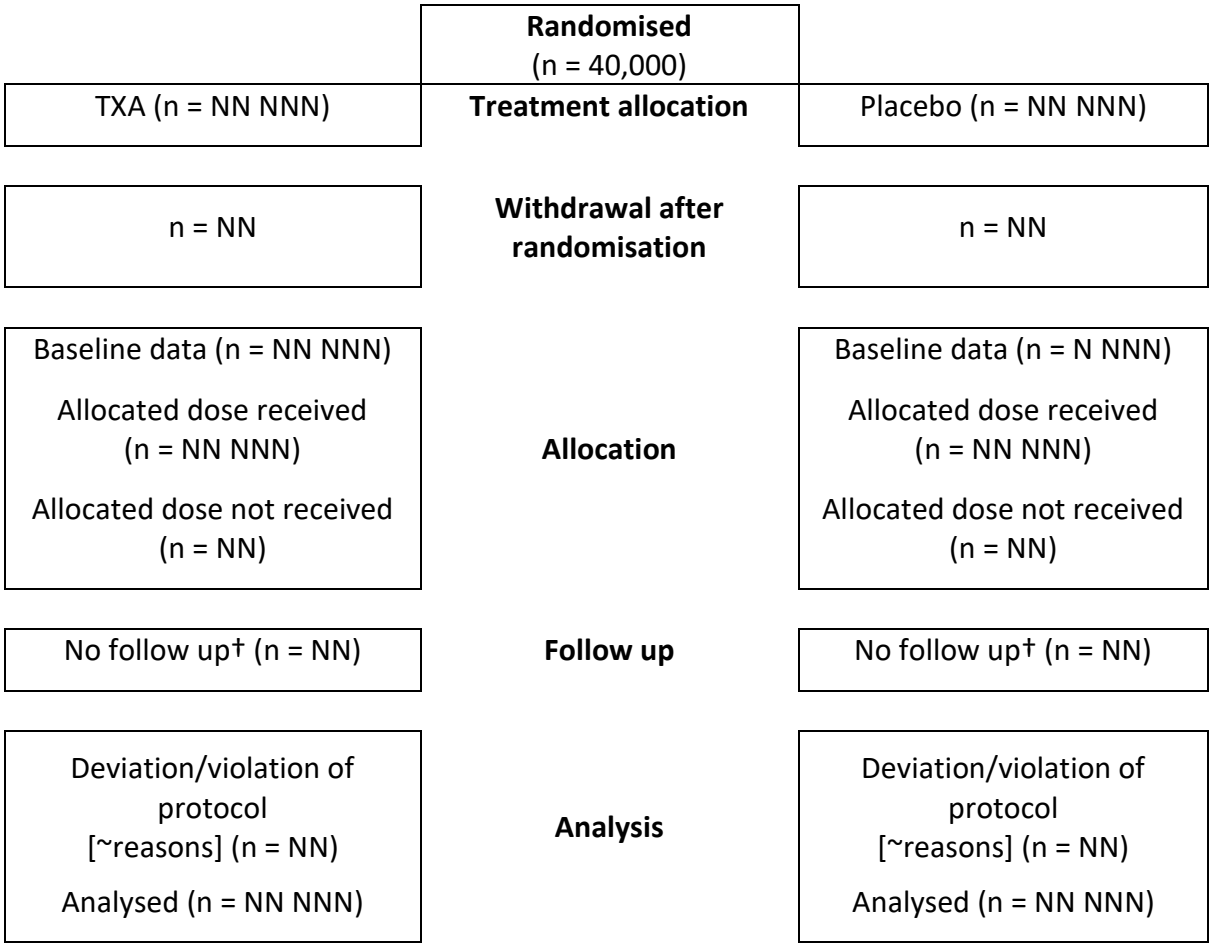
Appendix: Statistical Analysis Plan Shell Tables

PAPER A. Effects of TXA on bleeding-related outcomes and adverse events in mother and infant

Paper A - Figure 1: Trial Profile



† No follow-up relates to those participants where there is no information on the primary endpoint

