National Institute for Health and Care Excellence

Blood transfusion (update)

[A] Technical appendices for tranexamic acid for anticipated minor blood loss after surgery

NICE guideline NG24

Technical data underpinning the evidence review on the effectiveness of tranexamic acid for anticipated minor blood loss after surgery

November 2025

Draft for consultation

Copyright

Contents

Appendix A Review protocols

A.1.1 Clinical review protocol

The review protocol for the Jaiswal, et al 2025 review was pre-registered. The full protocol can be found on the PROSPERO database.

A.1.2 Economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).{NICE2014} **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high

	applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2005 or later but that depend on unit costs and resource data entirely or predominantly from before 2005 will be rated as 'Not applicable'. • Studies published before 2005 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

1

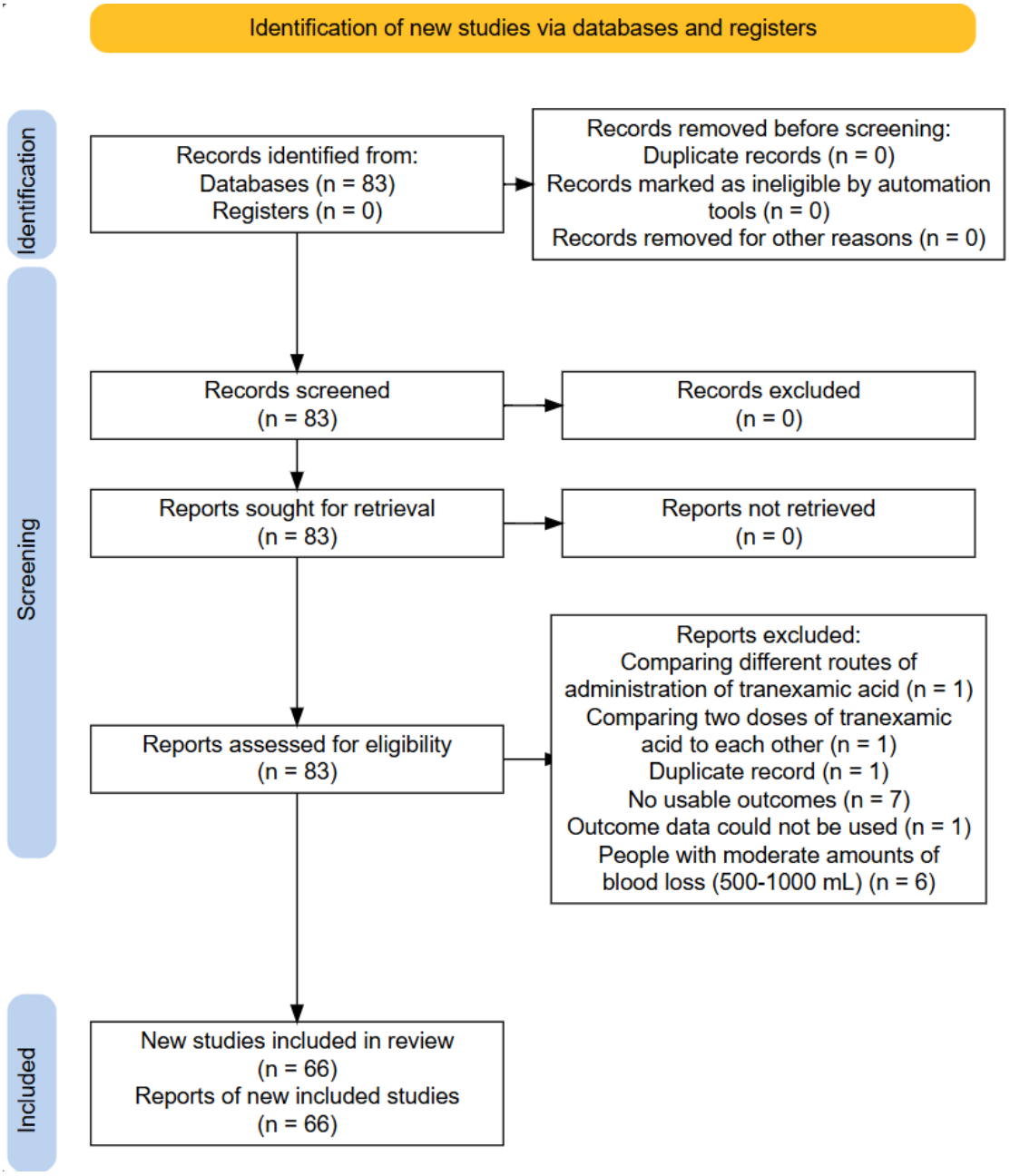
Appendix B Literature search strategies

For more information see Jaiswal, et al 2025.

Appendix C Study selection – effectiveness evidence

For the study selection in the original review, see Jaiswal, et al 2025.

Figure 1 Effectiveness evidence study selection



Appendix D Effectiveness evidence tables

D.1 Jaiswal, 2025

Bibliographic Reference	Jaiswal N; Robinson W; Ciminata G; Taylor-Rowan M; Morris T; Nevill C; Tahir H; Fisher E; Mulholland R; Davies A; Lumsden M; Noel-Storr A; Cooper N; Quinn T; Sutton A; Wu O; At what levels of expected blood loss from surgery is tranexamic acid (TXA) effective at reducing the need for blood transfusion?; 2025

D.1.1 Study details

Study design	Systematic review
Databases searched	Embase CENTRAL ClinicalTrials.gov International Clinical Trials Registry Platform MEDLINE CDSR
Dates searched	01/2015-2024
Sources of funding	Academic or government grant support NIHR grant funding
Matching inclusion criteria	Population: adults (above 16 years of age) Population: children (under 16 years of age) Population: low risk of blood loss (<500mL/1 unit expected blood loss) Population: moderate risk of blood loss (500mL-1L/1-2 units expected blood loss) Population: high risk of blood loss (>1L/>2 units expected blood loss) Study design: randomised controlled trials (RCTs)
Other important inclusion criteria	Moderate and high bleeding risk orthopaedic surgery trials were included, but other surgical disciplines were not included for this speciality.

Matching exclusion criteria	Study design: Non-randomised studies Conference abstracts
Other important exclusion criteria	People undergoing caesarean section (as the total blood loss estimated includes blood losses due to caesarean section surgery and post-partum losses, which could have an impact on the apparent efficacy of tranexamic acid).
Interventions of interest	Tranexamic acid (high, moderate and low risk groups) Placebo (high, moderate and low risk groups) No treatment (high, moderate and low risk groups)
Other interventions	Standard care
Comparisons of interest	Tranexamic acid to standard treatment (placebo/no treatment) (low risk group)
Outcomes of interest	Length of stay (hospitalisation) Number of patients needing transfusions Thrombotic complications DVT
Number of studies included in the review	173. Number of studies relevant to our review population: 65.
Comments	Protocol deviations: Did not analyse mortality, quality of life, blood volume transfused, surgical bleeding, post operative bleeding, adverse events (acute myocardial infarction, postoperative thrombosis and rate of serious adverse events) due to unavailability of data from published papers and reports. Had planned to use mean difference for total blood volume loss but used ratio of mean volume loss as it fitted the data better. Included additional primary outcomes - total blood volume loss, deep vein thrombosis.

