Tranexamic acid in life threatening bleeding

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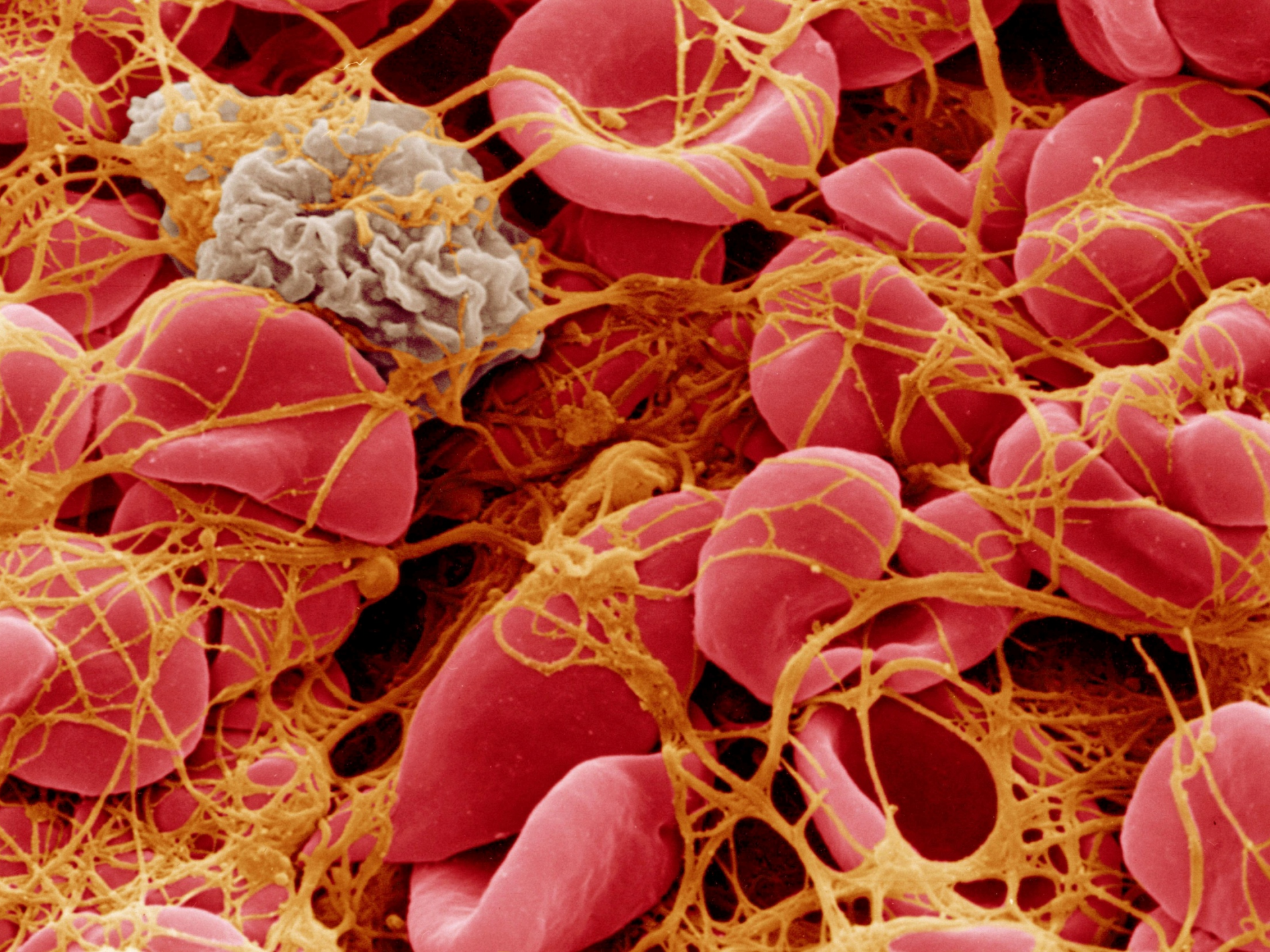
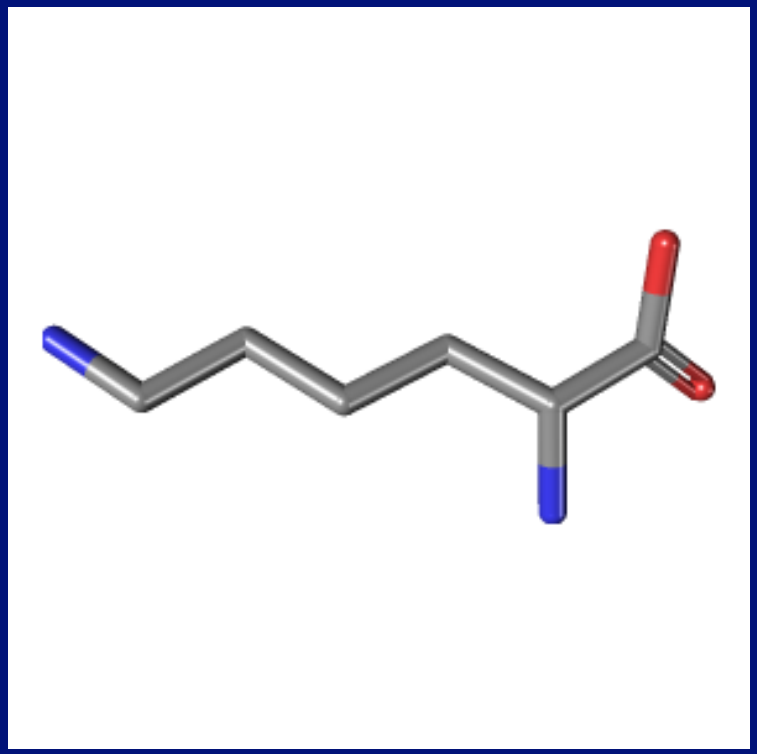
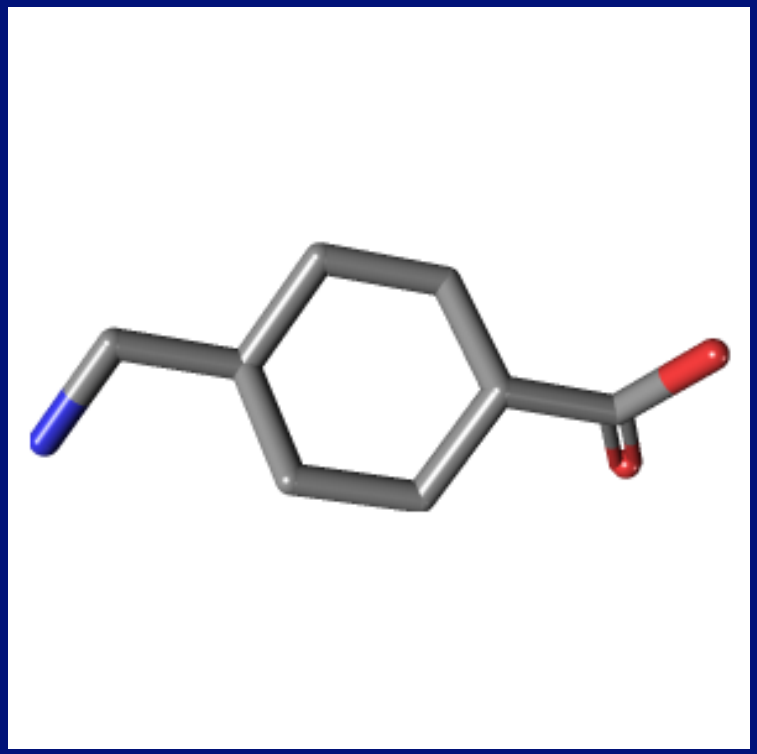