Paper A - Table 1. Baseline characteristics of participants prior to randomisation

Baseline characteristics	**TXA** (n = NN) n (%)	**Placebo** (n = NN) n (%)
Maternal age, years (mean, SD)		
Gestational age, weeks (mean, SD)		
Parity (including current pregnancy)		
1		
2		
3		
≥4		
Baseline anaemia (Hb g/L)		
Not anaemic (≥110)		
Mild (100-109)		
Moderate (70-99)		
Severe (<70)		
Missing		
Postpartum haemorrhage risk factors		
Increased maternal age (≥ 35 years)		
Parity (≥4)		
Hypertensive disorder		
Moderate or severe anaemia		
Fibroids		
Multiple pregnancy		
Preterm birth (<37 weeks)		
Abnormal placental implantation		
Antepartum haemorrhage or abruption		
Prolonged labour (>12 hours)		
Obstructed labour		
Dead foetus in utero		
Previous caesarean section		
Caesarean birth planned		
Emergency caesarean section		
Other		
Number of PPH risk factors		
1		
2		
≥3		

Abbreviations: TXA, Tranexamic Acid; PPH, Postpartum Haemorrhage; N, Number; SD, Standard Deviation; Hb, Haemoglobin.

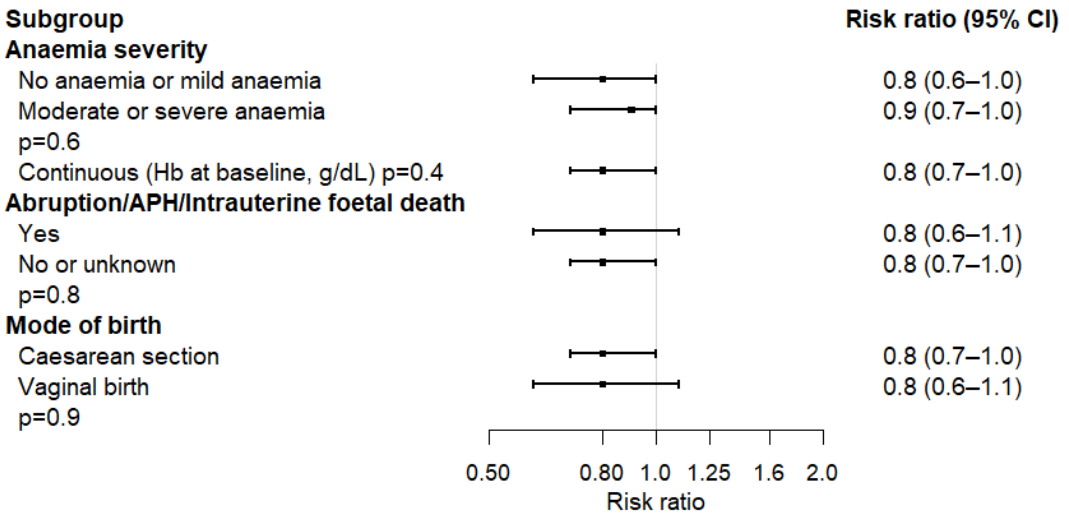
Paper A - Table 2. Effect of tranexamic acid on clinical diagnosis of postpartum haemorrhage, bleeding related death or near miss, blood loss and haemoglobin concentration

