

Supplementary Information:

Methodology

REBOA and RTACC Studies

Table S1: Overview of studies used to calculate REBOA outcomes

Reference	Location	Population size	RBC Units (Mean)	ISS	Mean Age	Mortality (%)	Complication
Low ¹	Unknown	15	N/A	N/A	N/A	13/15 (87)	None
Wolf & Berry ²	USA	1	12	N/A	43	0/1 (0)	None
Gupta ³	USA	21	N/A	N/A	25	14/21 (67)	Thrombosis (1 patient)
Matsuoka ⁴	Japan	1	N/A	N/A	47	0/1 (0)	None
Martinelli ⁵	France	13	19	48	42	7/13 (54)	Thrombosis (2 patients)
Brenner ⁶	USA	6	N/A	33.8 3	39.5	2/6 (33)	None
Ogura ⁷	Japan	7	12	50	62	1/7 (14)	None
Irahara ⁸	Japan	14	28.8	29.5	46.9	9/14 (64)	Acute kidney injury (1 patient)
Norii ⁹	USA/Japan	452	N/A	35.6	51.5	343/452 (76)	Unknown
Saito ¹⁰	Japan	24	15.6	47	59	17/24 (71)	Acute kidney injury (9 patients), Amputation (2 patients)
Moore ¹¹	USA	24	N/A	N/A	41	15/24 (63)	None
DuBose ¹²	USA	46	20.5	31	43.2	33/46 (72)	Pneumonia (2), DVT (2), Sepsis (3), Dialysis (2)

Table S2: Overview of studies used to calculate RTACC outcomes

Reference	Location	Population size	RBC units (Mean)	ISS	Mean age	Mortality (%)	Complications
Branney ¹³	USA	124	N/A	N/A	30	115/124 (92)	1 NI
Velmahos ¹⁴	South Africa	118	N/A	N/A	N/A	110/118 (93)	N/A
Durham ¹⁵	USA	124	N/A	N/A	N/A	119/124 (96)	N/A
Ivatory ¹⁶	USA	19	N/A	N/A	N/A	19/19 (100)	N/A
Feliciano ¹⁷	USA	185	N/A	N/A	N/A	180/185 (97)	N/A
Schwab ¹⁸	UK	31	N/A	N/A	N/A	30/31 (97)	N/A
Danne ¹⁹	USA	6	N/A	N/A	35.5	7/8 (88)	1 Empyema
Vij ²⁰	USA	2	N/A	N/A	n/a	2/2 (100)	N/A
Flynn ²¹	USA	6	N/A	N/A	n/a	6/6 (100)	N/A
MacDonald ²²	USA	9	N/A	N/A	n/a	9/9 (100)	N/A
Millikan ²³	USA	39	17	n/a	30.8	12/17 (71)	1 Pneumothorax
Van waes ²⁴	Netherlands	56	N/A	25	32	20/56 (36)	2 Reop, 1 NI
Lorenz ²⁵	USA	463	9	34	35	402/463 (87)	5 Reop + 3 NI
Abe ²⁶	Japan	367	N/A	34	56.7	355/367 (97)	N/A
Seamon et al. (AAST) ²⁷	global	856	N/A	N/A	N/A	796/856 (93)	8 NI
DuBose ¹²	global	68	20	31.5	40.8	55/68 (81)	2 Infection, 1 Haemothorax. 9 NI
Brautigan ²⁸	Unknown	47	N/A	N/A	N/A	34/47 (72)	5 NI
Seamon ²⁹	USA	50	28.6	39.4	N/A	42/50 (84)	N/A
Seamon EDT surv. ³⁰	USA	37	N/A	N/A	N/A	30/37 (81)	N/A
Ledgerwood ³¹	USA	40	N/A	N/A	32	34/40 (85)	1 Sepsis

NI - Neurological impairment

Mortality and Quality of Life of complications

As explained in the search strategy in the main body, the RTACC and REBOA papers did not contain sufficient data regarding complications to generate a cost-utility analysis so data regarding mortality, costs and utility for those complications reported in the RTACC/REBOA papers was identified from the following studies.