Lysine

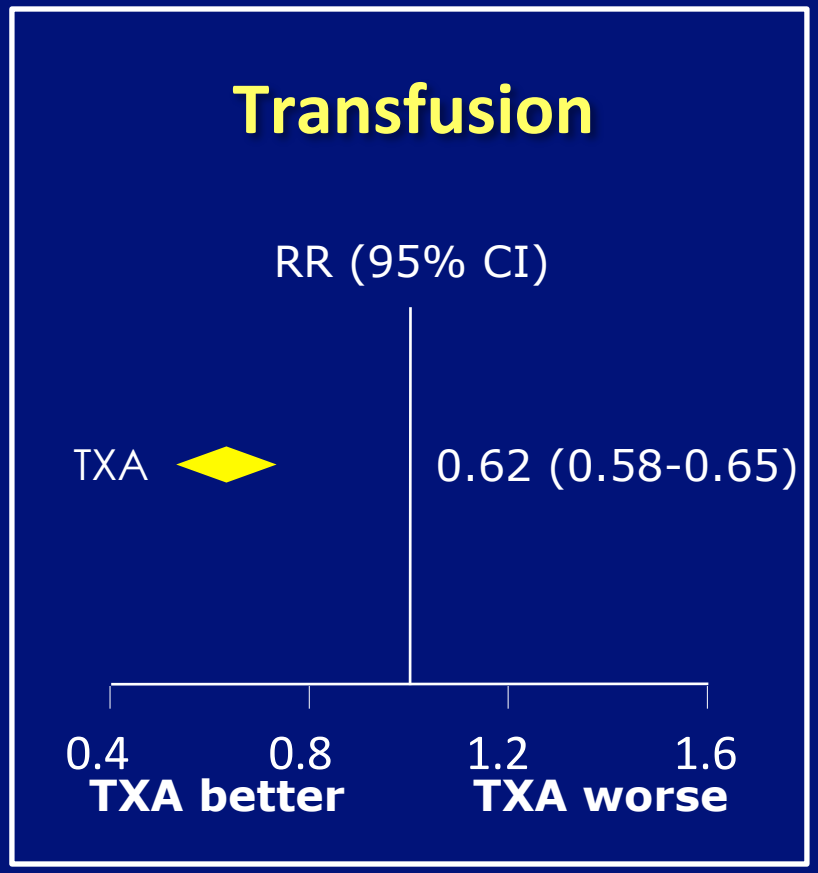


Tranexamic acid

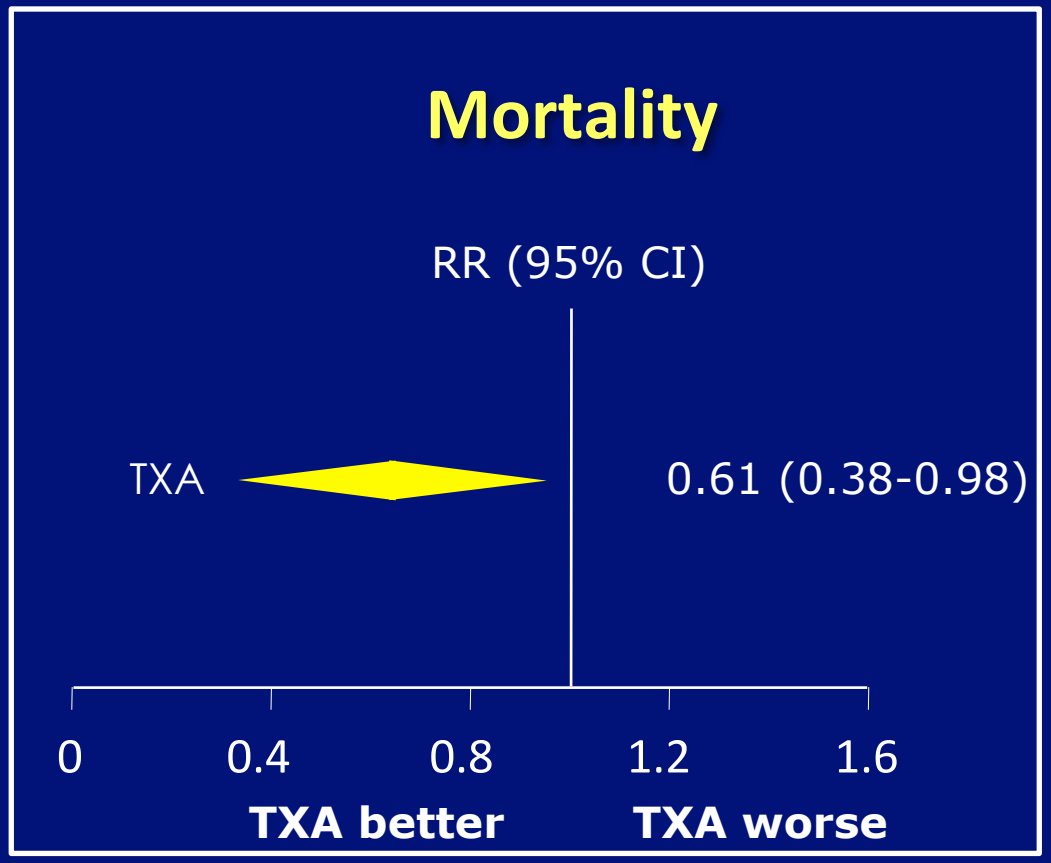


TXA reduces surgical bleeding

(Ker et al, BMJ 2012)



95 trials



72 trials

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery

Paul S. Myles, M.P.H., M.D., Julian A. Smith, F.R.A.C.S., Andrew Forbes, Ph.D., Brendan Silbert, M.B., B.S., Mohandas Jayarajah, M.B., B.S., Thomas Painter, M.B., Ch.B., D. James Cooper, M.D., Silvana Marasco, Ph.D., John McNeil, Ph.D., Jean S. Bussières, M.D., Shay McGuinness, M.B., Ch.B., Kelly Byrne, M.B., Ch.B., Matthew T.V. Chan, M.B., B.S., Ph.D., Giovanni Landoni, M.D., and Sophie Wallace, M.P.H., for the ATACAS Investigators of the ANZCA Clinical Trials Network*

ABSTRACT

BACKGROUND

Tranexamic acid reduces the risk of bleeding among patients undergoing cardiac surgery, but it is unclear whether this leads to improved outcomes. Furthermore, there are concerns that tranexamic acid may have prothrombotic and proconvulsant effects.