	TXA (n = NN)	Placebo (n = NN)	Estimate (95% CI) *
Clinical diagnosis of PPH	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Causes of PPH			
Uterine atony	NN (X%)	NN (X%)	-
Anaemia	NN (X%)	NN (X%)	-
Retained placenta/placental abnormalities/abruption	NN (X%)	NN (X%)	-
Tears/lacerations/episiotomy	NN (X%)	NN (X%)	-
Coagulopathy	NN (X%)	NN (X%)	-
Other	NN (X%)	NN (X%)	-
Unknown	NN (X%)	NN (X%)	-
Sensitivity analysis			
Exclusion of women with prophylactic non-trial TXA	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Covariate adjustment‡	-	-	X.XX (X.XX–X.XX)
Bleeding-related death or near miss†	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Death due to bleeding within 24 h of birth	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Severe PPH	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Major interventions for bleeding within 24h of birth	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Renal or cardiovascular dysfunction	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Measured blood loss, mL (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Blood loss category (mL)			X.XX (X.XX–X.XX)
0-299	NN (X%)	NN (X%)	-
300-499	NN (X%)	NN (X%)	-
500-999	NN (X%)	NN (X%)	-
1000-1499	NN (X%)	NN (X%)	-
≥1500	NN (X%)	NN (X%)	-
Intraoperative blood loss, mL (mean) ^	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Drape-measured blood loss, mL (mean) ^	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Peripartum haemoglobin change, g/L (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Postpartum haemoglobin (g/L (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Haemoglobin category			X.XX (X.XX–X.XX)
No anaemia (≥110)	NN (X%)	NN (X%)	-
Mild anaemia (100-109)	NN (X%)	NN (X%)	-
Moderate anaemia (70-99)	NN (X%)	NN (X%)	-
Severe anaemia (<70)	NN (X%)	NN (X%)	-

Abbreviations: TXA, Tranexamic Acid; CI, Confidence Interval; PPH, Postpartum Haemorrhage.
Causes of PPH are not mutually exclusive. Measured blood loss is calibrated obstetric drape measured blood loss for vaginal births and intraoperative plus drape measured blood loss for caesarean births. Postpartum Hb was corrected for blood transfusion given during CS and up to 24h after birth.

*Mean difference for continuous variables (measured blood loss, peripartum haemoglobin change and corrected postpartum haemoglobin), common OR for categorical variables (measured blood loss category and corrected postpartum haemoglobin category), and RR for the binary variables (clinical diagnosis of PPH and bleeding-related death or near-miss).
† Severe PPH is defined as peripartum Hb drop ≥25 g/L or measured blood loss ≥1500 mL. Major interventions for bleeding include hysterectomy, laparotomy, arterial embolization or ligation, uterine compression sutures, or a transfusion of ≥5 units of blood intraoperatively and up to 24 h after birth. Cardiovascular dysfunction was diagnosed based on shock, cardiac arrest, continuous vasoactive drugs, severe hypoperfusion, severe acidosis, and/or cardiopulmonary resuscitation. Renal dysfunction was diagnosed based on oliguria non-responsive to fluids or diuretics, dialysis for acute renal failure, and/or severe acute azotaemia.
‡ Adjusted for country, age, pre-birth haemoglobin, abnormal placental implantation, APH, dead foetus in utero, hypertensive disorder of pregnancy, fibroids, multiple pregnancy, and mode of birth.
^ Caesarean births only.

Paper A - Figure 2. Effect of tranexamic acid on clinical diagnosis of postpartum haemorrhage, by subgroups



Abbreviations: CI, Confidence Interval; APH, Antepartum Haemorrhage.
† p-values from adjusted tests of interaction in a Poisson model with robust error variance to assess evidence for whether the effect of treatment differs across subgroup categories.
‡ Anaemia severity analysis adjusted for APH, intrauterine foetal death and mode of birth.
Antepartum haemorrhage/APH/intrauterine foetal death analysis adjusted for anaemia severity, mode of birth, and time from randomisation to birth.
Mode of birth analysis adjusted for anaemia severity, APH, and time from randomisation to birth.

Paper A - Figure 3. Postpartum haemoglobin and measured blood loss by randomised group

Histogram(s) showing the distribution of transfusion-corrected postpartum Hb and measured blood loss by randomised group.

