; Prieto-Merino, D; et al



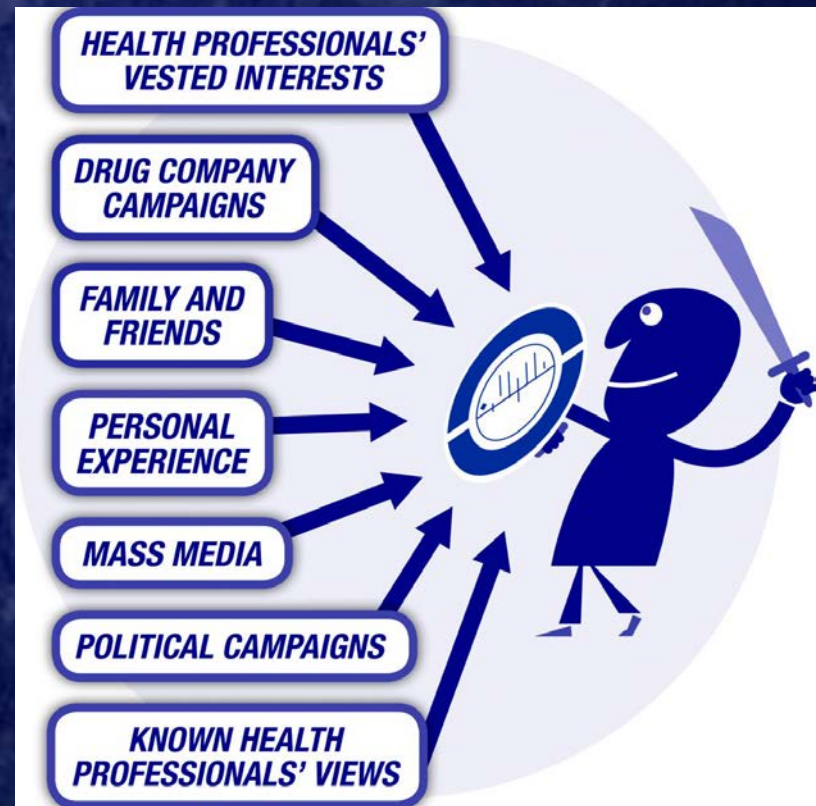
Early TXA

- **Lancet 2011; 377: 1096–101**
The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial
The CRASH-2 collaborators
- **Tranexamic acid should be given as early as possible to bleeding trauma patients. For trauma patients seen late after injury (>3h), tranexamic acid is less effective and could be harmful.**



TXA Cochrane

- Cochrane Database Syst Rev. 2011 Jan 19;(1) *Antifibrinolytic drugs for acute traumatic injury.* Roberts, I; Shakur, H; Ker, K; Coats, T; CRASH-2 Trial collaborators.
- “TXA safely reduces mortality in bleeding trauma patients without increasing the risk of adverse events.”



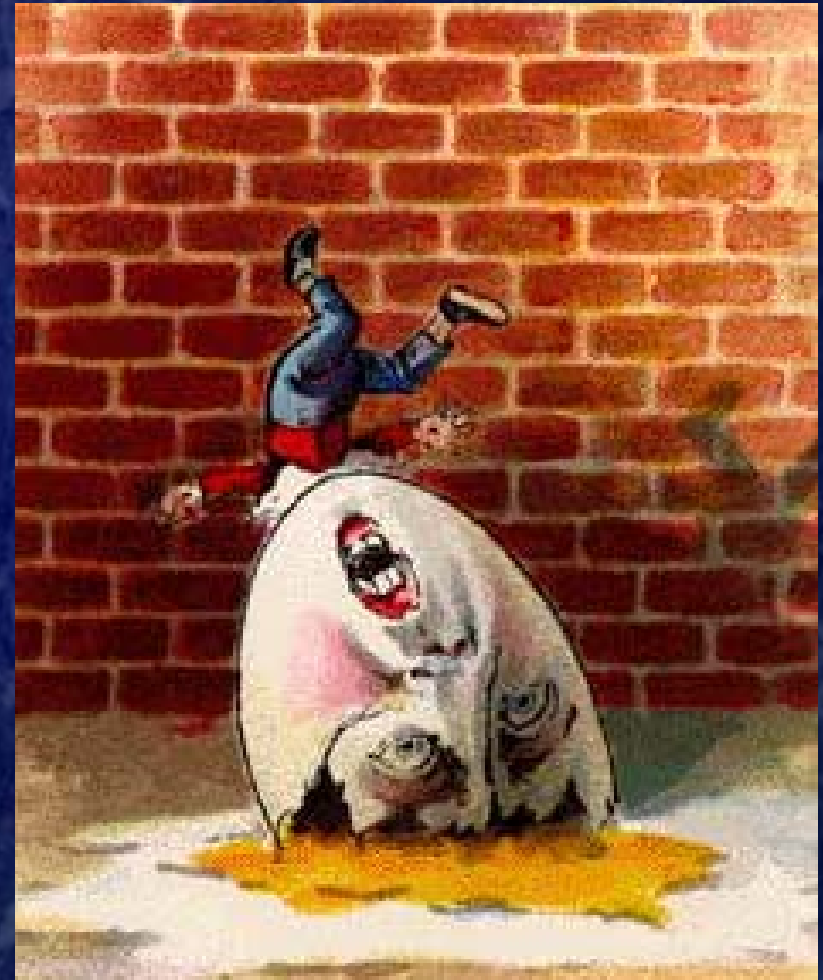
But what does TXA cost?

