Table 1. Characteristics of included studies

Paper	Study	N	Gender (M/F)	Mean age (years)	ASA grade (3 or 4)	Fracture type	Fracture surgical management	Duration of surgery (minutes)	Intervention	Control
Lee et al 2015 [19]	RCS	271	Interv: 32/52 Control: 53/134	Interv: 86.0 Control: 84.7	Interv: 57 Control: 137	Hip Fracture	Hemiarthroplasty: 271	Not documented	(N: 84) 1g IV TXA given at induction.	(N:187) No treatment control.
Sadeghi & Mehr - Aein 2007 [34]	DBL blind RCT	67	Interv: 17/15 Control: 24/11	Interv: 51.8 Control: 44.4	Not documented	Hip Fracture	Not documented	Not documented	(N:32) Single bolus of 15mg/kg IV TXA given at induction.	(N:35) Same volume of IV normal saline given to controls.
Zuffery at al. 2010 [16]	DBL blind RCT	110	Interv: 10/47 Control: 4/49	Interv: 81 Control: 82	Interv: 19 Control: 20	Cervical: 45 Trochanteric: 19 Unstable trochanteric/inter/subtrochanternic: 46	THR: 45 Hemiarthroplasty: 2 SHS: 41 IMN: 22	Interv: 64.0 Control: 64.0	(N:57) Two doses of IV TXA – 15mg/kg given at induction then another 3 hours later.	(N:53) Control group received 2 doses of IV placebo at same intervals.
Emara 2014 [17]	DBL blind RCT	60	Interv (IV): 12/8 Interv (Topical): 10/10 Control: 14/6	Interv (IV): 56.5 Interv (Topical): 55 Control: 56	Not documented	Hip Fracture	Hemiarthroplasty: 60	Interv (IV): 2.3 hrs Interv (Topical): 2.3 hrs	(N:20) IV TXA 10mg/kg as bolus pre incision then 5mg/kg/h infusion until end (N:20) Topical TXA 100mls NS with 1.5g TXA poured into surgical field for 5 mins	(N:20) Control received 20ml of normal saline pre-incision and 80ml/h of normal saline until end.100ml of normal saline poured into surgical field for 5 mins
Mohib et al. 2015 [18]	DBL blind RCT	100	Interv: 21/29 Control: 24/26	Interv: 69.0 Control: 70.0	Not documented	Intertrochanteric: 100	SHS: 100	Interv: 112.9 Control: 112.3	(N: 50)Two doses of IV 10mg/kg TXA at induction and 3 hours later.	(N:50) Controls: same amount saline.
Vijay et al 2013 [33]	DBL blind RCT	90	Interv: 10/35 Control: 10/35	Interv: 49.3 Control: 48.8	Interv: 0 Control: 0	Hip and Femoral fracture. No further details provided.	ORIF; hemiarthroplasty; THR. Frequencies not documented.	Interv: 118.7 Control: 117.3	(N: 45) 10mg/kg body weight IV TXA given 15min prior to incision.	(N:45) Controls: 1mg/kg body weight IV saline.
Tengberg et al 2016 [32]	DBL blind RCT	72	Interv: 7/26 Control: 14/25	Interv: 79.8 Control: 75	Interv: 5 Control: 12	Extracapsular (AO type 31-A2.2 to 31-A3): 72	Short intramedullary nail: 72	Not documented	(N: 33) 1g IV TXA as bolus pre incision then post-op 24hr infusion of 3g TXA	(N: 39) Controls: 5ml saline given pre incision and then 24 hour infusion of 1litre IV saline

Abbreviations: DBL = Double; RCT = Randomised controlled trial; RCS = Retrospective cohort study; Interv = Intervention group; THR = Total Hip replacement; SHS = Sliding hip screw; IMN = Intramedullary nail; ORIF = Open reduction internal fixation

Table 2. Synthesis of results for all outcomes & GRADE assessment: summary of findings