Paper A - Figure 4. Setting the results in the context of other trials of tranexamic acid – effect of tranexamic acid on clinical diagnosis of postpartum haemorrhage

Meta-analysis of large, high quality, randomised controlled trials of TXA for PPH, stratified by anaemia severity, APH, and mode of birth

Paper A - Table 3. Effect of tranexamic acid on maternal death, complications and interventions

	TXA (n = NN)	Placebo (n = NN)	Estimate (95% CI) *
Death (all-cause)	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Causes of death			
Bleeding	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Eclampsia	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Organ failure	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Pulmonary embolism	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Sepsis	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Other	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Vascular occlusive event †	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Deep vein thrombosis	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Pulmonary embolism	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Myocardial infarction	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Stroke	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Seizure †	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
By dose of TXA, g			
None	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
<2g	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
≥2g	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
(p=0.XXX) ‡			
Sepsis †	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Organ dysfunction †	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Coagulopathy †	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Intervention for bleeding	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Non-trial TXA	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Uterotonics	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Blood transfusion	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Surgical interventions	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Non-surgical interventions	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Cervical, vaginal or perineal sutures	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Length of surgery	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Length of hospital stay (days)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Days in ICU or HDU	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Transfer to another hospital	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Systolic blood pressure, mmHg	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Diastolic blood pressure, mmHg	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Heart rate, BPM	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)

Abbreviations: TXA = Tranexamic Acid; CS, Caesarean Section; ICU = Intensive Care Unit; HDU = High Dependency Unit; BPM Beats Per Minute.

Surgical interventions for bleeding include hysterectomy, laparotomy, arterial embolization or ligation and uterine compression sutures. Non-surgical interventions for bleeding include bimanual compression, external aortic compression, uterine tamponade, or packing.

† Prespecified AEs include death, vascular occlusive event, seizure, sepsis, organ dysfunction and coagulopathy.

‡ p-value from adjusted tests of interaction in a binomial or Poisson model with robust error variance to assess evidence for whether the effect of treatment differs across subgroup categories

*Mean difference for continuous variables (length of surgery, lengthy of hospital stay, days in ICU or HDU, blood pressure and heart rate) and RR for all other binary variables.

Paper A - Table 4. Safety and tolerability of tranexamic acid compared to placebo

	TXA (n = NN)	Placebo (n = NN)	Estimate (95% CI) *
Retching/vomiting episodes	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Nausea score (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Dizziness score (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Pain score - IM injection sites (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Pain score - IV injection site (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Adverse reaction - IM injection sites	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Adverse reaction - IV injection sites	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)

Abbreviations: TXA, Tranexamic Acid; CI, Confidence Interval; IM, Intramuscular; IV, Intravenous.
*Mean difference for continuous variables (nausea, dizziness, pain) and RR for all other binary variables.

