Supplementary Appendix

Tranexamic acid for the prevention of blood loss after vaginal delivery

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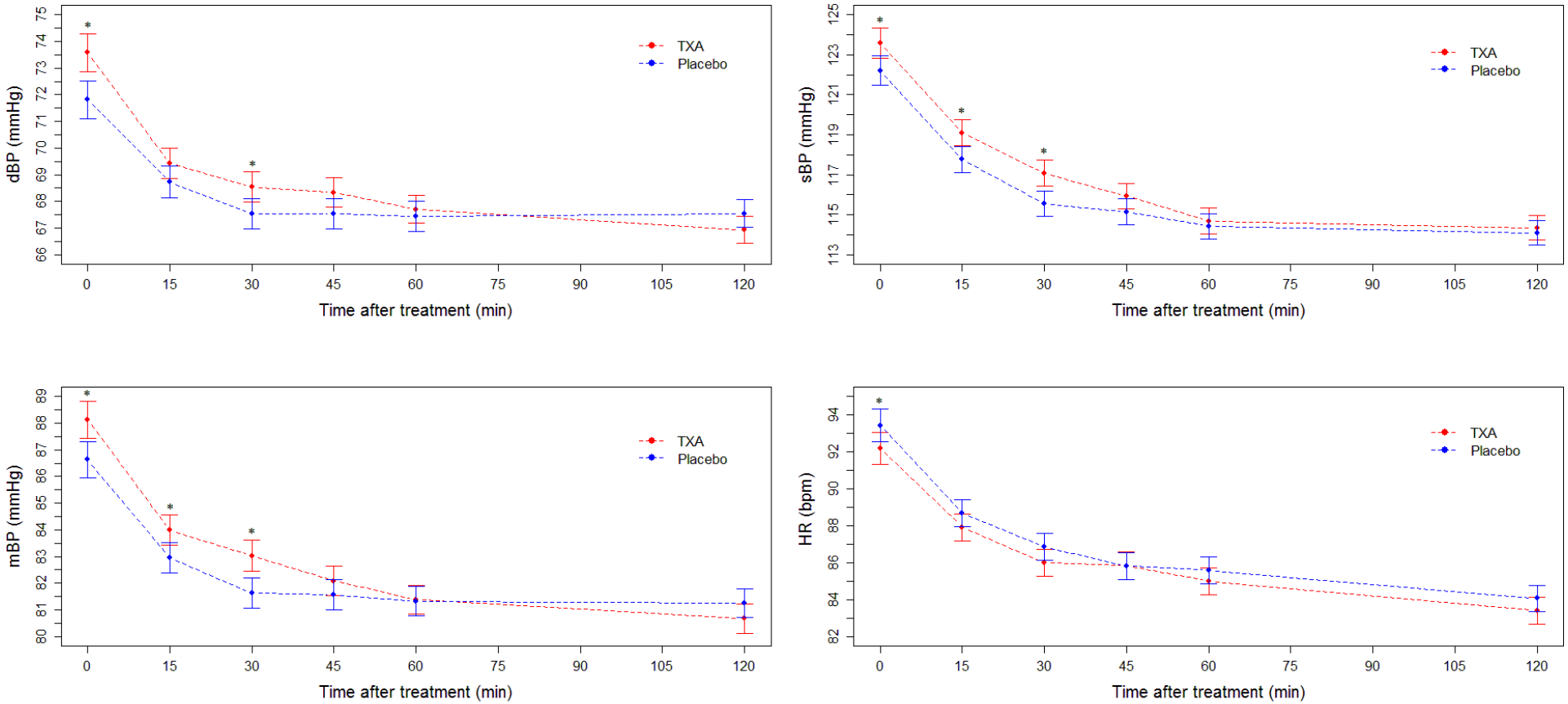
Figure S1. Hemodynamic parameters in the immediate postpartum, modified intention to treat population



Legend:

Results are mean (95% CI)

dBP: diastolic blood pressure, sBP: systolic blood pressure; mBP: mean blood pressure; HR: heart rate

