Tranexamic acid for the prevention of postpartum bleeding in women with moderate and severe anaemia: an international, randomised, double-blind, placebo-controlled trial

The WOMAN-2 Trial Collaborators

CLINICAL TRIALS UNIT

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

TRANEXAMIC ACID

A drug that reduces bleeding

Results from the WOMAN trial

World Maternal Antifibrinolytic Trial

20,000 WOMEN
21 COUNTRIES
193 HOSPITALS

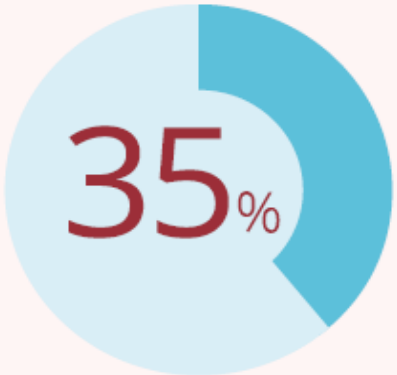
The drug could save

1/3

of women who would otherwise bleed to death after childbirth

An estimated **100,000** women die from severe bleeding after giving birth every year

The drug reduced the number of women bleeding to death after childbirth by more than 30%



The drug reduced the need for urgent surgery to control bleeding by more than 35%

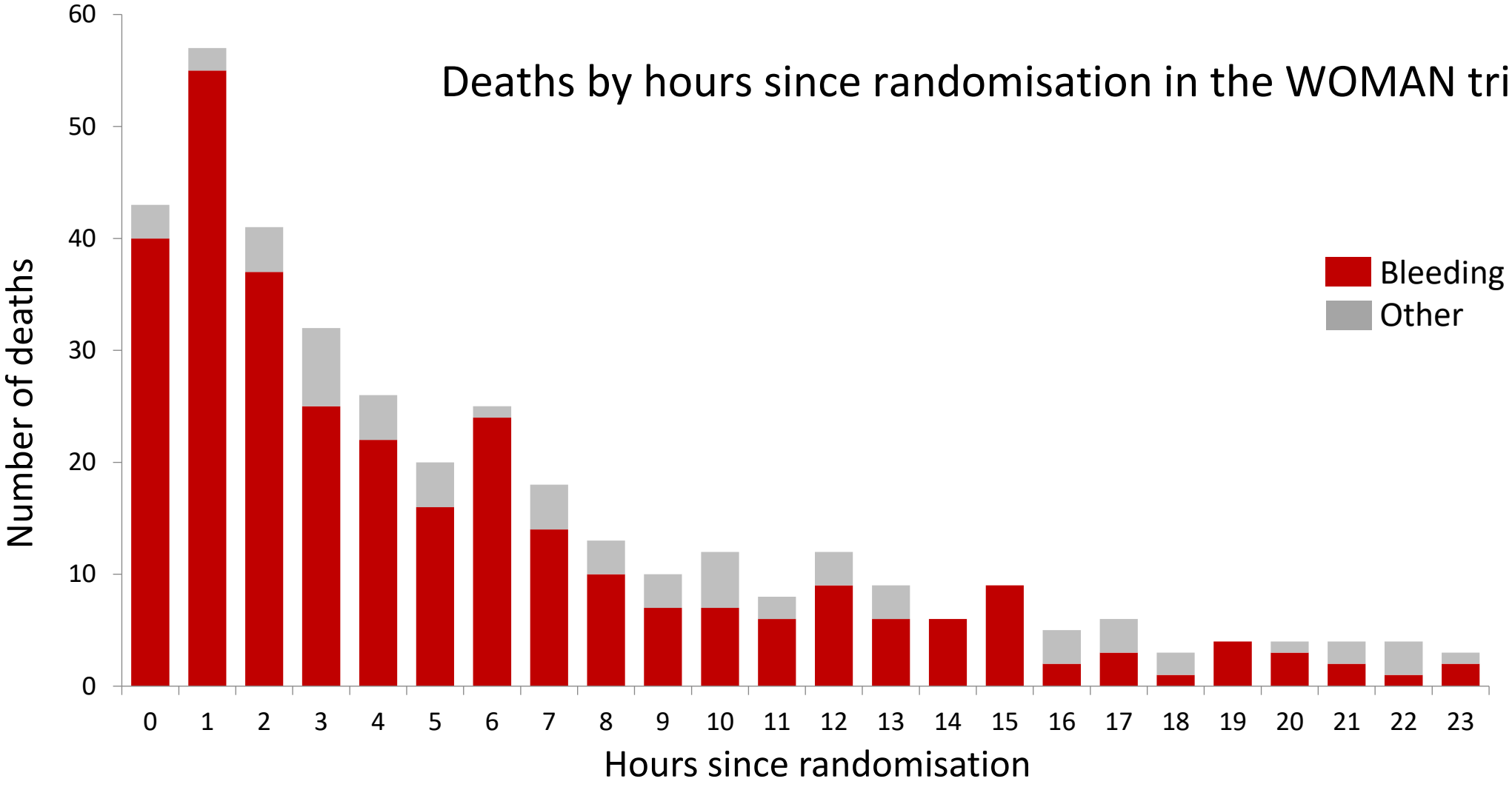
£2 ($2.5)

The cost of tranexamic acid in most countries

Source: The WOMAN trial (2017)
Credit: Rebeccah Robinson/LSHTM

Find out more at **womantrial.lshtm.ac.uk**

For some women treatment is too late



The WOMAN Trial Collaborators. Lancet. 2017 ; 389 (10084): 2105-16.