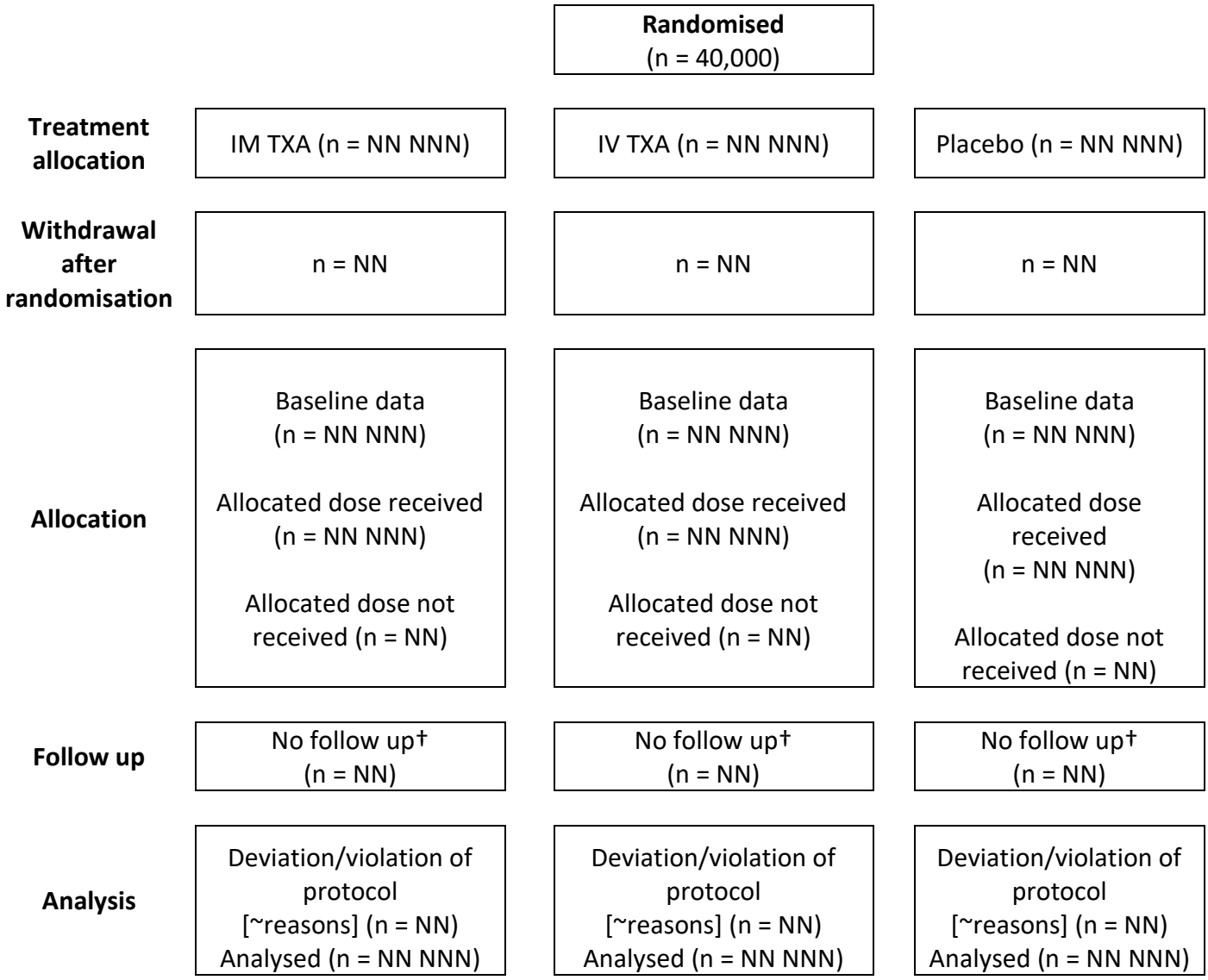
Paper A - Table 5. Effect of tranexamic acid on neonatal outcomes

	TXA (n = NN)	**Placebo** (n = NN)	**Risk ratio (95% CI)**
Stillbirth/intrapartum death	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Neonatal death	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Intracranial or pulmonary haemorrhage	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Bruising	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Thromboembolic event	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Seizure	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Breastfed	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Congenital and genetic abnormalities	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Cause of death			
A	N (X%)	N (X%)	-
B	N (X%)	N (X%)	-
C	N (X%)	N (X%)	-

Abbreviations: TXA, Tranexamic Acid; CI, Confidence Interval.

PAPER B. The effects of IM TXA on severe bleeding and adverse effects

Figure 1: Trial Profile



† No follow-up relates to those participants where there is no information on the primary endpoint

Paper B - Table 1. Baseline characteristics of participants prior to randomisation

Baseline characteristics	IM TXA (n = NN)		IV TXA (n = NN)		Placebo (n = NN)	
	n	(%)	n	(%)	n	(%)
Maternal age, years (mean, SD)						
Gestational age, weeks (mean, SD)						
Parity (including current pregnancy)						
1						
2						
3						
≥4						
Baseline anaemia (Hb g/L)						
Not anaemic (≥110)						
Mild (100-109)						
Moderate (70-99)						
Severe (<70)						
Missing						
Postpartum haemorrhage risk factors						
Increased maternal age (≥ 35 years)						
Parity (≥4)						
Hypertensive disorder						
Moderate or severe anaemia						
Fibroids						
Multiple pregnancy						
Preterm birth (<37 weeks)						
Abnormal placental implantation						
Antepartum haemorrhage or abruption						
Prolonged labour (>12 hours)						
Obstructed labour						
Dead foetus in utero						
Previous caesarean section						
Caesarean birth planned						
Emergency caesarean section						
Other						
Number of PPH risk factors						
1						
2						
≥3						

Abbreviations: TXA, Tranexamic Acid; PPH, Postpartum Haemorrhage; N, Number; SD, Standard Deviation; Hb, Haemoglobin.