*p <0.05 for difference between the 2 groups

Table S1: Exclusion criteria, TRAAP trial

Previous episode of venous thrombosis: deep vein thrombosis, pulmonary embolism
Previous episode of arterial thrombosis: myocardial infarction, stroke
Any known cardiovascular, kidney, or liver disorder
Autoimmune disease
Sickle cell disease
Condition at possibly increased risk of bleeding: severe hemorrhagic disease, placenta previa, placenta accrete spectrum, HELLP syndrome, multiple pregnancy
Condition that could impair initial hemostasis: in utero fetal death, administration of low-molecular-weight heparin or antiplatelet agents in the week before delivery
Epilepsy
Eclampsia
Poor comprehension of oral French

Table S2. Characteristics of participants at baseline, adherence to assigned intervention and other aspects of management of the third stage of labor, modified intention-to-treat population (expanded version of Table 1)*

Characteristic of participants at baseline	Tranexamic acid group (N=1945)	Placebo group (N=1946)
Age —yr	30.3±4.7	30.2±5.0
Geographical origin— no. (%)		
Europe	1540 (83.5)	1531 (82.8)
Sub-Saharan Africa	70 (3.8)	88 (4.8)
North Africa	172 (9.3)	176 (9.5)
Asia	43 (2.3)	39 (2.1)
Other	20 (1.1)	14 (0.8)
Non-French Nationality — no. (%)	161 (8.8)	162 (8.9)
Body-mass index before pregnancy ‡	23.3±4.4	23.5±4.6
Preexisting chronic hypertension — no. (%)	7 (0.4)	17 (0.9)
Preexisting diabetes mellitus — no. (%)	7 (0.4)	10 (0.5)
Primiparous — no. (%)	1025 (52.7)	1048 (53.9)
Any uterine scar — no. (%)	122 (6.3)	114 (5.9)
Previous cesarean delivery— no. (%)	101 (5.2)	107 (5.5)
History of postpartum hemorrhage— no. (%)	92 (4.7)	85 (4.4)
Tobacco use during pregnancy — no. (%)	247 (12.7)	284 (14.6)
Gestational diabetes — no. (%)	198 (10.2)	222 (11.4)
Gestational hypertensive disorders— no. (%)	37 (1.9)	47 (2.4)
Hospitalization during pregnancy longer than 24 hours — no. (%)	106 (5.4)	103 (5.3)

Induction of labor— no. (%)	384 (19.7)	410 (21.1)
Epidural analgesia— no. (%)	1908 (98.1)	1900 (97.6)
Oxytocin during labor— no. (%)	1135 (58.4)	1171 (60.2)
Duration of active phase of labor— hours		
Median (IQR)	2.3 (1.3-3.5)	2.3 (1.3-3.5)
Operative vaginal delivery — no. (%)	346 (17.8)	332 (17.1)
Vacuum	162 (46.8)	137 (41.3)
Forceps	184 (53.2)	195 (58.7)
Episiotomy— no. (%)	456 (23.4)	444 (22.8)
Perineal tear— no. (%)	1099 (56.5)	1119 (57.5)
Birth weight —g	3406±419	3384±425
Birth weight above 4000 g— no. (%)	165 (8.5)	142 (7.3)
Characteristics of participants at adherence to assigned intervention and other aspects of management of the third stage of labor		
Prophylactic oxytocin at birth — no. (%)	1922 (98.8)	1934 (99.4)
Study treatment — no. (%)		
Received assigned treatment	1902 (97.8)	1902 (97.7)
within two minutes of birth	1479 (76.0)	1490 (76.6)
within ten minutes of birth	1888 (97.1)	1889 (97.1)
Received no treatment	41 (2.1)	42 (2.2)
Received the opposite treatment	2 (0.1)	2 (0.1)
Interval between delivery and study treatment administration—min		
Median (IQR)	2 (1-2)	1 (1-2)
Cord clamping within two minutes of birth — no.	1594 (87.0)	1620 (88.2)

(%)		
Controlled cord traction — no. (%)	738 (42.5)	742 (42.8)
Graduated collector bag — no. (%)	1928 (99.2)	1931 (99.3)
Duration of the use of collector bag — min		
Median (IQR)	26 (17-38)	27 (18-40)
Duration of the third stage of labor – min		
Median (IQR)	6 (4-10)	6 (4-10)

* Plus-minus values are mean ±SD. There were no significant differences between the two groups.

‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

Table S3- Primary outcome analysis after imputation of missing value as failures, modified intention to treat population

Outcome	**Tranexamic Acid Group (N=1945)**	**Placebo Group (N=1946)**	**Risk Ratio (95% CI)**	**Unadjusted P value**
Primary outcome: PPH, defined by blood loss ≥500 mL, measured with a graduated collector bag – no./total no. (%)	180/1945 (9.3)	216/1946 (11.1)	0.83 (0.69-1.01)	0.06

95% CI and P values were not adjusted for multiple testing

Table S4. Blood sample results at day 2, and EPDS score, modified intention-to-treat population.

	Tranexamic Acid Group (N=1945)	**Placebo Group (N=1946)**	**RR (95% CI)**	**Mean difference (95% CI)**	**Unadjusted P value**
Blood sample results at day 2*					
Urea nitrogen – mmol/l	3.42±0.93 n=1730	3.42±0.96 n=1716		-0.00 (-0.06 to 0.06)	0.97
Creatinine – µmol/l	54.65±9.83 n=1784	54.91±10.16 n=1769		-0.26 (-0.91 to 0.40)	0.44
Prothrombin time – %	107.5±12.4 n=1756	107.5±12.1 n=1735		0.1 (-0.7 to 0.9)	0.87
Active prothrombin time – s	30.0±3.9 n=1749	30.0±3.8 n=1734		-0.0 (-0.3 to 0.3)	0.98
Fibrinogen – g/l	4.78±0.83 n=1688	4.76±0.82 n=1670		0.02 (-0.04 to 0.08)	0.50
Alanine transaminase – IU/l	19.3±24.0 n=1790	18.0±17.5 n=1767		1.3 (-0.0 to 2.7)	0.06
Aspartate transaminase – IU/L	32.9±17.5 n=1788	31.5±14.4 n=1769		1.3 (0.3 to 2.4)	0.01
Alanine transaminase> 2 N	32/1790 (1.8)	23/1767 (1.3)	1.37 (0.81-2.34)		0.24
Aspartate transaminase> 2 N	42/1788 (2.4)	33/1769 (1.9)	1.26 (0.80-1.98)		0.32
Total bilirubin –	4.6±5.1	4.5±2.7		0.1	0.36

µmol/l	n=1750	n=1746		(-0.1 to 0.4)	
Maternal satisfaction at day 2					
Completed questionnaires†	1526 (78.5)	1540 (79.1)			
Felt tired :	n=1590	n=1603			0.15
Not at all	96 (6.0)	115 (7.2)			
A little	558 (35.1)	525 (32.8)			
Moderately	612 (38.5)	616 (38.4)			
Very	297 (18.7)	303 (18.9)			
Extremely	27 (1.7)	44 (2.7)			
Felt anxious :	n=1538	n=1551			0.47
Not at all	783 (50.9)	765 (49.3)			
A little	533 (34.7)	536 (34.6)			
Moderately	180 (11.7)	193 (12.4)			
Very	37 (2.4)	53 (3.4)			
Extremely	5 (0.3)	4 (0.3)			
Felt satisfied with the delivery:	n=1591	n=1605			0.28
Not at all	1 (0.1)	3 (0.2)			
A little	3 (0.2)	10 (0.6)			
Moderately	36 (2.3)	40 (2.5)			
Very	766 (48.1)	752 (46.9)			
Extremely	785 (49.3)	800 (49.8)			
Felt satisfied with the	n=1581	n=1598			0.46

postpartum stay:					
Not at all	6 (0.4)	8 (0.5)			
A little	6 (0.4)	12 (0.8)			
Moderately	130 (8.2)	141 (8.8)			
Very	1006 (63.6)	980 (61.3)			
Extremely	433 (27.4)	457 (28.6)			
Today, what are your memories of your delivery?	n=1589	n=1603			0.20
Excellent	704 (44.3)	659 (41.1)			
Good	674 (42.4)	699 (43.6)			
Intermediate	172 (10.8)	191 (11.9)			
Bad	28 (1.8)	43 (2.7)			
Very bad	11 (0.7)	11 (0.7)			
EPDS at day 60‡					
Completed questionnaires	1394 (71.7)	1381 (71.0)			0.63
EPDS score	n=1394	n=1381			0.12
Median (IQR)	5 (2-8)	5 (2-8)			
EPDS score ≥12	156/1394 (11.2)	163/1381 (11.8)	0.95 (0.77-1.17)		0.61

95% CI and P values were not adjusted for multiple testing

* if no blood sample was available from day 2, measurement of blood parameters was assessed from a day-3 blood sample, if available. If no blood sample was available from day 2 or 3, measurement of blood parameters was assessed from a day-1 blood sample, if available.