- PLoS One. 2011 May 3;6(5):e18987. *Cost-effectiveness analysis of administering tranexamic acid to bleeding trauma patients using evidence from the CRASH-2 trial.* Guerriero, C; Cairns, J; Perel, P; Shakur, H; Roberts, I; CRASH 2 trial collaborators.
- The estimated incremental cost per LY gained of administering TXA is \$48 in Tanzania, \$66 in India and \$64, in the UK.



CRASH-2 TBI

- Health Technology Assessment 2012; Vol. 16: No. 13 March 2012 *CRASH-2 (Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage) intracranial bleeding study: the effect of tranexamic acid in traumatic brain injury – a nested, randomized, placebo-controlled trial* Perel, P; Al-Shahi Salman, R; Kawahara, T; et al.
- Study was a wash in terms of benefit to TBI patients
- Leaves the door open to pre-hospital use
 - Where the extent and nature of injuries may be unclear



How much will TXA help?

- **BMC Emerg Med. 2012 Mar 1;12:3. *Avoidable mortality from giving tranexamic acid to bleeding trauma patients: an estimation based on WHO mortality data, a systematic literature review and data from the CRASH-2 trial.* Ker, K; Kiriya, J; Perel, P; Edwards, P; Shakur, H; Roberts, I.**
- **3,996 deaths a year in the U.S. could be avoided if TXA was routinely given less than 1h after injury (or 3,497 if given in less than 3h)**



MATTERs II

- JAMA Surg. 2013
Mar;148(3):218-25.
Association of cryoprecipitate and tranexamic acid with improved survival following wartime injury: findings from the MATTERs II Study.
Morrison, JJ; Ross, JD;
Dubose, JJ; Jansen, JO;
Midwinter, MJ;
Rasmussen, TE.
- Tranexamic acid was independently associated with reduced mortality (OR - 0.61; 95% CI, 0.42-0.89; P = .01)



A Crack in the Wall?

- Do all trauma patients benefit from tranexamic acid? J Trauma Acute Care Surg. 2014 Jun;76(6):1373-8. Valle, Allen, and Van Haren et. Al.
- For the highest injury acuity patients, TXA was associated with increased, rather than reduced, mortality, no matter what time it was administered.

A Crack in the Wall?

