Tranexamic acid and the victim's right to effective healthcare

Ian Roberts

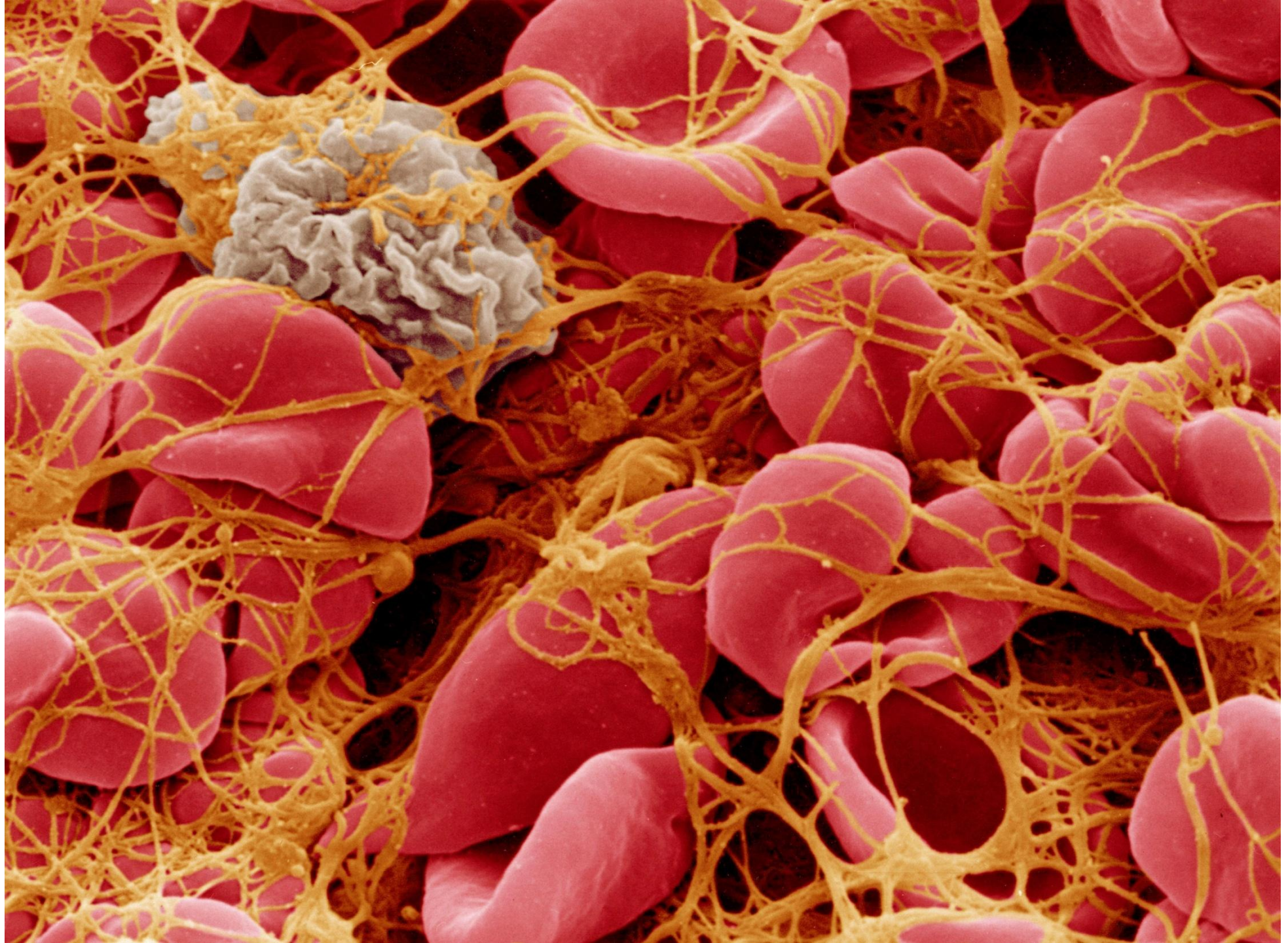
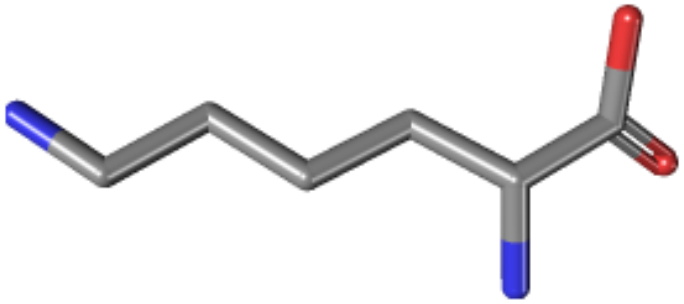


TABLE I

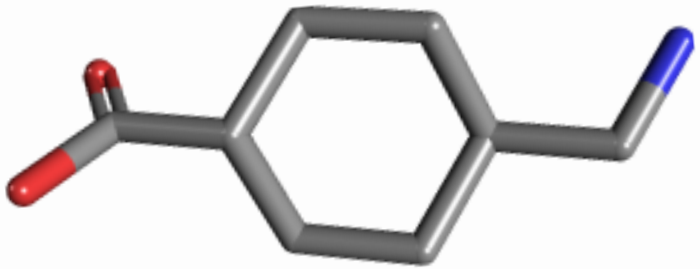
NATURAL AMINO ACIDS AND THEIR ACTION

Compound	Index of inhibition
Lysine	100
Lysine (D-form)	100
Lysine (DL-mixture)	100
Arginine	5
Histidine	5
Tryptophan	5
Asparagine	5
α,ε-Diaminopimelic acid	2
Cystine	3
Cysteine	1
α-Amino-*n*-butylic acid	<5
Valine	<5
Norvaline	<5
Leucine	<5
Norleucine	<5
Isoleucine	<5
Proline	<5
Serine	<1
Threonine	<1
Glycine	Slight activation
Alanine	Slight activation
Phenylalanine	Slight activation
Tyrosine	Slight activation
Oxyproline	Slight activation
Aspartic acid	Activation
Glutamic acid	Activation