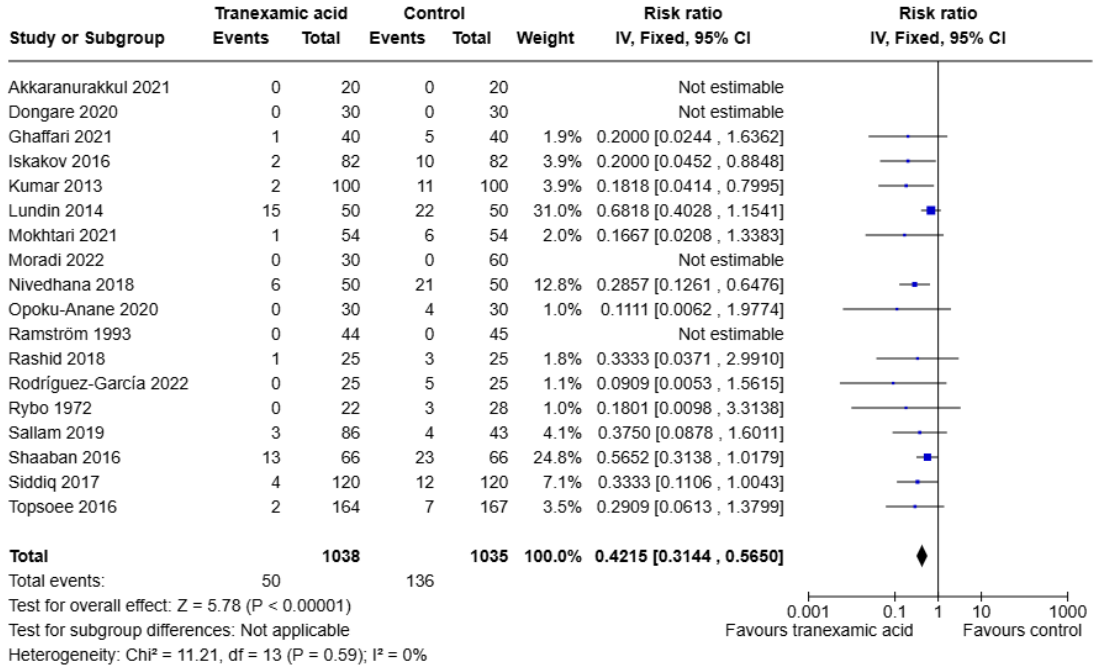
1
2

D.1.2 Critical appraisal - ROBIS systematic review checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	High
Overall study ratings	Applicability as a source of data	Fully applicable

Appendix E Forest plots

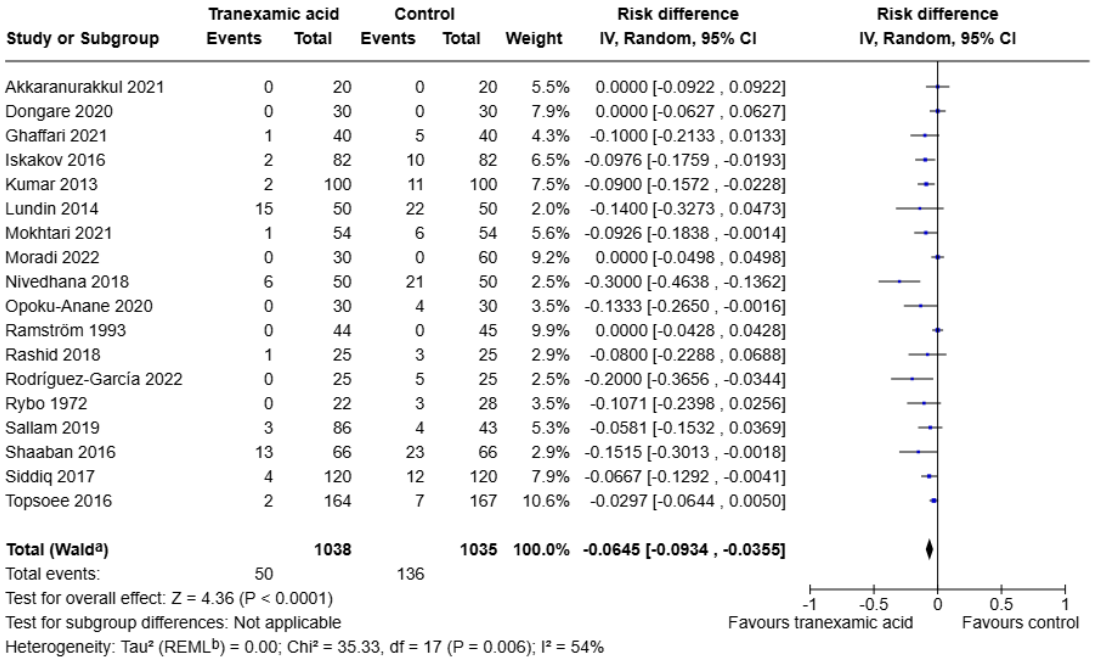
Figure 2 Proportion of patients requiring transfusion at end of study (risk ratio)



Abbreviations: CI: confidence intervals; df: Degrees of freedom; IV: Inverse variance; M-H: Mantel-Haenszel.

The risk ratio was used by the committee due to the limited number of studies that reported zero events in both study arms. However, both the risk ratio and risk difference were presented to the committee due to the differences between the approaches (for example: the GRADE showed the risk difference method to have a lower risk of bias but was downgraded more due to inconsistency).

Figure 3 Proportion of patients requiring transfusion at end of study (risk difference)



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 4 All-cause mortality at 30 days

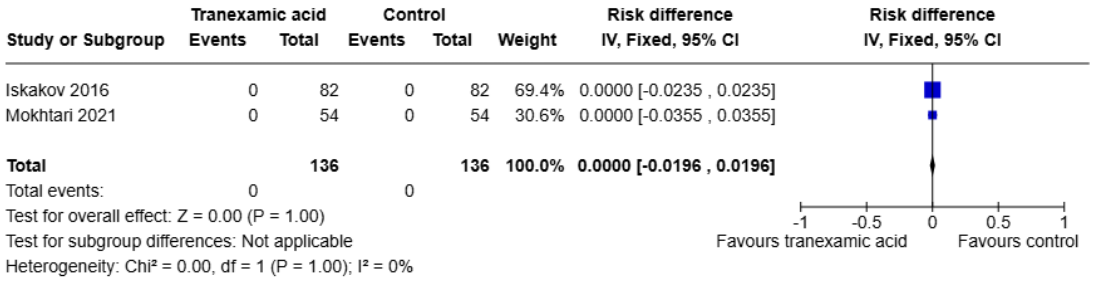
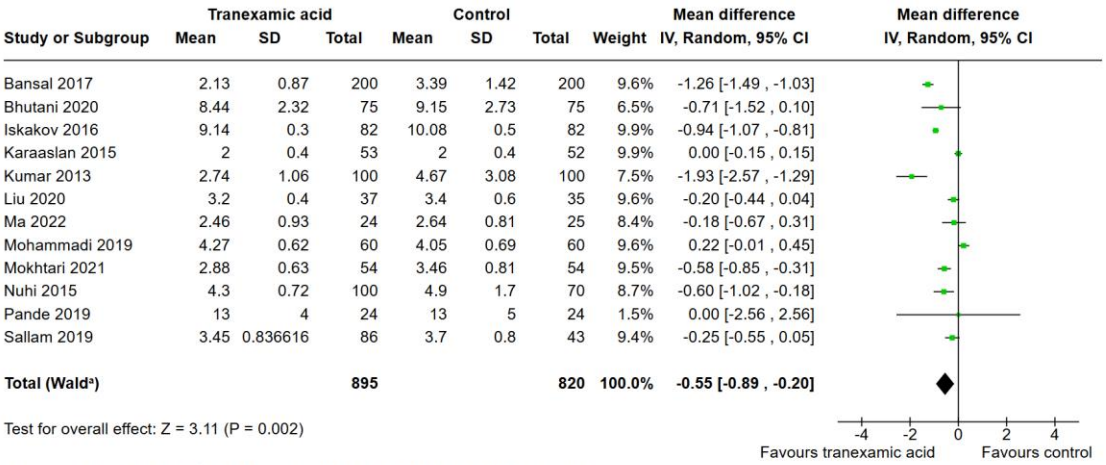


Figure 5 Length of stay (hospitalisation) at end of study (units: days, lower value is better)



Study or Subgroup	Tranexamic acid Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Bansal 2017	2.13	0.87	200	3.39	1.42	200	9.6%	-1.26 [-1.49 , -1.03]
Bhutani 2020	8.44	2.32	75	9.15	2.73	75	6.5%	-0.71 [-1.52 , 0.10]
Iskakov 2016	9.14	0.3	82	10.08	0.5	82	9.9%	-0.94 [-1.07 , -0.81]
Karaaslan 2015	2	0.4	53	2	0.4	52	9.9%	0.00 [-0.15 , 0.15]
Kumar 2013	2.74	1.06	100	4.67	3.08	100	7.5%	-1.93 [-2.57 , -1.29]
Liu 2020	3.2	0.4	37	3.4	0.6	35	9.6%	-0.20 [-0.44 , 0.04]
Ma 2022	2.46	0.93	24	2.64	0.81	25	8.4%	-0.18 [-0.67 , 0.31]
Mohammadi 2019	4.27	0.62	60	4.05	0.69	60	9.6%	0.22 [-0.01 , 0.45]
Mokhtari 2021	2.88	0.63	54	3.46	0.81	54	9.5%	-0.58 [-0.85 , -0.31]
Nuhi 2015	4.3	0.72	100	4.9	1.7	70	8.7%	-0.60 [-1.02 , -0.18]
Pande 2019	13	4	24	13	5	24	1.5%	0.00 [-2.56 , 2.56]
Sallam 2019	3.45	0.836616	86	3.7	0.8	43	9.4%	-0.25 [-0.55 , 0.05]
Total (Wald[a])			**895**			**820**	**100.0%**	**-0.55 [-0.89 , -0.20]**