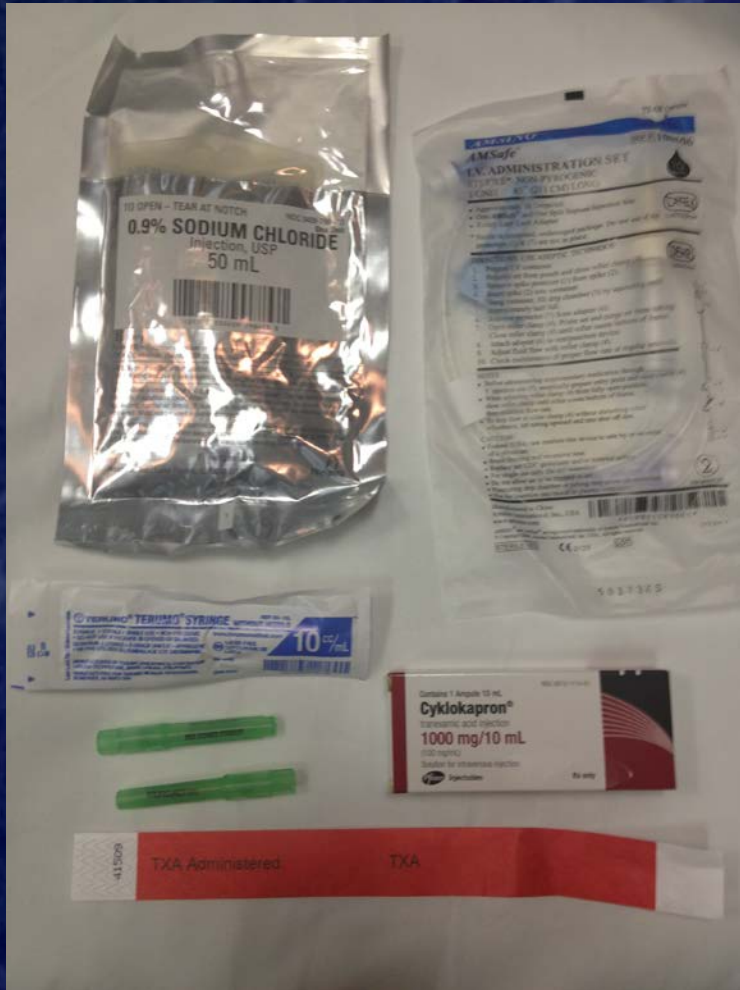
- Do all trauma patients benefit from tranexamic acid? J Trauma Acute Care Surg. 2014 Jun;76(6):1373-8. Valle, Allen, and Van Haren et. Al.
- This lack of benefit can probably be attributed to the rapid availability of fluids and emergency OR at this trauma center.

So what now?

- **TXA is EMS**
 - Give in the field, early and when there is no other option
 - Give in the outlying hospital, prior to transport
 - Use 1:1:1 in the trauma center +/- TXA (if < 3h) – the jury is still out.



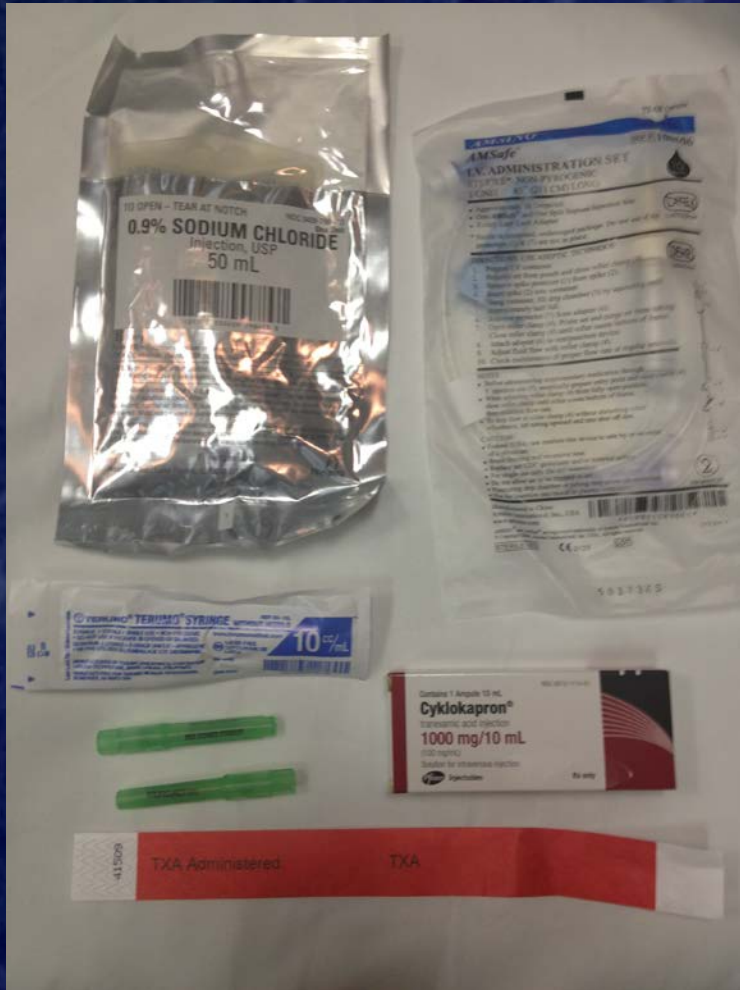
Tranexamic Acid (TXA)