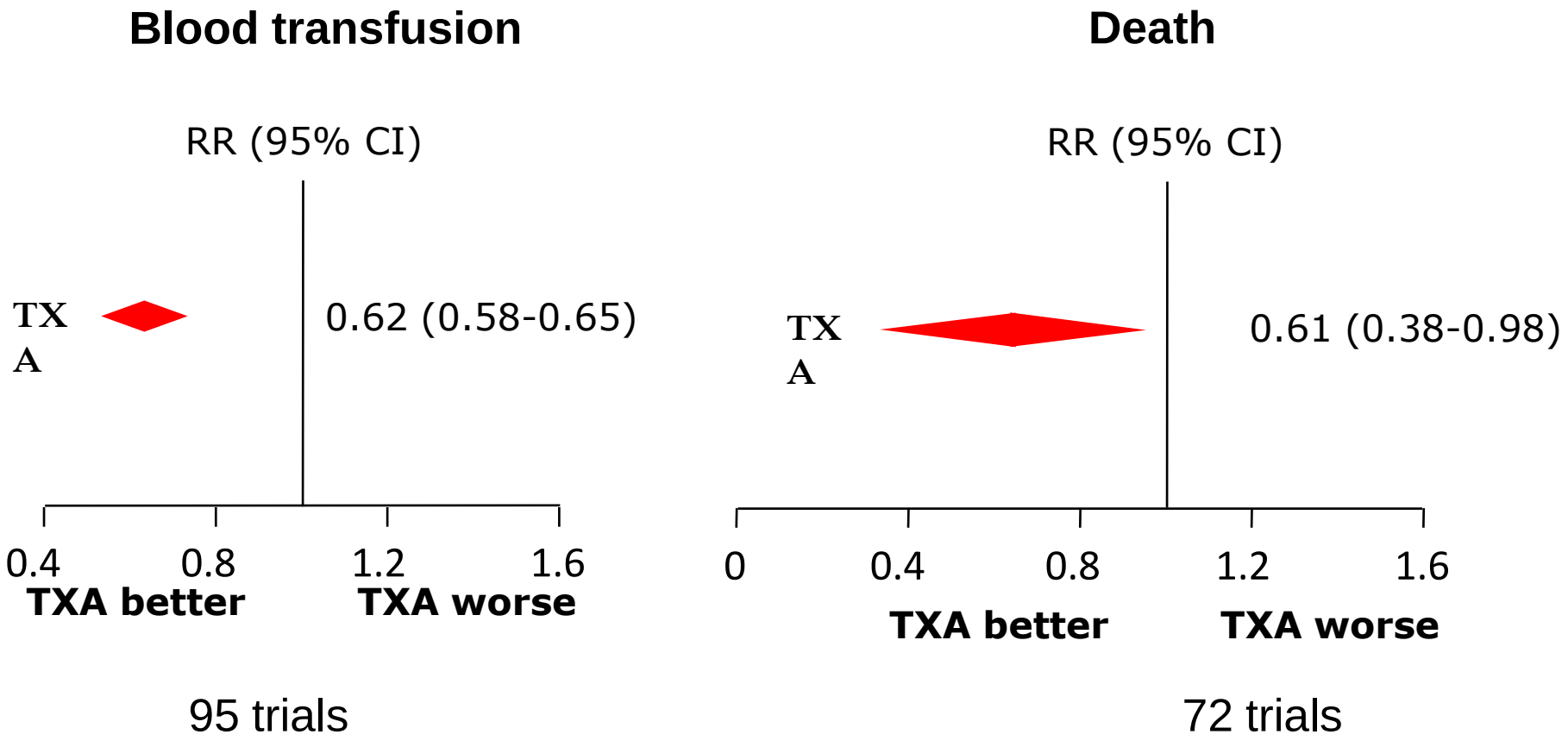
Lysine



Tranexamic acid



TXA reduces surgical bleeding

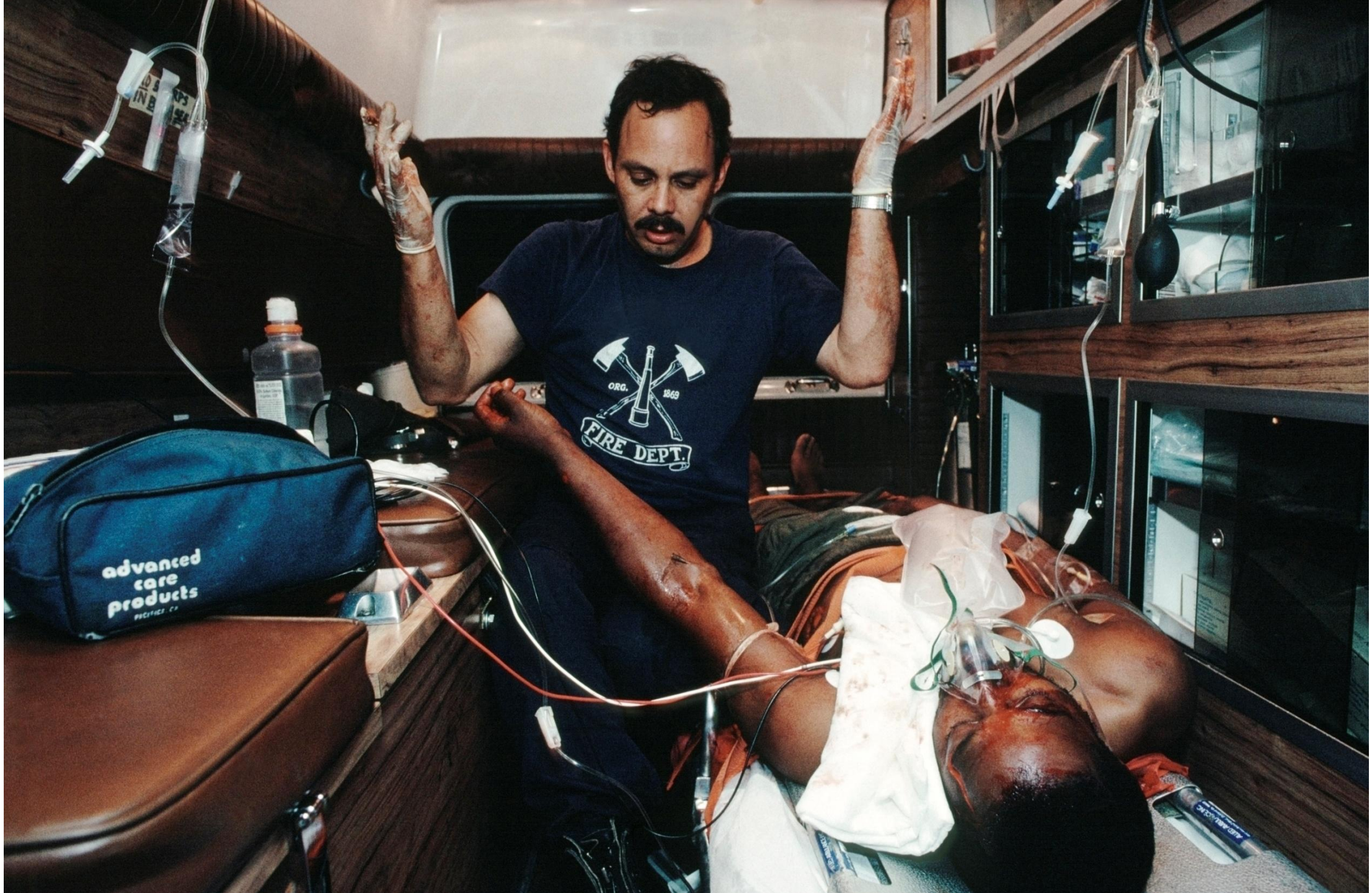


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery

Outcome	TXA N=2311	Placebo N=2320	RR (95%CI)	P value
Death	26 (1.1%)	33 (1.4%)	0.79 (0.47-1.32)	0.34
Re-operation	18 (0.8%)	50 (2.2%)	0.36 (0.21–0.62)	<0.001
Transfusion	876 (37.9)	1269 (54.7)		<0.001
MI	269 (11.6)	300 (12.9)	0.90 (0.77–1.05)	0.19
Stroke	32 (1.4)	35 (1.5)	0.92 (0.57–1.48)	0.81
PE	15 (0.6)	15 (0.6)	1.00 (0.49–2.05)	>0.99