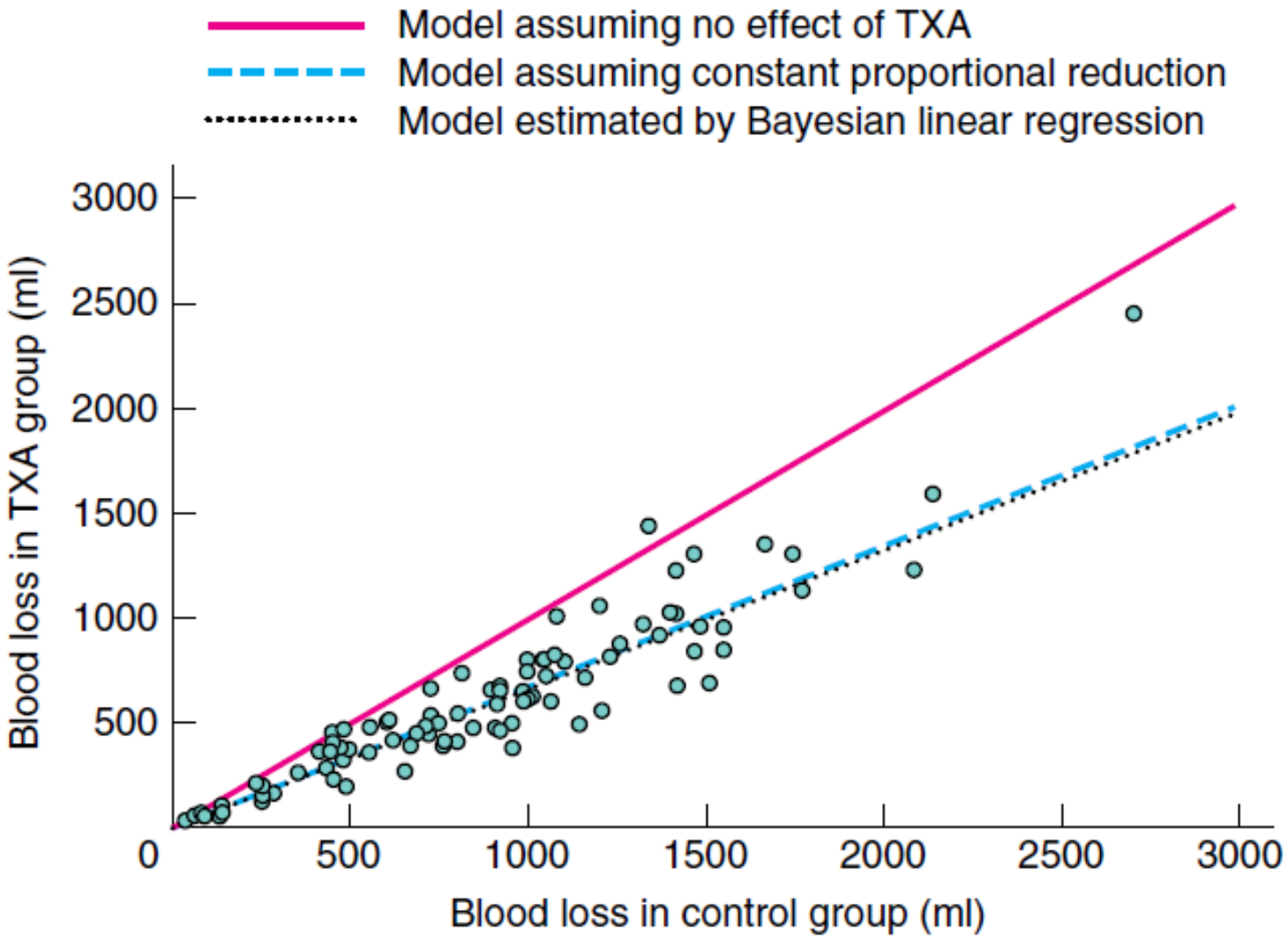
METHODS

In a trial with a 2-by-2 factorial design, we randomly assigned patients who were scheduled to undergo coronary-artery surgery and were at risk for perioperative complications to receive aspirin or placebo and tranexamic acid or placebo. The results of the tranexamic acid comparison are reported here. The primary outcome was a composite of death and thrombotic complications (nonfatal myocardial infarction, stroke, pulmonary embolism, renal failure, or bowel infarction) within 30 days after surgery.

Outcome or Event	Tranexamic Acid Group (N=2311)	Placebo Group (N=2320)	Risk Ratio (95% CI)	P Value
Primary outcome: death, myocardial infarction, stroke, renal failure, pulmonary embolism, or bowel infarction — no./total no. (%)	386/2310 (16.7)	420/2320 (18.1)	0.92 (0.81–1.05)	0.22
Death	26/2310 (1.1)	33/2320 (1.4)	0.79 (0.47–1.32)	0.43
Myocardial infarction	269/2310 (11.6)	300/2320 (12.9)	0.90 (0.77–1.05)	0.19
Stroke	32/2309 (1.4)	35/2320 (1.5)	0.92 (0.57–1.48)	0.81
Renal failure	98/2309 (4.2)	96/2320 (4.1)	1.03 (0.78–1.35)	0.88
Pulmonary embolism	15/2309 (0.6)	15/2320 (0.6)	1.00 (0.49–2.05)	>0.99
Bowel infarction	8/2309 (0.3)	3/2320 (0.1)	2.68 (0.71–10.09)	0.15
Primary outcome not including renal failure — no./total no. (%)*	324/2310 (14.0)	362/2320 (15.6)	0.90 (0.78–1.03)	0.14
Reoperation — no./total no. (%)				
Due to any cause	32/2310 (1.4)	65/2320 (2.8)	0.49 (0.32–0.75)	0.001
Due to major hemorrhage	18/2310 (0.8)	50/2320 (2.2)	0.36 (0.21–0.62)	<0.001
Due to cardiac tamponade	14/2310 (0.6)	23/2320 (1.0)	0.61 (0.32–1.19)	0.19
Transfusion of red cells during hospitalization — no./total no. (%)	759/2311 (32.8)	1086/2320 (46.8)		
No. of units of red cells that were transfused during hospitalization				<0.001