† Completed for the 5 questions, ‡ EPDS, Edinburgh Postnatal Depression Scale

Table S5. Outcome measures describing postpartum blood loss, per protocol 1 population*.

Outcome or event	**Tranexamic Acid Group (N=1467)**	**Placebo Group (N=1480)**	**Risk Ratio (95% CI)**	**Mean difference (95% CI)**	**Unadjusted P value**
Primary outcome: PPH, defined by blood loss ≥500 mL, measured with a graduated collector bag – no./total no. (%)	123/1461 (8.4)	136/1473 (9.2)	0.91 (0.72-1.15)		0.44
Blood loss > 500 mL, measured with a graduated collector bag – no./total no. (%)†	101/1461 (6.9)	122/1473 (8.3)	0.83 (0.65-1.08)		0.16
Clinically significant PPH according to caregivers – no./total no. (%)	120/1467 (8.2)	152/1480 (10.3)	0.80 (0.63-1.00)		0.05
Severe PPH, defined by blood loss ≥ 1000 mL – no./total no. (%)	42/1461 (2.9)	42/1473 (2.9)	1.01 (0.66-1.54)		0.97
Blood loss at 15 minutes – mL	131.0±148.1 n=1453	135.5±151.7 n=1463		-4.5 (-15.4 to 6.4)	0.42
Blood loss at bag removal – mL	202.9±276.0 n=1461	208.0±257.0 n=1473		-5.1 (-24.4 to 14.2)	0.60
Estimated total blood loss – mL	224.9±296.1 n=1465	237.5±299.0 n=1478		-12.5 (-34.0 to 9.0)	0.25

Additional uterotonics for excessive bleeding – no./total no. (%)	109/1467 (7.4)	141/1480 (9.5)	0.78 (0.61-0.99)		0.04
Blood transfusion – no./total no. (%)	15/1467 (1.0)	14/1480 (0.9)	1.08 (0.52-2.23)		0.83
Arterial embolisation or surgery for PPH – no./total no. (%)	3/1467 (0.2)	5/1480 (0.3)	0.61 (0.15-2.53)		0.73
Peripartum change in hemoglobin – g/dL‡	-0.77±1.22 (n=1394)	-0.80±1.30 (n=1371)		0.03 (-0.06 to 0.13)	0.49
Hemoglobin drop>2g/dL‡	196/1394 (14.1)	210/1371 (15.3)	0.92 (0.77-1.10)		0.35
Peripartum change in Hematocrit – %§	-2.06±3.89 (n=1330)	-2.08±4.19 (n=1316)		0.02 (-0.29 to 0.33)	0.91
Hematocrit drop>10%§	36/1330 (2.7)	39/1316 (3.0)	0.91 (0.58-1.43)		0.69

95% CI and P values were not adjusted for multiple testing

PPH, postpartum hemorrhage.

*Per-protocol 1 population was defined as women of the modified ITT population who received oxytocin and then the study medication within the 2 minutes after birth.

†Outcome was not prespecified in the protocol.

‡Prepartum hemoglobin level measured within eight months of gestation and arrival in labor ward in 1100 (79.8%) and 1094 (80.6%), at arrival in labor ward in 120 (8.7%) and 93 (6.9%), and between 5-7 months of gestation in 159 (11.5%) and 170 (12.5%) in tranexamic acid group and placebo group,

respectively; Postpartum hemoglobin level measured at day 2 postpartum in 1235 (89.6%) and 1228 (90.5%) and on another day between one and three days postpartum in 144 (10.4%) and 129 (9.5%) in tranexamic acid group and placebo group, respectively. In women transfused (respectively 15 and 14 in the TXA and placebo groups), one unit of packed red blood cells was considered equivalent to a 1g/dl decrease in Hb.