ORG. 1869
FIRE DEPT.
advanced care Products

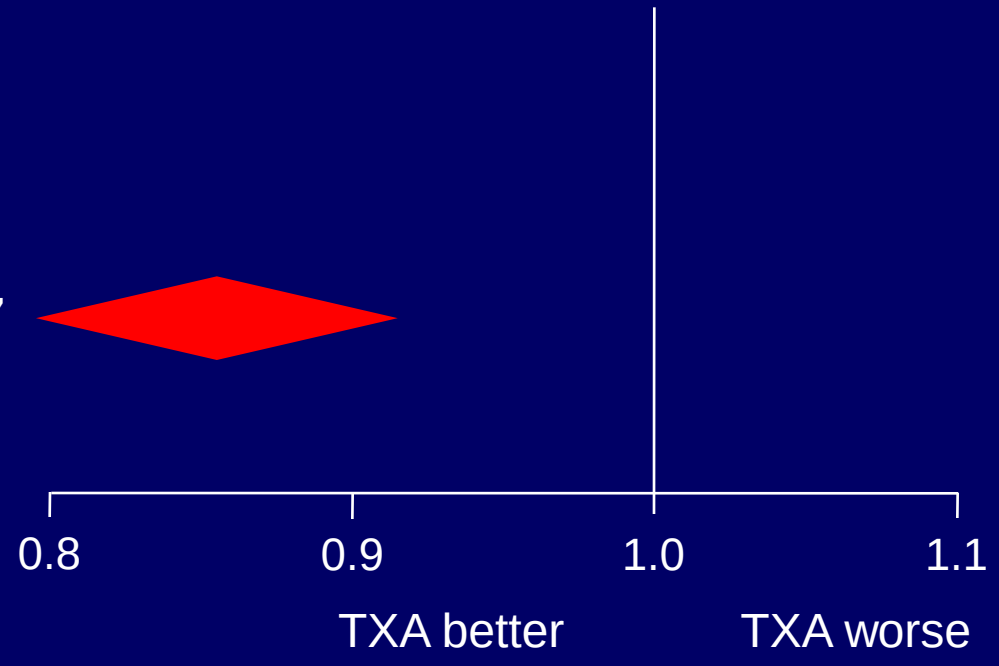

TOYOTA
adidas


CRASH 2
Clinical Randomisation of an
Antifibrinolytic in Significant Haemorrhage

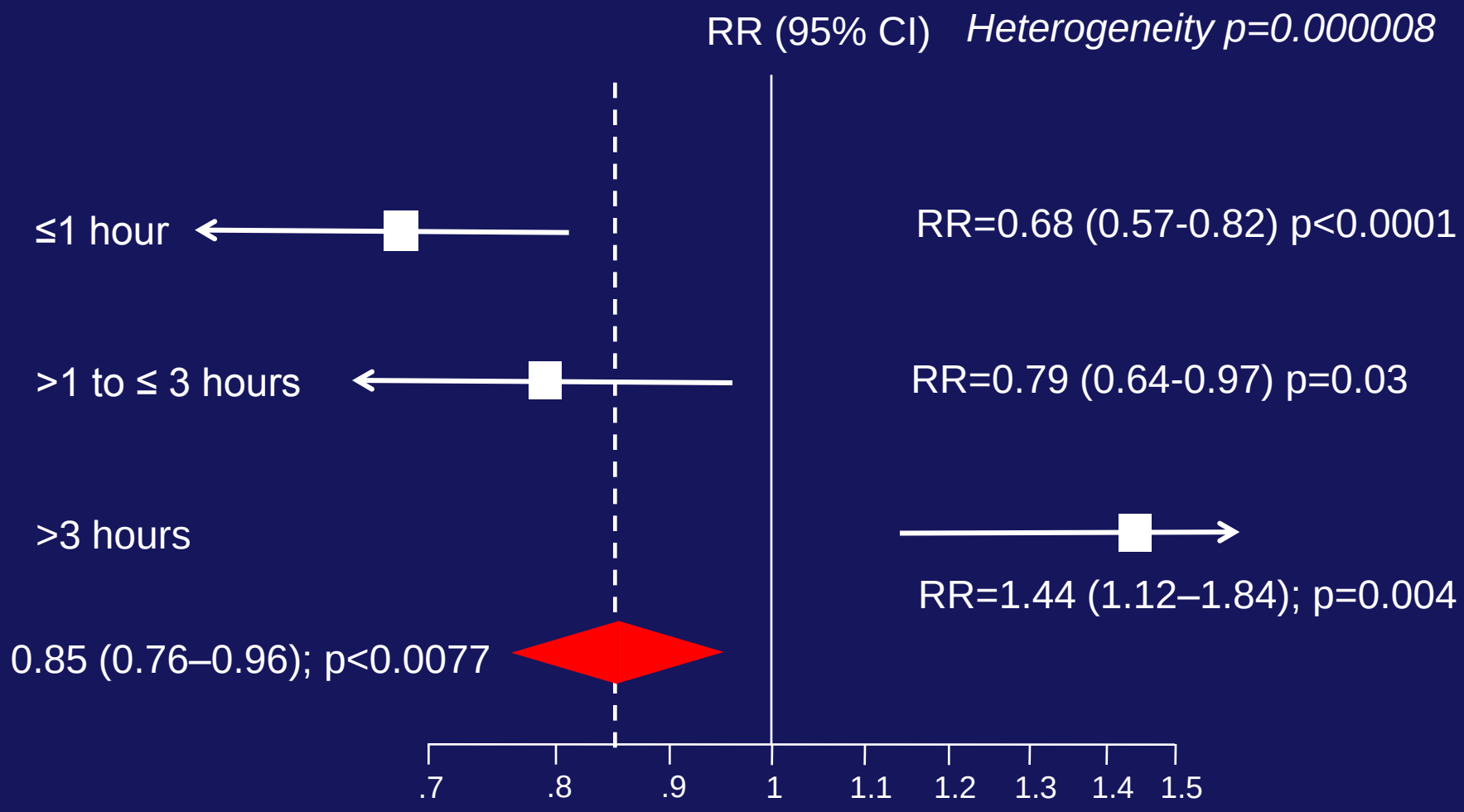
Death due to bleeding in trauma

TXA	Placebo	RR (95% CI)
(n= 10,060)	**(n= 10,067)**	
489 (5%)	574 (6%)	