Paper B - Table 2. Effect of IM tranexamic acid on a clinical diagnosis of postpartum haemorrhage, bleeding related death or near miss, blood loss and haemoglobin concentration (superiority analysis)

	IM TXA (n = NN)	Placebo (n = NN)	Estimate (95% CI) *
Clinical diagnosis of PPH	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Sensitivity analysis			
Exclusion of women with prophylactic non-trial TXA	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Covariate adjustment‡	-	-	X.XX (X.XX–X.XX)
Bleeding-related death or near miss†	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Death due to bleeding within 24 h of birth	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Severe postpartum haemorrhage	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Major interventions for bleeding within 24h of birth	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Renal or cardiovascular dysfunction	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Measured blood loss, mL (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Blood loss category			X.XX (X.XX–X.XX)
0-299	NN (X%)	NN (X%)	-
300-499	NN (X%)	NN (X%)	-
500-999	NN (X%)	NN (X%)	-
1000-1499	NN (X%)	NN (X%)	-
≥1500	NN (X%)	NN (X%)	-
Intraoperative blood loss, mL (mean) ^	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Drape-measured blood loss, mL (mean) ^	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Peripartum haemoglobin change, g/L (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Postpartum haemoglobin (g/L (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Haemoglobin category			X.XX (X.XX–X.XX)
No anaemia (≥110)	NN (X%)	NN (X%)	-
Mild anaemia (100-109)	NN (X%)	NN (X%)	-
Moderate anaemia (70-99)	NN (X%)	NN (X%)	-
Severe anaemia (<70)	NN (X%)	NN (X%)	-

Abbreviations: TXA, Tranexamic Acid; IM, Intramuscular; CI, Confidence Interval; PPH, Postpartum Haemorrhage.

Causes of PPH are not mutually exclusive. Measured blood loss is calibrated obstetric drape measured blood loss for vaginal births and intraoperative plus drape measured blood loss for caesarean births. Postpartum Hb was corrected for blood transfusion given during CS and up to 24h after birth.

*Mean difference for continuous variables (measured blood loss, peripartum haemoglobin change and corrected postpartum haemoglobin), common OR for categorical variables (measured blood loss category and corrected postpartum haemoglobin category), and RR for the binary variables (clinical diagnosis of PPH and bleeding-related death or near-miss).

† Severe PPH is defined as peripartum Hb drop ≥25 g/L or measured blood loss ≥1500 mL. Major interventions for bleeding include hysterectomy, laparotomy, arterial embolization or ligation, uterine compression sutures, or a transfusion of ≥5 units of blood intraoperatively and up to 24 h after birth. Cardiovascular dysfunction was diagnosed based on shock, cardiac arrest, continuous vasoactive drugs, severe hypoperfusion, severe acidosis,

and/or cardiopulmonary resuscitation. Renal dysfunction was diagnosed based on oliguria non-responsive to fluids or diuretics, dialysis for acute renal failure, and/or severe acute azotaemia.
‡ Adjusted for country, age, pre-birth haemoglobin, abnormal placental implantation, APH, dead foetus in utero, hypertensive disorder of pregnancy, fibroids, multiple pregnancy, and mode of birth.
^ Caesarean births only.

Paper B - Table 3. Effect of IM tranexamic acid on maternal death, complications, interventions and management (superiority analysis)

	IM TXA (n = NN)	Placebo (n = NN)	Estimate (95% CI) *
Death (all-cause)	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Cause of death			
Bleeding	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Other	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Vascular occlusive event ✝	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Deep vein thrombosis	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Pulmonary embolism	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Myocardial infarction	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Stroke	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Seizure ✝	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Sepsis ✝	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Organ dysfunction ✝	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Coagulopathy ✝	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Intervention for bleeding	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Non-trial TXA	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Uterotonics	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Blood transfusion	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Surgical interventions	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Non-surgical interventions	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Cervical, vaginal or perineal sutures	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Length of CS surgery	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Length of hospital stay (days)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Days in ICU or HDU	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Transfer to another hospital	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Systolic blood pressure, mmHg	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Diastolic blood pressure, mmHg	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Heart rate, BPM	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)

Abbreviations: TXA, Tranexamic Acid; CS, Caesarean Section; ICU = Intensive Care Unit; HDU = High Dependency Unit; BPM Beats Per Minute.