Table S3: Studies from which relevant mortality and utility values for complications were obtained

Reference	Location	Population	Complication studied	Mortality	Utility (EQ-5D)
Sprengers ³²	Netherlands	47	Limb ischaemia/Thrombosis	N/A	0.34
Lyaker ³³	USA	N/A	Limb Ischaemia/Thrombosis	4-15%	N/A
Galanaud ³⁴	Germany	1643	DVT	4.4%	N/A
Tennvall ³⁵	Sweden	310	Major lower limb amputation	N/A	0.31
Fortington ³⁶	Unknown	299	Major lower limb amputation	32.5%	N/A
Fagon ³⁷	France	1978	Pneumonia in ICU	52.4%	N/A
Ringburg ³⁸	Netherlands	246	Major trauma	N/A	0.73
Campbell ³⁹	UK	441	Length of stay after major trauma and bleeding	N/A	N/A
Xie ⁴⁰	USA	1040	Neurological impairment	N/A	0.69
Korosec ⁴¹	Slovenia	164	Sepsis	N/A	0.717
Granja ⁴²	Portugal	305	Sepsis	34%	N/A
Griffith ⁴³	USA	90	Haemothorax	2.2%	N/A
Yoon ⁴⁴	Unknown	370	Pneumothorax	3.3%	N/A
Sogaard ⁴⁵	Denmark	1,841	Empyema	10%	N/A
Morris ⁴⁶	USA	78	Dialysis	57%	N/A
Nisula ⁴⁷	Finland/Australia	635	Acute Kidney Injury	35.3%	N/A
NICE ⁴⁸	UK	N/A	Cost of Red Blood Cells	N/A	N/A

REBOA Probabilities

Probability at the exit of each chance node adds up to 1. The sources used to calculate probabilities are listed in Table S1.

Chance node A

- Node A1 “Definitive Intervention”: Of the 625 patients in the studies analysed who received REBOA, 558 survived to definitive procedure, either surgery or angioembolization or both. Probability is $558/(625-14+15)$: 0.936.
- Node A2 “Death”: 67 patients died before receiving any definitive intervention. Probability is thus $1-0.936 = 0.064$.

Chance Nodes B

- B1 “Survive”: From the studies analysed, 164 of 558 patients survived the definitive procedure, a probability of 0.29390681.
- B2 “Dead”: Probability of death was obtained by subtracting 1 from the probability of surviving.

Chance Nodes C

After surviving the definitive intervention, patients are admitted to intensive care. It was assumed that everyone received the same level of care and this was derived from Campbell et al.³⁹ The only complications considered were for those who survived to discharge as it was assumed that patients died prior to having the time to develop them. The studies analysed mentioned a number of complications related to the procedure and the level of care required. Some patients did not have any complications. No patient sustained any neurological impairment as a result of the procedure in the available literature. All studies commented on the presence or absence of all complications reported. Importantly, Norii et al.⁹, by far the largest study analysed, did not report on complications therefore this patient dataset was excluded. Data for complications was available for only 55 patients of the total thereby limiting the quality of the analysis.

- C1 “Pneumonia”: DuBose et al.¹² reported 2 patients with pneumonia
- C2 “Acute Kidney Injury”: Saito et al.¹⁰ and Irihara et al.⁸ reported a total of 10 cases of acute kidney injury from which total recovery occurred
- C3 “Leg Amputation”: 3 amputations were reported in Saito et al.¹⁰ resulting from the use of REBOA. Many studies had amputation as one of the consequences of the injuries sustained.
- C4 “Sepsis”: Sepsis was reported in 3 patients by DuBose et al.¹²
- C5 “Thrombosis”: Thrombosis leading to critical leg ischaemia requiring thrombectomy was reported in Martinelli et al.⁵ and Gupta et al.³ in a total of 3 patients.
- C6 “No Complication”: Patients who did not sustain any of the complications mentioned in this node were 30. This was obtained by subtracting those who did from the total patients that survived to discharge for whom data was available.
- C7 “Dialysis”: DuBose et al.¹² reported on 2 patients who developed end-stage renal failure requiring dialysis as an inpatient.
- C8 “Deep Vein Thrombosis”: DuBose et al.¹² reported on 2 patients who developed a DVT.

Chance Nodes D

- D1, D3, D5, D7, D9, D11, D13 “Survival”: Data on the survival following each of the complications was obtained from literature describing these complications in intensive care and major trauma patients, when possible. If there was no data describing mortalities in patients in these conditions then data was used from studies looking at the general population although this represents a limitation of our study.
- D2, D4, D6, D8, D10, D12, D14 “Death”: Mortality was obtained by subtracting the survival rates from 1.