0.85 (0.76–0.96) 2P=0.0077



Early treatment is essential



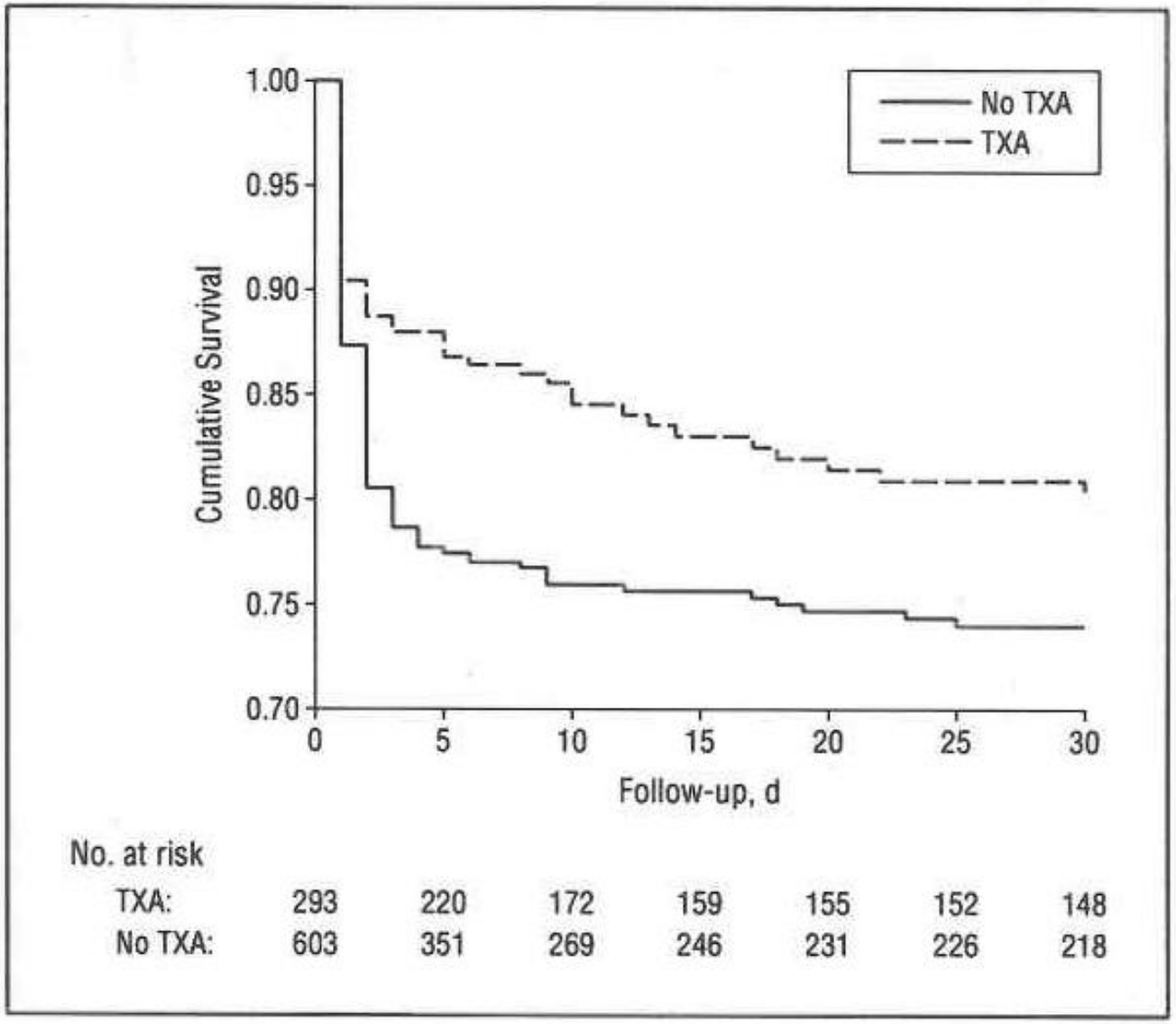


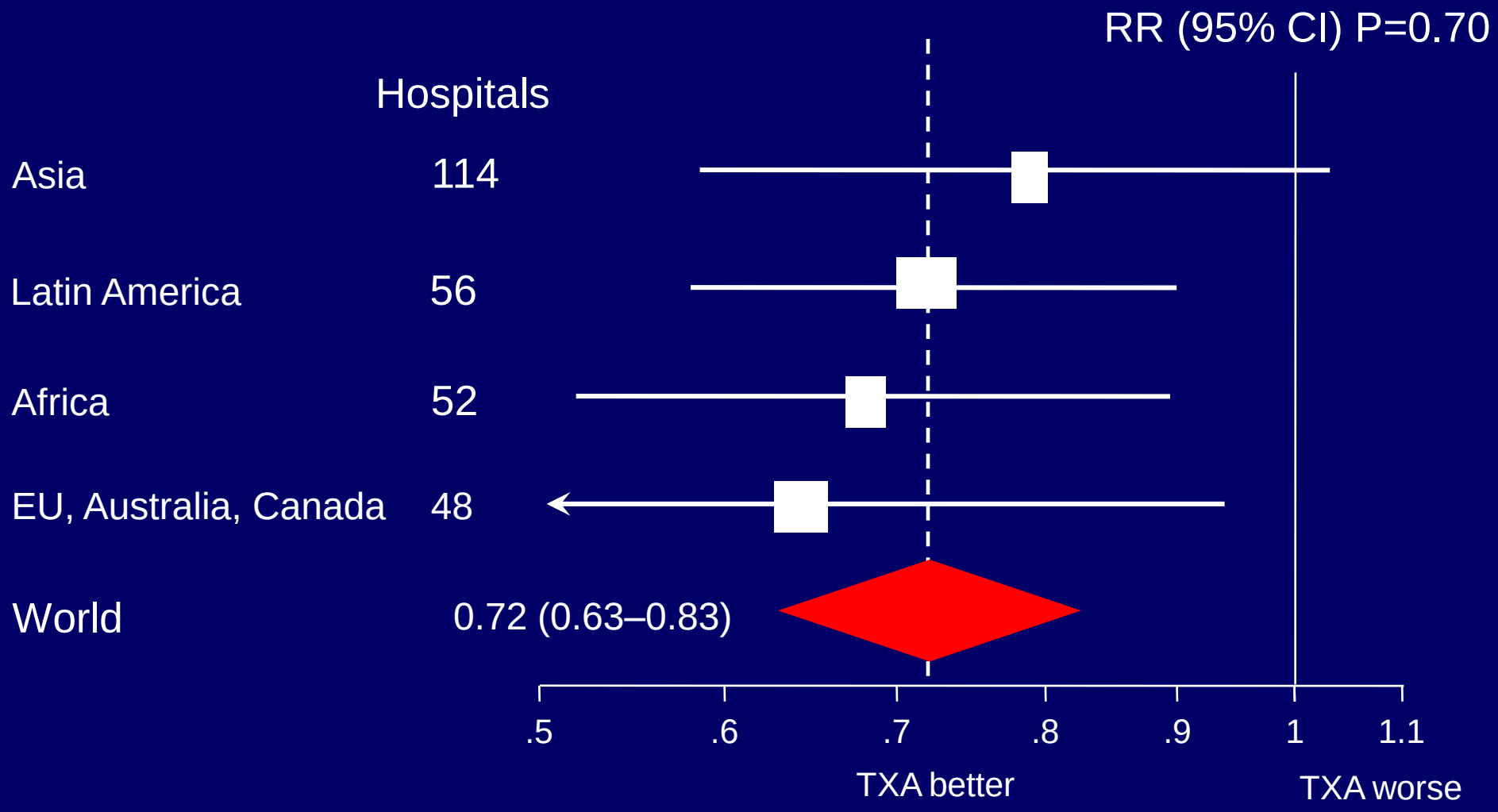
Figure 3. Kaplan-Meier survival curve of the overall cohort, including patients receiving tranexamic acid (TXA) vs no TXA. *P*=.006, Mantel-Cox log-rank test.