Test for overall effect: Z = 3.11 (P = 0.002)

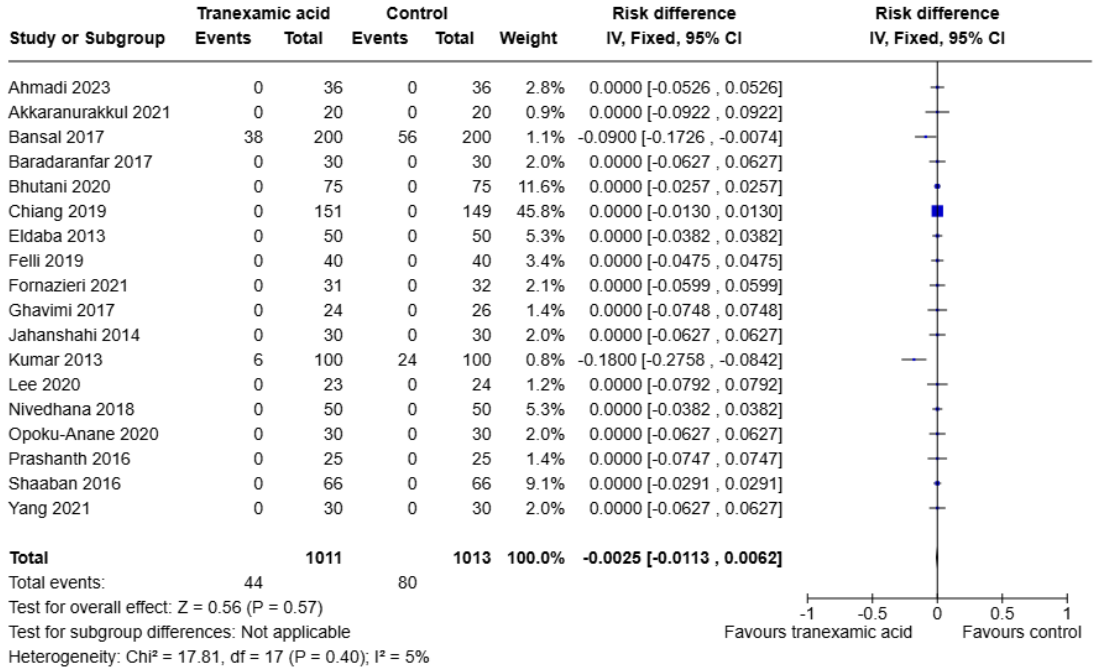
Heterogeneity: Tau² (REML[b]) = 0.31; Chi² = 196.03, df = 11 (P < 0.00001); I² = 95%

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 6 Serious adverse events at end of study



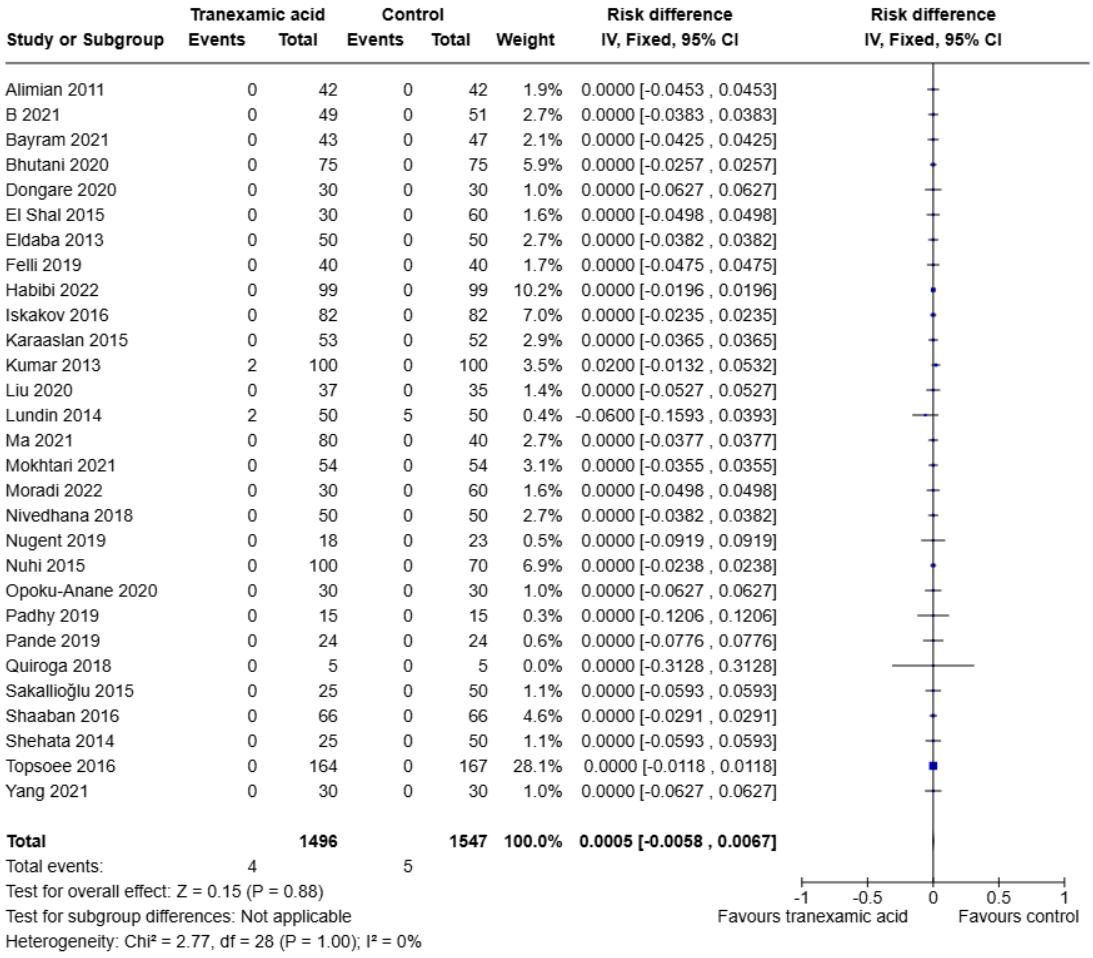
Study or Subgroup	Tranexamic acid Events	Total	Control Events	Total	Weight	Risk difference IV, Fixed, 95% CI
Ahmadi 2023	0	36	0	36	2.8%	0.0000 [-0.0526 , 0.0526]
Akkaranurakkul 2021	0	20	0	20	0.9%	0.0000 [-0.0922 , 0.0922]
Bansal 2017	38	200	56	200	1.1%	-0.0900 [-0.1726 , -0.0074]
Baradaranfar 2017	0	30	0	30	2.0%	0.0000 [-0.0627 , 0.0627]
Bhutani 2020	0	75	0	75	11.6%	0.0000 [-0.0257 , 0.0257]
Chiang 2019	0	151	0	149	45.8%	0.0000 [-0.0130 , 0.0130]
Eldaba 2013	0	50	0	50	5.3%	0.0000 [-0.0382 , 0.0382]
Felli 2019	0	40	0	40	3.4%	0.0000 [-0.0475 , 0.0475]
Fornazieri 2021	0	31	0	32	2.1%	0.0000 [-0.0599 , 0.0599]
Ghavimi 2017	0	24	0	26	1.4%	0.0000 [-0.0748 , 0.0748]
Jahanshahi 2014	0	30	0	30	2.0%	0.0000 [-0.0627 , 0.0627]
Kumar 2013	6	100	24	100	0.8%	-0.1800 [-0.2758 , -0.0842]
Lee 2020	0	23	0	24	1.2%	0.0000 [-0.0792 , 0.0792]
Nivedhana 2018	0	50	0	50	5.3%	0.0000 [-0.0382 , 0.0382]
Opoku-Anane 2020	0	30	0	30	2.0%	0.0000 [-0.0627 , 0.0627]
Prashanth 2016	0	25	0	25	1.4%	0.0000 [-0.0747 , 0.0747]
Shaaban 2016	0	66	0	66	9.1%	0.0000 [-0.0291 , 0.0291]
Yang 2021	0	30	0	30	2.0%	0.0000 [-0.0627 , 0.0627]
Total		**1011**		**1013**	**100.0%**	**-0.0025 [-0.0113 , 0.0062]**
Total events:	44		80			