Chance Nodes E

- E1 “Discharged with dialysis”: Morris et al.⁴⁶ reported that patients who required dialysis after major trauma required long-term dialysis in 18% of cases. It was assumed that this was haemodialysis.

- E2 “Discharged without dialysis”: This represents the remaining 82% of patients who did not require haemodialysis long-term.

RTACC Probabilities

Sources of all the data are delineated in Table S2.

Chance Node A (intervention, Death)

- The “Definitive Intervention” node values were calculated using the rates of patients undergoing RTACC as an intervention, who had data for mortality before arriving at the operating room (OR). Once the rates were found, these were converted into probabilities. The natural log calculations yielded the same values over the one-year study period.
- “Death” values were found by taking away the probability of getting to the OR from 1.

Chance Node B (Survival, Death)

- The “survival” patients were those who arrived to the OR and survived either a laparotomy or angioembolisation procedure. The data for this was limited, included in only 3 studies.
- Those in the “death” category was the mortality rate of the patients undergoing procedures. This was calculated using the number of patients receiving an intervention divided by the were the number of patients who died in the studies with data available for this node.

Chance Node C (Complications)

The rates of complications were assessed using only the values available in the studies reporting this variable. Many studies mentioned, but did not state the number of complications and were therefore excluded.

- C1 (No complications). “no complication” data was a composite of the other papers, once the incidence of complications was found, 1 take away the probabilities of other complications. In literature, the complication rates are reported to be 35%²⁶, our rate of 34% is close to the literature values.
- C2 (Sepsis). “sepsis” was reported in one study of 40 patients.
- C3 (Reoperations). For RTACC, “reoperation” is seen in 7 patients across 2 studies, in a total population of 519.
- C4 (Pneumothorax). “Pneumothorax” was a rare complication, seen in 1 out of 39 patients.
- C5 (Haemothorax). “Haemothorax” was seen in 1 patient out of 68.
- C6 (Empyema). “Empyema” was seen in 1 patient in a study where there were only 6 procedures observed. It is likely that this is overstated due to the small sample patient population.
- C7 (Infection). “Infection” is a more common complication of a thoracotomy due to the invasive and roadside element of this procedure. It was seen in two patients in a study of 68.
- C8 (Neurological Impairment). As the occlusion of the aorta limits blood flow to the brain “neurological impairment” was the most common complication observed and seen in 6 studies and one of the foci of the meta-analysis. In total, 29 patients survived with neurological impairment.

Chance Node D (survival, death)

- D1, D2, D3, D4, D5, D6, D7, D8, D9, D10, D11, D12. All these values were obtained from literature. The mortality rates were converted into probabilities to find the chance of dying. In order to get the “survival” node, the mortality probability was subtracted from 1. Those undergoing reoperation were assumed to have the same survival probability as those previously undergoing surgery, as is would be for the same procedure.

Sensitivity Analysis

The purpose of a sensitivity analysis is to assess the level of uncertainty in the model we created and whether changes in the data used impacted the overall probabilities, costs or utilities of each intervention as well as the overall ICER. The node column indicates which branch of the decision tree the calculation impacts, the categories where split for simplification of display. The variable column indicates the original value at the node identified from the first column and the alternative value given from literature. Once the alternative values had been inputted, we monitored the impact of this on the overall cost and utility of the REBOA or RTACC branch. Finally, these values were put into the ICER formula to demonstrate changes from the initial values. If the alternative value gave an overall ICER of less than £30,000 (the NHS' willingness-to-pay), then the alternative value was deemed to be cost-effective.

Table S4: Sensitivity analysis to determine impact of probability, cost and utility on ICER