✝ Prespecified AEs include death, vascular occlusive event, seizure, sepsis, organ dysfunction and coagulopathy.

*Mean difference for continuous variables (length of surgery, length of hospital stay, days in ICU or HDU, blood pressure and heart rate) and RR for all other binary variables.

Paper B - Table 4. Safety and tolerability of IM tranexamic acid compared to placebo (superiority analysis)

	IM TXA (n = NN)	**Placebo** (n = NN)	**Estimate (95% CI)** *
Retching/vomiting episodes	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Nausea score (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Dizziness score (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Pain score - IM injection sites (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Pain score - IV injection site (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Adverse reaction - IM injection sites	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Adverse reaction - IV injection sites	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)

Abbreviations: TXA, Tranexamic Acid; CI, Confidence Interval; IM, Intramuscular; IV, Intravenous.
*Mean difference for continuous variables (nausea, dizziness, pain) and RR for all other binary variables.

Paper B - Table 5. Effect of IM tranexamic acid on neonatal outcomes (superiority analysis)

	IM TXA (n = NN)	**Placebo** (n = NN)	**Risk ratio (95% CI)**
Stillbirth/intrapartum death	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Neonatal death	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Intracranial or pulmonary haemorrhage	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Bruising	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Thromboembolic event	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Seizure	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Breastfed	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Congenital and genetic abnormalities	N (X%)	N (X%)	X.XX (X.XX–X.XX)
Cause of death			
A	N (X%)	N (X%)	-
B	N (X%)	N (X%)	-
C	N (X%)	N (X%)	-

Abbreviations: TXA, Tranexamic Acid; IM, Intramuscular; CI, Confidence Interval.

Paper B - Table 6. Effect of IM versus IV tranexamic acid on a clinical diagnosis of postpartum haemorrhage, bleeding related death or near miss, blood loss and haemoglobin concentration (non-inferiority analysis)

	IM TXA (n = NN)	IV TXA (n = NN)	Estimate (95% CI) *
Clinical diagnosis of PPH	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Sensitivity analysis			
Exclusion of women with prophylactic non-trial TXA	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Covariate adjustment‡	-	-	X.XX (X.XX–X.XX)
Bleeding-related death or near miss†	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Death due to bleeding within 24 h of birth	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Severe postpartum haemorrhage	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Major interventions for bleeding within 24h of birth	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Renal or cardiovascular dysfunction	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Measured blood loss, mL (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Blood loss category			X.XX (X.XX–X.XX)
0-299	NN (X%)	NN (X%)	-
300-499	NN (X%)	NN (X%)	-
500-999	NN (X%)	NN (X%)	-
1000-1499	NN (X%)	NN (X%)	-
≥1500	NN (X%)	NN (X%)	-
Intraoperative blood loss, mL (mean) ^	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Drape-measured blood loss, mL (mean) ^	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Peripartum haemoglobin change, g/L (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Postpartum haemoglobin (g/L (mean)	XX (SD)	XX(SD)	X.XX (X.XX–X.XX)
Haemoglobin category			X.XX (X.XX–X.XX)
No anaemia (≥110)	NN (X%)	NN (X%)	-
Mild anaemia (100-109)	NN (X%)	NN (X%)	-
Moderate anaemia (70-99)	NN (X%)	NN (X%)	-
Severe anaemia (<70)	NN (X%)	NN (X%)	-

Abbreviations: TXA, Tranexamic Acid; IM, Intramuscular; IV, Intravenous; CI, Confidence Interval; PPH, Postpartum Haemorrhage.