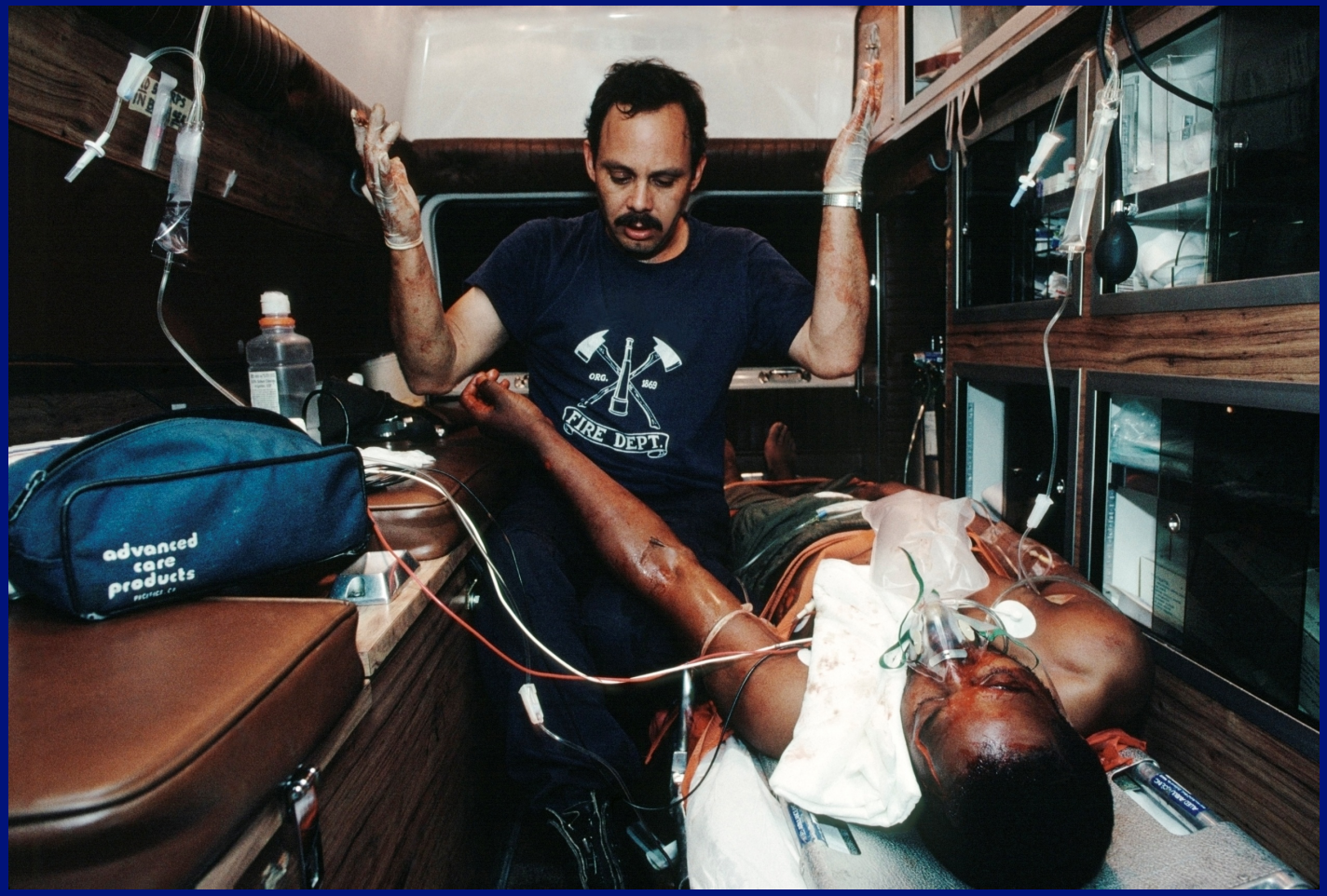
Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss

K. Ker, D. Prieto-Merino and I. Roberts




CRASH 2
Clinical Randomisation of an
Antifibrinolytic in Significant Haemorrhage

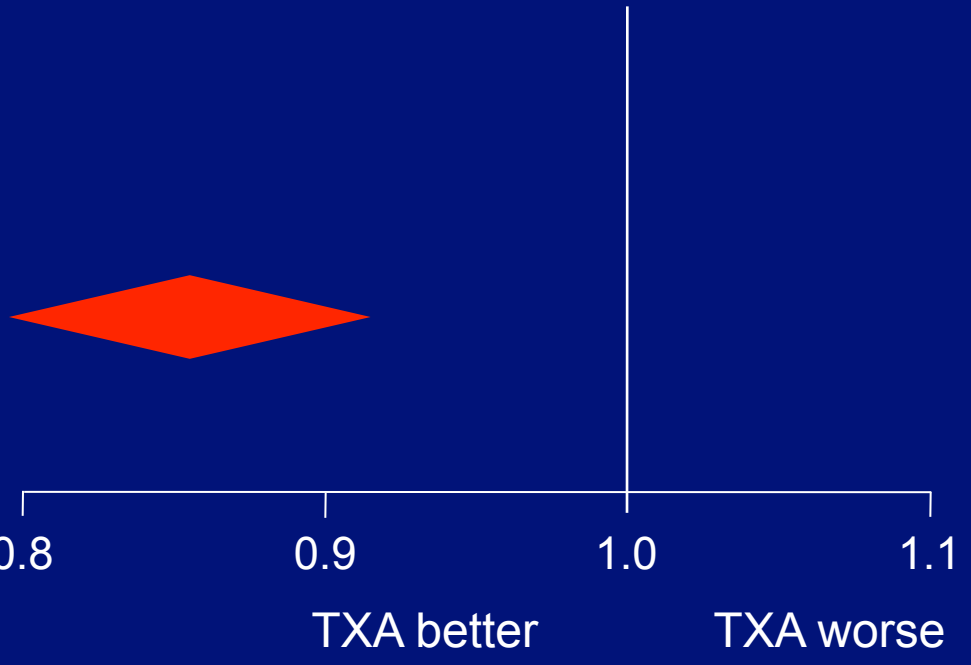
TXA reduces death from bleeding in trauma



