Haemorrhage alleviation with tranexamic acid - Intestinal system

BACKGROUND AND SCIENTIFIC RATIONALE

Protocol Code: ISRCTN11225767
Background and scientific rationale – version 2.0 date 23/07/2017

Gastrointestinal haemorrhage

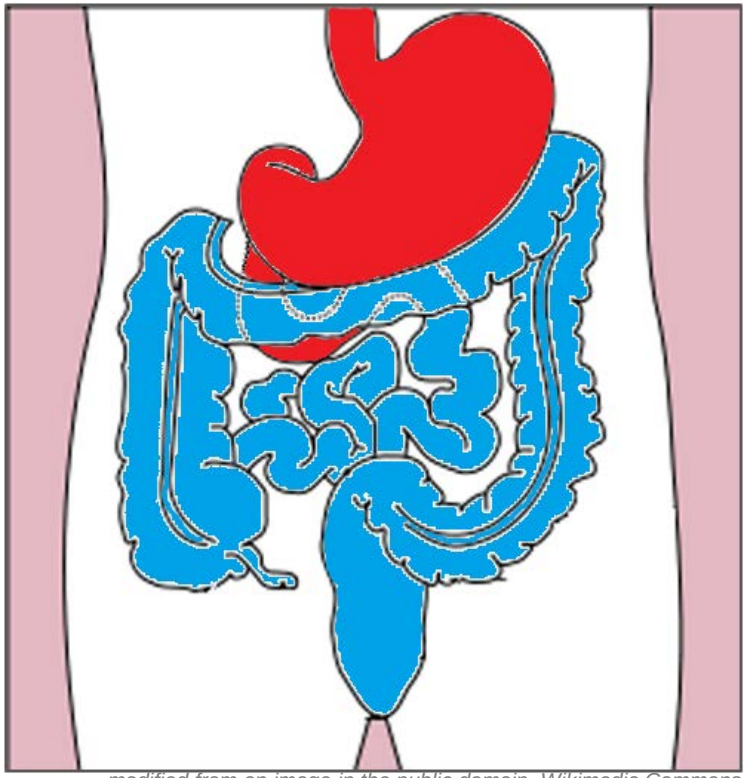
- A common emergency
- Important cause of mortality and morbidity
- Case fatality is high (10–20% in the UK)

- *Rockall TA et al. BMJ, 1995. 311(6999): p. 222-6.*
- *Williams JG et al. Gut, 2007. 56 Suppl 1: p. 1-113.*

Most common causes

- Cause varies by country, but in general:

- **Upper GI haemorrhage:**
  - Peptic ulcer
  - Oesophageal varices
- **Lower GI haemorrhage:**
  - Diverticular disease
  - Colitis
  - Cancer