Why WOMAN-2?

"Our women are different."

Professor Bukola Fawole (1960-2019)

The WOMAN-2 Trial

Aim

- To determine the effect of TXA on postpartum bleeding in women with moderate or severe anaemia

Trial design

- Randomised, double-blind, placebo-controlled trial
- 15 000 women with moderate or severe anaemia who are giving birth vaginally in hospitals
- Randomised to receive 1 g of TXA or matching placebo (sodium chloride 0.9%) intravenously immediately and no later than 15 minutes after the umbilical cord is cut or clamped

Inclusion criteria

- Women with moderate or severe anaemia (Hb level <100 g/L or PCV <30%), who have given birth vaginally and for who the responsible clinician is substantially uncertain whether to use TXA

The WOMAN-2 Trial

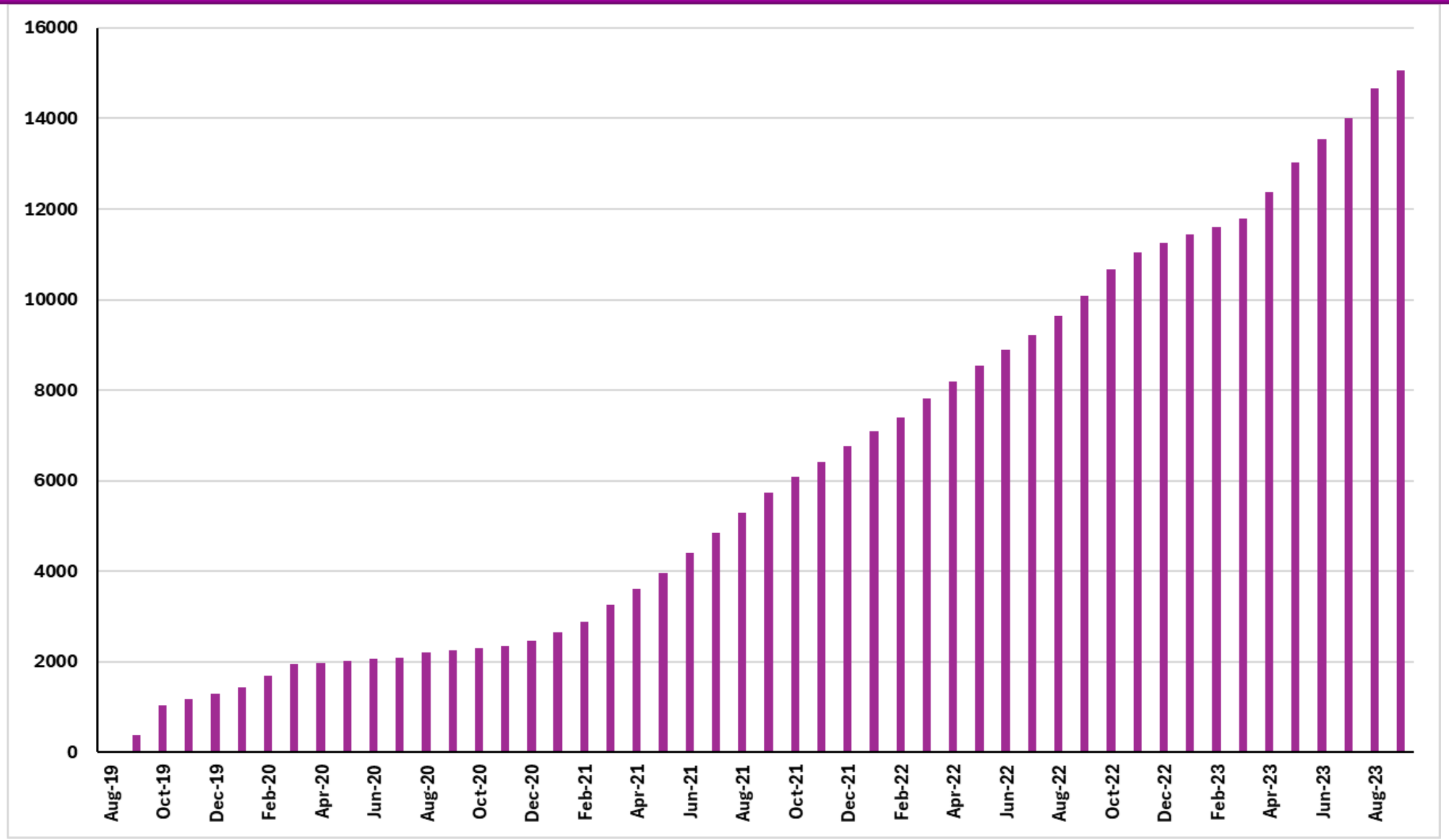
Exclusion criteria

- Women who are not legally adult (<18 years) and permission not provided by a guardian
- Women with a known allergy to TXA or its excipients
- Women who develop PPH before umbilical cord is clamped/cut