TXA within 3 hours of injury fatal or non fatal occlusive events

Thrombotic events[#]	TXA [n = 6784]	Placebo [n = 6700]	RR (95% CI)	p-value
Any event	98 (1·4%)	141 (2·1%)	0·69 (0·53 – 0·89)	0·004
Any arterial event	47 (0·7%)	81 (1·2%)	0.57 (0·40– 0·82)	0.002
Myocardial infarction	*23 (0·3%)*	*47 (0·7%)*	*0·48 (0·29 – 0·79)*	*0·003*
Stroke	*28 (0·4%)*	*40 (0·6%)*	*0·69 (0·42 – 1·12)*	*0·131*
Any venous event	60 (0·9%)	71 (1·1%)	0.83 (0·59– 1·17)	0.299
Pulmonary embolism	*42 (0·6%)*	*47 (0·7%)*	*0·88 (0·58 – 1·34)*	*0·555*
Deep vein thrombosis	*25 (0·4%)*	*28 (0·4%)*	*0·88 (0·51 – 1·51)*	*0·647*

Effect of early TXA on death due to bleeding

(by geographical region)



Ker et al. BMC Emergency Medicine 2012, 12:3
http://www.biomedcentral.com/1471-227X/12/3

BMC Emergency Medicine

RESEARCH ARTICLE Open Access

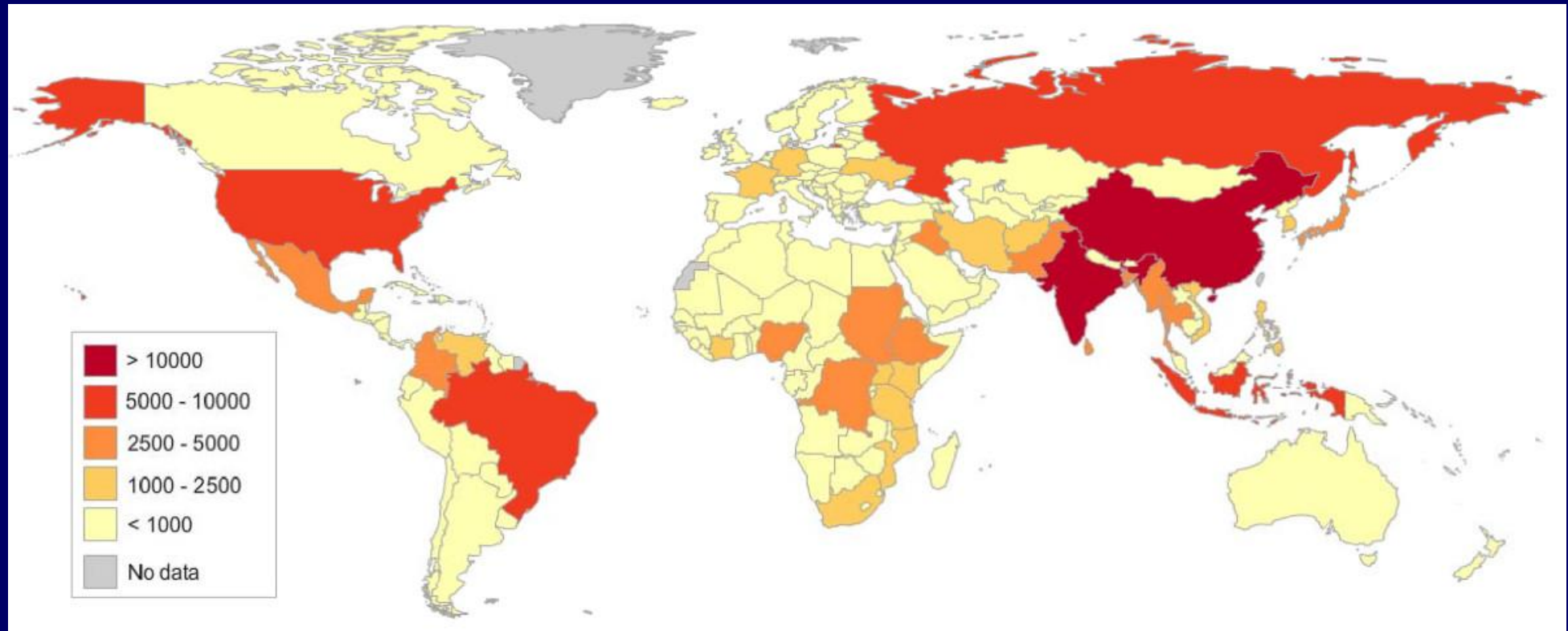
Avoidable mortality from giving tranexamic acid to bleeding trauma patients: an estimation based on WHO mortality data, a systematic literature review and data from the CRASH-2 trial

Katharine Ker*, Junko Kiriya, Pablo Perel, Phil Edwards, Haleema Shakur and Ian Roberts

Lives saved with TXA (every year)

TXA < 1 hour = 128,000 lives

TXA < 3hours =112,000 lives



Cost per life-year gained		US$1 m
• Insecticide treated bed net (malaria)	US$ 49	20,000
• Tranexamic acid for trauma (included on WHO list of essential medicines)	US$ 60*	17,000
• Antiretroviral treatment for HIV	US$ 1300	800

TXA included on WHO list of essential medicines in 2010

* Based on discounted life-year gained (DLYG)

TXA included in trauma treatment guidelines

Tranexamic Acid [875–879]

Presentation

Vial containing 500 mg tranexamic acid in 5 ml (100 mg/ml).

Indications

- Patients with **TIME CRITICAL** injury where significant internal/external haemorrhage is suspected.
- Injured patients fulfilling local Step 1 or Step 2 trauma triage protocol – **refer to Appendix in trauma emergencies overview (adults)**.

Actions

Tranexamic acid is an anti-fibrinolytic which reduces the breakdown of blood clot.

Contra-Indications

- Isolated head injury.
- Critical interventions required (if critical interventions leave insufficient time for TXA administration).
- Bleeding now stopped.

The effects of tranexamic acid in isolated TBI

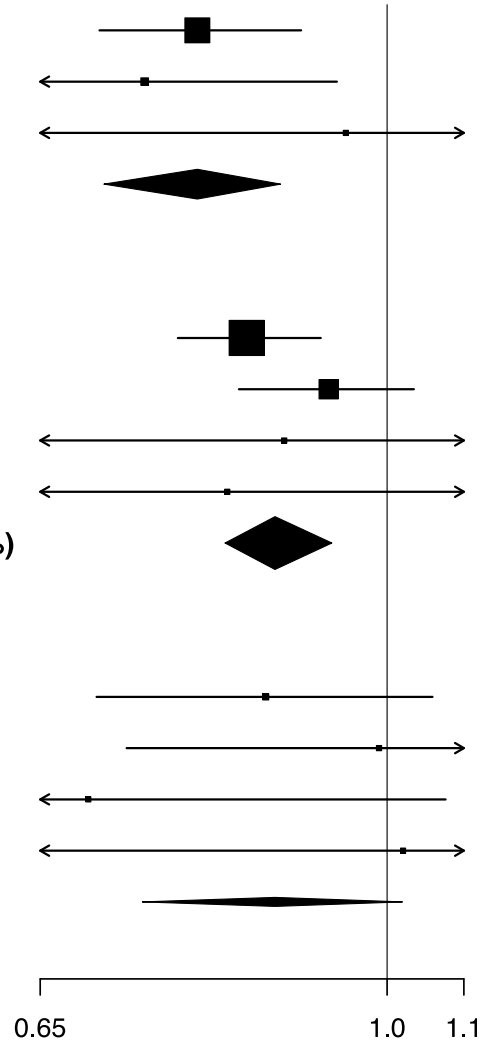
Effect of TXA on all-cause mortality within 24 hours and within 28 days (excluding patients with GCS 3 or bilateral unreactive pupils at baseline)