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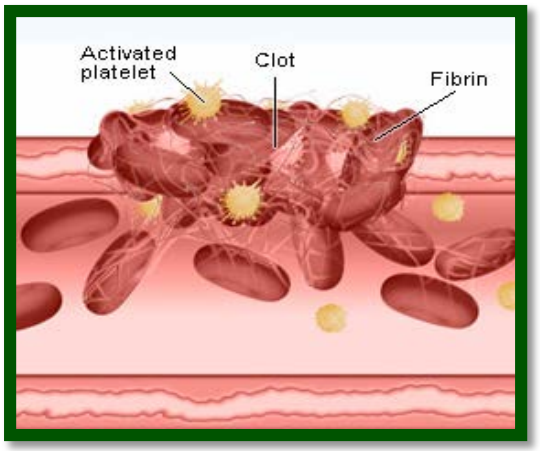
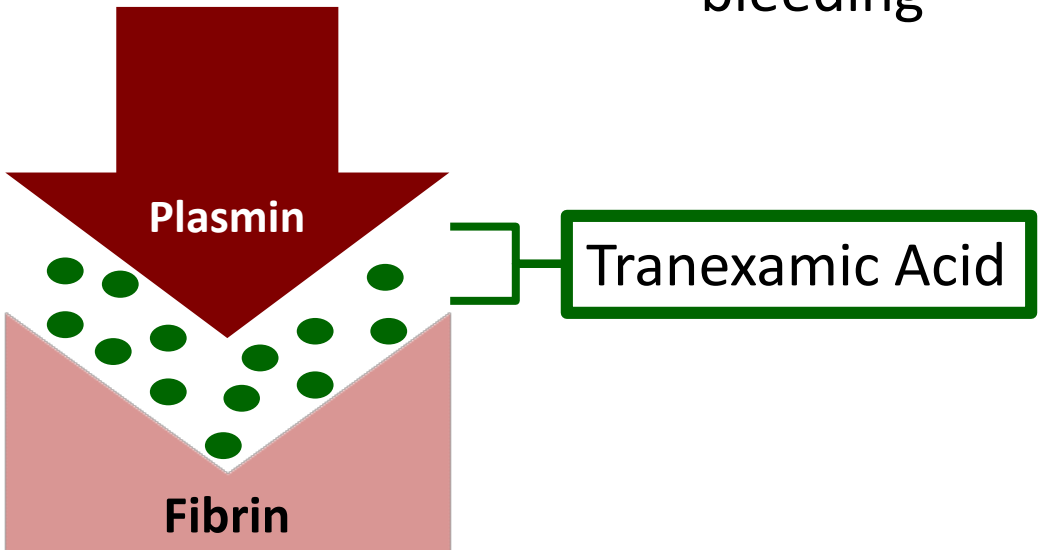
Fibrinolysis & Tranexamic Acid (TXA)

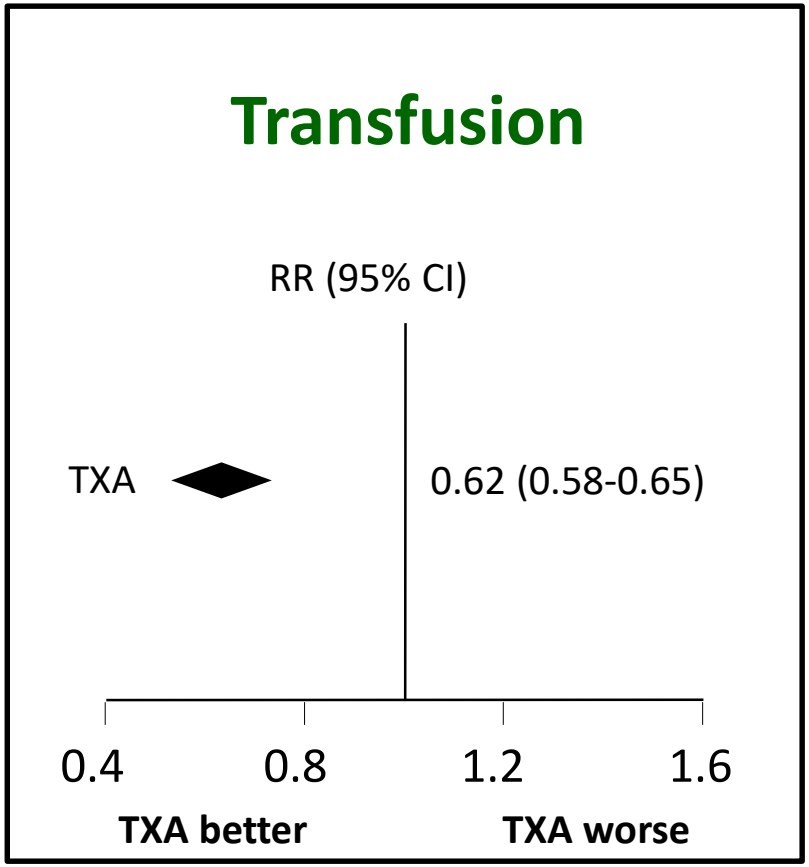


- At the site of damaged blood vessel, a fibrin blood clot forms
- Plasmin can impair clot stability and worsen bleeding
- TXA inhibits plasmin and reduces bleeding