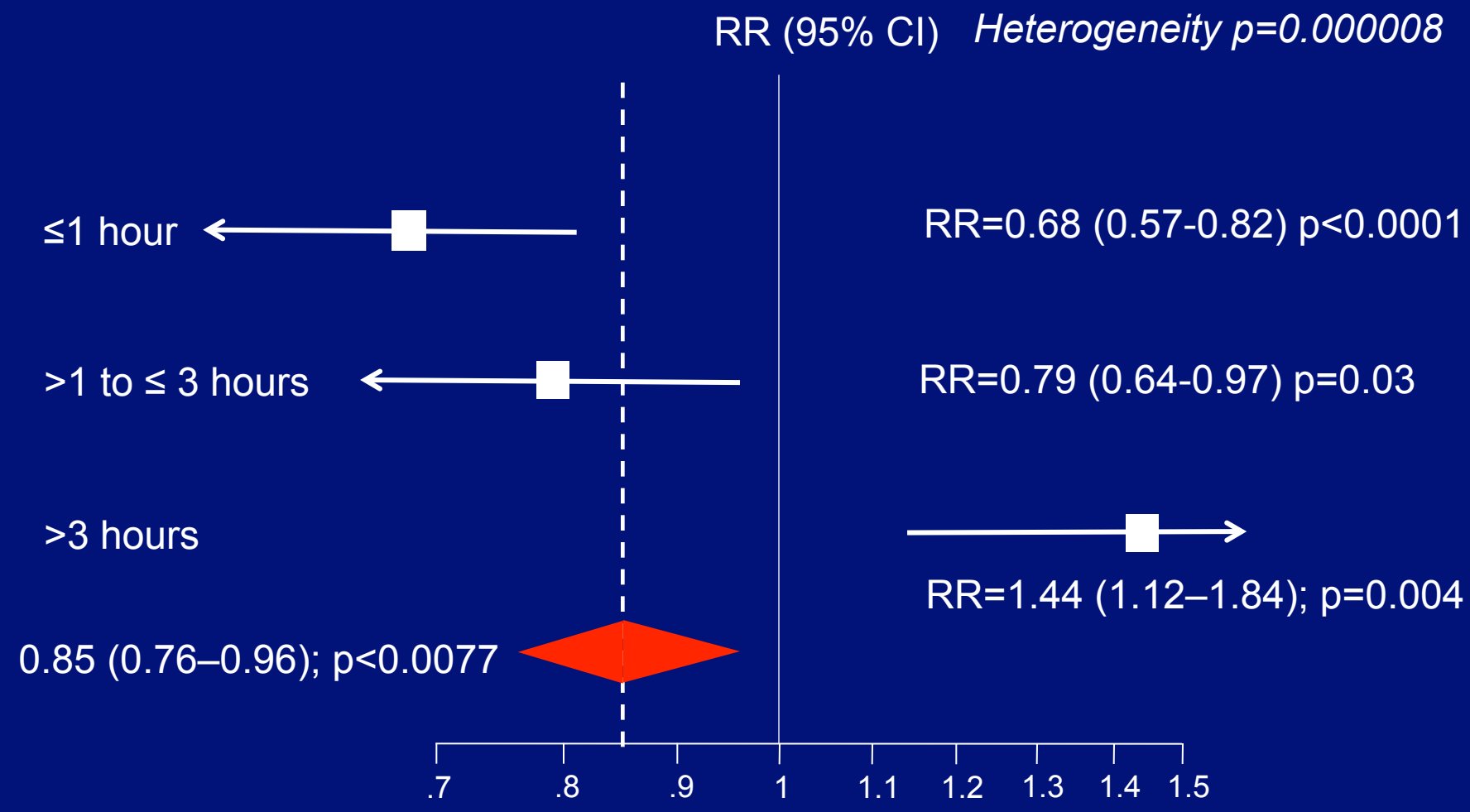
Death due to bleeding in trauma

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



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

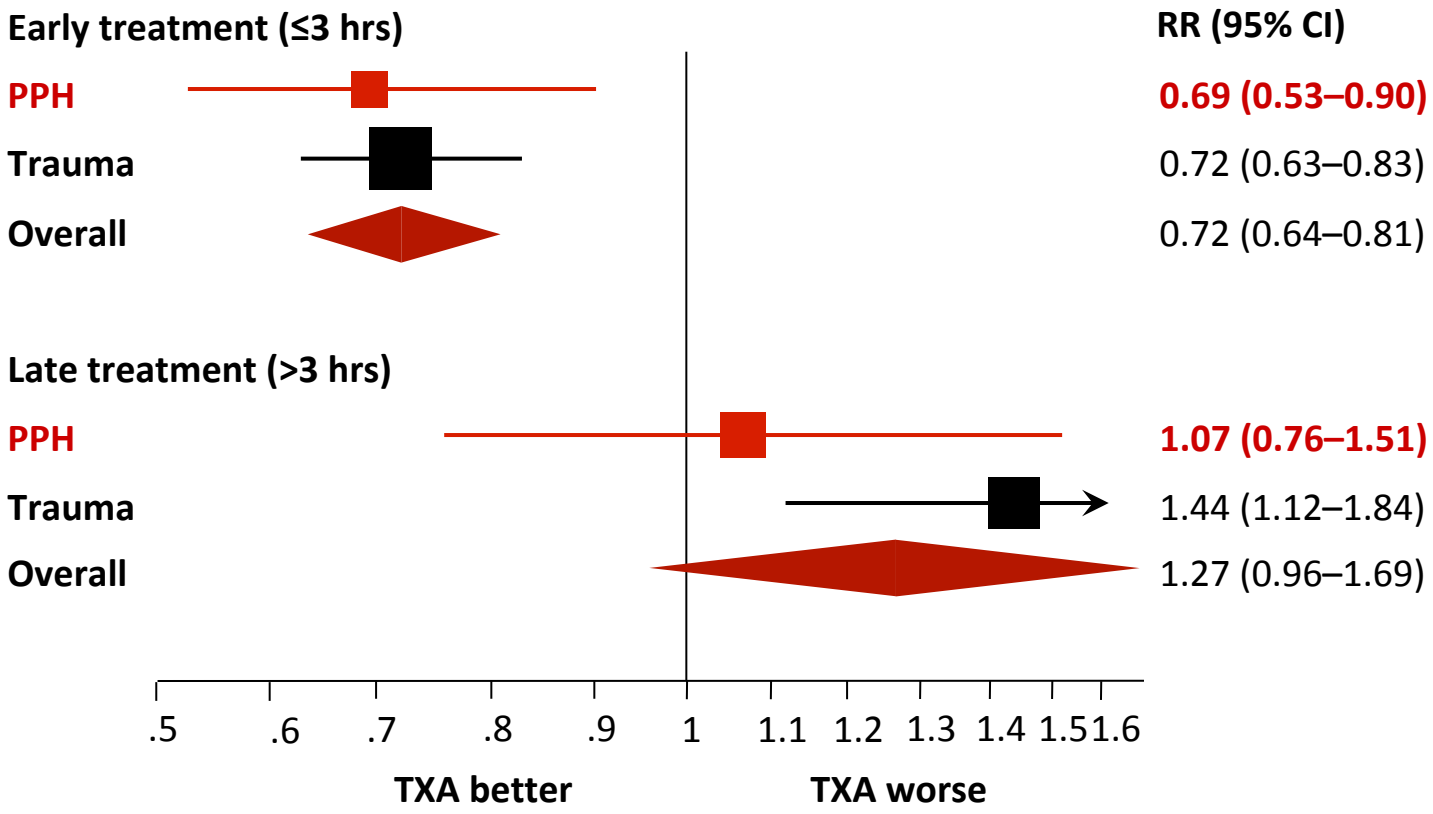
Thrombotic events[#]	TXA [n = 6784]	Placebo [n = 6700]	RR (95% CI)	p-value
Any event	98 (1·4%)	141 (2·1%)	0·69 (0·53 – 0·89)	0·004
Any arterial event	47 (0·7%)	81 (1·2%)	0.57 (0·40– 0·82)	0.002
Myocardial infarction	*23 (0·3%)*	*47 (0·7%)*	*0·48 (0·29 – 0·79)*	*0·003*
Stroke	*28 (0·4%)*	*40 (0·6%)*	*0·69 (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*

WOMAN Trial Collaborators

Death

Cause of death	TXA N=10036 n (%)	Placebo N=9985 n (%)	Risk ratio (95% CI)	P value
Bleeding	**155 (1.5)**	**191 (1.9)**	**0.81 (0.65–1.00)**	**0.045**
Pulmonary embolism	10 (0.1)	11 (0.1)	0.90 (0.38–2.13)	0.82
Organ failure	25 (0.3)	18 (0.2)	1.38 (0.75–2.53)	0.29
Sepsis	15 (0.2)	8 (0.1)	1.87 (0.79–4.40)	0.15
Eclampsia	2 (0.02)	8 (0.1)	0.25 (0.05–1.17)	0.06
Other	20 (0.2)	20 (0.2)	0.99 (0.54–1.85)	0.99
All causes	227 (2.3)	256 (2.6)	0.88 (0.74–1.05)	0.16