§Prepartum hematocrit measured within eight months of gestation and arrival in labor ward in 1046 (79.5%) and 1047 (80.4%), at arrival in labor ward in 126 (9.6%) and 97 (7.5%), and between 5-7 months of gestation in 143 (10.9%) and 158 (12.1%) in tranexamic acid group and placebo group, respectively; Postpartum hematocrit measured at day 2 postpartum in 1182 (89.9%) and 1179 (90.6%) and on another day between one and three days postpartum in 133 (10.1%) and 123 (9.4%) in tranexamic acid group and placebo group, respectively. In women transfused (respectively 15 and 14 in the TXA and placebo groups), one unit of packed red blood cells was considered equivalent to a 5% decrease in Ht.

Table S6. Adverse events, maternal satisfaction and EPDS scores, perprotocol 1 population*.

Adverse events	Tranexamic acid (N=1467)	Placebo (N=1480)	RR (95% CI)	Mean difference (95% CI)	Unadjusted P-value
In the delivery room – no./total no. (%)					
Vomiting or nausea	99/1467 (6.7)	46/1480 (3.1)	2.17 (1.54-3.06)		<0.001
Nausea	72/1467 (4.9)	38/1480 (2.6)	1.91 (1.30-2.81)		<0.001
Vomiting	53/1467 (3.6)	23/1480 (1.6)	2.32 (1.43-3.77)		<0.001
Photopsias	3/1467 (0.2)	5/1480 (0.3)	0.61 (0.14-2.53)		0.73
Dizziness	26/1467 (1.8)	26/1480 (1.8)	1.01 (0.59-1.73)		0.97
Postpartum up to three months after delivery – no./total no. (%)					
Completed forms – no. (%)	1393 (94.8)	1403 (95.0)			
Thromboembolic events					
Any thromboembolic	1/1393 (0.1)	3/1403 (0.2)	0.34		0.62

event			(0.03-3.22)		
Deep vein thrombosis	0/1393 (0.0)	1/1403 (0.1)	-	-	
Pulmonary embolism	0/1393 (0.0)	0/1403 (0.0)			
Ovarian vein thrombosis	0/1393 (0.0)	2/1403 (0.1)	-	-	
Superficial vein thrombosis	1/1393 (0.1)	0/1403 (0.0)	-	-	
Retinal vascular occlusion	0/1393 (0.0)	0/1403 (0.0)			
Myocardial infarction	0/1393 (0.0)	0/1403 (0.0)	-	-	
Stroke	0/1393 (0.0)	0/1403 (0.0)	-	-	
Seizure	1/1393 (0.1)	0/1403 (0.0)			
Renal failure	0/1393 (0.0)	0/1403 (0.0)	-	-	
Re-admission after discharge	16/1393 (1.1)	11/1403 (0.8)	1.46 (0.68-3.15)		0.32
Anticoagulant therapy at and after discharge	46/1382 (3.3)	46/1397 (3.3)	1.01 (0.68-1.51)		0.96
Blood sample results at day 2†					
Urea nitrogen – mmol/L	3.40±0.91 n=1308	3.40±0.93 n=1296		0.00 (-0.07 to 0.07)	0.98
Creatinine – µmol/L	54.43±9.76	55.10±10.36		-0.66	0.09

	n=1357	n=1345		(-1.42 to 0.09)	
Prothrombin time – %	107.1±12.5 n=1335	107.2±12.1 n=1329		-0.0 (-1.0 to 0.9)	0.96
Active prothrombin time – s	30.3±3.9 n=1329	30.2±3.9 n=1327		0.1 (-0.2 to 0.4)	0.72
Fibrinogen – g/L	4.78±0.83 n=1285	4.78±0.83 n=1271		-0.00 (-0.07 to 0.06)	0.96
Alanine transaminase – IU/L	19.2±26.2 n=1358	18.3±18.7 n=1345		0.9 (-0.8 to 2.7)	0.28
Aspartate transaminase – IU/L	32.8±18.3 n=1356	31.8±15.1 n=1347		1.0 (-0.3 to 2.2)	0.13
Total bilirubin – µmol/L	4.5±3.3 n=1329	4.5±2.7 n=1326		0.0 (-0.2 to 0.3)	0.84
Maternal satisfaction at day 2					
Completed questionnaires‡	1153 (78.6)	1168 (78.9)			
Felt tired :	n=1195	n=1209			0.44
Not at all	70 (5.9)	85 (7.0)			
A little	406 (34.0)	398 (32.9)			
Moderately	469 (39.2)	468 (38.7)			
Very	229 (19.2)	226 (18.7)			
Extremely	21 (1.8)	32 (2.6)			
Felt anxious :	n=1161	n=1176			0.46
Not at all	592 (51.0)	568 (48.3)			