Test for overall effect: Z = 0.56 (P = 0.57)

Test for subgroup differences: Not applicable

Heterogeneity: Chi² = 17.81, df = 17 (P = 0.40); I² = 5%

Figure 7 Thrombotic complications at end of study



Study or Subgroup	Tranexamic acid Events	Total	Control Events	Total	Weight	Risk difference IV, Fixed, 95% CI
Alimian 2011	0	42	0	42	1.9%	0.0000 [-0.0453 , 0.0453]
B 2021	0	49	0	51	2.7%	0.0000 [-0.0383 , 0.0383]
Bayram 2021	0	43	0	47	2.1%	0.0000 [-0.0425 , 0.0425]
Bhutani 2020	0	75	0	75	5.9%	0.0000 [-0.0257 , 0.0257]
Dongare 2020	0	30	0	30	1.0%	0.0000 [-0.0627 , 0.0627]
El Shal 2015	0	30	0	60	1.6%	0.0000 [-0.0498 , 0.0498]
Eldaba 2013	0	50	0	50	2.7%	0.0000 [-0.0382 , 0.0382]
Felli 2019	0	40	0	40	1.7%	0.0000 [-0.0475 , 0.0475]
Habibi 2022	0	99	0	99	10.2%	0.0000 [-0.0196 , 0.0196]
Iskakov 2016	0	82	0	82	7.0%	0.0000 [-0.0235 , 0.0235]
Karaaslan 2015	0	53	0	52	2.9%	0.0000 [-0.0365 , 0.0365]
Kumar 2013	2	100	0	100	3.5%	0.0200 [-0.0132 , 0.0532]
Liu 2020	0	37	0	35	1.4%	0.0000 [-0.0527 , 0.0527]
Lundin 2014	2	50	5	50	0.4%	-0.0600 [-0.1593 , 0.0393]
Ma 2021	0	80	0	40	2.7%	0.0000 [-0.0377 , 0.0377]
Mokhtari 2021	0	54	0	54	3.1%	0.0000 [-0.0355 , 0.0355]
Moradi 2022	0	30	0	60	1.6%	0.0000 [-0.0498 , 0.0498]
Nivedhana 2018	0	50	0	50	2.7%	0.0000 [-0.0382 , 0.0382]
Nugent 2019	0	18	0	23	0.5%	0.0000 [-0.0919 , 0.0919]
Nuhi 2015	0	100	0	70	6.9%	0.0000 [-0.0238 , 0.0238]
Opoku-Anane 2020	0	30	0	30	1.0%	0.0000 [-0.0627 , 0.0627]
Padhy 2019	0	15	0	15	0.3%	0.0000 [-0.1206 , 0.1206]
Pande 2019	0	24	0	24	0.6%	0.0000 [-0.0776 , 0.0776]
Quiroga 2018	0	5	0	5	0.0%	0.0000 [-0.3128 , 0.3128]
Sakallioğlu 2015	0	25	0	50	1.1%	0.0000 [-0.0593 , 0.0593]
Shaaban 2016	0	66	0	66	4.6%	0.0000 [-0.0291 , 0.0291]
Shehata 2014	0	25	0	50	1.1%	0.0000 [-0.0593 , 0.0593]
Topsoee 2016	0	164	0	167	28.1%	0.0000 [-0.0118 , 0.0118]
Yang 2021	0	30	0	30	1.0%	0.0000 [-0.0627 , 0.0627]
Total		**1496**		**1547**	**100.0%**	**0.0005 [-0.0058 , 0.0067]**
Total events:	4		5			

Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable
Heterogeneity: Chi² = 2.77, df = 28 (P = 1.00); I² = 0%

Figure 8 Infection at end of study

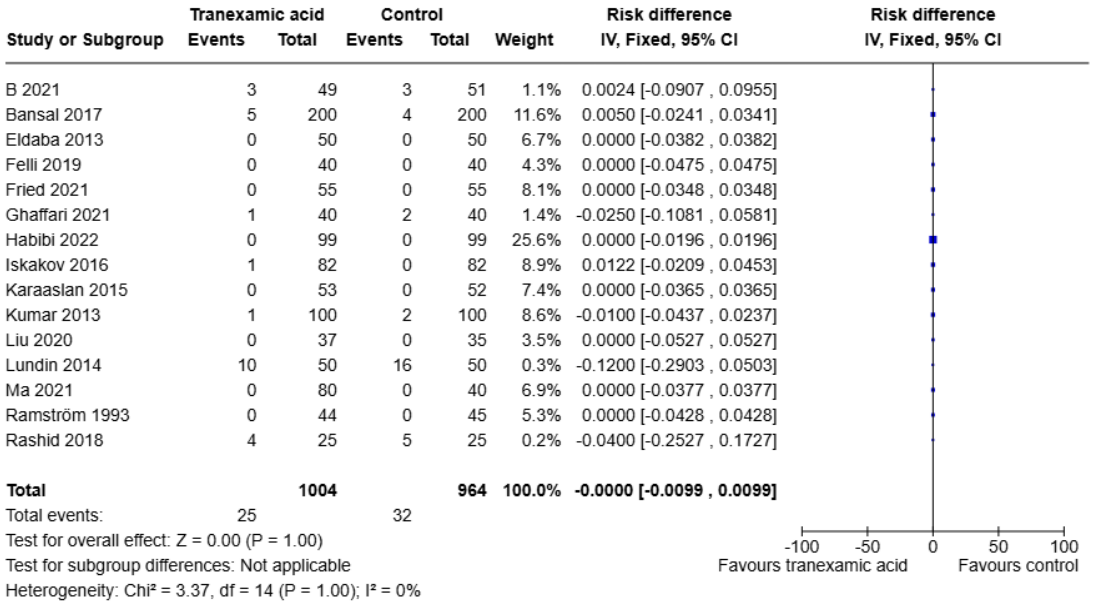
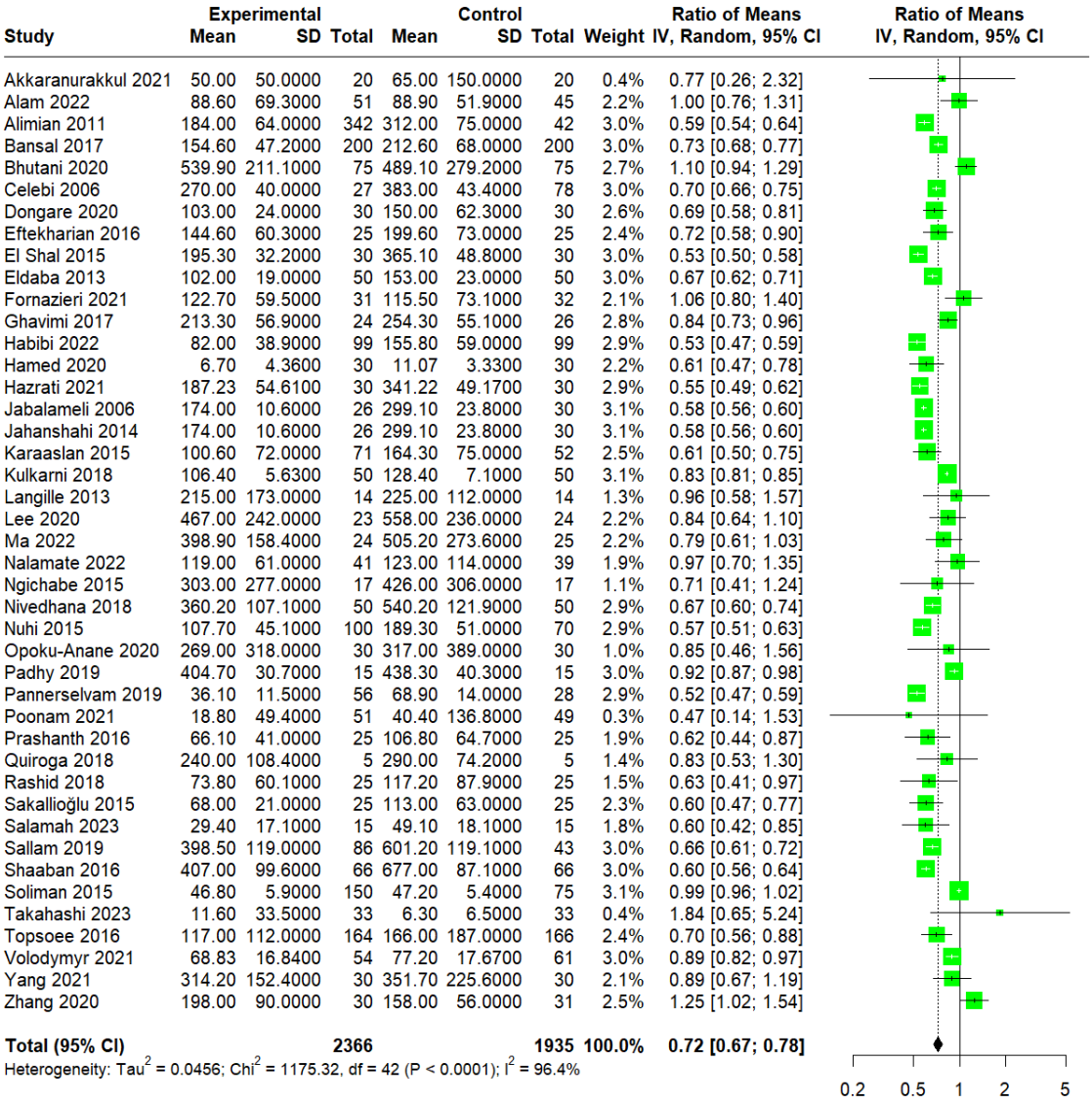