Outcomes	Intervention	Control	Relative effect (95% CI)	Inconsistency value (I^2)	Inconsistency (Chi^2) p value	Number of participants [Studies]	Quality of evidence	Comments
Post-operative blood transfusion	85 of 321	166 of 429	RR 0.54 (0.35, 0.85)	78%	p<0.0001	750 [16-19, 32-34]	Moderate	Serious imprecision
Post-operative haemoglobin	10.5 g/dl	10.0 g/dl	MD 0.81 (0.45, 1.18)	46%	p=0.10	638 [17-19, 32-34]	High	
Blood loss on 1st post-operative day	467mls	780mls	MD -341 (-672, -9.87)	100%	p<0.0001	197 [17, 31, 34]	Low	Serious inconsistency & serious imprecision
Peri-operative blood loss	415mls	568mls	MD -190 (-495, 115)	91%	p<0.0001	249 [16, 32, 34]	Low	Serious inconsistency & serious imprecision
Length of hospital stay	16.4 days	16.1 days	MD 0.26 (-4.05, 4.56)	77%	p=0.04	338 [19, 34]	Very low	Serious risk of bias, serious inconsistency & serious imprecision
Post-operative complications: 30 day mortality	9 of 206	11 of 314	RR 1.33 (0.53, 3.34)	0%	p=0.48	520 [16,19, 32, 34]	Moderate	Serious risk of bias
Post-operative complications: Stroke	2 of 110	1 of 112	RR 1.49 (0.24, 9.25)	0%	p=0.60	222 [16, 17, 32]	Low	Very serious imprecision
Post-operative complications: Thromboembolic events	16 of 289	10 of 394	RD 0.01 (-0.03, 0.05) *	68%	p=0.007	683 [16-19, 32, 31]	Low	serious inconsistency & serious imprecision
Post-operative complications: Pulmonary embolus	0 of 205	0 of 207	RD 0.00 (-0.02, 0.02) *	0%	p=1.00	412 [16-18, 32, 33]	Low	Very serious imprecision
Post-operative complications: DVT	10 of 172	4 of 168	RD 0.01 (-0.03, 0.04) *	43%	p=0.13	412 [16-18, 32, 33]	Low	Serious inconsistency & serious imprecision

Abbreviations: GRADE = Grading of Recommendations Assessment, Development and Evaluation;
CI =Confidence interval; RR =Relative risk; RD = Risk difference; MD = Mean difference. * risk difference calculated given zero-events were reported in some studies.

Table 3. Subgroup & Sensitivity analysis

Subgroup Analysis	Variable [Studies]	Transfusion	Post-operative haemoglobin	Day 1 post-operative blood loss	Peri-operative blood loss	Total Length of Hospital Stay	Thromboembolic events	30 day mortality	90 day mortality	PE	DVT	Stroke
Age	≥76 [16,19,32]	RR 0.67 (0.37, 1.22); I^2: 84%; Inconsistency Chi^2 p=0.002; N=453 *	MD 0.50 (0.10, 0.89); I^2: 0%; Inconsistency Chi^2 p=0.87; N=341		MD -47.6 (-127, 31.5); I^2: 0%; Inconsistency Chi^2 p=0.97; N=182 *		RD 0.00 (-0.07, 0.08); I^2: 69%; Inconsistency Chi^2 p=0.04; N=453	RR 1.61 (0.64, 4.03); I^2: 0%; Inconsistency Chi^2 p=0.41; N=453		RD 0.00 (-0.03, 0.03); I^2: 0%; Inconsistency Chi^2 p=1.00; N=182	RD 0.01 (-0.06, 0.07); I^2: 9%; Inconsistency Chi^2 p=0.29; N=182	RD 0.04 (-0.04, 0.04); I^2: 0%; Inconsistency Chi^2 p=0.32; N=182
	≤75 [17,18,33,34]	RR 0.48 (0.33, 0.72); I^2: 10%; Inconsistency Chi^2 p=0.35; N=297	MD 1.03 (0.46, 1.60); I^2: 64%; Inconsistency Chi^2 p=0.0004; N=297				RD 0.03 (-0.06, 0.12); I^2: 84%; Inconsistency Chi^2 p=0.002; N=230					
BMI	≤40 [16,17,32,34]	RR 0.73 (0.49, 1.11); I^2: 68%; Inconsistency Chi^2 p=0.02; N=289 *	MD 1.34 (0.76, 1.93); I^2: 0%; Inconsistency Chi^2 p=0.79; N=179	MD: -461 (-478, -444); I^2: 0%; Inconsistency Chi^2 p=0.43; N=107			RD 0.08 (-0.10, 0.26); I^2: 82%; Inconsistency Chi^2 p=0.003; N=222	RR 2.26 (0.48, 10.63); I^2: 0%; Inconsistency Chi^2 p=0.42; N=247		RD 0.00 (-0.03, 0.03); I^2: 0%; Inconsistency Chi^2 p=1.00; N=222	RD 0.04 (-0.02, 0.11); I^2: 65%; Inconsistency Chi^2 p=0.20; N=222	
	>40											
Hip fracture type	Intracapsular [17,19]											
	Extracapsular [18,32]	RR 0.67 (0.24, 1.87); I^2: 88%; Inconsistency Chi^2 p=0.004; N=172 *	MD 1.40 (-0.79, 2.01); I^2: 0%; Inconsistency Chi^2 p=0.85; N=212				RD -0.02 (-0.07, 0.04); I^2: 40%; Inconsistency Chi^2 p=0.20; N=172			RD 0.00 (-0.03, 0.03); I^2: 0%; Inconsistency Chi^2 p=1.00; N=172	RD -0.01 (-0.05, 0.03); I^2: 0%; Inconsistency Chi^2 p=0.49; N=172	