A little	399 (34.4)	421 (35.8)			
Moderately	137 (11.8)	142 (12.1)			
Very	29 (2.5)	42 (3.6)			
Extremely	4 (0.3)	3 (0.3)			
Felt satisfied with the delivery:	n=1196	n=1210			0.21
Not at all	1 (0.1)	3 (0.2)			
A little	2 (0.2)	9 (0.7)			
Moderately	24 (2.0)	22 (1.8)			
Very	583 (48.7)	572 (47.3)			
Extremely	586 (49.0)	604 (49.9)			
Felt satisfied with the postpartum stay:	n=1189	n=1206			0.76
Not at all	4 (0.3)	4 (0.3)			
A little	6 (0.5)	10 (0.8)			
Moderately	95 (8.0)	109 (9.0)			
Very	751 (63.2)	754 (62.5)			
Extremely	333 (28.0)	329 (27.3)			
Today, what are your memories of your delivery?	n=1196	n=1209			0.20
Excellent	523 (43.7)	501 (41.4)			
Good	512 (42.8)	520 (43.0)			
Intermediate	134 (11.2)	146 (12.1)			
Bad	18 (1.5)	34 (2.8)			

Very bad	9 (0.8)	8 (0.7)			
EPDS at day 60§					
Completed questionnaires	1049 (71.5)	1068 (72.2)			
EPDS score	n=1049	n=1068			0.23
Median (IQR)	4 (2-8)	5 (2-8)			
EPDS score ≥12	115 (11.0)	127 (11.9)	0.92 (0.73-1.17)		0.50

95% CI and P values were not adjusted for multiple testing

*Per-protocol 1 population was defined as women of the modified ITT population who received oxytocin and then the study medication within the 2 minutes after birth.

†if no blood sample was available at day 2, measurement of blood parameters was assessed from a day 3 blood sample, if available. If no blood sample was available from day 2 or 3, measurement of blood parameters was assessed from a day 1 blood sample, if available.

‡Completed for the 5 questions

§EPDS, Edinburgh Postnatal Depression Scale

Table S7. Outcome measures describing postpartum blood loss, per protocol 2 population*.

Outcome or event	**Tranexamic acid Group (N=1873)**	**Placebo Group (N=1878)**	**Risk Ratio (95% CI)**	**Mean difference (95% CI)**	**Unadjusted P value**
Primary outcome: PPH, defined by blood loss ≥500 mL, measured with a graduated collector bag – no./total no. (%)	153/1867 (8.2)	178/1870 (9.5)	0.86 (0.70-1.06)		0.15
Blood loss > 500 mL, measured with a graduated collector bag – no./total no. (%)†	124/1867 (6.6)	160/1870 (8.6)	0.78 (0.62-0.97)		0.03
Clinically significant PPH according to caregivers – no./total no. (%)†	147/1873 (7.8)	192/1878 (10.2)	0.77 (0.63-0.94)		0.01
Severe PPH, defined by blood loss ≥ 1000 mL – no./total no. (%)	46/1867 (2.5)	55/1870 (2.9)	0.84 (0.57-1.23)		0.37
Blood loss at 15 minutes – mL	130.7±145.0 n=1854	134.0±148.6 n=1856		-3.4 (-12.8 to 6.1)	0.48
Blood loss at bag removal – mL	199.7±263.0 n=1867	208.9±255.3 n=1870		-9.1 (-25.8 to 7.5)	0.28
Estimated total blood loss – mL	220.8±282.4 n=1870	235.6±291.4 n=1875		-14.8 (-33.2 to	0.11