	Deaths in TXA group (%)	Deaths in placebo group (%)	Risk ratio (95% CI)
Death within 24 hours			
CRASH-2	6.3	8.0	0.79 (0.70-0.90)
CRASH-3	2.9	3.9	0.74 (0.58-0.94)
Combined	**5.0**	**6.5**	**0.78 (0.70-0.87)**
Death within 28 days			
CRASH-2	12.1	14.3	0.84 (0.77-0.92)
CRASH-3	14.0	15.1	0.93 (0.83-1.03)
Combined	**12.8**	**14.6**	**0.88 (0.82-0.94)**

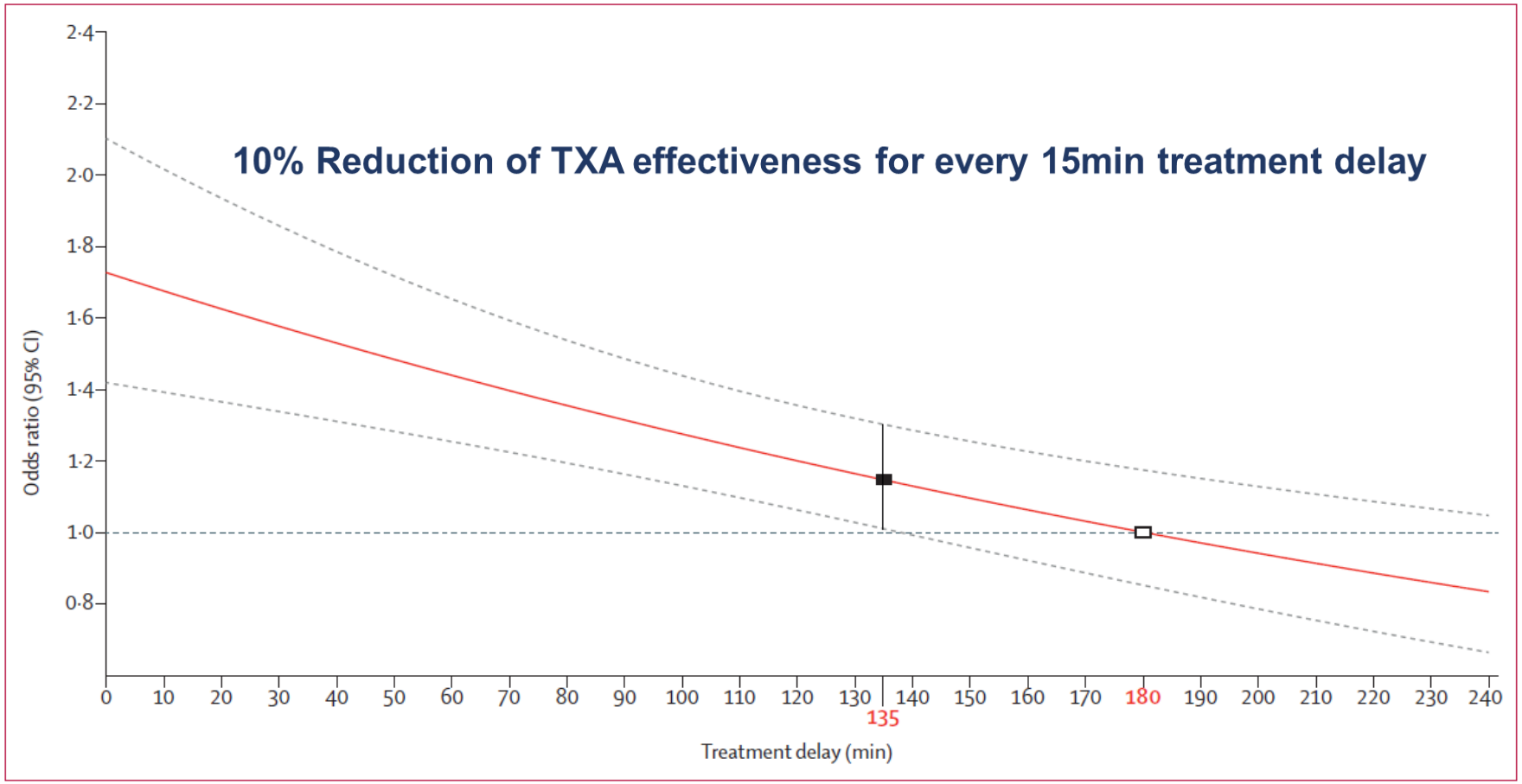
Risk ratios less than one mean there are fewer deaths in the TXA group

Effect of TXA on all-cause mortality at 24 hours and 28 days (all trials >500 patients)

Study	Tranexamic acid	Placebo	RR	95% CI
Death within 24 hours				
CRASH-2	410 / 6486 (6.3%)	513 / 6435 (8.0%)	0.79	(0.70-0.90)
CRASH-3	112 / 3880 (2.9%)	147 / 3757 (3.9%)	0.74	(0.58-0.94)
STAAMP	16 / 447 (3.6%)	17 / 453 (3.8%)	0.95	(0.49-1.86)
Pooled	**538 / 10813 (5.0%)**	**677 / 10645 (6.4%)**	**0.79**	**(0.70-0.88)**
Death at 28 days				
CRASH-2	784 / 6486 (12.1%)	923 / 6435 (14.3%)	0.84	(0.77-0.92)
CRASH-3	544 / 3880 (14.0%)	568 / 3757 (15.1%)	0.93	(0.83-1.03)
Rowell 2020	93 / 603 (15.4%)	50 / 285 (17.5%)	0.88	(0.64-1.20)
STAAMP	36 / 442 (8.1%)	45 / 452 (10.0%)	0.82	(0.54-1.24)
Pooled	**1457 / 11411 (12.8%)**	**1586 / 10929 (14.5%)**	**0.87**	**(0.82-0.93)**
Vasc. occlusive events				
CRASH-2	161 / 9655 (1.7%)	188 / 9682 (1.9%)	0.86	(0.70-1.06)
CRASH-3	77 / 5420 (1.4%)	76 / 5302 (1.4%)	0.99	(0.72-1.36)
Rowell 2020	44 / 657 (6.7%)	30 / 309 (9.7%)	0.69	(0.44-1.08)
STAAMP	2 / 447 (0.4%)	2 / 456 (0.4%)	1.02	(0.14-7.21)
Pooled	**284 / 16179 (1.8%)**	**296 / 15749 (1.9%)**	**0.87**	**(0.74-1.02)**