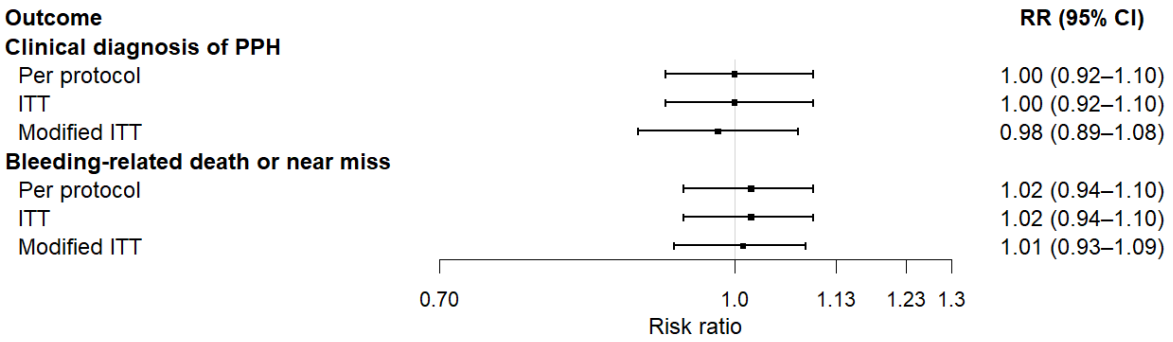
Causes of PPH are not mutually exclusive. Measured blood loss is calibrated obstetric drape measured blood loss for vaginal births and intraoperative plus drape measured blood loss for caesarean births. Postpartum Hb was corrected for blood transfusion given during CS and up to 24h after birth.

*Mean difference for continuous variables (measured blood loss, peripartum haemoglobin change and corrected postpartum haemoglobin), common OR for categorical variables (measured blood loss category and corrected postpartum haemoglobin category), and RR for the binary variables (clinical diagnosis of PPH and bleeding-related death or near-miss).

† Severe PPH is defined as peripartum Hb drop ≥25 g/L or measured blood loss ≥1500 mL. Major interventions for bleeding include hysterectomy, laparotomy, arterial embolization or ligation, uterine compression sutures, or a transfusion of ≥5 units of blood intraoperatively and up to 24 h after birth. Cardiovascular dysfunction was diagnosed based on shock, cardiac arrest, continuous vasoactive drugs, severe hypoperfusion, severe acidosis,

and/or cardiopulmonary resuscitation. Renal dysfunction was diagnosed based on oliguria non-responsive to fluids or diuretics, dialysis for acute renal failure, and/or severe acute azotaemia.
‡ Adjusted for country, age, pre-birth haemoglobin, abnormal placental implantation, APH, dead foetus in utero, hypertensive disorder of pregnancy, fibroids, multiple pregnancy, and mode of birth.
^ Caesarean births only.

Paper B - Figure 1. Effect of IM versus IV tranexamic acid on a clinical diagnosis of PPH and bleeding-related death or near miss (non-inferiority analysis)



Abbreviations: PPH, Postpartum Haemorrhage; IM, Intramuscular; IV, Intravenous; RR, Risk Ratio; CI, Confidence Interval; ITT, Intention to Treat.

Paper B - Table 7. Safety and tolerability of IM compared to IV tranexamic acid (superiority analysis)

	IM TXA (n = NN)	IV TXA (n = NN)	Estimate (95% CI) *
Retching/vomiting episodes	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Nausea score (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Dizziness score (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Pain score - IM injection sites (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Pain score - IV injection site (mean)	XX (SD)	XX (SD)	X.XX (X.XX–X.XX)
Adverse reaction - IM injection sites	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)
Adverse reaction - IV injection sites	NN (X%)	NN (X%)	X.XX (X.XX–X.XX)

Abbreviations: TXA, Tranexamic Acid; CI, Confidence Interval; IM, Intramuscular; IV, Intravenous.
* Mean difference for continuous variables (nausea, dizziness, pain) and RR for all other binary variables.