- **Kit Contents**
 - 50 mL bag 0.9% Normal Saline
 - 10 gtt / cc IV tubing
 - 10 cc syringe
 - Filter needle
 - 18g needle
 - 1 g / 10 mL ampule of Tranexamic Acid
 - Patient bracelet



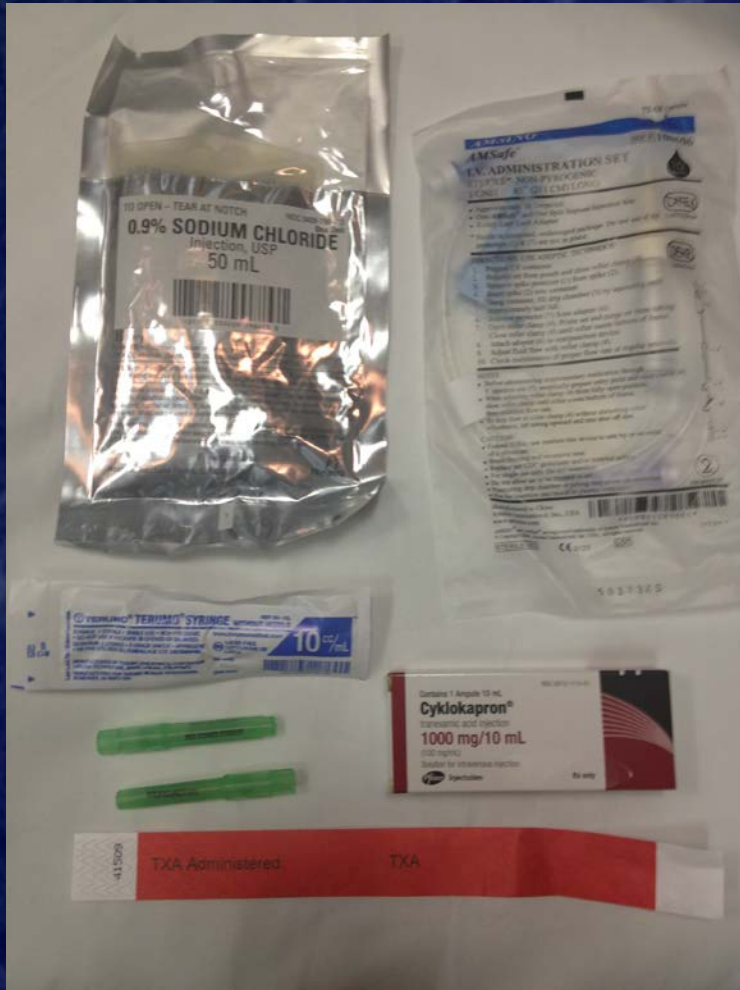
Tranexamic Acid (TXA)



- This is the Newark OH "kit" for TXA.
- Protocol in place 27 March 2013.
- Pushed 4 times in first year.
- Cost?
 - \$107.00 per kit.



Tranexamic Acid (TXA)



- It is **CHEAP!**
- It is **EASY!**
- And it **SAVES LIVES!**



Tranexamic Acid (TXA) versus Tissue Plasminogen Activator (tPA)

- **tPA**

- Key paper published in Lancet
- Unblinded trial
- No objective benefit proven, definite adverse effects observed
- Expensive, huge sales force and campaign
- Mandated by AHA and JC

- **TXA**

- Key paper published in Lancet
- Double blinded, randomized, placebo controlled trial
- Clear, objectively measured benefit without observed adverse effects
- Cheap, generic
- No US mandate



Any Questions?



<http://blogs.lshtm.ac.uk/news/2012/09/11/tranexamic-acid-manga-offers-comic-relief-for-medics/>