Follow-up

- Outcomes related to PPH collected at 24 hours, discharge, or death, whichever occurred first
- Other outcomes collected at day 42, discharge, or death, whichever occurred first
- Adverse events were monitored for up to 42 days after randomisation

Participant enrolment

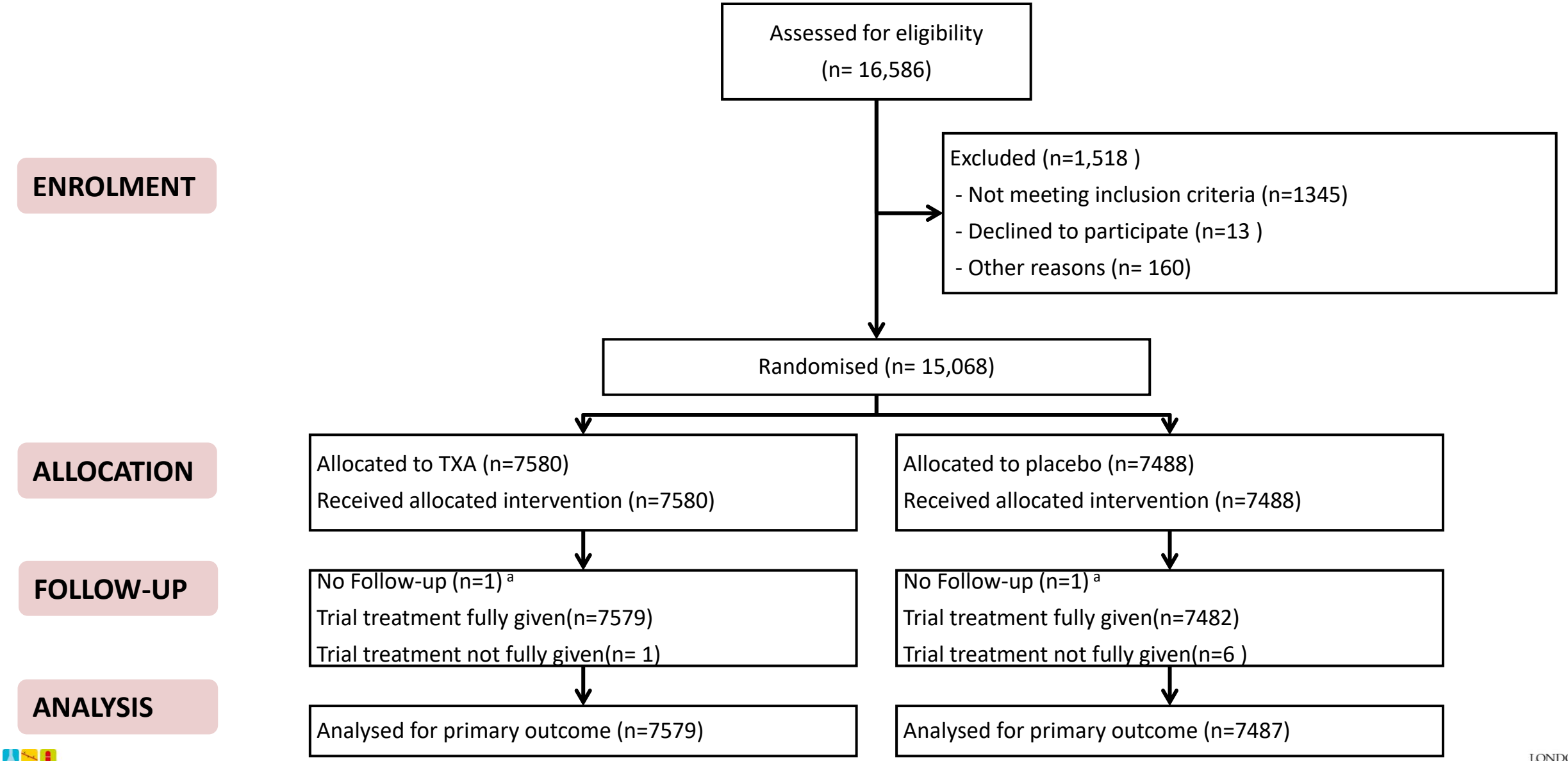


Participant enrolment

15, 068 participants randomised in Nigeria, Pakistan, Tanzania and Zambia

COUNTRY	RANDOMISED
Nigeria	1 326
Pakistan	11 025
Tanzania	2 029
Zambia	688
TRIAL	**15 068**