Death due to bleeding



Thromboembolic events

	TXA (N=10033) n (%)	Placebo (N=9985) n (%)	Risk ratio (95% CI)	P-value
Any event	30 (0.3)	34 (0.3)	0.88 (0.54–1.43)	0.60
Venous events (DVT, PE)	20 (0.2)	25 (0.3)	0.80 (0.44–1.43)	0.45
Deep vein thrombosis	3 (0.03)	7 (0.1)	0.43 (0.11–1.65)	0.20
Pulmonary embolism	17 (0.2)	20 (0.2)	0.85 (0.44–1.61)	0.61
Arterial events (MI, stroke)	10 (0.1)	9 (0.1)	1.11 (0.45–2.72)	0.83
Myocardial infarction	2 (0.02)	3 (0.03)	0.66 (0.11–3.97)	0.65
Stroke	8 (0.1)	6 (0.1)	1.33 (0.46–3.82)	0.60

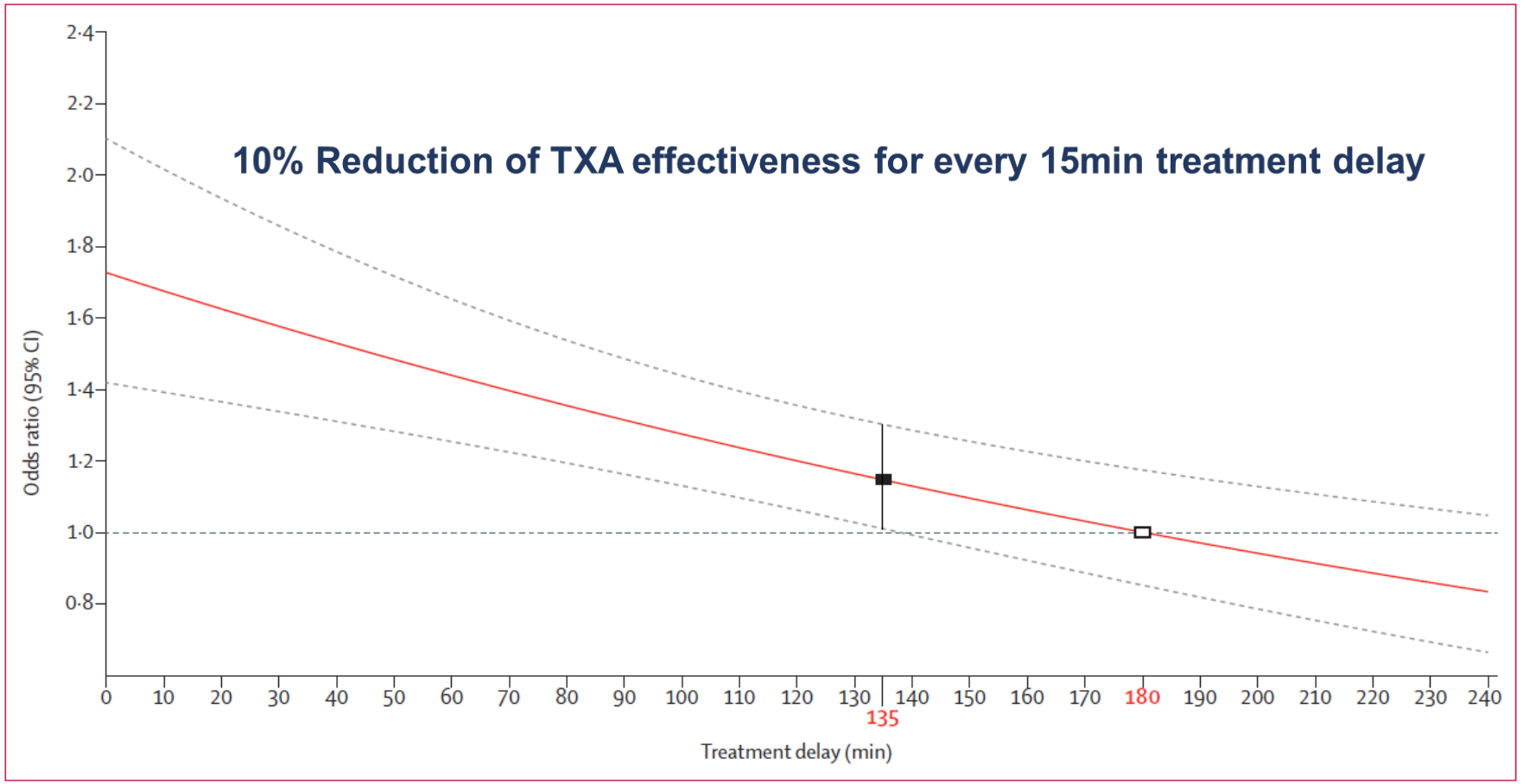
Lancet November 7th, 2017

Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: a meta-analysis of individual patient-level data from 40 138 bleeding patients

Interpretation Death from bleeding occurs soon after onset and even a short delay in treatment reduces the benefit of tranexamic acid administration. Patients must be treated immediately. Further research is needed to deepen our understanding of the mechanism of action of tranexamic acid.