				3.6)	
Additional uterotonics for excessive bleeding – no./total no. (%)	137/1873 (7.3)	178/1878 (9.5)	0.77 (0.62-0.96)		0.02
Blood transfusion – no./total no. (%)	16/1873 (0.9)	17/1878 (0.9)	0.94 (0.48-1.86)		0.87
Arterial embolisation or surgery for PPH – no./total no. (%)	3/1873 (0.2)	5/1878 (0.3)	0.60 (0.14-2.52)		0.73
Peripartum change in hemoglobin – g/dL‡	-0.77±1.23 (n=1777)	-0.78±1.28 (n=1747)		0.01 (-0.07 to 0.09)	0.78
Hemoglobin drop>2g/dL‡	258/1777 (14.5)	265/1747 (15.2)	0.96 (0.82-1.12)		0.59
Peripartum change in Hematocrit – %§	-2.03±3.88 (n=1692)	-2.00±4.10 (n=1672)		-0.03 (-0.30 to 0.24)	0.83
Hematocrit drop>10%§	45/1692 (2.7)	50/1672 (3.0)	0.89 (0.60-1.32)		0.56

95% CI and P values were not adjusted for multiple testing

PPH, postpartum hemorrhage.

*Per-protocol 2 population was defined as women of the modified ITT population who received oxytocin and then the study medication within 10 minutes after birth.

†Outcome was not prespecified in the protocol.

‡Prepartum hemoglobin level measured between eight months of gestation and arrival in labor ward in 1409 (80.0%) and 1407 (81.3%), at arrival in labor ward in 155 (8.8%) and 119 (6.9%), and between 5-7 months of gestation in 197 (11.2%) and 204 (11.8%) in tranexamic acid group and placebo group, respectively; Postpartum hemoglobin level measured at day 2 postpartum in 1605 (91.1%) and 1592 (92.0%) and on another day between one and three days postpartum in 156 (8.9%) and 138 (8.0%) in tranexamic acid group and placebo group, respectively. In women transfused (respectively 3 and 5 in the TXA and placebo groups), one unit of packed red blood cells was considered equivalent to a 1g/dl decrease in Hb.

§Prepartum hematocrit measured between eight months of gestation and arrival in labor ward in 1336 (79.7%) and 1343 (81.2%), at arrival in labor ward in 164 (9.8%) and 124 (7.4%), and between 5-7 months of gestation in 176 (10.5%) and 188 (11.4%) in tranexamic acid group and placebo group, respectively; Postpartum hematocrit measured at day 2 postpartum in 1534 (91.5%) and 1524 (92.1%) and on another day between one and three days postpartum in 142 (8.5%) and 131 (7.9%) in tranexamic acid group and placebo group, respectively. In women transfused (respectively 3 and 5 in the TXA and placebo groups), one unit of packed red blood cells was considered equivalent to a 5% decrease in Ht.

Table S8. Adverse events, maternal satisfaction and EPDS scores, perprotocol 2 population*.

Adverse events	Tranexamic acid (N=1873)	Placebo (N=1878)	RR (95% CI)	Mean difference (95% CI)	Unadjusted P value
In the delivery room – no./total no. (%)					
Vomiting or nausea	132/1873 (7.0)	61/1878 (3.2)	2.17 (1.61-2.92)		<0.0001
Nausea	99/1873 (5.3)	48/1878 (2.6)	2.07 (1.47-2.90)		<0.0001
Vomiting	73/1873 (3.9)	32/1878 (1.7)	2.29 (1.52-3.45)		<0.0001
Photopsias	4/1873 (0.2)	6/1878 (0.3)	0.67 (0.19-2.36)		0.75
Dizziness	40/1873 (2.1)	30/1878 (1.6)	1.34 (0.84-2.14)		0.22
Postpartum up to three months after delivery – no./total no. (%)					
Completed forms – no. (%)	1780 (95.0)	1787 (95.2)			
Thromboembolic events					
Any thromboembolic	1/1780 (0.1)	4/1787 (0.2)	0.25		0.37