Trial profile



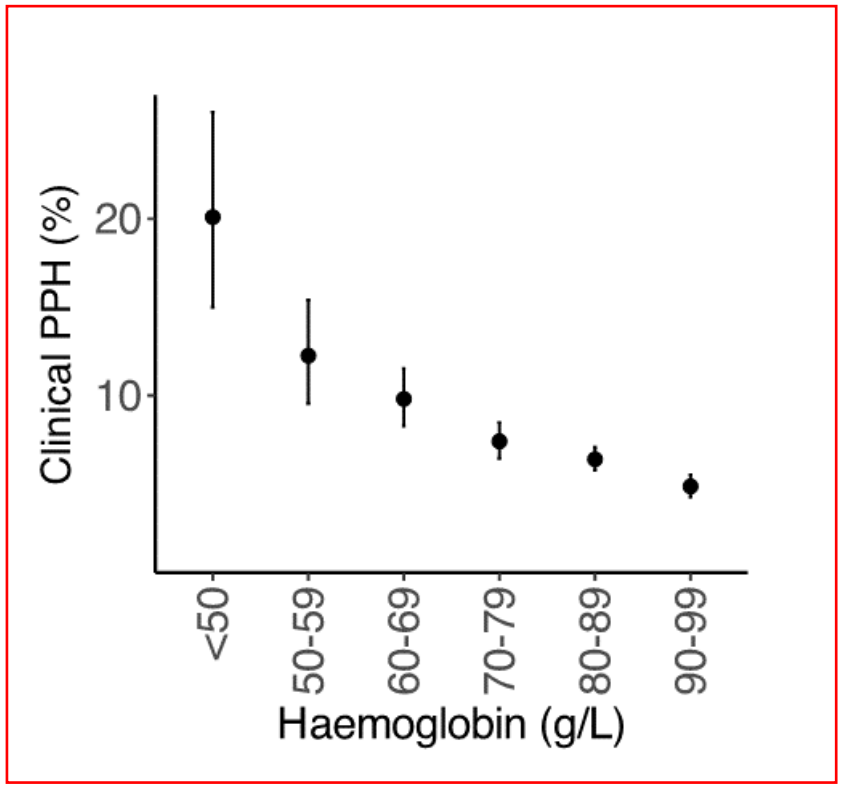
[a] = Patients for whom there is no information about the primary endpoint.

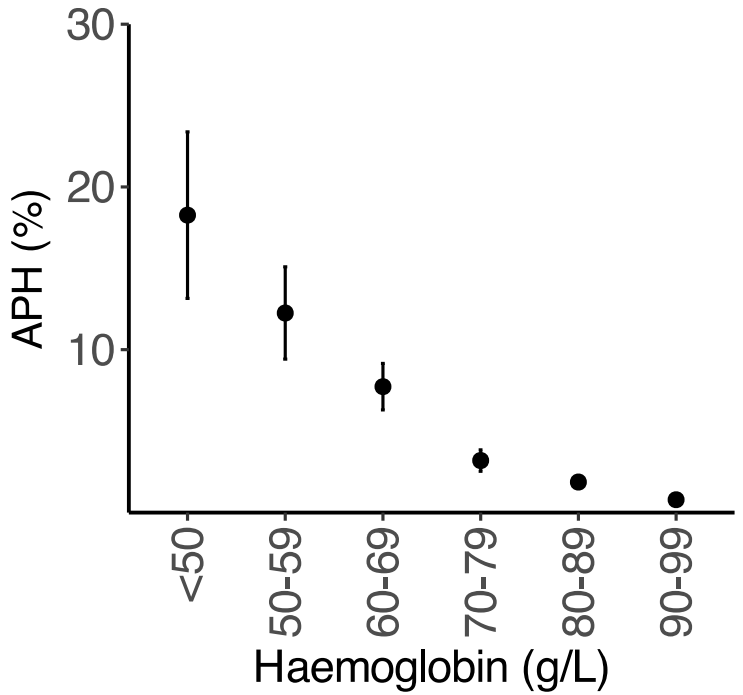
Baseline characteristics

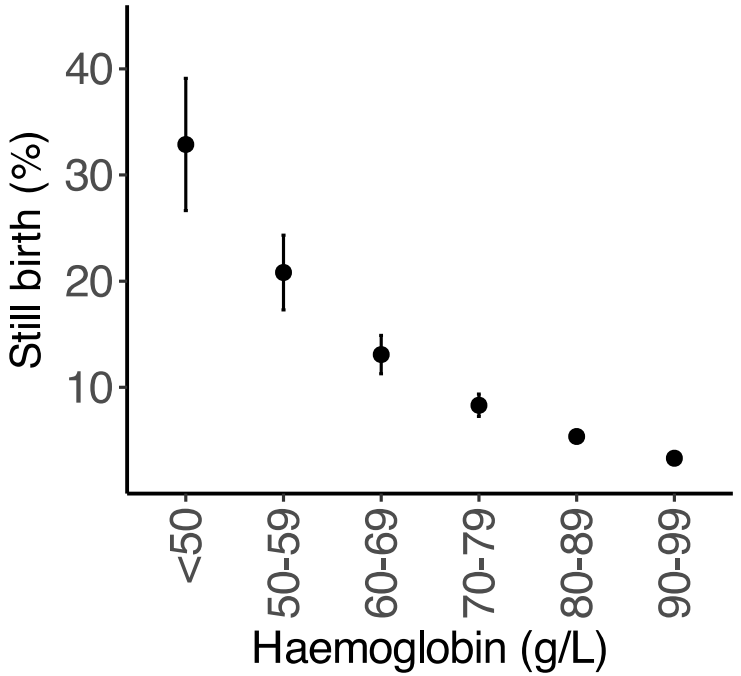
	Tranexamic acid group (n=7580)	Placebo group (n=7488)
Mean age, years	27·3 (5·6)	27·1 (5·6)
Haemoglobin, g/L		
Mean	82·7 (11·8)	82·8 (11·9)
Moderate (70–99 g/L)	6527 (86·1%)	6462 (86·3%)
Severe (<70 g/L)	1053 (13·9%)	1026 (13·7%)
Mean estimated gestation, weeks	37·4 (2·7)	37·4 (2·7)
Number of fetuses		
1	7290 (96·2%)	7195 (96·1%)
2	283 (3·7%)	285 (3·8%)
3	7 (0·1%)	8 (0·1%)
Placental abnormalities		
Abruption	210 (2·9%)	221 (2·3%)
Previa	15 (0·2%)	26 (0·4%)
Accreta	1 (<0·1%)	2 (<0·1%)
Antepartum haemorrhage	207 (2·7%)	228 (3·0%)
Pre-eclampsia	162 (2·1%)	159 (2·1%)