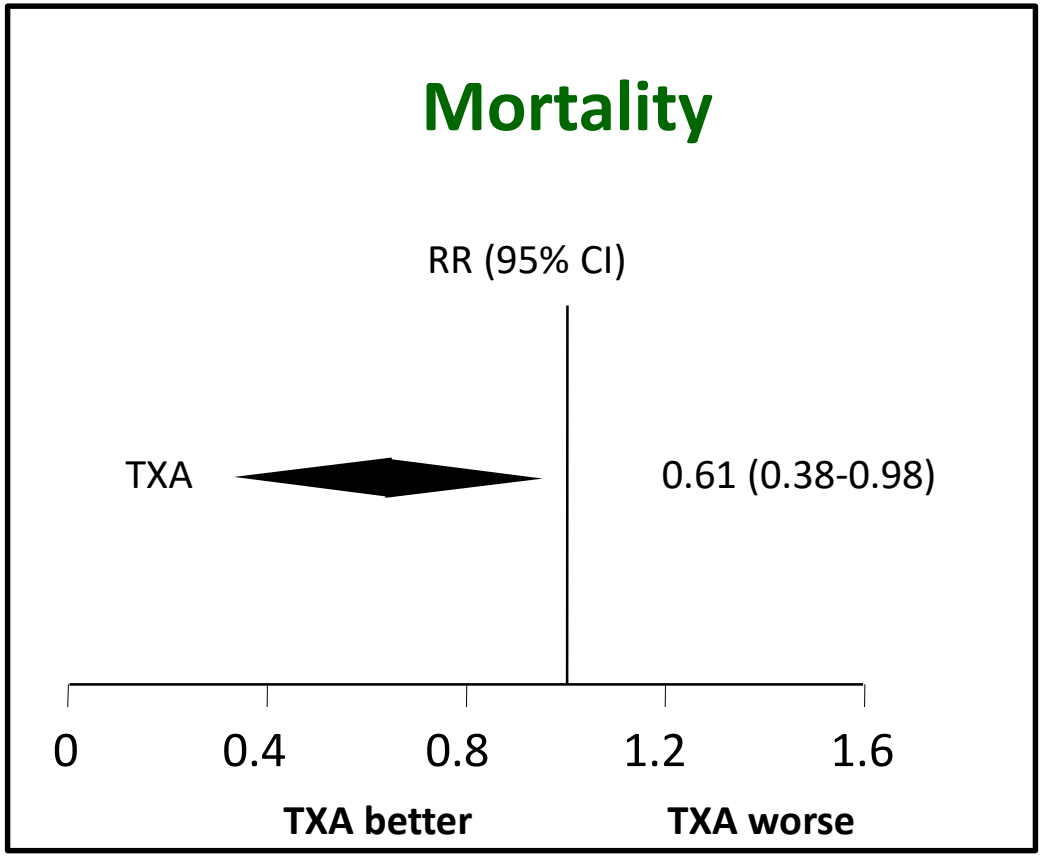


TXA use in surgery

TXA reduces bleeding in surgery



95 trials



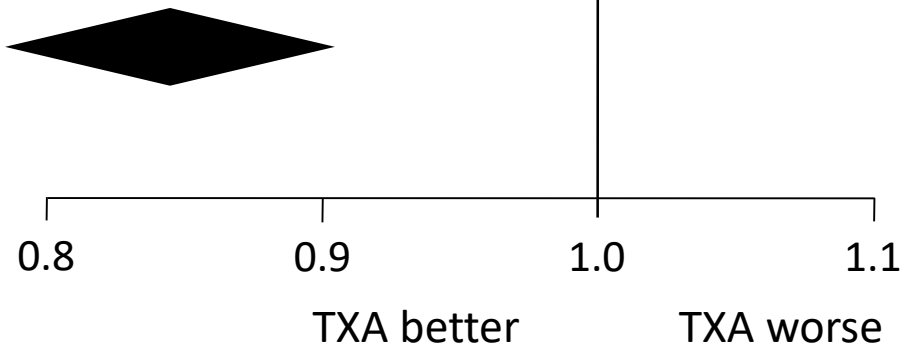
72 trials

Ker et al. BMJ 2012; 344:e3054

CRASH-2 trial results