event			(0.03-2.24)		
Deep vein thrombosis	0/1780 (0.0)	1/1787 (0.1)	-	-	
Pulmonary embolism	0/1780 (0.0)	0/1787 (0.0)			
Ovarian vein thrombosis	0/1780 (0.0)	2/1787 (0.1)	-	-	
Superficial vein thrombosis	1/1780 (0.1)	1/1787 (0.1)	-	-	
Retinal vascular occlusion	0/1780 (0.0)	0/1787 (0.0)			
Myocardial infarction	0/1780 (0.0)	0/1787 (0.0)	-	-	
Stroke	0/1780 (0.0)	0/1787 (0.0)	-	-	
Seizure	1/1780 (0.1)	0/1787 (0.0)			
Renal failure	0/1780 (0.0)	0/1787 (0.0)	-	-	
Re-admission after discharge	18/1780 (1.0)	15/1787 (0.8)	1.20 (0.61-2.38)		0.59
Anticoagulant therapy at and after discharge	55/1766 (3.1)	55/1780 (3.1)	1.01 (0.70-1.46)		0.97
Blood sample results at day 2†					
Urea nitrogen – mmol/L	3.41±0.92 n=1676	3.41±0.94 n=1666		-0.00 (-0.07 to 0.06)	0.89
Creatinine – µmol/L	54.68±9.81	54.95±10.20		-0.27	0.43

	n=1731	n=1717		(-0.94 to 0.40)	
Prothrombin time – %	107.5±12.4 n=1703	107.5±12.1 n=1685		-0.0 (-0.8 to 0.8)	>0.99
Active prothrombin time – s	30.0±3.9 n=1696	30.0±3.8 n=1684		-0.0 (-0.3 to 0.2)	0.85
Fibrinogen – g/L	4.78±0.84 n=1638	4.76±0.82 n=1621		0.02 (-0.04 to 0.08)	0.51
Alanine transaminase – IU/L	19.3±24.1 n=1735	18.1±17.7 n=1717		1.2 (-0.2 to 2.6)	0.10
Aspartate transaminase – IU/L	32.8±17.5 n=1733	31.6±14.5 n=1719		1.2 (0.2 to 2.3)	0.03
Total bilirubin – µmol/L	4.6±5.1 n=1698	4.5±2.7 n=1695		0.1 (-0.1 to 0.4)	0.34
Maternal satisfaction at day 2					
Completed questionnaires‡	1481 (79.1)	1493 (79.5)			
Felt tired :	n=1538	n=1553			0.16
Not at all	94 (6.1)	113 (7.3)			
A little	537 (34.9)	504 (32.5)			
Moderately	595 (38.7)	602 (38.8)			
Very	286 (18.6)	292 (18.8)			
Extremely	26 (1.7)	42 (2.7)			
Felt anxious :	n=1492	n=1503			0.52
Not at all	762 (51.1)	741 (49.3)			

A little	512 (34.3)	522 (34.7)			
Moderately	177 (11.9)	185 (12.3)			
Very	36 (2.4)	51 (3.4)			
Extremely	5 (0.3)	4 (0.3)			
Felt satisfied with the delivery:	n=1539	n=1554			0.20
Not at all	1 (0.1)	3 (0.2)			
A little	2 (0.1)	9 (0.6)			
Moderately	34 (2.2)	35 (2.3)			
Very	740 (48.1)	722 (46.5)			
Extremely	762 (49.5)	785 (50.5)			
Felt satisfied with the postpartum stay:	n=1529	n=1548			0.44
Not at all	6 (0.4)	8 (0.5)			
A little	6 (0.4)	12 (0.8)			
Moderately	125 (8.2)	137 (8.9)			
Very	970 (63.4)	944 (61.0)			
Extremely	422 (27.6)	447 (28.9)			
Today, what are your memories of your delivery?	n=1538	n=1553			0.19
Excellent	679 (44.1)	640 (41.2)			
Good	657 (42.7)	676 (43.5)			
Intermediate	165 (10.7)	184 (11.8)			
Bad	26 (1.7)	42 (2.7)			

Very bad	11 (0.7)	11 (0.7)			
EPDS at day 60					
Completed questionnaires	1345 (71.8)	1344 (71.6)			
EPDS score§	n=1345	n=1344			0.08
Median (IQR)	4 (2-8)	5 (2-8)			
EPDS score ≥12	146 (10.9)	158 (11.8)	0.92 (0.75-1.14)		0.46

95% CI and P values were not adjusted for multiple testing

*Per-protocol 2 population was defined as women of the modified ITT population who received oxytocin and then the study medication within 10 minutes after birth.

†if no blood sample was available at day 2, measurement of blood parameters was assessed from a day 3 blood sample, if available. If no blood sample was available from day 2 or 3, measurement of blood parameters was assessed from a day 1 blood sample, if available.

‡Completed for the 5 questions

§EPDS, Edinburgh Postnatal Depression Scale

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