Figure 9 Surgical bleeding at end of study



Appendix F GRADE summary

Table 1 Effectiveness evidence summary: tranexamic acid compared to control

Outcome	Number of studies	Sample size	GRADE components	GRADE	Effect measure	Effect size	Control group rate	Absolute effect (per 1000 people)	Reasons	Clinical importance
Proportion of patients requiring transfusion at end of study (risk ratio analysis), study types: randomised trials, scale: not applicable, units: not applicable	18	2073	Risk of bias: Very serious Indirectness: Not serious Inconsistency: Not serious Imprecision: Not serious Other considerations: None	Low	Risk Ratio	0.42146 (0.31437, 0.56502)	131 per 1000 people	70 fewer events, 95 fewer to 45 fewer	Risk of bias: Downgraded twice. Very serious risk of bias in the evidence contributing to the outcomes. More than 50% of the weight of the evidence came from studies at high risk of bias as per RoB2	Clinically important benefit (absolute effect exceeded 10% of control group rate)
Proportion of people requiring transfusion at end of study (risk difference analysis), study types:	18	2073	Risk of bias: Serious Indirectness: Not serious Inconsistency: Serious Imprecision: Not serious	Low	Risk Difference	-0.06447 (-0.09344, -0.0355)	131 per 1000 people	64 fewer events, 93 fewer to 35 fewer	Risk of bias: Downgraded once. Serious risk of bias in the evidence contributing to the outcomes. More than 50%	Clinically important benefit (absolute effect exceeded 10% of

randomised trials, scale: not applicable, units: not applicable			Other considerations: None						of the weight of the evidence came from studies at moderate or high risk of bias as per RoB2 Inconsistency: Downgraded once. Serious heterogeneity (I2 = 40 to 60%) unexplained by subgroup analysis. Random effects analysis used	control group rate)
All-cause mortality at 30 days, study types: randomised trials, scale: not applicable, units: not applicable	2	272	Risk of bias: Very serious Indirectness: Not serious Inconsistency: Not serious Imprecision: Not serious Other considerations: None	Low	Risk Difference	0 (-0.01962, 0.01962)	0 per 1000 people	0 fewer events, 20 fewer to 20 more	Risk of bias: Downgraded twice. Very serious risk of bias in the evidence contributing to the outcomes. More than 50% of the weight of the evidence came from studies at high	No clinically important difference (clinical importance: 1 per 1000)

									risk of bias as per RoB2	
Length of stay at end of study, study types: randomised trials, scale: not applicable, units: days	13	1749	Risk of bias: Serious Indirectness: Not serious Inconsistency: Very serious Imprecision: Very serious Other considerations: None	Very low	Mean Difference	-0.54595 (-0.86561, -0.22629)	Not applicable	Not applicable	Risk of bias: Downgraded once. Serious risk of bias in the evidence contributing to the outcomes. More than 50% of the weight of the evidence came from studies at moderate or high risk of bias as per RoB2 Inconsistency: Downgraded twice. Very serious heterogeneity (serious I2 = >60%) unexplained by subgroup analysis. Random effects analysis used Imprecision:	Clinically important benefit (decrease of more than half a day)

									Downgraded twice. Very serious imprecision because of small sample size compared to the optimal information size (OIS)	
Number of units of allogenic blood transfused at end of study, study types: randomised trials, scale: not applicable, units: units	1	150	Risk of bias: Not serious Indirectness: Not serious Inconsistency: Not serious Imprecision: Very serious Other considerations: None	Low	Mean Difference	-0.24 (-0.43962, -0.04038)	Not applicable	Not applicable	Imprecision: Downgraded twice. Very serious imprecision because of small sample size compared to the optimal information size (OIS)	Clinically important benefit (decrease in blood transfused)
Volume of allogenic blood transfused at end of study, study types: randomised trials, scale: not applicable, units: mL	1	120	Risk of bias: Not serious Indirectness: Not serious Inconsistency: Serious Imprecision: Not serious Other	Moderate	Mean Difference	-97.5 (-121.42, -73.58)	Not applicable	Not applicable	Inconsistency: Single study-downgraded once for inconsistency, as single study outcomes may otherwise receive	Clinically important benefit (decrease in blood transfused)

			considerations: None						favourable ratings for inconsistency by default	
Serious adverse events at end of study, study types: randomised trials, scale: not applicable, units: not applicable	18	2024	Risk of bias: Not serious Indirectness: Not serious Inconsistency: Not serious Imprecision: Not serious Other considerations: None	High	Risk Difference	-0.00252 (-0.01129, 0.00625)	79 per 1000 people	3 fewer events, 11 fewer to 6 more	No downgrading required	No clinically important difference (less than 10% of the control group rate)
Thrombotic complications at end of study, study types: randomised trials, scale: not applicable, units: not applicable	29	3043	Risk of bias: Serious Indirectness: Not serious Inconsistency: Not serious Imprecision: Very serious Other considerations: None	Very low	Risk Difference	0.00047 (-0.00576, 0.0067)	3 per 1000 people	0 fewer events, 6 fewer to 7 more	Risk of bias: Downgraded once. Serious risk of bias in the evidence contributing to the outcomes. More than 50% of the weight of the evidence came from studies at moderate or high risk of bias as per RoB2	No clinically important difference (less than 10% of the control group rate)