Node	Category	Descriptor	Variable		Δ Costs (£)		Δ Utility (QALY)		ICER (£/QALY)			Cost effective?
			Original	Alternative	Original	Alternative	Original	Alternative	Original	Alternative	% Change	
		Survival at RTACC/REBOA										
RE(A1)	Probability	Survival REBOA (min)	0.936	0.457	4575.45	1896.04	0.1025	0.0168	44617.4446	112800.02	152.82%	no
	Probability	Survival REBOA (max)	0.936	1.000	4575.45	4931.56	0.1025	0.1139	44617.4446	43280.63	-3.00%	no
RT(A1)	Probability	Survival RTACC (min)	0.522	0.000	4575.45	7577.46	0.1025	0.1673	44617.4446	45283.74	1.49%	no
	Probability	Survival RTACC (max)	0.522	1.000	4575.45	1824.23	0.1025	0.0432	44617.4446	42250.89	-5.30%	no
		Survival at Definitive Intervention										
RE(B1)	Probability	Survival REBOA (min)	0.294	0.162	4575.45	4238.76	0.1025	0.0291	44617.4446	145803.47	226.79%	no
	Probability	Survival REBOA (max)	0.294	1.000	4575.45	6377.73	0.1025	0.4959	44617.4446	12861.79	-71.17%	yes
RT(B1)	Probability	Survival RTACC (min)	0.173	0.095	4575.45	4611.46	0.1025	0.1308	44617.4446	35262.26	-20.97%	no
	Probability	Survival RTACC (max)	0.173	0.344	4575.45	4496.37	0.1025	0.0406	44617.4446	110808.90	148.35%	no
		Complications										
RE(C6)	Probability	No complications REBOA (min)	0.545	0.000	4575.45	5475.67	0.1025	0.0632	44617.4446	86643.39	94.19%	no
	Probability	No complications REBOA (max)	0.545	1.000	4575.45	3825.25	0.1025	0.1353	44617.4446	28263.94	-36.65%	yes
RT(C1)	Probability	No complications RTACC (min)	0.780	0.000	4575.45	4295.12	0.1025	0.1085	44617.4446	39590.62	-11.27%	no
	Probability	No complications RTACC (max)	0.780	1.000	4575.45	4655.54	0.1025	0.1009	44617.4446	46162.44	3.46%	no
		ISS										
RE(A1,A2) & RT(A1,A2)	Cost	REBOA/RTACC (min)	9487.00	7272.00	4575.45	4579.07	0.1025	0.1025	44617.4446	44652.76	0.08%	no
	Cost	REBOA/RTACC (max)	9487.00	14280.00	4575.45	4567.61	0.1025	0.1025	44617.4446	44541.03	-0.17%	no
		Blood Products										
RE(A1,A2)	Cost	REBOA (min)	18.60	12.00	4575.45	3493.81	0.1025	0.1025	44617.4446	34069.84	-23.64%	no
	Cost	REBOA (max)	18.60	28.80	4575.45	6247.07	0.1025	0.1025	44617.4446	60918.28	36.53%	no
RT(A1,A2)	Cost	RTACC (min)	11.30	9.00	4575.45	4953.34	0.1025	0.1025	44617.4446	48302.44	8.26%	no
	Cost	RTACC (max)	11.30	28.60	4575.45	1733.06	0.1025	0.1025	44617.4446	16899.88	-62.12%	yes
		Proportion Angio:Lap										
RE(A1)	Cost	REBOA (min)	0.474 Angio	0 Angio	4575.45	5817.63	0.1025	0.1025	44617.4446	56730.58	27.15%	no
	Cost	REBOA (max)	0.474 Angio	1 Angio	4575.45	3196.99	0.1025	0.1025	44617.4446	31175.44	-30.13%	no
RT(A1)	Cost	RTACC (min)	0.167 Angio	0 Angio	4575.45	4331.10	0.1025	0.1025	44617.4446	42234.76	-5.34%	no
	Cost	RTACC (max)	0.167 Angio	0.273 Angio	4575.45	4730.54	0.1025	0.1025	44617.4446	46129.81	3.39%	no
		Survey QoL Values										
RE(A1) & RT(A1)	Utility	ITU - REBOA/RTACC (min)	0.286	0.169	4575.45	4575.45	0.1025	0.1019	44617.4446	44904.24	0.64%	no
	Utility	ITU - REBOA/RTACC (max)	0.286	0.335	4575.45	4575.45	0.1025	0.1028	44617.4446	44498.42	-0.27%	no
RT(C4)	Utility	Pneumothorax (min)	0.237	-0.126	4575.45	4575.45	0.1025	0.1026	44617.4446	44616.31	0.00%	no
	Utility	Pneumothorax (max)	0.237	0.592	4575.45	4575.45	0.1025	0.1025	44617.4446	44618.55	0.00%	no
RT(C6)	Utility	Empyema (min)	0.233	-0.199	4575.45	4575.45	0.1025	0.1026	44617.4446	44613.17	-0.01%	no
	Utility	Empyema (max)	0.233	0.531	4575.45	4575.45	0.1025	0.1025	44617.4446	44620.40	0.01%	no
RT(C5)	Utility	Haemothorax (min)	0.237	-0.126	4575.45	4575.45	0.1025	0.1026	44617.4446	44616.35	0.00%	no
	Utility	Haemothorax (max)	0.237	0.592	4575.45	4575.45	0.1025	0.1025	44617.4446	44618.52	0.00%	no
		Note: Values in the table are rounded for display purposes. Therefore, they may not add up.										