Early treatment is essential



Effect of treatment delay on the survival benefit from tranexamic acid


South East Coast Ambulance Service NHS
KEEP CLEAR
POLI

TARN

THE TRAUMA AUDIT & RESEARCH NETWORK

YEAR 2017

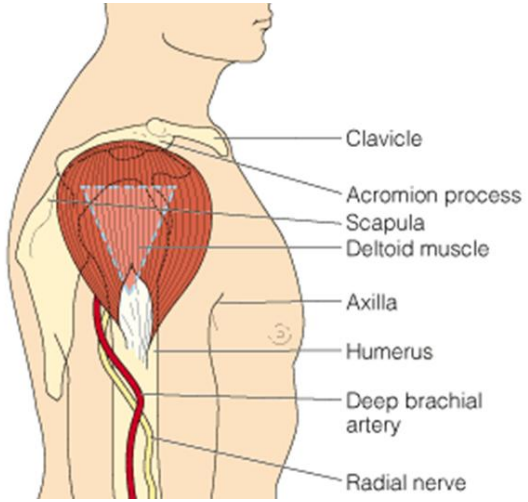
Average time to TXA treatment = 1.45 hours (0.85 – 2.50)

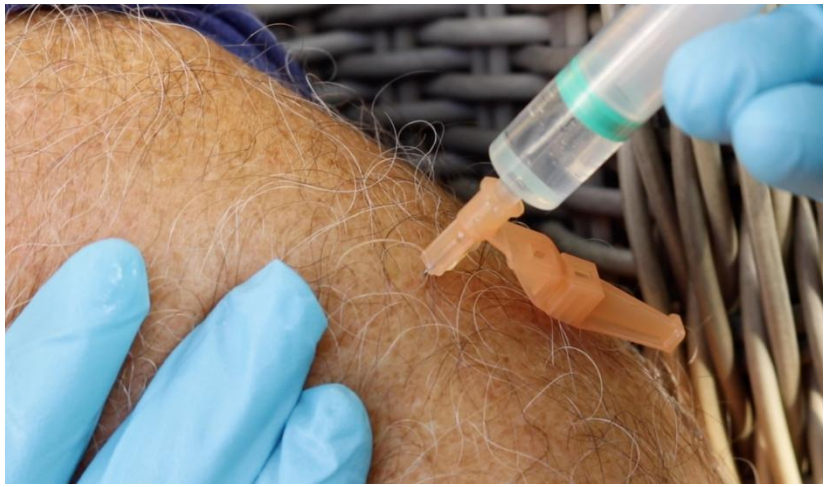
30% trauma patients received TXA within the first hour

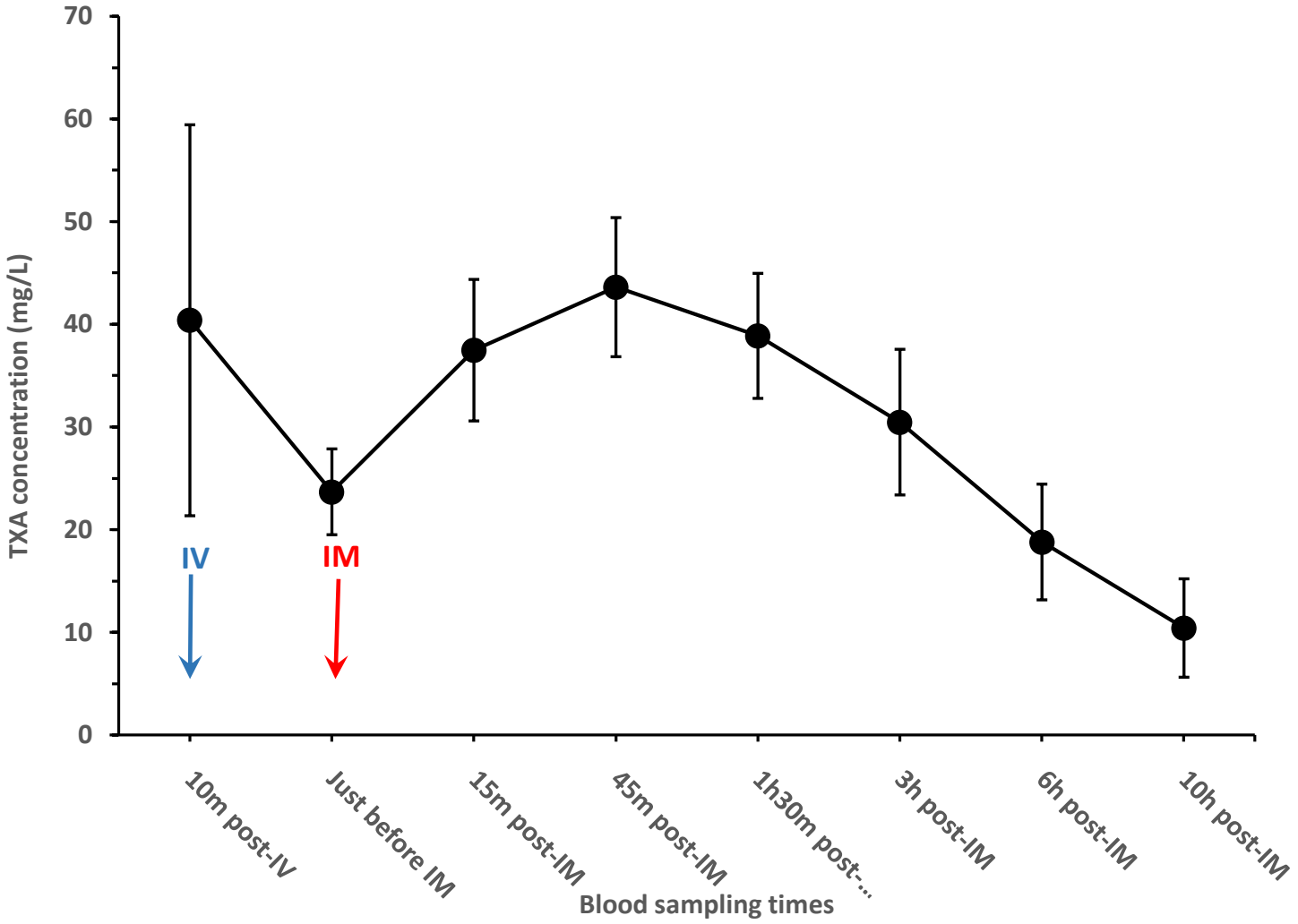
Average 50 minutes

Average 110 minutes

TXA is well tolerated and rapidly absorbed after IM injection







Accident victims could be saved in minutes with one simple injection

Kat Lay Health Correspondent

Thousands of lives could be saved each year by giving patients a simple injection to prevent severe bleeding at the scene of accidents, a study has found.

A cheap, widely available drug called tranexamic acid (TXA) encourages the blood to clot and can reduce deaths of injury victims by up to a third when given within an hour. Each 15 minute delay reduces its lifesaving potential by 10 per cent and at present only 3 per cent of trauma victims in the UK get it within the one-hour window.

The study, published in the *British Journal of Anaesthesia*, showed that TXA could be given as a simple intramuscular injection, in the same way as a flu jab, rather than via the more complicated intravenous line that is standard.

"Intramuscular TXA is like a vaccine against trauma death," said Dr Ian Roberts, from the London School of Hygiene and Tropical Medicine, who led the study. "An urgent injection of TXA is life-saving after serious injury, but patients are not being treated fast enough. A rapid intramuscular injection given by first responders or paramedics could mean the difference between life and death."