	Tranexamic acid group (n=7580)	Placebo group (n=7488)
Stillbirths per mother		
1	507 (6·7%)	509 (6·8%)
2	7 (0·1%)	13 (0·2%)
Macrosomia (>4000 g)	57 (0·8%)	51 (0·7%)
Assisted delivery		
Ventouse	119 (1·6%)	116 (1·5%)
Forceps	61 (0·8%)	63 (0·8%)
Other	35 (0·5%)	33 (0·4%)
Lacerations and tears		
Perineal	865 (11·4%)	923 (12·3%)
Cervical	165 (2·2%)	169 (2·3%)
Vaginal	85 (1·1%)	78 (1·0%)
Prophylactic uterotonics		
Oxytocin	7569 (99·9%)	7479 (99·9%)
Misoprostol	27 (0·4%)	22 (0·3%)
Ergometrine	3 (<0·1%)	8 (0·1%)
Prostaglandins	1 (<0·1%)	3 (<0·1%)

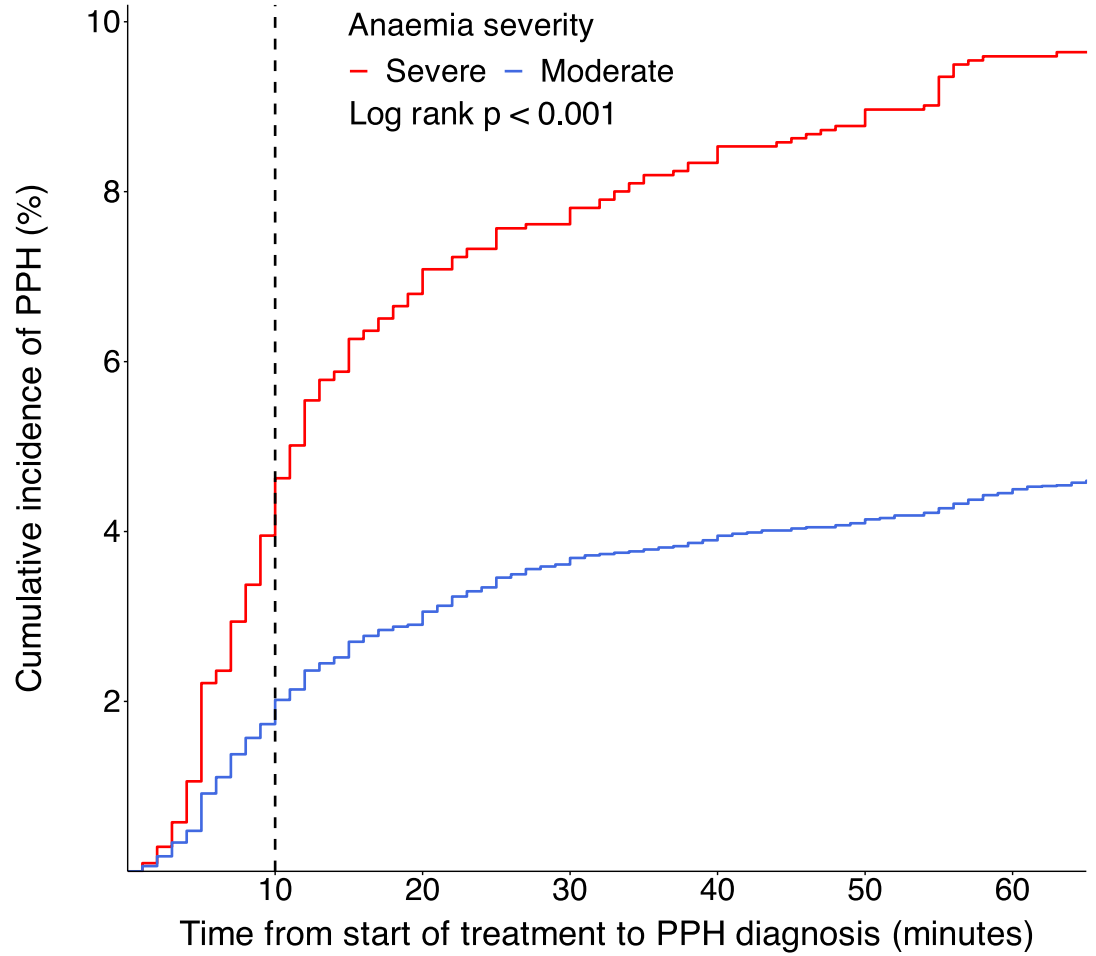
Baseline characteristics by maternal haemoglobin concentration