Discussion

Table S5 - List of assumptions used in study

Assumption	Rationale for assumption	Source (if applicable)
Length of ventilation/ICU/hospital stay	No sufficient data from studies on the overall length of stay, length of stay in ICU and duration and rate of use of invasive ventilation. Therefore, this analysis relied on data from this large UK study	Campbell ³⁹
TISS-28 Score	This score was calculated for a typical patient estimated by our group to reach the tariff for major trauma	Lefering ⁴⁹
Conscious level	Due to incomplete reporting of this measure all patients were assumed to be unconscious and intubated and ventilated by the time or during their A&E management.	N/A
Dialysis post-discharge	Most dialysis regimens in the UK involve 3 sessions per week. It was assumed this was the case for our patients	Fluck ⁵⁰
In-Hospital Dialysis	It was assumed that dialysis was required only during intensive care stay, when a patient is sickest and where the facilities for dialysis are available, and at the same rate as outpatient dialysis	N/A
Procedure location	It was assumed every REBOA/RTACC was performed in a major trauma centre	N/A
Pre-hospital costs	Pre-hospital costs were excluded because they are identical to both patient sets. It can be assumed that some patients were transported using air ambulances whilst others would be transported using conventional road ambulances. The different probabilities of both patient sets using either of these methods of transport could have impacted on the results but there was insufficient data for this.	N/A
ICU care	The tariff for ICU stay is agreed locally and is conditional on the number of organs supported. It was unknown how many organs were supported in each patient therefore this was eliminated from the costing altogether.	N/A

Pneumothorax, Haemothorax, Empyema	It was assumed all these complications occurred after ICU stay and took 5 days to resolve, except for empyema which took the full duration of general medical ward stay.	
Utilities derived from questionnaire	A questionnaire was undertaken with experienced medical professionals to reach to the utility of being in ICU, empyema, pneumothorax and haemothorax. No data was available on the utilities for these health states in the literature.	
Time of death	Patients who died are assumed to have survived to the end of the standardised admission as there was extremely sparse data on length of stay.	
Utility Ventilation	Assumed to be 0. Patients are unconscious and the health state is equivalent to being dead.	
Utility Neurological Impairment	There was no uniform definition in the literature on what the neurological outcomes were of those who suffered impairment. Therefore, it was assumed that the utility was the same as that of patient suffering from an ischaemic stroke.	Xie ⁴⁰
Utility Sepsis	Data using EQ-5D on the utility after severe sepsis in critical illness, our subset of patients, was derived from a study looking at this utility at 2 years. No available study was found using EQ-5D at 1 year or earlier that gave a concrete number. It was assumed that this utility would be the same from discharge, similar to what Brown (2007) assumed in their paper.	Korosec ⁴¹
Mortality Thrombosis Lower limb amputation DVT	Mortality for these three complications were not obtained for patients specific to major trauma. Evidence for patients in general was used. This is likely to understate the mortality as trauma patients are likely to be more unwell.	Fortington ³⁶ ; Lyaker ³³ ; Galanaud ³⁴
Mortality AKI	It was assumed nobody died within a year after admission with acute kidney injury. This was because the severity of the injury was low and no patient suffered any adverse outcome as a result. Patients with severe renal failure, requiring haemodialysis, were modelled separately	

Mortality infection	localised	<p>Two instances of localized infection at the site of thoracotomy were reported. None developed into sepsis. This was managed through a minor procedure. Therefore, it was assumed that this carries a mortality of 0.</p>	<p>DuBose ¹²</p>
Utility of reoperation		<p>As this is due to a re-bleed from the initial intervention and likely to occur within hours of being operated on initially, the utility is that of being ventilated, as this is the health state at the time. It was costed as a further major surgery.</p>	
Blood products		<p>It was assumed that only red blood cells were used. Only a very small amount of studies reported on the use of blood products other than red blood cells, therefore it was only quantified and costed for this use.</p>	

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