CRASH-2
Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage

Early treatment is essential



Effect of treatment delay on the survival benefit from tranexamic acid

TARN
THE TRAUMA AUDIT & RESEARCH NETWORK

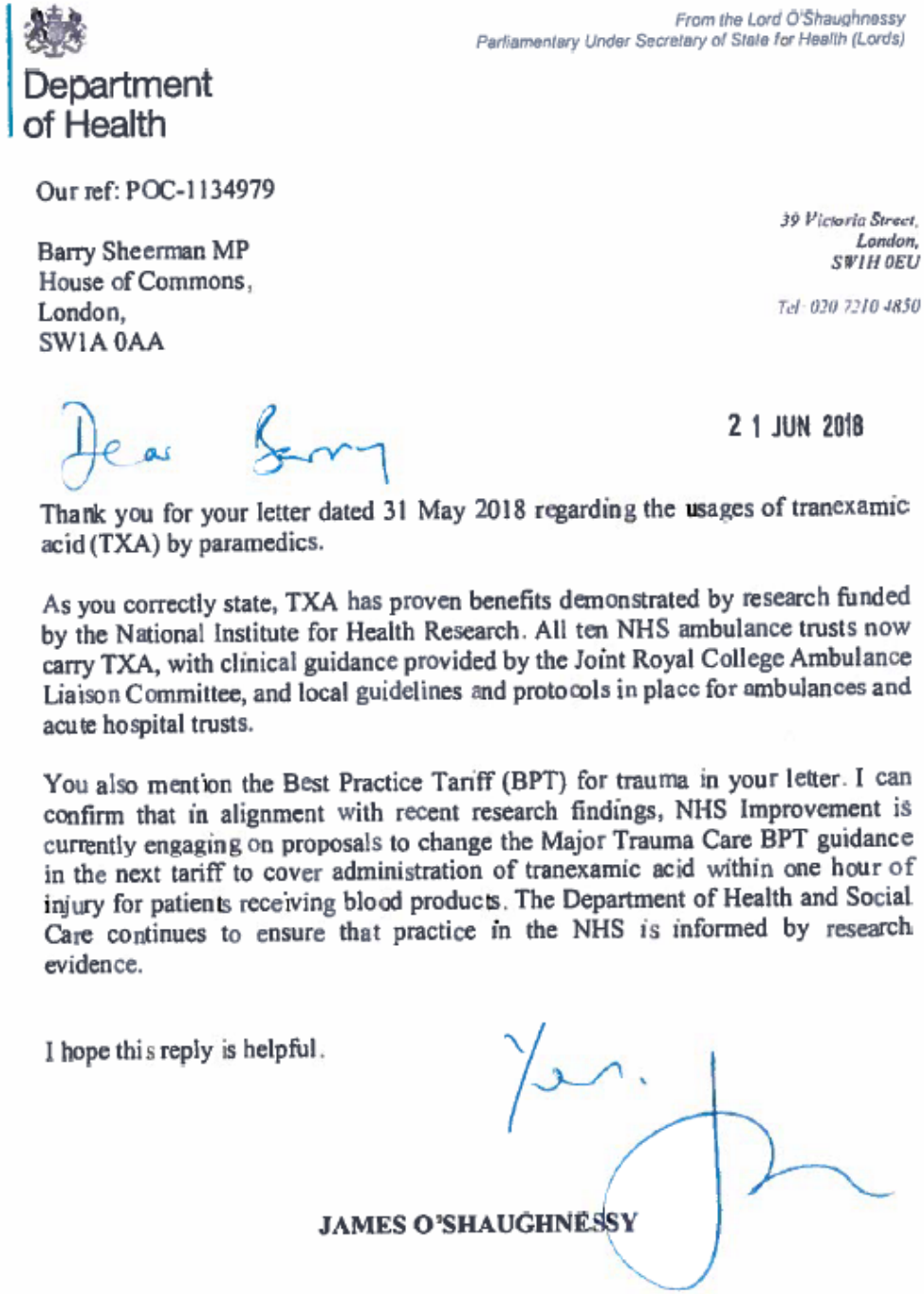
YEAR 2016

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

30% trauma patients received TXA within the first hour

median 49 minutes (33 – 72)

median 111 minutes (77 – 162)



Department of Health

From the Lord O'Shaughnessy
Parliamentary Under Secretary of State for Health (Lords)

Our ref: POC-1134979

Barry Sheerman MP
House of Commons,
London,
SW1A 0AA

39 Victoria Street,
London,
SW1H 0EU

Tel: 020 7210 4850

21 JUN 2018

Dear Barry

Thank you for your letter dated 31 May 2018 regarding the usages of tranexamic acid (TXA) by paramedics.

As you correctly state, TXA has proven benefits demonstrated by research funded by the National Institute for Health Research. All ten NHS ambulance trusts now carry TXA, with clinical guidance provided by the Joint Royal College Ambulance Liaison Committee, and local guidelines and protocols in place for ambulances and acute hospital trusts.

You also mention the Best Practice Tariff (BPT) for trauma in your letter. I can confirm that in alignment with recent research findings, NHS Improvement is currently engaging on proposals to change the Major Trauma Care BPT guidance in the next tariff to cover administration of tranexamic acid within one hour of injury for patients receiving blood products. The Department of Health and Social Care continues to ensure that practice in the NHS is informed by research evidence.

I hope this reply is helpful.

JAMES O'SHAUGHNESSY

Best practice tariff for trauma:

Incentive payment if "TXA given within 3 hours if patient receives blood within 6 hours.

in alignment with recent research..

"TXA within one hour for patients receiving blood products."