									Imprecision: Downgraded twice. Very serious imprecision because of small sample size compared to the optimal information size (OIS)	
Acute myocardial infarction at end of study, study types: randomised trials, scale: not applicable, units: not applicable	1	164	Risk of bias: Not serious Indirectness: Not serious Inconsistency: Serious Imprecision: Very serious Other considerations: None	Very low	Risk Difference	0 (-0.0235, 0.0235)	0 per 1000 people	0 fewer events, 24 fewer to 24 more	Inconsistency: Single study-downgraded once for inconsistency, as single study outcomes may otherwise receive favourable ratings for inconsistency by default Imprecision: Downgraded twice. Very serious imprecision as small sample	No clinically important difference (less than 10% of the control group rate)

									size and zero events in both study arms	
Infection at end of study, study types: randomised trials, scale: not applicable, units: not applicable	15	1968	Risk of bias: Not serious Indirectness: Not serious Inconsistency: Not serious Imprecision: Very serious Other considerations: None	Low	Risk Difference	-0.00002 (-0.00991, 0.00987)	33 per 1000 people	0 fewer events, 10 fewer to 10 more	Imprecision: Downgraded twice. Very serious imprecision because of small sample size compared to the optimal information size (OIS)	No clinically important difference (less than 10% of the control group rate)
Total blood loss volume at end of study, study types: randomised trials, scale: not applicable, units: not applicable	43	4301	Risk of bias: Serious Indirectness: Not serious Inconsistency: Very serious Imprecision: Not serious Other considerations: None	Very low	Ratio of Means	0.72 (0.67, 0.78)	Not applicable	Not applicable	Risk of bias: Downgraded once. Serious risk of bias in the evidence contributing to the outcomes. More than 50% of the weight of the evidence came from studies at moderate or high risk of bias as per RoB2 Inconsistency:	Clinically important benefit (ratio of means less than 0.8 indicating a reduction in total blood loss volume)

									Downgraded twice. Very serious heterogeneity (serious I2 = >60%) unexplained by subgroup analysis. Random effects analysis used	

1

Appendix G Economic evidence table

G.1 Tranexamic acid versus Standard care in those undergoing surgery categorised as low risk blood loss

G.1.1 Economic studies used in decision-making

Jaiswal, 2025

Table 2: Economic evidence study extraction table: Jasiwal, 2025

Section	Details for Jaiswal, 2025
Study details	**Economic analysis type:** Cost-utility **Analysis design:** Decision analytic model (decision tree) **Country setting:** UK **Perspective:** NHS and PSS **Time horizon:** 30 days **Discount rate per year:** NA (time horizon < 1 year)
Interventions	**Intervention 1:** Standard care Standard care without the administration of TXA. This included the usual surgical and peri-operative practices without the use of TXA to reduce blood loss. **Intervention 2:** Tranexamic acid (TXA) TXA was administered peri-operatively to patients undergoing surgery classified as low risk for blood loss. The typical dosing and administration assumed was 1 gram of TXA given by slow intravenous injection at the start and end of surgery, totalling 2 grams per surgery.
Population	**Population:** Adults undergoing surgery classified as low risk for blood loss. Low risk for blood loss was classified based on the risk stratification for procedural bleed risk as suggested by the International Society on Thrombosis and Haemostasis (ISTH), assuming <500mL of blood loss. The model did not consider surgeries with expected blood loss exceeding 500 mL, as these were categorized as moderate or high risk and were addressed separately in the previous NICE guideline (NG24). **Baseline characteristics** The economic evaluation used data from the associated clinical review and meta-analysis, which included 82 RCTs involving 8,506 participants undergoing surgery classified as low risk for blood loss. Start age = NR Male = 61% **Sub-group analyses:** Type of surgery

Section	Details for Jaiswal, 2025
	• General Surgery • Gynaecology • Otolaryngology • Orthopaedics • Urology The overall treatment effect for TXA was used in these sub-group analyses in the absence of any evidence for a treatment modifying effect of baseline risk.
Costs included	**Original currency & cost year:** 2024 UK pounds **Cost components incorporated:** TXA (£1.66 per patient), blood transfusion (£216.53 per unit of RBC), hospital stay (£345 per day)
Outcomes included	**Primary health outcome in economic analysis:** QALY **Key events modelled /analysed:** reduction in blood loss, reduction in transfusion requirements, reduction in hospital stay, improvement in QoL.
Data Sources	**Effectiveness data:** Systematic review and meta-analysis. **Baseline / epidemiological data:** Effect of TXA and risk of transfusion obtained from a systematic review and meta-analysis. The log odds of transfusion was estimated via meta-analysis using all the control arms from the trials identified in the clinical systematic review that reported transfusion rates. The relative effect of TXA on transfusion was reported as a log odds ratio and estimated from meta-analysis. Log odd transfusion (untreated): -1.605 Log odds ratio transfusion (TXA): -0.945 Difference in length of stay (days): 0.397 The above values are obtained using a random-effect model. **Quality-of-life weights:** EQ-5D-3L UK tariff (utility values obtained from NG24 – obtained from the 22nd Annual Health Survey for England). Utility of hospitalisation (per diem): 0.247 decrement **Costs and/or resource use:** Cost of TXA was based on 2g dose via slow IV injection and was taken from eMIT data (2024). It was assumed the surgery anaesthetist would administer TXA, so no staff was included in this cost. Blood transfusion cost per unit transfused included staff time both on the ward and at the blood bank, disposables, one unit of RBC and wastage per unit. Resources use based on Agrawal 2026 and NG24 committee opinion except for blood volume transfused. As no clinical evidence was identified in the systematic review on the number of units transferred. Clinical opinion of 1 unit of blood transferred was therefore used in the model. It was assumed all transfusions would be of red blood cells (RBC). Unit cost sources included: NHS Blood and Transplant list price (2023/2024) and PSSRU Health and Social Care unit costs 2023. The effect of TXA on length of stay was independent of the degree of blood loss in the control arms of the included studies. Given the wide variety of procedures that may be considered 'low' risk, the model did not

Section	Details for Jaiswal, 2025
	attempt to estimate an average cost per (excess) day in hospital for a particular array of procedures; rather a single unit cost per hospital day was applied (Hansard 2023)
Results: costs	**Total costs (per patient):** Intervention 1: £173.20 Intervention 2: £17.25 Incremental (2-1): saves £155.95: (95% CI: saves £25, saves £305; p=NR) **Breakdown of costs by key cost components** ***Cost of TXA*** Intervention 1: £0 Intervention 2: £1.66 ***Cost of Transfusion*** Intervention 1: £36.06 Intervention 2: £15.59 ***Cost of Length of stay*** Intervention 1: £137.14 Intervention 2: £0
Results: health outcomes	**QALYs (per patient):** Intervention 1: 0.000 Intervention 2: 0.000 Incremental (2-1): 0.000 (95% CI: NR; p=NR) **Average number of transfusions (per patient):** Intervention 1: 0.167 Intervention 2: 0.072 **Average length of stay (per patient):** Intervention 1: 0.398 Intervention 2: 0
Results: cost effectiveness	**Incremental cost-effectiveness ratios:** 2 vs 1: TXA dominates standard care (PSA) **Incremental net monetary benefit (NMB) (2 vs 1) at £20K per QALY gained threshold:** £161 (95% CI: £20, £315) The magnitude of net benefit is driven by savings in length of stay.
Results: Uncertainty	Sensitivity analyses: Varied the log odds and log odds ratio for transfusion, and the length of stay reduction, across quantiles of their respective distributions. With length of stay applied based on the clinical review, the results were not sensitive to variation of the log odds and log odds ratio for

Section	Details for Jaiswal, 2025
	transfusion. With length of stay effect removed, net benefit remains due to savings in blood transfusion. They also performed analyses at levels of transfusion risk less than or equal to 10% to assess how net benefit would be impacted by lower levels of risk than seen in the clinical review (17%). Savings remain positive with and without effect of length of stay included. Only when length of stay is excluded, and the level of blood transfusion is below 2% does the conclusion change and NMB become negative. <u>Scenario analyses:</u> When fixed effects model is applied to the meta-analysis (compared to random effects model in the base case): Transfusion log odds fixed effects NMB £164 Transfusion log OR fixed effects NMB £159 LOS fixed effects, NMB £234 All fixed effects NMB £232 Scenario analysis by surgery type (with LOS included/excluded) General surgery –, NMB £156 / £14 Gynaecology – NMB £168 / £26 Otolaryngology – NMB £142 / £0 Plastic surgery – NMB £165 / £23 Urology – NMB £156 / £13 Overall, the model found that fewer than one transfusion avoided for every 100 cases TXA given would offset the cost of TXA. **Probabilistic:** Probability Intervention 2 cost-effective (£20K threshold): 99% Uncertainty in clinical parameters is based on the findings of the meta-analysis. A probability distribution was not applied to either the cost of TXA or blood transfusion, but the model did assume a standard error for the cost of a hospital ward day equal to 15% of the mean.
Health inequalities assessment	NR
Comments	**Source of funding:** NIHR Evidence Synthesis Programme (NIHR153934) **Other:** Thrombotic complications not included
Rating: Applicability	Directly applicable UK study, QALYs
Rating: Quality/ limitations	Minor limitations Mortality not included in the analysis.