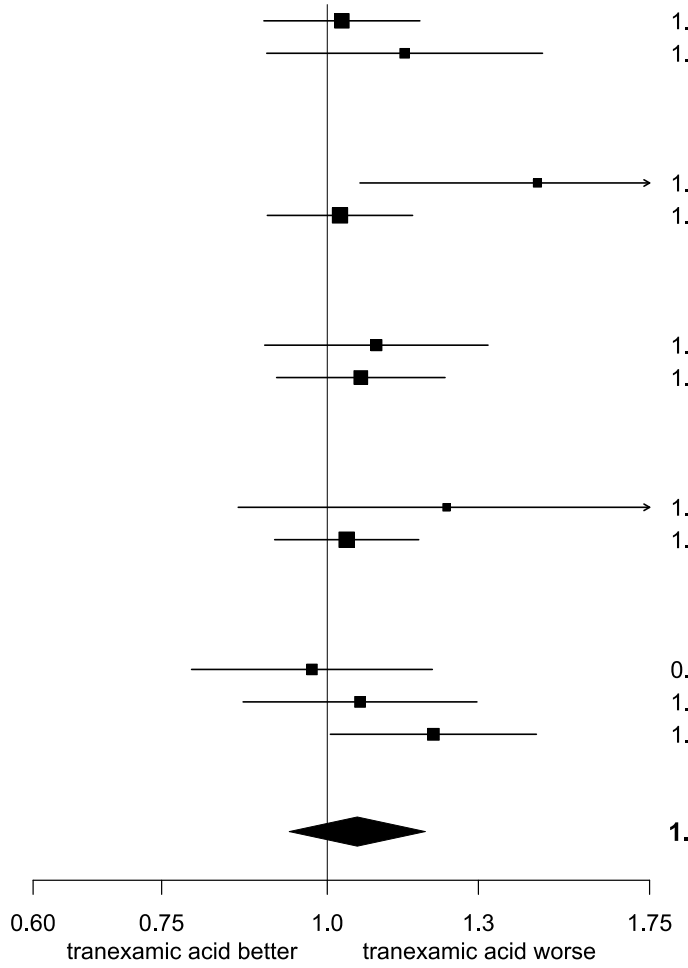
Women with anaemia bleed faster and decompensate sooner



TXA in women with moderate & severe anaemia

Outcome is clinically diagnosed postpartum haemorrhage

	Tranexamic acid allocated N = 7579	Placebo allocated N = 7487	RR	95% CI
Anaemia severity				
Moderate (70-99g/L)	401/6527 (6%)	387/6461 (6%)	1.03	(0.90-1.17)
Severe (<70 g/L)	129/1052 (12%)	110/1026 (11%)	1.14	(0.90-1.45)
p=0.44				
Antepartum haemorrhage				
Yes	68/207 (33%)	52/228 (23%)	1.44	(1.06-1.96)
No	462/7372 (6%)	445/7259 (6%)	1.02	(0.90-1.16)
p=0.044				
Traumatic birth				
Yes	175/1071 (16%)	170/1133 (15%)	1.09	(0.90-1.32)
No	355/6508 (5%)	327/6354 (5%)	1.06	(0.92-1.23)
p=0.83				
Any pain control				
Yes	63/925 (7%)	49/885 (6%)	1.23	(0.86-1.77)
No	467/6654 (7%)	448/6602 (7%)	1.03	(0.91-1.17)
p=0.37				
Risk of PPH				
Low	171/5151 (3%)	169/4957 (3%)	0.97	(0.79-1.20)
Medium	170/1816 (9%)	169/1911 (9%)	1.06	(0.86-1.30)
High	189/612 (31%)	159/619 (26%)	1.20	(1.01-1.44)
p=0.31				
Overall	**530/7579 (7%)**	**497/7487 (7%)**	**1.05**	**(0.94-1.19)**



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Lancet 2024; 404: 1645-56

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TXA in women with moderate & severe anaemia

	Tranexamic acid (n=7579)	Placebo (n=7487)	RR	95% CI	p value
Estimated blood loss (ml)					
Mean(SD)	309·8 (193·9)	310·8 (191·5)	-0·95	(-7·10-5·21)	0·76
Haemoglobin* (g/L)					
Mean(SD)	82·2 (15·5)	82·1 (15·7)	0·12	(-0·26-0·50)	0·54
Vascular occlusive event**					
Any event	0	0			
Death or near miss death***					
Any death or near miss	122 (1·6%)	137 (1·8%)	0·88	(0·69-1·12)	0·30