Subgroup Analysis	Variable [Studies]	Transfusion	Post-operative haemoglobin	Total post-operative blood loss	Peri-operative blood loss	Total Length of Hospital	Thromboembolic events	30 day mortality	90 day mortality	PE	DVT	Stroke

				Stay					
Vijay et al. 2013 removed	[16-19,32,34]	RR 0.58 (0.36, 0.92); I^2: 78%; Inconsistency Chi^2 p=0.0003; N=660	MD 1.01 (0.50, 1.51); I^2: 43%; Inconsistency Chi^2 p=0.14; N=548	MD: -461 (-478, -444); I^2: 0%; Inconsistency Chi^2 p=0.43; N=107	RD 0.02 (-0.04, 0.08); I^2: 75%; Inconsistency Chi^2 p=0.0003; N=593		RD 0.02 (-0.02, 0.02); I^2: 0%; Inconsistency Chi^2 p=1.00; N=322	RD 0.03 (-0.02, 0.08); I^2: 58%; Inconsistency Chi^2 p=0.07; N=322	
Lee et al. 2015 removed	[16-18,32-34]	RR 0.60 (0.39, 0.92); I^2: 76%; Inconsistency Chi^2 p=0.001; N=479	MD 1.00 (0.47, 1.54); I^2: 53%; Inconsistency Chi^2 p=0.08; N=369		RD 0.02 (-0.04, 0.09); I^2: 77%; Inconsistency Chi^2 p=0.001; N=412	RR 2.26 (0.48, 10.63); I^2: 0%; Inconsistency Chi^2 p=0.42; N=479			

Abbreviations: CI = confidence intervals; I^2 = inconsistency value; N = number of cases; RR = Risk ratio; RD = risk difference (calculated given zero-events were reported in some studies). * denotes result that has ceased to become statistically significant after subgroup analysis.

Supplementary Table 1. Search strategy

1. Tranexamic acid
2. hip fracture
3. femoral fracture
4. neck of femur
5. extracapsular
6. intracapsular
7. subcapital
8. transcervical
9. basicervical
10. intertrochanteric
11. subtrochanteric
12. hemiarthroplasty
13. total hip arthroplasty
14. sliding hip screw
15. dynamic hip screw
16. intramedullary nail
17. femoral nail
18. cannulated screws
19. open reduction internal fixation
20. OR/1-11
21. OR/12-19
22. AND/1,20,21

Supplementary table 2. Risk of bias assessment for individual studies

RCT Studies	**Random sequence generation**	**Allocation concealment**	**Blinding of participants & personnel**	**Blinding of outcome assessment**	**Incomplete outcome data**	**Selective reporting**	**Other bias**	**Other bias explanation**
Emara et al 2014 [17]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk	Low risk	
Mohib et al 2015 [18]	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	
Sadeghi et al 2007 [34]	Low risk	Low risk	Low risk	Unclear risk	Unclear risk	High risk	Low risk	
Vijay et al 2013 [33]	High risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	High risk	unclear frequency of distal or proximal femoral fracture
Zufferey et al 2010 [16]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	
Tengberg et al 2015 [32]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Significant baseline differences in treatment groups
Observational studies	**Bias due to confounding**	**Bias in participant selection**	**Bias in classification of interventions**	**Bias due to departures from intended interventions**	**Bias due to missing data**	**Bias in measurement of outcomes**	**Bias in selection of the reported result**	**Overall bias**
Lee et al 2015 [19]	Serious risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk	Serious risk

Risk of bias assessment was performed using the Cochrane Collaboration's risk of bias tool for RCT's. Each domain was classified as either unclear, low or high risk. The Risk of Bias in non-randomised studies – of interventions (ROBINS-I) tool was used for observational studies. Each domain was classified as low risk, moderate risk, serious risk, and critical risk or not interpretable. An overall bias assessment was then made using the same scale.