Section	Details for Jaiswal, 2025
	Inclusion criteria were based on a list of surgeries classified as low-risk (based on ISTH guidance). However, many included studies observed volumes of blood loss in the trial control arms equal to, or greater than, surgeries classed as moderate or high risk of blood loss (i.e. >= 0·5 litres). Length of stay can be heavily influenced by the healthcare system the study is conducted in. Therefore, any non-NHS setting may not be reflective of UK current practice. No mention of thrombotic complications. Clinical review reports reduced pain for those receiving TXA vs no TXA post operatively. This potentially could have been used to estimate QoL

Abbreviations: CI= confidence interval; DA=deterministic analysis; eMIT=electronic market information tool; EQ-5D= euroqol five-dimensional questionnaire with three levels; ICER=incremental cost-effectiveness ratio; ISTH= international society on thrombosis and haemostasis; IV= intravenous; LOS=length of stay; PSA=probabilistic sensitivity analysis; NA=not applicable; NR=not reported; PSS= Personal Social Services; QALY=quality-adjusted life-year; QoL= quality of life; RBC= red blood cell; RCT=randomised controlled trial; TXA=tranexamic acid.

Appendix H Excluded studies

Effectiveness

Table 3 Studies excluded from the effectiveness review

Study	Reason for exclusion
Abdul, Ishaq F, Amadu, Motunrayo B, Adesina, Kike T et al. (2019) Adjunctive use of tranexamic acid to tourniquet in reducing haemorrhage during abdominal myomectomy - A randomized controlled trial. European journal of obstetrics, gynecology, and reproductive biology 242: 150-158	People with moderate amounts of blood loss (500-1000 mL)
Aboelsuod, Mohamed Abdelgawad Abdelhalim, Abdalla, Abdalla Mohamed, Ahmed, Ismail Mohamed Abdelgawad et al. (2023) Clinical efficacy of local infiltration of lidocaine and tranexamic acid application in tonsillar region on postoperative pain and bleeding during tonsillectomy: prospective, randomized, double-blind controlled study. Ain-Shams Journal of Anesthesiology 15(1): 90-90	No usable outcomes
Abtahi, Mojtaba, Kargoshai, Amir-Abbas, Shetabi, Hamidreza et al. (2023) The Effect of Tranexamic Acid Local Injection on Bleeding during and after Tonsillectomy: A Double-Blind Randomized Placebo-Controlled Trial. World journal of plastic surgery 12(3): 31-36	Surgical bleeding reported as a median (IQR) – given the abundant reporting of this outcome, that this value could not be meta-analysed with the other data, and that it was assessed that this would not add any value to the existing evidence (as it was showing the same effect as other studies). It was agreed to not add this to the report.
Batagello, Carlos A, Vicentini, Fabio C, Monga, Manoj et al. (2022) Tranexamic acid in patients with complex stones undergoing percutaneous nephrolithotomy: a randomised,	People with moderate amounts of blood loss (500-1000 mL)

Study	Reason for exclusion
double-blinded, placebo-controlled trial. BJU international 129(1): 35-47	
Caglar, G S, Tasci, Y, Kayikcioglu, F et al. (2008) Intravenous tranexamic acid use in myomectomy: a prospective randomized double-blind placebo controlled study. European journal of obstetrics, gynecology, and reproductive biology 137(2): 227-31	People with moderate amounts of blood loss (500-1000 mL)
Choudhury, Sunirmal; Dutta, Avisek; Pal, Dilip Kumar (2023) Comparison of efficacy of tranexamic acid irrigation versus intravenous injection for preventing blood loss in percutaneous nephrolithotomy. Journal of Clinical Urology 16(2): 108-112	Comparing different routes of administration of tranexamic acid
Grundsell, H; Larsson, G; Bekassy, Z (1984) Use of an antifibrinolytic agent (tranexamic acid) and lateral sutures with laser conization of the cervix. Obstetrics and gynecology 64(4): 573-6	No usable outcomes
Haddady-Abianeh, Shahriar, Rahmati, Javad, Delavari, Changiz et al. (2022) Comparison of the Effect of Injectable Tranexamic Acid and Inhaled Desmopressin in Controlling Bleeding and Ecchymosis in Open Rhinoplasty. World journal of plastic surgery 11(3): 24-27	No usable outcomes
Karaaslan, Fatih; Karaoğlu, Sinan; Yurdakul, Emre (2015) Reducing Intra-articular Hemarthrosis After Arthroscopic Anterior Cruciate Ligament Reconstruction by the Administration of Intravenous Tranexamic Acid: A Prospective, Randomized Controlled Trial. The	Duplicate reference

Study	Reason for exclusion
American journal of sports medicine 43(11): 2720-6	
Mackenzie, Samuel P, Spasojevic, Miloš, Smith, Margaret et al. (2022) The effect of single-dose, preoperative intravenous tranexamic acid on early postoperative pain scores after rotator cuff repair: a double-blind, randomized controlled trial. Journal of shoulder and elbow surgery 31(7): 1399-1408	No usable outcomes
Mitra, Sukanya, Jain, Kompal, Singh, Jasveer et al. (2022) Topical vs. intravenous administration of tranexamic acid to minimize blood loss in abdominal hysterectomy perioperatively: A randomized controlled study. Journal of anaesthesiology, clinical pharmacology 38(2): 233-239	No usable outcomes
Mohammadi Sichani, Mehrdad, Kazemi, Reza, Nouri-Mahdavi, Kia et al. (2019) Re-evaluation of the efficacy of tranexamic acid in reducing blood loss in percutaneous nephrolithotomy: a randomized clinical trial. Minerva urologica e nefrologica = The Italian journal of urology and nephrology 71(1): 55-62	People with moderate amounts of blood loss (500-1000 mL)
Mousavi, Hamid; Akbari-Aghdam, Hossein; Entezari, Reza (2023) The effect of tranexamic acid injection during anterior cruciate ligament reconstruction surgery on postoperative bleeding, pain and swelling. European journal of orthopaedic surgery & traumatology : orthopedie traumatologie 33(3): 639-644	No usable outcomes
Nicholson, Thema A, Kirsch, Jacob M, Churchill, Ryan et al. (2022) The effect of tranexamic acid for visualization on pump	No usable outcomes

Study	Reason for exclusion
pressure and visualization during arthroscopic rotator cuff repair: an anonymized, randomized controlled trial. Journal of shoulder and elbow surgery 31(11): 2211-2216	
Shady, Nahla W.; Sallam, Hany F.; Fahmy, Huda (2018) Reducing blood loss during open myomectomy with intravenous versus topical tranexamic acid: A double-blinded randomized placebo-controlled trial. Middle East Fertility Society Journal 23(3): 225-231	People with moderate amounts of blood loss (500-1000 mL)
Shafa, Amir, Besharati, Shima, Shetebi, Hamidreza et al. (2022) Comparative study of the effect of administering two doses of tranexamic acid in patients undergoing adenotonsillectomy. International journal of physiology, pathophysiology and pharmacology 14(4): 233-239	Comparing two doses of tranexamic acid to each other
Singh, Dr. Dhara and Bindal, Dr. Jyoti (2020) The effect of prophylactic use of intravenous tranexamic acid in hysterectomy of benign diseases. International Journal of Clinical Obstetrics and Gynaecology 4(3): 93-97	People with moderate amounts of blood loss (500-1000 mL)

Economic

No economic study was reviewed at full text and excluded from this review.

Appendix I Research recommendations

Research recommendation

What is the clinical and cost-effectiveness of tranexamic acid compared to placebo for children and young people undergoing surgery in reducing the risk of post-operative infection, length of stay and the need for a blood transfusion?

Why this is important

Children are at a higher risk of adverse outcomes from blood loss. Due to the average body weight of a child being lower than that of an adult, their blood volume is lower and the amount of blood loss required before they begin to experience systemic problems is significantly less. Children can also have physiological differences to adults which may means that they respond differently to medication and so taking care to ensure that medication can be prescribed appropriately in a paediatric population is important.