**corrected for the effect of blood transfusion*

***pulmonary embolism, deep vein thrombosis, stroke and myocardial infarction*

****Death from any cause or near-miss death from PPH. Near miss death for PPH is defined by the WHO as severe PPH (blood loss of 1000ml+), surgical intervention for bleeding (hysterectomy for bleeding, laparotomy, embolization, uterine compression sutures, arterial ligation), failure to form clots, transfusion of >5 units, cardiovascular dysfunction (shock, cardiac arrest, continuous vasoactive drugs, severe hypoperfusion, severe acidosis, CPR), renal dysfunction diagnosed (oliguria non-responsive to fluids or diuretics, dialysis for acute renal failure, severe acute azotemia)*

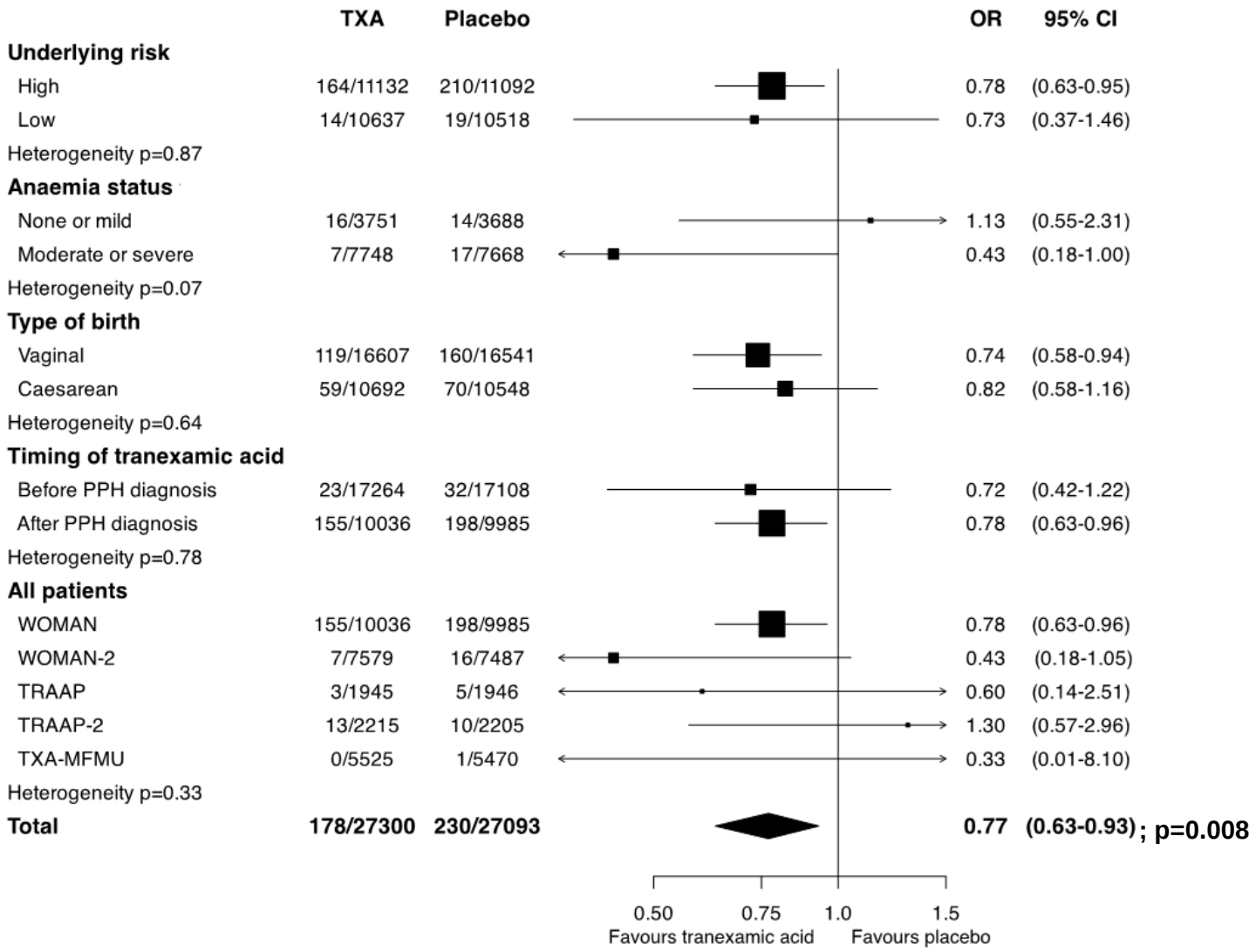
Effect of TXA on life-threatening bleeding

Tranexamic acid for postpartum bleeding: a systematic review and individual patient data meta-analysis of randomised controlled trials