TXA reduces death due to bleeding in trauma patients

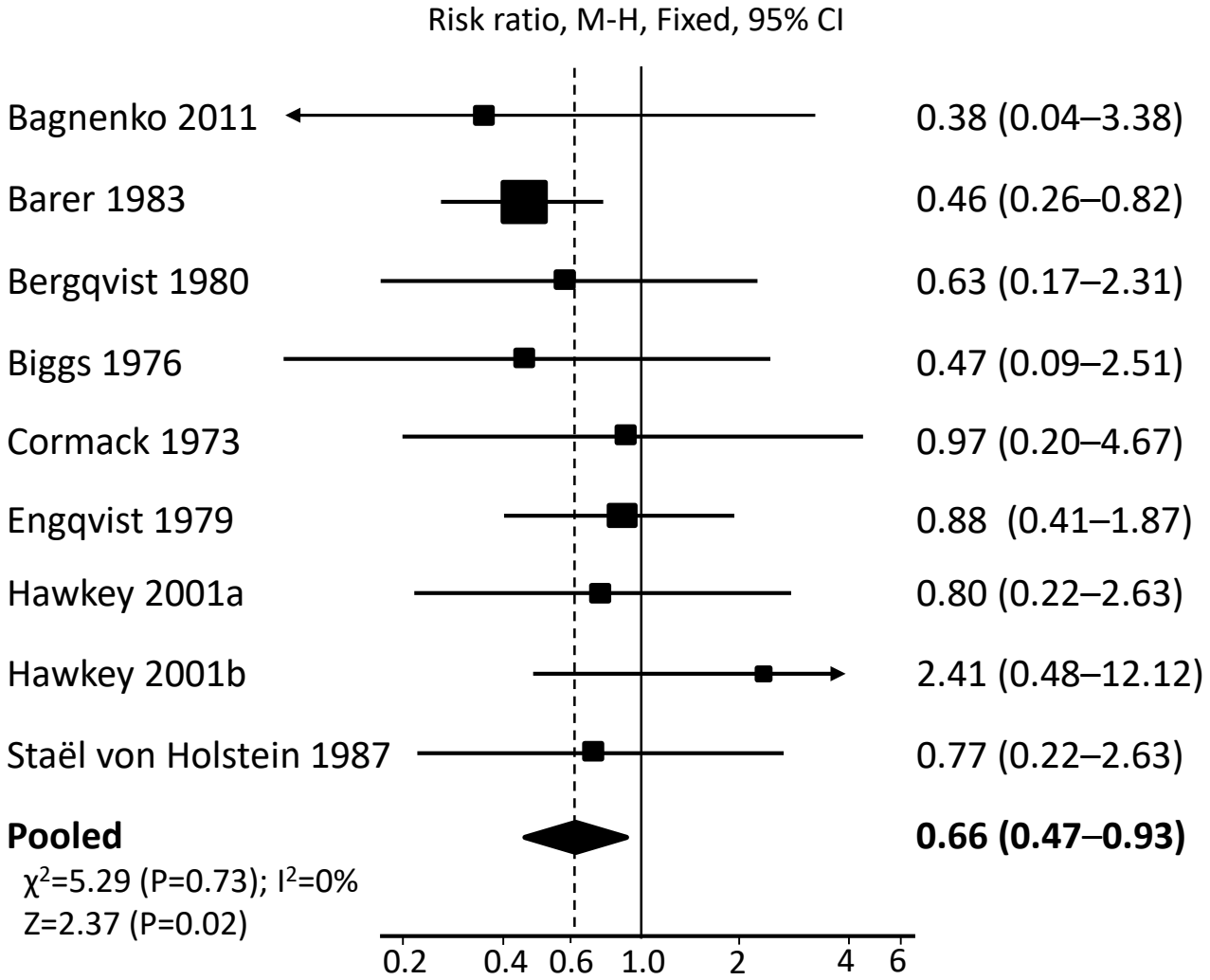
TXA-allocated (n=10,060)	Placebo-allocated (n=10,067)	Risk ratio (95% CI)
489 (4.9%)	574 (5.7%)	**0.85 (0.76–0.96) 2P=0.0077**