Blood transfusion can be a highly costly procedure, as blood donation levels are generally lower than the supply available in the UK. It is also associated with potential risks such as transfusion reactions, serious allergic reactions and rarely infection. Therefore, where possible, finding alternatives to blood transfusion so that it can be provided to those who require it the most when they need it is preferable.

In this guideline, NICE has made a weak recommendation for tranexamic acid to reduce the need for blood transfusions for children. No specific recommendation was made for young people. Instead it was agreed that the same recommendations as adults could be applied in most cases. This was in part due to a lack of evidence to show clinical and cost effectiveness in this population. Further research may allow for stronger recommendations to be

made in the future and allow for better outcomes for children and young people long term.

Rationale for research recommendation

Importance to the population

Children and young people with significant bleeding may benefit from alternatives to blood transfusion (for example: tranexamic acid) if they are safe to give. Having a blood transfusion poses risks and so providing an alternative can be useful for some people.

Children and young people have specific outcomes that are more likely to be important to them that will not be captured in research for adults. Conducting research specific to children that focusses on their needs is important to ensure this is understood.

Relevance to NICE guidance

The current Blood Transfusion guideline recommends that tranexamic acid is considered for children and young people. Further research into the clinical and cost-effectiveness is required to strengthen this recommendation.

Relevance to the NHS

Providing further clarity on the effectiveness of the medicine for children and young people will allow for clearer guidance on the implementation of the treatment for this population, allowing for more consistent care to be delivered across the NHS.

The review for the Blood transfusion guideline was limited in the number of studies conducted in a UK NHS health setting context. Therefore, being able to provide that information with cost-effectiveness evidence would allow for greater understanding of the applicability of the evidence to this health context

allowing for better certainty in the current findings and the findings for children.

National priorities

This falls within the James Lind Alliance top 10 priorities for blood transfusion and blood donation areas for research (priority 7 – what are the best drug alternatives to blood transfusion to reduce and prevent bleeding?)

Current evidence base

The current evidence review showed that there is limited evidence investigating the efficacy of tranexamic acid for children and young people where there is an anticipated minor blood loss. The previous guideline review showed there is limited evidence where there is anticipated moderate and severe blood loss. The safety review showed there is limited evidence where there is any blood loss. However, it is known that analysis of the TARN data did not show an increase in the number of thromboembolic events in paediatric trauma (though this did not include adverse events like seizures) and the TIC-TOC trial is currently being developed to investigate the safety of tranexamic acid for children and young people in the trauma setting.

Therefore, the committee agreed that further research into the effectiveness in a surgical setting was important for developing the current evidence base.

Equality considerations

Providing more certainty to the care of children and young people helps to reduce inequalities in their care compared to adults.

Providing an alternative to blood transfusions is useful for reducing health inequalities for people who are more likely to bleed, people who are more likely to need blood transfusions and people who may have reasons to refuse a blood transfusion.

Table 4 Research recommendation protocol outline

Population	Children and young people (1 to 17) undergoing cardiac and non-cardiac surgery who are anticipated to have any blood loss
Interventions	Tranexamic acid 15 mg/kg (maximum 1 gram) over 10 minutes before the start of surgery with more tranexamic acid providing during surgery if needed dependent on the duration of surgery and volume of blood loss Route is not specified. Could include intravenous, topical, oral or a combination of approaches.
Comparator	No tranexamic acid
Outcomes	• Proportion of children requiring blood transfusion • All-cause mortality at 30 days • Quality of life • Pain • Time to return to feeding • Length of stay (hospitalisation) • Number of units of allogenic blood transfused • Serious adverse events including cardiovascular or respiratory adverse events, thrombotic complications, infection, seizures Cost effectiveness
Study type	Randomised controlled trial (RCT)
Timeframe	30 days
Other information	Information should be provided about the surgery type; how much blood was lost and how this was determined. Study should be sufficiently powered to capture events (in particular for children requiring blood transfusion).

Research recommendation

What is the clinical and cost-effectiveness of tranexamic acid compared to placebo for people having specific vascular surgery procedures in reducing limb-related thromboembolic events, pain and infection?

Why this is important

Blood transfusion can be a highly costly procedure, as blood donation levels are generally lower than the supply available in the UK. It is also associated with potential risks such as transfusion reactions, serious allergic reactions and rarely infection. Therefore, where possible, finding alternatives to blood transfusion so that it can be provided to those who require it the most when they need it is preferable.

Vascular surgery is a field of surgery where thrombotic complications are more common and can have very significant effects. In the National Comparative Audit of NICE Quality Standard QS138, the uptake of the previous recommendation was lowest amongst this speciality. When conducting the systematic review, no evidence was found to indicate that tranexamic acid was clinically effective or safe for people undergoing vascular surgery procedures. While the committee agree that the evidence from other areas can be broadly applied to this speciality, they also agree that further evidence about which surgeries have greater benefit from tranexamic acid may help to give better specificity to vascular surgery recommendations in the future, and help to improve the uptake of the recommendations. They noted that while tranexamic acid for surgeries that anticipate higher levels of blood loss (such as abdominal aortic aneurysm repair) may be more acceptable, there may be less acceptance of surgeries that anticipate lower levels of blood loss due to the catastropic risks of thromboembolic events. Taking that in mind, the committee agreed that this question was of great importance for this speciality.

Rationale for research recommendation

Importance to the population

People undergoing vascular surgery are generally more likely to have thromboembolic events due to the natural history of their conditions and more likely to have significant bleeding events due to a combination of the surgery being performed and medication being provided to reduce the likelihood of them having thromboembolic events. Therefore, understanding if providing tranexamic acid for any specific vascular surgery procedures a) provides any benefit, b) adds any risks (given that it works as an anti-fibrinolytic and the safety review showed a very small increase in the risk of thromboembolic events), c) the best strategy to use after weighing up the benefits and the risks.

Relevance to NICE guidance

The current NICE guidance included no evidence for vascular surgery. This group has previously shown lower uptake of recommendations about tranexamic acid. Providing further clarity may allow for more specific guidance to be provided for this subgroup and for more reassurance to improve uptake of the guidance in the future.

Relevance to the NHS

Providing more certainty about the use of tranexamic acid will allow for more consistent care across the NHS.

The review for the Blood transfusion guideline was limited in the number of studies conducted in a UK NHS health setting context. Therefore, being able to provide that information with cost-effectiveness evidence would allow for greater understanding of the applicability of the evidence to this health context allowing for better certainty in the current findings and the findings for people having specific vascular surgery procedures.

National priorities

This falls within the James Lind Alliance top 10 priorities for blood transfusion and blood donation areas for research (priority 7 – what are the best drug alternatives to blood transfusion to reduce and prevent bleeding?)

Current evidence base

The current evidence base is very limited regarding vascular surgery making it difficult to comment on the efficacy and safety in this population. Further research is required to allow more conclusions to be drawn for specific procedures for this subgroup.

Equality considerations

Providing an alternative to blood transfusions is useful for reducing health inequalities for people who are more likely to bleed, people who are more likely to need blood transfusions and people who may have reasons to refuse a blood transfusion.

Table 5 Research recommendation protocol outline

Population	Adults (over the age of 16) undergoing vascular surgery who are anticipated to have any blood loss. Subgroup by the surgical procedure being performed. For example (but not limited to): • Aneurysm repair • Arteriovenous fistula surgery • Arteriovenous graft surgery • Carotid angioplasty and stenting • Carotid endarterectomy • Endovascular repair • Peripheral bypass surgery • Thromboendarterectomy • Vein ligation and stripping
Interventions	Tranexamic acid 1 gram before the start of surgery with more tranexamic acid providing during surgery if needed dependent on the duration of surgery and volume of blood loss.

	Route is not specified. Could include intravenous, topical, oral or a combination of approaches.
Comparator	No tranexamic acid (usual care)
Outcomes	• Proportion of adults requiring blood transfusion • All-cause mortality at 30 days • Quality of life • Pain • Limb ischaemia • Surgical site infection • Graft or stent occlusion • Amputation • Length of stay (hospitalisation) Cost effectiveness
Study type	Randomised controlled trial (RCT)
Timeframe	30 days
Other information	Information should be provided about how much blood was lost and how this was determined. Study should be sufficiently powered to capture events (in particular for adults requiring blood transfusion).

1