Katharine Ker, Loïc Sentilhes, Haleema Shakur-Still, Hugo Madar, Catherine Deneux-Tharaux, George Saade, Luis D Pacheco, François-Xavier Ageron, Raoul Mansukhani, Eni Balogun, Amy Brenner, Danielle Prowse, Monica Arribas, Homa Ahmadzia, Rizwana Chaudhri, Oladapo Olayemi, Ian Roberts, for The Anti-fibrinolytics Trialists Collaborators Obstetric Group

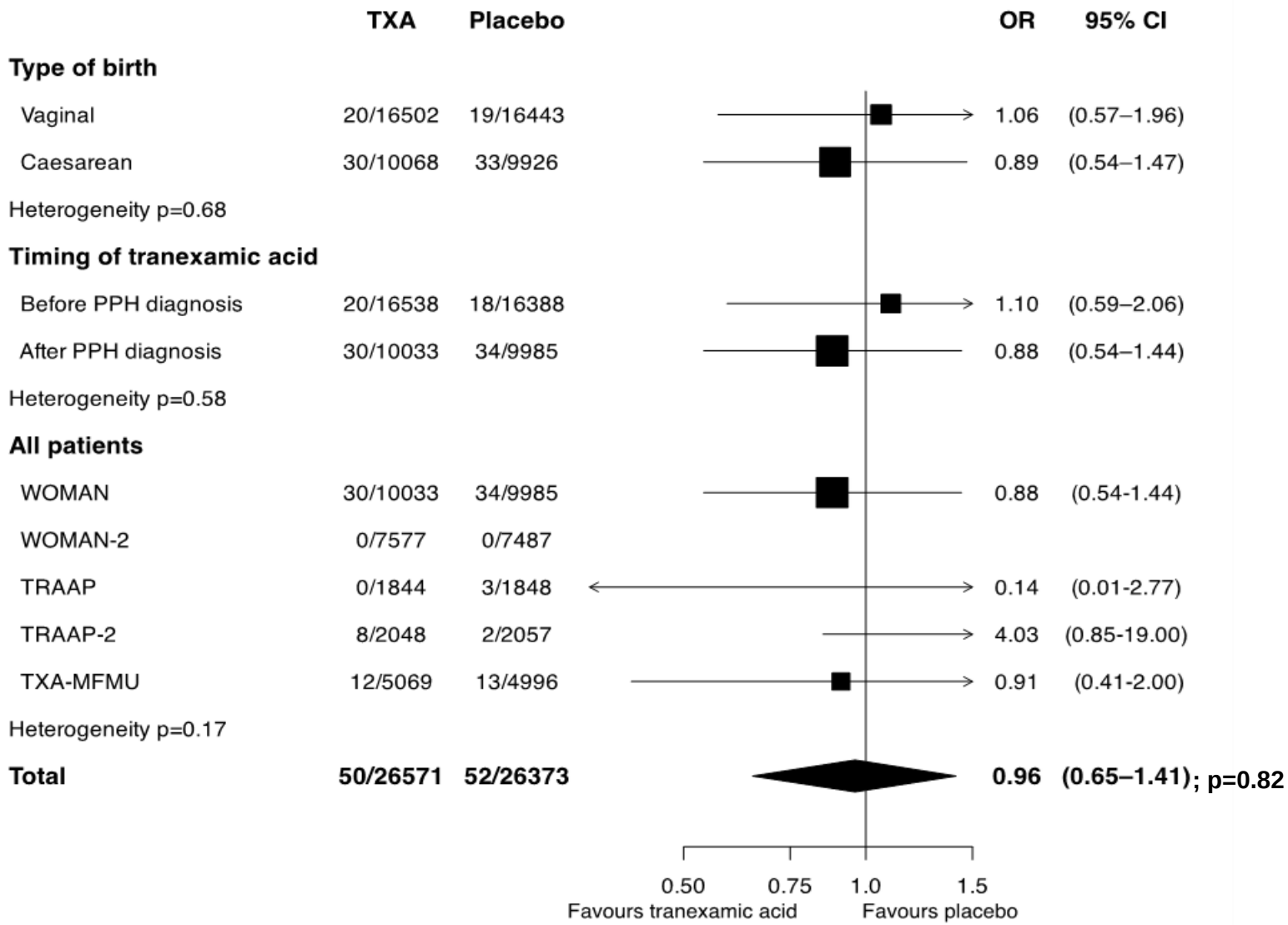
Lancet 2024; 404: 1657–67

Effect of TXA on life-threatening bleeding*



*death or surgical intervention for bleeding (laparotomy, embolization, uterine compression sutures, or arterial ligation) within 24 hours after birth.

Effect of TXA on fatal or non-fatal thromboembolic events



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Implications for obstetric care

- **Tranexamic acid did not prevent clinically diagnosed postpartum haemorrhage in women with moderate or severe anaemia**
- **No evidence of adverse effects**
- **Anaemia is a strong risk factor for life-threatening bleeding after birth. So, we must prevent and treat anaemia in women of childbearing age.**
- **There is strong evidence that TXA reduces life-threatening bleeding. We must make sure that TXA is available for all women who need it.**

Funded by:

Gates Foundation

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https://www.lshtm.ac.uk/research/centres-projects-groups/the-woman-trials