The drug is rapidly absorbed from muscles into the blood, and there were no local side-effects other than some redness and swelling. "I think we can start using it this way immediately," said Dr Roberts.

"If you could just get to the scene of an injury — somebody lying on the floor by the road, or at the foot of a ladder — you just do the basics, sort out airway, breathing, and then you could very quickly give an injection of the intramuscular dose of tranexamic acid, and it's absorbed into the blood so quickly that you get therapeutic effect really, really quickly.

"At the moment in the NHS tranexamic acid is used but patients aren't getting it quick enough. It's most effective when given within an hour of injury, and the hours just disappear so quickly. It takes time for the ambulance to arrive, time for paramedics to orientate themselves to what's going on. It takes a little time to put in an intravenous line — sometimes they just say, well, let's leave that for the hospital.

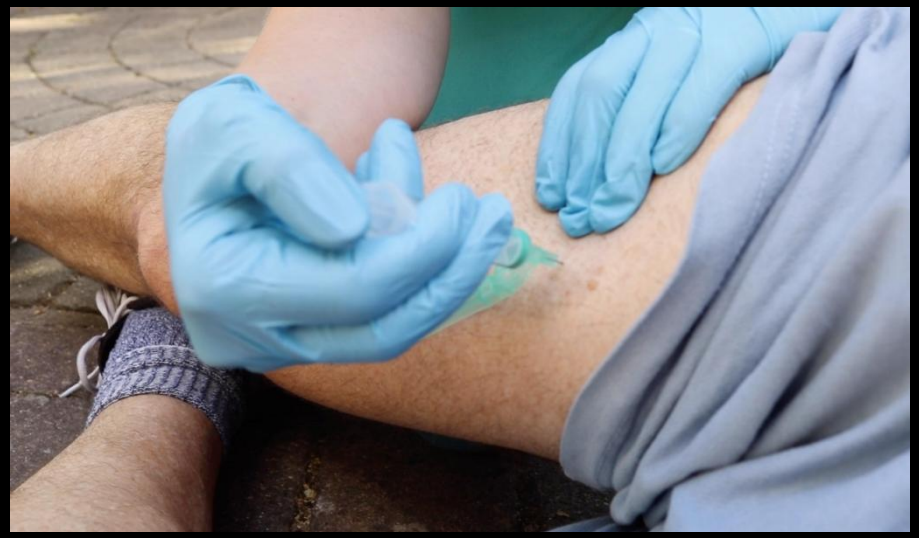
"This way, you can just inject it intramuscularly and forget about it."

The study involved 30 bleeding trauma patients at London hospitals, who were given their first dose of TXA intravenously but the second via intramuscular injection.

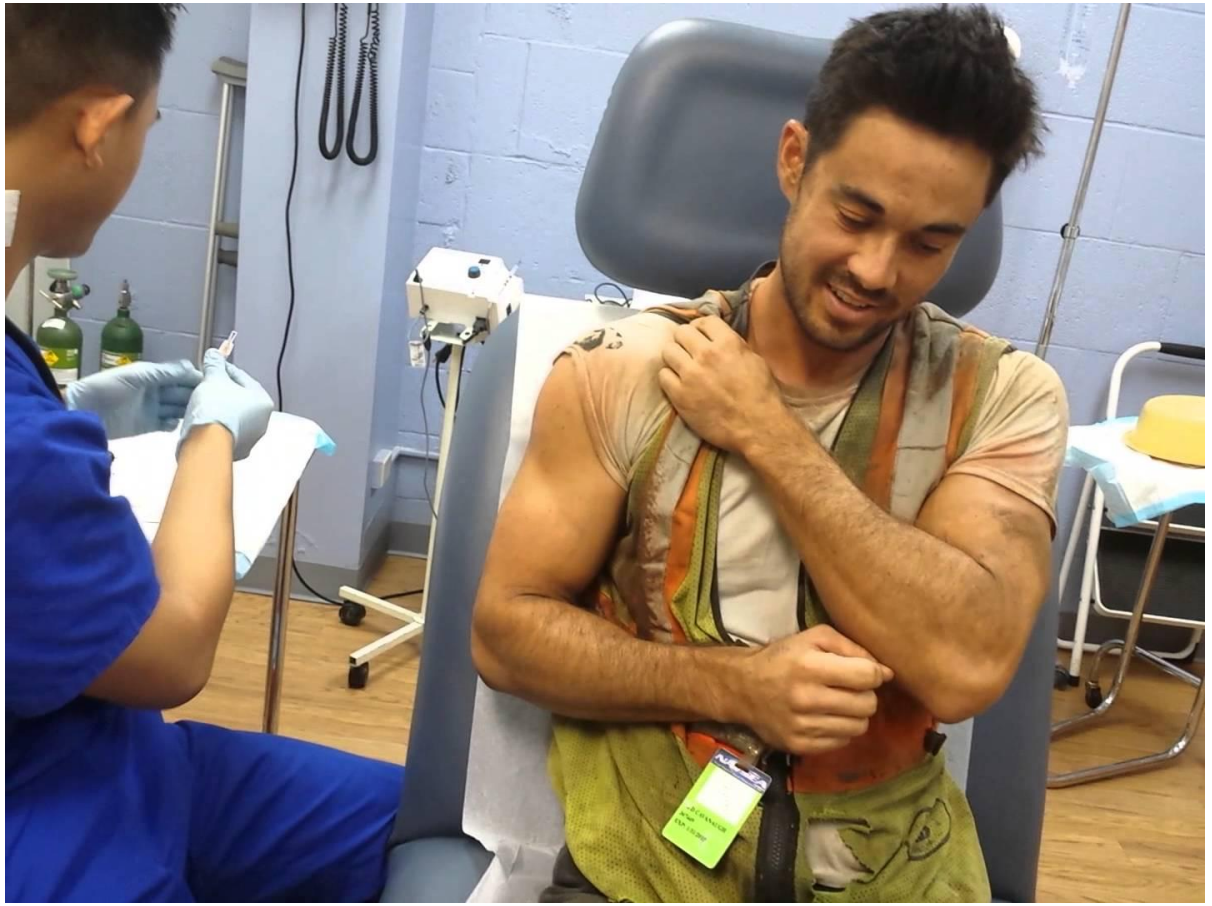
Tests showed that TXA was rapidly absorbed from muscle and reached the necessary level to save lives within 15 minutes in all patients.

Dr Roberts said that the finding was particularly useful for low and middle-income countries, where first responders are least likely to be able to give intravenous injections. More than 90 per cent of trauma deaths occur in those countries, and up to 80 per cent before the patient arrives at hospital.

The research team is also working with the British military on an Epipen-style autoinjector that could be used on the battlefield. Dr Roberts said the intramuscular injection could be "a game-changer" for a variety of trauma victims. "A simple auto injector device that could be used by lay first responders or police officers — before the ambulance arrives — could save thousands of lives each year," he said. "It could also be used by wounded soldiers either on themselves or a buddy."



Tranexamic acid ‘vaccination’ against serious bleeding



Prehospital trauma care evolution, practice and controversies: need for a review

Mathew Varghese

"Other than tranexamic acid and pain killers, there is very little role for any drugs in the prehospital setting for trauma victims."

Most trauma victims do not get TXA

The failure of global implementation is a bleeding tragedy