The CRASH-2 Collaborators. The Lancet. 2010; 376(9734):23-32

TXA in upper GI bleeding

TXA may reduce death in GI bleeding but the quality of the trials is poor

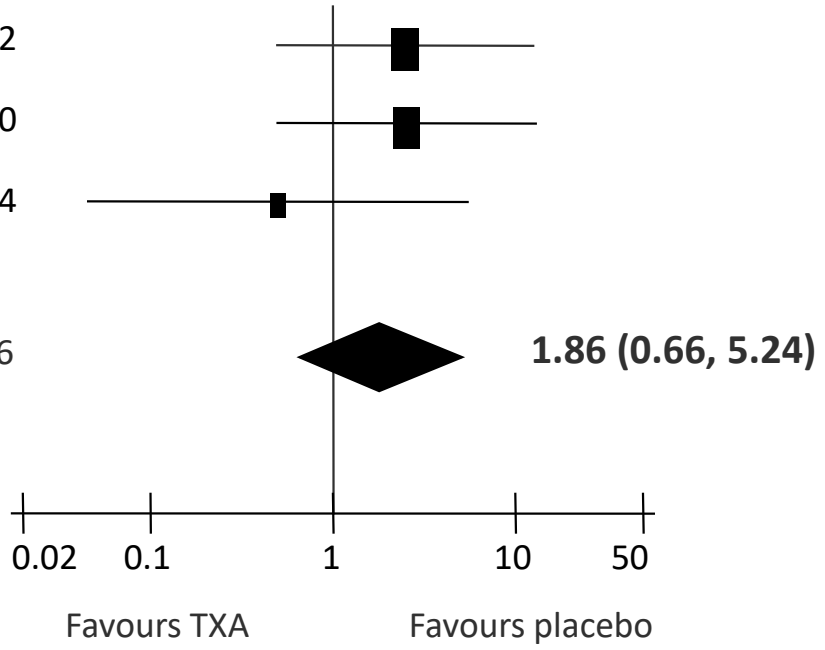


Manno D et al. BMJ 2014; 348:g1421

TXA in upper GI bleeding (2)

Trials are too small to assess the effect of TXA on thromboembolic events

	TXA		Placebo		Risk Ratio (95% CI)
	Events	*Total*	*Events*	*Total*	
Engquist 1979	5	102	2	102	
Barer 1983	5	256	2	260	
von Holstein 1987	1	164	2	164	
Total	11	522	6	526	**1.86 (0.66, 5.24)**



Rationale for Halt-it

- GI bleeding is an important cause of death
- TXA reduces bleeding in surgery
- TXA reduces death due to bleeding in trauma patients
- TXA may reduce deaths in GI bleeding but the evidence is poor
- TXA could reduce death and morbidity in GI bleeding

- The HALT-IT trial will provide reliable evidence about the effect of tranexamic acid on mortality and morbidity in patients with significant gastrointestinal bleeding.
- The effect of TXA on the risk of thromboembolic events will also be assessed.

Aims

To quantify the effect of TXA on mortality and morbidity

- **Primary outcome:** death in hospital within 28 days of randomisation (cause-specific mortality will also be recorded)

- **Secondary outcomes:**
  - Death from haemorrhage
  - Re-bleeding
  - Need for surgery or radiological intervention
  - Blood product transfusion
  - Thromboembolic events
  - Other adverse medical events
  - Patient's selfcare capacity
  - Days spent in ICU or HDU
  - Patient status (death, hospital readmission) at 12 months*

* England and Wales only

Study characteristics

- **Trial design:** randomised, double blind, placebo controlled
- **Target sample size:** 12,000 adults with acute significant upper or lower GI bleeding
- **Where?** Worldwide

Rationale for eligibility

- Adult with significant upper or lower GI bleeding
- **Uncertainty principle:** the responsible clinician is substantially uncertain as to whether or not to use TXA

If the clinician believes there is a clear indication for, or clear contraindication to, tranexamic acid use, the patient should not be randomised.

JOIN THE GLOBAL COLLABORATION

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Haltit
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