Intramuscular TXA in healthy volunteers

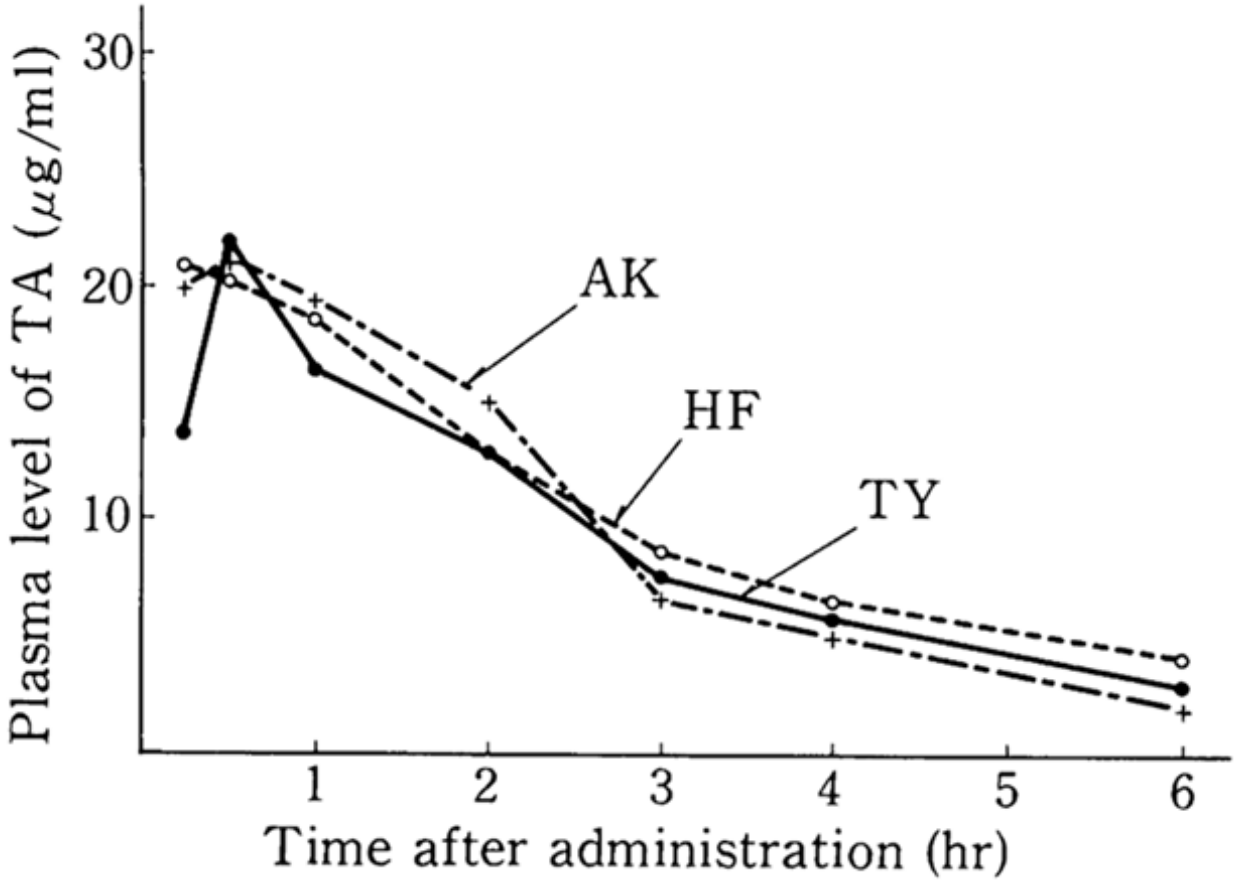
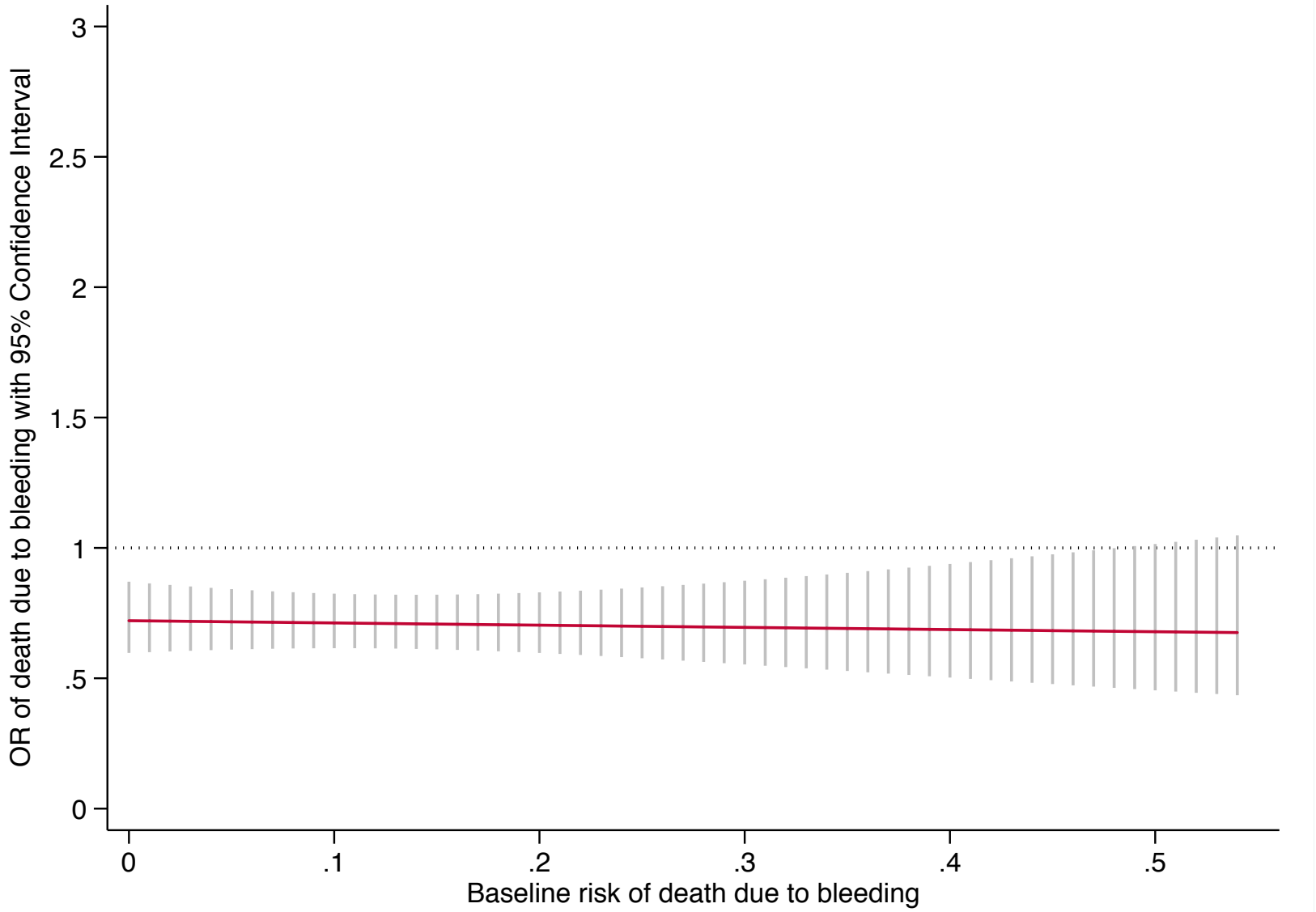


Fig. 5 Plasma levels of TA 500 mg/man, i. m.

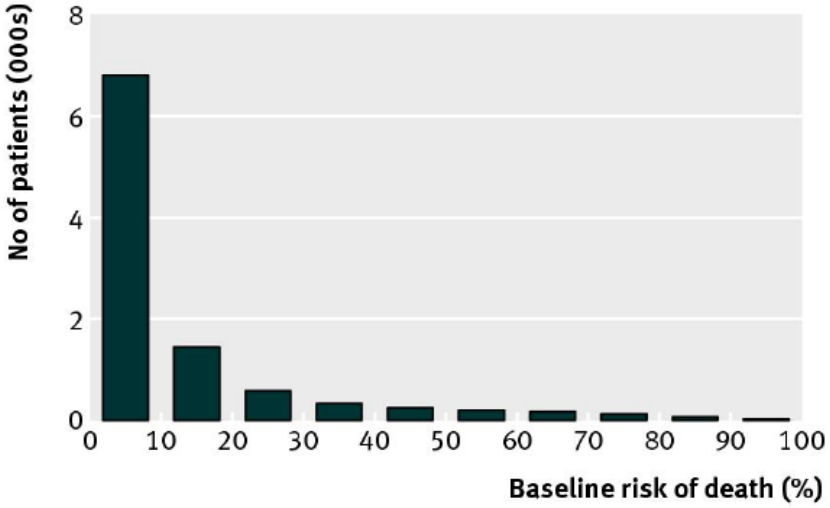
TXA: Same benefit regardless of baseline risk

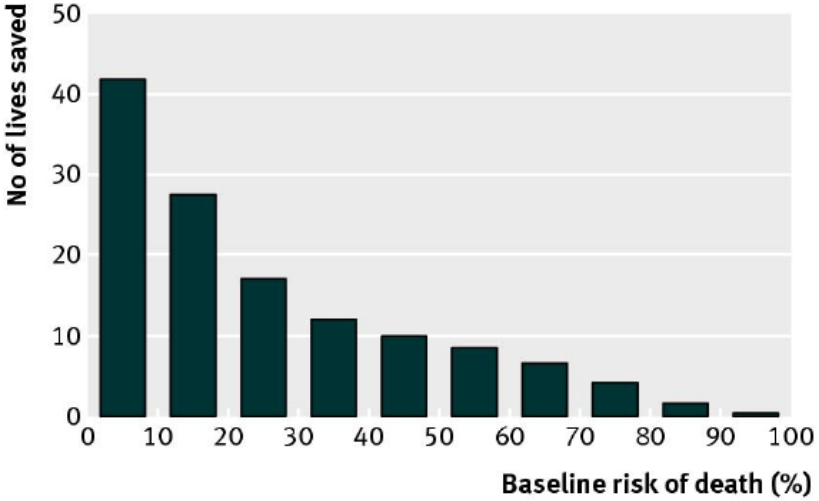
(Francois Agero)



Most trauma patients have a low baseline risk

We need to treat all trauma patients





Tranexamic acid

Safely prevents bleeding

Give it early to all patients at risk

Not about massive transfusion

Not about acute traumatic coagulopathy

Tranexamic acid ‘vaccination’ against serious bleeding